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Efficient transfer hydrogenation reactions with quinazoline-based ruthenium complexes

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ABSTRACT

(4-Phenylquinazolin-2-yl)methanamine was synthesized in high yield by starting from naturally and commercially available glycine in a few steps. The ligand was reacted with $RuCl_2(PPh_3)_3$ and $RuCl_2(PPh_3)$ dppb to obtain *N*-heterocyclic ruthenium(II) complexes. We have examined these catalysts in transfer hydrogenation of acetophenone derivatives and excellent conversions of up to 99% and high TOF values of up to 118,800 h^{-1} using 0.1 mol % of catalyst were achieved.

Hydrogen transfer reduction processes have attracted significant interest from synthetic chemists as a result of their operational simplicity and high selectivity.[1] Applications using a small amount of a catalyst are important in green chemistry. The ability to reduce the C=O and C=N group by transfer hydrogenation creates the need for designing new ligands and preparing metal complexes (Rh, Pt, Ir, Pd, Os and Ru).[2,3] After Noyori et al., discovered the BINAP-Ru-catalyst system including a 1,2-diamine, which has been shown to be highly efficient for the reduction of ketones, attention has been paid towards this type of complex with different P and N ligand combinations.[4] Organometallic complexes containing nitrogen donor ligands generally exhibit high reactivity; hence, *N*-heterocyclic catalysts, having appropriate geometric structures to generate complexes with metals have attracted attention.[5–10] Baratta and co-workers have synthesized several catalysts bearing amine and pyridyl donor groups for transfer hydrogenation of ketones.[11–14] In a similar vein, the large number of efficient ruthenium complexes containing pyridyl,[15–18] pyrazolyl,[19–21] imidazolyl,[5,22,23] benzimidazolyl,[24,25] oxazolinyl,[26] and aminophosphines[27] have been widely used.

Ligands bearing a quinazoline structure have been used in various reactions such as catalytic asymmetric organozinc addition[28,29] and asymmetric allylic alkylation.[30] Also, the use of ruthenium complexes of quinazoline for transfer hydrogenation has been applied for the first time in this study. For this purpose, the readily available amino acid glycine was used to synthesize (4-phenylquinazolin-2-yl)methanamine. The quinazoline ligand was coordinated with $RuCl_2(PPh_3)$dppb and $RuCl_2(PPh_3)_3$ and the catalytic activity of the complexes in transfer hydrogenation reactions of acetophenone derivatives was investigated.

The quinazoline compound **7** was easily synthesized starting from glycine according to the general synthetic route outlined in Scheme 1. In the first step, glycine (**1**) was protected with Boc_2O in the presence of Na_2CO_3. Protected glycine **2** was converted into *tert*-butyl {2-[(2-carbamoylphenyl)amino]-2-oxoethyl}carbamate (**3**) via treatment with anthranilamide, ethyl chloroformate and Et_3N. Cyclization of this amide was achieved using NaOH in EtOH at ambient temperature. 4-Chloroquinazoline **5** was obtained by chlorination of quinazolinone derivative **4** by treatment with phosphoryl chloride and *N*,*N*-diethylaniline. The synthesis of **6** was accomplished by a Suzuki coupling reaction using phenylboronic acid and a catalytic amount of $Pd(PPh_3)_4$ (2 mol %) at reflux under an N_2 atmosphere. The 4-phenylquinazoline amine **7** was finally obtained by removal of the Boc group by treatment of **6** with TFA.

Treatment of $RuCl_2(PPh_3)$dppb and $RuCl_2(PPh_3)_3$ with 1.2 equiv of 4-phenylquinazoline **7** in the presence of Et_3N and ^iPrOH at reflux temperature for three hours resulted in the formation of ruthenium complexes **8** and **9** in moderate yields (Scheme 2).

Due to the fact that the quinazoline ligand bears two nitrogen atoms, it can be expected that two types of ruthenium complexes

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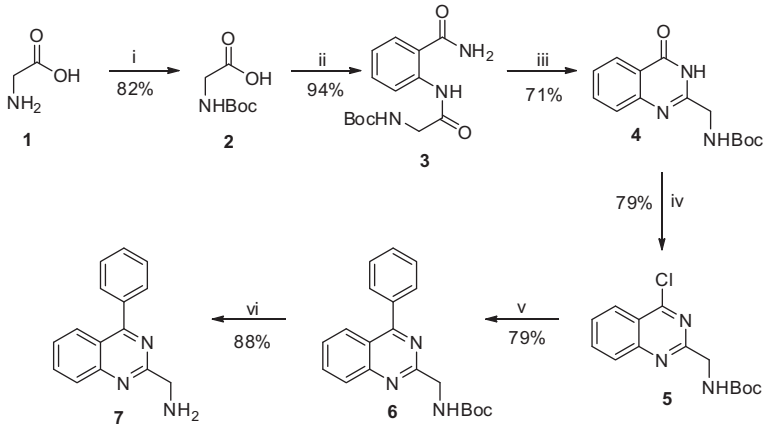
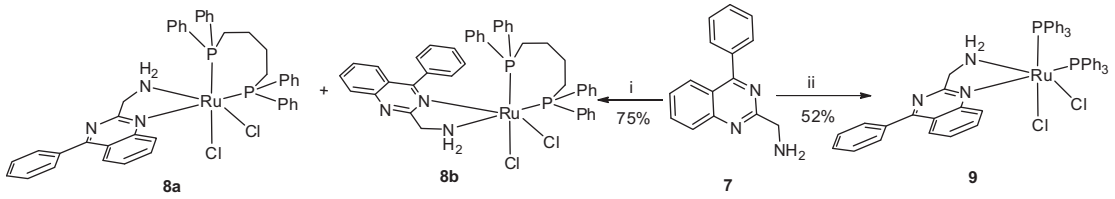


Scheme 1. Synthesis of (4-phenylquinazolin-2-yl)methanamine (**7**). Reagents and conditions: (i) Boc_2O, Na_2CO_3, THF/H_2O, rt, 48 h; (ii) anthranilamide, ethyl chloroformate, Et_3N, THF, rt, 48 h; (iii) NaOH, EtOH, rt, 24 h; (iv) $POCl_3$, *N*,*N*-diethylaniline, benzene, reflux, 40 min; (v) $PhB(OH)_2$, Na_2CO_3, $Pd(PPh_3)_4$, EtOH/DME, reflux, 2 h; (vi) TFA, CH_2Cl_2, rt, 6 h.



Scheme 2. Reagents and conditions: (i) $RuCl_2(PPh_3)_3$, Et_3N, ^{i}PrOH, reflux, 3 h; (ii) $RuCl_2(PPh_3)$dppb, Et_3N, ^{i}PrOH, reflux, 3 h.

will occur in equal amounts according to the positions of the nitrogen atoms on the quinazoline. However, interaction of $Ru(PPh_3)dppbCl_2$ and the quinazoline ligand gave complexes **8a** and **8b** in a ratio of about 4:1, that was determined from the ^{1}H NMR spectrum. The ^{1}H NMR spectrum exhibited one doublet at 10.42 ppm which was attributed to one of the complexes and one doublet at 9.02 ppm for the other in the ratio 4:1. This ratio was also observed for several signals at 8.47, 8.02, 6.66 and 6.43 ppm against signals at 8.53, 8.18, 6.32 and 6.03 ppm due to the aromatic protons. Similarly, the ^{31}P NMR spectrum confirmed this observation. The ^{31}P NMR spectrum showed two doublets at 52.6 ppm and 40.6 ppm [^2J(P,P) = 39.1 Hz] for the major complex and two doublets at 55.1 ppm and 40.2 ppm [^2J(P,P) = 38.6 Hz] for the minor complex in $CDCl_3$. The mixture of ruthenium complexes **8a**,**b** was washed several times with diethyl ether and hexane. As a result, it was observed that the minor signals had disappeared from both the ^{1}H and ^{31}P NMR spectra. To prepare complex **9**, the quinazoline ligand **7** was treated with $Ru(PPh_3)_3Cl_2$ using the same procedure and its formation was evident from the singlet at 29.2 ppm in the ^{31}P NMR spectrum.

To obtain reliable results, full geometry optimizations for the ground states of the studied complexes **8a**,**b** were performed by the application of density functional theory (DFT) calculations. The B3LYP/LANL2DZ level of theory was used to obtain the geometry optimized structures of **8a** and **8b** (Fig. 1). The calculated structural parameters (bond lengths and angles) of the equilibrium geometries together with the calculated zero-point corrected energies for the complexes are given in Table 1. The experimental

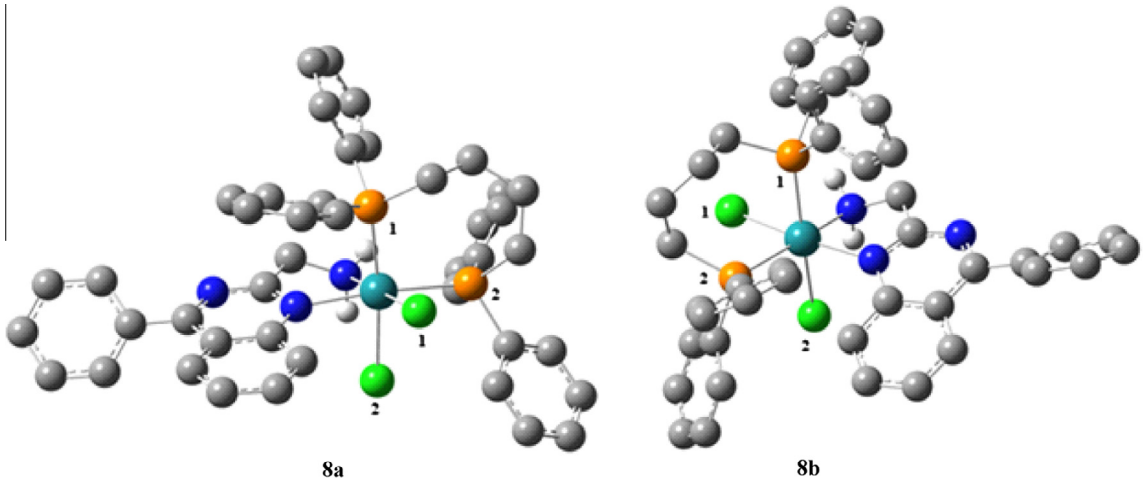


Figure 1. Geometry optimized structures of complexes **8a** and **8b** computed at the B3LYP/LANL2DZ level of theory. Hydrogen atoms are omitted for clarity.