186. Ruthenium-Catalyzed Enantioselective Hydrogenation of 1,3-*O*-Disubstituted 1,3-Dihydroxypropan-2-ones

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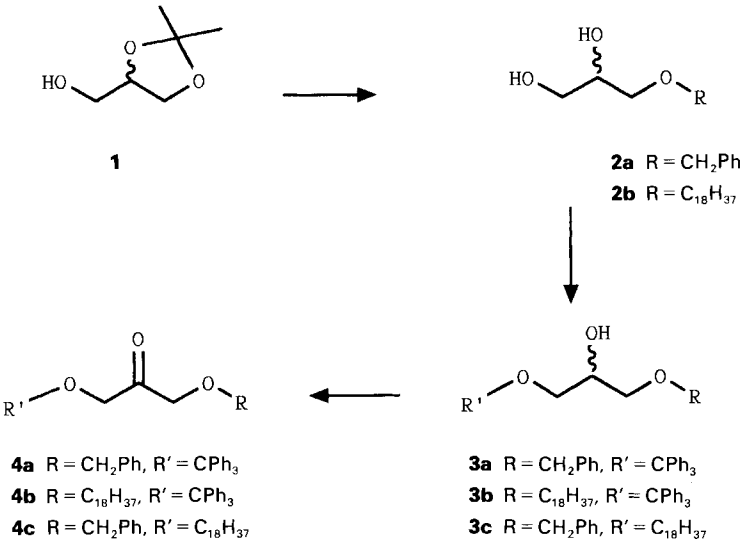
Optically active 1,3-*O*-disubstituted glycerols were obtained by enantioselective homogeneous hydrogenation of the corresponding 1,3-*O*-disubstituted 1,3-dihydroxypropan-2-ones with different Ru^{II}-binap complexes. The highest enantioselectivities were obtained with dimeric chloro-ruthenium complexes on the substrates bearing bulky trityloxy groups.

Introduction. – Optically active 1,3-glycerol derivatives are important and versatile key building blocks for the preparation of a large variety of compounds that are biologically important or are of interest in biochemical research such as phospholipids [1], PAF (platelet activating factor) [2], β-blockers [3], prostaglandins [4], and other compounds [5].

These compounds are usually prepared from the chiral pool substances such as D-mannitol, L-arabinose, L-ascorbic acid, D- or L-tartaric acid, L-serine. New approaches to synthesizing chiral glycerol derivatives are based on enzymatic differentiation of enantiotopic hydroxymethyl groups of glycerol [6] or enantioselective microbial reduction of monoesters of 1,3-dihydroxypropanone [7]. Prompted by the reports on the impressive enantioselective activity of Ru^{II}-binap (binap: atropisomeric chiral diphosphines (+)-(*R*)- and (−)-(*S*)-bis(diphenylphosphino)-1,1′-binaphthalene) catalysts in the reduction of a large variety of prochiral ketones [8] [9], we have investigated the possibility of the enantioselective reduction of some prochiral diethers of 1,3-dihydroxypropanone with different Ru^{II}-binap complexes. Part of this work concerning some preliminary results in the catalytic reduction of **4a** and **4b** has been object of a short communication [10].

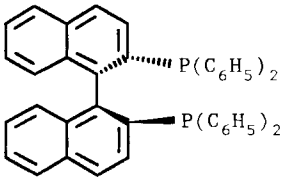
Results and Discussion. – The substrates investigated together with the synthesis sequence are reported in the *Scheme*; they are prepared in good yields from racemic 1,2-*O*-isopropylideneglycerol (**1**). The unprotected primary OH group is functionalized with a benzyl or an octadecyl group followed by acetonide removal to give the diols **2a** and **2b**.

Tritylation of **2a** and **2b** affords the diethers **3a** and **3b**; the reaction of **2a** with octadecyl *para*-toluenesulfonate gives the diether **3c**. The secondary alcohols are oxidized to the corresponding ketones **4a**, **4b**, and **4c** with pyridinium chlorochromate in dry CH_2Cl_2.

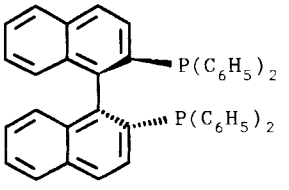


The Ru complexes used in enantioselective reduction are prepared according to literature procedures: they are the dimers $[Ru_2((S)\text{-binap})_2Cl_4]NEt_3$ (**1S**) and $[Ru_2((R)\text{-binap})_2Cl_4]NEt_3$ (**1R**) [11], the cationic arene complexes [Ru(benzene)((*S*)-binap)Cl]Cl (**2S**) and [Ru((*S*)-binap)(*p*-cymene)I]I (**3S**) [12]; the 'preformed' $[Ru((S)\text{-binap})Cl_2]_n$ (**4S**) is prepared from the combination of (*S*)-binap and $[Ru(benzene)Cl_2]_2$ in DMF [13]; the complex **5S** of empirical formula $[Ru((S)\text{-binap})Cl_2]$ is prepared by mixing $[Ru((S)\text{-binap})(OCOCH_3)_2]$ and HCl in a 1:2 ratio in CH_2Cl_2 [14].

The complexes **1S**, **1R**, **2S**, and **3S** give satisfactory elemental analysis and spectroscopic data in agreement with the data reported in the literature. All the complexes are also characterized by MS. The fast-atom ionization technique makes it possible to obtain information about the molecular weight of the Ru complexes by investigating the posi-



(*S*)-binap



(*R*)-binap

1S $[Ru_2((S)\text{-binap})_2Cl_4]NEt_3$
1R $[Ru_2((R)\text{-binap})_2Cl_4]NEt_3$
2S [Ru(benzene)((*S*)-binap)Cl]Cl
3S [Ru(*p*-cymene)((*S*)-binap)I]I
4S $[Ru((S)\text{-binap})Cl_2]_n$ from $[Ru(benzene)Cl_2]_n$ + (*S*)-binap
5S $[Ru((S)\text{-binap})Cl_2]_n$ from $[Ru((S)\text{-binap})(CH_3COO)_2]$ + HCl

tive-ion spectra. The FAB^+ mass spectra do not show appreciable differencies in the different matrices used (*cf. Exper. Part*); higher sensitivities are obtained, however, using nitrobenzyl alcohol.

The relative intensities of the principal Ru-containing positive ions observed in the FAB^+ mass spectra of the complexes **1S**, **1R**, **4S**, and **5S** are summarized in *Table 1*.

Table 1. *Relative Intensities of the Principal Ru-Containing Positive Ions Observed in the FAB^+ Mass Spectra of Ru Complexes* **1S**, **4S**, *and* **5S**

Ion	*m/z*	Rel. intensity [%]		
		1S	**4S**	**5S**
$[Ru_2(binap)_2Cl_4]NEt_3^+$	1689	–		
$[Ru_2(binap)_2Cl_4]^+$	1588	3		
$[Ru_2(binap)_2Cl_3]^+$	1553	8		
$[Ru(binap)Cl_2]^+$	794	–	7	6
$[Ru(binap)Cl]^+$	759	48	64	50
$[Ru(C_{44}H_{31}P_2)]^+$ (−HCl)	723	100	100	100
$[Ru(C_{38}H_{26}P_2)]^+$ ($-C_6H_6$)	645	32	44	28
$[Ru(Cl_{32}H_{21}P)]^+$ ($-PPh_2H$)	537	44	41	60

Obviously, the dimers **1S** and **1R** give the same spectra, although the Et_3N adducts are never detectable. All the complexes show a parent ion of low intensity (3–7%) and a base peak corresponding to the fragment $[Ru(C_{44}H_{31}P_2)]^+$ (*m/z* 723) arising from the loss of HCl from $[Ru(binap)Cl]^+$ (*m/z* 759); this fragmentation is supported in all the complexes by a metastable peak at *m/z* 689.7. The absence of ions of *m/z* > 794 in the spectra of **4S** and **5S** may indicate that these two complexes are essentially monomeric.

The relative intensities of the positive ions observed in the FAB^+ mass spectra of the cationic Ru-arene complexes **2S** and **3S** are summarized in *Table 2*. Both give a parent ion of 7% and 5% intensity and base peak corresponding to the fragment $[Ru(binap)Cl]^+$ (*m/z* 759) and $[Ru(binap)I]^+$ (*m/z* 851); these fragments undergo the loss of HCl or HI as evidenced by a metastable peak at *m/z* 688.7 and 614.2, respectively.

Table 2. *Relative Intensities of the Principal Ru-Containing Positive Ions Observed in the FAB^+ Mass Spectra of Ru Complexes* **2S** *and* **3S**

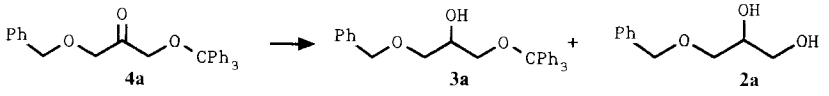
Ion	*m/z*	Rel. intensity [%] **2S**	Ion	*m/z*	Rel. intensity [%] **3S**
$[Ru(binap)(benzene)Cl]^+$	837	7	[Ru(binap)(*p*-cymene)I]	985	5
$[Ru(binap)(benzene)]^+$	802	5	$[Ru(binap)(p\text{-cymene})]^+$	858	7
$[Ru(binap)Cl]^+$	759	100	$[Ru(binap)I]^+$	851	100
$[Ru(C_{44}H_{31}P_2)]^+$ (−HCl)	723	64	$[Ru(C_{44}H_{31}P_2)]^+$ (−HI)	723	38
$[Ru(C_{38}H_{26}P_2)]^+$ ($-C_6H_6$)	645	44	$[Ru(C_{38}H_{26}P_2)]^+$ ($-C_6H_6$)	645	21
$[Ru(C_{32}H_{21}P)]^+$ ($-PPh_2H$)	537	68	$[Ru(C_{32}H_{21}P)]^+$ ($-PPh_2H$)	537	21

Interestingly, the molecular complexes **1S**, **1R**, **4S**, and **5S** give similar mass spectra below *m/z* 759; the dimers **1S** and **1R**, however, do not show any detectable peak at *m/z* 794 corresponding to the fragment $[Ru(binap)Cl_2]^+$ arising from the splitting of the dimeric cage. Even if great care must always be taken when making predictions concern-

ing bond dissociations from ion intensities, it appears that the dimeric cage in the complexes **1S** and **1R** is relatively stable and undergoes fragmentation to low m/z ions rather to the monomeric unit $[Ru(binap)Cl_2]^+$.

The results of enantioselective hydrogenation of 1-(benzyloxy)-3-(trityloxy)propan-2-one (**4a**) are compiled in *Table 3*. The dimeric complexes **1S** and **1R** show a high chemoselectivity and a remarkable enantioselectivity; (*S*)- or (*R*)-1-(benzyloxy)-3-(trityloxy)propan-2-ol (**3a**) is the only product formed in 86% and 87% e.e., respectively

Table 3. *Enantioselective Hydrogenation of 1-(Benzyloxy)-3-(trityloxy)propan-2-one* (**4a**)[a])



4a **3a** **2a**

Entry	Catalyst	Temp. [°C]	Time [h]	**3a**			**2a**		
				Conversion [%][b])	e.e. [%][c])	Configuration[d])	Conversion [%][b])	e.e. [%][c])	Configugation[d])
1	**1R**	25	88	70	86	(*S*)	–	–	–
2	**1S**	25	87	67	87	(*R*)	–	–	–
3	**1R**	60	24	18	60	(*S*)	–	–	–
4[e])	**1S**	60	24	–	–	–	100	0	–
5	**2S**	60	24	31	51	(*R*)	38	29	(*R*)
6	**2S**	100	1	32	40	(*R*)	< 2		
7	**3S**	60	24	7	35	(*R*)	75	10	(*R*)
8[f])	**3S**	60	23	40	8	(*R*)	–	–	–
9[g])	**2S**	25	80	41	49	(*R*)	< 2		

[a]) All reactions were carried out in CH_2Cl_2 if not otherwise stated; substrate concentrations 0.1M; catalyst concentration 0.001M; molar substrate/catalyst ratio 100:1; pressure 100 Kgw cm^{-2} (1 Kgw cm^{-2} = 9.81×10^4 Pa).

[b]) Isolated yield after flash chromatography.

[c]) Determined by HPLC on chiral stationary phase.

[d]) Determined by the sign of rotation.

[e]) MeOH as solvent.

[f]) Molar Et_3N/catalyst ratio 2:1.

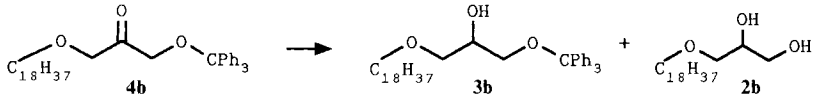
[g]) Substrate concentrations 0.002M; catalyst concentration 0.001M; pressure 100 Kgw cm^{-2}, temperature 60°. After 30 min, the autoclave was cooled to 25° and 98 equiv. of substrate, dissolved in the minimum amount of solvent, were added.

(*Entries 1* and *2*). An increase in temperature leads to a decrease in the steric control (*Entry 3*). MeOH as solvent (*Entry 4*) increases the catalytic activity, but the only product is 3-(benzyloxy)propane-1,2-diol (**2a**) in an almost racemic form and Ph_3COH. The cationic arene complexes **2S** and **3S** are totally inactive at room temperature; on increasing the temperature to 60°, they become more active than the corresponding dimers (*Entries 5* and *7*). This higher reactivity is associated with a decreased enantioselectivity, and the cleavage of the O–CPh_3 bond becomes predominant giving **2a** as the major product. When the hydrogenation is performed at high temperature (*Entry 6*) for a short period, the major product is **3a** which is formed in reasonable yields, and only traces of **2a**

are detectable. The cleavage of the O–CPh_3 bond is due to the catalytic action of the halogenidric acids arising from the heterolytic activation of the molecular hydrogen. In fact, when the hydrogenation is performed in the presence of 2 equiv. of Et_3N (with respect to the catalyst; *Entry 8*), only **3a** is formed.

In *Table 4*, the results of the asymmetric hydrogenation of 1-(octadecyloxy)-3-(trityloxy)propan-2-one (**4b**) are summarized. The dimers **1S** and **1R** show a high enantioselectivity; (*R*)- or (*S*)-1-(octadecyloxy)-3-(trityloxy)propan-2-ol (**3b**) is the only product formed in 89% and 86% e.e., respectively (*Entries 1* and *2*). Previously, we described an

Table 4. *Enantioselective Hydrogenation of 1-(Octadecyloxy)-3-(trityloxy)propan-2-one* (**4b**)[a])



Entry	Catalyst	Temp. [°C]	Time [h]	**3a**			**2b**		
				Conversion [%][b])	e.e. [%][c])	Configuration[d])	Conversion [%][b])	o.p. [%][e])	Configuration[d])
1	**1S**	25	87	73	89	(*R*)	–	–	–
2	**1R**	25	87	60	86	(*S*)	–	–	–
3	**3S**	25	70	–	–	–	–	–	–
4	**3S**	60	24	–	–	–	80	67	(*R*)
5	**4S**	25	24	50	20	(*R*)	–	–	–

[a]) All reactions were carried out in CH_2Cl_2 if not otherwise stated; substrate concentrations 0.1M; catalyst concentration 0.001M; molar substrate/catalyst ratio 100:1; pressure 100 Kgw cm^{-2} (1 Kgw cm^{-2} = 9.81×10^4 Pa).

[b]) Isolated yield after flash chromatography.

[c]) Determined by HPLC on chiral stationary phase.

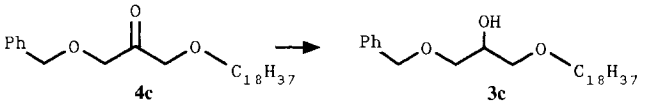
[d]) Determined by the sign of rotation.

[e]) Specific optical rotation (+)-(*R*)-**2b**: $[\alpha]_D^{25} = +2.36$ ($c = 7$, THF) [2].

enantiodifferentiation higher than 96% e.e. [10]; these results had been obtained by polarimetric measurements based on the specific optical rotation values $[\alpha]_D = -4.59$ and $[\alpha]_D = +4.70$ for (–)-(*S*)- and (+)-(*R*)- **3b**, respectively [2]. The cationic arene complex **3S** is almost inactive at room temperature (*Entry 3*); the same catalyst at 60° (*Entry 4*) gives exclusively 3-(octadecyloxy)propane-1,2-diol (**2b**) in 67% o.p. The catalyst **4S**, prepared '*in situ*' in DMF from a combination of (*S*)-binap and $[(C_6H_6)RuCl_2]_2$ according to [13] (*Entry 5*) gives exclusively **3b** with a moderate 20% e.e. It is worth mentioning that the catalyst **4S** under the same conditions reduces ethyl 3-oxobutanoate to ethyl (*S*)-hydroxybutanoate quantitatively in 87% e.e.

In *Table 5*, the results of enantioselective hydrogenation of 1-(benzyloxy)-3-(octadecyloxy)propan-2-one (**4c**) are compiled; the catalysts **1S**, **1R**, and **3S** reduce the ketone to the corresponding (*R*)- or (*S*)-1-(benzyloxy)-3-(octadecyloxy)propan-2-ol (**3c**) with moderate e.e. (27%, 21%, and 13%, respectively, *Entries 1*, *2*, and *3*). The catalyst **5S**, prepared '*in situ*' according to [14] by treating [Ru((*S*)-binap)$(CH_3COO)_2$] with HCl in CH_2Cl_2, gives **3c** as a racemic mixture (*Entry 4*).

Table 5. *Enantioselective Hydrogenation of 1-(Benzyloxy)-3-(octadecyloxy)propan-2-one* (**4c**)[a])



4c **3c**

Entry	Catalyst	Temp. [°C]	Time [h]	**3c**		
				Conversion [%][b])	e.e. [%][c])	Configuration[d])
1	**1S**	25	89	84	27	(*R*)
2	**1R**	25	88	81	21	(*S*)
3	**3S**	60	24	81	13	(*R*)
4	**5S**	25	24	50	0	–

[a]) All reactions were carried out in CH_2Cl_2 if not otherwise stated; substrate concentrations 0.1M; catalyst concentration 0.001M; molar substrate/catalyst ratio 100:1; pressure 100 Kgw cm^{-2} (1 Kgw cm^{-2} = 9.81×10^4 Pa).

[b]) Isolated yield after flash chromatography.

[c]) Determined by HPLC on chiral stationary phase.

[d]) Determined by the sign of rotation.

The experimental results indicate that the dimers **1S** and **1R** give the best enantioselecitivity in the catalytic reduction of disubstituted 1,3-dihydroxypropan-2-one among the Ru-catalyst precursors investigated, notwithstanding the similar solvent and pressure conditions. The high level of enantioselectivity usually shown by the different Ru complexes with binap-type ligands is related to the possibility for the substrate to coordinate simultaneously with a second directing group making five or six-membered chelate rings with high sterical demand [15]. This is a well established feature in the stereocontrolled reduction of olefins with rhodium- or iridium-phosphine complexes [16] and in the kinetic resolution of racemic allylic alcohols by Ru^{II}-binap complexes [17]. In the present case, however, the chelating ability of the substrates depends upon the basicity of the ether-type O-atoms which are known to be weakly coordinating, and which are weaker directing groups than amido, hydroxy, or ester functions. Rather surprisingly, **2a** is obtained in a racemic mixture (in MeOH) or in a very low e.e.-%, in spite of the fact that α-hydroxy-ketones are good substrates in the enantioselective hydrogenation [13]. This is probably due to the solvent and/or to the nature of the catalyst. Preliminary results indicate that **1S** reduces quantitatively the hydroxy-ketone $Ph-CH_2-O-CH_2-CO-CH_2-OH$ to (*R*)-**2a** with an e.e. close to 90% in CH_2Cl_2 [18].

The distinctive features of the substrates investigated under similar reaction conditions seem to surface that each Ru complex should generate equilibrium mixtures of different catalytically active species. It is probable that when the substrate to be reduced is strongly coordinating, like the most studies β-keto-esters of β-diketones, the different Ru catalysts can exert comparable enantioselectivity essentially because of the chelating ability of the substrate [9] [19] [20].

The mass spectrometric observation of the relative stability of the dimeric cage together with the results of the catalytic reductions could indicate that **1S** and **1R** might maintain their dimeric structure during the catalytic cycle, at least in CH_2Cl_2.

Also the presence of a bulky Ph_3CO group greatly contributes to the enantioselectivity of the reaction as is shown comparing the efficient reduction of **4a** and **4b** (87–89% e.e.) to the moderate 27–21% e.e. reduction of **4c**.

The cleavage of the O–CPh_3 bond in the substrates **4a** and **4b** is related both to the presence of catalytic amounts of halogenidric acid, generated by the activation of molecular hydrogen and to the temperature of the reaction. In fact the cationic complex **2S**, heated at 60° for 30 min in the presence of 2 equiv. of substrate under 100 Kgw/cm^2 of H_2, cooled to 25° followed by the addition of 98 equiv. of **4a**, gives the reduction product **3a** in 49% e.e. and only traces of **2a** (*Table 3, Entry 9*).

The products derived from the cleavage of the O–CH_2Ph bond have never been detected; it is worth mentioning that the dimeric catalyst **1S** reduces dibenzyl(β-oxophenethyl)amine to dibenzyl(β-hydroxyphenethyl)amine in 83% e.e. without any detectable debenzylation product.

We wish to express our sincere thanks to *Johnson Matthey* for the generous loan of ruthenium trichloride (to *E. C.*).

Experimental Part

General. (–)-(*S*)- and (+)-(*R*)-2,2′-Bis(diphenylphosphino)-1,1′-binaphthalene, ((–)-(*S*)- and (+)-(*R*)-binap) are commercially available and were purchased from *Fluka AG*. All reactions with air- and moisture-sensitive solvents and reagents were carried out under a positive pressure of dry Ar. Solvents were distilled under dry N_2 and degassed with Ar prior to use. Solvent mixtures for TLC (silica-gel plates, *Merck 5715*) and column flash chromatography (silica gel, *Merck 9385*) are specified by volume-to-volume ratio. HPLC: on a *Chiralcel-OD* column (250 × 4.6 mm I.D.) from *Daicel* using a *Waters 510* pump and a *Pye Unicam Pu 4025 UV* detector (λ = 254 nm), processed on a *Waters 740* data module. ^{1}H-NMR: *Bruker WP80* and *Varian XL200*, in $CDCl_3$, with TMS as an internal standard. ^{31}P-NMR: in $CDCl_3$ with H_3PO_4 as an external standard. MS: on a double focusing, reverse geometry *VG 7070 EQ* instrument; FAB^+ spectra: carried out in different matrices (glycerol, thioglycerol, nitrobenzyl alcohol) using a Xe-atom beam with a translational energy of 8 KeV. The quoted *m/z* were the peaks in the multiplet which arose from the most abundant ruthenium and chlorine isotopes.

1. Synthesis of 1,3-*O*-Disubstituted 1,3-Dihydroxypropan-2-ones 4. – *3-(Benzyloxy)propane-1,2-diol* (**2a**). *3-(Octadecyloxy)propane-1,2-diol* (**2b**), *1-(Benzyloxy)-3-(trityloxy)propan-2-ol* (**3a**), *1-(Octadecyloxy)-3-(trityloxy)propan-2-ol* (**3b**), and *1-(Benzyloxy)-3-(octadecyloxy)propan-2-ol* (**3c**) were prepared from racemic 1,2-*O*-isopropylideneglycerol following literature methods [2]; all compounds had spectroscopic and physical properties in accordance with those reported in the literature.

1-(Benzyloxy)-3-(trityloxy)propan-2-one (**4a**). Pyridinium chlorochromate (4.63 g, 21.5 mmol) and AcONa (0.353 g, 4.3 mmol) were suspended in CH_2Cl_2 (100 ml), and a soln. of **3a** (6.09 g, 14.3 mmol) in CH_2Cl_2 (50 ml) was added in one portion. The mixture was refluxed for 2 h, cooled, filtered through a short pad of *Florisil*, and concentrated. Column flash chromatography on silica gel (toluene/AcOEt 97:3) followed by crystallization from MeOH gave 3.12 g (7.37 mmol; 51.5%) of **4a** as a white solid. ^{1}H-NMR: 7.6–7.1 (*m*, 20 H); 4.5 (*s*, 2 H); 4.3 (*s*, 2 H); 3.9 (*s*, 2 H).

1-(Octadecyloxy)-3-(trityloxy)propan-2-one (**4b**). Pyridinium chlorochromate (1.57 g, 7.28 mmol) and AcOEt (0.118 g, 1.4 mmol) were suspended in CH_2Cl_2 (100 ml), and a soln. of **3b** (2.84 g, 4.84 mmol) in CH_2Cl_2 (50 ml) was added. The mixture was refluxed for 4 h, cooled, filtered through a short pad of *Florisil*, and concentrated. Column flash chromatography on silica gel (toluene/AcOEt 97:3) afforded 1.7 g (2.90 mmol; 60%) of **4b** as a white solid. ^{1}H-NMR: 7.6–7.2 (*m*, 15 H); 4.3 (*s*, 2 H); 3.9 (*s*, 2 H); 3.4 (*t*, 2 H); 1.3 (br. *s*, 32 H); 0.9 (*t*, 3 H).

1-(Benzyloxy)-3-(octadecyloxy)propan-2-one (**4c**). The compound was prepared from **3c** in a similar way to **4b**. Column flash chromatography (toluene/AcOEt 98:2) afforded 2.06 g (4.74 mmol; 65.2%) of **4c** as a white solid. ^{1}H-NMR: 7.35 (*s*, 2 H); 4.6 (*s*, 2 H); 4.25 (*s*, 2 H); 4.2 (*s*, 2 H); 3.45 (*t*, 2 H); 1.3 (br. *s*, 32 H); 0.9 (*t*, 3 H).

2. Synthesis of the Ru^{II} Complexes. – The Ru^{II} complexes were prepared according to literature procedures with minor modifications.

[Ru_2((S)-binap)$_2Cl_4$]NEt_3 (**1S**). $[RuCl_2(COD)]_n$ (0.112 g, 0.402 mmol), (*S*)-binap, (0.298 g, 0.464 mmol) and Et_3N (0.35 ml) were dissolved in 7 ml of toluene and refluxed for 3 h. The soln. was cooled giving a light orange mass; toluene was removed with a syringe and the residue washed with toluene (2 × 5 ml). The solid was dried *in vacuo* and washed with Et_2O (3 × 5 ml). The orange-brown powder was dissolved in CH_2Cl_2 (10 ml), and the soln. was filtered through a frit. Et_2O (40 ml) was stratified over the CH_2Cl_2 soln.; by slow diffusion a red-orange light mass was formed. The solvent was carefully eliminated with a cannula, and the residue was washed twice with Et_2O (2 × 10 ml) and dried *in vacuo* to give 82.3 mg (21%) of **1S**. Anal. calc. for $C_{94}H_{79}Cl_4NP_4Ru_2$ (1690.51): C 66.79, H 4.71, N 0.83; found: C 66.15, H 4.38, N 0.57.

[Ru_2((R)-binap)$_2Cl_4$]NEt_3 (**1R**). The complex was prepared as described for **1S** in 19% yield. Anal. calc. for $C_{94}H_{79}Cl_4NP_4Ru_2$ (1690.51): C 66.79, H 4.71, N 0.83; found: C 64.78, H 4.07, N 0.70.

The complex *[Ru((S)-binap)Cl(C_6H_6)]Cl* (**2S**) and *[Ru((S)-binap)I(p-cymene)]I* (**3S**) were prepared according to [12]; *[Ru((S)-binap)Cl_2]* (**4S**) was prepared from $[RuCl_2(C_6H_6)]_2$ and (*S*)-binap according to [13].

[Ru((S)-binap)Cl_2] (**5S**). Freshly distilled CH_2Cl_2 was saturated with anh. HCl for 5 min; a volume of the solvent was prelevated with a syringe under a positive pressure of Ar, added to 100 ml of H_2O, and titrated with 0.1M NaOH. [Ru((*S*)-binap)$(OCOCH_3)_2$] (50.5 mg, 0.6 mmol), prepared according to [21], was dissolved in 5 ml of CH_2Cl_2, and the proper amount of CH_2Cl_2 saturated with HCl (2 equiv.) was added; the stirred soln. turned from orange to light brown. After 15 min, the soln. was evaporated to dryness, diluted with CH_2Cl_2 (5 ml), and evaporated. The dilution and evaporation were repeated three times; finally the brown precipitate was left under vacuum overnight.

Catalytic Reduction. – *General Procedure.* A weighed amount of catalyst was dissolved in a known amount of CH_2Cl_2 in a *Schlenk* tube under Ar; in another *Schlenk* tube more than 1 mmol of the substrate was dissolved in 5 ml of CH_2Cl_2 under Ar. With a syringe, 1.1 mmol of the substrate and 0.011 mmol of the catalyst were transferred into a third *Schlenk* tube, CH_2Cl_2 was added to obtain 11 ml of soln., which was stirred for 30 min under Ar. A stainless steel autoclave was pressurized to 100 Kgw/cm^2 and vented five times; 10 ml of the substrate/catalyst soln. were introduced into the autoclave with a syringe through a serum cap; the autoclave was pressurized to 100 Kgw/cm^2 and heated in a thermoregulated oil bath. After the reaction, the autoclave was carefully vented, the resulting orange-yellow soln. was concentrated on a rotatory evaporator, and the oily residue was separated by column flash chromatography. The workup conditions were as follows; reduction of **4a** to **3a** and **2a**: silica gel, toluene/AcOEt 9:1; reduction of **4b** to **3b** and **2b**: silica gel, toluene/AcOEt 9.5:0.5; reduction of **4c** to **3c**: silica gel, toluene/AcOEt 9:1.

The enantiomeric composition was determined by HPLC on a chiral stationary phase under the following conditions: **3a**: hexane/EtOH/H_2O 90.63:9.06:0.3, flow rate 0.2 ml/min; **2a**: hexane/i-PrOH 90:10, flow rate 1 ml/min; **3b** and **3c**: hexane/i-PrOH 99.4:0.6, flow rate 1 ml/min. The enantiomeric composition of **2b** was determined by comparing the optical rotation value with that reported in [2].

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