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Scope, mechanism and diene inhibition of isomerization of allylic alcohols to saturated ketones catalyzed by ruthenium(II)-cyclopentadienyl complexes

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Abstract

The isomerization of 3-buten-2-ol to butanone catalyzed by Ru(II)Cp-complexes (Cp = η^5-cyclopentadienyl) with phosphine and amine ligands is described. The reaction catalyzed by $[RuCp(MeCN)_3](PF_6)$ and two equivalents of triphenylphospine is first order in substrate with a k_{ini} of 0.43 h^{-1} and an initial TOF of 13,000 h^{-1}. The catalyst precursor complex [RuClCp(dppb)] (dppb = bis(diphenylphosphino)butane) has been characterized by X-ray diffraction. This compound features a seven-membered ring incorporating the ruthenium centre and the dppb ligand.

Combination of two equivalents of primary, secondary or tertiary amines and $[RuCp(MeCN)_3](PF_6)$ results in active catalyst precursors. Within each group, increasing the bulk of the ligand gives lower isomerization rates. The combined effects of optimal pK_a, nucleophilicity and steric bulk make RuCp-complexes with secondary amines the most active precursors. With di-*n*-butylamine, 745 turnovers can be reached after 1 h. ^{31}P NMR spectra indicate that the resting state in the catalytic cycle is a complex in which 3-buten-2-ol is η^2-coordinated through the alkene moiety. This implies that coordination of the oxygen moiety and concomitant β-hydrogen abstraction is the rate-limiting step. A counterintuitive result is that allylic alcohols bind stronger to RuCp complexes with phosphine ligands than dienes. Inhibition of the catalyst appears to be a result of interaction of the diene with a ruthenium–allyl alcohol complex, which is sufficiently strong to prevent coordination of the oxygen moiety of the allylic alcohol. This hinders orientation of the allylic alcohol substrate in a suitable way to undergo β-hydrogen abstraction, thereby blocking isomerization catalysis.

Keywords: Isomerization; Allylic alcohols; Ruthenium; Cyclopentadienyl; Diene inhibition

1. Introduction

With a growing demand for environmentally benign organic reactions, homogeneously catalyzed reactions that are atom efficient receive increasing attention [1]. Isomerization of allylic alcohols forms an elegant shortcut to carbonyl compounds [2,3] in a completely atom-economical process that offers potentially several useful applications in natural-product synthesis [4–6] and in bulk chemical processes. As an example of the latter, butanone (methyl ethyl ketone, MEK) is a Mton-per-year scale solvent traditionally produced from butenes [7,8]. This process requires the use of stoichiometric

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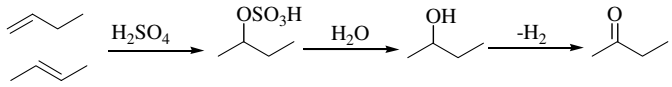


Scheme 1. Present-day synthesis of MEK from a mixture of butenes.

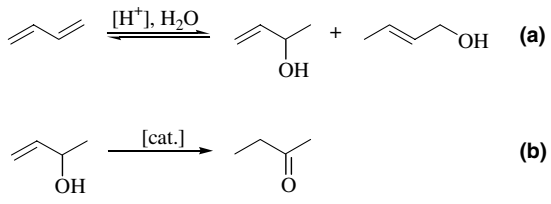
amounts of concentrated sulfuric acid as shown in Scheme 1.

A viable alternative route starting from 1,3-butadiene would need water as only other stoichiometric reagent. After acid-catalyzed hydration of butadiene (Scheme 2(a)), the 1,2-addition product 3-buten-2-ol can be isomerized to MEK (Scheme 2(b)). As the equilibrium of Scheme 2 a lies for 97% on the left-hand side, a process in which both reactions take place in one reactor is preferable in order to circumvent an extensive butadiene recycle. The key reaction in this process is selective isomerization of the secondary allylic alcohol to the saturated ketone *in the presence of dienes*.

The feasibility of the one-pot synthesis of MEK from 1,3-butadiene was shown by Drent and co-workers [9]. The maximum conversion was obtained with a catalytic system formed by in situ mixing of a ruthenium(III) salt and 2,2′-bipyridine (bpy) or 1,10-phenanthroline (phen) [9,10]. A subsequent investigation in our group of possible deactivation routes for this type of catalyst [11] led to the discovery of a significantly improved system [12].

Yet, the most active catalyst precursor thus far for the overall hydration-isomerization reaction, [$RuCl_3$(dmso)(phen)], is only moderately active in isomerization of allylic alcohols in the absence of dienes [11]. This prompted us to investigate alternative catalyst precursors with higher intrinsic isomerization activities. Ruthenium-cyclopentadienyl complexes with phosphine ligands have been shown by Trost and co-workers [13,14] and Slugovc et al. [15,16] to be active isomerization catalysts. Indeed, [RuClCp(PPh_3)$_2$] in the presence of silver(I) salts with non-coordinating anions proved to be extremely active in the isomerization of 3-buten-2-ol [17]. Likewise, application of didentate phosphine ligands gave high turnover numbers to MEK [17].

Unfortunately, none of these RuCp-catalyst precursors showed any isomerization activity in the presence of dienes. Recently, a bis(allyl)-ruthenium(IV) complex has been proved to catalyze the isomerization of allylic alcohols efficiently and, interestingly, the complex remains active in the presence of dienes [18]. The discoveries of systems that are able to catalyze the isomerization of allylic alcohols in the presence of dienes uptil now have had a serendipitous character. The strong inhibitory effect of dienes on most catalysts has been poorly understood.



Scheme 2. Acid-catalyzed hydration of 1,3-butadiene (a) followed by isomerization (b) yields MEK in a complete atom-economical process.

In this paper the results are described of a study on the use of the ruthenium(II)-cyclopentadienyl moiety in combination with various ligands as catalyst precursors for the isomerization of 3-buten-2-ol to MEK. Next to phosphine ligands, which have been discussed in the literature previously [14,15,17], for the first time ligands containing nitrogen-donor atoms are included in this study intending to explore the scope of this catalytic system. Furthermore, the mechanism of the isomerization is investigated by ^{31}P NMR spectroscopy both in the absence and the presence of dienes in an attempt to shed light on the intriguing effect of dienes on the isomerization reaction.

2. Results and discussion

2.1. RuCp-complexes containing monodentate or didentate phosphine ligands

2.1.1. Isomerization of 3-buten-2-ol

The complex [RuClCp(PPh_3)$_2$] is synthetically readily accessible [19] and forms a convenient precursor to analogous complexes with monodentate and didentate phosphine ligands [17]. In the publications of Trost on the isomerization of allylic alcohols, catalyzed by [RuClCp(PPh_3)$_2$], a low substrate-to-catalyst ratio of 100 was employed [13,14]. The catalytic efficiency of the RuCp-moiety can be increased considerably by using [RuCp(MeCN)$_2$(PPh_3)]$^+$ as catalyst precursor [15,16]. This complex has been prepared quantitatively from [RuCp(MeCN)$_3$](PF_6) (**1**) and triphenylphosphine by Slugovc et al. [15,16]. To avoid tedious synthetic procedures and allow for faster screening of catalytic activity of various ligands in combination with the RuCp-moiety, an in situ strategy is adopted here.

The presence of substitutionally labile acetonitrile ligands [20] makes **1** an ideal starting complex for in situ testing. When **1** is used as catalyst precursor, only low turnover numbers (TONs; 115 after 1 h; see Table 2) are obtained. In the presence of **1** and two equivalents of triphenylphosphine, a fast isomerization of 3-buten-2-ol to MEK takes place, after a negligible induction period (Fig. 1). A similar behaviour is observed if one

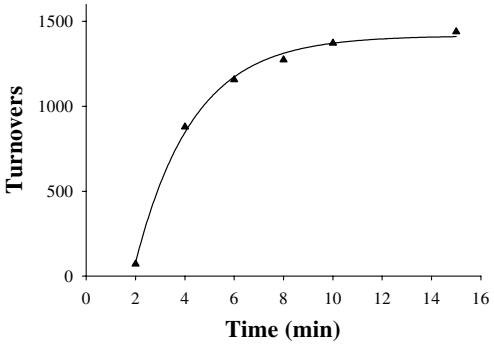


Fig. 1. Isomerization of 3-buten-2-ol to MEK, catalyzed by **1** with 2 equiv. of triphenylphosphine in diglyme. $T = 100$ °C. Substrate/catalyst precursor = 1640.

equivalent of triphenylphosphine is employed. The reaction is first order in substrate with a k_{ini} of 0.43 h^{-1} and an initial TOF of 13,000 h^{-1}. This TOF is significantly higher than obtained with **1** alone and comparable to the activity reported for the isolated complex $[RuCp(MeCN)_2(PPh_3)]^+$ [15].

As can be seen from Fig. 1, a full conversion of 3-buten-2-ol is not obtained. This is probably due to the formation of small amounts of 1,3-butadiene through reversion of the hydration reaction depicted in Scheme 2a under the reaction conditions, which inhibits the isomerization reaction severely.

Several ruthenium(II)-cyclopentadienyl complexes with didentate phosphine ligands [21], obtained by reacting in each case the appropriate ligand with a solution of $[RuClCp(PPh_3)_2]$ in toluene, have been used previously as catalyst precursor as well [17]. Upon increasing the carbon-chain length between the phosphorus-donor atoms, the reactivity of the resultant ruthenium complexes increases. Thus, initial turnover frequencies in the series range from 530 h^{-1} for a C_1 chain (dppm ligand) to 18,000 h^{-1} for a C_4 chain (dppb ligand) [17]. All complexes with didentate phosphine ligands are less active than $[RuClCp(PPh_3)_2]$. The proposed mechanism of isomerization of allylic alcohols involves the dissociation of one phosphine moiety (see Section 2.4). The increased reactivity with increasing chain length in the phosphine ligand has been ascribed to the greater ease of ring opening of larger chelate rings. Indeed, complexes with didentate phosphine ligands that are extremely rigid, such as with a phenylene or ethene bridge, show no catalytic activity at all [17].

2.1.2. Crystal structure determination of [RuClCp(dppb)]

Even though ruthenium(II)-cyclopentadienyl complexes with didentate phosphine ligands are known for quite some time and their use is widespread, only a few solid-state structures have been reported. Notably, of the catalyst-precursor series mentioned in the previous section, only the structures of the chloride complexes containing the dppm [22] and the dppe [22,23] ligands have been published. An interesting seven-membered ring is obtained with dppb as ligand. An ORTEP drawing of [RuClCp(dppb)] is shown in Fig. 2. Some selected bond lengths and angles are given in Table 1. The solid-state structure shows that the dppb ligand coordinates in a didentate fashion and this implies that isomerization of allylic alcohols catalyzed by RuCp-complexes with this ligand is only possible after opening up of the chelate ring.

In all respects, the structure of [RuClCp(dppb)] is analogous to the previously reported complexes in the series. The ruthenium centre may be considered to be in a pseudo-octahedral environment (three-legged piano stool). The Ru(1)–Cl(2) bond length of 2.4404(4) Å falls in the range of 2.430–2.453 Å observed for similar ruthenium(II)–cyclopentadienyl chloride complexes [22,24].

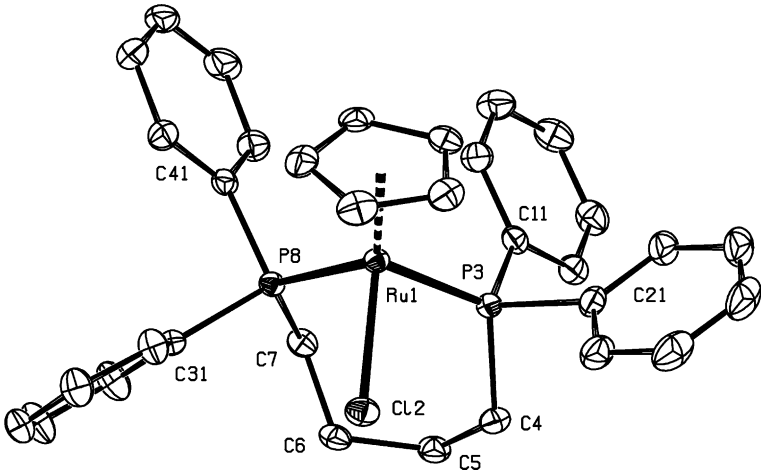


Fig. 2. ORTEP drawing and numbering scheme of [RuClCp(dppb)]. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level.

Table 1
Selected bond lengths and angles for [RuClCp(dppb)]

Bond lengths (Å)			
Ru(1)–Cl(2)	2.4404(4)	P(8)–C(7)	1.8330(17)
Ru(1)–P(3)	2.2810(5)	C(4)–C(5)	1.533(3)
Ru(1)–P(8)	2.2809(6)	C(5)–C(6)	1.530(3)
Ru(1)–Cp	1.8508(9)	C(6)–C(7)	1.542(3)
P(3)–C(4)	1.8503(19)		
Angles (°)			
Ru(1)–P(3)–C(11)	118.46(7)	P(8)–Ru(1)–Cl(2)	91.09(2)
Ru(1)–P(8)–C(31)	115.84(6)	P(8)–C(7)–C(6)	112.81(12)
P(3)–Ru(1)–P(8)	93.64(2)	C(4)–C(5)–C(6)	116.35(16)
P(3)–Ru(1)–Cl(2)	88.66(2)	C(5)–C(6)–C(7)	113.93(15)
P(3)–C(4)–C(5)	118.95(15)		

The Ru(1)–P(3) and Ru(1)–P(8) bond lengths are identical and consistent with distances found in a series of complexes containing the Cp–Ru–Cl fragment [24]. As expected, the P(3)–Ru(1)–P(8) bite angle (93.64(2)°) is considerably larger than that found for complexes with a C_2 chain between the phosphorus atoms (82.37–83.48°). The smallest bite angle for this series is found with the dppm ligand (72.07°) [22]. The seven-membered chelate ring is in a twist-chair conformation, with all groups attached to this ring staggered with respect to each other.

The ruthenium phosphorus distances are slightly longer than those found in the analogous hydride complex [RuCpH(dppb)] (2.2809(6)–2.2810(5) vs 2.2451(8)–2.2463(8) Å) [25]. The C_4-bridge appears to be in the same configuration in both complexes, since absolute differences between the corresponding torsion angles are less than 4° [25].

2.2. Isomerization of 3-buten-2-ol catalyzed by RuCp-complexes containing didentate ligands with phosphorus and nitrogen donor atoms

In several homogeneously catalyzed reactions, it proved beneficial to replace one phenyl group in triphenylphosphine by a pyridine moiety, either because of the additional basic function or because of the coordination of the nitrogen donor atom. Addition of two equivalents of 2-(diphenylphosphino)pyridine (2-PPh_2py) to **1** gives rise to two complexes as evidenced by ^{1}H NMR, ^{31}P NMR and mass spectrometry. The main product (>90%) exhibits a singlet in the ^{31}P NMR spectrum at 51.5 ppm, close to the singlet found for [RuClCp(PPh_3)$_2$], thus suggesting monodentate coordination of the ligand through the phosphorus atom. The other small singlet at 0.35 ppm may result from a complex in which the ligand is monodentately coordinated through nitrogen. From the facts that all signals in the ^{31}P NMR spectrum stem from symmetrical complexes and that no free ligand (−3.5 ppm) is observed, it can be concluded that 2-(diphenylphosphino)pyridine primarily behaves as a monodentate phosphine, to give [RuCp(MeCN)(2-PPh_2py-κP)$_2$]$^+$. [RuCp(MeCN)-(2-PPh_2py-κP)$_2$]$^+$ catalyzes the isomerization of 3-buten-2-ol to MEK as shown in Fig. 3(a). The reaction is not simply first order in substrate and the catalyst is considerably deactivated with time. The initial rate (k_{ini} = 0.39 h^{-1}) is of the same order as for **1** with triphenylphosphine (vide supra). However, the catalyst is deactivated much faster and the total turnover number is circa 30% lower.

Addition of two equivalents of 2-(diphenylphosphinoethyl)pyridine (2-PPh_2Etpy) to **1** results in the formation of two different species as evidenced most clearly by ^{31}P NMR. One species gives rise to a singlet, indicating two equivalent phosphorus atoms. This complex, which is by far the dominant species (>80%), is analogous to the complexes found with triphenylphosphine and 2-PPh_2py, viz. monodentate coordination of the phosphine with a pendant ethylpyridine group ([RuCp-(MeCN)(2-PPh_2Etpy-κP)$_2$]$^+$). The second species exhibits two doublets in the ^{31}P NMR spectrum. These signals suggest a minor fraction in which one ligand is coordinated in a monodentate fashion, while another ligand is coordinated through both the phosphorus atom and the nitrogen atom, viz. [RuCp(2-PPh_2Etpy-κP)(2-PPh_2Etpy-κP,κN)]$^+$. This hypothesis is corroborated by the ^{1}H NMR spectrum, which contains a small doublet at low field (9.3 ppm). Such a doublet can be as-

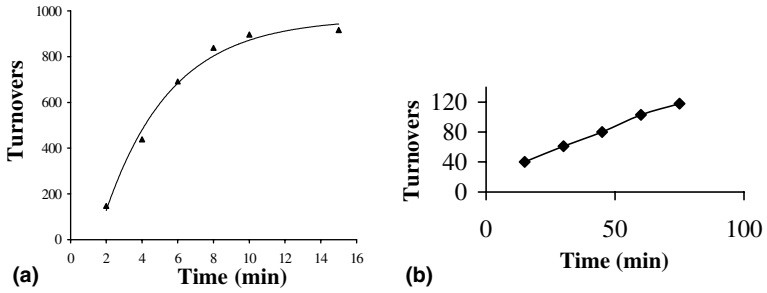


Fig. 3. Isomerization of 3-buten-2-ol to MEK, catalyzed by **1** with (a) 2 equiv. of 2-PPh_2py in diglyme and (b) 2 equiv. of 2-PPh_2Etpy in diglyme. T = 100 °C. Substrate/catalyst precursor = 1640.

cribed to the *ortho* hydrogen of a coordinated pyridine moiety (see also Section 2.3). The catalytic activity in the isomerization of 3-buten-2-ol of the ruthenium-cyclopentadienyl complex with 2-PPh_2Etpy is low (Fig. 3b).

The results indicate that both P,N-ligands behave mainly as monodentate phosphines when reacted in situ with **1**. The presence of a pyridine moiety is not beneficial to catalytic activity. Significant inhibition of the catalysts is observed as can be derived from Figs. 3. The inhibition is possibly caused by 1,3-butadiene, which can be formed under the reaction conditions from the substrate by dehydration. Indeed, in the presence of isoprene (2-methyl-1,3-butadiene), no activity is obtained with either ligand. The different reaction profile that is obtained when 2-PPh_2Etpy is used as the ligand is probably in part due to oxidation of the ligand during isomerization. The free ligand 2-PPh_2Etpy is more susceptible to air oxidation than 2-PPh_2py or triphenylphosphine as can be seen from the facile oxidation of 2-PPh_2Etpy in the solid state upon exposure to air.

2.3. Isomerization of 3-buten-2-ol catalyzed by RuCp-complexes containing amines

2.3.1. Ligand type dependency

Literature on allylic-alcohol isomerization reactions is dominated by complexes with phosphine ligands [2,3]. Ligands with donor atoms from the same group have been explored to a much lesser extent. In particular, isomerization catalyzed by RuCp-complexes with amine ligands to the best of our knowledge has not been reported.

An in situ strategy has been adopted in which two equivalents of ligand are added to a solution of **1** and 3-buten-2-ol in diglyme. The results are shown in Table 2. The result of entry 1 demonstrates that **1** by itself is only moderately active. Complex **1** in combination with two equivalents of an amine in some cases results in the formation of more active catalyst precursors for the isomerization of 3-buten-2-ol to MEK. Addition of two equivalents of primary (entries 2–4), secondary (entries 5–7) and tertiary amines (entries 8–9) results in active catalyst precursors. Within each group, increasing the bulk of the ligand gives lower isomerization rates

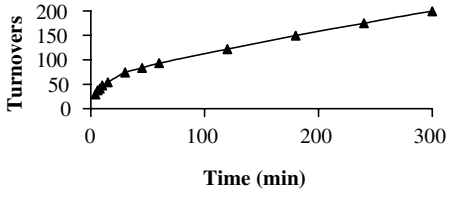


Fig. 4. Isomerization of 3-buten-2-ol, catalyzed by **1** with 2 equiv. of pyridine in diglyme. T = 100 °C. Substrate/catalyst precursor = 1640.

Table 2
Isomerization of 3-buten-2-ol to MEK, catalyzed by in situ mixtures of **1** with amine ligands[a]

Entry	Ligand	Turnovers [b]	pK_a [c]
1	MeCN	115	–
2	*n*-Propylamine	260	10.61
3	Isopropylamine	180	10.60
4	Aniline	55	4.62
5	Piperidine	235	11.27
6	Di-*n*-butylamine	745	10.60
7	Di-*n*-hexylamine	525	10.6
8	Triethylamine	460	10.74
9	Tri-*n*-butylamine	155	10.75
10	Pyridine	95	5.2
11	1-Methylimidazole	25	7.25
12	2,2′-Bipyridine[d]	0	4.35[e]
13	tmen[d]	25	10.01

[a] Solvent: diglyme (15 ml), toluene (4.0 mmol) as internal standard; ligand/ruthenium = 2; substrate/catalyst precursor = 1640; T = 100 °C.
[b] Turnovers determined by GLC after 1 h.
[c] Value for the corresponding ammonium salt. Taken from [26].
[d] Ligand/ruthenium = 1. tmen: *N*,*N*,*N*′,*N*′-tetramethylethylene diamine.
[e] Taken from [27].

(e.g., entry 6 vs. 7 and 8 vs. 9). Aromatic amines with relatively low pK_a-values all result in lower activity than of **1** alone (entries 4, 10–11). The combined effects of optimal pK_a, nucleophilicity and steric bulk make ruthenium(II)–cyclopentadienyl complexes with secondary amines the most active catalyst precursors. With its most prominent exponent, di-*n*-butylamine, 745 turnovers can be reached after one hour (entry 6). The application of didentate ligands (entries 12–13) does not give active catalysts. The strong chelate coordination and consequent difficulty in opening of the ring to create a vacant site hamper catalysis as was described for didentate phosphines in Section 2.1.1.

To put the results with nitrogen-donor ligands in perspective it should be noted that, although ruthenium(II)–cyclopentadienyl complexes with phosphorous ligands show initial activities of thousands per hour, the majority of transition-metal complexes only reach TOFs around 20 h^{-1} and maximum TONs of ca. 100 in allyl alcohol isomerization [2].

The catalyst precursors obtained from **1** and the amines shown in Table 2 are stable and active in isomerization catalysis for prolonged periods. This is exemplified in Fig. 4, in which a profile of isomerization of 3-buten-2-ol catalyzed by **1** with two equivalents of pyridine in time is depicted. From the figure, it becomes apparent that at least two different catalytic species must be present in solution in different stages of the reaction. In the first 30 min, a relatively active species catalyzes the isomerization (k = 0.16 h^{-1}, TOF = 215 h^{-1}), which then changes to another species that is considerably less active ($k_{apparent}$ = 0.044 $mol^{-1}\,l^{-1}\,h^{-1}$, TOF = 25 h^{-1}), but that retains its activity overnight (23 h) with only slight

deactivation. The relatively low activity of this catalytic species in combination with the large excess of substrate gives an apparent zeroth reaction-order in 3-buten-2-ol.

The proposed isomerization mechanism (see Section 2.4) contains a step in which an allylic alkoxide, obtained by deprotonation of the substrate, is coordinated to the ruthenium centre. Since amines are bases, it might be expected that the initial rate acceleration when amine ligands are used compared to **1** as catalyst precursor is due to an increased alkoxide concentration. Bäckvall reported a significant rate increase with several ruthenium catalyst precursors upon addition of catalytic amounts of K_2CO_3 [28]. However, no rate enhancement was observed for $[RuClCp(PPh_3)_2]$ with K_2CO_3 [28]. When under our experimental conditions $[RuClCp(PPh_3)_2]$ is used in combination with AgOTs and various amounts of bases (K_2CO_3, NaOH) a lower rate is observed, presumably due to coordination of the bases to the ruthenium centre. A large excess of potassium *t*-butoxide in combination with **1** yields 510 turnovers after one hour, demonstrating that deprotonation of the allylic alcohol is beneficial, but this cannot be the only effect of amines. No clear trend is observed with amine pK_a. The use of stronger bases (e.g., piperidine, tri-*n*-butylamine) does not result in higher activity and amines with similar pK_a values may differ considerably in resulting activity of the precursor complexes. If the rate-increasing effect of amines were solely due to their basic properties, more sterically hindered amines should result in higher activity. Yet, the opposite is observed.

2.3.2. Influence of ligand-to-ruthenium ratio

Not only the type of amine, but also the relative amount of ligand proves to be an important factor for activity. In Fig. 5(a) are plotted the various activities of **1** with different amounts of di-*n*-butylamine. Clearly, two equivalents of ligand are most beneficial. Both less than two equivalents and more than two equivalents to **1** cause a steep drop in activity. At high ligand concentrations, even lower activity than with **1** alone is observed.

A slightly different behaviour is observed with pyridine as ligand, as shown in Fig. 5(b). Here, the highest initial activity is found with one equivalent of pyridine. However, the catalytically active species is deactivated rapidly. With two equivalents of pyridine, slower deactivation is observed and therefore a higher TON is attained in the long run.

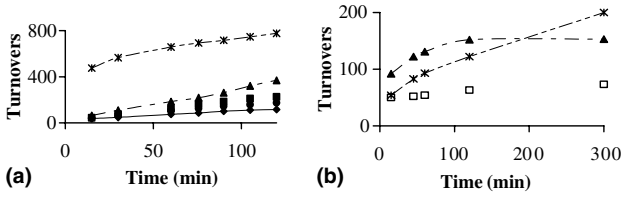
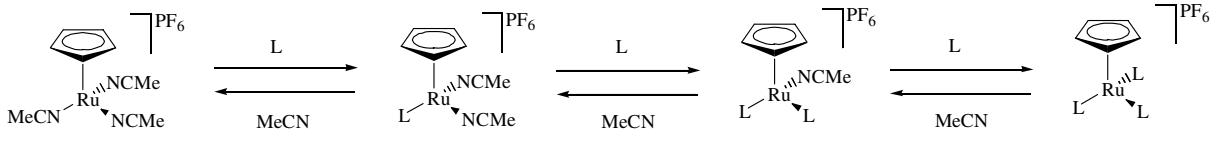


Fig. 5. Effect of ligand to ruthenium ratio for catalyst precursors formed in situ from **1** and (a) di-*n*-butylamine or (b) pyridine for the isomerization of 3-buten-2-ol to MEK in diglyme. $T = 100$ °C. (◆) 10 equiv., (■) 5 equiv., (□) 4 equiv., (∗) 2 equiv., (▲) 1 equiv., (●) no ligand.

Addition of two equivalents of pyridine to **1** gives a mixture of complexes, containing one, two and three pyridine molecules coordinated to the ruthenium centre, respectively (see Scheme 3). In the ^1H NMR spectrum in $CDCl_3$ at 50 °C, RuCp-complexes with coordinated pyridine ligands can be observed, while MEK is being formed. The pronounced effect of the ligand-to-ruthenium ratio is most likely due to shifting of the equilibria towards inactive species fully saturated with amine upon use of more equivalents of ligand. The fact that an increased amount of amine does not lead to an increased rate, but that optimum activity is found at two equivalents, again suggests that the positive effect of amine ligands is not exclusively due to their basic properties.

In concurrence with the results depicted in Fig. 4, it appears from Fig. 5 that at least two different catalytically active species are present successively. This becomes most obvious from the curve with two equivalents of di-*n*-butylamine. In the first 30 min, fast isomerization takes place, thereafter MEK is steadily formed but at much lower rate. All results are consistent with a ruthenium(II)-cyclopentadienyl complex with one amine ligand as the most active catalyst. Depending on the amount of ligand and the ligand type, this species is formed next to species with two and three amine ligands. At higher ligand concentrations, the latter two species dominate and isomerization rates go down. Deactivation may take place by ligand redistribution, which gives rise to the initial complex **1** and species with two and three amine ligands (Scheme 3). The concentrations of the active species with one amine ligand and without amine ligands thereby become lower and reach a steady state. Ligand disproportionation has also proved to be a major deactivation route in the synthesis of MEK from 1,3-butadiene catalyzed by ruthenium complexes with phenanthroline ligands [12].



Scheme 3. Equilibrium formation of several ruthenium complexes.

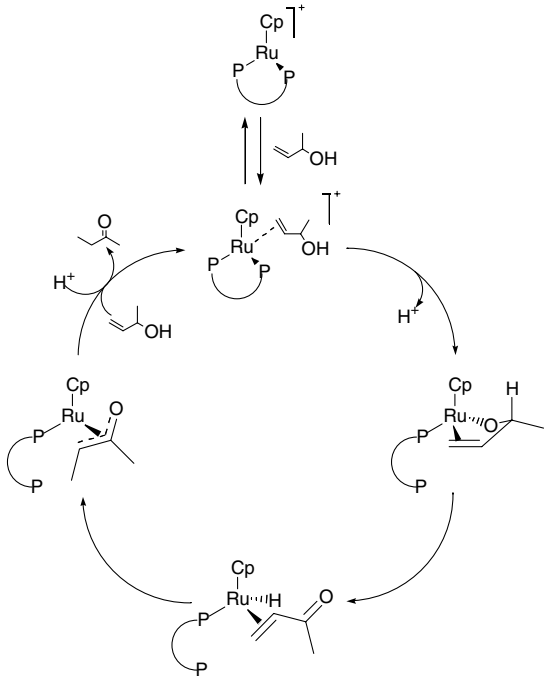
2.3.3. Inhibition by dienes

The results of isomerization experiments in the presence of isoprene are reported in Table 3. A much lower isomerization rate is observed for all catalyst precursors. However, it is interesting to note that **1** in combination with nitrogen donor ligands is significantly less inhibited by isoprene than if **1** is used in combination with triphenylphosphine. If the activity of **1** with various ligands under diene-free conditions is taken into account, it can be deduced that ruthenium(II)-cyclopentadienyl complexes with amines are more resistant to isoprene compared to ruthenium(II)-cyclopentadienyl complexes with triphenylphosphine by a factor of ca. 50. Yet, the activities are all far too low to be attractive in the direct hydration-isomerization reaction to produce MEK from 1,3-butadiene on an industrial scale.

2.4. Mechanism and diene inhibition of the isomerization of allylic alcohols catalyzed by RuCp-complexes with phosphine ligands

All RuCp-complexes described in this paper are extremely effectively poisoned by isoprene, while some of these complexes are under diene-free conditions among the best catalyst precursors for allyl alcohol isomerization. Several RuCp-complexes with didentate phosphine ligands catalyze an entirely different reaction of 3-buten-2-ol in the presence of isoprene [17]. The recent discovery of a catalyst precursor that is much less affected by isoprene [18] makes it even more interesting to study the effect of dienes on the isomerization reaction.

An intramolecular mechanism has been proposed for the isomerization of allylic alcohols by ruthenium(II)-cyclopentadienyl complexes with phosphine ligands [14,17]. This mechanism is depicted for complexes with didentate ligands in Scheme 4. A ^{31}P NMR study on the behaviour of [RuClCp(dppe)] towards allylic alcohols showed that initial coordination of the allylic alcohol to the ruthenium centre takes place at the alkene moiety and that the resultant species forms the resting state of the catalytic cycle (top of the catalytic cycle in Scheme 4) [17]. This implies that the next step, viz. coordination of the oxygen moiety and concomitant β-hydrogen abstraction is the rate-determining step. [RuClCp(PPh_3)$_2$] reacted analogously; the first step in the catalytic cycle after initial complexation is in this case didentate coordination of the allyl alcohol with concomitant dissociation of one triphenylphosphine ligand [17]. It is interesting to note that in these studies, allylic alcohols with an internal double bond react much slower and significant peaks for unreacted [RuCp(dppe)]$^+$ are still visible in the ^{31}P NMR spectra [17].



Scheme 4. Mechanistic proposal for the isomerization of allylic alcohols, catalyzed by ruthenium-cyclopentadienyl complexes with didentate phosphorous ligands (P^P) [17].

Table 3
Isomerization of 3-buten-2-ol to MEK catalyzed by **1** with different ligands in the presence of isoprene[a]

Entry	Ligand	Turnovers
1	MeCN	3
2	PPh_3	2
3	Piperidine	5
4	Di-*n*-hexylamine	7
5	Di-*n*-butylamine	15

[a] Solvent: diglyme (15 ml), isoprene (2 ml); ligand/ruthenium = 2; T = 100 °C, t = 1 h. Turnovers determined by GLC with toluene as internal standard. Substrate/catalyst precursor = 1640. Isoprene/ruthenium = 2000.

With monodentate triphenylphosphine ligands in [RuClCp(PPh_3)$_2$], refluxing in isoprene leads to the formation of a ruthenium–isoprene complex (presumably η^4-coordinated) as determined with mass spectrometry. A strong η^4-coordination of isoprene vs. a weaker η^2-coordination of allylic alcohols, preventing the required initial coordination of the substrate as shown in Scheme 4, at first sight may be an explanation for the absence of activity upon addition of isoprene. ^{31}P NMR has been used to study the effect of the addition of isoprene to a mixture of allyl alcohol and ruthenium-cyclopentadienyl complexes with phosphine ligands. Thus, the interaction between [RuCp(dppe)]$^+$, obtained after reaction of [RuClCp(dppe)] with AgOTs, and isoprene and allyl alcohol has been considered. The latter substrate is isomerized to propanal, analogously to 3-buten-2-ol. Surprisingly, addition of an excess of isoprene (ca. 1000 equiv. to ruthenium) to a solution of

$[RuCp(dppe)]^+$ in $CDCl_3$ at room temperature results in only partial coordination of the substrate. Around 50% of the ruthenium complex remains "free" (Fig. 6(a)), even after prolonged stirring. This seems to contradict the idea of strong coordination. Moreover, both phosphorus atoms are bound to the ruthenium centre and isoprene is therefore most likely coordinated in an η^2-fashion. The result of subsequent addition of allyl alcohol (ca. 10 equiv. to ruthenium) is depicted in Fig. 6(b). Although a small amount of isoprene is still coordinated, two doublets resulting from allyl alcohol coordination appear. Obviously, allyl alcohol coordinates first to the "free" $[RuCp(dppe)]^+$ and indeed the singlet at 77.5 ppm has disappeared. Comparison of the integrals leads to the conclusion that in addition to complexation to the "free" ruthenium centres, a significant amount of isoprene is displaced. Thus, allyl alcohol binds more strongly to $[RuCp(dppe)]^+$ than does isoprene!

In Fig. 7 the results are shown of the reversed route. Addition of a few drops of allyl alcohol gives instantaneous, complete formation of [RuCp(allyl alcohol)-(dppe)]$^+$ (Fig. 7(a)). Subsequent addition of 1 ml of isoprene does not change the spectrum at all (Fig. 7(b)): again the preferential coordination of allyl alcohol is demonstrated. With other didentate phosphine ligands and with 3-buten-2-ol as substrate, comparable results are obtained. If $[RuCp(PPh_3)_2]^+$ is used at room temperature, no coordination of isoprene is observed with ^{31}P NMR (Figure S1). Addition of allyl alcohol leads to instantaneous formation of the adduct (Figure S2), again confirming the preferential coordination of the substrate rather than the inhibitor. It should be noted that at room temperature, isomerization occurs under diene-free conditions, while in the presence of isoprene no activity is observed.

Counter intuitively, the poisoning effect of isoprene is not caused by preferential initial coordination. Still, isoprene is a strong poison and it must therefore interact further in the catalytic cycle. In the presence of isoprene, other ruthenium species (such as ruthenium–allyl) cannot be detected with ^{31}P NMR. The absence of methyl vinyl ketone (MVK) in the GLC-chromatograms with ruthenium-cyclopentadienyl complexes further suggests that inhibition occurs before possible formation of a ruthenium-hydride species (cf. Scheme 4). Apparently, isoprene interacts with the ruthenium–allyl alcohol complex sufficiently strong to prevent coordination of the oxygen moiety of the allylic alcohol. This hinders

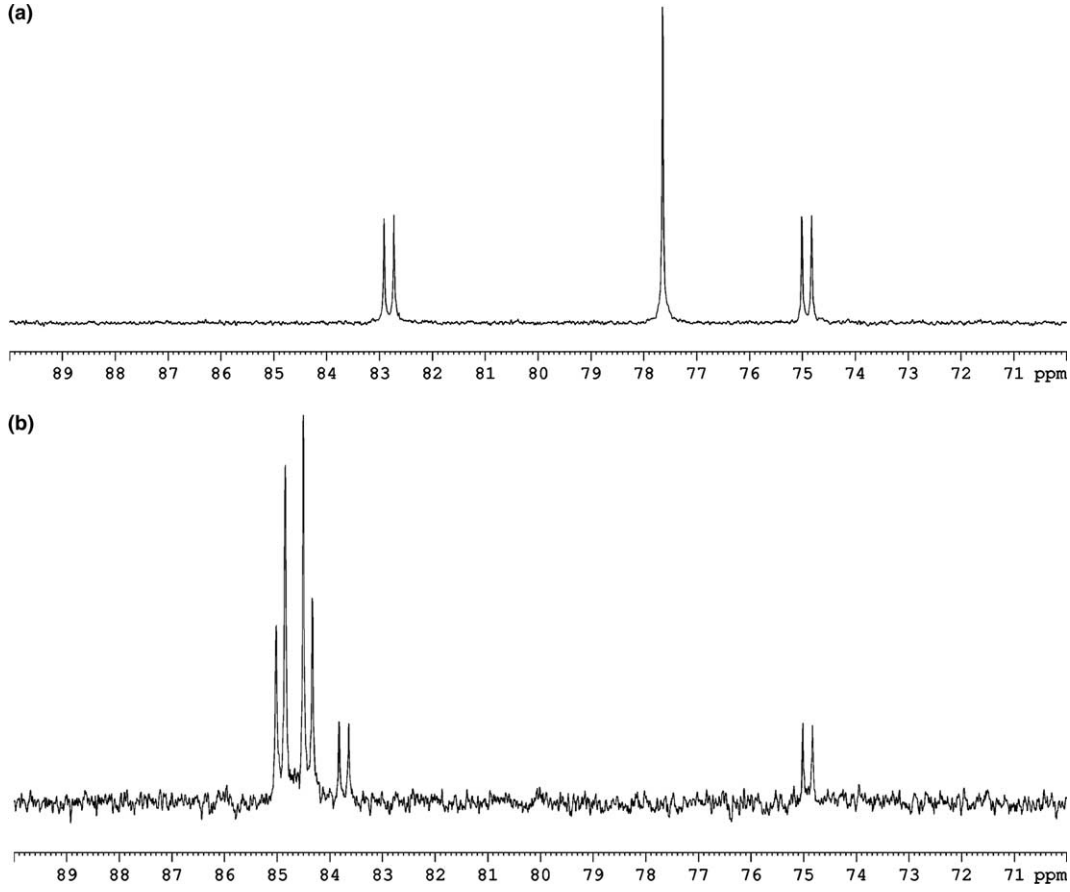


Fig. 6. ^{31}P NMR spectra recorded at room temperature in $CDCl_3$ of $[RuCp(dppe)]^+$ (77.5 ppm) with (a) isoprene (~1000 equiv. to ruthenium) and (b) after subsequent addition of allyl alcohol (~10 equiv. to ruthenium).

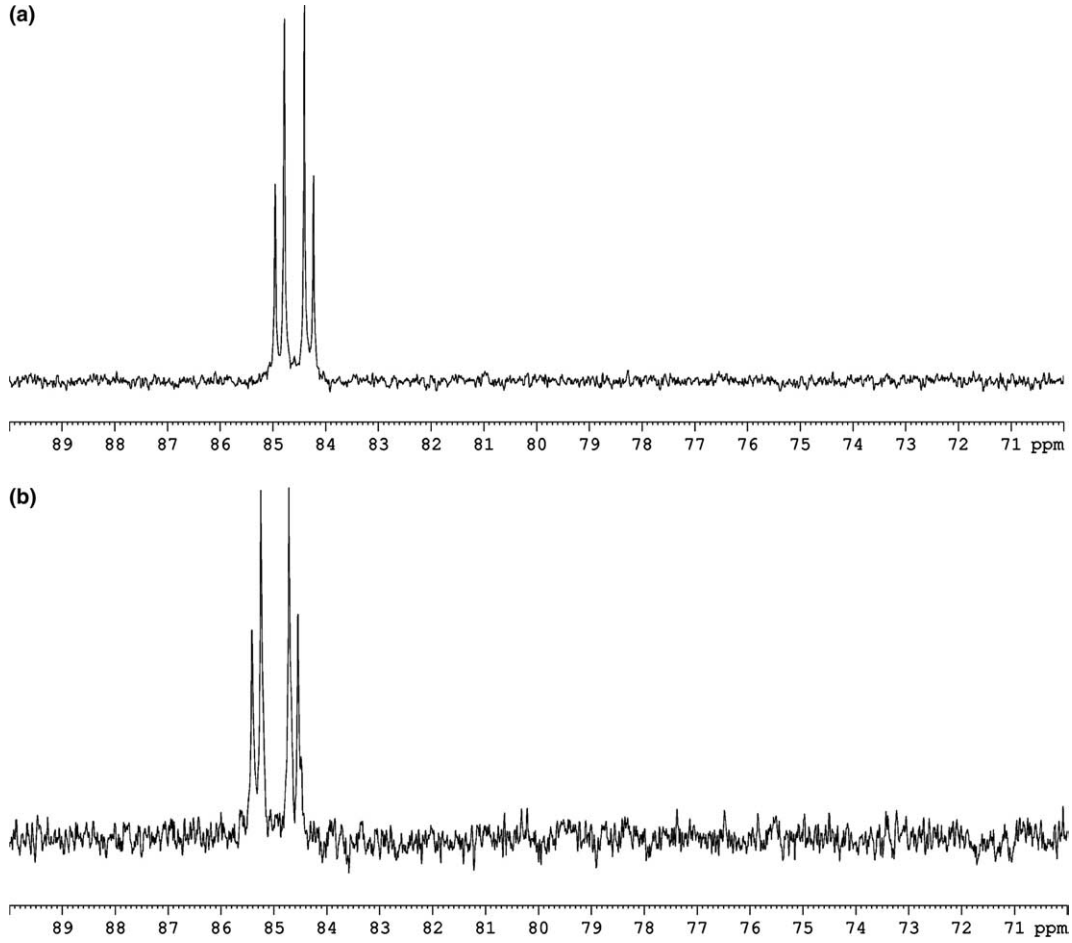


Fig. 7. ^{31}P NMR spectra recorded at room temperature in $CDCl_3$ of $[RuCp(dppe)]^+$ with (a) allyl alcohol (~10 equiv. to ruthenium) and (b) after subsequent addition of isoprene (~1000 equiv. to ruthenium).

orientation of the allylic alcohol substrate in a suitable way to undergo β-hydrogen abstraction, thereby hampering isomerization catalysis. The RuCp-complexes behave differently from ruthenium–phenanthroline complexes [11]. With the latter type of complexes, significant amounts of MVK are formed and indirect evidence exists for the formation of ruthenium–allyl species. Different inhibition pathways must exist for different types of ruthenium complexes.

3. Conclusions

A series of ligands have been tested in situ with $[RuCp(MeCN)_3](PF_6)$ for the isomerization of 3-buten-2-ol to MEK. The most active catalyst precursor is obtained with triphenylphosphine ($k_{ini} = 0.43\ h^{-1}$, TOF = 13,000 h^{-1}). Substitution of a phenyl moiety in triphenylphosphine by a pyridine group, or introduction of pyridine as a pendant group results in stronger deactivation. Several amine ligands have for the first time shown to result in active catalyst precursors for the isomerization of allylic alcohols. The most active precursor is obtained with di-*n*-butylamine (745 turnovers after one hour). Amine ligands with relatively low pK_a values result in lower activity than if $[RuCp(MeCN)_3](PF_6)$ (115 turnovers after one hour) is used alone. A ligand to metal ratio of two yields the most active precursors; a steep drop in activity is observed with either more or less equivalents of ligand. The results indicate that the activity of $[RuCp(MeCN)_3](PF_6)$ in the presence of amines is not solely due to the basic function of the ligands.

The mechanism of isomerization catalyzed by RuCp-complexes has been studied in the presence and absence of dienes. ^{31}P NMR spectra indicate that the resting state in the catalytic cycle is a complex in which 3-buten-2-ol is η^2-coordinated through the alkene moiety. This implies that coordination of the oxygen moiety and concomitant β-hydrogen abstraction is the rate-determining step. It has been shown that allylic alcohols bind stronger to RuCp-complexes than dienes. Inhibition of the allyl alcohol isomerization reaction must be a result of an interaction of the diene to a ruthenium–

allyl alcohol complex sufficiently strong to prevent coordination of the oxygen moiety of the allylic alcohol. This hinders orientation of the allylic alcohol substrate in a suitable way to undergo β-hydrogen abstraction, thereby blocking isomerization catalysis.

4. Experimental

4.1. General

Silver(I) salts, allylic alcohols, isoprene, phosphines, amines and other reagents were commercially available and used as received. Solvents were of reagent grade. The ligands 2-PPh_2py [29] and 2-PPh_2Etpy [30] and the complex [RuCp(MeCN)$_3$](PF_6) [31] were prepared according to the literature procedures. The syntheses of [RuClCp(dppe)] and [RuClCp(dppb)] are described elsewhere [17]. All syntheses and catalytic reactions were performed in an argon atmosphere using standard Schlenk techniques. Quantitative gas liquid chromatography analyzes was carried out on a Chrompack apparatus equipped with a CP Sil 5CB column (50 m × 0.4 μm) with toluene or anisole as internal standard. ^{1}H NMR spectra (199.5 MHz) were performed on a Jeol JNM 200 FTNMR spectrometer. Proton chemical shifts (δ) are reported in ppm relative to TMS ($\delta = 0$). ^{31}P{^{1}H}NMR spectra (121.5 MHz) were recorded on a Bruker DPX 300 spectrometer. Chemical shifts (δ) are reported in ppm relative to external 85% aqueous H_3PO_4 ($\delta = 0$). Mass spectra were recorded on a Finnigan MAT TSQ-70 equipped with a custom-made electrospray interface (ESI) in acetonitrile/water or methanol/water.

4.2. Formation of [RuCp(MeCN)(PPh_3)$_2$](PF_6) by in situ mixing of **1** and triphenylphosphine

In an NMR tube, **1** was mixed with two equivalents of triphenylphosphine at room temperature in $CDCl_3$. ^{1}H NMR ($CDCl_3$): δ = 7.5–7.3 (m, 30H, PPh_3), 4.43 (s, 5H, Cp), 2.12 (s, 3H, MeCN). ^{31}P NMR ($CDCl_3$): δ = 51.5. The signal for the PF_6 anion was outside the measured range ($\delta = -143.5$ [20]). ESI-MS: *m/z* 732 ([RuCp-(MeCN)(PPh_3)$_2$]$^+$), 691 ([RuCp(PPh_3)$_2$]$^+$), 510 ([RuCp-(MeCN)$_2$(PPh_3)]$^+$), 470 ([RuCp(MeCN)(PPh_3)]$^+$).

4.3. Formation of [RuCp(MeCN)(2-PPh_2py)$_2$](PF_6) by in situ mixing of **1** and 2-PPh_2py

In an NMR tube, **1** was mixed with two equivalents of 2-PPh_2py at room temperature in $CDCl_3$. ^{1}H NMR ($CDCl_3$): a qualitative description is given here; the different complexes have not been assigned nor have the integrals been ascertained. δ = 8.8 (d, minor, ArH), 8.7 (d, minor, ArH), 7.9–7.1 (m, major, ArH), 4.05 (s, minor, Cp), 4.4 (s, major, Cp), 2.12 (s, minor, MeCN), 2.0 (s, major, MeCN). ^{31}P NMR ($CDCl_3$): δ = 51.5 (major), 0.35 (minor). ESI MS: *m/z* 733 ([RuCp-(MeCN)(2-PPh_2py)$_2$]$^+$), 692 ([RuCp(2-PPh_2py)$_2$]$^+$), 512 ([RuCp-(MeCN)$_2$(2-PPh_2py)]$^+$), 471 ([RuCp(MeCN)-(2-PPh_2py)]$^+$).

4.4. Formation of [RuCp(MeCN)(2-PPh_2Etpy)$_2$](PF_6) by in situ mixing of **1** and 2-PPh_2Etpy

In an NMR tube, **1** was mixed with two equivalents of 2-PPh_2Etpy at room temperature in $CDCl_3$. ^{1}H NMR ($CDCl_3$): a qualitative description is given here; the different complexes have not been assigned nor have the integrals been ascertained. δ = 9.3 (d, major, ArH), 8.5 (d, minor, ArH), 7.8–7.1 (m, major, ArH), 4.45 (s, minor, Cp), 4.4 (s, major, Cp), 2.0 (s, major, MeCN). The signals for the bridge were observed in the range 3.5–0.8. ^{31}P NMR ($CDCl_3$): δ = 49 (major), 42.5 (d, ^2J(PP) = 49 Hz, minor), 38.2 (d, ^2J(PP) = 49 Hz, minor). ESI MS: *m/z* 748 ([RuCp(MeCN)(2-PPh_2Etpy)$_2$]$^+$), 499 ([RuCp(MeCN)$_2$(2- PPh_2Etpy)]$^+$), 458 ([RuCp-(MeCN)(2-PPh_2Etpy)]$^+$).

4.5. Reaction of **1** with two equivalents of pyridine and 3-buten-2-ol

In an NMR tube, **1** was mixed with two equivalents of pyridine at room temperature in $CDCl_3$. Next, 3-buten-2-ol was added and the tube was heated to 50 °C. ^{1}H NMR ($CDCl_3$): 8.77 (d, ArH), 8.57 (d, ArH), 8.24 (d, ArH), 7.8–7.7 (m, ArH), 7.38 (t, ArH), 7.33 (t, ArH), 7.22 (t, ArH), 4.22 (s, Cp), 2.42 (br s, MeCN), 2.0 (br s, MeCN). These peaks are in addition to the signals of 3-buten-2-ol and MEK. The three doublets and three triplets indicate the coexistence of three different pyridine-containing complexes.

4.6. Mass spectrometry on reaction mixture of [RuClCp(PPh_3)$_2$] with isoprene

A solution of [RuClCp(PPh_3)$_2$] in isoprene was refluxed for 2 h. ESI MS: *m/z* 497 ([RuCp(isoprene)-(PPh_3)]$^+$).

4.7. NMR experiments with [RuClCp(dppe)] and substrates with double bond moieties

To a solution of [RuClCp(dppe)] in $CDCl_3$ was added AgOTs (10% excess to ruthenium). Next, the substrate was added and after stirring, a ^{31}P NMR spectrum was recorded at room temperature. Recording at higher temperatures (up to 50 °C) resulted in analogous spectra. No other species were observed. ^{31}P NMR ($CDCl_3$): [RuCp(dppe)]$^+$: δ = 77.5. [RuCp(allyl alcohol)-(dppe)]$^+$: δ = 85.3 (d, 1P, ^2J (PP) = 21 Hz), 84.5 (d, 1P,

^2J (PP) = 21 Hz). *[RuCp(1-octene)(dppe)]*$^+$: δ = 83.5 (d, 1P, ^2J (PP) = 22 Hz), 82.9 (d, 1P, ^2J (PP) = 22 Hz), 77.5 ([RuCp(dppe)]$^+$, ca. 5%). *[RuCp(2-buten-1-ol)(dppe)]*$^+$: δ = 81.1 (d, 1P, ^2J (PP) = 22 Hz), 80.5 (d, 1P, ^2J (PP) = 22 Hz), 77.5 ([RuCp(dppe)]$^+$, ca. 50%). *[RuCp(isoprene)(dppe)]*$^+$: δ = 82.9 (d, 1P, ^2J (PP) = 22 Hz), 74.9 (d, 1P, ^2J (PP) = 22 Hz), 77.5 ([RuCp(dppe)]$^+$, ca. 50%).

4.8. Isomerization of 3-buten-2-ol to MEK

In a typical experiment, 3-buten-2-ol (46 mmol), a catalyst complex (0.008 mmol), a ligand if appropriate, AgOTs (0.010 mmol) if appropriate and anisole or toluene (3.7 mmol) were brought into a two-neck round bottom flask equipped with a reflux condenser and a septum. Next, the flask was lowered into a pre-heated oil bath of 100 °C. After one hour a sample was taken with an airtight syringe, and analyzed by ^{1}H NMR and/or GLC. In some cases, several samples were taken at certain time intervals (see text). In cases where isoprene was used, 2 ml (20 mmol) was added to the reaction mixture prior to heating.

4.9. X-ray crystallographic study of [RuClCp(dppb)]

Crystals of the compound suitable for X-ray analysis were obtained by vapour-phase diffusion of *n*-hexane into a toluene solution of [RuClCp(dppb)] at room temperature. Pertinent data for [RuClCp(dppb)]: $C_{33}H_{33}ClP_2Ru$, M_r = 628.05, colour orange, prism-shaped crystal (0.07 × 0.18 × 0.18 mm), monoclinic, space group $P2_1/c$ with a = 12.7294(12), b = 15.8421(12), c = 16.520(2) Å, β = 123.071(9)°, V = 2791.7(6) Å^3, Z = 4, D_c = 1.4943(3) g cm^3, μ(Mo Kα) = 0.79 mm^{-1}. 30990 Reflections were measured (6362 independent, R_{int} = 0.0363, 1.6° < θ < 27.5°, T = 150 K, Mo Kα radiation, graphite monochromator, λ = 0.71073 Å) on a Nonius-Kappa CCD diffractometer on rotating anode; no absorption correction was applied. The structure was solved by automated direct methods [32].

Hydrogen atoms were located on a difference Fourier map and their coordinates were introduced as parameters in the refinement. Hydrogen atoms were described with isotropic displacement parameters, all other atoms with anisotropic displacement parameters. Full-matrix least-squares refinement on F^2 [33] resulted in a final R_1 value of 0.0226 [for 5814 $I > 2(I)$], wR_2 = 0.0546, GoF = 1.043. Final residual density was in the range −0.54 to 0.40 e Å^3. Geometric calculations and molecular graphics were performed with the PLATON package [34].

Details on the crystal structure determination have been deposited at the Cambridge Crystallographic Data Centre (Deposition No. CCDC-251670) for [RuClCp(dppb)].

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Appendix A. Supplementary material

^{31}P NMR spectra of the reaction of [RuCp(PPh$_3$)$_2$]$^+$ with isoprene (Figure S1) and subsequently allyl alcohol (Figure S2). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2004.11.017.

References

[1] B.M. Trost, Acc. Chem. Res. 35 (2002) 695.
[2] R.C. Van der Drift, E. Bouwman, E. Drent, J. Organomet. Chem. 650 (2002) 1.
[3] R. Uma, C. Crevisy, R. Gree, Chem. Rev. 103 (2003) 27.
[4] Y.E. Raifeld, G.Y. Vid, I.E. Mikerin, B.M. Arshava, A.A. Nikitenko, Carbohydrate Res. 224 (1992) 103.
[5] H.M. Hull, R.G. Jones, D.W. Knight, J. Chem. Soc., Perkin Trans. 1 (1998) 1779.
[6] A. Krief, A.M. Laval, Bull. Soc. Chim. France 134 (1997) 869.
[7] R.E. Kirk, D.F. Othmer (Eds.), Encyclopedia of Chemical Technology, vol. 8, Wiley-Interscience, New York, 1995, p. 985.
[8] W. Neier, G. Strehlke, in: W. Foerst (Ed.), Ullmann's Encyclopaedia, vol. A4, VCH, München, 1985, p. 475.
[9] F. Stunnenberg, F.G.M. Niele, E. Drent, Inorg. Chim. Acta 222 (1994) 225.
[10] E. Drent, EP457387, 1991.
[11] R.C. Van der Drift, J.W. Sprengers, E. Bouwman, W.P. Mul, H. Kooijman, A.L. Spek, E. Drent, Eur. J. Inorg. Chem. (2002) 2147.
[12] R.C. Van der Drift, W.P. Mul, E. Bouwman, E. Drent, Chem. Commun. (2001) 2647.
[13] B.M. Trost, R.J. Kulawiec, Tetrahedron Lett. 32 (1991) 3039.
[14] B.M. Trost, R.J. Kulawiec, J. Am. Chem. Soc. 115 (1993) 2027.
[15] C. Slugovc, E. Ruba, R. Schmid, K. Kirchner, Organometallics 18 (1999) 4230.
[16] C. Slugovc, E. Ruba, R. Schmid, K. Kirchner, K. Mereiter, Monatsh Chem. 131 (2000) 1241.
[17] R.C. Van der Drift, M. Vailati, E. Bouwman, E. Drent, J. Mol. Catal. A 159 (2000) 163.
[18] V. Cadierno, S.E. Garcia-Garrido, J. Gimeno, Chem. Commun. (2004) 232.
[19] M.I. Bruce, C. Hameister, A.G. Swincer, R.C. Wallis, Inorg. Synth. 21 (1982) 78.
[20] E. Rüba, W. Simanko, K. Mauthner, K.M. Soldouzi, C. Slugovc, K. Mereiter, R. Schmid, K. Kirchner, Organometallics 18 (1999) 3843.
[21] In this paper, the following abbreviations for phosphine ligands have been used: dppm = 1,1-bis(diphenylphosphino)methane;

dppe = 1,2-bis(diphenylphosphino)ethane; dppb = 1,4-bis(diphenylphosphino)butane.
[22] W.H. Pearson, J.E. Shade, J.E. Brown, T.E. Bitterwolf, Acta Crystallogr., Part C 52 (1996) 1106.
[23] S. Suravajjala, L.C. Porter, Acta Crystalogr., Part C 49 (1993) 1456.
[24] The CCDC search for structures matching [$RuClCpP_2$] returned 16 complexes with didentate phosphorous ligands, of which 10 contained an all-carbon bridge and two phenyl groups at each phosphorus atom.
[25] H. Guan, M. Iimura, M.P. Magee, J.R. Norton, K.E. Janak, Organometallics 22 (2003) 4084.
[26] R.T. Morrison, R.N. Boyd, Allin and Bacon, Boston, 1976, p. 729 and 749.
[27] S.T. Howerd, J. Am. Chem. Soc. 118 (1996) 10269.
[28] J.-E. Bäckvall, U. Andreasson, Tetrahedron Lett. 34 (1993) 5459.
[29] T.J. Barder, F.A. Cotton, G.L. Powel, S.E. Tetrick, R.A. Walton, J. Am. Chem. Soc. 106 (1984) 1323.
[30] S.D. Toto, J.T. Doi, J. Org. Chem. 52 (1987) 4999.
[31] B.M. Trost, C.M. Older, Organometallics 21 (2002) 2544.
[32] G.M. Sheldrick, University of Göttingen, Germany, 1986.
[33] G.M. Sheldrick, University of Göttingen, Germany, 1997.
[34] A.L. Spek, J. Appl. Crystallogr. 36 (2003) 7.