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Highly Diastereoselective, Enantioselective Cyclization of Symmetrical 3,4-Disubstituted 4-Pentenal Using Chiral Rhodium(I)-complex

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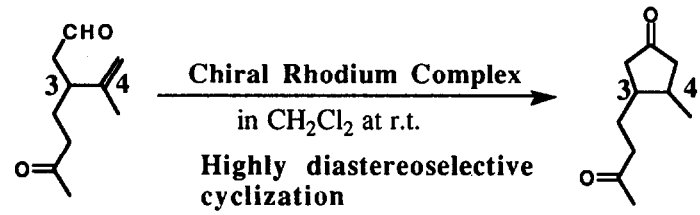
Key Words; enantioselective cyclization; cationic rhodium, neutral rhodium; chiral ligand; BINAP; 3,4-disubstituted cyclopentanone; diastereoselective cyclization; 3-isopropenyl-4-methyl-4-penten-1-al

Abstract: Concurrent introduction of two chiral centers at 3,4-positions of cyclopentanone from symmetrical 1 was achieved in diastereoselective and enantioselective fashion by combination of BINAP and cationic Rh(I)(or neutral).

Stereoselective cyclization under mild reaction conditions has been the subject of extensive study, in view of its importance as an indispensable reaction for the synthesis of natural products. In recent years several excellent methods have been developed for the enantioselective generation of stereocenters. Above all, it is well known that metal-catalyzed cyclization[1] plays an essential role in the synthesis of structurally complex organic molecules. Previously we reported[2,3] that 3R (or S), 4-disubstituted 4-pentenals by combination of cationic $Rh^+ClO_4^-$ and R (or S)-BINAP as chiral phosphine ligand are cyclized into cis-3R (or S), 4S (or R)-disubstituted cyclopentanone (92-94%d.e.), and combination of 3S (or R),4-disubstituted 4-pentenals and cationic $Rh^+ClO_4^-$ with R (or S)-BINAP affords trans-3S (or R), 4S (or R)-disubstituted cyclopentanone in highly diastereoselective manner (>99 d.e.)(scheme1). In short, R-BINAP affords the C_4-S-configuration, and S-BINAP generates the C_4-R, regardless of the C_3-configuration.



Scheme 1

The above chiral Rh(I)-catalyzed cyclization prompted us to examine the concurrent introduction of two desired asymmetric centers at 3,4-positions of cyclopentanone from prochiral, symmetrical 3-isopropenyl-4-methyl-4-penten-1-al (1), by combination of BINAP and cationic Rh(I) (or neutral). Cyclization of the aldehyde (1)[4] using neutral RhCl with chiral ligand such as chiral BINAP,[5] DIPMC,[6] and DIOP[7] is summarized in table 1. Chiral Rh(I)(BINAP)Cl-catalyzed cyclization proceeded to afford the cis-isomer in highly diastereoselective (94%d.e.)[8] and enantioselective (>99%e.e.)[9,10] manner, although the yields were unsatisfactory. The preferential cyclization into the cis-(3S,4R)-isomer indicates that the C_3-position of the symmetrical aldehyde 1

plays the role of S-configuration in the case of R-BINAP to suggest the matched pair of C_3(S) and R-BINAP. The formation of cis-(3R,4S)-isomer indicates the matched pair of C_3(R) and S-BINAP.[11] On the other hand, DIPMC and DIOP afforded comparatively good yields, but were not very effective in respect of the diastereoselectivity and enantioselectivity.

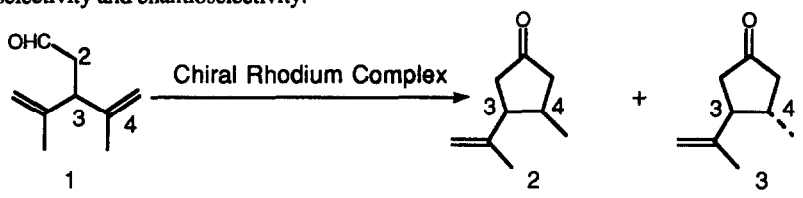


Table 1. Neutral RhCl(Ligand)-catalyzed cyclization

Entry	Ligand	Time (h)	Yield (%)	Cis : Trans (2) (3)	e.e. (%)	Abs. Config. (2)
1	(R)-BINAP	72	25	**97 : 3**	**>99**	3S,4R
2	(S)-BINAP	72	31	**97 : 3**	**>99**	3R,4S
3	(+)-DIPMC	1	74	73 : 27	36	3S,4R
4	(+)-DIOP	1	71	71 : 29	74	3S,4R

Reaction was carried out in CH_2Cl_2 at R. T. under an Ar atmosphere using Rh-complex (0.5 eq.).

Table 2. Cationic Rh(ligand)ClO_4-catalyzed cyclization

Entry	Ligand	Time (h)	Yield (%)	Cis : Trans (2) (3)	e.e. (%)	Abs. Config. (3)
1	(R)-BINAP	0.5	81	**3 : 97**	**>99**	3S,4S
*2	(S)-BINAP	1	84	**4 : 96**	**>99**	3R,4R
3	(+)-DIPMC	12	0			
4	(+)-DIOP	12	0			

Under the same conditions as the case of table 1, Rh-complex (0.05eq.) was used. *Reaction was carried out at 0°C.

As shown in table 1, the matched pair of C_3S (or R) and neutral Rh(I)[R (or S)-BINAP)]-complex to afford the cis-isomer suggested that, for the matched pair[12] of the cationic Rh((R)-BINAP)$^+ClO_4^-$,[13] the C_3 in the aldehyde 1 should play the role of S-configuration. As shown in table 2, the expected Rh(I)-catalyzed cyclization reaction of the aldehyde 1 using a catalytic amount (0.05eq.) of cationic Rh(R-BINAP) proceeded smoothly to afford the trans-(3S,4S)-cyclopentanone via the matched pair of C_3(S) for R-BINAP, (or S-BINAP and C_3(R) for trans-(3R,4R)-isomer) in highly diastereoselective (94% d.e.), enantioselective (>99% e.e.) manner, and in good yield. Each reaction was completed much faster than in the case of neutral Rh(I)-complex. Thus, the first concurrent introduction of two asymmetric centers in Rh-catalyzed cyclization made it possible to prepare freely the 4-stereoisomers of 3,4-disubstituted cyclpentanone from the common prochiral substrate. It is noteworthy that no cyclization was observed in cationic Rh(DIOP or DIPMC)$^+ClO_4^-$, while neutral Rh-complex with these ligands afforded fairly good yields.[14]

Now, neutral Rh-catalyzed cyclization to 3,4-cis-cyclopentanone may be explained by the following mechanistic consideration. It is assumed[3] that the Rh(I)-catalyzed cyclization of 4-penten-1-al to the

cyclopentanone proceeds via i) the oxidative addition of the aldehyde to Rh(I), ii) addition of Rh-H to the coordinated double bond to form a 6-membered ring including Rh, iii) then reductive cyclization to the cyclopentanone. The high stereoselectivity in this cyclization may be explained by Fig. 1. In this case, two phosphines in R-BINAP coordinate in such a way that one phenyl function of P_1 occupies axial (β) position, and that of P_2 occupies axial (α) position. Therefore, the β-site of P_1 and the α-site of P_2 may be sterically hindered. It is likely that the methyl function of the substrate occupies a less hindered position (P_2β-side) and R (isopropenyl) occupies the position to release the steric repulsion by Rh-H, as shown in Fig. 1A. The steric repulsion between Rh-H and isopropeny function as depicted in Fig. 1B may be released by facile conversion from Fig. 2B to favorable Fig. 2A, which may be induced by lower energy, as shown in Fig. 2. Thus, addition of Rh-H to the double bond and subsequent reductive cyclization affords the cis-isomer in highly stereocontrolled manner. On the other hand, it is difficult to explain reasonably the trans-cyclization using cationic Rh-complex. However, the formation of the trans-(3S,4S)-isomer by R-BINAP may be explained by assuming a cyclization via the unstable intermediate C with sterically unfavorable factors ((i) methyl function to occupy the hindered site, and (ii) steric repulsion between Rh-H and isopropenyl group) as shown in Fig. 3. That is to say, if asymmetric cyclization from the unstable Fig. 3C proceeds much faster than from other possible stable intermediates, the formation of the trans-(3S,4S)-isomer may be explained. Support of this assumption is provided by the finding that, in catalytic hydrogenation of a acylamino-cinnamic acid using cationic Rh-complex with Chiraphos (or DIPAMP) as ligand, the predominant enantiomer arises from the less stable (minor) diastereomer of the catalyst-substrate by virture of its much faster hydrogenation than from the stable (predominant) diastereomer.[15]

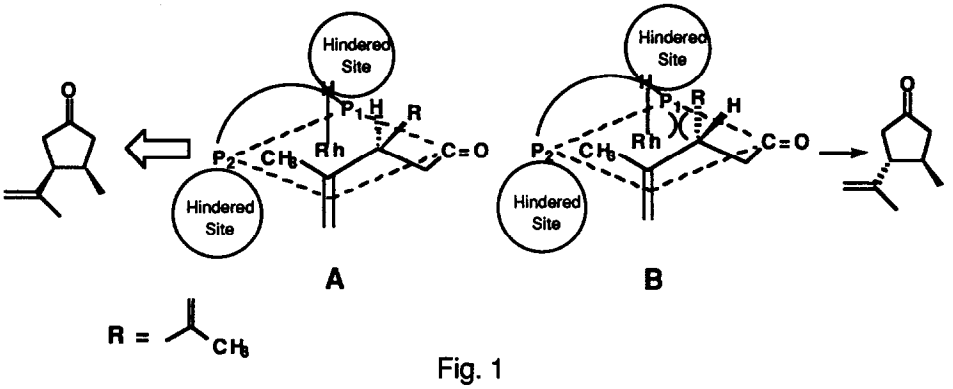


Fig. 1

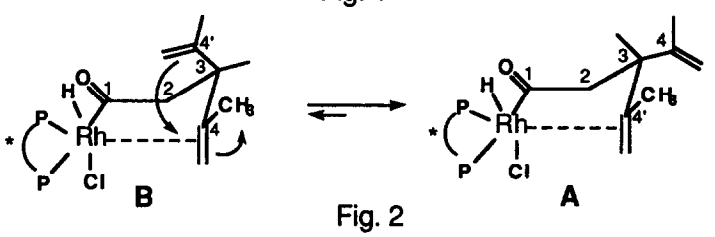


Fig. 2

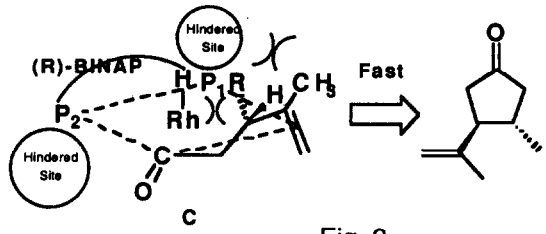
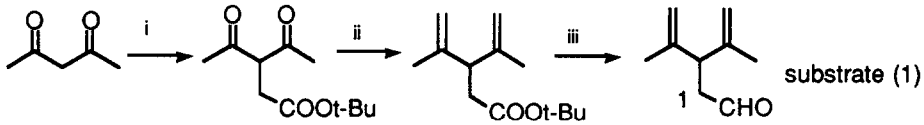


Fig. 3

References and notes

1. For example, see Takemoto, T.; Nishikimi, Y.;Sodeoka, M.;Shibasaki, M. Tetrahedron Lett. 1992, 33, 3527-3530, and 3531-3532. Adams, J.; Spero, D.M. Tetrahedron 1991, 47, 1765-1808.
2. Wu, X-M.; Funakoshi, K.; Sakai, K. Tetrahedron Lett. 1992, 33, 6331-6334.
3. Taura, Y.; Tanaka, M.; Wu, X-M.; Funakoshi, K.; Sakai, K. Tetrahedron 1991, 47, 4879-4888, and references cited therein.
4. Substrate (1) was prepared as follows.



i) NaH/ $BrCH_2COOt$-Bu (65%) ii) Ph_3PCH_3Br/KOt-Bu (80%) iii) DIBAL/CH_2Cl_2 (61%)

5. Commercially available S(-)-BINAP and R(+)-BINAP were used.
6. Glaser, R.; Geresch, S.; Blummernfeld, J.; Twaik, M. Tetrahedron 1978, 34, 2405-2408. (+)-DIPMC: (1S,2S)-(+)-1,2-Bis(diphenylphosphinomethyl)-cyclohexane, and also see ref. 3.
7. Kagan, H.B.; Dang, T.P. J. Am. Chem. Soc. 1972, 94, 6429-6433. (+)-DIOP: (4S,5S)-(+)-4,5-Bis(diphenylphosphinomethyl)-2,3-dimethyl-1,3-dioxolane, and also see ref. 3.
8. The ratio of 3,4-cis-cyclopentanone to 3,4-trans-isomer was determined by comparison of the 270 ^{1}H-NMR spectral data, in which cis- and trans-methyl signals at C_4 appear at δ 0.82 and 1.08, respectively. See Inoue, K.; Sakai, K. Bull. Chem. Soc. Japan 1978, 51, 2361-2365.
9. The enantiomeric excess was definitively determined from the ^{13}C-NMR spectral data, after acetalization with (2R,3R)-butanediol/ p-TsOH in refluxing in benzene.
10. The absolute confuguration of cyclized products was determined from previous finding[2] that cationic Rh-complex with R-BINAP and neutral Rh-complex with R-BINAP afford 3S- and 3R-configuration, respectively.
11. These results are consistent with the previous finding (see ref.2) that combination of 3R-substrate and neutral Rh-complex with S-BINAP (or 3S and R-BINAP) yields cis-(3R,4S)-isomer (or 3S,4R-isomer) with high diastereoselectivity (>99% d.e.).
12. In previous paper (see ref.2), combination of the 3R-substrate (or 3S) and cationic Rh-complex with S-BINAP(or R) afforded high diastereoselectivity (>99% d.e.).
13. a) Miyashita, A.; Takaya, H.; Souchi, T.; Noyori, R. Tetrahedron 1984, 40, 1245-1253. b) Inoue, S.; Takaya, H.; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R.; J. Am. Chem. Soc. 1990, 112, 4897-4905, and ref. cited therein.
14. It was difficult to explain reasonably for this unexpected findings.
15. Morrison, J.D. "Asymmetric Synthesis" Volume 5, Academic Press 1985, New York, p46-66.

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