ASYMMETRIC SYNTHESIS BY CHIRAL RUTHENIUM COMPLEXES

VI [*]. ENANTIOMER-DISCRIMINATION IN THE HYDROGEN TRANSFER FROM RACEMIC ALCOHOLS TO PROCHIRAL KETONES IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$

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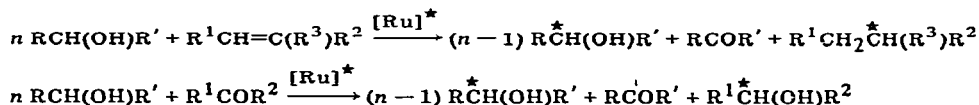*Istituto di Chimica Organica dell'Università di Firenze, via Gino Capponi, 9, 50121 Firenze (Italy)*

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Summary

Hydrogen transfer from racemic alcohols to prochiral ketones in the presence of $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$ has been examined. The enantiomer-discrimination is influenced by the structure of the reactants, temperature and the excess of phosphine present.

Introduction

Hydrogen transfer carried out in the presence of a chiral catalyst offers the possibility of obtaining two optically active products at the same time. If the hydrogen acceptor is a prochiral compound and the hydrogen donor a racemic species, the possibility exists of carrying out an enantioface-discriminating hydrogenation together with an enantiomer-discriminating dehydrogenation (Scheme 1). A few examples of such combined processes, have appeared in the literature, and all involve ruthenium catalysis [1—8].

$$n \ RCH(OH)R' + R^1CH=C(R^3)R^2 \xrightarrow{[Ru]^*} (n-1) \ R\overset{*}{C}H(OH)R' + RCOR' + R^1CH_2\overset{*}{C}H(R^3)R^2$$

$$n \ RCH(OH)R' + R^1COR^2 \xrightarrow{[Ru]^*} (n-1) \ R\overset{*}{C}H(OH)R' + RCOR' + R^1\overset{*}{C}H(OH)R^2$$

[*] : chiral carbon atom in optically active compounds
$[Ru]^*$: catalytic complex containing optically active ligand

SCHEME 1

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[*] For part V see ref. 12.

We report now the results of an investigation of the possibility of using the reversible hydrogen transfer between racemic alcohols and prochiral ketones in the presence of a chiral catalyst as a synthetic tool and aiming at the same time to gain useful information on the mechanism of the hydrogen transfer itself. $H_4Ru_4(CO)_8[(-)-DIOP]_2$, previously shown to catalyze several asymmetric reactions [1,8—14], was used as the catalytic precursor.

Results and discussion

In Table 1 we show the results of experiments in which the enantiomer-discriminating dehydrogenation * of $(R)(S)$-pentan-2-ol or $(R)(S)$-1-phenyl-ethanol was examined in the presence of various hydrogen acceptors at 120°C using an initial alcohol/ketone molar ratio of two. The values of the enantioface-discrimination are also given.

With pentan-2-ol the enantiomeric-discrimination is 0 in the presence of 3-methylbutan-2-one and 1.6% in the presence of acetophenone. The pre-dominant configuration of the residual alcohol is (S). For each test the enan-tiomer-discrimination was lower than the enantioface-discrimination, which reached 8.4% in the case of 1-phenyl-3-methylbutan-1-one. It will be seen that 3-methylbutan-2-one does not induce enantiomer-discrimination in the dehydro-genation of (R,S)-pentan-2-ol while it does so when 1-phenylethanol is the hydrogen donor (Table 1).

The behaviour of alcohols with a same acceptor is shown in Table 2. When acetophenone is the acceptor the enantiomer-discrimination for a series of methyl alkyl carbinols increases with increasing length of the alkyl group; thus it is 0 for butan-2-ol and 2.5% for octan-2-ol. The configuration of the residual alcohol is (S) in the case of pentan-2-ol and (R) in the case of octan-2-ol. The enantioface-discrimination increases as the molecular weight of the donor increases.

The effect of temperature on the enantiomer-discrimination was examined using the (R,S)-1-phenylethanol/1-phenyl-3-methylbutan-1-one system in the range 100—140°C (Table 3). Increase of temperature from 100 to 120°C lowers the enantiomer-discrimination from 6.8 to 1.1%; a further increase to 140°C does not cause much change in the discrimination, but the configuration of the predominantly dehydrogenated enantiomer is opposite to that of the predom-inantly dehydrogenated enantiomer at lower temperatures. The enantioface-discrimination falls from 13.9 (T 100°C) to 4.3% (T 140°C), the predominant enantiomer being always (S).

At 140°C a clear dehydrogenation of the alcohol also occurs, with formation of free hydrogen (5%). Such dehydrogenation could, in principle, be stereo-selective [3,17—21] and therefore could also be responsible of the observed change of the enantiomeric excess of the remaining donor substrate as the tem-perature is increased. Experiments at 120°C with 1-phenylethanol in the absence of an acceptor, however, showed that the residual alcohol is not

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* The enantiomer-discrimination is given by the ratio between the observed optical purity of the residual alcohol and the maximum optical purity obtainable for complete discrimination at the same conversion.

TABLE 1

ENANTIOMER-DISCRIMINATION IN THE HYDROGEN TRANSFER FROM RACEMIC ALCOHOLS TO PROCHIRAL KETONES IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$ (T 120°C; $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$ 50 mg; mol H donor/mol H acceptor = 0.5; reaction mixture 30 ml)

H donor	H acceptor	Reaction time (h)	Conv. (%)	Residual H donor $\alpha^{20}_{D(l=1)}$ (neat) (°)	O.P.[b,e] (%)	Conf.[f]	Discrimination (%)	Alcohol formed[a] O.P.[e] (%)	Conf.[f]
CH₃CH(OH)CH₂CH₂CH₃	CH₃CO(CH₂)₃CH₃	88	13.3	+0.014	0.13	(S)	0.85	1.2	(R)
	CH₃COCH(CH₃)₂	288	14.2	0.000	0.0	—	0.0	0.7	(R)
	CH₃COC₆H₅	142	15.9	+0.048	0.3	(S)	1.6	2.8	(S)
	C₆H₅COCH₂CH(CH₃)₂	159	14.4	+0.026	0.2	(S)	1.2	8.4[d]	(S)
C₆H₅CH(OH)CH₃	CH₃COCH(CH₃)₂	308	22.0	+0.124[c]	0.29	(R)	1.0	0.2[d]	(R)
	C₆H₅COCH₂CH(CH₃)₂	233	18.3	+0.108[c]	0.25	(R)	1.1	6.8	(S)

[a] Data from ref. 12. [b] $[\alpha]^T_{Dmax}$ from ref. 12. [c] Measured at 25°. [d] $\alpha^{25}_{D(l=1)}$ −0.009°. [e] O.P. = optical purity. [f] Conf. = configuration.

TABLE 2

ENANTIOMER-DISCRIMINATION IN THE HYDROGEN TRANSFER FROM ALCOHOLS TO ACETOPHENONE IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$ (T 120°C; $H_4Ru_4(CO)_8[(-)$-DIOP$]_2$ 50 mg; mol H donor/mol H acceptor = 0.5; reaction mixture 30 ml)

H donor	Reaction time (h)	Conv. (%)	Residual H donor $\alpha^{20}_{D(l=1)}$ (neat) (°)	O.P.[b,f] (%)	Conf.[g]	Discrimination (%)	1-Phenylethanol[a] O.P.[f] (%)	Conf.[g]
CH₃CH(OH)CH₂CH₃	116	13.8	0.000	0.0	—	0.0	1.5	(S)
CH₃CH(OH)CH₂CH₂CH₃	142	15.9	+0.048	0.3	(S)	1.6	2.8	(S)
CH₃CH(OH)(CH₂)₅CH₃	94	24.4	−0.096[c]	0.8[d]	(R)[c]	2.5	3.1	(S)

[a] Data from ref. 12. [b] $[\alpha]^T_{Dmax}$ from ref. 12. [c] Measured at 18°C. [d] $[\alpha]^{18}_{Dmax}$ +11.76 [15]. [e] Ref. 16. [f] O.P. = optical purity. [g] Conf. = configuration.

TABLE 3

ENANTIOMER-DISCRIMINATION IN THE HYDROGEN TRANSFER FROM 1-PHENYLETHANOL TO 1-PHENYL-3-METHYLBUTAN-1-ONE IN THE PRESENCE OF H$_4$Ru$_4$(CO)$_8$[(—)-DIOP]$_2$ (H$_4$Ru$_4$(CO)$_8$[(—)-DIOP]$_2$ 50 mg; mol H donor/mol H acceptor = 0,5; reaction mixture 30 ml)

T (°C)	Reaction time (h)	Conv. (%)	Residual 1-phenylethanol			Discrimination (%)	1-Phenyl-3-methylbutan-1-ol		
			$\alpha_D^{25}(l=1)$ (neat) (°)	O.P. a,f (%)	Conf. g		$\alpha_D^{26}(l=1)$ (°)	O.P. a,f (%)	Conf. g
100	592	15.9	+0,594	1,34	(R)	6,8	−0,758 b	13,9	(S)
120	233	18.3	+0,108	0,26	(R)	1,1	−0,369 c	6,8	(S)
140	65	27,3 d	−0,164	0,37	(S)	1,3	−0,230 e	4,3	(S)

a [α]$^T_{Dmax}$ from ref. 12, b Measured in solution (c 16,92, n-heptane), c Measured in solution (c 16,82, n-heptane), d 4,9% Dehydrogenation, e Measured in solution (c 16,73, n-heptane), f O.P. = optical purity, g Conf. = configuration.

TABLE 4

REDUCTION OF ACETOPHENONE BY HYDROGEN TRANSFER FROM PROPAN-2-OL (H_4Ru_4-$(CO)_8[(—)-DIOP]_2$ 200 mg: mol acetophenone/mol propan-2-ol = 0.5; T 120°C; reaction mixture 120 ml)

Reaction time (h)	Yield (%)	Reaction product: 1-phenylethanol		
		α_D^{25} (l=1) (neat) (°)	O.P. [a] (%)	Conf. [b]
51	13.4	—1.953	4.4	(S)
111	34.9	—1.906	4.3	(S)
350	44.0	—1.054	2.5	(S)
580	60.0	n.d. [c]	n.d.	n.d.
730	60.0	—0.200	0.5	(S)

[a] O.P. = optical purity. [b] Conf. = configuration. [c] n.d. = not determined.

optically active (2.8% dehydrogenation after 112 h). Experiments with pentan-2-ol gave similar results (1.5% dehydrogenation after 38 h).

The enantiomer-discrimination was usually lower than the enantioface-discrimination, which itself occurs only to a rather limited extent. The low optical yields obtained with this catalytic system may be attributed not only to its poor selectivity at relatively high reaction temperatures but also to racemization of the alcohols in the reaction mixture.

The temperature effect may reasonably be ascribed to the predominance of different intermediates at different temperatures. Thus (—)-(R)-1-phenylethanol (optical purity 2.24%) heated at 120°C for 235 h in the presence of H_4Ru_4-$(CO)_8[(—)-DIOP]_2$ undergoes an 18.3% racemization, and acetophenone and hydrogen are formed (4.4%) at the same time. In the absence of the catalyst under the same conditions neither racemization nor dehydrogenation of the substrate occurs. Racemization of optically active alcohols occurs also under transfer conditions, as shown by the results of experiments carried out with the acetophenone/propan-2-ol system and interrupted after various times (Table 4). The optical purity of 1-phenylethanol falls from 4.3 after 5 h to 0.5% after 730 h.

The low optical yields and the long reaction times required do not make this reaction an attractive synthetic process.

The small but definite influence of the structure of the acceptor on the enantiomer-discrimination of the donor and, conversely, the influence of the structure of the donor on the enantioface-discrimination of the acceptor suggest that in this reaction, as in other transfer reactions [4,7,22], both acceptor and donor are present in the catalytically active intermediate.

Experimental section

Hydrogen transfer experiments, separation, characterization of products and determinations of properties were made as previously described [12]. Reagents were commercial products except for 1-phenyl-3-methylbutan-1-one and (—)-(R)-1-phenylethanol which were prepared as previously described [12].

Racemization of (—)-(R)-1-phenylethanol

(—)-(R)-1-phenylethanol (3 ml), $[\alpha]_D^{25}$ —0.978, optical purity 2.24%, and $H_4Ru_4(CO)_8[(—)\text{-}DIOP]_2$ (10 mg) were heated together under nitrogen at 120°C for 235 h in an autoclave. The gases were analyzed by GLC, which showed the presence of hydrogen (2 mt Porapak Q, 20°C, thermal conductivity detector). The liquid phase contained 1-phenylethanol and acetophenone in the ratio 95.6/4.4. The 1-phenylethanol, recovered by preparative GLC, had $[\alpha]_D^{25}$ —0.799, optical purity 1.83%, racemization 18.3%.

Dehydrogenation of racemic alcohols

(a) (R)(S)-1-Phenylethanol (10 ml) and $H_4Ru_4(CO)_8[(—)\text{-}DIOP]_2$ (50 mg) were heated together for 112 h at 120°C under nitrogen in an autoclave. GLC showed that hydrogen was present in the gas phase, and that in the liquid phase 1-phenylethanol and acetophenone were present in the ratio 97.2/2.8. The recovered 1-phenylethanol had α_D^{25} 0.000°.

(b) (R)(S)-Pentan-2-ol (10 ml) and $H_4Ru_4(CO)_8[(—)\text{-}DIOP]_2$ (50 mg) were heated together for 38 h at 120°C giving hydrogen and pentan-2-one (1.5%). The residual alcohol had α_D^{25} 0.000°.

Acknowledgements

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