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GENERAL SYNTHESIS OF NOVEL CHIRAL RUTHENIUM CATALYSTS AND THEIR USE IN ASYMMETRIC HYDROGENATION

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Abstract : The first general synthesis of mononuclear hexacoordinate chiral ruthenium-complexes is presented. Four chiral ruthenium(II)(2-methylallyl)$_2$ complexes containing Diop, Chiraphos, Norphos, and Binap were prepared in 50-71% yield under mild conditions, and were found to be effective for asymmetric hydrogenation of unsaturated carboxylic acids to give the corresponding saturated derivatives attaining 90% optical purity.

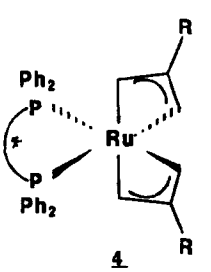
During the past twenty years asymmetric synthesis using homogeneous catalysis has become a powerful tool in organic chemistry. Catalytic asymmetric hydrogenation by means of a large variety of rhodium complexes with chiral ligands such as Diop, Bppm, Chiraphos, etc, has been extensively used to achieve high enantioselectivity.[1] In contrast, there are relatively few reports on corresponding ruthenium complexes.[2] Some cluster ruthenium complexes of Diop are known and are effective as catalysts for asymmetric hydrogenation under quite drastic conditions.[2e] With the advent of the first ruthenium Binap complexes **1** described by Ikariya,[3] the situation changed, and outstanding performance of various Binap-ruthenium complexes **2**, **3**[4] have been described by Noyori and Saburi for reduction of carbon-carbon double-bonds[3,5] and carbonyl groups.[6] However, the synthesis of ruthenium mononuclear catalyst from polymeric(RuCl$_2$(COD))$_n$ as starting material requires the presence of triethylamine and is executed in toluene at reflux,[3,4] to cleave the halogeno- bridged structure. The development of ruthenium-chemistry for homogeneous asymmetric synthesis requires mild and reliable synthesis of chiral ruthenium catalysts.
In this note we wish to report a convenient and general synthetic method for the preparation of new family of chiral bidentate phosphine ruthenium bis-allyl complexes of type **4** which were also found to catalyze asymmetric hydrogenation of olefins.

Ru_2Cl_4(-)$BINAP_2$, NEt_3

1

(BINAP)RuX_2

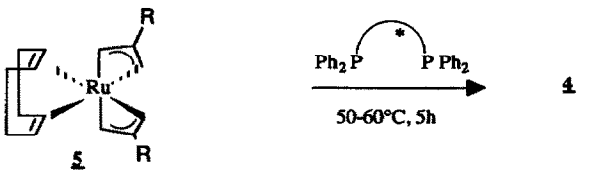
2 : X = Cl, Br, I
3 : X = OAc



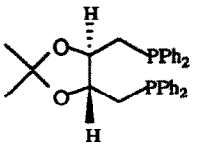
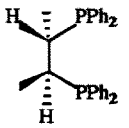
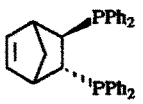
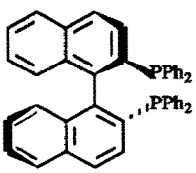
4

Allylic Grignard reagents are known to react with polymeric, halogeno-bridged complexes such as $(RuX_2diene)_n$ with formation of mononuclear ruthenium complexes of type $(Ru(All)_2diene)$ (All = Allyl or 2-methylallyl).[8] We found that Ru(2-methylallyl)$_2$COD **5** was an excellent starting material for a facile synthesis of a wide range of bidentate chiral phosphine complexes **4**.[9] These complexes can be prepared by simple displacement of 1,5-cyclooctadiene (COD) of **5** by the appropriate chiral ligand as shown in Table I. These catalysts are also convenient precursors for the preparation of the corresponding chiral ruthenium acetate and bromide complexes.[10]

Table I : Preparation of catalysts (4a-4d) by displacement of cyclooctadiene



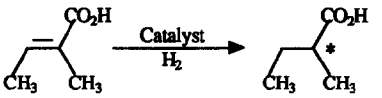
5 **4**

Entry	Ligand	Yield	Aspect
4a[a]	 (R,R)-(-)DIOP	71	(yellow)[12]
4b[a]	 (2S, 3S)-(-)CHIRAPHOS	67	(pale yellow)[13]
4c[a]	 (R,R)-(-)NORPHOS	51	(brown)
4d[b]	 (S)-(-)BINAP	50	(pale brown)[14]

*a) Under argon a mixture of CODRu(methylallyl)$_2$ (0.1g, 0.314 mmol) and the appropriate chiral ligand (1 equivalent) in degassed hexane (2 mL) was heated at 50-60°C for 5 h. The resulting colored crystalline complex (**4a-4c**) was collected by filtration, washed with hexane(2mL) and the powder was dried in vacuo.*

b) (-) Binap was heated with 2 mL of hexane-toluene mixture (5/3). After 8h at 60-70°C, the clear solution was evaporated under reduced pressure,and the resulting solid was washed with hexane (2 mL) and dried in vacuo.

These new chiral ruthenium complexes were found to catalyze hydrogenation, and in this preliminary study tiglic acid 6 was hydrogenated in quantitative yield into saturated acid. The results are summarized in Table II.



6 7

Table II : Hydrogenation of Tiglic Acid (6).[a]

Entry	Ligand	Press (atm)	Temp. (°C)	Yield[b] (%)	ee[c]	conf.
1	(-)-Diop	50	20	100	46	R
2	(-)-Diop	15	20	100	46	R
3	(-)-Diop	3	20	100	51	R
4	(-)-Diop	50	0-5	100	51	R
5	(-)-Diop	15	50	100	38	R
6	(-)-Chiraphos	15	20	100	30	S
7	(+)-Norphos	3	20	100	4	S
8	(+)-Binap	3	20	100	90	R

a) Reaction was executed with stirrring in a stainless steel autoclave in methanol solution (2-3 ml) of the substrate (1 mmol) with exclusion of air during 24-60 h. b) Determined by ^1H NMR. c) ee were determined by H.P.L.C. analysis of the amide prepared by condensation of R-1-(1-naphthylethylamine) and the saturated acid.

A systematic study revealed that the degree of enantioselection is only slightly dependant upon hydrogen pressure. The reaction of 6 in methanol using Ru-Diop as a catalyst at initial hydrogen pressure of 50, 15 and 3 atm. gave the saturated acid in 46 and 51% ee respectively (entries 1-3). The level of asymmetric induction increased by decreasing reaction temperature. Thus using Ru-Diop as a catalyst the reduction of tiglic acid 6 gave an enantiomeric excess reaching 51% at 0-5°C under 50 atm but only 46% at 20°C. (compare entries 1 and 4).

The present study reveals a direct comparison in the efficiency of different optically active chelating biphosphanes ruthenium-allyl hexacoordinate complexes. These complexes are slightly more efficient (2-3 atm.) than the corresponding Ru(II)-acetate.

Ru(II)-Norphos gave poor enantioselectivity (4% : entry 7), with Ru-Chiraphos the formation of saturated acid is observed with 30% ee (entry 6). The ruthenium complex 4a possessing Diop ligand proved to be efficient and rather high enantiomeric excess up to 51% ee is obtained (entry 4), when tiglic acid is the substrate. Noteworthy with the Ru(II)-(2-methylallyl)$_2$ complex bearing Binap ligand a very high enantioselectivity is observed up to 90% ee (entry 8).

In conclusion, new chiral Ru(II) complexes with allyl ligand are easy prepared. These complexes have good activity (2-3 atm) as catalysts for asymmetric hydrogenation with high enantioface discriminating activity (up to 90%).

Out of this work, a systematic study is now possible with ruthenium complexes bearing a large variety of chiral ligands as in the case of rhodium and iridium, which is under active investigation in this laboratory.

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10) To our knowledge few racemic monodentate ruthenium(Allyl)$_2$ complexes (e. g. triphenylphosphines and trialkylphosphites) have been described, see ref 8a and M. Cooke, R. J. Goodfellow, M. Green and G. Parker, *J. Chem. Soc.(A)*, **1971**, 16-20. This methodology has already been extended to 12 other chiral ligands / S. Mallart, C. Pinel, unpublished work in this laboratory.

11) All new chiral ruthenium hexacoordinates complexes have been characterized by ^1H, ^{13}C, ^{31}P NMR, IR, mass spectrum, elementary analysis.

12) 4a : ^1H NMR (250 MHz, C_6D_6) : 1.0 (m, 2H) ; 1.3 (s, 6H) ; 1.32 (q, J = 14.5 Hz, 4H) ; 2.04 (s, 6H) ; 2.55 (m, 2H) ; 2.79 (dd, J_1 = 8.5 Hz, J_2 = 13 Hz, 6H) ; 3.25 (t, J = 13 Hz, 6H) ; 4.15 (m, 2H) ; 6.8-8.0 (m, 20H, aromatics). ^{13}C NMR (62 MHz, C_6D_6) : 25.77 ; 27.2 ; 31.5 (m) ; 42.5 ; 48.31 (m) ; 78.8 ; 95.7 ; 107.9 ; 127-140 (aromatics). ^{31}P NMR (100 MHz, C_6D_6) : 36 (ref : H_3PO_4 75%). IR (Nujol) : 1595, 1240 cm^{-1}. $[\alpha]_D^{25}$ = +202 (c = 0.43, toluene). m. p. = 204°C (decomposition).

13) 4b : ^1H NMR (250 MHz, C_6D_6) : 1.06 (d, J = 6.5 Hz, 2H) ; 1.12 (d, J = 6.5 Hz, 2H) ; 1.24 (q, J = 2.5 Hz, 6H) ; 1.61 (d, J = 2.5 Hz, 2H) ; 1.74 (d, J = 2.5 Hz, 2H) ; 2.15 (s, 6H) ; 6.8-8.0 (m, 20H, aromatics). ^{13}C NMR (62 MHz, C_6D_6) : 18.4 ; 26.1 ; 40.3 (m) ; 44.3 (d, J = 28 Hz) ; 44.7 (d, J = 28 Hz) ; 45.9 ; 97.1 ; 127-133 (aromatics). ^{31}P NMR (100 MHz, C_6D_6) : 87.6 (ref : H_3PO_4 75%). IR (Nujol) : 1580, 1085, 1015, 760, 720 cm^{-1}. $[\alpha]_D^{25}$ = +60 (c = 0.2, toluene). m. p. = 183°C (decomposition).

14) 4d : ^1H NMR (250 MHz, C_6D_6) : 0.35 (s, 2H) ; 0.96 (d, J = 7 Hz, 2H) ; 1.21 (d, J = 2.5 Hz, 2H) ; 2.1 (s, 2H) ; 2.46 (s, 2H) ; 6.0-8.0 (m, 32H, aromatics).^{31}P NMR (100 MHz, C_6D_6) : 42.2 (ref : H_3PO_4 75%).
$[\alpha]_D^{25}$ = +280° (c = 0.3, toluene). m. p. = 230°C (decomposition).