Homogeneous Catalysis

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Ruthenium(IV) Complexes Featuring P,O-Chelating Ligands: Regioselective Substitution Directly from Allylic Alcohols**

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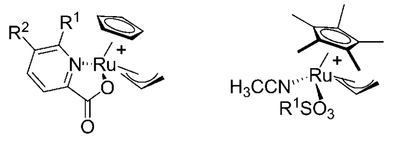
Transition metal catalyzed regioselective C- and O-allylation reaction is a powerful tool to access chiral branched compounds.[1] In particular, ruthenium complexes featuring [Ru(Cp*)] and [Ru(Cp)] (Cp* = η_5-C_5Me_5, Cp = cyclopentadienyl) moieties have received special attention in allylation reactions, as some of them are able to promote the selective formation of branched or linear products directly from allylic alcohols with water as the only by-product.[2–4] Therefore, several new ruthenium(IV) complexes have emerged as efficient precatalysts to achieve these transformations. However, in most reports branched-type products were obtained from branched allylic alcohol substrates, whereas the use of linear starting substrates resulted in a loss of selectivity.[5] Recently, monocationic [Ru^{IV}(Cp)]-based catalysts containing a five-membered pyridine-2-carboxylato N,O chelate have been successfully used,[2] and even applied in an enantioselective intramolecular allylation thereby avoiding the selectivity issue (Figure 1).[2c] Dicationic [Ru(Cp*)(allyl)(MeCN)$_2$]$^{2+}$ complexes[3a,b] and catalytic systems generated from [Ru(Cp*)(CH$_3$CN)$_3$]PF$_6$ (**A**) in the presence of sulfonic acid derivatives represent other types of catalyst precursors used with success in regioselective C allylation (Figure 1).[5,6] In contrast, P,O chelates have received less attention. A notable example has been reported for [Ru$_3$(CO)$_{12}$] and diphenylphosphino benzoic acid (DPPBA; **1a**) to afford a ruthenium(II) [Ru(π-allyl)(CO)$_2$(κ^2-DPPBz)] (DPPBz = diphenylphosphino benzoate) complex featuring a six-membered P,O chelate, which allowed linear allylation of nucleophiles from allyl acetates.[7] To the best of our knowledge, anionic phosphine monosulfonate ligands[8] have never been applied in allylation reactions with ruthenium. These ligands have been widely used because of their water solubility properties, and have found applications in copolymerization processes with ethylene involving palladium and nickel as transition metals.[9] They have also been applied to hydroformylations employing rhodium[10] and to palladium-catalyzed Heck coupling reaction.[11]



Kitamura[2]
isolated complexes

Pregosin[6b]
proposed active species

Figure 1. Active complexes in substitution from allyl alcohol derivatives.

Herein, we report the synthesis of novel ruthenium(IV) allyl complexes bearing DPPBz and diphenylphosphinobenzene sulfonate (DPPBS) ligands, and their catalytic activities in regioselective allylation reactions of various nucleophiles, starting from both branched and linear allylic derivatives are compared.

Reaction of [Ru(Cp*)(CH$_3$CN)$_3$]PF$_6$ (**A**)[12] with ligand **1a** in the presence of crotyl alcohol **2a** using dichloromethane as the solvent gave the Ru^{IV} complex **B**, bearing the six-membered ring P,O chelate, in an excellent 90% yield (Scheme 1). Surprisingly, the reaction of **A** with *o*-diphenylphosphinobenzenesulfonic acid ligand **1b** did not afford the analogous complex **C** (see Scheme 2), but led to the formation of the allylphoshonium salt **3a**, and the starting ruthenium complex **A** was recovered regardless of the solvent used. However, in the absence of **A**, no allylphosphonium salt **3a** was formed at room temperature, indicating that a ruthenium-catalyzed allylation of **1b** was involved.

We believe the difference in the reactivities between **1a** and **1b** is related to the zwitterionic nature of **1b** and to the stability of the corresponding ruthenium(IV) species under acidic conditions. Therefore, to avoid the presence of acid, treatment of compound **1b** with potassium *tert*-butoxide in methanol and then successive addition of **A** and allyl chloride **4a** afforded the expected complex **C** in 80% yield after crystallization (Scheme 2).

The solid-state structure of complex **B** clearly demonstrates that the phosphino carboxylate coordinates as a bidentate ligand through both the phosphorous and oxygen atoms. The allyl moiety shows an *endo* configuration and a *cis* relationship between the methyl substituent and the carboxylate moiety (Figure 2).[13] As observed in most ruth-

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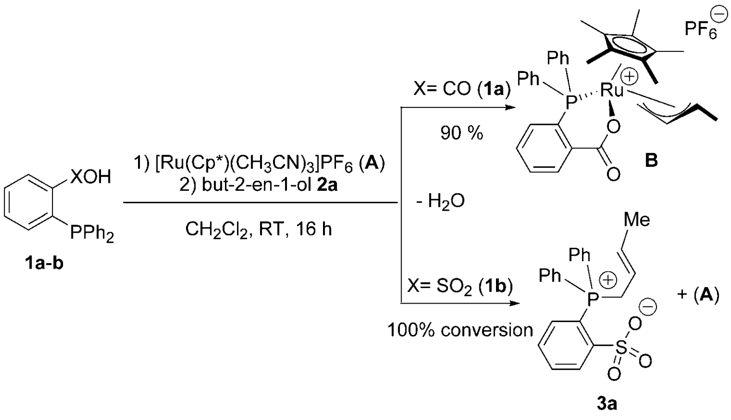
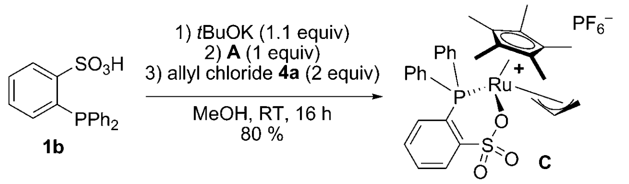


Scheme 1. Reactivity of $[Ru(Cp^*)(CH_3CN)_3]PF_6$ (**A**) with **1a** and **1b**.



Scheme 2. Preparation of complex **C**.

enium(IV) complexes bearing an unsymmetrical allylic ligand, the distance from the ruthenium center to the substituted carbon atom of the allylic ligand is longer than that to the terminal CH_2 group, leading to a distorted π-allyl ligand coordination.[14]

Structural information on the complex **C** was also provided by the X-ray diffraction study which showed the ruthenium atom to be coordinated by the P,O chelate (Figure 3).[15] Whereas the half-chair conformation of the six-membered metallacycle was found to be *exo* for **B**, the structure of **C** revealed an *endo* conformation. Notably, the ruthenium complex **C** is closely related to the active species $[RuCp^*(RSO_3)(allyl)(MeCN)][RSO_3]$ proposed by Pregosin and coworkers when they used [**A** + RSO_3H] as a catalyst precursor (Figure 1).[6b]

With these complexes in hand, we performed a comparative study of complexes **B** and **C** as precatalysts for the O allylation of *p*-methoxyphenol (**5a**) in the presence of cinnamyl chloride (**4b**; Table 1). Reaction with **B** appeared to be regioselective, thereby favoring the branched product, and the best result was obtained using dimethyl carbonate (DMC) as the solvent; this reaction led to a branched/linear

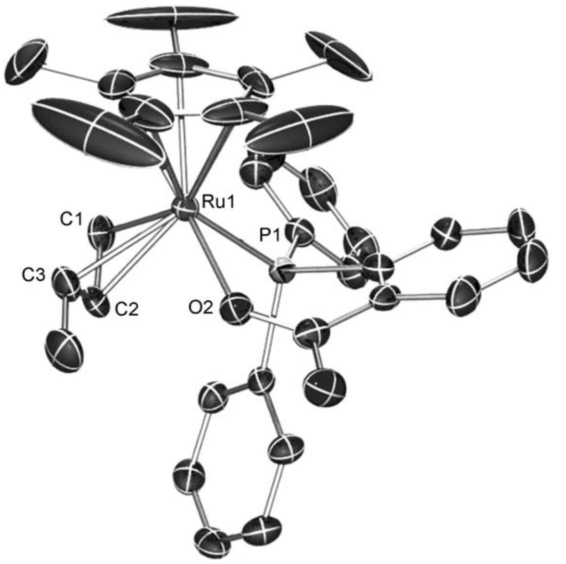


Figure 2. Thermal ellipsoids diagram (50%) of **B**·MeOH. All hydrogen atoms, MeOH, and the PF_6 moiety are omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru(1)–O(2) 2.096, Ru(1)–P(1) 2.374, Ru(1)–C(1) 2.203, Ru(1)–C(2) 2.184, Ru(1)–C(3) 2.316, C(1)–C(2) 1.427, C(2)–C(3) 1.383; O(2)-Ru(1)-P(1) 76.82, C(1)-Ru(1)-C(3) 64.51.

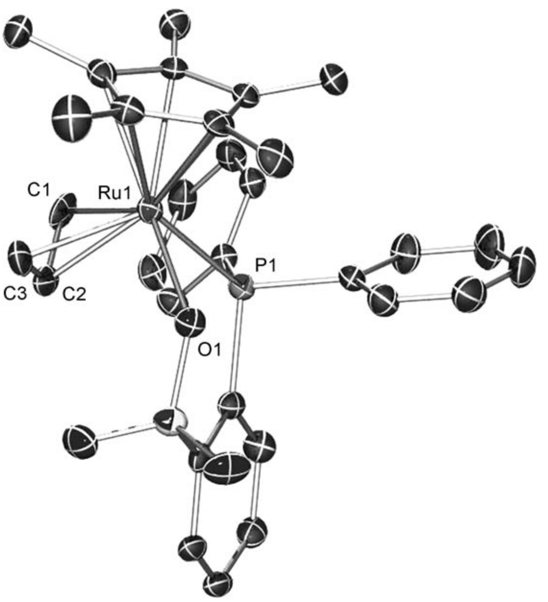
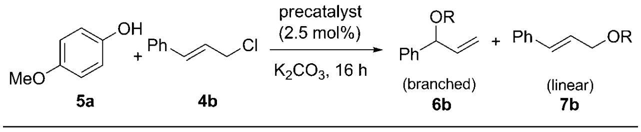


Figure 3. Thermal ellipsoids diagram (50%) of **C**. All hydrogen atoms and the PF_6 moiety are omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru(1)–O(1) 2.136, Ru(1)–P(1) 2.421, Ru(1)–C(1) 2.224, Ru(1)–C(2) 2.162, Ru(1)–C(3) 2.225, C(1)–C(2) 1.407, C(2)–C(3) 1.386; O(1)-Ru(1)-P(1) 77.10, C(1)-Ru(1)-C(3) 64.32.

Table 1: O Allylation of **5a** with cinnamyl chloride **4b**.[a]



Entries	Catalyst	Solvent	*T* [°C]	**6b**/**7b**[b]	Yield [%][c]
1	**B**	CH_3CN	40	86:14	77
2	**B**	CH_2Cl_2	40	81:19	71
3	**B**	DMC	40	94:6	93
4	**C**	CH_3CN	RT	98:2	95
5	**C**	CH_2Cl_2	RT	97:3	95

[a] All reactions were carried out at 0.08 M concentration in specified solvent for 16 h under inert atmosphere with **4b**/**5a**/[Ru]/K_2CO_3 in 1.1:1:0.025:1.1 molar ratio. [b] Ratio determined by ^1H NMR analysis of the crude reaction mixture. [c] Yield of isolated products.

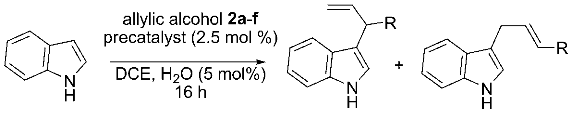
(**6b**/**7b**) ratio of up to 94:6 (Table 1, entry 3). Notably, moderate heating was necessary to achieve full conversion of the starting material **5a** (Table 1, entries 1–3), thereby highlighting the lower activity which results from the presence of the electron-rich phosphine as compared with our previous results based on analogous ruthenium precatalysts featuring an N,O chelate.[16] The presence of the more electron-deficient sulfonate moiety in **C** was expected to lead to more reactive ruthenium species and indeed, good reactivity and regioselectivity were obtained at room temperature using either acetonitrile or dichloromethane (Table 1, entries 4 and 5).[6b] Moreover, the reaction was faster and full conversion of **5a** occurred within six hours in dichloromethane. In the presence of precatalyst **A** or **C**, no reaction occurred when an allylphosphonium was treated with **5a**, which tends to demonstrate that the cationic complex **C** is the active species during the allylation reactions.[17]

We then explored the reactivity of various allylic alcohols **2** in the C allylation of indole **8** (Table 2). When the indole **8** was treated with 1.2 equivalents of allyl alcohol **2c** in the presence of **B** at 60 °C, 3-allylindole (**9c**) was obtained in 85 % yield (Table 2, entry 1). Interestingly, **C** gave the same product **9c**, even at room temperature and it was isolated in 83 % yield (Table 2, entry 2).

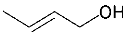
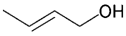
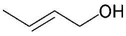
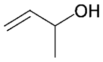
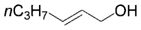
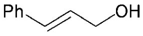
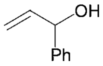
The scope of this catalytic reaction was then evaluated starting from various allylic alcohols. For substituted allyl alcohols the reaction was carried out at 60 °C with an additional catalytic amount of **1b** (6 mol %), to ensure complete conversion within 16 hours, and in the presence of water to avoid diallyl ether formation as a side reaction. Therefore, reaction of but-3-en-2-ol (**2d**) or crotyl alcohol **2a** in the presence of an extra catalytic amount of **1b** afforded the branched 3-allylated compound **9a** in good yield with excellent regioselectivity (Table 2, entries 3 and 4). The other purely aliphatic linear hex-2-en-1-ol (**2e**) also led to the branched product with remarkable regioselectivity in favor of **9e** (Table 2, entry 5).

The reaction of the branched and linear isomers of cinnamyl alcohol **2b** and vinyl benzyl alcohol **2f** proceeded smoothly, giving a regioselectivity of up to 98:2 (Table 2, entries 6, 7). The use of a tertiary alcohol such as dimethyl vinyl methanol (**2g**) resulted in the formation of the branched product **9g** as the major compound (Scheme 3).

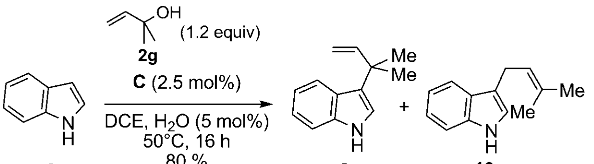
Table 2: Regioselective allylation of indole with allylic alcohols **2a**–**f**.[a]



8 **9a-c,e** **10a-c,e**

Entry	Catalyst	*T* [°C]	Alcohol **2**		**9**/**10**[b]	R	Product (yield)[c]
1	**B**	60		**2c**	–	H	**9c** (85 %)
2	**C**	25		**2c**	–	H	**9c** (83 %)
3[d]	**C**	60		**2a**	97:3	Me	**9a** (84 %)
4[d]	**C**	60		**2d**	99:1	Me	**9a** (88 %)
5[d]	**C**	60		**2e**	98:2	*n*Pr	**9e** (91 %)
6[d]	**C**	60		**2b**	97:3	Ph	**9b** (85 %)
7[d]	**C**	60		**2f**	98:2	Ph	**9b** (88 %)

[a] All reactions were carried out at 0.08 M concentration in 1,2-dichloroethane for 16 h under inert atmosphere with **2**/**8**/[Ru] in 1.2/1/0.025 molar ratio. [b] Ratio determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Major product and yield of isolated product. [d] Reactions were performed with **C**/**1b** in 0.025:0.06 molar ratio.



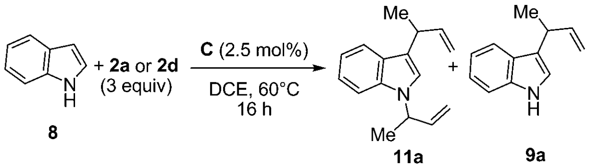
8 **9g** **10g**

95 : 5

Scheme 3. Regioselective allylation of **8** with tertiary alcohol **2g**. DCE = 1,2-dichloroethane.

For these reactions we propose that the benefit of a catalytic excess of ligand **1b** might result from its ability to facilitate the allyl formation through alcohol protonation, but we cannot exclude a possible counteranion exchange for complex **C** (PF_6^- to sulfonate), which would lead to the formation of dicationic allyl ruthenium diphosphine species.[4,18] This new catalytic system is highly regioselective for the formation of branched products starting from either branched or linear allylic alcohols. It represents a complementary catalytic system to previous ones, which were either unreactive or much less regioselective, especially when starting from linear substrates.[5,6a]

The difference of reactivity between linear and branched starting allyl alcohols **2** was next investigated for the diallylation of **8** in the presence of an excess amount of alcohol. Therefore, the reaction of **8** in the presence of three equivalents of crotyl alcohol **2a** and a catalytic amount of **C** resulted in the complete consumption of the indole **8** to afford mono C-allylated compound **9a** and a small amount of diallylated product **11a** (Scheme 4). However, the use of the branched allylic alcohol **2d** gave the diallylated product **11a** as the major compound with a high level of regioselectivity in favor of the dibranched product. The double allylation of indoles at the same position has been reported, but only starting from allyl alcohol itself leading to only one possible product corresponding to N-allylated **9c**. For comparison, a



8 **11a** **9a**

from **2a**: yields : 8% 83%
2d: yields : 75% 11%

Scheme 4. Allylation of **8** from linear and branched allyl alcohols. Yields shown are those of isolated products.

similar reaction of **8** with allyl alcohol **2c** afforded 90% of diallylated compound with traces of mono 3-allylindole **9c**.

In conclusion, we have reported the preparation and structural characterization of new ruthenium(IV) complexes featuring P,O-chelating ligands. The cationic $[\mathrm{Ru(Cp^*)(\pi\text{-}C_3H_5)(\widehat{PSO_2O})}]$ **C** has been shown to be an active precatalyst for regioselective allylation reactions either with allylic chlorides or alcohols. Excellent regioselectivities for the formation of branched products were obtained starting from branched, but also, more gratifyingly from linear allylic alcohols. The first example of doubly regioselective disubstitution of indole at the N1- and C3-positions leading to the dibranched diallylated indole is presented.

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Keywords: allylic compounds · homogeneous catalysis · phosphorus · P,O chelate · ruthenium

[1] a) *Comprehensive Organic Synthesis*, *Vol. 4* (Eds.: S. A. Godleski, B. M. Trost, I. Fleming), Pergamon, New York, **1991**, pp. 585–661; b) J. Tsuji, *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*, Wiley, Chichester, **2000**, p. 109; c) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921; d) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336.

[2] a) H. Saburi, S. Tanaka, M. Kitamura, *Angew. Chem.* **2005**, *117*, 1758; *Angew. Chem. Int. Ed.* **2005**, *44*, 1730; b) S. Tanaka, H. Saburi, M. Kitamura, *Adv. Synth. Catal.* **2006**, *348*, 375; c) S. Tanaka, T. Seki, M. Kitamura, *Angew. Chem.* **2009**, *121*, 9110; *Angew. Chem. Int. Ed.* **2009**, *48*, 8948.

[3] a) A. B. Zaitsev, S. Gruber, P. S. Pregosin, *Chem. Commun.* **2007**, 4692; b) S. Gruber, A. B. Zaitsev, M. Wörle, P. S. Pregosin, *Organometallics* **2008**, *27*, 3796; c) I. F. Nieves, D. Schott, S. Gruber, P. S. Pregosin, *Helv. Chim. Acta* **2007**, *90*, 271.

[4] a) J. A. van Rijn, M. Lutz, L. S. von Chrzanowski, A. L. Spek, E. Bouwman, E. Drent, *Adv. Synth. Catal.* **2009**, *351*, 1637; b) J. A. van Rijn, M. A. Siegler, A. L. Spek, E. Bouwman, E. Drent, *Organometallics* **2009**, asap.

[5] see supporting information: A. B. Zaitsev, S. Gruber, P. A. Plüss, P. S. Pregosin, L. F. Veiros, M. Wörle, *J. Am. Chem. Soc.* **2008**, *130*, 11604.

[6] a) A. B. Zaitsev, H. F. Caldwell, P. S. Pregosin, L. F. Veiros, *Chem. Eur. J.* **2009**, *15*, 6468; b) S. Gruber, A. B. Zaitsev, M. Wörle, P. S. Pregosin, *Organometallics* **2009**, *28*, 3437.

[7] a) M. Kawatsura, F. Ata, S. Wada, S. Hayase, H. Uno, T. Itoh, *Chem. Commun.* **2007**, 298; b) M. Kawatsura, F. Ata, T. Hirakawa, S. Hayase, T. Itoh, *Tetrahedron Lett.* **2008**, *49*, 4873.

[8] a) A. T. Brandvold, US Pat. US5760286, **1998**; b) E. Drent, W. Sjardijn, J. C. L. J. Suykerbuyk, K. Wanninger, World Pat. 00/06615, **2000**; c) W. Weng, Z. Shen, R. F. Jordan, *J. Am. Chem. Soc.* **2007**, *129*, 15450.

[9] For selected references see: a) E. Drent, R. van Dijk, R. van Ginkel, B. van Oort, R. I. Pugh, *Chem. Commun.* **2002**, 744; b) W. Weng, Z. Shen, R. F. Jordan, *J. Am. Chem. Soc.* **2007**, *129*, 15450; c) T. Kochi, S. Noda, K. Yoshimura, K. Nosaki, *J. Am. Chem. Soc.* **2007**, *129*, 8948; d) L. Betucci, C. Bianchini, C. Claver, E. J. Garcia Suarez, A. Ruiz, A. Meli, W. Oberhauser, *Dalton Trans.* **2007**, 5590; e) S. Liu, S. Borkar, D. Newsham, H. Yennawar, A. Sen, *Organometallics* **2007**, *26*, 210; f) A. Nakamura, K. Munakata, T. Kochi, K. Nozaki, *J. Am. Chem. Soc.* **2008**, *130*, 81128.

[10] L. Bettucci, C. Bianchini, A. Meli, W. Oberhauser, *J. Mol. Catal. A* **2008**, *291*, 57.

[11] T. Schultz, A. Pfaltz, *Synthesis* **2005**, 1005.

[12] a) A. M. McNair, D. C. Boyd, K. R. Mann, *Organometallics* **1986**, *5*, 303; b) B. M. Trost, P. L. Fraisse, Z. T. Ball, *Angew. Chem.* **2002**, *114*, 1101; *Angew. Chem. Int. Ed.* **2002**, *41*, 1059.

[13] Crystal data: $\mathrm{C_{34}H_{40}F_6O_3P_2Ru}$, $M_r = 773.67$, orthorhombic, space group $P2_12_12_1$, $Z = 4$, $a = 9.4887(2)$ Å, $b = 10.9680(2)$ Å, $c = 32.3709(5)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $U = 3368.91(11)$ Å^3, $T = 150(1)$ K, $F(000) = 1584$, $\mathrm{Mo_{K\alpha}}$ radiation ($\lambda = 0.71073$ Å), $\mu = 0.627\ \mathrm{mm^{-1}}$, 26050 reflexions measured in the range $2.65 \le \theta \le 26.99$, 26050 unique,($R_{\mathrm{int}}$=0.0296) which were used in all calculations. The structure was refined by using full-matrix least-squares on F^2 to $R_1 = 0.0299$, $wR_2 = 0.0681$, $S = 0.989$, for 7257 reflections ($> 2\sigma$) and 437 refined parameters, R_1(all data) 0.0360, wR_2(all data) = 0.0693, goodness-of-fit on $F^2 = 0.989$. CCDC 727698 (**B**·MeOH) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[14] a) C. Bruneau, J.-L. Renaud, B. Demerseman, *Chem. Eur. J.* **2006**, *12*, 5178; b) R. Hermatschweiler, I. Fernandez, P. S. Pregosin, E. J. Watson, A. Albinati, S. Rizzato, L. F. Veiros, M. J. Calhorda, *Organometallics* **2005**, *24*, 1809.

[15] Crystal data: $\mathrm{C_{31}H_{34}F_6O_3P_2RuS}$, $M_r = 763.65$, monoclinic, space group $P2_1/n$, $Z = 4$, $a = 9.0076(3)$ Å, $b = 12.1942(5)$ Å, $c = 28.6987(9)$ Å, $\alpha = 90°$, $\beta = 94.039(4)°$, $\gamma = 90°$, $U = 3144.45(19)$ Å^3, $T = 150(2$ K, $F(000) = 1552$, $\mathrm{Mo_{K\alpha}}$ radiation ($\lambda = 0.71073$ Å), $\mu = 0.735\ \mathrm{mm^{-1}}$, 12814 reflexions measured in the range $2.71 \le \theta \le 27.00$, 26050 unique,($R_{\mathrm{int}}$=0.0396) which were used in all calculations. The structure was refined by using full-matrix least-squares on F^2 to $R_1 = 0.0436$, $wR_2 = 0.0908$, $S = 0.911$, for 6594 reflections ($> 2\sigma$) and 412 refined parameters, R_1(all data) 0.0808, wR_2(all data) = 0.0853, goodness-of-fit on $F^2 = 0.911$. CCDC 726159 (**C**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[16] a) H. J. Zhang, B. Demerseman, L. Toupet, Z. Xi, C. Bruneau, *Adv. Synth. Catal.* **2008**, *350*, 1601; b) M. Achard, N. Derrien, H. J. Zhang, B. Demerseman, C. Bruneau, *Org. Lett.* **2009**, *11*, 185; c) H. J. Zhang, B. Demerseman, L. Toupet, Z. Xi, C. Bruneau, *Organometallics* **2009**, *28*, 5173; d) B. Sundararaju, M. Achard, G. V. M. Sharma, C. Bruneau, *Org. Biomol. Chem.* **2009**, *7*, 3906.

[17] see supporting information for details.

[18] For dicationic allyl ruthenium complexes see: M. D. Mbaye, B. Demerseman, J. L. Renaud, L. Toupet, C. Bruneau, *Angew. Chem.* **2003**, *115*, 5220; *Angew. Chem. Int. Ed.* **2003**, *42*, 5066.