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Novel ruthenium(II) complexes with chelating 1,2,4-triazole NHC ligands and their catalytic activity in the transfer hydrogenation of ketones

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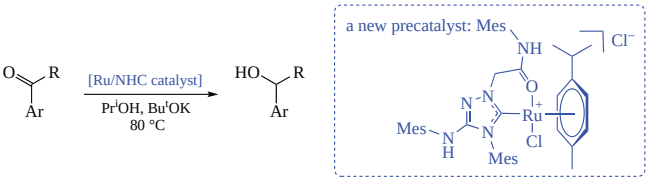
A series of novel ruthenium(II) complexes with nitron-type N-heterocyclic carbene ligands containing chelating (*N*-arylcarbamoyl)methyl or carboxymethyl groups have been synthesized. Their evaluation as precatalysts in the hydrogenation of ketones has revealed that the complex containing three *N*-mesityl groups (one on the carbamoylmethyl moiety and two on the triazole moiety) is the most efficient one.



Keywords: ruthenium complexes, N-heterocyclic carbene, Nitron, chelating ligands, hemilabile, catalysis, transfer hydrogenation, ketones, secondary alcohols.

Ruthenium(II) complexes with N-heterocyclic carbene ligands (Ru/NHC) have been widely used as homogeneous catalysts for hydrogenation/dehydrogenation reactions.[1–3] N-Heterocyclic carbene (NHC) ligands, due to their strong sigma-donating ability and variability of steric parameters,[4] provide high stability and excellent catalytic activity of Ru/NHC systems in hydrogenation/dehydrogenation reactions.[5] For example, some of Ru/NHC systems based on bidentate NHCs containing a chelating C-donor,[6] N-donor,[7–10] and P-donor[11,12] group showed very high activities in the transfer hydrogenation (TH) of ketones to alcohols at the level of 0.01 mol% Ru loading [Figure 1(*a*)]. Remarkably, most of these catalysts were based on abnormal imidazole-type and mesoionic 1,2,3-triazole-type NHC ligands. It has been proposed that the excellent performance of these ligands in TH reactions might be related to their enhanced electron-donating ability compared to the usual NHCs.[11,13,14]

Nitron and its derivatives represent another type of NHC ligands with interesting electronic properties that have attracted much attention in the last decade [see Figure 1(*b*)].[15–24] Recently, it has been demonstrated that metal complexes with the nitron-type ligands [Figure 1(*b*)] could be deprotonated at the RNH group of the NHC ligand in the presence of bases.[17,25,26] The deprotonation transforms the nitron-type NHC ligand into its anionic form and significantly enhances the electron donation of the NHC to the metal, leading to the stabilization of the metal–NHC bond and the increase in the electron density on the metal [Figure 1(*c*)].[17] For example, nickel complexes with nitron-type NHC ligands showed enhanced activity in the catalysis of the Suzuki–Miyaura cross-coupling of unactivated aryl chlorides.[26] However, ruthenium complexes with nitron-type ligands remain understudied. To the best of our knowledge, only a few examples of Ru complexes with nitron have been described in the literature,[16,27] while catalytic properties have been studied for only one of these complexes, on an example of ketone α-alkylation with benzyl alcohol.[16]

In this work, we report the first synthesis of Ru^{II} complexes with chelated nitron-type NHC ligands containing a hemilabile *N*-carboxymethyl or *N*-carbamoylmethyl side arm and the evaluation of their catalytic properties in the base-mediated ketone transfer hydrogenation reactions [Figure 1(*d*)].

The alkylation of 3-arylamino-1,2,4-triazoles **1a–c** with *N*-aryl-2-chloroacetamides or methyl chloroacetate afforded nitron-type NHC proligands **2a–c** and **3a–c**, respectively (Scheme 1). The reaction was selective, involving the sterically more accessible N^1 atom of the triazole ring. Complexes **4a–c** or **5a–c** were synthesized by the reaction of compounds **2a–c** or **3a–c** with Ag_2O and subsequent transmetallation of the thus formed crude Ag/NHC species with $[RuCl_2(p\text{-cymene})]_2$, similarly to the described procedure.[9,28] The moderate yields (35–47%) of complexes **4a–c** and **5a–c** can be attributed to losses during isolation and purification by column chromatography.

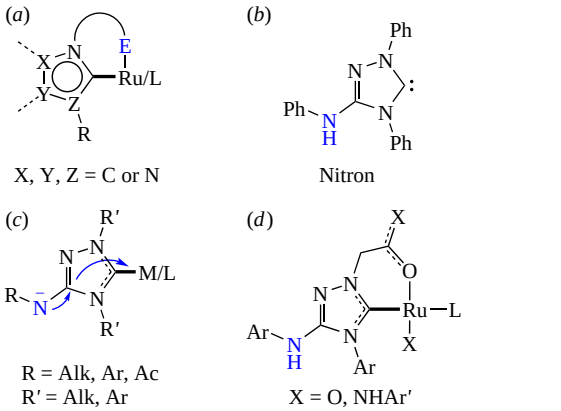
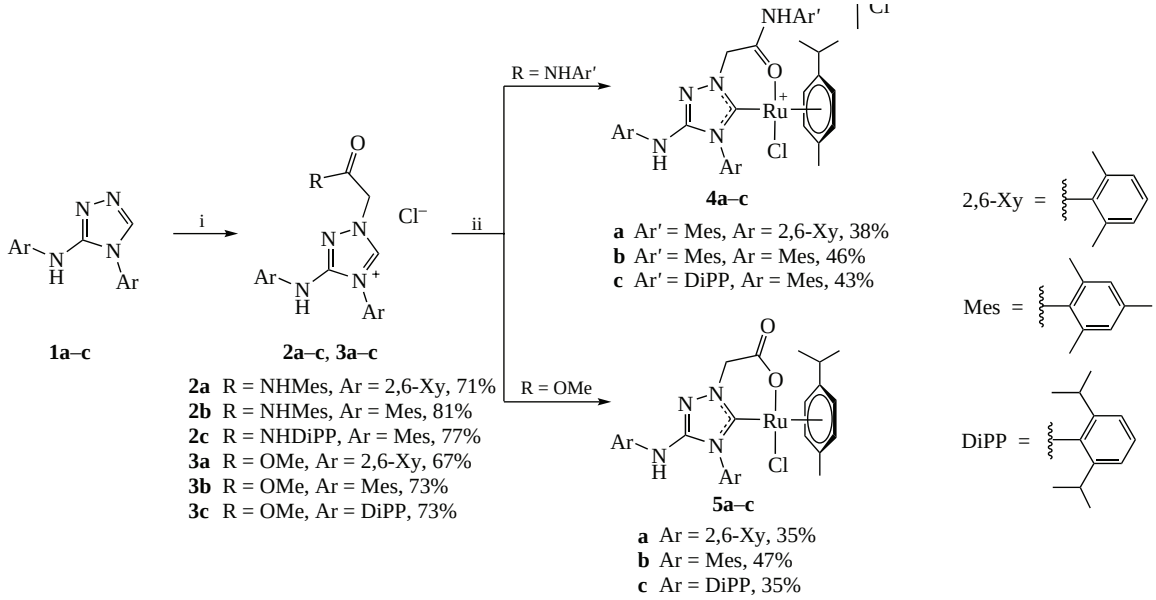


Figure 1 (*a*) General structure of Ru complexes with chelating NHC ligands used in catalysis of hydrogenation reactions; (*b*) nitron in carbene tautomeric form; (*c*) general structure of metal complexes with deprotonated nitron-type NHC ligands; and (*d*) general structure of new Ru^{II} complexes with chelating nitron-type NHC ligands.



Scheme 1 *Reagents and conditions*: i, 3-arylamino-1,2,4-triazole **1a–c** (1.24 mmol), $ClCH_2C(O)R$ (1.35 mmol), DMF (6 ml), 90 °C, 16 h; ii, azolium salt **2a–c** or **3a–c** (0.2 mmol), Ag_2O (0.1 mmol), CH_2Cl_2 (4 ml), room temperature, 24 h, then $[RuCl_2(p\text{-cymene})]_2$ (0.1 mmol), room temperature, 24 h.

The structures of compounds **2a–c**, **3a–c**, **4a–c** and **5a–c** were confirmed by ^1H and ^{13}C NMR spectra, high-resolution mass spectra and single crystal X-ray study of complex **5b** (Figure 2). The NMR spectra of compounds **2a–c** and **3a–c** are similar to those of other nitron-type salts.[17] The direction of alkylation of compounds **1a–c** at the N^1 atom of the triazole ring was also confirmed by two-dimensional ^1H–^{13}C HMBC spectra of compounds **2c** and **3b** (see Online Supplementary Materials, Figures S9 and S15). The HMBC spectra show correlation peaks between the methylene protons for the CH_2 group (5.28 ppm for **2c** and 5.33 ppm for **3b**) of a substituent on the N^1 atom and the C^5 atom of the triazole ring (142.2 ppm for **2c** and 142.4 ppm for **3b**), whereas no correlation was observed between the protons for the methylene group and the C^3 atom of the triazole ring (152.2 ppm for **2c** and **3b**). The NMR spectra of complexes **4a–c** and **5a–c** are similar to those of Ru^{II} complexes with imidazole-type NHC ligands containing hemilabile *N*-carbamoylmethyl and *N*-carboxylatomethyl chelating groups with *p*-cymene co-ligands.[9,29–31] The pseudotetrahedral arrangement of the ligands creates a stereogenic center at the Ru atom, leading to the doubling of some ^{13}C NMR signals in the spectra of compounds **4a–c** and **5a–c** due to the existence of two stereoisomers, as reported for Ru complexes with chelating NHC ligands and *p*-cymene co-ligands.[29–32] The clearly observed NH signal in the range of 12.38–12.54 ppm confirms the coordination of the chelated (*N*-arylcarbamoyl)methyl group to the ruthenium atom *via* the carbonyl oxygen atom, as previously observed in similar Ru^{II} complexes with imidazole-type NHC ligands.[9,29]

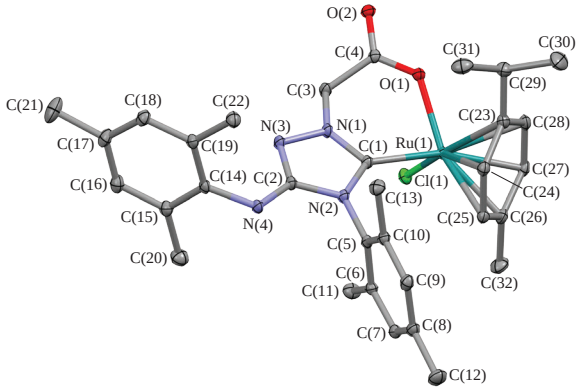


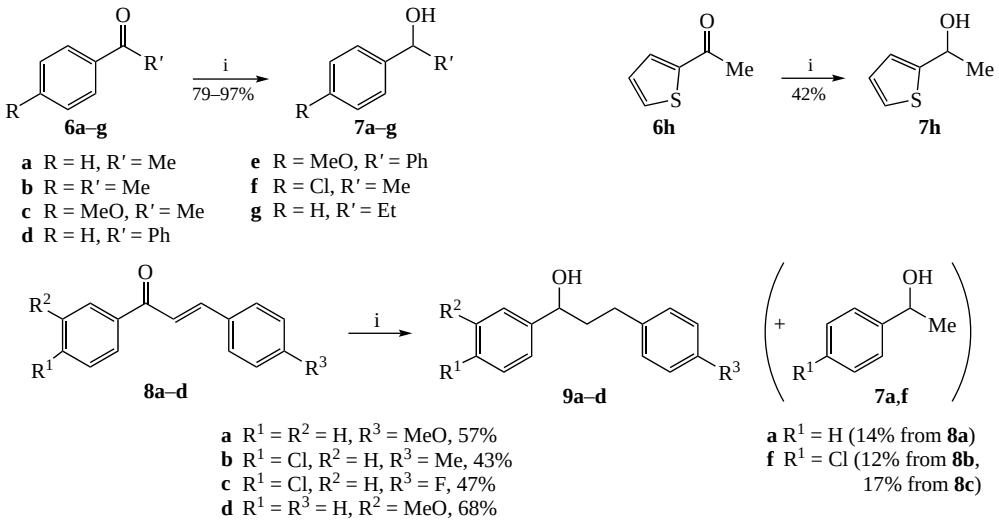
Figure 2 X-ray structure of compound **5b**, $p = 50\%$. Disorder and solvated $CHCl_3$ molecules are omitted. Hydrogen atoms are not shown for clarity.

According to the X-ray data,† the molecule of the complex **5b** adopts the three-legged piano stool geometry (Figures 2 and S1). The lengths of the Ru–$C_{(NHC)}$ [2.0585(9) Å), Ru–O (2.1070(7) Å] and Ru–Cl [2.4137(2) Å] bonds are close to the lengths of these bonds in Ru/NHC complexes with similar imidazole-type NHC ligands and a *p*-cymene coligand.[28,30]

The obtained Ru/NHC complexes **4a–c** and **5a–c** were investigated as potential precatalysts for the transfer hydrogenation (TH) of ketones. The catalytic activity of the obtained complexes was evaluated on the example of the hydrogenation of acetophenone **6a** to 1-phenylethanol **7a** under conditions commonly used for Ru/NHC catalyzed TH of ketones, using Pr^iOH as the hydrogen source and Bu^tOK as the base (Scheme 2, Table 1).[12,30,31] At 0.5 mol% loading, complexes **4a–c** with a carbamoylmethyl chelating arm provided sufficiently higher yields of **7a** (71–96%, entries 1–3) than complexes **5a–c** with a carboxylate chelating arm (40–55%, entries 4–6). Most likely, the higher performance of complexes **4a–c** may be related to the higher coordination lability of the chelating carbamoylmethyl group. However, all the Ru/NHC complexes studied showed significantly higher catalytic performance than the $[RuCl_2(p\text{-cymene})]_2$ complex (25%, entry 7). These results confirm the importance of NHC ligands in providing high catalytic performance of ruthenium active species in catalysis of the TH reaction. Among the Ru/NHC complexes investigated (entries 1–6), compound **4b** provided the highest yield of **7a** (entry 2). Experiments aimed at reducing the **4b** loading (entries 8–12) showed that the conditions of entry 9 (0.25 mol% **4b** loading, 5 h reaction time) can be accepted as optimal. Further

† *Crystal data for* **5b**. $C_{32}H_{39}ClN_4O_2Ru \cdot 2CHCl_3$, $M_r = 886.93$, monoclinic, $P2_1/_n$ at 99.9(7) K, $\lambda = 0.71073$ Å, $a = 15.63046(14)$, $b = 15.26918(12)$ and $c = 16.84325(14)$ Å, $\beta = 97.6546(8)°$, $V = 3984.06(6)$ Å^3, $Z = 4$, $D_x = 1.479$ g cm^{-3}, $\mu(MoK\alpha) = 0.898$ mm^{-1}, $F(000) = 1808$. Total of 96417 reflections were measured and 16732 independent reflections ($R_{int} = 0.046$) were used. The refinement converged to $wR_2 = 0.0731$ and GOF = 1.035 for all independent reflections [$R_1 = 0.0264$ was calculated against F for 15303 observed reflections with $I > 2\sigma(I)$].

CCDC 2306474 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.



Scheme 2 *Reagents and conditions*: i, **6a**–**h** or **8a**–**d** (0.5 mmol), **4b** (0.0025 mmol, 0.25 mol%), Bu^{t}OK (0.05 mmol), Pr^{i}OH (2 ml), 80 °C, 5 h. Isolated yields of **7a**–**h** and **9a**–**b** are presented.

Table 1 Comparison of Ru/NHC complexes in the transfer hydrogenation of **6a**.[a]

Entry	[Ru] (mol%)	*t*/h	Yield of **7a** (%)[b,c]
1	**4a** (0.5)	3	79
2	**4b** (0.5)	3	96
3	**4c** (0.5)	3	71
4	**5a** (0.5)	3	40
5	**5b** (0.5)	3	55
6	**5c** (0.5)	3	47
7	$[RuCl_2(p\text{-cymene})]_2$ (0.5)	3	25
8	**4b** (0.25)	3	82
9	**4b** (0.25)	5	95
10	**4b** (0.25)	10	96
11	**4b** (0.1)	3	10
12	**4b** (0.1)	10	57

[a] Reagents and conditions: **6a** (0.5 mmol), [Ru] (0.5–2.5 μmol, 0.1–0.5 mol%), Bu^{t}OK (0.05 mmol, 10 mol%), Pr^{i}OH (2 ml), 80 °C, 3–10 h. [b] The yield was determined by GC-MS. [c] Mean values derived from two independent experiments are given; the maximum deviation of the experimental data from the mean values presented did not exceed 5%.

reduction of the loading to 0.1 mol% resulted in a significant decrease of the **7a** yield, even when the processing was extended to 10 h (entry 12).

With the optimized conditions in hand, the catalytic efficiency of complex **4b** was evaluated in the TH of various ketones (see Scheme 2). Aryl ketones **6a**–**g** were converted to the corresponding benzylic alcohols **7a**–**g** in high yields (79–97%). However, 2-acetylthiophene **6h** or chalcones **8a**–**d** were converted into alcohols **7h** (42%) or **9a**–**d** (43–68%) in moderate yields. Predictably, the hydrogenation of chalcones involved both C=O and C=C bonds, similarly to other Ru/NHC catalysts.[33] The modest yield of thienylethanol **7h** can be explained by a stronger coordination of the thiophene moiety to the ruthenium atom thus causing partial deactivation of the catalyst.[34,35] The moderate yields of compounds **9a**–**d** are also related to the insufficient selectivity of the reaction due to the partial cleavage at the C=C bond leading to by-products **7a**,**f** which were isolated in 12–17% yield (see Scheme 2). Similar reactivity of chalcones in Ru-catalyzed TH reactions has been reported in the literature.[33] The observed catalytic performance of complex **4b** in the TH of ketones of type **6** is at the level of most-efficient phosphine-free Ru/NHC precatalysts with NHC ligands containing a hemilabile chelating O-donor group.[3] However, complex **4b** is significantly inferior in catalytic performance to the best phosphine-free catalysts based on abnormal and mesoionic NHC ligands with N-donor chelating moieties, which showed high performance at even 0.01 mol% loading.[13,14,34]

In conclusion, Ru^{II} complexes with nitron-type NHC ligands containing chelating (*N*-arylcarbamoyl)methyl or carboxymethyl groups have been synthesized and characterized. Evaluation of these complexes in the catalysis of the ketone transfer hydrogenation showed a better catalytic efficiency of the complexes with the (*N*-arylcarbamoyl)methyl group, the complex with three *N*-mesityl groups being the most efficient.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.04.023.

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