Homogeneous Catalysis

Cyclometalated Ruthenium(II) Complexes as Highly Active Transfer Hydrogenation Catalysts**

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Complexes of platinum group metals with PCP pincer ligands are currently being investigated in both stoichiometric and catalytic reactions.[1] Conversely, cyclometalated complexes

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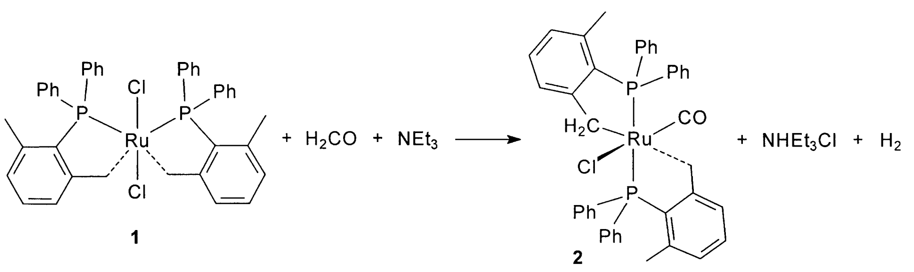
with simple PC ligands[2] have attracted comparatively less attention in catalysis, with the exception of the palladium derivatives used for Heck-type reactions.[3] Thus, despite the large number of ruthenium compounds that have been found to be highly efficient reagents and catalysts for a variety of organic transformations,[4] very few examples of ruthenium catalysts with PC ligands have been reported.[5] In this context, the development of simple routes for the preparation of ruthenium complexes with PC ligands showing features similar to the PCP pincer derivatives would prove useful. Of the many synthetic procedures known, the cyclometalation of *ortho*-methylated aryl phosphanes offers a simple route for the preparation of stable five-membered chelate complexes.[2] Recently, we have studied the coordination chemistry of the bulky phosphanes $(2,6\text{-Me}_2C_6H_3)PR_2$ (R = Ph, cyclohexyl (Cy)) which were found to stabilize rare examples of 14-electron Ru^{II}[6] and Pt^{II}[7] complexes through δ-agostic interactions of the *ortho*-methyl groups. As expected, these ligands undergo facile cyclometalation reactions to give stable compounds in which a carbon donor atom forms a σ bond to the metal center, as found for Pt^{II}[7] and Os^{II} complexes.[8] Thus, starting from the 14-electron compound $[RuCl_2\{(2,6\text{-Me}_2C_6H_3)PPh_2\}_2]$ (**1**),[6] we report herein the synthesis of a new class of complexes containing the anionic $[(2\text{-CH}_2\text{-6-MeC}_6H_3)PPh_2]^-$ ligand and a first application of these robust metal–carbon compounds containing a σ bond in catalytic transfer hydrogenation.[9] Among the new cyclometalated complexes, the derivative bearing 2-(aminomethyl)pyridine was found to be extremely active for the reduction of a large number of ketones with turnover frequency (TOF) numbers up to 63000 h^{-1} and quantitative formation of the alcohol when using a very high substrate/catalyst ratio (up to 10000:1).

Treatment of **1** with formaldehyde in the presence of triethylamine afforded the thermally stable five-coordinate ruthenium(II) complex **2** [Eq. (1)].[10]



(1)

In this reaction one phosphorus center undergoes cyclometalation with one δ-agostic *ortho*-methyl group and the addition of formaldehyde leads to coordination of a CO ligand with extrusion of dihydrogen. The ^{1}H NMR spectrum of **2** shows one signal at $\delta = 1.60$ ppm (CD_2Cl_2) corresponding to two *ortho*-methyl groups. This resonance remains as a singlet even at −90 °C, which indicates there is a low energy barrier to rotation of the xylyl group, in contrast to **1**. The X-ray structure of a single crystal of **2** is shown in Figure 1.[11]

The ruthenium center is in a distorted octahedral environment with two phosphorus atoms in a *trans* arrangement, and with the chloride and the carbonyl group *cis* to the strong σ-donating alkyl ligand. The coordination sphere is completed by an *ortho*-methyl group with a Ru···C10 distance of 2.765(10) Å, which is longer than the value detected in **1** (mean value 2.651(1) Å). The hydrogen atoms of the agostic methyl group have been located by refining the torsion angle that maximizes the electron density of the group. It is noteworthy that the hydrogen atoms are "tilted" away from the metal center, which is in agreement with other complexes with δ-agostic *ortho*-methyl groups.[6,7]

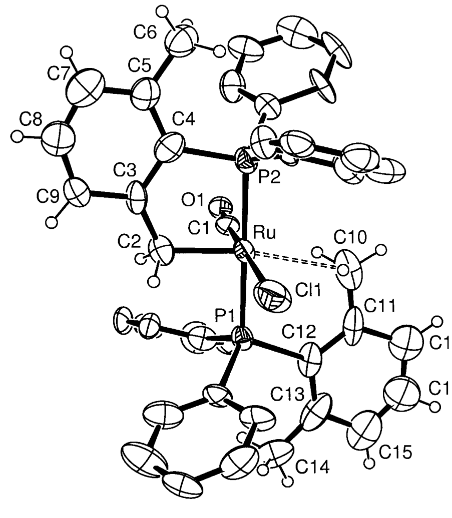
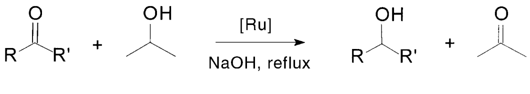


Figure 1. ORTEP representation of complex **2** in the solid state. Thermal ellipsoids are at 40% probability. The labels for the phenyl carbon atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Ru-C(1) 1.780(9), Ru-C(2) 2.043(8), Ru···C(10) 2.765(10), Ru-Cl(1) 2.525(4), Ru-P(1) 2.351(3), Ru-P(2) 2.349(3); C(1)-Ru-C(2) 90.2(4), C(2)-Ru-P(2) 84.8(2), C(2)-Ru-P(1) 95.1(2), C(2)-Ru-Cl(1) 91.7(3), P(1)-Ru-P(2) 179.8(2), C(1)-Ru-Cl(1) 176.1(3), Ru-P(1)-C(12) 112.1(4).

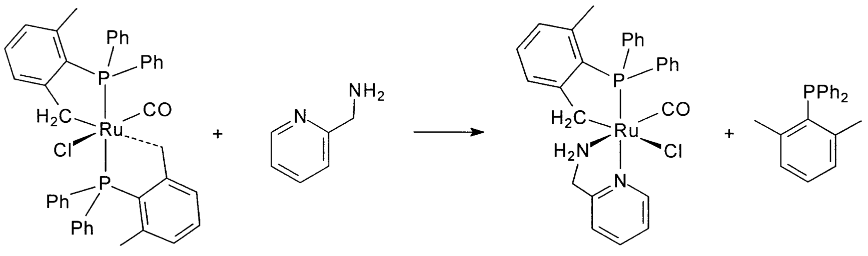
Complex **2** undergoes facile displacement of the $(2,6\text{-Me}_2C_6H_3)PPh_2$ group with phosphorus or nitrogen ligands to afford a new class of cyclometalated derivatives of general formula $[\overline{RuCl(CO)\{(2\text{-C}}H_2\text{-6-MeC}_6H_3)PPh_2\}L_n]$ ($n = 1$, 2). Although the corresponding five-coordinate derivative is obtained with the bulky phosphane PCy_3, reaction of **2** with two equivalents of $PMePh_2$ leads to the six-coordinate compound $[\overline{RuCl(CO)\{(2\text{-C}}H_2\text{-6-MeC}_6H_3)PPh_2\}(PMePh_2)_2]$ (**3**).[12] These complexes have been proven to catalyze the reduction of acetophenone to 1-phenylethanol through hydrogen transfer using 2-propanol as the hydrogen source [Eq. (2)].



(2)

R, R' = alkyl, aryl

Importantly, the systems comprised of **2** and bidentate nitrogen ligands were found to be very active. Whereas complete conversion of acetophenone is achieved with **2**/ethylendiamine in 0.5 h (ketone/Ru/NaOH = 1000:1:20; TOF = 2800 h^{-1}), the reduction occurs within a few minutes with **2**/2-(aminomethyl)pyridine. Treatment of **2** with an equimolar amount of the latter ligand affords the highly efficient catalyst **4**,[13] which exhibits the same activity of the in situ prepared **2**/2-(aminomethyl)pyridine system [Eq. (3)].

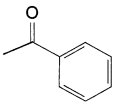
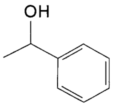
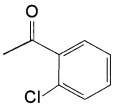
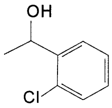
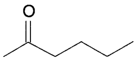
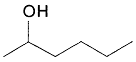
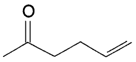
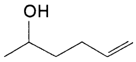
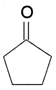
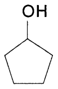
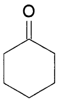
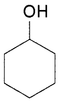
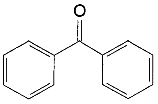
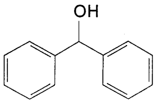
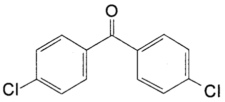
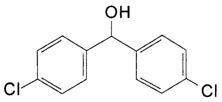


2

4

(3)

Table 1: Reduction of ketones (0.1 M) with **4** (0.05 mol%) and NaOH (2 mol%) in 2-propanol at 82 °C.

Ketone	Alcohol	Conversion [%][a] (min)	TOF [h^{-1}][b]
		98 (5)	60000
		99 (10)	28800
		99 (10)	63000
		95 (10)	30000
		99 (10)	33600
		99 (15)	19000
		95 (5)	36000
		98 (10)	17700

[a] The conversion was determined by GC analysis. [b] Turnover frequency (moles of ketone converted into alcohol per mole of catalyst per hour) at 50% conversion.

Attempts to obtain suitable crystals of **4** for X-ray analysis failed. The proposed structure was supported by ^{1}H NMR and ROESY experiments; the latter showed NOE correlations between the protons of the {$RuCH_2$} moiety and those of the pyridine ligand. The carbon atoms of the pyridine ligand appear as singlets in the $^{13}C\{^1H\}$ NMR spectrum, whereas the CH_2NH_2 group *cis* to the phosphorus center appears as a doublet at $\delta = 48.8$ ppm ($^3J(C,P) = 2.9$ Hz). Furthermore, the IR spectrum of **4** shows a $\tilde{\nu}_{CO}$ band at a low wavenumber (1912 cm^{-1}), which is consistent with a strong σ-donating ligand in the *trans* position.

A large number of alkyl aryl, dialkyl (linear and cyclic), and diaryl ketones can be converted into alcohols *quantitatively*, within a few minutes at 82 °C using catalyst **4** and a substrate/**4** ratio of 2000:1 or higher. The turnover frequencies at 50 % conversion are in the range 17700–63000 h^{-1} (Table 1), depending on the stereoelectronic features of the substrate, and these values are among the highest reported in the literature.[1i,9b,14]

It is noteworthy that ketones containing an olefinic function (such as 5-hexen-2-one) can be selectively converted into the corresponding alcohol without hydrogenation or isomerization of the double bond. The high catalytic performance of **4** enables this complex to be used for preparative purposes with a substrate/catalyst ratio of up to 10000:1. Benzhydrols, which are important intermediates for the synthesis of pharmaceuticals, can now be easily prepared from diaryl ketones by transfer hydrogenation, instead of using dihydrogen.[15] Thus, starting from 3.64 g of benzophenone (0.1 M in 2-propanol) and 1.2 mg of **4** (ketone/**4**/NaOH = 10000:1:200) benzhydrol can be formed in 2 h under reflux conditions (90 % yield of isolated product).

According to the mechanism proposed by Noyori and coworkers for Ru^{II}–amine complexes, it is likely that **4** reacts with the base to afford the corresponding amide compound on elimination of HCl. The subsequent reaction with 2-propanol leads to the key ruthenium hydride amine species that reduces the ketone to the alcohol with the formation of the amide, which closes the cycle.[16a] Alternatively, the active hydride catalyst may be generated from **4** through the alkoxide route.[16b] The very high catalytic performance of **4** can be ascribed to the presence of a bifunctional Ru-H/N-H motif,[17] which is associated with the stable Ru−C σ bond. It is noteworthy that the catalytically active species is not extremely sensitive to oxygen and, in addition, deactivation occurs slowly during catalysis, as proven by the fact that subsequently added acetophenone (up to three times) undergoes quantitative conversion. Therefore, catalyst **4** can be used in a very low amount (0.01 mol %), in contrast to the most active ruthenium catalysts which undergo rapid leaching. Since chiral ligands related to 2-(aminomethyl)pyridine have been recently employed in asymmetric hydrogen-transfer reactions with ruthenium,[18] their use with **2** holds promise for obtaining high-speed enantioselective catalysts.

In summary, the δ-agostic compound **2**, prepared from the 14-electron species **1**, gives access to the synthesis of a new class of cyclometalated derivatives. Complex **4**, prepared from **2** and 2-(aminomethyl)pyridine, is one of the most active catalysts for the reduction of ketones in 2-propanol by a hydrogen-transfer reaction. The presence of a robust cyclometalated metal–carbon bond apparently allows the formation of long-living catalytic species, which may have great potential for use in other catalytic reactions and synthetic methods.

Experimental Section

2: Triethylamine (1.90 mL, 13.6 mmol) and formaldehyde (1.00 mL, 37 % solution in water, 13.4 mmol) were added to a suspension of **1** (2.00 g, 2.66 mmol) in ethanol (40 mL) under argon. The mixture was refluxed for 2 h and then concentrated to half its volume. After filtration, the product was dried under reduced pressure. Yield: 1.60 g (81 %).

4: 2-(Aminomethyl)pyridine (90 μL, 0.87 mmol) and $CaCO_3$ (39 mg, 0.39 mmol) were added to a solution of **2** (535 mg, 0.72 mmol) in dichloromethane (10 mL) under argon. The suspension was heated at reflux overnight, filtered, and concentrated. The product was precipitated with diethyl ether, filtered, and dried under reduced pressure. Yield: 308 mg (76 %).

Typical procedure for the catalytic hydrogen-transfer reaction: Complex **4** (2.8 mg, 5.0 μmol) was dissolved in a 0.04 M solution of NaOH in 2-propanol (5 mL). The ketone (2 mmol) was dissolved in 2-propanol (19 mL) and the solution was heated to reflux under argon. Addition of the solution of **4** (1 mL) resulted in the immediate reduction of the ketone and the yield was determined by GC analysis (ketone/**4**/NaOH = 2000:1:40; ketone 0.1 M).

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Keywords: cyclometalation · homogeneous catalysis · noncovalent interactions · P ligands · ruthenium

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[10] **2**: ^{1}H NMR (200.1 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 7.8$–6.9 (m, 26 H; aromatic protons), 3.48 (d, J(H,H) = 13.4 Hz, 1 H; $RuCH_2$), 3.29 (dd, J(H,H) = 13.4 Hz, J(H,P) = 5.4 Hz, 1 H; CH_2), 1.76 (s, 3 H; CH_3), 1.64 ppm (s, 6 H; CH_3); $^{31}P\{^1H\}$ NMR (81.0 MHz, $CDCl_3$, 20 °C, H_3PO_4): $\delta = 53.7$ (d, J(P,P) = 301 Hz; PC), 32.8 ppm (d, J(P,P) = 301 Hz; P); IR (nujol): $\tilde{\nu}(CO) = 1923\ cm^{-1}$; elemental analysis (%) calcd for $C_{41}H_{37}ClOP_2Ru$: C 66.2, H 5.0; found: C 65.9, H 5.0.

[11] Crystal structure analysis of **2**, $C_{41}H_{37}ClOP_2Ru$, $M_r = 744.17$, monoclinic, space group $P2_1$, $a = 9.502(3)$, $b = 9.974(3)$, $c = 19.771(6)$ Å, $\beta = 111.98(2)°$, $V = 1737.5(9)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.422\ g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 0.652\ mm^{-1}$, $F(000) = 764$, $2.16 < \theta < 29.94°$. Final $R1 = 0.0497$, $wR2 = 0.1454$, $S = 1.045$ for 412 parameters and 9754 reflections, 9401 unique ($R_{int} = 0.0393$), max positive and negative peaks in ΔF map 0.691 and -0.821 e Å^{-3}. Data were were collected at 150(2) K on a Nonius DIP-1030H system with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å).

[12] The molecular structure of **3** is related to that of **2** with two $PMePh_2$ ligands *trans* to the cyclometalated phosphane. **3**·0.5 Et_2O: $C_{49}H_{49}ClO_{1.50}P_3Ru$, $M_r = 891.31$, monoclinic, space group $C2/c$, $a = 21.735(5)$, $b = 10.385(3)$, $c = 37.589(6)$ Å, $\beta = 94.50(2)°$, $V = 8458(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.400\ g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 0.586\ mm^{-1}$, $F(000) = 3688$, $2.17 < \theta < 27.10°$. Final $R1 = 0.0462$, $wR2 = 0.1459$, $S = 1.060$ for 506 parameters and 10511 reflections, 6096 unique ($R(int) = 0.0470$), residuals in ΔF map 0.680, -0.778 e Å^{-3}. Data were collected at 150(2) K on a Nonius DIP-1030H system with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å). CCDC-224572 (**2**) and CCDC-224573 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk)..

[13] **4**: ^{1}H NMR (200.1 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 9.01$ (d, J(H,H) = 5.6 Hz, 1 H; o-C_5H_4N), 7.92–6.88 (m, 16 H; aromatic protons), 4.35 (d pseudo t, J(H,H) = 16.1 Hz, J(H,H) = 4.4 Hz, 1 H; CH_2N), 4.01 (d pseudo t, J(H,H) = 16.2 Hz, J(H,H) = 6.4 Hz, 1 H; CH_2N), 3.05 (m, 1 H; NH_2), 2.95 (d, J(H,H) = 14.9 Hz, 1 H; $RuCH_2$), 2.15 (d, J(H,H) = 14.8 Hz, 1 H; $RuCH_2$), 1.85 (m, 1 H; NH_2), 1.76 ppm (s, 3 H; CH_3); $^{13}C\{^1H\}$ NMR (50.3 MHz, $CDCl_3$, 20 °C, TMS): $\delta = 205.4$ (d, J(C,P) = 19.1 Hz; CO), 164.1 (d, J(C,P) = 31.8 Hz; CCH_2Ru), 159.7 (s; $NCCH_2$), 152.3 (s; o-C_5H_4N), 141.3 (s, $CCCH_3$), 136.4 (s; p-C_5H_4N), 135.1–120.9 (aromatic carbon atoms), 48.8 (d, J(C,P) = 2.9 Hz; CH_2NH_2), 23.1 (d, J(C,P) = 3.6 Hz; $RuCH_2$), 22.3 ppm (d, J(C,P) = 3.8 Hz; CH_3); $^{31}P\{^1H\}$ NMR (81.0 MHz, $CDCl_3$, 20 °C,

H_3PO_4): $\delta = 67.9$ ppm (s). IR (nujol): $\tilde{\nu}(CO) = 1912\ cm^{-1}$; elemental analysis (%) calcd for $C_{27}H_{26}ClN_2OPRu$: C 57.7, H 4.7, N 5.0; found: C 57.3, H 4.6, N 5.0.

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