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Catalytic Activity of bis-Phosphine Ruthenium(II)-Arene Compounds

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Abstract: This overview presents recent work on the coordination chemistry and catalytic activity of bis-phosphine ruthenium(II)-arene complexes, $[RuCl(PPh_3)(PR_3)(\eta^6\text{-arene})]^+$, carried out in the Laboratory of Organometallic and Medicinal Chemistry at the EPFL.

Keywords: Arene ligands · Hydrogenation catalysis · Mechanism · Phosphine ligands · Ruthenium

Introduction

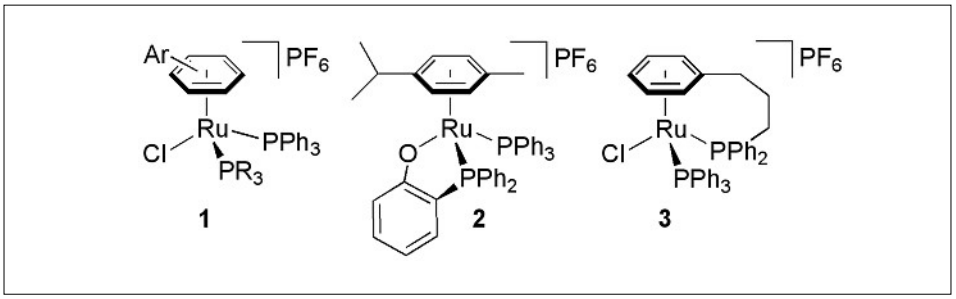
Half sandwich ruthenium(II)-arene complexes are an important and widely used class of organometallic compound, which exhibit a diverse range of coordination chemistry and show considerable potential as precursors for catalytic organic transformations.[1,2] Among these complexes, those bearing one monodentate phosphine ligand have been established as useful catalyst precursors for a wide range of reactions.[3] Notable examples include hydrogenation,[4] free-radical polymerisation,[5] hydration of terminal alkynes,[6] and olefin metathesis reactions.[7] Ruthenium(II)-arene complexes bearing the versatile water-soluble phosphine 1,3,5-triaza-7-phosphatricyclo-[3.3.1.1]decanephosphine (PTA)[8] have also recently found promising applications in medicinal chemistry.[9]

Compared to mono-phosphine complexes, the catalytic activity of bis-phosphine ruthenium(II)-arene complexes remains largely unexplored.[6a,10] This is somewhat surprising given the utility of mono-phosphine and related diphosphine complexes.[2a,f,11] As a large number of molecular catalysts require dissociation of a phosphine ligand in order for the catalysts to enter the catalytic cycle,[12] we decided to investigate the reactivity and catalytic activity of a variety of bis-phosphine ruthenium(II)-arene complexes containing a triphenylphosphine ligand (**1**–**3**, Scheme 1); the results are summarized herein.[13,14]

Synthesis and Phosphine Exchange Dynamics

Bis-phosphine complexes are readily prepared by further addition of phosphine to mono-phosphine complexes, $[RuCl_2(PR_3)(\eta^6\text{-arene})]$, in polar solvents in the presence of chloride abstracting agents.[1] Alternatively, the facile substitution of acetonitrile by phosphine ligands in $[RuCl(NCMe)(PPh_3)(\eta^6\text{-arene})]^+$ provides a mild, selective and reliable route to **1a**–**f**.[13] This procedure is also useful for the preparation of cationic pendant diphosphine complexes of the formulation $[RuCl(\kappa^1\text{-(P-P)})(p\text{-cymene})]PF_6$ (P-P = dppm, *cis*-PPh_2CH-$CHPPh_2$, dppe, dppp, dppf), which afford κ^2-diphosphine complexes *via* dissociative substitution of triphenylphosphine upon heating in 1,2-dichloroethane ($\Delta S^{\ddagger}$, +23 – +77 $Jmol^{-1}K^{-1}$),[15] and has been used to prepare a mixed triphenylphosphine-PTA complex.[16]

Complexes **1**–**3** exhibit varying degrees of phosphine dissociation in solution as evidenced by substitution reactions with excess $P(p\text{-tol})_3$ in THF.[13] The complexes with the most crowded coordination spheres, *i.e.* **1b**–**1d**, show appreciable PPh_3 substitution at ambient temperature, whereas those complexes with less bulky co-ligands or tethered phosphine ligands require elevated temperatures for PPh_3 exchange to



Scheme 1. Bis-phosphine complexes **1** [arene = *p*-cymene: PR_3 = $PPhMe_2$ (**1a**), PPh_3 (**1b**), $P(p\text{-tol})_3$ (**1c**), $PPh_2{}^iPr$ (**1d**); arene = PhMe: PR_3 = $PPhMe_2$ (**1e**), PPh_3 (**1f**)], **2** and **3**.

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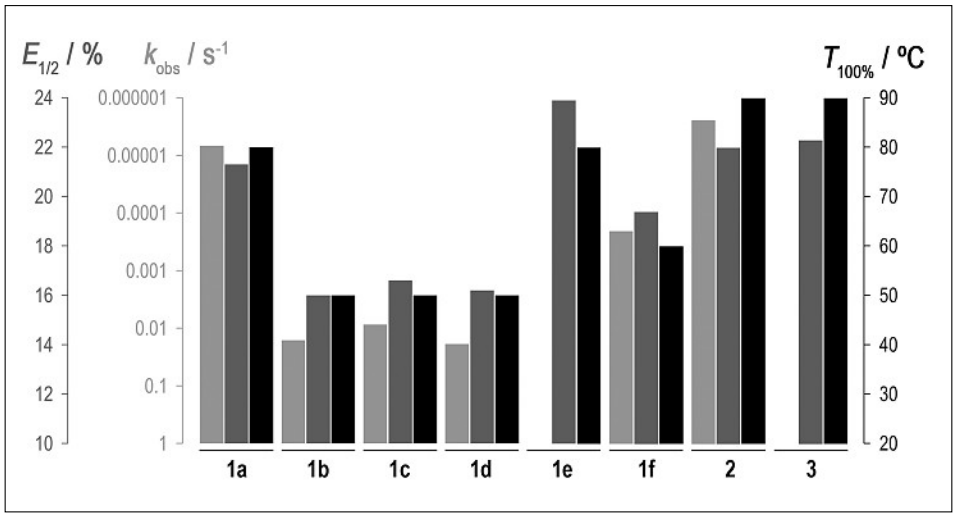


Fig. 1. Structure–activity correlations: rate of (first) PPh_3 exchange with P(*p*-tol)$_3$ in THF at 60°C [left bar, k_{obs} / s^{-1}]; Normalised Collision Energy[17] required to obtain 50% relative fragmentation of PPh_3 [central bar, $E_{1/2}$ / %]; temperature required for 100% hydrogenation of styrene (conditions given in text) [right bar, $T_{100\%}$ / °C].

occur. Kinetic measurements showed that the rate of exchange at 60 °C decreases in the order **1b** ≈ **1c** ≈ **1d** > **1f** > **1a** > **2** > **3**; no exchange is observed for **1e** even after 60 hours. These observations have been further substantiated by gas phase studies using tandem electrospray ionisation mass spectrometry (ESI-MS/MS).[13] Collision induced dissociation of PPh_3 was found to be the primary pathway for the parent ions using this technique and furthermore, by monitoring changes in the relative intensity of the parent ion fragments as the collison energy was increased, a qualitative dissociation energy scale was established for this process. These gas phase data showed excellent agreement with the solution-phase kinetic data; the ease in dissociation decreasing in the order **1b** ≈ **1c** ≈ **1d** > **1f** > **1a** > **2** > **3** > **1e** (see Fig. 1).

The importance of these processes on the catalytic chemistry of the bis-phosphine complexes was established by screening their catalytic activity as a function of temperature using the hydrogenation of styrene to ethyl benzene in THF as a benchmark (0.05 mol%, 50 bar H_2, 1 h).[13] Consistent with an initiation step involving dissociation of a phosphine ligand, the catalytic activity of the bis-phosphine complexes showed strong correlation with the ease of phosphine dissociation. For instance, complexes **1b–d**, which exhibit facile PPh_3 dissociation, are active at T ≥ 30 °C and are characterised by turnover frequencies of ≥ 2000 h^{-1} at 50 °C. To obtain equivalent rates of hydrogenation with the other bis-phosphine complexes higher temperatures were required; temperature required **1b** ≈ **1c** ≈ **1d** < **1f** < **1a** < **1e** < **2** ≈ **3** (see Fig. 1). Under identical conditions the diphosphine complex [RuCl(κ^2-dppm)(*p*-cymene)]PF_6 is only active at T ≥ 80 °C and the mono-phosphine complex [$RuCl_2(PPh_3)$(*p*-cymene)] remained essentially inactive up to 90 °C.

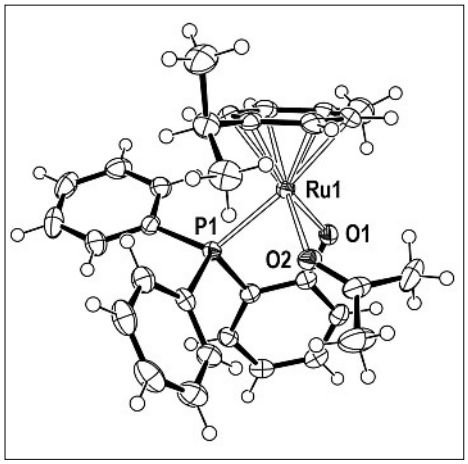


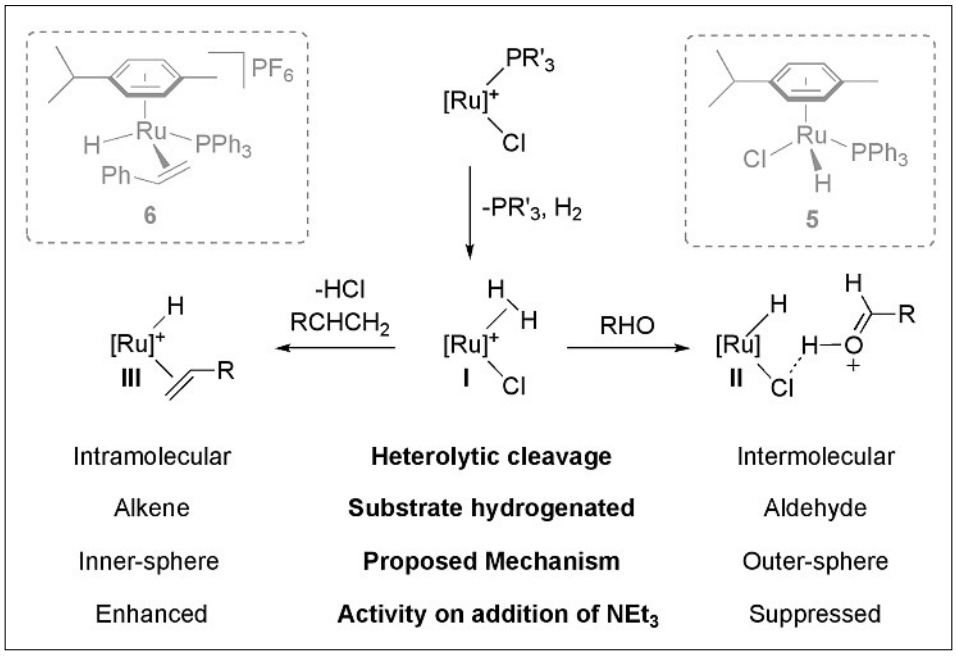
Fig. 2. ORTEP representation of the bis-phosphine analogue [Ru(κ^2-$PPh_2C_6H_4O$)($OCMe_2$)(*p*-cymene)]$^+$; thermal ellipsoids drawn at 50% probability.

Chemoselective Hydrogenation

The reduction of carbonyl compounds to alcohols is an important reaction in organic chemistry. On the laboratory scale, stoichiometric hydride reagents, such as sodium borohydride and lithium aluminium hydride, are often the reagents of choice, operating under mild conditions with high selectivity for the reduction of C=O bonds over C=C bonds.[18] On a larger scale, heterogeneous catalysts such as Pd/C and Pt/C represent a more economical method for carrying out this reduction, although the conditions used are often forcing and can result in problems with chemoselectivity or functional group tolerance.[18a] The development of highly selective homogeneous catalysts that operate under mild conditions is thus of ongoing interest for improving atom efficiency and reducing cost. However, the usefulness of a large number of homogenous catalysts is hindered by low chemoselectivity (generally selective for C=C bonds) and reductions in activity by decarbonylation.[18] The most successful homogeneous catalysts for this process are arguably ruthenium-based diamino–bisphosphine (or diphosphine) complexes, selective for the reduction of ketone and aldehyde groups.[19] With these catalysts, α,β-unsaturated carbonyl compounds can be reduced with C=O selectivities of >99% and turnover numbers of up to 10,000. Other notable examples are ruthenium-$PPh_2(C_6H_4$-3-$SO_3Na)$ or $P(C_6H_4$-3-$SO_3Na)_3$ systems, which show pH-tunable selectivity for the hydrogenation of unsaturated aldehydes under biphasic conditions,[20] although other catalysts are also known.[21]

Following screening of the bis-phosphine complexes catalytic activity, **1c** was chosen for further investigation and consequently found to be an active precursor for the reduction of aldehydes in toluene (0.1 mol%, 50 °C, 50 bar H_2, 2 h).[14] For example, benzaldehyde and 3-phenylpropionaldehyde were hydrogenated with turnover frequencies of 325 and 400 h^{-1}, respectively. Although styrene was also reduced under these conditions (280 h^{-1}), a competition experiment using a 1:1 mixture of styrene and benzaldehyde demonstrated a high degree of chemoselectivity for the hydrogenation of the carbonyl group (82% selectivity) with this catalyst. This high selectivity was further affirmed by experiments employing the α,β-unsaturated aldehyde *trans*-cinnamaldehyde, which underwent almost exclusive hydrogenation of the aldehyde functionality (>99%). Complex **1b** and [RuCl(P(*p*-tol)$_3)_2$(*p*-cymene)]PF_6 (**4**), both showed similar chemoselectivity during this reaction, with the activity decreasing in the order; **1b** (405 h^{-1}) > **1c** (370 h^{-1}) > **4** (250 h^{-1}).

Two different catalytic cycles for the hydrogenation of aldehydes and alkenes have been proposed for the bis-phosphine systems.[14] Common to both proposals is a reactive dihydrogen complex (**I** in Scheme 2), generated following a rate-limiting dissociation of a phosphine ligand (in agreement with the observed structure–activity trends noted above). The observed chemoselectivity is attributed to a preferential intermolecular heterolytic cleavage of dihydrogen in **I** by the substrate, which leads to a mono-hydride complex and an activated aldehyde molecule (**II**); hydrogenation is completed following outer-sphere hydride transfer from the metal. These suggestions are supported by the isolation and reactions of the mono-hydride complex [RuHCl(PPh_3)(*p*-cymene)] (**5**, Scheme 2) and base poisoning



Scheme 2.

experiments; NEt_3 acting as a competitive base, suppressing activity. Intramolecular heterolytic cleavage of dihydrogen in **I** with the loss of HCl is suggested to lead to alkene hydrogenation *via* an alternative inner-sphere pathway. This later proposal is supported by enhancements in alkene hydrogenation activity on addition of NEt_3 (and in more basic solvents such as THF) and the isolation of the olefin-hydride complex $[RuH(\eta^2\text{-}CH_2CHPh)(PPh_3)(p\text{-cymene})]PF_6$ (**6**, Scheme 2). Both proposals are upheld by a computational analysis, notably, the calculated energy barrier for the intermolecular heterolytic cleavage of dihydrogen in **I** (leading to **II**) is 3.5 times lower than the corresponding intramolecular process (leading to **III**) – in agreement with the observed selectivity.

Summary and Concluding Comments

A general and mild method for the preparation of bis-phosphine complexes has been developed and their phosphine dissociation characteristics have been established. These later characteristics showed good correlation with the complexes catalytic activity; those with more crowded coordination spheres showing facile phosphine dissociation and high catalytic activity. Based on these structure–activity relationships a smaller range of bis-phosphine complexes were selected for further investigation and found to be both active and chemoselective catalysts for the hydrogenation of aldehydes in the presence of olefinic bonds. Alkene hydrogenation could also be achieved, particularly under basic conditions that promote intramolecular heterolytic cleavage of dihydrogen and loss of HCl. A 'non-classical' ionic outer-sphere mechanism is proposed for the hydrogenation of aldehydes. Mechanisms of this type are an emerging class in transition metal catalysis and this system helps to further establish them in the field.[22] Useful attributes of the bis-phosphine complexes, which make them attractive targets for further investigation, are their ease in preparation, air and moisture stability, and the relatively mild conditions under which they operate. The dual activity of these complexes for both C=C and C=O bonds is, however, a limitation that needs to be addressed by further ligand design before they can be applied more widely; for the (desirable) hydrogenation of carbonyl compounds. A specific example of ligand refinement, based upon the mechanistic proposals, is a structural analogue containing a labile acetone ligand and *ortho*-oxy substituted triphenylphosphine, $[Ru(\kappa^2\text{-}PPh_2C_6H_4O)(OCMe_2)(p\text{-cymene})]PF_6$ (Fig. 2). This catalyst precursor shows reduced activity for the hydrogenation of alkenes, while maintaining high activity for the hydrogenation of aldehydes.[14]

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