Enantioselective Transfer Hydrogenation of Aromatic Ketones Catalyzed by New Diaminodiphosphine Ru(Ⅱ) Complexes*

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Chiral biphosphine ligands provide a useful tool for preparing optically active secondary alcohols and have been the interesting subject of numerous investigations[1]. However, it is noted that in the field of enantioseletive transfer hydrogenation, the mostly used chiral auxiliary ligands should contain nitrogen as the donor atom[2]. Recently, the importance of nitrogen donors has been reviewed[3] and some chiral ruthenium complexes bearing nitrogen donors have been developed[4]. In the past few years, we have been interested in the synthesis of well-designed polydentate ligands possessing two "soft" phosphorus atoms and two "hard" nitrogen atoms as chelating ligands[5~8]. These ligands can act as bi-, tri- and tetradentate ligands, depending on the reaction conditions and display some interesting structures, chemical and catalytic properties[9]. This communication reports the synthesis and characterization of some new chiral Ru(Ⅱ) complexes with a similar structure *N*, *N*′-bis[*o*-(diphenylphosphino)benzylidene]propane-1, 2-diamine(P_2N_2Me-Ru(Ⅱ)Cl_2 for abbriviation) and *N*, *N*′-bis[*o*-(diphenylphosphino)benzyl]propane-1, 2-diamine($P_2N_2H_4Me$-Ru(Ⅱ)Cl_2 for abbriviation), their application in the enantioselective transfer hydrogenation of aromatic ketones as well.

When a mixture of *o*-(diphenylphosphino)benzylaldehyde and (*R*)-propane-1, 2-diamine in a molar ratio of 2∶1 was stirring in dichloromethane with an excess of Na_2SO_4 as a dehy-

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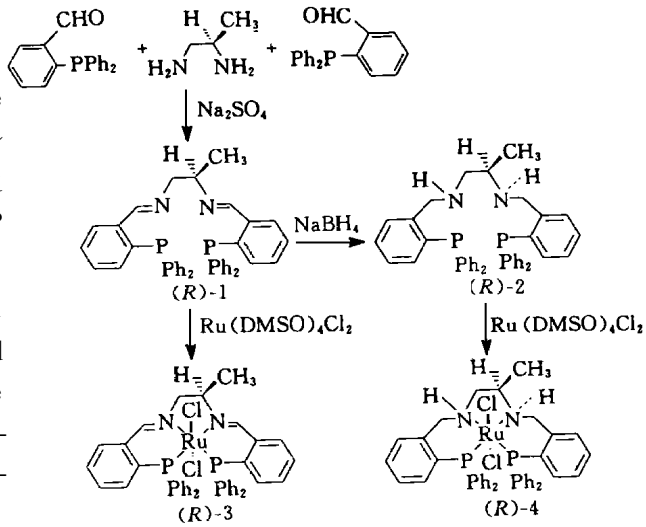
drating agent, a tetradentate (*R*)-*N*, *N*′-bis [*o*-(diphenylphosphino) benzylidene] propane-1, 2-diamine [(*R*)-1] was produced in a 83%～88% yield (Scheme 1). ^{1}H NMR ($CDCl_3$): δ 8.75 for Ph—CH═N; ^{31}P NMR($CDCl_3$), δ – 11.81, – 12.44. Furthermore, the reduction of (*R*)-1 with an excess of $NaBH_4$ was carried out in refluxing ethanol to afford the corresponding (*R*)-*N*, *N*′-bis [*o*-(diphenylphosphino) benzyl] propane-1, 2-diamine [(*R*)-2] in a 68%—73% yield(^{1}H NMR($CDCl_3$): δ 4.14 for Ph_ CH_2_; ^{31}P NMR($CDCl_3$), δ – 15.41, – 15.51).



Scheme 1

The interaction of an equimolar mixture of *trans*-$RuCl_2(DMSO)_4$ and (*R*)-1 in refluxing toluene gave a dark-red solution. This solution was concentrated under reduced pressure and the crude product was chromatographed on a silica gel column (2 cm × 12 cm) with CH_2Cl_2 as the eluent solvent, giving a red colour ruthenium complex containing (*R*)-*N*, *N*′-bis [*o*-(diphenylphosphino) benzylidene] propane-1, 2-diamine [(*R*)-3] (yield 78%～82%, ^{1}H NMR ($CDCl_3$): δ 8.76 for Ph_ CH═N_; ^{31}P NMR($CDCl_3$), δ 48.12, 48.51).

A yellow Ru(Ⅱ) complex (*R*)-4 was prepared by the similar procedure and CH_2Cl_2/acetone (1∶1 V/V) was used as eluent solvent when a silica gel column was used. The ^{31}P NMR spectrum of (*R*)-4 exhibits two singlets of equal intensity at δ 45.18 and 43.88, which suggest that the two phosphine groups are non-equivalent and coordinated to ruthenium atom. ^{1}H NMR (500 MHz $CDCl_3$) for (*R*)-4: δ 0.91(d, *J* = 5.8 Hz, 3H, _ CH_3), 3.28(t, 1H, _ CH_2), 3.01(d, 1H, _ CH_2), 4.62(s, 1H, _ NH_), 3.95(t, *J* = 12 Hz, 1H, _ NH_). 3.54(m, 1H, —HC⟩), 3.70(d, *J* = 12 Hz, 1H, $PhCH_2$_), 4.06(d, *J* = 12 Hz, 1H, $PhCH_2$_), 4.75(d, *J* = 11 Hz, 1H, $PhCH_2$_), 4.80(t, *J* = 11 Hz, 1H, $PhCH_2$_), 6.82～7.34(m, 28 Hz, C_6H_5_). ^{31}P NMR($CDCl_3$) for (*R*)-4: δ 45.18, 43.88. m.p. 226～228 ℃. Anal. Calcd. (%) for (*R*)-4 0.5 C_6H_{14} (837.79): C 63.11; H 5.61; N 3.36; Found: C 63.04; H 5.46; N 3.35. IR(KBr), $\tilde{\nu}$/cm^{-1}: 3 450m, 3 057m, 2 867m, 1 474s, 1 431vs, 1 089s, 1 027w, 950s, 744s, 692vs, 516vs. Ligands (*S*)-1, (*S*)-2 and Ru(Ⅱ) complexes (*S*)-3, (*S*)-4 were easily prepared by means of the above similar procedures.

A suitable crystal of complex (*R*)-3 for X-ray diffraction was grown from a CH_2Cl_2/hexane mixture. The structure analysis of (*R*)-3 revealed a distorted octahedral *trans*-configuration for the complex(Fig. 1). The crystal data for (*R*)-3 $C_{41}H_{36}N_2P_2Cl_2Ru$ are as follows: *M* = 790.67, monoclinic, space group $P2_1$, *a* = 1.156 9(1) nm, *b* = 1.507 9(1) nm, *c* = 1.197 2(1) nm, β = 97.42(1)°, *V* = 2.071 13 nm^3, *Z* = 2, D_c = 1.540 g/cm^3, μ = 78.1 cm^{-1}, *F*(000) = 976. The two chloro-ligands in the axial position are mutually *trans* to each other

and the (*R*)-1 ligand acts as a tetradentate ligand around the Ru center with the two phosphino-groups *cis* to each other. The attempt to get a suitable crystal of complex (*R*)-4 for structure analysis is still unsuccessful. However, based on the spectroscopic data and the molecular structures of *trans*-$RuCl_2(P_2N_2)$ and *trans*-$RuCl_2(P_2N_2H_4)$[9,10], the structure of ruthenium complex (*R*)-4 is assignable to an analogy of complex (*R*)-3.

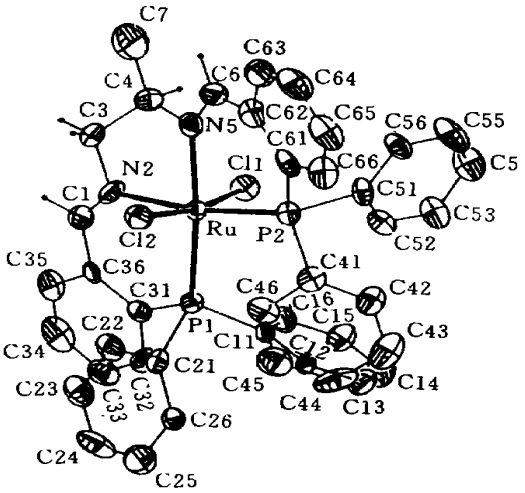
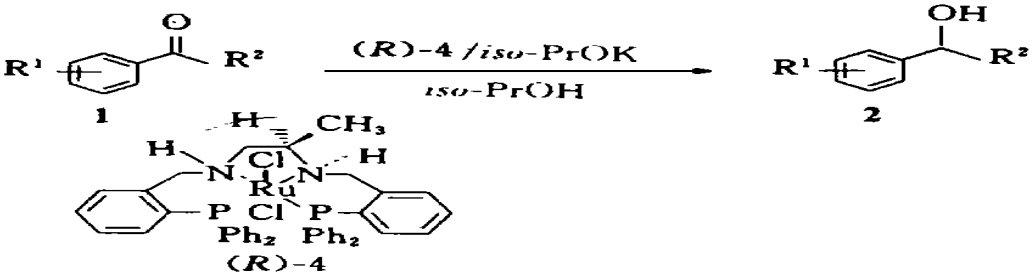


Fig. 1 Molecular structure of complex (*R*)-3.

Complexes (*R*)-3, (*S*)-3, and (*R*)-4, (*S*)-4 have been tested as catalysts for the enantioseletive transfer hydrogenation of aromatic ketones in an *iso*-PrOH solution (Scheme 2). The catalytic hydrogenation of acetophenone (**1**a) was conducted using some potassium 2-propoxide (1_ 3 equiv. with respect to Ru) as a promoter (Table 1).



a. R^1= H, R^2= Me; *b*. R^1= H, R^2= Et; *c*. R^1= Cl, R^2= Me; *d*. R^1= OCH_3, R^2= Me.

Scheme 2

Table 1 Asymmetric transfer hydrogenation of ketones catalyzed by chiral $P_2N_2Me_2$-Ru(Ⅱ)Cl_2 and $P_2N_2H_4Me$-Ru(Ⅱ)Cl_2 complexes*

Ketone substrate	Catalyst	*n*(S)∶*n*(C)∶*n*(*iso*-PrOK)[a]	Condition		Alcohol product		
			t/℃	*t*/h	Yield(%)[b]	*e.e.*(%)[c]	Config.[d]
1a	(*R*)-3	100∶1∶5	40	22	63	26	*S*
1a	(*S*)-3	100∶1∶5	40	22	65	14	*R*
1a	(*S*)-3	100∶1∶5	30	46	90	91	*S*
1b	(*S*)-4	100∶1∶2	45	48	55	88	*S*
1b	(*R*)-4	100∶1∶5	30	46	73	91	*R*
m-**1**c	(*S*)-4	100∶1∶2	30	24	99	87	*S*
p-**1**c	(*S*)-4	100∶1∶2	30	24	82	89	*S*
m-**1**d	(*S*)-4	100∶1∶2	30	24	72	85[e]	*S*
p-**1**d	(*S*)-4	100∶1∶2	30	24	49	87[e]	*S*

* Conditions: catalysts 0.01 mmol; solvent *iso*-PrOH 20 mL; *a*. S/C/*iso*-PrOK= ketone/Ru/*iso*-PrOK; *b*. GLC analysis; *c*. capillary GLC analysis using a chiral Chrompack CD-cyclodextrin-β-236 M-19 column unless otherwise specified; *d*. determined by comparison of the retention time of each of the enantiomers on the GLC traces with literature values; *e*. determined by HPLC analysis using a Daicel Chiralcel OB column (10∶90 2-propanol-hexane).

The concentration of *iso*-PrOK is an important factor for the catalytic activity and the

catalytic system is inactive without a basic co-catalyst. The increase of reaction temperature accelerates the reaction rate with a slight loss of enantiomeric purity of the product. The ketones possessing an eletron-donating substituent such as methoxyl to the para position tend to lower the rate, but still show high stereoselectivity. It is noteworthy that the diimino complexes (*R*)-3 or (*S*)-3 and the diamino complexes (*R*)-4 or (*S*)-4 display the differences in reactivities and enantioseletivities. Complex (*R*)-4 or (*S*)-4 with sp^3 hybridized nitrogens containing N_H bonds showed the higher reaction rate and enantioselectivity. The detailed reaction mechanism is now under investigating.

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