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HIGHLY EFFECTIVE CATALYTIC ASYMMETRIC SYNTHESIS OF R-(-)-PANTOLACTONE[1)]

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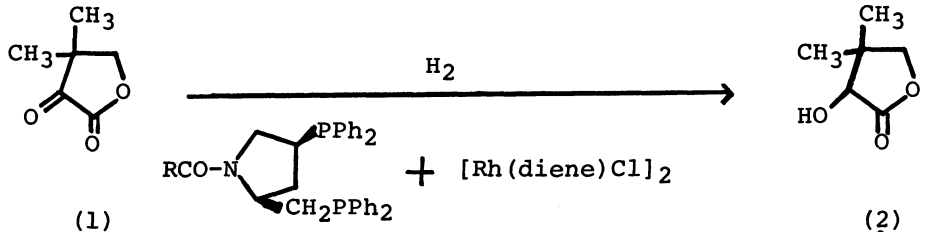
The sterically smaller N-substituents of methylpyrrolidinebisphosphines as chiral ligands in benzene except BPPM and BZPPM gave the better optical yields of R-(-)-pantolactone. Thus, BPPM-, FPPM-, APPM-, BZPPM- and PPPM-[Rh(1,5-cyclooctadiene)Cl]$_2$ complexes gave 80.5, 78.9, 73.4, 78.5 and 67.5% optical yields respectively.

Recently, We have developed a simple chiral synthesis of R-(-)-pantolactone(2) in 54.6-59.2% optical yields by asymmetric hydrogenation of α-keto-β,β-dimethyl-γ-butyrolactone(1)[2)] as an application of the successful hydrogenation of the α-keto-esters catalyzed by BPPM-rhodium complex[3)], and also from our continued interest in the effects of the modified N-substituents of BPPM on the asymmetric hydrogenation of the conformationally fixed cyclic keto ester, since the modification of the N-substituent of BPPM afforded a dramatic effect on the optical yields of N-benzyloxycarbonylalanine[4)], isoquinoline alkaloid salsolidine[5)] and β-amino acids[6)] in their asymmetric syntheses.

We wish to describe here a systematic investigation of the chiral synthesis of this simple α-hydroxy lactone using new chiral bisphosphines; BPPM[7)], FPPM[8)], APPM[4)], BZPPM[6)] and PPPM[4)], and rhodium(diene) complexes; [Rh(1,5-hexadiene)Cl]$_2$ and [Rh(1,5-cyclooctadiene)Cl]$_2$, to clarify the N-substituent effects[9)].



(1) (3) (4) (2)

3a, RCO-= $(CH_3)_3COCO-$ (BPPM)
3b, RCO-= HCO- (FPPM)
3c, RCO-= CH_3CO- (APPM)
3d, RCO-= C_6H_5CO- (BZPPM)
3e, RCO-= $(CH_3)_3CCO-$ (PPPM)

4f, diene= 1,5-hexadiene
4g, diene= 1,5-cyclooctadiene

Table I. Asymmetric hydrogenation of α-keto-β,β-dimethyl-γ-butyrolactone[a)]

Chiral reagent (RCO-)		[Rh(diene)Cl]$_2$	Conversion[b)] (%)	$[\alpha]_D^{20}$ (H_2O)	Optical y. (%)	(conf.)[c)]
$(CH_3)_3COCO$-	(BPPM)	1,5-hexadiene	100	-27.7	54.6[d)]	(R)
HCO-	(FPPM)	1,5-hexadiene	100	-38.1	75.1	(R)
CH_3CO-	(APPM)	1,5-hexadiene	100	-35.9	70.8	(R)
C_6H_5CO-	(BZPPM)	1,5-hexadiene	100	-38.5	75.9	(R)
$(CH_3)_3CCO$-	(PPPM)	1,5-hexadiene	100	-30.0	59.2[d)]	(R)
$(CH_3)_3COCO$-	(BPPM)	1,5-cyclooctadiene	100	-40.8	80.5	(R)
HCO-	(FPPM)	1,5-cyclooctadiene	100	-40.0	78.9	(R)
CH_3CO-	(APPM)	1,5-cyclooctadiene	100	-37.2	73.4	(R)
C_6H_5CO-	(BZPPM)	1,5-cyclooctadiene	100	-39.8	78.5	(R)
$(CH_3)_3CCO$-	(PPPM)	1,5-cyclooctadiene	100	-34.2	67.5	(R)

a) All hydrogenations were run with 5 mmole of substrate, 0.025 mmole of [Rh(diene)Cl]$_2$ and 0.06 mmole of bisphosphine in 3 ml of benzene at 50°C for 45 h under an initial hydrogen pressure of 50 atm. b) Vpc analysis. c) Calculated on the basis of the reported value for optically pure R-2; $[\alpha]_D^{25}$-50.7°(c 2.05, H_2O)(E.T.Stiller, S.A.Harris, J.Finkelstein, J.C.Keresztesy and K.Folkers, J.Am.Chem.Soc., 62, 1785(1940)). d) Data from ref. 2.

Table I shows clearly that the steric bulkiness of the N-substituents(RCO-) of 3 plays an important role in affecting the optical yields of 2, whereas their polar effects are almost negligible at least in this condition, and also the catalyst from the bisphosphine and [Rh(1,5-cyclooctadiene)Cl]$_2$ gave the better optical yields than the catalyst of [Rh(1,5-hexadiene)Cl]$_2$ especially when BPPM was used as a ligand, although no plausible interpretation of these facts is obtained in this stage.

It should be also noted that the sterically smaller N-substituents of the bisphosphines as chiral ligands in benzene except BPPM and BZPPM gave the better optical yields of R-(-)-pantolactone. These facts may suggest that the further modification of the N-substituent and phosphine group of BPPM is possible for the match of substrate structure towards complete stereospecificity[10)].

REFERENCES AND NOTES

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8) K.Achiwa, The 15th symposium on peptide chemistry, November 1977 (Osaka). FPPM(3b); mp 125-126°C, $[\alpha]_D^{20}$-38°(c 0.684, benzene).
9) Acidity orders of RCOOH in 3; $(CH_3)_3COCOOH < (CH_3)_3CCOOH \approx CH_3COOH < C_6H_5COOH < HCOOH$. Steric bulkiness orders of R in 3; $H < CH_3 < C_6H_5 < (CH_3)_3C$.
10) Further refinement of the reaction conditions using BPPM as a ligand gave a 86.7% optical yield of R-(-)-pantolactone(I.Ojima, T.Kogure, T.Terasaki and K.Achiwa).

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