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Review

Current advances on ruthenium(II) *N*-heterocyclic carbenes in hydrogenation reactions

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ABSTRACT

This review provides a brief overview of advances on ruthenium(II) *N*-heterocyclic carbene complexes (NHCs) applied for hydrogenation reactions undertaken during the last five years. Several structural motifs, containing mono-, bi-, tri- and tetradentate binding modes of the NHCs are discussed in combination with a variety of different wingtip substituents to provide active catalysts for hydrogenation reactions. While bidentate ligands afford the more active catalysts than their monodentate analogues, pincer ligands must be chosen carefully to enable the formation of a free coordination site in catalysis. Transfer hydrogenation and direct hydrogenation of ketones and aldehydes, olefins, nitriles, imines and esters are summarized, showing the trend towards hydrogen transfer from other sources than hydrogen gas. Recently developed chiral NHCs offer the opportunity for asymmetric transformations as a possible pathway to access natural products.

Contents

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1. Introduction

Hydrogenation reactions are widely applied in industry, for instance for the synthesis of pharmaceuticals or for petrochemical transformations [1,2]. A variety of functional groups, e.g. aldehydes, ketones, olefins and nitriles, can be reduced by homogeneous catalysis [3]. Several organometallic compounds are reported for these transformations, ruthenium complexes being among the most widespread examples in current research. In particular, ruthenium(II) *N*-heterocyclic carbenes (NHCs), which have been widely applied in metathesis reactions [4–6], belong to the most thoroughly studied compounds that are able to catalyze hydrogenation reactions [7]. The possibility of designing both the backbone and wingtip substituents of the carbene ligands allows the synthesis of a large variety of sterically and electronically different catalysts for task-specific hydrogenation reactions [8], as well as for tandem catalysis that combines metathesis or C—C coupling reactions with hydrogenation [9,10].

This review provides an overview of recent advances in the field of hydrogenation reactions catalyzed by ruthenium(II) NHCs. Different reaction types are presented and the most important structural motifs for each are discussed.

2. Transfer hydrogenation of aldehydes and ketones

The catalytic transfer hydrogenation reaction (TH) is one of the most commonly employed methods for the transformation of aldehydes and ketones to the respective alcohols [11–13]. Apart from the simplification of the reaction setup [14], TH provides safer reaction conditions compared to direct hydrogenation (HY), since no hydrogen gas is necessary [15]. The reaction is usually carried out with *iso*-propanol (^{i}PrOH), used as solvent, or formic acid as hydrogen donors. Other examples of hydrogen donors, such as glycerol, exist likewise, but appear only more recently in the literature and will not be part of this review. A detailed summary of these advances is given by *Voutchkova-Kostal* et al. [16].

Ruthenium(II) NHCs are widely examined for the homogeneous TH of various carbonyl compounds using ^{i}PrOH [17]. Mostly, acetophenone is used as a model substrate, but related aldehydes and ketones are examined as well, to evaluate the scope and potential of the catalyst. To improve the catalytic activity and to retard decomposition, NHCs with varying structures and properties were considered. The most recent advances in this field are elucidated below.

2.1. Hydrogenation reactions with monodentate NHC complexes

The first approaches towards metal complexes containing NHC ligands feature monodentate binding modes of the carbene to the metal [17]. To date, these complexes are the most thoroughly examined ruthenium(II) NHCs, mostly exhibiting the general structure shown in Fig. 1.

Ruthenium complexes of the depicted motif, containing a cymene and two chloride ligands, are accessible by the straightforward reaction of the commercially available [(*p*-cymene)$RuCl_2$]$_2$ with the respective silver(I) NHC at room temperature (RT) in dichloromethane under mild conditions [18]. Improvements of the catalytic properties of these complexes are realized by varying the wingtip substituents R^1 and R^2. *Yaşar* et al. compared the activities of asymmetrically substituted ruthenium(II) NHCs in the TH of acetophenone. Maintaining the *N*-methyl moiety, different wingtips on the other *N*-atom were investigated (Scheme 1) [19].

The substrate was reacted in ^{i}PrOH at 80 °C, using a substrate: catalyst:base (S:C:B) ratio of 1:0.0075:2, with KOH as base. While it is possible to achieve conversions of 93% and 96% of acetophenone to 1-phenylethanol with catalysts **1** and **2** in 30 min, catalyst **3** is slightly less active with a conversion of 85% in the same time (Table 1, entries 1–3). It is noticeable that a high amount of KOH was used in this reaction, although prior findings have shown that the base itself already catalyzes TH reactions [20,21]. This behavior is underlined by a blank experiment without catalyst, affording 15% conversion under the same reaction conditions (T = 80 °C, solvent = ^{i}PrOH, B = KOH, S:B = 1:2, t = 30 min). However, having performed optimization reactions, the authors declare the S:B ratio employed as ideal amount of base for the examined catalytic reactions.

A similar trend for the activities of catalysts **1**–**3** was observed for *p*-chloro-acetophenone as substrate, however exhibiting much higher TOFs of up to 5200 h^{-1} with **1** when decreasing the catalyst loading (Table 1, entries 4–15). The latter could be reduced as low as 0.025 mol%, to obtain a turnover number (TON) of 2600, an indicator for the high stability of the complexes. The authors judge that the steric demand of the *N*-substituents R as well as their low electron donating ability is responsible for the distinct increase in catalytic activity with **1**. No proof regarding the electronic nature of the complexes was provided to confirm this assumption (single crystal X-ray structure, DFT calculations). Substrates with electron-withdrawing moieties are also reduced more easily. This conclusion is based on experiments conducted with a catalyst loading of 0.750 mol%, since a decrease of the catalyst loading was not carried out with the acetophenone substrate.

The beneficial influence of bulky electron-donating wingtip substituents is underlined by investigations of *Günay* et al., who examined phenyl (Ph) (**4**), mesityl (Mes) (**5**), 2,3,5,6-tetramethylphenyl (**6**) and 2,3,4,5,6-pentamethylphenyl (**7**) as *N*-aryl substituents (Fig. 2 and Table 2) [22]. The most active catalyst for the conversion of acetophenone proved to be **7**, albeit with a TOF of only 46.5 h^{-1} and a moderate TON of 186 (entry 4). Complex **6** affords comparable results (entry 3), while **4** and **5** are much less active catalysts (entries 1 and 2). It has to be mentioned that these turnovers are low compared with previous publications and the medium TONs hint towards average stability of the catalysts. Nevertheless, the results underline the influence of steric demand and concurrent electron-donating properties on the NHC backbone, which are both stated as a reason for the better catalytic performance of **7** [22].

An elongation of the alkyl chain from methyl (Me) to *N*-butyl (^{n}Bu) however resulted in a slight decrease of the TOF to 40.5 h^{-1} under the same reaction conditions as used before (T = 82 °C, solvent = ^{i}PrOH, B = KOH, S:C:B = 1:0.005:0.05, 81% conversion in

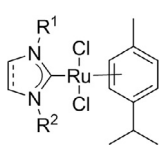
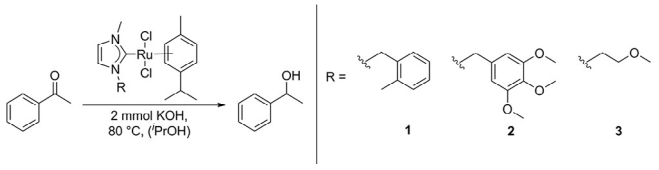


Fig. 1. General structure of a ruthenium(II) monodentate NHC. R^1 = aryl, R^2 = alkyl or aryl.



Scheme 1. Different aryl- and alkyl- wingtip substituents examined in the TH of acetophenone by *Yaşar* et al. S:C:B = 1:0.0075:2, t = 30 min [19].