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$RuCl_2$[*S*-BINAP]-catalyzed synthesis of aldehydes and ketones by dehydrogenation of alcohols

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Abstract

$RuCl_2$[*S*-BINAP] catalyzed dehydrogenation of alcohols into aldehydes or ketones has been investigated. Among many H-acceptors screened, diphenylacetylene (tolane) was the most suitable judged from its smooth reduction. Electron rich and deficient analogues of tolane have been synthesized. Based on competition experiments between these H-acceptors a tentative catalytic cycle for the $RuCl_2$[*S*-BINAP] catalyzed dehydrogenations is proposed.

Keywords: Dichloro[(*S*)-(-)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]ruthenium(II) catalyst; Catalytic dehydrogenations; Alcohols; Ligands; Hydride acceptors

1. Introduction

In the field of aldehyde and ketone synthesis, a problem of continuing interest is the development of a general, highly efficient method for the conversion of alcohols into aldehydes or ketones under mild reaction conditions without producing waste. Several effective ruthenium catalysts for dehydrogenations have been described previously, ranging in formal oxidation state from +8 to 0. For oxidation of primary alcohols the atom economical perruthenate-catalyzed reaction with oxygen is of prime importance [1a,1b]. Also dichlororutheniumtristriphenylphosphine-mediated processes with the aid of *meta*-iodosobenzoic acid [2a], oxygen-hydroquinone [2b] or TEMPO [2c] and ruthenium(0) on alumina with molecular oxygen as oxidant [3] are selective and high yielding. For the less-demanding oxidation of secondary alcohols tetra-isopropyl-ammoniumperruthenate [4], rutheniumdioxide [5], ruthenium dichloride [6a,6b] and ruthenium on alumina [7a] or with ceriumdioxide [7b,7c] have been applied. Recently, we described the dihydroruthenium-carbonylbistriphenylphosphine-trifluoroacetic acid-mediated dehydrogenation to ketones in the absence of hydrogen acceptor [8].

During exploration of these reactions an unprecedented [9] dichloro[(*S*)-(-)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]ruthenium(II) or $RuCl_2$[*S*-BINAP] catalyzed dehydrogenation of alcohols was discovered. With $RuCl_2$[*S*-BINAP], an active catalyst, the dehydrogenation of primary and secondary alcohols into aldehydes and ketones can be performed upon treatment with only 2 molar equiv of tolane in *p*-xylene as solvent at 130 °C, giving aldehydes or ketones in high yield and selectivity. As an example, the dehydrogenation of 1-octanol is depicted in Fig. 1.

It is noteworthy that the $RuCl_2$[*S*-BINAP] catalyzed dehydrogenations do not need additional ligand to suppress consecutive reactions such as ester formation as was previously shown with the $Ru_3(CO)_{12}/PPh_3$ catalytic system [10].[1]

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[1] In a previous paper $Ru_3(CO)_{12}$ is described as a different catalyst in similar dehydrogenations of alcohols. Differences between both catalysts can best be defined as a slight excess of PPh_3 in ligand with respect to Ru(0) for the less stable $Ru_3(CO)_{12}$ giving a faster dehydrogenation for secondary than primary alcohols, while $RuCl_2$[*S*-BINAP] gives a more stable Ru(II) complex and is stoichiometric in ligand showing a reverse dehydrogenation rate for primary and secondary alcohols.

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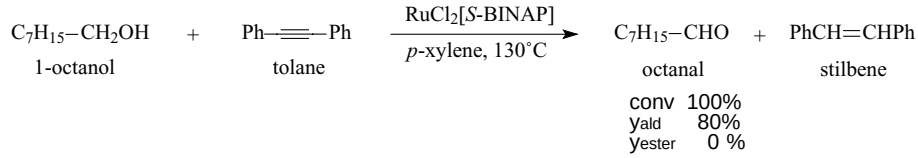


Fig. 1. Irreversible hydrogen transfer from alcohols to tolane, exemplified for 1-octanol.

In general, it can be stated that low valent ruthenium species are excellent catalysts for hydrogen transfer reactions because of their low redox potentials and high affinity towards heteroatoms [11]. Although ruthenium complexes can promote hydrogen transfer from hydrocarbons [12], aldehydes [13], amines [14] and cyclic ethers [15], hydrogen donors are frequently alcohols [12,16–27].[2]

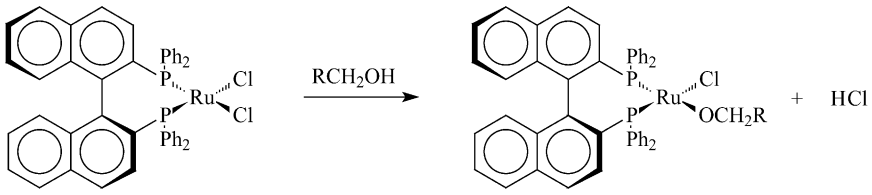
2. Results and discussion

The $RuCl_2$[*S*-BINAP] complex was tested as a catalyst for dehydrogenation of various primary alcohols as substrates. The results collected in Table 1 reveal catalytic activity in dehydrogenation.

1-Octanol (entry 1) is dehydrogenated nearly quantitatively within 2 h. When longer aliphatic alcohols like 1-decanol (entry 2) and 1-dodecanol (entry 3) were dehydrogenated, the reaction rate decreases. Selectivity, however, remains constant at about 80%. In the dehydrogenation of L-citronellol (entry 4), the double bond is not hydrogenated. Hydrogen transfer seems to be negligible to the isolated double bond. All alcohols containing terminal vinyl or ethynyl groups, like in entry 5, yielded a lot of by-products and were for this reason not further investigated. Alcohols containing non-terminal ethynyl groups like 9-hexadecyn-1-ol (entry 6) always showed a decrease in selectivity due to the partial hydrogenation of the triple bond. Moreover in this case, the hydride can be transferred in an intra- or intermolecular fashion to the triple bond of 9-hexadecyn-1-ol or to the actual H-acceptor tolane. Dehydrogenation of more sterically hindered and electronically different primary aliphatic 2-ethyl-1-hexanol (entry 7), cyclohexylmethanol (entry 8) and 2-phenylethanol (entry 9) was sluggish presumably due to difficulties to expose the primary hydroxyl group to the catalytically active center.

Catalytic dehydrogenation of various primary allylic and benzylic alcohols, see Table 2, indicate that the formation of conjugated systems during dehydrogenation increased selectivity.

(*E*,*Z*)-3,7-Dimethyl-2,6-octadien-1-ol (geraniol) could be dehydrogenated into the corresponding aldehyde without hydrogenation of the double bonds in a selectivity of 81% (entry 1), similar to L-citronellol. However, when 3-phenyl-2-propen-1-ol (cinnamyl alcohol) (entry 2) was used, the observed selectivity increased to 100%. Selectivities higher than 90% were observed for benzyl alcohol (entry 3) and *p*-methoxybenzyl alcohol (entry 4). Apparently, the dehydrogenation of primary aliphatic alcohols is accompanied by loss of about 20% in contrast to that of benzylic and allylic alcohols where no product loss was observed. To solve this problem of an incomplete mass balance, the dehydrogenation of 1-octanol was studied in more detail. First it was observed that the reaction is disturbed by opening the reaction tube for sampling. The disturbance is either due to loss of hydrogen chloride that is present as a gas in the reaction tube and/or to the sensitivity of the catalyst towards oxygen. Formation of hydrogen chloride can be expected as a result of the reaction of the alcohol with the ruthenium catalyst to form a ruthenium alkoxide species, see Eq. (1) [23]:

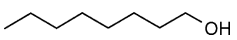
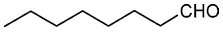
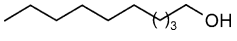
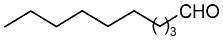
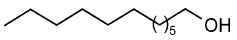
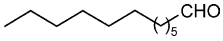
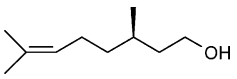
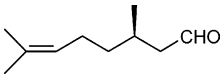
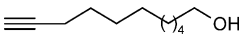
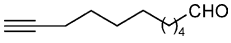
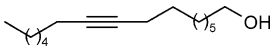
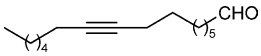
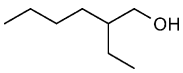
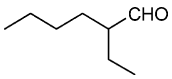
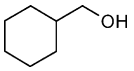
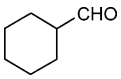
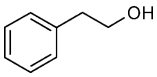
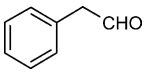


(1)

Furthermore, to examine the influence of the catalyst on the extent of mass balance incompleteness, experiments with different amounts of catalyst were performed. More incompleteness occurs when a larger amount of catalyst is used. All reaction mixtures were distilled (130 °C, 10^{-1} Torr), ^{1}H- and ^{13}C-NMR spectra of the residues did not show ruthenium alkoxide species. However, IR-spectrometry revealed a strong absorption peak at 1960 cm^{-1} for all residues. Since metal carbonyl complexes [28] and metal hydrides

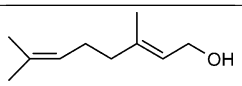
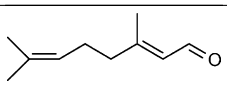
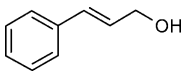
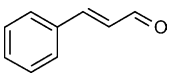
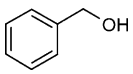
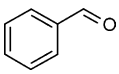
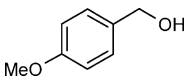
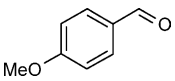
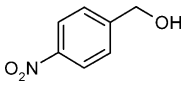
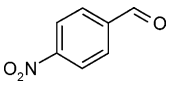
[2] The possible intermediacy of a dihydridoruthenium species in basic conditions was kindly suggested by a reviewer. *Additional comment*: the intermediacy of a RuHCl species has been adopted in the catalytic cycle, see Fig. 4.

Table 1
$RuCl_2$[*S*-BINAP] catalyzed dehydrogenation of a series of primary alcohols at 130 °C in *p*-xylene with tolane as hydrogen acceptor[a,b]

Entry	Substrate	Product	Time (h)	Conv. (%)	S_{ald} (%)	Y_{ald} (%)
1			2	100	81	81
2			4	92	80	74
3			5	85	80	68
4			2	94	73	68
5			4	100	40	40
6			2	100	97[c]	97
7			5	85	84	71
8			2	79	87	69
9			2	60	53	32

[a] See Section 9 for the recipe; Y_{ald} = conv. × selectivity (S_{ald}) as measured by GC.
[b] All experiments were performed in *p*-xylene as a solvent at 130 °C in the presence of 2 molar equiv of tolane as H-acceptor and 5 mol% $RuCl_2$[*S*-BINAP] as catalyst.
[c] After 5 h the selectivity in the aldehyde had decreased to 82%.

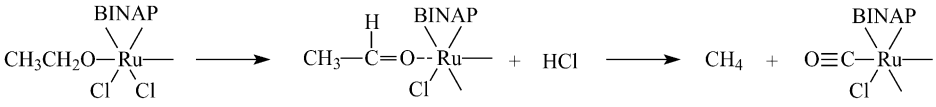
Table 2
$RuCl_2$[*S*-BINAP] catalyzed dehydrogenations of primary allylic and benzylic alcohols at 130 °C in *p*-xylene with tolane as hydrogen acceptor[a,b]

Entry	Substrate	Product	Time (h)	Conv. (%)	S_{ald} (%)	Y_{ald} (%)
1			2	100	81	81
2			2	100	100	100
3			4	100	92	92
4			4	100	99	99
5			4	98	58[c]	56

[a] All experiments were performed in *p*-xylene as solvent at 130 °C in the presence of 2 molar equiv of tolane as H-acceptor and 5 mol% $RuCl_2$[*S*-BINAP].
[b] Y_{ald} = conv. × selectivity (S_{ald}) as measured by GC.
[c] Due to the low solubility of *p*-nitrobenzyl alcohol in *p*-xylene the conversion and yield data are not accurate.

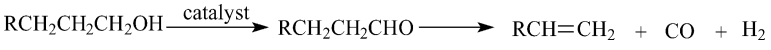
[13,29] feature absorptions in this region, an experiment was performed using a longer chain primary aliphatic alcohol than 1-octanol thus preventing evaporation of the lower molecular weight by-products. When 1-dodecanol was used undecene (6%) could be identified as a by-product. This observation would imply that dehydroformylation is an important consecutive reaction during the catalytic dehydrogenation of primary aliphatic alcohols. Indeed, Chatt et al. [30] have reported that decarbonylation of an alcohol occurs in the presence of ruthenium chloride

triphosphine complexes to form a ruthenium carbonyl complex and a degraded fragment of the alcohol, e.g. methane from ethanol, see Eq. (2). Likewise, Crabtree and coworkers [31] recently reported the decarbonylation of aldehydes catalyzed by rhodium complexes with tridentate phosphine ligands:



(2)

Thus the dehydrogenation of alcohols with $RuCl_2$[*S*-BINAP] gave dehydroformylation of an aldehyde into an unsaturated aliphatic compound together with a ruthenium carbonyl species. The dehydroformylation can schematically be presented as depicted in Eq. (3):



(3)

The difference in selectivity between allylic and benzylic primary alcohols (100%) and other primary aliphatic alcohols (80%) can be ascribed to the reluctance of conjugated aldehydes to undergo dehydroformylation (see Tables 1 and 2).

Subsequently, several secondary alcohols were tested. Although selectivities are high as is demonstrated in Table 3, the reactions are quite slow.

When a secondary benzylic alcohol like 1-phenylethanol (entry 3) was used as a substrate, the reactivity increased compared to aliphatic alcohols like 2-decanol and 4-*t*-butylcyclohexanol (entries 1 and 2). This increase in reactivity can be attributed to stabilization of the product by conjugation with the phenyl group. Oxidation of 6-phenyl-5-hexyn-3-ol (entry 4) led to the formation of several products that could be identified with GC/MS: 6-phenyl-5-hexyn-3-one (25%), 6-phenyl-5-hexen-3-ol (16%) and 6-phenyl-5-hexen-3-one (39%). Formation of the latter two implies that intra- and/or intermolecular hydrogen transfer occurs.

The Δ5(6)-(3-hydroxy)-steroids cholesterol (entries 5-7) and *trans*-dehydroandrosterone (entry 8) could be dehydrogenated in high yield. Unfortunately, migration of the double bond from the Δ5(6) to the Δ4 position occurred in both steroids investigated. The low reactivity of *trans*-dehydroandrosterone (entry 8) as compared to cholesterol (entry 5) is remarkable. An explanation for the low reactivity of *trans*-dehydroandrosterone may be an interaction of the carbonyl functionality associated with carbon atom number 17 with the catalyst. Such an interaction may have a retarding effect on the dehydrogenation as a result of a smaller fraction of the active species in the catalytic cycle. 4-Cholestene-3-one could be isolated from the reaction mixture in 65% yield (entry 5) by flash chromatography on silica–gel with a mixture of dichloromethane/diethyl ether as eluent in a purity of about 98%, judged from ^{1}H- and ^{13}C-NMR data.

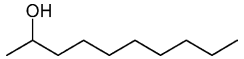
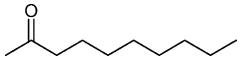
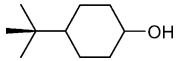
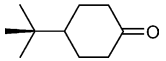
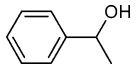
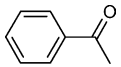
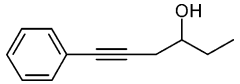
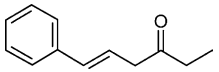
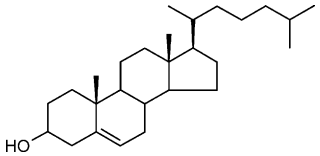
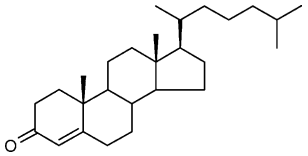
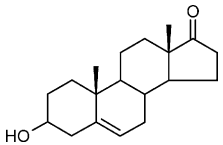
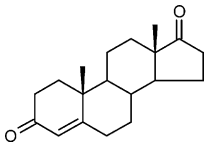
Although Bäckvall and coworkers [32] reported the selective dehydrogenation of cholesterol into 4-cholestene-3-one with acetone as solvent and hydrogen acceptor using a ruthenium dimer as catalyst, the $RuCl_2$[*S*-BINAP] complex showed little activity (entry 6). When cyclohexanone was used as solvent and hydrogen acceptor, aldol condensation products of cyclohexanone could be identified with GC/MS (entry 7).

The difference in reaction rate between primary and secondary alcohols is quite remarkable. The turnover frequencies for the $RuCl_2$[*S*-BINAP] catalyzed dehydrogenations are typically 4–10 h^{-1} for primary alcohols while secondary alcohols are generally oxidized with a rate of 0.1–1 h^{-1}. When compared to the $Ru_3(CO)_{12}/PPh_3$ catalytic system, previously reported by us [10], the $RuCl_2$[*S*-BINAP] catalyzed dehydrogenations of primary and secondary alcohols show opposed reactivity. This observation can be rationalized in terms of differences in steric crowding to be overcome in the catalytic cycle.

Furthermore, the $RuCl_2$[*S*-BINAP] complex was tested as a dehydrogenation catalyst of two diols. As indicated in Table 4, decane-1,10-diol could be dehydrogenated to the dialdehyde in high yield (entry 1) and only 15% 10-hydroxy-decanal could be identified. However, special chemoselectivity was observed compared to the former results in the dehydrogenation of 1,2-octanediol (entry 2). In this reaction formally not the primary but the secondary hydroxyl group was dehydrogenated selectively. The α-hydroxy-ketone, 1-hydroxy-2-octanone, could be characterized in the reaction mixture by GC/MS, IR, ^{1}H- and ^{13}C-NMR. However, the observed chemoselectivity could arise from initial dehydrogenation of the primary alcohol to the aldehyde followed by consecutive enolization and enol-keto tautomerization to the thermodynamically more stable ketone.

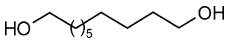
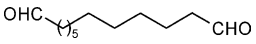
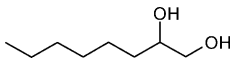
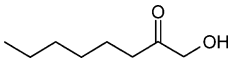
One could question the use of a complex chiral catalyst like $RuCl_2$[*S*-BINAP] in our work. One of the reasons not to use the racemic catalyst is that it is more expensive. In addition, it is known that homogeneous ruthenium catalysts bearing chiral phosphine ligands are extremely useful in enantioselective hydrogenation processes [9]. The best known examples of homogeneously catalyzed enantioselective dehydrogenation processes are displayed by rhodium(I)- and ruthenium(II)-BINAP complexes developed by Noyori et al. (For synthesis of these complexes [37a], for an example of the first efficient dehydrogenation process via hydrogen transfer (using other ligands) [37b].). In our work the chiral $RuCl_2$[*S*-BINAP] catalyst

Table 3
$RuCl_2$[*S*-BINAP] catalyzed dehydrogenations of a variety of secondary alcohols at 130 °C in *p*-xylene with tolane as hydrogen acceptor[a,b]

Entry	Substrate	Product	Time (h)	Conv. (%)	S_{ket} (%)	Y_{ket} (%)
1			24	34	85	29
2			24	47	87	41
3			5	30	70	21
4			24	79	50	39
5			48	100	97	97
6			16	14	50[c]	7
7			72	30	77[d]	23
8			170	87	96	83

[a] Again experiments were performed in *p*-xylene as a solvent at 130 °C in the presence of 2 molar equiv of tolane and 5 mol% $RuCl_2$[*S*-BINAP]. Y_{ket} are not isolated yields.
[b] Y_{ket} = conv. × selectivity (S_{ket}) as measured by GC.
[c] The reaction was performed without tolane in 10 ml of refluxing acetone as solvent and hydrogen acceptor.
[d] The reaction was performed without tolane in 10 ml of refluxing cyclohexanone as solvent and hydrogen acceptor.

Table 4
$RuCl_2$[*S*-BINAP] catalyzed dehydrogenations of various diols at 130 °C in *p*-xylene with tolane as hydrogen acceptor[a,b]

Entry	Substrate	Product	Time (h)	Conv. (%)	S_{ald} (%)	Y_{ald} (%)
1			2	100	67	67
2			2	83	84	70

[a] Both experiments were performed in *p*-xylene as a solvent at 130 °C in the presence of 3 molar equiv of tolane as H-acceptor and 5 mol% $RuCl_2$[*S*-BINAP].
[b] $Y_{ald/ket}$ = conv. × selectivity ($S_{ald/ket}$) as measured by GC.

was investigated for the enantioselective dehydrogenation of racemic 1-phenylethanol and 1-phenyl-2-propanol. Both reactions were performed in *p*-xylene as a solvent at 130 °C in the presence of 2 molar equiv tolane and 5 mol% $RuCl_2$[*S*-BINAP]. Furthermore, a small amount of K_2CO_3 was added to accelerate the reaction. After 2 h both reactions had reached 50% conversion and were then stopped. Disappointingly, no chiral enrichment of one of the stereoisomers of 1-phenylethanol and 1-phenyl-2-propanol was observed.

3. Effect of solvent

An elaborate screening of the influence of the solvent on the catalytic dehydrogenation has been performed. In the experiments always 1-octanol, 2 molar equiv of tolane as H-acceptor and 5 mol% $RuCl_2$[*S*-BINAP] as catalyst have been used. Performing the reaction in solvents like *p*-xylene, toluene, decaline and chlorobenzene results in moderate to good selectivities and yields. However, small amounts of ester are produced. Polar aprotic solvents like NMP, DMF and DMA tend to inhibit the reaction. Polar protic solvents like phenol also inhibit the reaction. The best results are obtained in *p*-xylene and toluene. The lower yield and conversion using toluene compared to *p*-xylene can entirely be ascribed to the lower reaction temperature that causes a decrease in reaction rate.

4. Effect of base

In order to investigate the influence of base on the catalytic dehydrogenation of 1-octanol several experiments were executed in *p*-xylene at 130 °C in the presence of 2 molar equiv of tolane as H-acceptor and 5 mol% $RuCl_2$[*S*-BINAP]. When bases like potassium carbonate (K_2CO_3) or potassium acetate (KOAc) as HCl acceptors are added, reaction rates increase. However, selectivity decreases concomitantly leading to considerable ester formation. Presumably double introduction of alkoxy substituents onto the ruthenium center occurs which in an intramolecular process may lead to the formation of ester and concomitantly of a dihydridoruthenium species (see footnote 2).

The accelerating effect of K_2CO_3 was also examined with secondary alcohols as substrates. The presence of K_2CO_3 increases the reaction rate drastically while selectivities remain excellent. As stated before, secondary alcohols are generally dehydrogenated at a turnover frequency of 0.1–1 h^{-1} without addition of a base. Adding 10 mol% of K_2CO_3 relative to the substrate enhanced turnover frequencies to 1–5 h^{-1}, implying an accelerating effect of the base in the order of 10.

5. Screening of H-acceptors

Since tolane is a relatively expensive hydrogen acceptor, other hydrogen acceptors were investigated in the catalytic dehydrogenation of 1-octanol into octanal. In addition, the

Table 5
$RuCl_2$[*S*-BINAP] catalyzed dehydrogenation of 1-octanol into octanal at 130 °C in *p*-xylene (influence of the type and amount of H-acceptor)[a]

Entry	H-acceptor	Acceptor/ substrate ratio	Time (h)	Conv. (%)	S_{ald} (%)	Y_{ald} (%)	Y_{est} (%)
1	1-Phenylpropyne	2	2	70	84	59	–
2	Dehydrolinalool	2	2	69	83	57	–
3	Nitrobenzene	2	2	34	<3	<1	–
4	*m*-Dinitrobenzene	1	2	41	<2	<1	–
5	Tolane	1	2, 7	78, 95	65, 47	51, 45	8, 17
6	Tolane	2	2, 8	100, 100	81, 70	81, 70	<1, 6
7	Tolane	3	2	88	52	46	<1

[a] Y_{ald} = conv. × selectivity (S_{ald}) as measured by GC.

influence of the amount of tolane was studied. The results in Table 5 indicate that alkynes like 1-phenylpropyne or dehydrolinalool are superior to nitro compounds such as nitrobenzene and *m*-dinitrobenzene. At around 2 molar equiv of tolane relative to the alcohol substrate an optimum appeared to be present. When the amount of tolane is reduced the reaction rate decreases and ester formation becomes favorable. This might rely on the presence of vacant coordination sites allowing for ester formation when relatively few acceptor molecules are present. However, increasing the amount of tolane above 2 molar equiv also decreases the reaction rate, presumably due to the occupation of all vacant coordination sites by the acceptor. In conclusion, a delicate balance in acceptor usage exists to obtain optimal yields of aldehyde. Furthermore, selectivity decreases with time probably due to conversion of the aldehyde into the ester in the presence of the ruthenium catalyst.

In order to obtain information about the catalytic cycle substituted analogues of tolane have been synthesized. In the catalytic cycle the H-acceptor has to coordinate to the metal center first. After coordination hydride is transferred from the metal center to the H-acceptor. Electron rich H-acceptors coordinate well to the metal center but are poor hydride acceptors.

The opposite is true for electron deficient H-acceptors. These compounds would take up the hydride easily but would not coordinate very well. For this reason, the MeO (electron rich) and CF_3 (electron deficient) substituted analogues of tolane have been synthesized (Fig. 2) [33].

Both substituted analogues could be isolated in 80% yield and were studied in the dehydrogenation of 1-octanol. The results of the experiments with different H-acceptors are depicted in Table 6.

The results in Table 6 demonstrate that tolane was more efficient than the electron rich 4-MeO-tolane and the electron deficient 4-CF_3-tolane. The performance of 4-CF_3-tolane as H-acceptor was less than that of 4-MeO-tolane. Both tolane and 4-MeO-tolane coordinate better to the metal center than 4-CF_3-tolane does. Due to the less favored complexation of 4-CF_3-tolane as compared to tolane and 4-MeO-tolane, the rate of hydride insertion is lower compared to that of the other two H-acceptors. The difference between tolane and the electron rich 4-MeO-tolane can be explained by realizing that the electron rich H-acceptor will take up the hydride with some more difficulty than tolane does despite faster complexation. In addition, experiments with equimolar mixtures of two H-acceptors were performed. The results of these experiments are collected in Table 7.

Table 6
$RuCl_2$[(*S*)-BINAP] catalyzed dehydrogenation of 1-octanol at 130 °C in *p*-xylene with tolane and substituted analogues as H-acceptor

H-acceptor	Conv. alcohol (%)[a]	Yield aldehyde (%)[b]
Tolane	100	80
4-MeO-tolane	79	64
4-CF_3-tolane	42	29

[a] Reaction time was 2 h.
[b] Y_{ald} = conv. × selectivity (S_{ald}) as measured by GC.

Table 7
$RuCl_2$[(*S*)-BINAP] catalyzed dehydrogenation of 1-octanol at 130 °C in *p*-xylene with equimolar mixtures of H-acceptors

H-acceptor	Conv. alcohol (%)[a]	Yield aldehyde (%)[b]
Tolane/4-MeO-tolane	77	63
Tolane/4-CF_3-tolane	70	57
4-MeO-tolane/4-CF_3-tolane	63	50

[a] Reaction time was 2 h.
[b] Y_{ald} = conv. × selectivity (S_{ald}) as measured by GC.

Table 8
$RuCl_2$[(*S*)-BINAP] catalyzed dehydrogenation of 1-octanol at 130 °C in *p*-xylene: conversions of the H-acceptors in the mixed experiments

H-acceptor mixture[a]	Conv. (%)[b,c]
Tolane/4-MeO-tolane	32/30
4-MeO-tolane/4-CF_3-tolane	9/34

[a] 1:1 mixture.
[b] Maximal 50%.
[c] Measured by GC.

To our surprise, the conversion of 4-CF_3-tolane into 4-CF_3-stilbene is faster than the conversion of tolane or 4-MeO-tolane into the corresponding stilbene compounds, see Table 8.

The conversion of tolane and 4-MeO-tolane into the corresponding stilbenes is within experimental error the same indicating that both compounds are comparable in combined coordination and H-acceptor properties. From the mixture of 4-MeO-tolane/4-CF_3-tolane the overall conversion was expected to be considerably lower compared to that of tolane/MeO-tolane. Interestingly, the conversion of CF_3-tolane is higher than that of 4-MeO-tolane indicating that both H-acceptors play an important role in the dehydrogenation. The asymmetry introduced by the substituents on the hydride acceptor may also influence the coordinating and hydride accepting properties of the H-acceptor.

6. Effect of a radical scavenger on the catalytic reaction

Furthermore, experiments were performed with a radical scavenger to determine whether the dehydrogenation of alcohols is a one or two electron process. In the presence of equimolar amounts of 2,6-di-tert-butyl-4-methylphenol as a radical scavenger (compared to the substrate), after 2 h the reaction was complete. Without radical scavenger the same result was found. Hence, it can be concluded that the dehydrogenation is not of a radical nature, see Fig. 3.

7. Towards unraveling the catalytic cycle

Since the $RuCl_2$[*S*-BINAP] complex is not simply a well defined monometallic catalyst and very little mechanistic

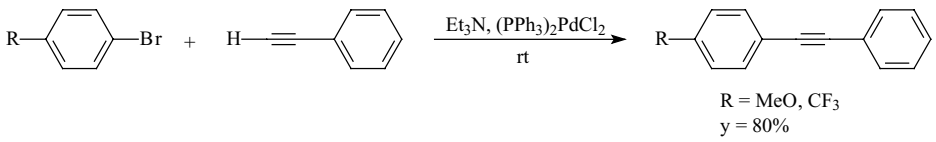


Fig. 2. Substituted analogues of tolane with electron releasing or electron withdrawing substituents.

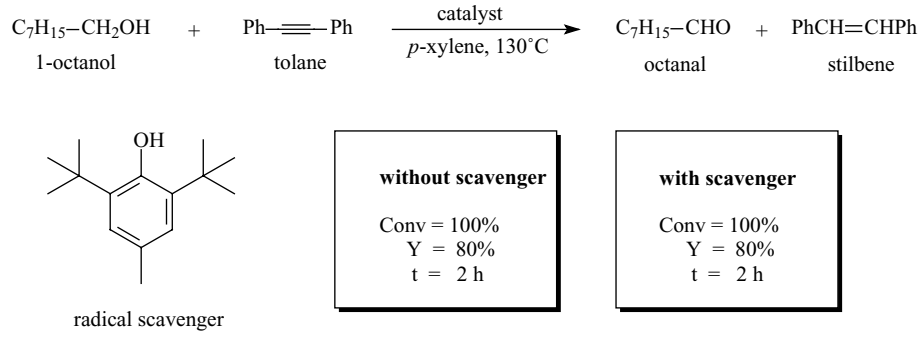


Fig. 3. Addition of a radical scavenger revealed the concertedness of the dehydrogenation.

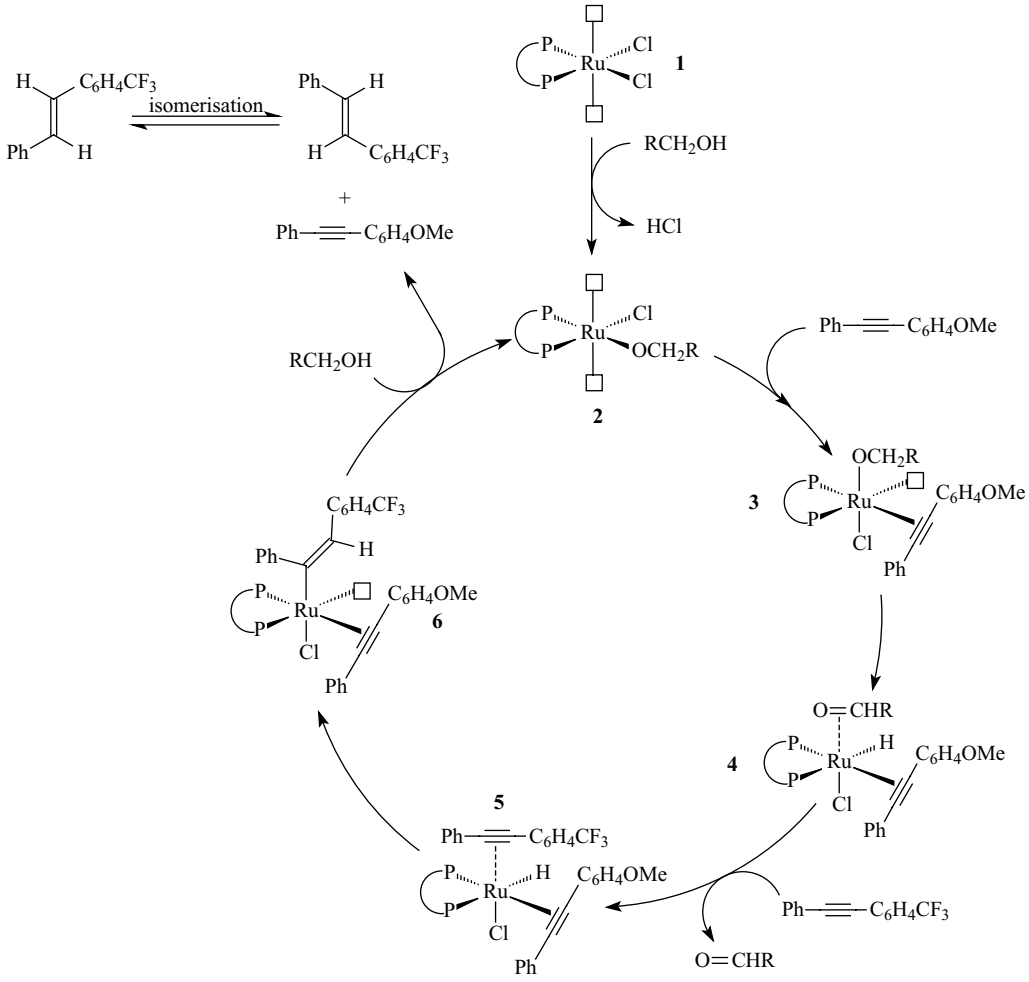


Fig. 4. Tentative mechanism for the $[RuCl_2[S\text{-BINAP}]]_x$ catalyzed dehydrogenation of alcohols.

information is available about ruthenium-BINAP catalyzed reactions, it was difficult to obtain information about the catalytic cycle describing the dehydrogenations of alcohols. Nevertheless, based on the results obtained so far, particularly from the competition experiments with the electron rich and deficient tolane analogues, a tentative catalytic cycle was proposed, see Fig. 4. In this simplified cycle the multinuclear $[RuCl_2[S\text{-BINAP}]]_x$ complex is proposed to be defragmented into the monometallic ruthenium complex. Subsequently, an alcohol inserts into the complex **1** liberating hydrogen chloride and giving a coordinatively unsaturated ruthenium alkoxide species **2**. In the next step the electron rich 4-MeO-tolane ligand coordinates with ruthenium affording **3**. Then β-hydrogen elimination from the alkoxide ligand gives rise to a ruthenium hydride species and one aldehyde or ketone molecule **4** which is released from the complex with concomitant generation of a free coordination site. Subsequently, the electron deficient 4-CF_3-tolane can coordinate to the metal center due to the enhanced electron density introduced by the electron rich 4-MeO-tolane **5**. Then, the hydride is transferred to the 4-CF_3-tolane, giving the coordinatively unsaturated ruthenium alkoxide species **6**. Finally, oxidative addition of alcohol and simultaneous release of 4-MeO-tolane and 4-CF_3-tolane to generate a free coordination site restore the coordinatively unsaturated ruthenium alkoxide species **2** and completes the catalytic cycle. Due to the high reaction temperature partial isomerization of *cis*-stilbenes occurs into the *trans* isomer. Furthermore, dehydrocarbonylation of **4** may occur to give a ruthenium carbonyl species and a free alkene.

About the catalytic cycle the following remarks need to be made: (a) since none of the intermediates proposed has been isolated, the suggested cycle is merely plausible, (b) it is not unlikely that dinuclear ruthenium complexes could participate in the cycle since they are initially present in the catalyst and (c) several catalytically active ruthenium carbonyl species could be formed during and dehydroformylation.

8. Conclusions

The dehydrogenation of various primary and secondary alcohols into the corresponding aldehydes and ketones is efficiently catalyzed with $RuCl_2$[*S*-BINAP], when ligating tolane is used as H-acceptor. The turnover frequencies for primary allylic and benzylic alcohols are typically 4–10 h^{-1}, while secondary alcohols are generally dehydrogenated at a rate of 0.1–1 h^{-1}. The difference in reaction rates between primary and secondary alcohols may originate from differences in steric crowding in the complex. The product loss of about 20% which is observed when primary aliphatic alcohols not leading to conjugated aldehydes are used as substrates, can be partly attributed to dehydroformylation. Addition of a base has a strongly accelerating effect on the catalytic dehydrogenation ensuring that secondary alcohols could be converted quantitatively into the corresponding ketones within a few hours. From all H-acceptors screened in the catalytic hydrogen transfer reaction, tolane performed best. Competition experiments between electron rich 4-MeO-tolane and the electron deficient 4-CF_3-tolane revealed cooperativity, one being easier ligating, the other acting better as H-acceptor. Addition of a radical scavenger had no negative influence on the oxidation reaction, thus proving that it is not a radical process. Although Noyori et al. reported that BINAP catalysts are very effective in enantioselective hydrogenation processes [37], no enantioselective dehydrogenation of racemic 1-phenylethanol and 1-phenyl-2-propanol could be achieved. In contrast to the $Ru_3(CO)_{12}$-based catalyst [10], attempts to isolate catalytic intermediates were not successful. Although a corner of the veil has been raised, more efforts have to be expended to elucidate the structure of the intermediates and unravel the exact catalytic cycle. Here the H-acceptor plays presumably an important role as ligand.

9. Experimental

9.1. General

All starting materials were obtained from commercial suppliers and used as received. $RuCl_2$[*S*-BINAP] was obtained from STREM Chemicals, Inc., France. All reactions were performed under an atmosphere of dry argon. Analytical thin layer chromatography was performed on Kieselgel 60 F-254 precoated silica gel plates. Visualization was accomplished with UV light or iodine vapor. Column chromatography was performed on Merck silica gel 60 or on Merck aluminum oxide 90. ^{1}H-NMR, ^{13}C-NMR and ^{31}P-NMR-spectra were recorded on a 400 MHz NMR (Varian Mercury, 400 MHz for ^{1}H-NMR and 100 MHz for ^{13}C-NMR), or on a 300 MHz NMR (Varian Gemini, 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR). Proton chemical shifts (δ) are reported in ppm downfield from tetramethylsilane (TMS) whereas the carbon chemical shifts are reported in ppm downfield of TMS using the resonance of the deuterated solvent as internal standard. The phosphorus shifts were referenced to 85% H_3PO_4. IR-spectra were recorded on a Perkin Elmer ATR-IR Spectrum One. MALDI-TOF-spectra were obtained on a PerSeptive Biosystems Voyager DE PRO spectrometer using α-cyano-4-hydroxycinnamic acid as a matrix. GC analyses were performed using a Zebron ZB-35 or a Chirasil-Dex-CB column on a Perkin Elmer Autosystem in combination with a flame ionization detector. Conversion and yields were determined relative to 1,3,5-tri-*tert*-butylbenzene as internal standard. GC/MS measurements were obtained with a Shimadzu GC/MS-QP5000 using a Zebron ZB-35 column.

9.2. $RuCl_2$[S-BINAP] catalyzed dehydrogenations, general procedure

All catalytic dehydrogenation experiments were performed in a dry, oxygen-free argon atmosphere. A typical experiment was performed as follows. An oven-dry 40 ml Radley carousel reaction tube was flushed with argon before it was charged with $RuCl_2$[*S*-BINAP] (71.5 mg, 0.090 mmol) and tolane (700 mg, 3.90 mmol). Alcohol (2.00 mmol) and internal standard (1,3,5-tri-*tert*-butylbenzene, 81 mg, 0.33 mmol) dissolved in *p*-xylene (2.50 ml) was added to the mixture. A small aliquot was taken from the alcohol/internal standard solution for GC analysis. The reaction tube was placed in a 12 tube Radley reaction carousel and the mixture was heated to 130 °C and stirred with a magnetic stirrer. Small aliquots of reaction mixture could be taken for GC analysis. The conversions and yields were determined with GC. The products were characterized (GC) by comparison with authentic samples.

9.3. Octanal

1-Octanol was oxidized in 2 h according to the general procedure described above (Table 1, entry 1). The product was characterized (GC) by comparison with an authentic sample. The yields were determined with GC. The reaction mixture was purified by bulb-to-bulb distillation yielding octanal in 81%. The spectral data were in accordance with literature [34].

9.4. 2-Phenylethanal

2-Phenylethanol was oxidized in 2 h according to the general procedure described above (Table 1, entry 9). The product was characterized (GC) by comparison with authentic samples. The yields were determined with GC (32%). The spectral data was in accordance with literature [35].

9.5. (E,Z)-3,7-Dimethyl-2,6-octadienal (Geranial)

Geraniol was oxidized in 2 h according to the general procedure described above (Table 2, entry 1). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC (81%). The spectral data was in accordance with literature [36].

9.6. 3-Phenyl-2-propenal

Cinnamyl alcohol was oxidized in 2 h according to the general procedure described above (Table 2, entry 2). The product was characterized (GC) by comparison with an authentic sample. The yields were determined with GC (100%). The spectral data was in accordance with literature [28].

9.7. Benzaldehyde

Benzyl alcohol was oxidized in 4 h according to the general procedure described above (Table 2, entry 3). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC (92%). The spectral data was in accordance with literature [34].

9.8. 2-Decanone

2-Decanol was oxidized in 24 h according to the general procedure described above (Table 3, entry 1). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC (29%). The spectral data was in accordance with literature [34].

9.9. 4-Cholestene-3-one

Cholesterol was oxidized in 48 h according to the general procedure described above (Table 3, entry 6). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC. Purification of the reaction mixture by flash column chromatography (silica, with dichloromethane/ether, 20:1) yielded 4-cholestene-3-one as a light brown/white powder (97%). The spectral data was in accordance with literature [32].

9.10. Androst-4-ene-3,17-dione

3-Hydroxyandrost-5-en-17-one was oxidized in 17 h according to the general procedure described above (Table 3, entry 8). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC. Purification of the reaction mixture by flash column chromatography (silica, with dichloromethane/diethyl ether, 20:1) yielded androst-4-ene-3,17-dione as a white powder (83%). The spectral data was in accordance with literature [32].

9.11. 1,10-Decanediol

1,10-Decanediol was oxidized in 2 h according to the general procedure described above (Table 4, entry 1). The product was characterized (GC) by comparison with an authentic sample. The yields were determined with GC (67%). The spectral data was in accordance with literature [38].

9.12. 1-Hydroxy-2-octanone

1,2-Octanediol was oxidized in 2 h according to the general procedure described above (Table 4, entry 2). The product was characterized (GC) by comparison with an authentic sample. The yield was determined with GC (70%). The spectral data were in accordance with literature [39].

9.13. Screening of H-acceptors

Analogous to the general procedure, the oxidation of 1-octanol was performed with 2 equiv of the alternative H-acceptors. All reactions were stopped after 5 h. The conversion was monitored by GC analysis.

9.14. 4-Trifluoromethyl-diphenylethyne

See Ref. [10] for details about the synthesis.

9.15. 4-Methoxy-diphenylethyne

See Ref. [10] for details about the synthesis.

9.16. Dehydrogenation in the presence of equimolar mixtures of H-acceptors

Analogous to the general procedure, the dehydrogenation of 1-octanol was performed in the presence of a 1 to 1 mixture of H-acceptors (total 2 equiv of H-acceptor). All reactions were stopped after 2 h. The conversion was monitored by GC analysis (Tables 6–8).

9.17. Dehydrogenation in the presence of a radical scavenger

The dehydrogenation of 1-octanol was performed according to the general procedure in the presence of 2,6-di-*tert*-butyl-4-methylphenol (427 mg, 1.94 mmol). The conversion was monitored by GC analysis (Fig. 3).

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