Tetrahedron Letters, Vol. 33, No. 42, pp. 6331-6334, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Highly Enantioselective Cyclization Using Cationic Rh(I) with Chiral Ligand

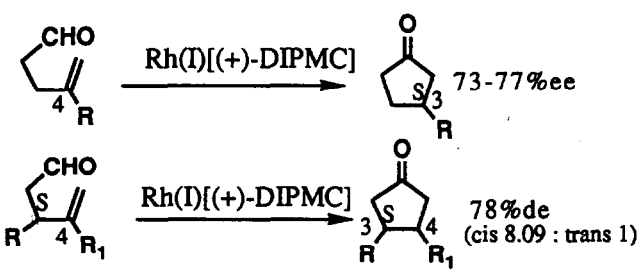
Xiao-Ming Wu, Kazuhisa Funakoshi, and Kiyoshi Sakai*

Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan

Key Words: enantioselective cyclization; cationic rhodium; chiral ligand; BINAP; 3,4-disubstituted cyclopentanone; 3-substituted cyclopentanone; diastereoselective cyclization

Abstract: *Highly diastereoselective cyclization (>99% de) of 3R (or S) 3,4-disubstituted 4-pentenals into the corresponding 3,4-cis(or trans)-disubstituted cyclopentanone and highly enantioselective cyclization (>99% ee) of 4-substituted 4-pentenals into 3-substituted cyclopentanone were achieved by using cationic $Rh^+(BINAP)ClO_4^-$.*

One of the indispensable reactions for the synthesis of natural products is stereoselective cyclization under mild reaction conditions. It is well known that metal-catalyzed cyclization plays an essential role in the synthesis of a structurally complex organic molecule.[1,2] Previously, we had reported that asymmetric cyclization of prochiral 4-substituted 4-pentenals by Rh(I) with (+)-DIPMC[3] as chiral phosphine ligand affords 3-substituted cyclopentanone with 73-77% ee, and the absolute stereochemistry of the C_4 of main products (at best 78% de) in Rh(I)[(+)-DIPMC]-catalyzed cyclization of 3,4-disubstituted 4-pentenals is R-configuration, regardless of the absolute configuration at C_3 of the substrate (Scheme 1). In this paper, we report highly diastereoselective cyclization (>99% de) of (3R or S)-3,4-disubstituted 4-pentenals and highly enantioselective cyclization (>99% ee) of 4-substituted 4-pentenals using Rh(I) with BINAP.[4]



Scheme 1

Substrates,[3] which could be readily prepared from (R) [or (S)]-limonene, were subjected to asymmetric cyclization using RhCl(BINAP). A mixture of the substrate (1eq.) and a neutral rhodium complex, RhCl[(R or S)-BINAP] (0.5 eq.) in CH_2Cl_2 was stirred at room temperature; the results are summarized in Table 1.[5] The cyclization reaction proceeded with high diastereoselectivity, and the (3R,4S)-cis-cyclopentanone with >99% de from 3R-substrate and the (3S,4R)-cis-isomer with >99% de from 3S-substrate were obtained, respectively, by

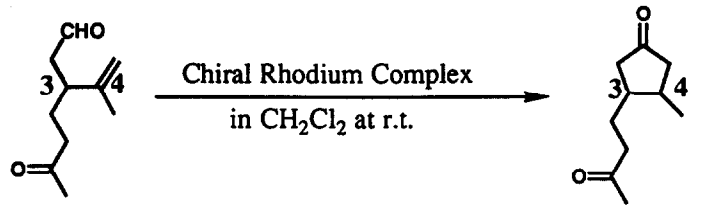


Table 1. Diastereoselective Cyclization by Neutral RhCl(Ligand) (0.5 eq.)

Entry	Substrate	Ligand(BINAP)	Yield(%)	Cis : Trans
1	3R	(R)-(+)	12	18 : 82
2	3R	(S)-(-)	29	>99
3	3S	(R)-(+)	34	>99
4	3S	(S)-(-)	25	26 : 74

Reaction was not completed even in 70-120 h.

Table 2. Diastereoselective Cyclization by Cationic [Rh (Ligand)]ClO_4 (0.1 eq.)

Entry	Substrate	Ligand(BINAP)	Yield(%)	Cis : Trans
1	3R	(R)-(+)	74	97 : 3 [a]
2	3R	(S)-(-)	85	>99
3	3S	(R)-(+)	86	>99
4	3S	(S)-(-)	82	96 : 4 [a]

Each reaction was completed in 2-4 h at R.T. a: Reaction was carried out at 0°C.

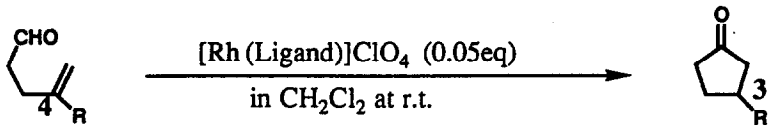


Table 3. Enantioselective Cyclization by Cationic Rh(I) Complex

Entry	Substrate	Ligand(BINAP)	Yield (%)	ee (%)	Abs. Config.
1	R = t-Bu	(S)-(-)	87	>99	S
2	R = t-Bu	(R)-(+)	86	>99	R
3	R = Dmp*	(S)-(-)	84	>99	S
4	R = Dmp	(R)-(+)	88	>99	R
5	R = Mcx*	(S)-(-)	94	>99	S
6	R = Mcx	(R)-(+)	92	>99	R
7	R = n-Bu	(S)-(-)	90	91[a]	S
8	R = n-Bu	(R)-(+)	92	92[a]	R
9	R = i-Pr	(S)-(-)	70	74[a]	S
10	R = i-Pr	(R)-(+)	74	78[b]	R
11	R = cHex*	(S)-(-)	95	65	S
12	R = cHex	(R)-(+)	90	67	R

Each reaction was completed in 0.5-2 h at R.T.

a: Reaction was carried out at 0°C; b: Reaction was carried out at -10°C.

*Dmp = 1,1-dimethylpropyl, Mcx = 1-methylcyclohexyl, cHex = cyclohexyl

using (S)-(-)-BINAP or (R)-(+)-BINAP. However, when (R)-(+)-BINAP for 3R-substrate and (S)-(-)-BINAP for 3S-substrate were used, [3R(or S),4R(or S)]-trans-cyclopentanone was obtained in the ratio of 82 to 18 (cis-isomer) or in the ratio of 74 to 26 (cis-isomer). This reaction was much slower than in the case of RhCl[(+)-DIPMC] or Wilkinson complex and resulted in poor yield, in which the substrate was substantially recovered.

Next, our attention was directed to asymmetric cyclization by a cationic rhodium complex with chiral ligand, ([Rh(chiral ligand)]ClO_4).[6] As shown in Table 2, asymmetric cyclization of (3R or S)-3,4-disubstituted 4-pentenals by $Rh^+ClO_4^-$ with (R)-(+)[or S-(-)]-BINAP as chiral ligand proceeded in good yield and in highly diastereoselective manner to afford (3R,4S)-cis-cyclopentanone (cis 97:trans 3) from 3R-substrate and [Rh(R)-(+)-BINAP]ClO_4, and (3S,4R)-cis-cyclopentanone (cis 96:trans 4) from 3S-substrate and [Rh(S)-(-)-BINAP]ClO_4. Combination of 3R-substrate and (S)-(-)-BINAP, or 3S-substrate and (R)-(+)-BINAP, respectively, gave the diastereomerically pure trans-isomers (>99% de) in good yield. In addition, each reaction proceeded much faster than in the case of neutral rhodium [RhCl(BINAP)]. Thus, this cyclization reaction is advantageous for the stereospecific synthesis of stereoisomer of 3,4-disubstituted cyclopentanone by using either (R)-(+)- or (S)-(-)-BINAP as ligand. The most remarkable difference between neutral Rh-complex and cationic Rh-complex for asymmetric cyclization into 3,4-disubstituted cyclopentanone is that (R)-(+)-BINAP in neutral Rh-complex affords (4R)-cyclopentanone, while (R)-(+)-BINAP in a cationic Rh-complex yields (4S)-isomer. Similarly, (S)-(-)-BINAP in a neutral Rh-complex affords (4S)-isomer, and (S)-(-)-BINAP in a cationic Rh-complex gives (4R)-isomer. That is to say, this stereoselective cyclization reaction is achieved regardless of the configuration at C_3, and indicates that, in neutral and cationic Rh-complex, each stereochemical course of the aldehyde hydrogen to the double bond via the acylrhodium complex is essentially reversed.

The success of diastereoselective cyclization to 3,4-disubstituted cyclopentanones by cationic Rh-complex prompted us to examine the asymmetic cyclization of prochiral 4-pentenals. As shown in Table 3, 4-substituted 4-pentenals were rapidly cyclized into 3-substituted cyclopentanones in highly enantioselective fashion (>99% ee), when R is a quaternary carbon such as t-Bu, 1,1-dimethylpropyl, and 1-methyl-1-cyclohexyl. Thus, this highly enantioselective cyclization coupled with the practical advantage, in which the employed cationic Rh-complex is only 0.05 eq. for the substrate (1.0 eq.), provides a convenient procedure for the synthesis of chiral 3-substituted cyclopentanones. However, the enantioselectivity in cyclization decreased when the carbon adjacent to the double bond is secondary or tertiary. The order of decrease is tertiary carbon > secondary carbon, as illustrated by the example of R=Bu (secondary carbon, 79% ee) and i-Pr (tertiary carbon, 69% ee) or cyclohexyl (tertiary carbon, 65% ee, 67% ee).[7] 4-Substituted 4-pentenals were not cyclized into the 3-substituted cyclopentanone by the neutral rhodium complex, RhCl[(R or S)-BINAP]. This finding suggests the neutral rhodium catalyst is less active than the cationic Rh-complex. The inversion of absolute configuration at C_3 in the cyclized products is only due to the CIP (Cahn, Ingold, Prelog) rule, and the steric course of addition of the aldehyde hydrogen to the double bond via the acylrhodium complex is essentially the same even for 4-substituted 4-pentenals as well as in the case of 3,4-disubstituted 4-pentenals.

The cyclization mechanism in neutral RhCl with (R)-(+) [or (S)-(-)]-BINAP as ligand is assumed to be similar to the case of RhCl[(+)-DIPMC].[3] As shown in Fig. A, two phosphines coordinate in such a way that one functional group (phenyl) of P_1 occupies axial (β) bond and that of P_2 occupies axial (α). That is to say, β-side of P_1 and α-side of P_2 may be sterically hindered. It is desired that, in the acylrhodium hydrogen intermediate obtained by the oxidative addition of the aldehyde carbon-hydrogen to rhodium, the double bond coordinates in such a way that R-substituent of the substrate is located at the same side as the hydrogen, because steric repulsion

between R and hydrogen is smaller than that of R and Cl. Therefore, it is reasonable that the R-substituent occupies a less hindered β-side of P_2, and subsequent insertion of the double bond into Rh-H and then reductive elimination affords the cyclopentanone with S-configuration.[8] The reasonable explanation for the finding that the asymmetric cyclization using the cationic Rh-complex affords the reversed configuration to the case of neutral rhodium remains unsolved.

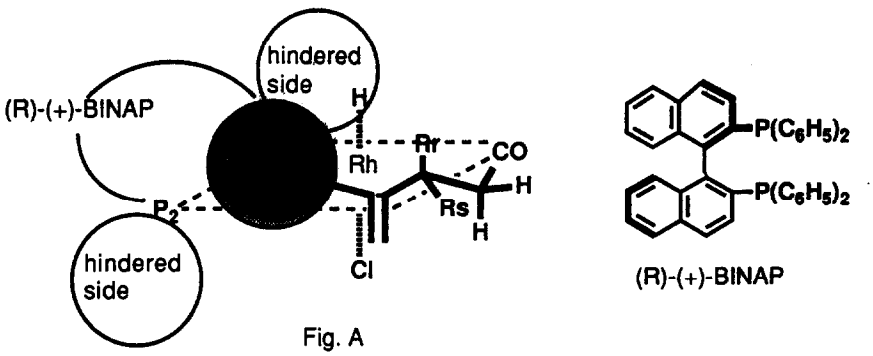


Fig. A

References and Notes

1. Harrington, P.J. " Transition Metals in Total Synthesis ", John Wiley and Sons, 1990 (New York).
2. Sakai, K.; Wu X-M,; Hata, T.; Marubayashi, N.; Funakoshi, K. J. Chem. Soc. Perkin Trans. 1, 1991, 2531-2536. See references cited therein.
3. (+)-DIPMC: (1S,2S)-(+)-1,2-Bis(diphenylphosphinomethyl)-cyclohexane (commercially available). Taura, Y.; Tanaka, M.; Wu, X-M.; Funakoshi, K.; Sakai, K. Tetrahedron 1991, 47, 4879-4888. See references cited therein.
4. Commercially available S(-)-BINAP and R(+)-BINAP were used.
5. The ratio of 3,4-cis-cyclopentanone to 3,4-trans-cyclopentanone was determined by comparison of 270 ^{1}H-NMR spectra, in which cis- and trans-methyl signals appear at δ 0.94 and 1.14, respectively. See Inoue, K.; Sakai, K. Bull. Chem. Soc. Japan 1978, 51, 2361-2365. The optical purity in Table 3 was definitively determined from the 500 MHz ^{1}H-NMR and ^{13}C-NMR spectra, after acetalization with (2R,3R)-butanediol/p-TsOH in refluxing benzene. The absolute stereochemistry in Table 3 was determined by comparison with the sign of the reported specific rotation (entry 1,2,7,8,9,10; see Corey, E.J.; Naef, R.; Hannon, H.J. J. Am. Chem. Soc. 1986, 108, 7114-7116. Posner, G.H.; Frye, L.L.; Hulce, M. Tetrahedron 1984, 40, 1401-1407) and by similarity of ^{1}H-NMR spectra. That is to say, two HCO protons of 2R,3R-butanedioxy acetal of 3S-substituted cyclopentanones were usually observed at lower field than that of 3R-substituent (unpublished data).
6. Miyashita, T.; Takaya, H.; Souchi, T.; Noyori, R. Tetrahedron 1984, 40, 1245-1253.
7. Reasonable explanation for the lower enantioselectivity of tertiary carbon than secondary carbon was not obtained.
8. In the presence of substituents at the C_3, R-configuration should be obtained.

(Received in Japan 11 July 1992)