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ASYMMETRIC CYCLIZATION REACTIONS BY Rh(I) WITH CHIRAL LIGANDS

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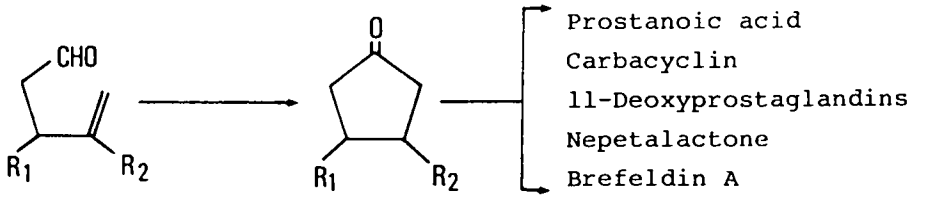
Summary: Cyclization of prochiral 4-butyl-4-penten-1-al by Rh(I)-complex with chiral phosphine ligand afforded 4-butylcyclopentanone with 73% ee. 3(S),4-Disubstituted 4-penten-1-al and 3(R)-isomer were preferentially cyclized to cis-cyclopentanone and trans-cyclopentanone, respectively.

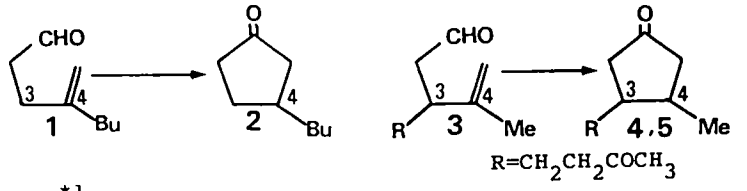
Rh(I)(Wilkinson)-catalyzed cyclization of 4-penten-1-als to cyclopentanones was explored by our laboratory[1a] and subsequently developed[1b] into the stereocontrolled cyclization of 3,4-disubstituted 4-penten-1-als to cis-3,4-disubstituted cyclopentanones; this method has been widely applied to the synthesis of several natural products[2].

This practical method for the construction[1] of a five-membered ring prompted us to examine the cyclization reactions by Rh(I)-complex with chiral ligand. It was previously reported by James and Young[3] that the cyclization of racemic 2-methyl-2-phenyl-4-penten-1-al with $[Rh(chiraphos)_2]Cl$ at 160°C afforded 2-methyl-2-phenyl-cyclopentanone with maximum 52% e.e (40-50% yield).[3] The employed Rh(I)-complex was apparently unsatisfactory in cyclization conditions, chemical yield, and optical purity.



cis

In this paper, we report on the asymmetric cyclization of prochiral 4-butyl-4-penten-1-al (1), and 3(R)(or 3(S)),4-disubstituted 4-penten-1-als (3a,b) by Rh(I) with chiral phosphine ligand. A mixture of 4-butyl-4-penten-1-al (1)[4], Rh(I)-complex prepared from $RhCl(cyclooctene)_2$, and chiral phosphine ligand[5] in CH_2Cl_2 was stirred at room temperature under an Ar atomosphere. The employed chiral phosphine ligands possess two diphenylphosphine in the molecule, and in this respect differ significantly from Wilkinson complex, but the expected cyclization into the five-membered ring proceeded smoothly. The results are summarized in Table 1 (see Scheme 1). Among the tested ligands, (+)-(1S,2S)-trans-1,2-bis(diphenylphosphinomethyl)cyclohexane (I) with C_2-axis afforded 4-butylcyclopentanone (2) with 73% e.e[6] (78% chemical yield).



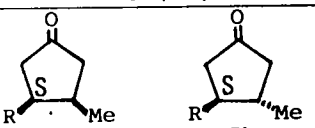
3a; 3R
3b; 3S
4a; 3R, cis
4b; 3S, cis
5a; 3R, trans
5b; 3S, trans

Table 1*1

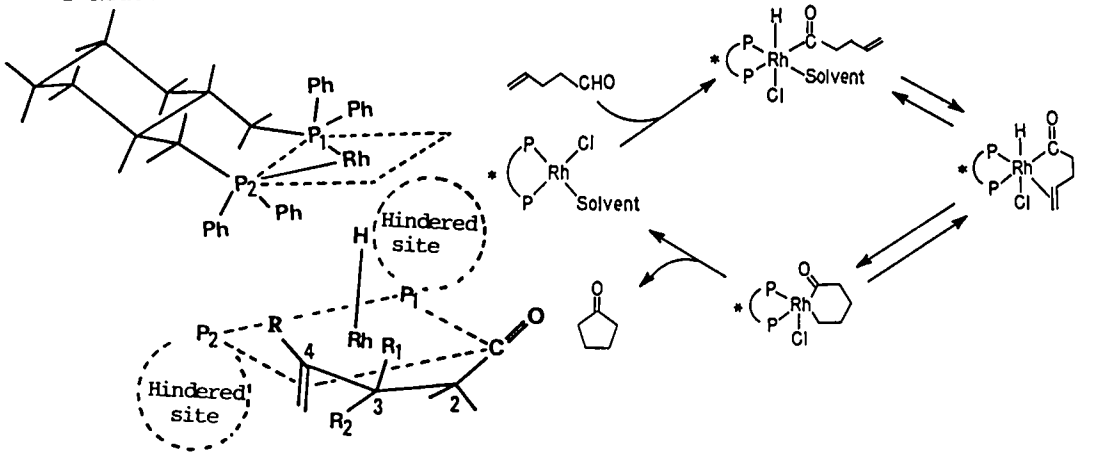
1 → 2					
	Time(h)	Yield(%)	$[\alpha]_D^{25}$ (c, $CHCl_3$)	Opt. Yield (% e.e)	Abs. Config.
BPPM	71	45	-58.6°(3.30)	46	S
(+)-DIOP	14	64	-0.83°(2.95)	6	S
(+)-I	2.5	78	-99.3°(5.70)	73	S

*1 Reaction conditions: Chiral Rh(I)-complex, 0.5 eq., Room Temp.

Table 2*2 (R=$CH_2CH_2COCH_3$)

3 → 4,5				
Substrates	3b(3S)		3a(3R)	
Products	 4b cis	5b trans	4a cis	5a trans
(+)-DIOP Yield(%)	79		75	
Ratio	1.91 : 1		1 : 1.30	
(+)-I Yield(%)	79		60	
Ratio	3.13 : 1		1 : 2.24	

*2 Reaction conditions: Chiral Rh(I)-complex, 0.5 eq., Room Temp., 20 h.



However, (+)-DIOP with C_2 axis resulted in lower optical purity (only 6% e.e).

Next, our attention was directed to cyclization of 3,4-disubstituted 4-penten-1-al (3)[7] by Rh(I) with chiral ligand. Previously, we reported[1b] that 3,4-disubstituted 4-penten-1-als were stereoselectively cyclized to cis-3,4-disubstituted cyclopentanone by Rh(I)-complex(Wilkinson). In preliminary cyclization of (±)-3 by Rh(I) with chiral ligand (I), it was found that a mixture of 3,4-cis and trans[8]-cyclopentanone was obtained in the ratio of 1.20(cis) to 1.00(trans). This result is in contrast to the case of Wilkinson-complex to afford stereoselectively cis-3,4-disubstituted cyclopentanone. To clarify this remarkable difference, 3a(3R) and 3b(3S) were independently subjected to cyclization reactions by Rh(I) with chiral ligand ((+)-I or (+)-DIOP). As shown in Table 2, 3b(3S) was cyclized by Rh(I) with (+)-I to afford mainly 3,4-cis-compound (4b) in the ratio of 3.13 to 1 (5b), while 3a(3R) was cyclized mainly to 3,4-trans-compound (5a) in the ratio of 2.24 to 1 (4a) in 60% yield. (+)-DIOP also afforded 4b in the ratio of 1.91 to 1 (5b) for cyclization of 3b, and 5a in the ratio of 1.30 to 1 (4a) for that of 3a. It is noteworthy that the absolute stereochemistry of C_4 of main products in this cyclization reaction using (+)-I or (+)-DIOP as ligand, is usually R-configuration, regardless of the configuration at C_3 of the aldehyde (3).

The generally accepted mechanism for the cyclization of 4-penten-1-al with Rh(I)-complex to cyclopentanone is as follows (Scheme 2).[9] The oxidative addition of the aldehyde carbon-hydrogen bond affords the acylrhodium hydrogen intermediate. Subsequent addition of Rh-H bond to the coordinated double bond forms the six-membered ring including Rh; then reductive elimination affords cyclopentanone. In the case of ligand such as (+)-I, it is likely that two phosphines, each with two phenyl functions, coordinate in such a way that phenyl function of one phosphine (P_1) occupies axial(β) bond and that of the other (P_2) occupies axial(α) (Fig. 1). That is to say, the assumption that β-side of P_1 and α-side of P_2 are sterically hindered, allows R=Bu substituent to occupy less hindered space such as β-side of P_2 (see Fig. 2, R_1=R_2=H). Thus, the above asymmetric cyclization can be explained.

In 3S (or 3R)-substituent, the preferential cyclization to 3,4-cis (or 3,4-trans)-disubstituted cyclopentanone may be rationalized as follows. In R=Me, methyl function approaches to occupy a less hindered space (P_2-β-face) similar to that in the case of Bu, and it is clear from Fig. 2 (3S: R_1=H, R_2=$CH_2CH_2COCH_3$; 3R: R_1=$CH_2CH_2COCH_3$, R_2=H) that 3S (or 3R)-substituent is cyclized to be 3,4-cis (or trans)-substituents. However, it is also likely that a smaller Me function than Bu occupies a hindered space (P_1-β-side). This assumption provides rational explanation for the findings that the 3,4-trans-cyclopentanone (5b) and the 3,4-cis-cyclopentanone (4a) are obtained from 3S-substituted 4-penten-1-al (3b) and

3R-substituted 4-penten-1-al (3a), respectively.

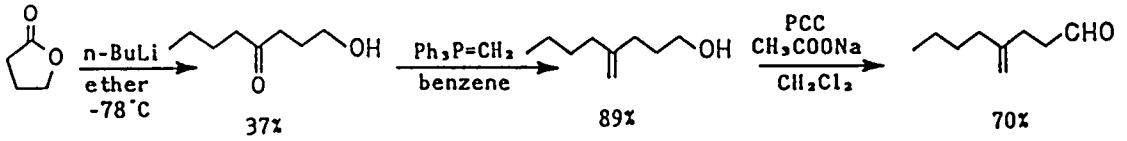
References and Notes

1) a; K.Sakai, J.Ide, O.Oda, and N.Nakamura, Tetrahedron Lett., 1972, 1287. b; K.Sakai, Y.Ishiguro, K.Funakoshi, K.Ueno, and H.Suemune, ibid., 25, 961 (1984). c; R.C.Larock, K.Oertle, and G.F.Potter, J. Am. Chem. Soc., 102, 190 (1980). d; C.F.Lochow, and R.G.Miller, ibid., 98, 1281 (1976). For the cyclization of 6-octen-1-als by Rh(I)-complex, see K.Sakai, and O.Oda, Tetrahedron Lett., 1972, 4375; K.Funakoshi, N.Togo, and K.Sakai, ibid., 30, 1095 (1989).

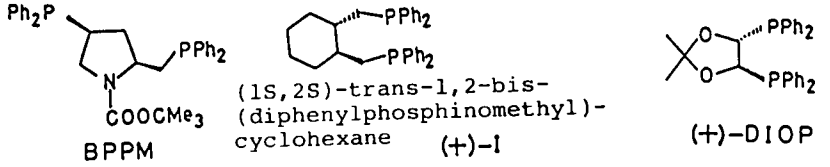
2) H.Suemune, T.Kawahara, and K.Sakai, Chem. Pharm. Bull., 34, 550 (1986); K.Ueno, H.Suemune, S.Saeki, K.Sakai, ibid., 33, 4021 (1985); X.-F.Xie, Y.Ichikawa, H.Suemune, and K.Sakai, ibid., 35, 1816 (1987); H.Suemune, H.Maruoka, S.Saeki, and K.Sakai, ibid., 34, 4629 (1986); H.Suemune, K.Oda, S.Saeki, and K.Sakai, ibid., 36, 172 (1988).

3) B.R.James and C.G.Young, J. Chem. Soc., Chem. Commun., 1983, 1215. Optical purity (52% e.e) was estimated by using the reported specific rotation of a standard sample.

4) 4-Bu-4-penten-1-al was synthesized as follows.



5) Structure of chiral ligands and the used abbreviations



6) Optical purity of cyclized 4-butylcyclopentanone (2) was determined by the examination of the ^{13}C-NMR spectra of diastereomers, which were obtained by acetalization of butylcyclopentanone with (2R,3R)-2,3-butanediol/p-TsOH. The absolute stereochemistry of 2 was determined to be S-configuration by comparison with sign of the reported specific rotation. See E.J.Corey, R.Naef, and F.J.Hannon, J. Am. Chem. Soc., 108, 7114 (1986).

7) For the preparation of 3a(3R) and 3b(3S), see ref. 1b and 2.

8) It was difficult to separate 3,4-cis and trans-mixtures by silica-gel column chromatography. The ratio of 3,4-cis-cyclopentanone to 3,4-trans isomer was determined by comparison of 100 ^{1}H-NMR spectra, in which cis- and trans-methyl signals appear at δ 0.94 and δ 1.14, respectively. See K.Inoue, J.Ide, and K.Sakai, Bull. Chem. Soc. Japan, 51, 2361 (1978).

9) R.E.Campbell, Jr.,C.F.Lochow, K.P.Vora, and R.G.Miller, J. Am. Chem. Soc., 102, 5824 (1980).

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