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Catalytic allylation of phenols : chloride-free route towards epoxy resins

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Cationic ruthenium-Cp-diphosphine complexes as catalysts for the allylation of phenols with allyl alcohol

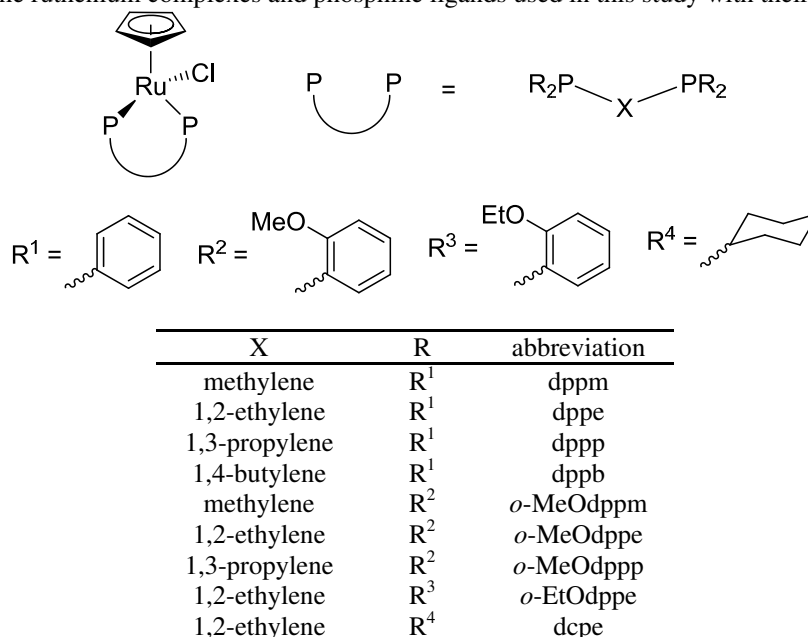
Abstract

A new catalytic method has been investigated to obtain either O- or C-allylated phenolic products using allyl alcohol or diallyl ether as the allyl donor. With the use of new cationic ruthenium(II) complexes as catalyst, both reactions can be performed with good selectivity. Active cationic Ru(II) complexes, having cyclopentadienyl and bidentate phosphine ligands are generated from the corresponding Ru(II) chloride complexes with a silver salt. The structures of three novel (diphosphine)Ru(II)CpCl catalyst precursor complexes are reported. It appears that the structure of the bidentate ligand has a major influence on catalytic activity as well as chemoselectivity. In addition, a strong cocatalytic effect of small amounts of acid is revealed. Model experiments are described that have been used to build a reaction network that explains the origin and evolution in time of both O-allylated and C-allylated phenolic products. Some mechanistic implications of the observed structure vs. performance relation of the [RuCp(diphosphine)]⁺ complexes and the cocatalytic role of added protons are discussed.

2.1 Introduction

For catalytic allylation reactions, allyl substrates with good leaving groups like carboxylate and halide have been employed in combination with ruthenium and palladium catalysts. In these reactions generally a stoichiometric amount of base is added to induce O-allylation, thereby producing inorganic salts as sideproducts.¹⁻³ In the context of the development of an environmentally benign catalytic route to epoxy resins, the O-allylation of phenols is desired.⁴ Allyl phenyl ethers can be epoxidized to obtain glycidyl ethers, which are currently produced on a multi-hundred kilotonne/year scale in the epoxy resin industry via the conventional epichlorohydrin route with the coproduction of stoichiometric amounts of chloride salt waste. From an environmental and atom-efficiency point of view it would be attractive to use allyl alcohol as the allyl donor, as only water is coproduced. However, the Pd systems for phenol allylation all use stoichiometric amounts of base [Ti(O*i*Pr)₄] to induce O-allylation,⁵ or Lewis acid (BEt₃) to promote C-allylation.⁶ With such Pd systems, electron-rich phenols such as 3,5-dimethoxyphenol and 1-naphthol were selectively C-allylated with allyl alcohol into 4-allyl-3,5-dimethoxyphenol and 2-allyl-1-naphthol, respectively, of which the latter does not require the use of a stoichiometric amount of base.^{5,7} In one example, C-allylation of phenols in an aqueous environment is induced by adding large amounts of base to the system.⁸ The yields in this system are very low. Using a Pd/Ti(O*i*Pr)₄ system, also aniline can be allylated with allyl alcohol.⁹ Although O-allylation of aliphatic alcohols was previously reported,¹⁰ phenols appeared to be much less reactive.

Only a few examples report catalytic allylation of phenols using allyl alcohol without the need of stoichiometric additives, which are based on ruthenium catalysts.^{11,12} Pregosin and co-workers have described a system that is able to C-allylate phenols.¹¹ Finally, a CpRu(diphosphine) system was reported earlier with which both O- and C-allylated products were formed. It was proposed that under the applied reaction conditions a thermal uncatalyzed Claisen rearrangement of O-allylated product occurred resulting in a mixture of O- and C-allylated products.¹² In the present chapter, the influence of the diphosphine ligand (Table 2.1)

Table 2.1. The ruthenium complexes and phosphine ligands used in this study with their abbreviations.

in cationic Ru(II) Cp complexes on their performance in the catalytic allylation of 4-*tert*-butylphenol with allyl alcohol is explored. It will be shown that chemoselectivity of cationic RuCp(diphosphine) complexes, in situ produced from the corresponding neutral Ru chloride precursor by addition of AgOTs (in the absence of AgOTs hardly any activity is observed), is decisively controlled by the diphosphine ligand. In particular, it will be shown that the steric properties of the diphosphine ligand are also critically important for the Ru-catalyzed conversion of the O-allylated product into thermodynamically more favourable C-allylated products. In addition, evidence will be given of a strong cocatalytic effect of small amounts of added acid, not only on the rate, but surprisingly also on the course of the allylation reactions.

2.2 Results and discussion

2.2.1 Synthesis

The new ruthenium complexes were successfully synthesized by displacement of the monodentate triphenylphosphine in [RuCpCl(PPh₃)₂] with bidentate phosphine ligands, with complex yields in the range of 80–85%. Reaction temperatures below 100 °C were used in the synthesis of the complexes with the ligands bearing *ortho*-substituents on the phenyl rings. When higher temperatures were used, methyl chloride or ethyl chloride was eliminated from the complex, resulting in a chelating phenolate group.¹³ For the unsubstituted ligands, a slight excess of ligand was used to ensure complete conversion of the starting material. The excess of ligand and the displaced triphenylphosphine could be easily separated from the product by

flushing the reaction mixture over a small silica gel column with toluene. The orange product band is immobile when toluene is used as the eluents and it can be eluted with ethyl acetate. Exactly one equivalent of the ortho-substituted ligands compared to ruthenium was used, as it proved to be difficult to remove excess of ligand from the mixture, either by flash silica gel chromatography or crystallization. All complexes have been characterized with ^1H - and ^{31}P NMR spectroscopy and elemental analysis.

2.2.2 Crystal Structures

The molecular structures of $[\text{RuCpCl}(o\text{-EtOdppe})]$, $[\text{RuCpCl}(o\text{-MeOdppm})]$ and $[\text{RuCpCl}(o\text{-MeOdppp})]$ are shown in Figure 2.1. Selected bond distances and angles are listed in Table 2.2. The binding of the ruthenium ion to the bidentate phosphine ligand is slightly asymmetrical in $[\text{RuCpCl}(o\text{-EtOdppe})]$ and $[\text{RuCpCl}(o\text{-MeOdppp})]$, while in $[\text{RuCpCl}(o\text{-MeOdppm})]$ the Ru–P distances are equal. The distances of the ruthenium centre to the cyclopentadienyl group and the chloride anion are similar for all three compounds and are comparable to those of related ruthenium complexes.¹⁴⁻¹⁷ The distance of the oxygen atoms O(17) and O(47) to Ru is too large [3.7932(17)–4.2351(14) Å] for all of the structures to be considered as an interaction, however, they are close enough to sterically block the metal centre. The two other oxygen atoms, O(27) and O(37), are relatively far away from the ruthenium atom [5.1764(15)–5.3428(13) Å]. The P...O distances are smaller than the sum of the van-der-Waals radii. The bite angles of the phosphine ligands very clearly reflect the

Table 2.2. Selected bond lengths and angles for the complexes $[\text{RuCpCl}(o\text{-EtOdppe})]$ (a), $[\text{RuCpCl}(o\text{-MeOdppm})]$ (b) and $[\text{RuCpCl}(o\text{-MeOdppp})]$ (c).

	(a)	(b)	(c)
<i>Bond distances (Å)</i>			
Ru(1)-Cl(2)	2.4456(13)	2.4363(5)	2.4653(4)
Ru(1)-P(3)	2.2711(16)	2.2947(4)	2.2967(4)
Ru(1)-P(7)	2.2958(14)	2.2926(4)	2.2644(4)
Ru(1)-Cp	1.8395(5)	1.8386(2)	1.8449(1)
Ru(1)...O(17)	4.094(4)	3.7975(14)	3.8416(13)
Ru(1)...O(47)	3.927(4)	3.7932(17)	5.2343(15)
Ru(1)...O(27)	5.260(4)	5.2606(16)	5.3428(13)
Ru(1)...O(37)	5.298(3)	5.1764(15)	4.2351(14)
P(3)...O(17)	2.967(5)	2.9073(13)	2.9365(13)
O(17)...O(27)	3.443(6)	4.649(2)	3.7891(19)
O(37)...O(47)	4.174(5)	4.760(2)	3.176(2)
<i>Angles (°)</i>			
P(3)-Ru(1)-P(7)	83.43(6)	72.145(16)	92.591(15)
P(3)-Ru(1)-Cl(2)	86.10(5)	90.147(16)	85.646(15)
P(7)-Ru(1)-Cl(2)	91.55(5)	90.131(16)	86.753(15)

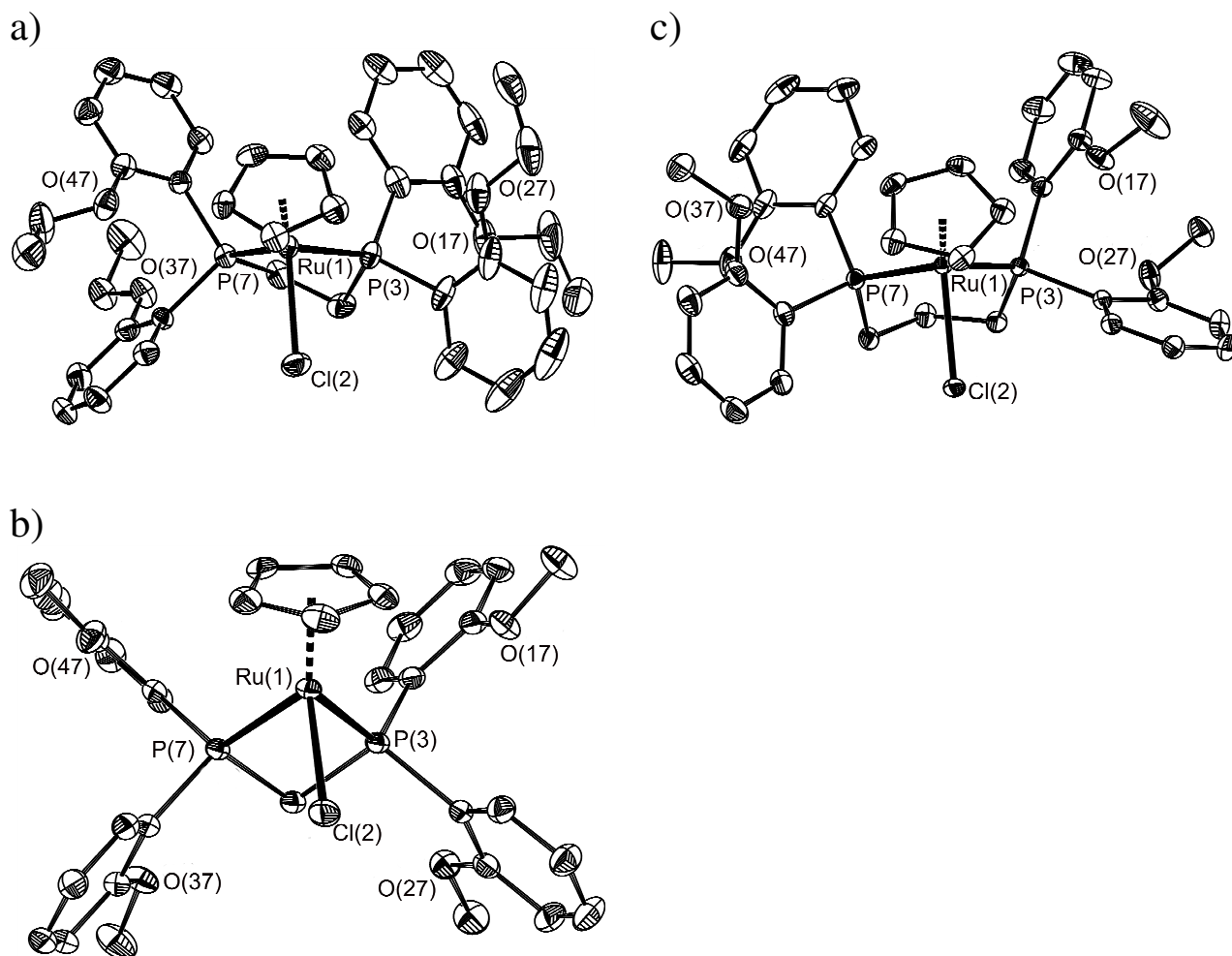
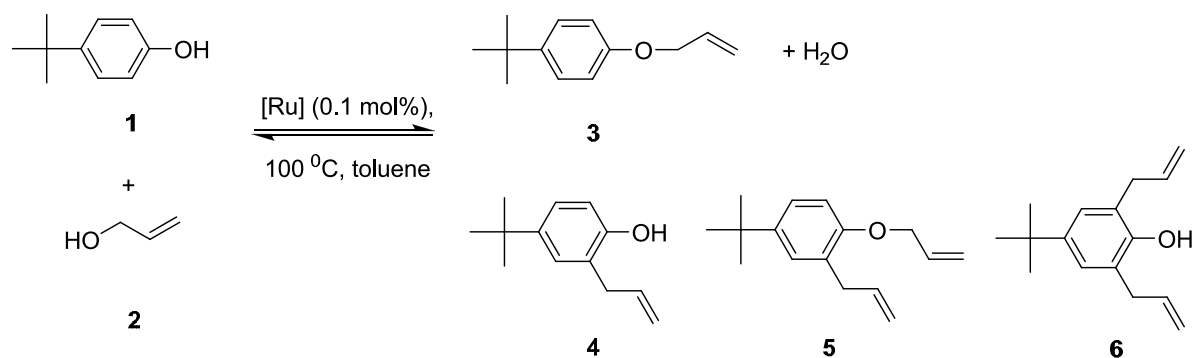


Figure 2.1. Displacement ellipsoid plots of a) $[\text{RuCpCl}(o\text{-EtOdppe})]$, b) $[\text{RuCpCl}(o\text{-MeOdppm})]$ and c) $[\text{RuCpCl}(o\text{-MeOdppp})]$ with the adopted atom labelling. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms are omitted for clarity. The (disordered) solvent molecules in the structure of $[\text{RuCpCl}(o\text{-MeOdppm})]$ are not shown.

increase of the carbon chain bridge in these three complexes, going from 72 via 83 to 93° for the methylene, ethylene and propylene bridges, respectively.

2.2.3 Catalytic Allylation

The complexes were tested in the reaction shown in Scheme 2.1. A low catalyst loading of 0.1 mol% was used at a temperature of 100 °C. Apart from the O-allylated product **3**, the C-allylated products **4–6** were observed (Scheme 2.1). The products were isolated and characterized by NMR and GC/MS. The evolution of phenol-derived products in a typical experiment, using $[\text{RuCp}(o\text{-EtOdppe})](\text{OTs})$ as catalyst precursor, is shown in Figure 2.2. From this it can be seen that in the first 30 min the formation of O-allylated product **3** is very rapid, however, after about one hour the amount of **3** starts to decrease in time. A similar (but less pronounced) concentration profile is observed for **5**.



Scheme 2.1. Model reaction of 4-*tert*-butylphenol **1** and allyl alcohol **2** catalyzed by ruthenium complexes showing the multiple of phenol-derived products **3-6**.

The concentration of C-allylphenols **4** and **6** steadily increases in time. After long reaction times (>12 h) almost only the C-allylated products **4** and **6** are observed. These concentration profiles thus indicate that the growth of **4** and **6** occurs at the cost of respectively **3** and **5** by a consecutive reaction. Apparently, **4** and **6** are the thermodynamic end products.¹⁸

After the first hour, the conversion of phenol hardly changes, however, the product composition changes in a major way. It thus appeared that the selectivity of the phenol allylation reaction to the respective products (**3-6**) is reaction time-dependent, but the product composition also strongly depends on the structure of the Ru catalyst used. The results for a series of Ru phosphine complexes are listed in Table 2.3; some clear trends can be observed.

Looking at the phosphines with unsubstituted phenyl groups, there is an optimum in activity with a 1,2-ethylene bridging group in the ligand. [RuCp(dppm)](OTs) (entry 1) is more than an order of magnitude less active ($k = 0.06\text{ h}^{-1}$) than [RuCp(dppe)](OTs) (entry 2, $k = 1.19\text{ h}^{-1}$),¹⁹ while the high selectivity for the C-allylated product **4** with the small bite-angle ($\sim 72^\circ$) dppm ligand is remarkable. This suggests that the formation of the C-allylated product requires a relatively large free coordination space at Ru for this reaction to occur. Increasing

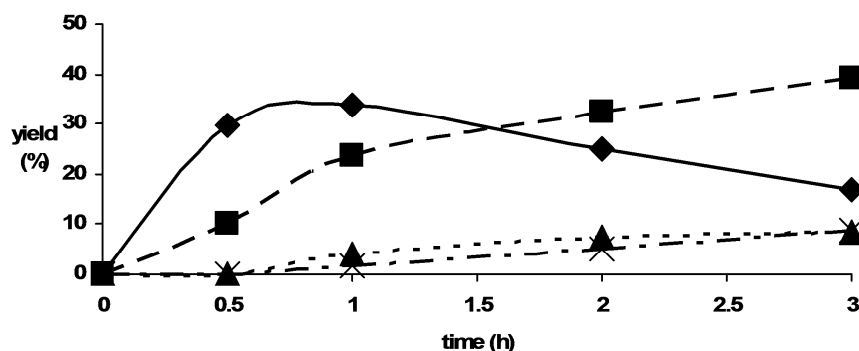


Figure 2.2. Formation of phenol-derived products in the reaction of 4-*tert*-butylphenol with allyl alcohol in time in a typical experiment; (\blacklozenge) **3** (\blacksquare) **4** (\blacktriangle) **5** (\times) **6**. Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/[RuCp(*o*-EtOdppe)]/AgOTs = 1000/1000/1/2, toluene, 100 °C. 5 mmol of phenol was used.

Table 2.3. Reaction of 4-*tert*-butylphenol (**1**) with allyl alcohol (**2**) catalyzed by different [RuCp(PP)]⁺ complexes. ^a

entry	RuCp(PP) PP =	conversion of 1			k ^c (h ⁻¹)	selectivity (%)							
		conversion of 1				3	4	3		4		5	6
		0.5 h	1 h	3h				0.5 h ^e	1 h ^e	3 h			
1	dppm	3	7	21	0.06	8	92	3	89	2	93	2	3
2	dppe	45	56	72	1.19	47	47	38	53	4	56	12	28
3	dppp	24	42	53	0.55	80	20	70	30	44	47	6	3
4	dppb ^b	0	0	0	0	-	-	-	-	-	-	-	-
5	PPh ₃ ^b	0	0	0	0	-	-	-	-	-	-	-	-
6	dcpe	4	10	34	0.08	81	19	76	18	76	22	1	1
7	<i>o</i> -MeOdppm	6	15	39	0.12	13	84	7	90	4	90	0	6
8	<i>o</i> -MeOdppe	44	53	60	1.15	58	42	39	51	12	74	5	9
9	<i>o</i> -EtOdpe	40	63	73	1.02	67	33	53	38	23	54	11	12
10	<i>o</i> -MeOdppp	0	7	21	0.07	-	-	99	1	87	13	0	0
11	<i>o</i> -EtOdppe ^d	80	84	87	3.22	92	8	81	13	53	20	18	9

^a Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/[Ru]/AgOTs = 1000/1000/1/2, toluene, 100 °C.

^b active in the isomerization of allyl alcohol into propanal.

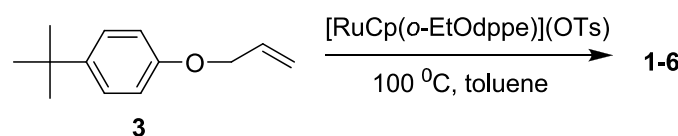
^c after 0.5 h

^d with diallyl ether instead of allyl alcohol.

^e in cases **3** and **4** do not add up to 100%, the remainder is product **5** and **6**

the bridge length from 1,2-ethylene to 1,3-propylene (bite angles respectively ~83° and 92°) leads to a decrease in activity (entry 3, $k=0.55\text{ h}^{-1}$), but with a significant increase in selectivity for O-allylation. In contrast, with a 1,4-butylene bridge (bite angle 94°, entry 4), all activity for allylation is lost. Instead, the complex appears active in the isomerization of allyl alcohol into propanal. The complex with two monodentate phosphine ligands (entry 5) is a very active catalyst in this isomerization reaction, in agreement with a prior report,²⁰ and shows no activity at all towards allylation. When the phenyl groups of the thus far most active dppe complex are replaced by cyclohexyl groups, the initial activity drops considerably (from $k=1.19\text{ h}^{-1}$ to $k=0.08\text{ h}^{-1}$), but the selectivity for O-allylation increases significantly from 40% to 76% (entry 6).

When the phenyl groups of the phosphines are substituted with ortho-methoxy groups, a similar reactivity pattern is observed. [RuCp(*o*-MeOdppm)](OTs) (entry 7) is, like its unsubstituted analogue, very selective in the formation of C-allylated product **4**. There is again an optimum in activity with an ethylene bridging group (entries 8 and 9). The complexes with a methylene or 1,2-ethylene bridge in the ligand (entry 7–9) show a similar or higher activity compared to their unsubstituted analogues (entry 1 and 2). The [RuCp(*o*-MeOdppp)](OTs) complex, however (entry 10), unexpectedly is considerably less active than its unsubstituted analogue, but it is highly selective for the formation of **3**. Having a very similar activity as the catalyst based on dppm (entry 1), the contrast in chemoselectivity is remarkable. Finally, not only allyl alcohol can be used as allylating agent, but also diallyl ether (entry 11). In all reactions diallyl ether is formed initially from allylation of allyl alcohol itself, forming water in the process. The diallyl ether further reacts with **1** to form **3–6**. It

Table 2.4. Reaction of **3** in the presence of [RuCp(*o*-EtOdppe)](OTs) and different additives.^a


entry	additives	conversion of 3 (%)	selectivity (%)			
			1	4	5	6
1	-	0	0	0	0	0
2	H ₂ O ^b	99	20	55	3	22
3	<i>p</i> -cresol ^c	92	40	54	2	4
4	HOTs ^d	86	33	40	3	24
5	camphor sulfonic acid	49	28	44	21	7

^a Reaction conditions: ratio **3**/[RuCpCl(*o*-EtOdppe)]/AgOTs = 1000/1/2, 100 °C, 2 h. If added, additives in ratio **3**/H₂O/cresol/HX = 1000/1000/1000/2

^b after 18 h

^c yields are total of both 4-*tert*-butylphenol and *p*-cresol derived products

^d HOTs = *p*-toluenesulfonic acid

appears that the activity and selectivity of the catalyst are highly enhanced if diallyl ether is used as the allyl source, possibly because less water is formed.

2.2.4 Reactivity of Allyl Ethers

An intriguing aspect of the evolution of products in the course of the reaction shown in Figure 2.2, is the question by which mechanism the concentration of initially formed O-allylated products **3** (and **5**) decrease at longer reaction times, while in parallel C-allylated products **4** (and **6**) steadily increase. As it is observed that diallyl ether can also be used as allylating agent as a substitute for allyl alcohol, it was suspected that the product ether **3** itself would also show reactivity towards the catalyst. Thus, phenyl allyl ether **3** was exposed to several conditions and additives to investigate its reactivity both under thermal conditions in the absence of the ruthenium catalyst as well as under prevailing catalytic conditions. The results are given in Table 2.4. When **3** is exposed to allylation reaction conditions with any of the reagents present in a typical reaction mixture, but in the absence of a catalyst, no reaction is observed, thus excluding the possibility of a thermal Claisen-type rearrangement. Adding only [RuCp(*o*-EtOdppe)](OTs) to **3** in toluene also gives no conversion (entry 1). In contrast, when both the Ru catalyst and a stoichiometric quantity of water with respect to **3** are present, compound **3** is fully converted in 18 h to give 4-*tert*-butylphenol, allyl alcohol, and C-allylated products **4–6** (entry 2). Under these conditions conversion of **3** takes place only after an induction period of several hours. However, when a stoichiometric amount of *p*-cresol is added, a conversion of **3** of 92% is observed after only two hours residence time; not only products **4–6**, but also the analogous *p*-cresol-derived allylation products are formed as well

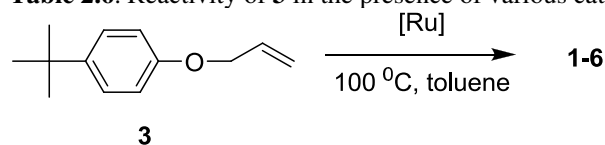
as 4-*tert*-butylphenol by transesterification. At this stage it is hypothesized that the added *p*-cresol – or likewise the 4-*tert*-butylphenol generated by the hydrolysis of **3**, – would function as an acidic cocatalyst, and have a devastating effect on the selectivity for O-allylation to give C-allylation instead. Therefore, the activated Ru catalyst is supplemented with a catalytic amount of hydrated *p*-toluenesulfonic acid (HOTs·xH₂O) and observed that **3** was now reacted to form **1** and products **4–6** with a conversion of 86% in only two hours. When this reaction is performed with a catalytic amount of camphorsulfonic acid under strictly anhydrous conditions (entry 5), a conversion of **3** of 49% after two hours is achieved to give again a mixture of products **1–6**. It should be noted that the combined amount of **5** and **6** is equal to the amount of **1**, since the total number of allyl moieties remains constant. In summary, in the presence of Ru catalyst and water, hydrolysis of **3** to phenol **1** and allyl alcohol **2** can take place, showing that O-allylation is a reversible reaction that is thermodynamically limited. The conversion to O-allylated product in a batch allylation process will thus be limited by the concentration of water in the reaction medium at reaction temperature. However, the utilization of an apolar solvent such as toluene allows the reaction to proceed beyond its thermodynamic equilibrium as the solubility of water in the reaction medium is low and water will form a separate phase. In order to prevent the reversed reaction of **3** in a batch process, an experiment was executed in which water was removed from the system by means of a Dean–Stark trap. A conversion of 85% with a selectivity towards O-allylated product **3** of 80% was observed after 30 min. An initial catalyst TOF of about 1700 h⁻¹ was thus achieved. For the reaction of the phenol **1** and allyl alcohol **2** with [RuCp(*o*-EtOdppe)](OTs) as catalyst, it was found that adding catalytic amounts of a Brønsted acid affects both the selectivity and the rate of the reaction. When a catalytic amount (2 equivalents on Ru-complex) of strong acid in the form of HOTs is added the rate of the reaction increases in a dramatic way to an initial turnover frequency of 6200 h⁻¹ in the first 5 min, while for this catalytic system the selectivity completely shifts towards C-allylation. For the acidic system in the absence of Ru complex, no activity is observed, excluding the possibility of an acid-catalyzed reaction.

Table 2.5. Reaction of 4-*tert*-butylphenol (**1**) with allyl alcohol (**2**) catalyzed by different [RuCp(PP)]⁺ complexes in the presence of added HOTs.^a

entry	RuCp(PP) PP =	conversion of 1 (%)			k (h ⁻¹)	selectivity (%)							
		0.5 h	1 h	3h		0.5 h ^b		1 h ^b		3 h			
						3	4	3	4	3	4	5	6
1	dppm	26	47	64	0.60	100	0	80	20	44	48	4	4
2	dppe	65	65	66	2.10	0	85	0	85	0	84	0	16
3	dppp	70	74	80	2.41	35	47	24	52	2	69	4	25
4	dppb	19	44	58	0.42	100	0	100	0	83	13	4	0

^a Reaction conditions: ratio 4-*tert*-butylphenol/allyl alcohol/[Ru]/AgOTs/HOTs = 1000/1000/1/2/2, toluene, 100 °C (reaction shown in Scheme 1)

^b in the cases that **3** and **4** do not add up to 100, the remainder is product **5** and **6**

Table 2.6. Reactivity of **3** in the presence of various catalysts [RuCp(PP)](OTs) and added HOTs.^a

entry	RuCp (PP) PP=	conversion of 3 (%)		selectivity (%) ^b			
		1 h	3 h	1	4	5	6
1	dppm	7	17	28	36	21	15
2	dppe	79	88	26	42	6	26
3	dppp	86	97	26	45	3	26
4	dppb	2	2	1	99	0	0

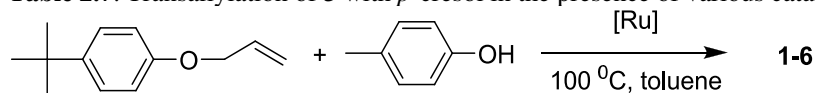
^a Reaction conditions: ratio **3**/[Ru]/AgOTs/HOTs = 1000/1/2/2, 100 °C

^b after 3 h

2.2.5 Catalyst Performance vs. Catalyst Structure

The effect of acid addition was also studied for CpRu(PP) complexes in the direct allylation of **1** with **2** (Table 2.5; to be compared to Table 2.3). The product development graphs for the reactions given in Table 5 are given in the Supporting Information. The rate of the allylation reaction for all four catalysts is strongly enhanced by the addition of two equivalents of HOTs (Table 2.5). The effect of acid on the selectivity of the reaction is not the same for all catalysts. For [RuCp(dppe)](OTs) and [RuCp(dppp)](OTs) the selectivity shifts towards C-allylation. Unexpectedly, for [RuCp(dppm)](OTs), O-allylation becomes favored, with an initial selectivity of 100% for **3** after 30 min. Surprisingly, also [RuCp(dppb)](OTs) becomes active for O-allylation. The isomerization of allyl alcohol into propanal, observed with this catalyst under neutral conditions, is apparently blocked by addition of acid. This latter observation could be rationalized by the fact that the formation of a Ru(II)-allyl alcoholate intermediate, being the first step in the isomerization reaction,¹² is suppressed in acidic conditions.

The reaction of **3** into **1–6** with these four catalysts in the presence of added HOTs was also investigated (Table 2.6). [RuCp(dppm)](OTs) shows only low conversion of **3** into C-

Table 2.7. Transallylation of **3** with *p*-cresol in the presence of various catalysts [RuCp(PP)](OTs).^a

entry	RuCp (PP) PP=	Conversion of 3 (%)				selectivity (%) ^b	
		1 h	3 h	1	4	5	6
1	dppm	0	0	-	-	-	-
2	dppe	99	99	50	50	0	0
3	dppp	80	91	50	50	0	0
4	dppb	19	49	49 ^c	0	0	0

^a Reagents and conditions: ratio **3**/*p*-cresol/[Ru]/AgOTs = 1000/1000/1/2, 100 °C

^b after 3 h; yields are total of both *tert*-butylphenol and *p*-cresol derived products

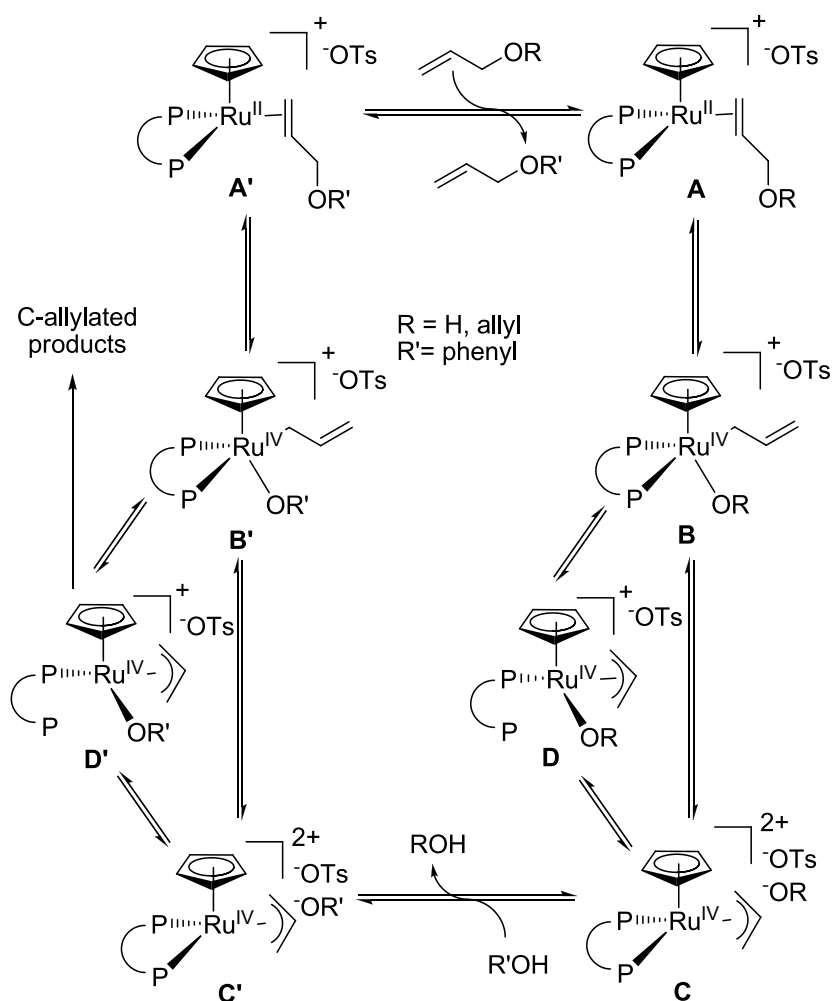
^c remaining 51% = *t*-Buphenyl and *p*-cresyl allyl ethers

allylated products, while [RuCp(dppb)](OTs) appears to be hardly active at all. In contrast, [RuCp(dppe)](OTs) and [RuCp(dppp)](OTs) are very active for the conversion of **3** to C-allylated products.

The apparent unreactivity of **3** with [RuCp(dppm)](OTs) and [RuCp(dppb)](OTs), prompted us to investigate the transallylation of **3** with *p*-cresol in the absence of additional acid (Table 2.7). For [RuCp(dppm)](OTs) the reactivity is extremely low. As expected, [RuCp(dppe)](OTs) and [RuCp(dppp)](OTs) behave very similar to [RuCp(*o*-EtOdpe)](OTs) and rapidly produce a large quantity of C-allylated products. Surprisingly, [RuCp(dppb)](OTs) in the presence of acid is quite active in the transallylation of **3** with *p*-cresol, but is only producing O-allylated products. Apparently, for this catalyst C-allylation is blocked; only after longer reaction times (6–18 h) do C-allylated products slowly appear. Apparently, the result from Table 2.6, entry 4, should be interpreted such that this catalyst is reactive with **3**, but rapidly regenerates it again in the absence of other phenol moieties.

2.2.6 Mechanistic Considerations

It is well-known that the activation of allyl-X (X= halide, carboxylates, alkoxide, etc) substrates by L₂CpRu(II)X complexes in allylation reactions proceeds via oxidative addition to give intermediate L_nCpRu(IV)(allyl)X₂ complexes (n=1 for σ-allyl, n=0 for π-allyl).²¹ The initially formed product of oxidative addition appeared to be a σ-allyl species which only after dissociation of a phosphine or CO ligand converted into the thermodynamically more stable π-allyl species. Reasoning along these lines with allyl alcohol as substrate in the present study, its oxidative addition in [Ru(II)Cp(PP)(allyl alcohol)](OTs) (Scheme 2.2, A, R = H) will initially produce [(PP)CpRu(IV)(σ-allyl)OH](OTs) (B, R = H). When σ- to π-allyl rearrangement occurs, to prevent a 20- electron species either a π-allyl dicationic complex (C)

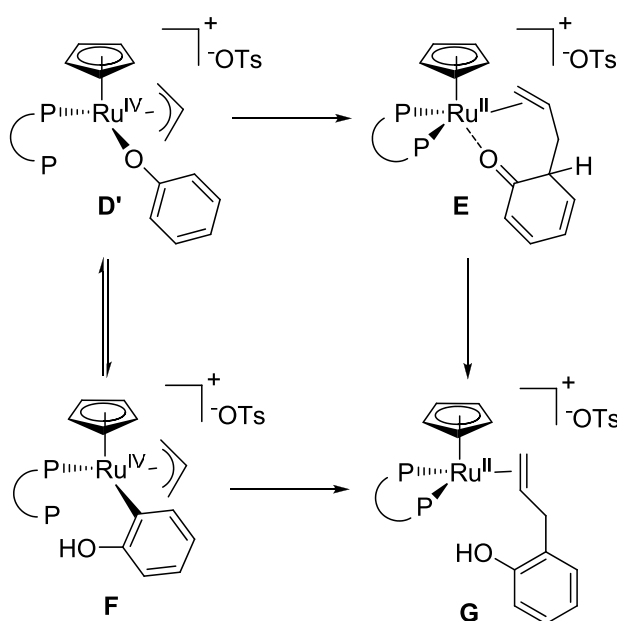


Scheme 2.2. Proposed catalytic cycle for allylation. **B**, **C**, **D** ($R = \text{H}$, allyl) and **B'**, **C'**, **D'** ($R = \text{phenyl}$) are isomeric 18-electron species formed after oxidative addition.

is formed, or a phosphine must dissociate (**D**). Displacement of the hydroxide anion by phenolate in an acid-base reaction from species **C** will be fast and results in the species $[(\text{PP})\text{CpRu}(\text{IV})(\pi\text{-allyl})](\text{phenolate})(\text{OTs})$ (**C'**, $R' = \text{Ph}$) while H_2O is coproduced. Due to the coordinating nature of the phenolate anion, strongly attracted to the positively charged $\text{Ru}(\text{IV})$, either species **B'** or **D'** will be formed. After reductive elimination, $\text{Ru}(\text{II})$ -bound product is obtained (**A'**) or C-allylated products are irreversibly formed. Complexes of type **B**, **C** and **D** must play a central role in the reaction network of all possible allylation reactions. A third possibility is reductive elimination of the phenyl allyl ether **3** from **B'**, **C'** or **D'** ($R' = \text{Ph}$), a step that is also reversible. The final option is the irreversible formation of the C-allylated product **4**. Likewise, the products **5** and **6** can be formed starting from **4** and allyl alcohol. When **4** is present in a significant concentration, exchange of phenolates could occur in intermediates **B'**, **C'** and **D'**. The occurrence of exchange also rationalizes the observations in Table 2.4 and Table 2.6 that reaction products **5** + **6** are produced in stoichiometric amounts on **1**; these products can only be formed when phenolate **1** is exchanged for

phenolate **4**, regenerating **1** in the process. Since the O-allylation steps all are reversible while formation of the C-allylated products is irreversible, all initially formed phenyl ether products can thus eventually be converted, if a sufficient amount of **2** is available, into fully C-allylated product **6** as is observed after long reaction times (e.g., 18 h).

A σ - π allyl interconversion of the (PP)CpRu(IV)allyl phenolate complex (Scheme 2, **B'**, for R'=Ph) will be dependent on the chelating strength of PP, which is expected to decrease in the order dppp > dppe > dppm. O-Allylated product **3** will be formed from **B'** (for R'=Ph) in a microscopic analogous reverse of the oxidative addition of allyl alcohol **2** to complex **A'** (for R'=Ph). However, C-allylation is generally thought to proceed via π -allyl species. For instance, C-allylation catalyzed by [Cp*Ru(IV)(MeCN)₂(π -allyl)]²⁺ complexes was proposed to proceed via Friedel–Crafts-type attack of the π -allyl moiety of these strongly electrophilic complexes at phenol.¹¹ Based upon the observed dependence of the allylation selectivity on the structure of the applied phosphine bidentate ligand and its chelating strength, a hypothesis that C-allylation also requires activation of the phenol via its O-atom at ruthenium is favored (Scheme 2.3). If the isomeric π -allyl species **C'** and **D'** are more abundantly present, due to weak chelation or space around ruthenium, reductive elimination of O-allylated product will be relatively slow, as this proceeds via the σ -allyl intermediate **B'**. It is proposed that C-allylated products are formed starting from intermediate **D'** (Scheme 2.3). The mechanism could proceed via an intramolecular Friedel–Crafts reaction, in which the phenolate ring has to reorientate in the same plane as the allyl group, and for which sufficient space around



Scheme 2.3. Proposed mechanism for C-allylated products via either Friedel–Craft or *ortho*-metallation.

ruthenium is needed, forming species **E** (Scheme 2.3). After tautomerization the C-allylated product is formed (**G**). Another mechanism could proceed via an ortho-metallation-type reaction, for which space around ruthenium is also required in order to activate the C-H bond, forming species **F**; after reductive elimination species **G** is then formed.

2.2.7 Effect of the Acid

The working hypothesis is thus summarized: more free coordination space at Ru is required for C-allylation. Therefore weakly chelating and/or small bite angle phosphine ligands give more selective catalysts for C-allylation, whereas stronger chelating, and/or larger bite angle ligands give catalysts which show higher selectivity for O-allylation. The rate-determining step in the allylation reaction with allyl alcohol is generally proposed to involve the oxidative addition of allyl alcohol, as OH is considered to be a poor leaving group.¹¹ Often intermediate protonation of allyl alcohol is implicated to increase the reactivity of allyl alcohol for allylation reactions.^{10,11,22,23} The strong increase in allylation reaction rate observed with addition of a catalytic quantity of a strong acid such as HOTs (Table 2.5), can thus be explained by protonation of the allyl alcohol, making H₂O the better leaving group. By the same reasoning, the protonation of the allyl ether **3** at the phenoxy group, makes the phenol a good leaving group, thus rationalizing the promoting effect of acid on the rate of activation of allyl ether **3** (Table 2.6). A strongly electrophilic, dicationic [(PP)CpRu(IV)(π -allyl)]²⁺ species (type **C**) is created and phosphine dissociation is not necessary to form the stable, resting state π -allyl species. Phenol may assist in the oxidative addition, perhaps as a proton donor or otherwise in hydrogen bonding and a concerted mechanism, as is clear from the transallylation results shown in Table 2.4. However, the oxidative addition also occurs in the presence of much weaker acids, such as 1-octanol. In both cases, the addition of a strong acid results in a strongly increased rate of reaction. The dramatic change in the reactivity of the catalyst [RuCp(dppb)]⁺ upon addition of acid is indicative of a change in the formed intermediate. It has been reported that oxidative addition of allyl alcohol in the absence of acid does take place, the reaction medium becoming more basic,²⁴ which supports our theory on initial hydroxyl anion formation. The microscopic reverse of the acid-catalyzed oxidative addition of phenyl allyl ether, that is, the formation of **3** by coordination of phenol to the Ru(IV) centre via (concerted) deprotonation and reductive elimination of **3** is expected to be more facile and thus occurs with higher rate in the presence of acid. As the rates of the reactions shown in Scheme 2.3 towards either species **E** or **F** are expected to be relatively

insensitive to acid, it can be rationalized that even with small bite angle dppm as well as the large bite angle ligand dppb an increased selectivity for O-allylation is observed in the presence of a catalytic quantity of acid. However, the cause of this increased selectivity is different for the two catalysts. While [RuCp(dppm)](OTs) undergoes the oxidative addition of allyl alcohol with a slightly higher rate than that of **3** (still being slow for both), [RuCp(dppb)](OTs) performs the oxidative addition of **3** in a higher rate, however, it is hardly able to produce C-allylated products. The complexes [RuCp(dppe)](OTs) and [RuCp(dppp)](OTs) react in such a high rate, that whereas oxidative addition of **3** as well as the reductive elimination to **3** has become more facile, the high rate of C-allylation with these catalysts makes that the reaction rapidly proceeds to the thermodynamic sink of C-allylated products.

2.3 Conclusions

In summary, a catalytic system has been developed that can catalyze both O- as well as C-allylation of phenols, without the need of any stoichiometric amounts of additives. It was shown that the O-allylated products are reversibly formed, while C-allylated products are produced irreversibly. Small quantities of an acid can fulfil a strong rate-promoting role. It is proposed that protons strongly reduce the activation barriers for oxidative addition and reductive elimination at the RuCp(PP) centre, for both of the substrate allyl alcohol as well as product allyl ether compounds. It has been unambiguously demonstrated that a Ru-catalyzed conversion of O-allylated products to the thermodynamically more favourable C-allylated products may readily occur under allylation conditions. Thus, C-allylated products can ultimately be catalytically produced in high yield by allylation of phenols with allyl alcohol. The efficiency of the consecutive C-allylation is, however, strongly dependent on the structural characteristics of the Ru complex as appears from the results given in Table 2.3. It appears that restricted coordination space at the ruthenium centre favours the formation of the O-allylated product, while sufficient space, either due to weak chelation and/or small bite angle, favours C-allylation. The addition of catalytic amounts of acid strongly promotes the rate of the reaction. The chelate strength plays a less dominant role in the acidic system, because the bidentate phosphine is less likely to dissociate and thus the bite angle seems to be determining selectivity.

2.4 Experimental

General remarks. All reactions were performed under an argon atmosphere using standard Schlenk techniques. Solvents were dried and distilled by standard procedures and stored under argon. The phosphine ligands dppm, dppe, dppp, dppb, dcpe, and triphenylphosphine were commercially available and used as received. The synthesis of the substituted phosphine ligands *o*-MeOdppm,²⁵ *o*-MeOdppe,²⁶ *o*-MeOdppp,²⁷ and *o*-EtOdppe²⁸ has been previously reported in literature. RuCl₃·3H₂O (Johnson & Matthey) was used as received. [RuCpCl(PPh₃)₂],¹⁴ [RuCpCl(dcpe)],²⁹ [RuCpCl(dppm)],¹⁵ [RuCpCl(dppe)],¹⁶ [RuCpCl(dppp)], [RuCpCl(dppb)],³⁰ [and [RuCpCl(*o*-MeOdppe)]¹² were prepared according to literature procedures. C,H,N,S analyses were performed on a Perkin Elmer 2400 Series II analyzer.

NMR Experiments. ¹H NMR spectra (300 MHz), and ³¹P{¹H}NMR spectra (121.4MHz) were measured on a Bruker DPX-300. Chemical shifts are reported in ppm. Proton chemical shifts are relative to TMS, and phosphorus chemical shifts are relative to 85% aqueous H₃PO₄. The spectra were taken at room temperature.

General procedure for RuCpCl(PP) synthesis. A solution of RuCpCl(PPh₃)₂ (72 mg, 0.1 mmol) and the bidentate phosphine ligand (0.1 mmol) in 5 ml toluene was stirred for 16 h at 90 °C. The solution was cooled to room temperature and flushed over a column of silica gel (3 g, d = 1 cm) with 15 ml of toluene to remove the triphenylphosphine. Finally, the orange product was eluted with ethyl acetate until the eluents was colorless. The solution was then concentrated in *vacuo* to approximately 1 ml and the product precipitated with petroleum ether.

RuCpCl(*o*-EtOdppe) was obtained as a yellow / orange solid in a yield of 63 mg (81%). Crystals suitable for X-ray diffraction were obtained by slow diffusion of n-hexane into a solution of the complex in toluene. Anal. Calcd for C₃₉H₄₅ClO₄P₂Ru·0.5(toluene): C, 62.07; H, 6.01. Found: C, 61.76; H, 5.99. ¹H-NMR (CDCl₃): δ 8.20-8.11 (m, 2H, ArH), 7.24-7.17 (m, 4H, ArH), 6.99 (t, 2H, *J* = 7 Hz, ArH), 6.96 (bs, 2H, ArH), 6.69-6.61 (m, 6H, ArH), 4.56 (s, 5H, Cp), 3.69-3.56 (m, 8H, OCH₂), 2.63 (m, 4H, CH₂), 0.85 (t, 6H, *J* = 7 Hz, CH₃), 0.77 (t, 6H, *J* = 7 Hz, CH₃). ³¹P{¹H}-NMR (CDCl₃): δ 68.1.

RuCpCl(*o*-MeOdppm) was obtained as an orange solid in a yield of 58 mg (82%). Crystals suitable for X-ray diffraction were obtained by slow diffusion of n-hexane into a solution of the complex in toluene. Anal. Calcd for C₃₄H₃₅ClO₄P₂Ru·1.5(water): C, 53.94; H, 5.06. Found: C, 54.09; H, 4.96. ¹H-NMR (CDCl₃): δ 8.05 (d, 2H, *J* = 5 Hz, ArH), 7.60-7.54 (m, 4H, ArH), 7.28-7.14 (m, 4H, ArH), 6.96-6.75 (m, 6H, ArH), 4.50 (s, 5H, Cp), 3.65 (s, 6H, OMe), 3.62 (s, 6H, OMe), 2.77 (s, 2H, CH₂). ³¹P{¹H}-NMR (acetone-d₆): δ 4.1.

RuCpCl(*o*-MeOdppp) was obtained as a yellow solid in a yield of 52 mg (71%). Crystals suitable for X-ray diffraction were obtained by slow diffusion of n-hexane into a solution of the complex in toluene. Anal. Calcd for C₃₆H₃₉ClO₄P₂Ru·1.33(toluene): C, 63.53; H, 5.84. Found: C, 63.90, H, 5.39. ¹H-NMR (CDCl₃): δ 7.36-7.29 (m, 4H, ArH), 7.04-6.99 (m, 4H, ArH), 6.82 (t, 4H, *J* = 7 Hz, ArH), 6.65-6.61 (m, 4H, ArH), 4.28 (s, 5H, Cp), 3.36 (s, 6H, OMe), 3.27 (s, 6H, OMe), 2.8-2.4 (br m, 6H, CH₂). ³¹P{¹H}-NMR (acetone-d₆): δ 40.2.

General procedure for catalytic reactions. 5 mmol of 4-*tert*-butylphenol (or in some experiments 4-*tert*-butylphenyl allyl ether), 0.005 mmol of the ruthenium complex, 0.01 mmol of AgOTs and, if indicated, 0.01 mmol of additive were charged into the reaction vessel

and flushed with argon. Degassed and dried toluene was added (5 ml) and the mixture was stirred for five minutes. Allyl alcohol (or diallyl ether) was added (5-10 mmol) and the reaction was stirred for 3 hours at 100 °C. Samples were taken at certain time intervals with an airtight syringe and analyzed by gas chromatography. To isolate and characterize compounds **3-6**, preparative HPLC purification was performed for selected experiments; the isolated yields corresponded with the yields found by GC. The NMR and mass spectra of the products **3-6** were in agreement with the data found in literature.³¹

GLC method. Quantitative gas liquid chromatography analyses were carried out on a Varian CP-3800 apparatus equipped with a VF-1ms (25 m × 0.25 mm) column with decane as internal standard. The temperature gradient used was: isothermal for 5 minutes at 40 °C, heating 10 °C/ minute to 250 °C and finally isothermal for 5 minutes at 250 °C.

X-ray crystal structure determinations. X-ray intensities were measured on a Nonius Kappa CCD diffractometer with rotating anode (graphite monochromator, $\lambda = 0.71073 \text{ \AA}$) up to a resolution of $(\sin \theta/\lambda)_{\max} = 0.65 \text{ \AA}^{-1}$ at a temperature of 150 K. The structures were solved with automated Patterson methods (program DIRDIF-99³²). Refinement was performed with

Table 2.8. Crystal data and structure refinement for the complexes RuCpCl(*o*-EtOdppe), RuCpCl(*o*-MeOdppm) and RuCpCl(*o*-MeOdppp).

	RuCpCl(<i>o</i>-EtOdppe)	RuCpCl(<i>o</i>-MeOdppm)	RuCpCl(<i>o</i>-MeOdppp)
formula	C ₃₉ H ₄₅ ClO ₄ P ₂ Ru	C ₃₄ H ₃₅ ClO ₄ P ₂ Ru · C ₇ H ₈ + disordered solvent	C ₃₆ H ₃₉ ClO ₄ P ₂ Ru
fw	776.21	798.21 [*]	734.13
crystal colour	orange	orange	yellow
crystal size [mm ³]	0.21 x 0.15 x 0.12	0.30 x 0.27 x 0.24	0.30 x 0.15 x 0.12
crystal system	orthorhombic	triclinic	triclinic
space group	Pna2 ₁ (no. 33)	P $\bar{1}$ (no. 2)	P $\bar{1}$ (no. 2)
a [Å]	26.5195(11)	12.14373(15)	10.08714(17)
b [Å]	12.5266(2)	13.22525(15)	11.00266(14)
c [Å]	11.0325(4)	14.98261(17)	15.7896(3)
α [°]	-	66.472(1)	73.742(1)
β [°]	-	79.779(1)	85.868(1)
γ [Å ³]	-	65.088(1)	80.460(1)
V [Å ³]	3665.0(2)	2000.82(5)	1658.47(5)
Z	4	2	2
D _x [g/cm ³]	1.407	1.325 [*]	1.470
μ [mm ⁻¹]	0.627	0.576 [*]	0.688
abs. corr. method	none	multi-scan	multi-scan
abs. corr. range	-	0.69 – 0.87	0.70 – 0.92
refl. (meas./unique)	41239 / 8439	27030 / 8759	24452 / 7567
param./restraints	439 / 3	466 / 0	421 / 0
R1/wR2	0.0498 / 0.0861	0.0287 / 0.0801	0.0227 / 0.0520
[I > 2 σ (I)]			
R1/wR2 [all refl.]	0.0859 / 0.0999	0.0321 / 0.0822	0.0283 / 0.0541
S	1.105	1.050	1.069
Flack parameter	-0.06(4)	-	-
$\rho_{\min/\max}$ [e/Å ³]	-0.72 / 0.88	-0.79 / 0.95	-0.47 / 0.37

[*] Derived parameters do not contain the contribution of the disordered solvent.

SHELXL-97³³ against F^2 of all reflections. Geometry calculations, illustrations, and checking for higher symmetry was performed with the PLATON program.³⁴

The crystal of [RuCpCl(*o*-EtOdppe)] was cracked into two fragments. The orientation matrices of both fragments were taken into account during intensity integration with the program EvalCCD.³⁵ Refinement was performed on a HKLF5 file.³⁶ Hydrogen atoms were introduced in calculated positions and refined with a riding model. One ethyl group was refined with a disorder model.

The crystal of [RuCpCl(*o*-MeOdppm)] contained large voids (211.6 Å³ / unit cell) filled with disordered solvent molecules. Their contribution to the structure factors was secured by back-Fourier transformation using the SQUEEZE routine of the program PLATON,³⁴ resulting in 22 electrons / unit cell. Hydrogen atoms were introduced in calculated positions. The hydrogen atoms of the Cp-ligand were refined freely with isotropic displacement parameters; all other hydrogen atoms were refined with a riding model.

In [RuCpCl(*o*-MeOdppp)] hydrogen atoms were introduced in calculated positions. The hydrogen atoms of the Cp-ligand were refined freely with isotropic displacement parameters; all other hydrogen atoms were refined with a riding model. Relevant crystal structure and refinement data are provided in Table 2.8.

2.5 References

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