CHEMISTRY LETTERS, pp. 305-308, 1989.

Efficient Asymmetric Hydrogenations of (Z)-2-Acetamidoacrylic Acid Derivatives with the Cationic Rhodium Complex of (2S,4S)-MOD-BPPM[1)]

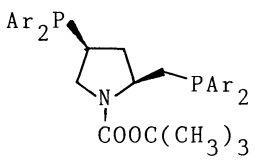
Hisashi TAKAHASHI and Kazuo ACHIWA*
School of Pharmaceutical Sciences, University of Shizuoka,
2-2-1 Oshika, Shizuoka 422

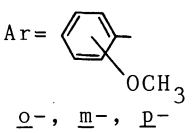
The preparation of (2S,4S)-MOD-BPPM ((2S,4S)-N-(t-butoxycarbonyl)-4-[[bis(4'-methoxy-3',5'-dimethylphenyl)]phosphino]-2-[[[bis(4'-methoxy-3',5'-dimethylphenyl)]phosphino]methyl]pyrrolidine) and its application to highly effective asymmetric hydrogenations of (Z)-2-acetamidoacrylic acid derivatives are described.

Recently, we have prepared the methoxy-substituted BPPM ((2S,4S)-N-(t-butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine)[2)] analogues and clarified the effects of the methoxy groups on catalytic activities and enantioselectivities in the hydrogenation of (Z)-2-acetamidocinnamic acid catalyzed by the rhodium complexes of them.[3)] When p-methoxy-BPPM (**4**) was used as a ligand, the hydrogenation proceeded smoothly with a very high substrate to catalyst ratio due to the electron donating factor of the p-methoxy group. The catalytic activity of m-methoxy-BPPM (**3**)-rhodium complex is lower than the other ones by the electron attracting factor of the m-methoxy group. o-Methoxy-BPPM (**2**) gave a much higher optical yield than the other ligands but accelerated the reaction rate less than p-methoxy-BPPM (**4**). This lesser activation of hydrogenation by o-methoxy-BPPM may be rationalized under the assumption that the steric factor of the o-methoxy group affects on the rate of the oxidative addition of molecular hydrogen to the rhodium.

On the other hand, Kagan and co-workers have reported that m-methyl substituted DIOP ((2R,3R)-2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)-butane) analogue gave a higher optical yield and accelerated the reaction rate slightly more than DIOP in the hydrogenation of (Z)-2-acetamidocinnamic acid.[4)]

From these asymmetric hydrogenation findings, here we wish to report the asymmetric hydrogenation of (Z)-2-acetamidoacrylic acid derivatives (**5**) with high catalytic activity and enantioselectivity leading to optically active N-acetyl-α-amino acid (**6**) catalyzed by cationic rhodium complex of (2S,4S)-MOD-BPPM ((2S,4S)-N-(t-butoxycarbonyl)-4-[[bis(4'-methoxy-3',5'-dimethylphenyl)]phosphino]-2-[[[bis-



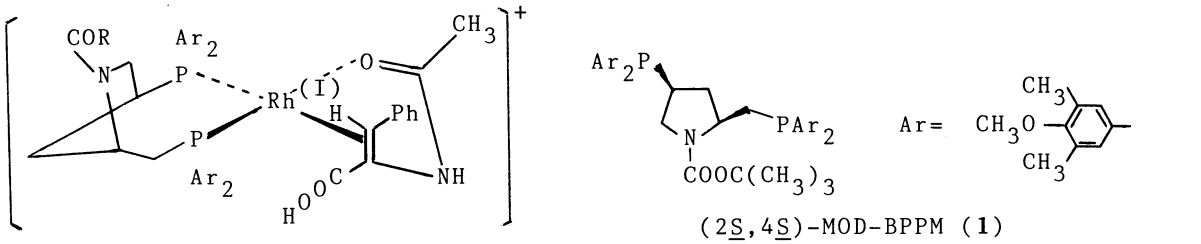


o-, m-, p-

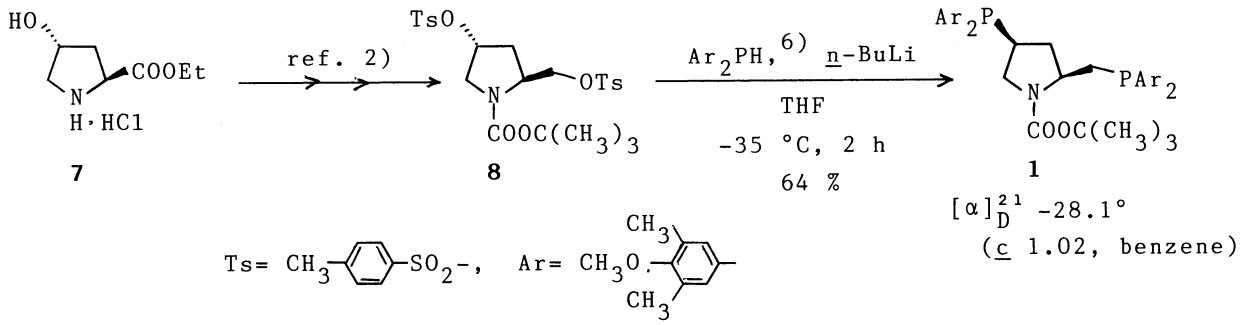
o-methoxy-BPPM (**2**)
m-methoxy-BPPM (**3**)
p-methoxy-BPPM (**4**)

(4'-methoxy-3',5'-dimethyl)]phosphino]methyl]pyrrolidiene) (**1**) which has been designed on the respective control concept[5] to develop efficient chiral catalysts for asymmetric hydrogenations. As shown in Scheme 1, m-dimethyl groups on the diphenylphosphine of **1** oriented cis to the prochiral group of substrate was expected to enhance the enantioselectivity of asymmetric hydrogenation, and p-methoxy and m-dimethyl groups on the other diphenylphosphine oriented trans to the prochiral group were also expected to accelerate its reaction rate in comparison with those of BPPM.

The (2S,4S)-MOD-BPPM (**1**) was prepared easily from the ditosylate[2] (**8**) by the similar method reported previously[3] as indicated in Scheme 2.



Scheme 1.

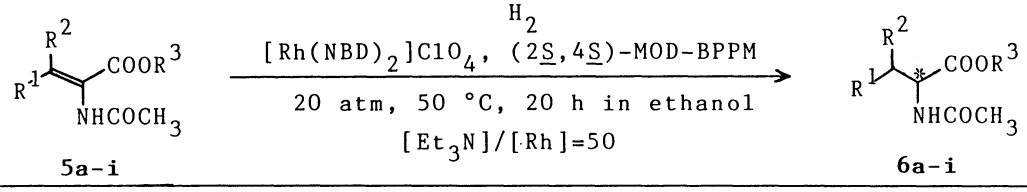


Scheme 2.

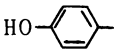
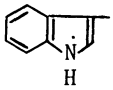
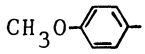
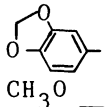
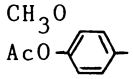
The results of asymmetric hydrogenations of **5a-l** are summarized in Table 1. Typical hydrogenations were carried out in the presence of a cationic rhodium catalyst (0.5-0.01 mol%) prepared in situ by mixing $[Rh(NBD)_2]ClO_4$ and **1** in a ratio of 1 : 1.2 and triethylamine ($[Et_3N]/[Rh]=50$) at 50 °C for 20 h in ethanol under the initial hydrogen pressure of 20 atm, unless otherwise noted.

Table 1 shows that high enantioselectivities are generally obtained. N-Acetyl-(R)-phenylalanine derivatives (**6f-g, 6j-l**) were given with high optical yields. In particular, (2S,4S)-MOD-BPPM-rhodium complex was found to give (R)-**6f**

Table 1. Asymmetric Hydrogenations of (Z)-2-Acetamidoacrylic Acid Derivatives[a)]



5a-i **6a-i**

Entry	Substrates				[Subst.]/[Rh]	Products[b)]		
		R^1-	R^2-	R^3-			%ee[c)]	Confign.
1	**5a**	H-	H-	H-	1000	**6a**	95.0	R
2	**5b**	H-	H-	CH_3-	1000	**6b**	81.6	R
3	**5c**	$(CH_3)_2CH$-	H-	H-	1000	**6c**	89.8	R
4[d)]	**5d**	CH_3SCH_2-	H-	H-	500	**6d**	69.0	R
5[e)]	**5e**	CH_3-	CH_3-	H-	1000	**6e**	58.6	R
6	**5f**		H-	H-	1000	**6f**	97.8	R
7	**5f**		H-	H-	10000	**6f**	98.0	R
8[f)]	**5f**		H-	H-	2000	**6f**	98.6	R
9	**5g**		H-	CH_3-	1000	**6g**	85.1	R
10	**5h**		H-	H-	1000	**6h**	79.6	R
11	**5i**		H-	H-	1000	**6i**	89.2	R
12	**5j**		H-	H-	1000	**6j**	88.6	R
13	**5k**		H-	H-	1000	**6k**	91.7	R
14	**5l**		H-	H-	1000	**6l**	91.3	R

a) All hydrogenations were carried out with [Substrate]=0.5 M in ethanol. b) The chemical yields were quantitative. The conversions were 100 %, which were determined by ^{1}H-NMR analysis. c) Calculated on the basis of the optical rotations of pure enantiomers: (R)-(+)-**6a** $[\alpha]_D^{25}$ +66.5° (c 2.0, H_2O); (S)-(-)-**6b** $[\alpha]_D^{25}$ -91.7° (c 2.0, H_2O); (S)-(-)-**6c** $[\alpha]_D^{26}$ -32.2° (c 1.0, EtOH); (S)-(-)-**6d** $[\alpha]_D^{20}$ -20.8° (c 4.0, MeOH); (S)-(+)-**6f** $[\alpha]_D^{26}$ +46.0° (c 1.0, EtOH); (S)-(+)-**6g** $[\alpha]_D^{25}$ +21.4° (c 1.9, MeOH); (S)-(+)-**6h** $[\alpha]_D^{27}$ +51.5° (c 1.0, MeOH); (S)-(+)-**6i** $[\alpha]_D^{15}$ +25.0° (c 1.0, 95% EtOH); (S)-(+)-**6j** $[\alpha]_D^{21}$ +67.5° (c 5.0, EtOH); (S)-(+)-**6k** $[\alpha]_D^{18}$ +53.4° (c 1.8, EtOH); (S)-(+)-**6l** $[\alpha]_D^{20}$ +40.7° (c 1.0, MeOH). d) Conditions: 20 atm, rt, 24 h. e) Reaction time: 45 h. The reduction product was converted to N-acetylvaline methyl ester with CH_2N_2 in ether and the optical yield was calculated using the optical rotation of pure methyl ester: N-acetyl-(S)-(-)-valine methyl ester $[\alpha]_D^{25}$ -47.6° (c 7.8, H_2O). f) Conditions: 1 atm, rt, 45 h.

with very high enentioselectivity (98 %ee) as well as very high catalytic activity ([Substrate]/[Rh]=10000) in hydrogenation of **1f** (entry 7). It is noteworthy that asymmetric hydrogenation of sulfur containig or tetrasubstituted dehydroamino acid (**5d** or **5e**) also proceeded smoothly, although the catalytic activity and the enantioselectivity are relatively low (entries 4-5). Asymmetric hydrogenations of methionine and valine precurcers catalyzed by (2S,4S)-BPPM-rhodium complex did not proceed smoothly and enantioselectivities were low.[7] In general, the hydrogenation catalyzed by MOD-BPPM-rhodium complex proceeded with higher enantioselectivities under milder conditions compared with that when BPPM-rhodium complex was used as a chiral catalyst.[2,8]

The MOD-BPPM-rhodium complex was found to be a very efficient catalyst for asymmetric hydrogenation of (Z)-2-acetamidoacrylic acid derivatives. These experimental findings offer practical synthetic method for optically active α-amino acids and their derivatives and the respective control concept is also useful for asymmetric hydrogenation of (Z)-2-acetamidoacrylic acids.

References

1) Asymmetric Reactions Catalyzed by Chiral Metal Complexes XXXIII.
2) K. Achiwa, J. Am. Chem. Soc., 98, 8265 (1976).
3) H. Takahashi and K. Achiwa, Chem. Pharm. Bull., 36, 3230 (1988).
4) T. P. Dang, J. C. Poulin, and H. B. Kagan, J. Organomet. Chem., 91, 105 (1975).
5) M. Chiba, H. Takahashi, H. Takahashi, T. Morimoto, and K. Achiwa, Tetrahedron Lett., 28, 3675 (1987).
6) T. Morimoto, M. Chiba, and K. Achiwa, Tetrahedron Lett., in press.
7) J. W. Scott, D. D. Keith, G. Nix, D. R. Parrish, S. Remington, G. P. Roth, J. M. Townsend, D. Valentine, and R. Yang, J. Org. Chem., 46, 5086 (1981).
8) I. Ojima, T. Kogure, and N. Yoda, J. Org. Chem., 45, 4728 (1980).

(Received November 26, 1988)