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

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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 are 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].

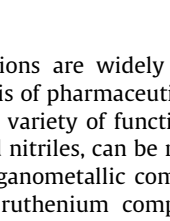
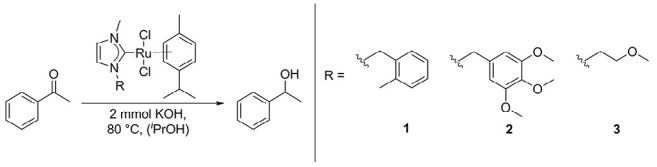


Fig. 1. General structure of a ruthenium(II) monodentate NHC. R^1 = aryl, R^2 = alkyl or aryl.



Scheme 1. Different aryl- and alkyl- wingtip substituents examined in the TH of acetophenone by *Yaşar* et al. 0 S:C:B = 1:0.0075:2, t = 30 min [19].

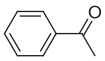
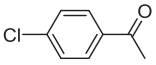
The substrate was reacted in ^{i}PrOH at 80 °C, using a substrate:-catalyst:base (S:C:B) ratio of 1:0.0075:2, with KOH as base. While it is possible to achieve conversions of 93% and 96% of acetophenone to 1-phenylethanol with catalysts **1** and **2** in 30 min, catalyst **3** is slightly less active 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 4 h). The authors presume that the larger ^{n}Bu group shields the

Table 1
TH of acetophenone (entries 1–3) and *p*-chloro-acetophenone (entries 4–15) described by *Yaşar* et al. [19].

Entry	Substrate	Catalyst (loading)	Conversion [%]	TOF [h^{-1}]	TON
1		**1** (0.750 mol%)	93	248	124
2		**2** (0.750 mol%)	96	256	128
3		**3** (0.750 mol%)	85	227	114
4		**1** (0.750 mol%)	100	267	134
5		**2** (0.750 mol%)	97	259	130
6		**3** (0.750 mol%)	92	245	123
7		**1** (0.375 mol%)	93	496	248
8		**2** (0.375 mol%)	97	481	241
9		**3** (0.375 mol%)	90	433	217
10		**1** (0.100 mol%)	95	1900	950
11		**2** (0.100 mol%)	94	1880	940
12		**3** (0.100 mol%)	89	1780	890
13		**1** (0.025 mol%)	65	5200	2600
14		**2** (0.025 mol%)	56	4480	2240
15		**3** (0.025 mol%)	51	4080	2040

(Reaction conditions: T = 80 °C, solvent = ^{i}PrOH, Base B = KOH, S:B = 1:2, t = 30 min.)

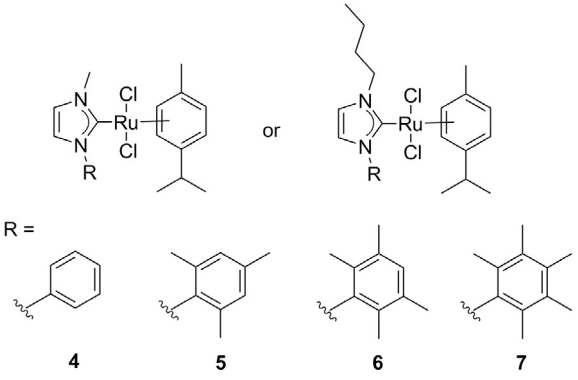


Fig. 2. *N*-Aryl wingtip substituents investigated in TH by *Günay* et al. [22].

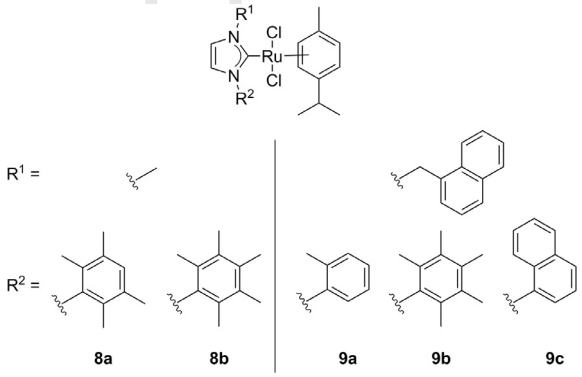


Fig. 3. Variation of the wingtip substituents R^1 and R^2 with moieties of distinct steric bulk [24].

active side of the catalyst and thereby decreases its activity, while additional methyl groups on the aromatic wingtip influence mainly the electronic properties through electron-donation to the metal. Consequently, the basicity of the metal increases and an enhanced catalytic activity is observed. However, no single crystal X-ray structures were provided, and no additional confirmation for this assumption was supplied.

Papish et al. investigated the influence of an ethoxyethyl compared to a pentyl wingtip, maintaining an ethyl moiety on the second nitrogen atom [23]. A slight increase of the TOF from 94 h^{-1} to 110 h^{-1} was observed in the TH of acetophenone when using the pentyl wingtip (S:C:B = 200:1:25, TOF calculated at t = 1 h). The authors state, however, that no preference for the alkyl to the ether moiety can be concluded due to the small difference of the TOFs. Besides investigations on the nature of the aliphatic wingtip and the chain length of one of the *N*-alkyl substituents, the impact of sterically bulky moieties on both nitrogen atoms was examined (Fig. 3) [24]. Experimental results demonstrated the higher activity of methyl-substituted NHCs **8** in comparison to *N*-naphthalene moieties **9**, when the second *N*-substituent is not varied (Table 3).

Even though a broad variety of conversions is obtained for different acetophenone-related substrates, *N*-methyl-substituted NHCs exhibit higher conversions than their naphthalene counterparts in almost every case. In Table 3, some examples are given to demonstrate this trend (**8a** and **b** vs. **9a**, **b** and **c**). Especially when comparing the direct analogues **8b** and **9b**, significantly higher TOFs can be observed for the *N*-methyl-substituted NHC **8b**. For the shown substrates (Table 3), low to medium TONs can be achieved with catalysts **8** and **9**, while for *p*-chlorobenzaldehyde the loading of **8a** can be reduced to 0.125 mol% to obtain a better TON of 360. This behavior evidences a higher, albeit still average, stability of the catalyst when transforming certain substrates with the best-performing catalyst in the row.

Also for catalytic measurements with **8** and **9**, a comparably high amount of base was used and a blank test without catalyst proved poor conversion of *p*-chloroacetophenone (2% in 30 min, T = 80 °C, solvent = ^{i}PrOH, S:B = 1:1). A single crystal X-ray structure was provided only for **8b**, but it was assumed that the naphthalene moiety impedes the catalytic activity by its bulkiness, shielding the metal and hindering the formation of the active species. Nevertheless, to determine the exact impact of certain wingtip moieties, additional methods should be applied (single crystal X-ray diffraction, calculations).

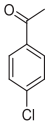
Besides the mentioned "classic" *N*-heterocyclic carbenes that contain imidazolium-based ligands, NHCs containing a triazole skeleton play a significant role as catalysts in TH reactions [25].

Table 2
TH of acetophenone with NHCs **4**–**7** with methyl as the second wingtip substituent [22].

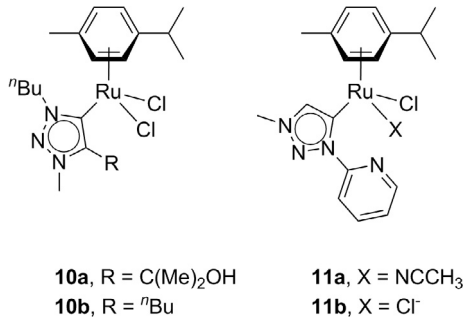
Entry	Catalyst	Conversion [%]	TOF [h^{-1}]	TON
1	**4**	34	17.0	68
2	**5**	45	22.5	90
3	**6**	85	42.5	170
4	**7**	93	46.5	186

(Reaction conditions: T = 82 °C, solvent = ^{i}PrOH, B = KOH, S:C:B = 1:0.005:0.05, t = 4 h.)

Table 3
TH of different substrates with catalysts **8** and **9** [24].

Entry	Catalyst	Substrate	Conversion [%]	TOF [h^{-1}]	TON
1	**8a**		20	80	40
2	**8b**		12	48	24
3	**9a**		5	20	10
4	**9b**		3	12	6
5	**9c**		11	44	22
6	**8a**		99	396	198
7	**8b**		84	336	168
8	**9a**		13	52	26
9	**9b**		15	60	30
10	**9c**		14	56	28
11	**8a**		36	144	72
12	**8b**		55	220	110
13	**9a**		23	92	46
14	**9b**		30	120	60
15	**9c**		40	160	80

(Reaction conditions: T = 80 °C, solvent = ^{i}PrOH, B = KOH, 0.5 mol% catalyst loading, S:C:B = 1:0.005:1, t = 30 min.)



10a, R = $C(Me)_2OH$ **11a**, X = $NCCH_3$
10b, R = ^{n}Bu **11b**, X = Cl^-

Fig. 4. Monodentate ruthenium(II) NHCs based on triazoles. For the cationic complex **11a**, $^-$OTf was used as counterion [26,27].

Only few examples of monodentate triazole-based NHCs on ruthenium(II) were examined in TH recently (Fig. 4) [26,27].

A comparison of the catalytic activities of **10** and **11** shows the advantageous influence of an alkyl substituent on the triazole ligand instead of a pyridine moiety (Table 4). For alkyl substituted triazoles (entries 1 and 2), a similar conversion can be observed in half the time as used for the complexes with pyridine wingtips (entries 3 and 4), leading to a ca. three-fold increase in the calculated TOF. The stability of the catalysts, on the other hand, does not differ significantly, no matter which substituent is applied, as can be seen from the comparably low TONs with constant catalyst loading of 1 mol%.

A higher TOF can be reached varying the wingtip from $C(Me)_2$-OH (**10a**) to ^{n}Bu (**10b**) (entries 1 and 2). An even larger difference is observed by changing the co-ligands from acetonitrile (**11a**) to chloride (**11b**). While 48% of acetophenone is converted within one hour using **11b** (entry 4), almost full conversion is reached with **11a** (entry 3). This indicates a faster dissociation of acetonitrile in comparison to chloride to create a vacant coordination site on the metal.

It was further shown that the examined ruthenium(II) triazoles are more active in TH than their iridium(III) analogues [26], an observation which is in accord with previous results for related complexes [28,29]. NMR experiments with ^{i}PrOH-d_7 indicate a monohydride inner-sphere mechanism, although the respective Ru–H species has not yet been isolated [27].

Several other examples of monodentate ruthenium(II) NHCs with different substitution patterns on the wingtips and the backbone of the carbene emerged during the last years [30–34], comprising redox-switchable complexes, where the catalytic activity can be tuned by the addition of a reductant or an oxidant [35]. Published results include complexes with cyclopentadienyl or benzyl moieties instead of a cymene backbone and different ancillary ligands apart from chloride (CO, pyridine, acetonitrile) [16,36,37]. However, no general correlation between the activity of the catalysts in the TH of acetophenone (TOFs between 20 h^{-1} and 700 h^{-1}) and the ligands employed can be found.

In summary, several ruthenium(II) compounds containing a monodentate NHC and a cymene ligand in the presence of chloride anionic ligands have been reported, since they can easily be synthesized from $[(p\text{-cymene})RuCl_2]_2$ as starting material. These complexes are active catalysts in the transfer hydrogenation of acetophenone-related substrates, with TOFs of up to 5200 h^{-1}. It has been noted that an increase of the steric demand on one of the *N*-substituents leads to higher activities, while the incorporation of a second bulky moiety on the other nitrogen atom in addition shows the opposite effect. Due to lacking evidence (X-ray structures, DFT calculations), it is not generally clear whether electronic or steric parameters are the reason for this trend. However, also the substrate itself influences the catalytic activity strongly and divergent conversions are found for donor- and acceptor-

Table 4
TH of ketone substrates catalyzed by **10** and **11** [26,27].

Entry	Catalyst	Conversion [%]	Time [h]	TOF [h^{-1}]	TON
1[a]	**10a**	78	0.5	210[c]	78
2[a]	**10b**	88	0.5	310[c]	88
3[b]	**11a**	88	1.0	88	88
4[b]	**11b**	48	1.0	48	48

(Reaction conditions: T = 82 °C, solvent = ^{i}PrOH, B = KOH, 1 mol% catalyst loading, S:C:B = 1:0.01:0.1. [a]Benzophenone used as substrate. [b]Acetophenone used as substrate. [c]TOF calculated at 50% conversion.)

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substituted acetophenone derivatives. In general, monodentate NHCs can be fine-tuned in a fashion to design highly active catalysts, but it has to be admitted that the best performances were reached with their polydentate analogues [36].

2.2. Hydrogenation reactions with polydentate NHC complexes

This part of the review will deal with bi-, tri- and tetradentate ruthenium(II) NHC complexes, displaying normally bound, abnormal or mesoionic and triazole carbene ligands. Some examples of chloride- or NHC-bridged ruthenium monobimetallic species have furthermore appeared in the literature more recently [38,39]. It must be noted, however, that they exhibit moderate activities in the TH of aldehydes and ketones when compared to monomeric ruthenium complexes, with TOFs below 500 h^{-1}.

Similar to the monodentate ruthenium(II) NHCs described above, the synthesis of bidentate carbenes is often carried out using [(*p*-cymene)$RuCl_2$]$_2$ and the respective silver(I) NHC. The latter is mostly formed *in situ* from Ag_2O and the respective imidazolium salt. In this manner, it was possible to synthesize several complexes of the general structure shown in Fig. 5 [39–42]. In most cases, PF_6^- is used for the preparation of cationic ruthenium(II) NHC complexes due to its low coordination ability and to avoid halogen mixing resulting from the transmetallation step [43,44].

Depending on the wingtip-substituent R, different catalytic activities are obtained. Table 5 shows some examples of transfer hydrogenation reactions with catalysts of the general structure shown in Fig. 5.

Despite varying reaction conditions (catalyst loading, amount of base), Table 5 demonstrates that TOFs lie within the range that *Crabtree* et al. found for related ruthenium complexes[45] and that catalysts show medium stability in the range of the examined catalyst loadings, evidenced by the calculated TONs.

In addition to the bidentate "classic" NHCs shown in Fig. 5, a related triazole complex **12** (Fig. 6) with a coordinating pyridine wingtip was prepared, based on the structures of **11a** and **b** (chapter 2.1, Fig. 4) [27]. The group of *Albrecht* compared the catalytic activity of **12** with its monodentate equivalents. While full conversion of acetophenone was observed within 4 h using **10a** and **b**, only 58% was reached with **12** in the same time. The authors conclude that the chelating effect of the pyridine substituent reduces the catalytic activity of the complex by inhibiting the formation of a reactive hydride species. It is indeed likely that the acetonitrile and chloride ligands of **11a** and **b** dissociate more readily than the pyridine substituent of **12** and thus enable a faster formation of the catalytically active species.

These findings are in agreement with previous studies of the group [46]. Contradicting results were reported by *Košmrlj*, *Sarkar* et al., mentioning TOFs up to 3000 h^{-1} in the TH of acetophenone with a similar bidentate NHC (0.01 mol% catalyst loading, 89% conversion within 3 h) [28]. Even higher turnovers were obtained with a pyrimidine instead of a pyridine wingtip. It must be admitted, however, that higher temperatures (T = 100 °C) and base amounts (17 mol% KOH) were used for these catalytic experiments. Both parameters can influence the rate of the reaction and no direct comparison with the previously mentioned complexes can be provided therefore.

Superior results were obtained with compounds **13**, **14** and **15** (Fig. 7), which bear two triazole wingtip ligands instead of the pyridine moiety [47]. They can be obtained similarly from [(*p*-cymene)$RuCl_2$]$_2$ by transmetallation and subsequent anion exchange with AgOTf for **14** and **15**.

Complexes **13**, **14** and **15** were examined in the TH of acetophenone (Table 6). Tridentate NHC **14** reaches the highest initial TOF of 1100 h^{-1}, followed by **15** (initial TOF = 580 h^{-1}) and the bidentate complex **13** (initial TOF = 280 h^{-1}). Although the initial TOFs are high, overall turnovers fall short compared to related ruthenium (II) compounds [48–50]. Still, the initial TOFs hint on a fast catalyst activation and subsequent deactivation. The latter becomes evident with the calculated TONs, especially for **13** and **14**, since no full conversion was reached under the applied conditions, while TONs do not exceed a value of 200 (Table 6). A higher TON could possibly be obtained for **15** by decreasing the catalyst loading, but it was not examined in the work.

The lower catalytic activity of **13** in comparison to **14** most likely results from the slower activation of **13** affording the same active hydride species. Accordingly, the triazole moiety is supposed to dissociate easier than the chloride anionic ligand to form a vacant coordination site for the substrate. Despite different initial TOFs of the two complexes, both eventually reach the same conversion of the substrate [47]. A fast catalyst activation (initial TOF = 580 h^{-1}) was found likewise for **15** (Fig. 7), where the NHC is a CCC pincer ligand, featuring an abnormal binding mode of the wingtip triazoles [47]. This tridentate complex also seems to be more robust than **13** and **14**, concluding from its kinetic profile and the higher overall TOF and TON. Both the chelating effect of the pincer ligand and the electron donating properties of the mesoionic carbene were attributed for the steady catalytic performance of **15**.

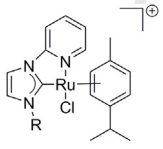
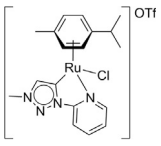


Fig. 5. General structure of bidentate ruthenium(II) NHCs synthesized from [(*p*-cymene)$RuCl_2$]$_2$.



12

Fig. 6. Ruthenium(II) triazole **12** with a coordinating pyridine backbone [27].

Table 5
TH of acetophenone with bidentate ruthenium(II) NHCs bearing different wingtip substituents.

Entry	R	Ru [mol%]	Base [mol%]	Conversion [%]	Time [min]	TOF [h^{-1}]	TON
1 [40]	^{n}Bu	0.5	10	76	70	130	152
2[a] [41]	Me	5	20	96	60	19	19
3 [42]	Ph	1	12	55	60	58	55
4 [42]	Mes	1	12	79	60	84	79
5[b] [39]	Bz	0.5	100	>99	120	199	200

(Reaction conditions: T = 80–82 °C, solvent = ^{i}PrOH, B = KOH. [a]Benzophenone was used as substrate. [b]NaOH was used as base.)

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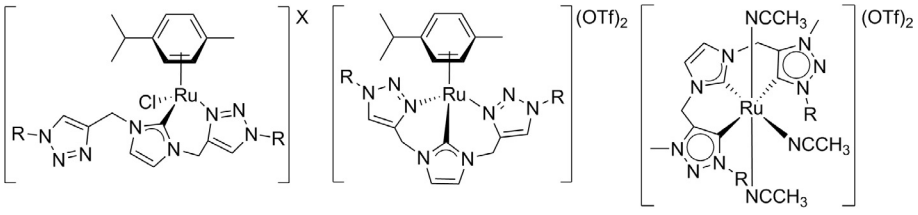


Fig. 7. Ruthenium(II) NHCs **13**, **14** and **15** bearing triazole wingtips. X = $^{-}PF_6$, ^{-}OTf; R = Mes [47].

Table 6
TH of acetophenone with catalysts **13**–**15** [47].

Entry	Catalyst	Conversion [%]	Time [min]	TOF [h^{-1}]	TON
1	**13**	85 (6)	180 (4)	57 (280)	170
2	**14**	84 (19)	120 (2)	84 (1100)	168
3	**15**	98 (10)	80 (2)	151 (580)	196

(Reaction conditions: T = 82 °C, solvent = ^{i}PrOH, B = Na^{i}OPr, 0.5 mol% catalyst loading, S:C:B = 1:0.005:0.05. Numbers in brackets refer to initial TOFs.)

Besides **14** and **15**, several other tridentate pincer complexes are applied in the TH of aldehydes and ketones (Fig. 8) [47,51,52]. In comparison to their mono- and bidentate analogues, they apparently show larger variations with respect to their activities in TH. While **16** exhibits similar properties to its bidentate counterpart (with only one pyridine moiety bound to ruthenium) [51], NHC **17** displays a much lower activity than the bidentate pyrazole-NHC [52]. It must be noted, however, that **17** was compared to analogue mono-NHCs instead of the directly related bis-NHC. The lower conversion with **17** was thus attributed to coordinative saturation in the case of the bis-NHC.

The same abnormally bound triazole pattern as in **15** can be observed for **18** (Fig. 9) [53]. Unlike **15**, complex **18** does not provide satisfactory results in TH, only affording quantitative conversion of acetophenone within 14 h (1 mol% catalyst loading). This behavior might be explained by the already mentioned influence of chelating ligands on the stability of the complex. While in case of **15** a high coordination ability of the ligand renders the catalyst more active through increasing robustness, the same property might also result in an absent free coordination site for the substrate in **18**. The ancillary ligands presumably reinforce this property, since acetonitrile is supposed to dissociate much easier than chloride or CO.

The tridentate CCC pincer complexes **19** (Fig. 9) on the other hand are quite active in TH reaching TOFs up to 3300 h^{-1} (Table 7) [50]. Therefore pincer ligands must be applied in a way to create robust catalysts, but not to hinder the dissociation of a leaving group to afford a free coordination site for the substrate.

Catalyst **19** was examined in the TH of different substrates, varying the wingtip substituents R and the leaving group L (Table 7). The best results were obtained with cyclohexanone as substrate (entries 7–9), as observed similarly for other ruthenium (II) NHC complexes [28,51]. The conversion of benzophenone is limited in comparison with other examined substrates (entries 4–6). Acetophenone affords TOFs in between of ca. 2100–2500 h^{-1} (entries 1–3), indicating that electron-rich ketones are easily reduced with this type of catalysts by contrast to ketones that contain electron-withdrawing backbones. When reacting cyclohexanone under the identical conditions, but without **19** (T = 82 °C, solvent = ^{i}PrOH, B = 20 mol% NaOH, t = 3 h), only 18% conversion were observed, hinting on the catalytic influence of the base itself.

It is noteworthy that NHCs with a methyl wingtip (entries 1, 4 and 7) lead to slightly higher conversions than their ^{t}Bu analogues (entries 2, 5 and 8). The difference, however, is not significant due

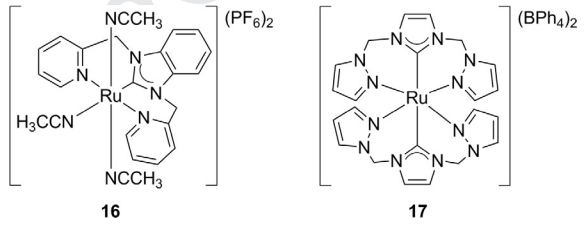


Fig. 8. NCN pincer complexes **16** and **17** [51,52].

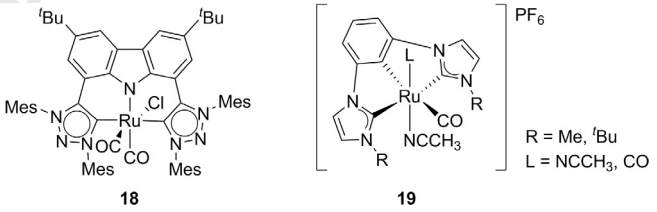


Fig. 9. CNC and CCC pincer complexes **18** and **19** [50,53].

to the prevalence of the unchanged NHC skeleton. A likewise alteration from the acetonitrile ligand to iodide or bromide or from L = CO to L = $NCCH_3$ (uneven entries) does not affect the catalytic activities considerably. Overall, the results obtained with **19** show the advantage of pincer NHC complexes compared to the previously discussed structures. A comparably high catalytic activity is evidenced by the TOF value, lying in the range of ca. 2000–3300 h^{-1} and thus higher than for several mono- and bidentate examples. The superior stability can be concluded from TONs up to nearly 9900, resulting from low catalyst loadings of 0.01 mol%. An even higher TON might be achieved by further decreasing the catalyst loading, but no experiment was conducted to prove this assumption.

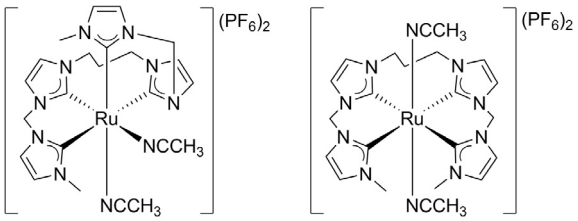
Ruthenium(II) complexes with structures related to **19**, containing two NHC moieties, have been reported in the literature [7,11]. Tetra-NHCs on the other hand are mostly known for other transition metals, particularly for iron and nickel [54–58]. *Kühn* et al. recently published two ruthenium(II) tetra-NHCs that proved to be very active in TH (Fig. 10) [59].

While a conversion of 94% acetophenone within 30 min was observed for **21** (0.1 mol% catalyst loading, TOF at 50% conversion = 4500 h^{-1}), complex **20** afforded a TOF^{50} of 110,000

Table 7
Catalytic activities of pincer NHCs **19** in the TH of different substrates [50].

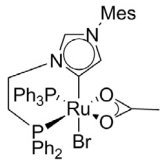
Entry	Substrate	R	L	Conversion [%]	TOF [h^{-1}]	TON
1		Me	CO	74	2467	7400
2		^{t}Bu	CO	65	2167	6500
3		Me	$NCCH_3$	67	2234	6700
4		Me	CO	60	2000	6000
5		^{t}Bu	CO	58	1934	5800
6		Me	$NCCH_3$	60	2000	6000
7		Me	CO	97	3233	9700
8		^{t}Bu	CO	96	3200	9600
9		Me	$NCCH_3$	99	3300	9900

(Reactions conditions: T = 82 °C, solvent = ^{i}PrOH, B = NaOH, 0.01 mol% catalyst loading, S:C:B = 1:0.0001:0.2, t = 3 h.)



20 **21**

Fig. 10. Ruthenium(II) tetra-NHCs **20** and **21** synthesized by *Kühn* et al. [59].



22

Fig. 11. Bidentate CP-linked ruthenium(II) NHC **22** [48].

h^{-1} (0.1 mol% catalyst loading, 98% conversion within one minute). This value displays one of the highest TOFs measured for ruthenium(II) NHCs in TH to date. Even superior results could be obtained with the bidentate CP-linked abnormal NHC **22** (Fig. 11) [48]. Already the complex itself catalyzes the conversion of acetophenone with a TOF[50] of 38,000 h^{-1} (Table 8, entry 1).

Application of additives, e.g. ethylenediamine, leads to a further increase of activity to 140,000 h^{-1} (Table 8, entries 2–5). The higher catalytic activity observed with primary and secondary amine additives is attributed to the *NH effect*, which improves the catalytic properties of transition metal complexes through bifunctional catalysis. This means that ligands with an NH group can operate as hydrogen carriers, facilitating the transfer of hydrogen from ^{i}PrOH, H_2, etc. to the substrate. No direct coordination of the substrate to the metal is required in this case, and an outer-sphere mechanism is often proposed for the respective examples [60,61]. Thus, primary amines do not only serve as ligands, but are also involved in the hydrogen transfer to the substrate [62–65].

While exhibiting an extraordinarily high catalytic activity and TOF, an average stability and TON of **22** seems to be observed for catalyst loadings of 0.05 mol%. However, a decrease of the catalyst loading when ethylenediamine was added evidences a relatively high stability, obtaining a TON of 8600 with a catalyst loading of 0.01 mol%. Complex **22** is among the most active ruthenium(II) catalysts for TH reactions, and more effective than related NHCs [11,50,59,66,67]. The combination of an abnormal NHC motif with phosphine ligands leads to an easy substitution of the anionic ligand in *trans* position to the phosphine and the formation of catalytically active hydride species in basic media [68,69]. The same beneficial properties of an abnormal NHC/phosphine were reported recently for a heterobimetallic Ru/Pd complex that catalyzes a coupled TH and Suzuki-Miyaura reaction [9].

In summary, several ruthenium(II) NHCs with a variety of different structure motifs were examined for the transfer hydrogenation of aldehydes and ketones in the last few years. Pincer complexes display good activity due to their high stability, albeit the set of ligands must be chosen carefully to allow binding of the substrate to the metal or to enable the proceeding of an outer-sphere mechanism through bifunctional catalysis. An increase of the basicity at the metal center, effected by ligands with electron-donor properties, has a beneficial effect in TH. Among the recently published examples, tetra-NHCs **20** and **21** as well as the abnormal CP-linked NHC **22** show the highest activity in the transfer hydrogenation of ketones.

3. Direct hydrogenation of aldehydes and ketones

Hydrogenation reactions are among the most widely exerted transformations in industry to produce agrochemicals, pharmaceu-

Table 8
TH of acetophenone catalyzed by **22** [48].

Entry	Additive	Conversion [%]	Time [min]	TOF[50] [h^{-1}]	TON
1	–	97	120	38,000	1940
2	Ethylenediamine	97	20	58,000	1940
3	Ampy[a]	85	1	15,000	1700
4	Benzylamine	95	8	34,000	1900
5[b]	Ethylenediamine	86	60	140,000	8600

(Reaction conditions: T = 82 °C, solvent = ^{i}PrOH, B = 2 mol% Na^{i}OPr, 0.05 mol% catalyst loading. [a]ampy = 2-aminomethylpyridine. [b]0.01 mol% catalyst loading.)

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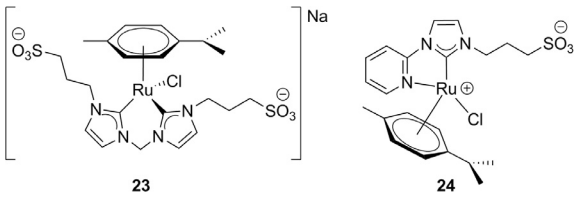


Fig. 12. Ruthenium(II) NHCs applied for the HY of ketones in aqueous conditions [40,74].

ticals and fine chemicals. Rather than the already discussed transfer hydrogenation reactions (chapter 2), direct hydrogenation under H_2 pressure (HY) is applied in industry, where heterogeneously catalyzed processes prevail. In the beginning of transition-metal catalyzed homogenous hydrogenation, this approach was pursued likewise, and a broad range of ruthenium complexes emerged [70,71]. By contrast, current research focuses mainly on hydrogen transfer from other sources than molecular hydrogen, such as ^{i}PrOH or formic acid, due to safety and handling issues [11,16].

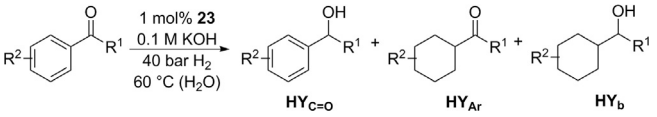
The application of ruthenium(II) NHCs as catalysts in direct hydrogenation in the last years is limited to few examples. These include the HY under specific conditions, such as in aqueous environment, or the improvement of certain catalyst properties through tuning of the ligands. Hydrogenation reactions with ruthenium NHC nanoparticles are further known [72], but will not be discussed in this review. This chapter elucidates the latest advances in this field, emphasizing reactions in water and the development of ligand properties, which highly affect the catalytic performance of the examined complexes.

3.1. Hydrogenation reactions in water

Hydrogenation reactions in water are favorable from an environmental point of view, avoiding organic solvents, e.g. tetrahydrofuran, toluene or propanol. Several ruthenium(II) NHCs are known to catalyze transformations in water, but only a few examples show their potential in hydrogenation reactions [73]. A requirement for this advance is the solubility of catalysts under the adapted conditions. *Kühn* et al. synthesized sulfonate-appended ruthenium(II) NHCs **23** and **24** (Fig. 12) that dissolve in aqueous solution owing to the anionic moieties [40,74].

Bis-NHC **23** was employed for the HY of diverse aromatic carbonyl substrates (Scheme 2 and Table 9) [74]. Basically three different hydrogenation products are possible, where either only the carbonyl moiety ($\mathbf{HY_{C=O}}$), only the aromatic ring ($\mathbf{HY_{Ar}}$), or both ($\mathbf{HY_b}$) are reduced. In fact, all mentioned products were observed in different ratios (Table 9). While the hydrogenation of phenol leads mainly to the completely hydrogenated product $\mathbf{HY_b}$ (entry 1), benzaldehyde is almost selectively transformed at the carbonyl position to $\mathbf{HY_{C=O}}$ (entry 3). It must be noted that aldehydes are generally more prone to hydrogenation than ketones, and a tendency for complete HY is observed for most of the examined ketone substrates (entries 4–6), especially for acetophenone (entry 2). Moreover, when a longer reaction time is considered (24 h instead of 4 h), the product ratio shifts considerably towards $\mathbf{HY_b}$ in all cases.

Albeit good conversions are obtained with **23**, mechanistic studies revealed the decomposition of this catalyst, resulting in the dissociation of one NHC moiety and the reduction of the backbone. This behavior was not observed for **24**, which has a pyridine instead of a second NHC coordinated to the metal (Fig. 12) [40]. The reduction of acetophenone proceeds smoothly within 3 h in a 6 M HCO_2Na/HCO_2H aqueous buffer (Scheme 3).

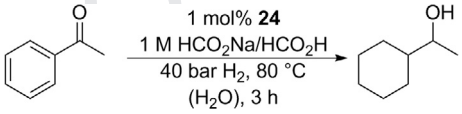


Scheme 2. HY of aromatic carbonyl substrates catalyzed by **23** [74].

Table 9
HY of aromatic carbonyl substrates catalyzed by **23** [74].

Entry	Substrate	$\mathbf{HY_{C=O}/HY_{Ar}/HY_b}$	Time [h]
1	Phenol	0/1/98	2
2	Acetophenone	11/12/77	2
3	Benzaldehyde	94/0/6	4
4	*o*-Methyl-acetophenone	59/20/17	4
5	*o*-Hydroxy-acetophenone	14/7/9	4
6	*p*-Acetyl-acetophenone	57/6/32[a]	4

(Reaction conditions: T = 60 °C, p = 40 bar H_2, solvent = H_2O, B = 0.1 M KOH, 1 mol% catalyst loading. [a]$\mathbf{HY_b}$ refers to the mono-hydrogenated acetyl.)



Scheme 3. HY of acetophenone catalyzed by **24** [40].

Table 10
HY of acetophenone catalyzed by **24** with varying catalyst loadings [40].

Entry	Catalyst loading [mol%]	Yield [%]	$\mathbf{HY_{C=O}/HY_{Ar}/HY_b}$
1	1	100	0/0/100
2	0.4	100	0/0/100
3	0.2	100	1/1/98
4	0.1	100	7/17/75
5	0.05	90	41/31/19
6	0.03	59	31/21/7

(Reaction conditions: T = 80 °C, p = 40 bar H_2, solvent = H_2O, 1 M HCO_2Na/HCO_2H, t = 2 h. HY was performed with a previously prepared catalyst solution.)

Compared to its iridium and osmium counterparts, the ruthenium NHC is more active and outperforms even the rhenium analogue [40]. It was observed however that the activity drops with lower catalyst loadings (Table 10), a sign of catalyst deactivation. Especially at loadings of 0.03 mol% (entry 6), this behavior is obvious with a yield of 59%. Nevertheless, an overall TON of 1967 can be calculated under these circumstances, outperforming the stability of some of the previously mentioned examples.

Another drawback was noted when catalytic activities of **24** were compared for TH and HY reactions. While the TH of acetophenone proceeds quantitatively within 70 min, HY requires an induction period of 3 h to form the catalytically active species. This behavior, apart from safety and instrumental issues, represents another distinct disadvantage of HY compared to TH. These challenges explain the decreasing number of investigations in the field of direct hydrogenation reactions and the trend towards hydrogen transfer reactions from ^{i}PrOH and other sources.

3.2. Ligand effects on hydrogenation reactions

The influence of ligands with amine groups in catalysis is widely referred to as *NH effect* [62], promoting the activity of the catalyst (see chapter 2.4) [48]. Usually bidentate amines, such as ethylenediamine or benzylamine, are used as chelating ligands. *Elsevier* et al. examined the effect of different amine wingtip substituents on the hydrogenation of acetophenone [75]. Therefore,

complex **25a** was synthesized, based on the structures of previously known **25b** and **25c** [76,77] (Fig. 13). They contain aniline-, ethylamine- and benzylamine-derived wingtips to compare the impact of the ring-size of the obtained chelates on HY reactions.

Among the depicted complexes, **25a** performs best in the HY of acetophenone, followed by **25b**. Both contain a 6-membered metal-ligand system, seemingly favored over the 7-membered ring present in **25c**. The superiority of **25a** was attributed to the conjugated system, which is a result of the phenyl backbone. This renders the NHC more electron-rich and increases its donor ability. It has to be mentioned, however, that **25c** was previously found to achieve higher maximum TOFs of 883 h^{-1} when decreasing the catalyst concentration to S:C:B = 1200:1:8 [76].

Regarding the catalytic activity of **25a**, the ^{n}Bu moiety was furthermore found to enhance the performance of the complex in comparison to methyl or ethyl wingtips (Table 11).

The kinetic profile reveals that the length of the alkyl chain mainly influences the initial activation of the catalyst to form the active hydride species. This behavior was attributed to the steric effect of the ^{n}Bu group, providing access for the hydrogen molecule, but inhibiting the coordination of the comparably bulkier substrate to the metal. Thus, the formation of the hydride species is facilitated by hampering the competitive action. Besides the activity of the catalyst, the TON and thus the stability of **25a** seems low at a first glance, but it has to be noted that the catalyst loading was not decreased below 0.5 mol% in catalytic experiments to really determine if catalyst deactivation is an issue in this case.

Even if an outer-sphere mechanism was found for a related structure to **25c**, it is not clear if hydrogenation reactions with ruthenium(II) pincer NHC complexes follow generally an inner- or an outer-sphere mechanism [62,75,78–80], and a thorough investigation of the process depending on the catalyst is still desirable.

The influence of certain ligand motifs on catalysis was also studied for pincer complexes **26a** and **b** (Fig. 14).

The HY of acetophenone-derived substrates proceeded quantitatively within 24 h, affording the desired alcohols (Scheme 4). Interestingly, neither the confirmation of the carbonyl and acetate ancillary ligands, nor the substitution R^1 and R^2 on the ligand's backbone influence the activity of the catalyst, reaching quantitative conversion for all R^1, R^2 = H, Me, ^{i}Pr, Ph. However, samples were only taken after 24 h reaction time, impeding valuable conclusions on the catalyst activation. It is noteworthy that, under the applied conditions, no HY of the aromatic ring was observed, as is the case for other catalysts, e.g. **23** and **24**, providing chemoselectivity for the carbonyl group in presence of aromatic double bonds.

Depending on the moieties R^1 and R^2 on the ligand backbone, even low enantioselectivity was observed (up to 60% *ee* for **26a**, R^1 = Ph, R^2 = H). Since the steric outcome of the reaction is moderate, these results will not be discussed in detail in this review. A section on asymmetric reactions with superior enantioselectivity is provided in the following chapter.

Table 11
Varying the steric demand of the wingtip substituent on **25a** in the HY of acetophenone [75].

Entry	Wingtip	Conversion [%]	TOF [h^{-1}]	TON
1	Me	99	909	198
2	Et	99	915	198
3	^{n}Bu	99	1543	198

(Reaction conditions: T = 50 °C, p = 25 bar H_2, solvent = THF, B = KO^{t}Bu, 0.5 mol% catalyst loading, S:C:B = 200:1:8, t = 30 min. TOFs were calculated at 50% conversion of acetophenone.)

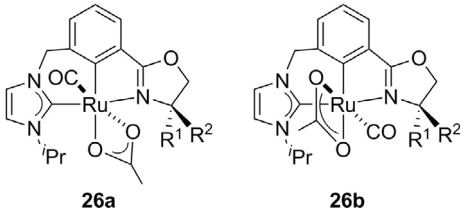
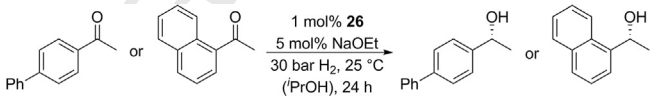


Fig. 14. Pincer complexes **26a** and **b** for the HY of ketone substrates [81].



Scheme 4. HY of ketones by pincer catalysts **26a** and **b** [81].

4. Asymmetric reduction by direct and transfer hydrogenation

Asymmetric hydrogenations are an important reaction type for the production of pharmaceuticals, natural products and flavor molecules [82–85]. Ruthenium(II) complexes are known for their activity in these reactions [86], featuring ligands such as chiral diamines[87] and a wide range of phosphines, with the most widespread being (*R*)-BINAP [82,88,89]. Only few NHC ligated ruthenium(II) compounds are established for asymmetric transformations [90], mostly originating from the group of *Glorius* [91]. Recent advances made in this field will be discussed in this chapter.

4.1. Hydrogenation of C=C double bonds

The stereoselective reduction of double bonds is important for the synthesis of several types of natural products, such as flavones and indolizines. When NHCs are applied for these transformations, they are mostly used as additives to create the active species

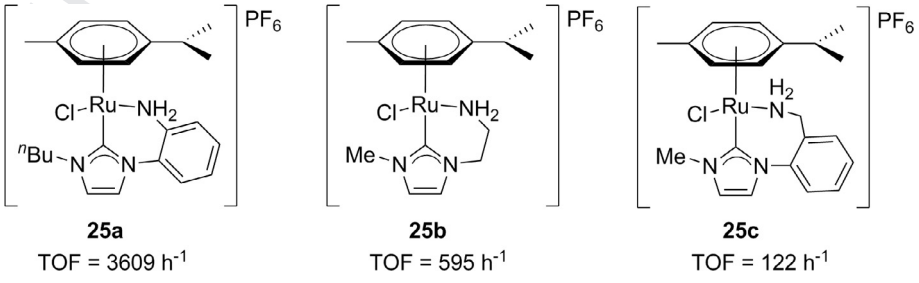
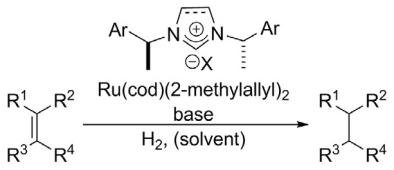
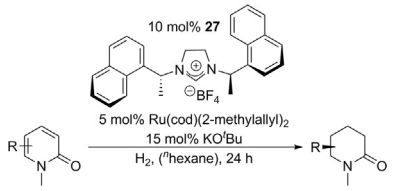


Fig. 13. Ruthenium(II) NHCs with aniline-, ethylamine- and benzylamine-derived chelating wingtips. TOFs were calculated at 50% conversion of acetophenone. Reaction conditions: T = 50 °C, p = 25 bar H_2, solvent = THF, B = KO^{t}Bu, S:C:B = 600:1:8 [75].



Scheme 5. Asymmetric hydrogenation of double bonds with a ruthenium(II) NHC catalyst. X = Cl^-, BF_4^-.

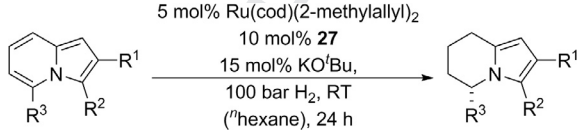


Scheme 6. Asymmetric hydrogenation of 2-pyridones with **27**. Reaction conditions: T = 25–60 °C, p = 10–120 °C [92].

Table 12
Improving the reaction conditions for the asymmetric hydrogenation of 2-pyridones with **27** [92].

Entry	H_2 pressure [bar]	Temperature [°C]	Conv. [%]	e.r.
1	10	30	<99	78:22
2	10	60	<99	68:32
3	40	40	<99	79:21
4	80	50	<99	75:25
5	120	25	<99	83:17

(Reaction conditions: solvent = ^{n}hexane, B = 15 mol% KOH, 10 mol% **27**, 5 mol% Ru(cod)(2-methylallyl)$_2$, t = 24 h.)



Scheme 7. HY of indolizine substrates [93].

Table 13
Asymmetric hydrogenation of different indolizine substrates with the general structure shown in Scheme 7 [93].

Entry	R^1	R^2	R^3	e.r.
1	H	^{n}Bu	Me	97:3
2	H	^{n}Bu	^{n}Pr	91:9
3	H	^{n}Bu	^{n}Undec	91:9
4	CO_2Et	H	Me	91:9
5	Ph	H	Me	95:5
6	*p*-F(C_6H_5)	H	Me	94:6
7[a]	*p*-OMe(C_6H_5)	H	Me	–

(Reaction conditions: T = RT, p = 100 bar H_2, solvent = ^{n}hexane, B = 15 mol% KO^{t}Bu, 10 mol% NHC **27**, 5 mol% Ru(cod)(2-methylallyl)$_2$, t = 24 h. Full conversion was reached for all substrates but *p*-OMe(C_6H_5). [a]No conversion.)

in situ, with Ru(cod)(2-methylallyl)$_2$ as catalyst precursor (Scheme 5).

A proof for the applicability of this system is given by the reduction of 2-pyridones [92]. By adding imidazolium salt **27** to the reaction mixture, several substrates with the pyridone skeleton can be hydrogenated under pressure (Scheme 6).

The reaction conditions were optimized with 6-methyl-2-pyridone as substrate. While a high conversion is obtained for any applied temperature and pressure, the conditions influence the enantiomeric ratio notably (Table 12). Optimum conditions have been reached at 25 °C with a hydrogen pressure of 120 bar (e.r. = 83:17, entry 5). It is remarkable that the amount of base used in the experiments is comparably high (15 mol%), but no control was run with different concentrations or no base at all to determine its impact on the catalytic reactions.

Variation of the solvent from ^{n}hexane to a 1:1 mixture of ^{t}-AmOH:^{n}hexane results in an increased stereoselectivity (e.r. = 94:6). It must be noted that the temperature has to be decreased to −10 °C to achieve this high enantiomeric ratio. To extend the substrate scope, several moieties on 2-pyridone (Scheme 6) were examined under optimized conditions. Among various aryl- and methyl-substituted substrates, no general trend can be observed. Still, the best e.r. is obtained with the previously investigated 6-methyl-2-pyridone, followed by 3-methyl-2-pyridone (e.r. = 82:18). All other compounds reached medium enantiomeric ratios below 80:20.

NHC **27** was then successfully applied for the HY of alkaloid substrates (Scheme 7) [93]. For almost all examined moieties R^1, R^2 and R^3, good to excellent e.r. were observed (Table 13).

An increase of the bulkiness of R^3 decreases the e.r. slightly (entries 1–3), aryl moieties for R^1 by contrast enhance the enantioselectivity for phenyl and *p*-fluorophenyl substituents (entries 5 and 6). A shift of R^3 from the 5- to the 7- or 8-position results in a strong decrease of e.r. below 75:25. With the methyl-group in 6-position, no conversion was observed.

After extending the substrate scope to various compounds that exhibit a natural product skeleton [94,95], investigations were directed to a more detailed mechanistic study. By exposing NHC **27** to Ru(cod)(2-methylallyl)$_2$ under catalytic conditions (KO^{t}Bu, ^{n}-hexane), bis-NHC **28a** was formed (Fig. 15) [96].

The isolation of this species and its application in catalysis revealed an induction period of 3 h under H_2 pressure before the actual hydrogenation reaction starts. NMR and MS experiments indicate that the active species **28b** is formed under hydrogen pressure. The hydrogenation of the previously examined substrates is thus assumed to proceed via this active catalyst.

Besides mechanistic investigations, attempts were made to further increase the activity and selectivity of the catalyst. *Zhou* et al. compared NHCs with different wingtips for the hydrogenation of quinoxalines and thiophenes (Fig. 16) [97].

It was observed that the wingtip substituent not only influences stereo- but also regioselectivity. When 2,3-diphenylquinoline is reduced, two different products are found (Scheme 8) [97].

Product **30b** is only favored over **30a** (99% vs. <1%) when the cyclohexyl-substituted NHC **29b** is added. The application of all other depicted NHCs affords **30a**. In neither case complete hydrogenation of both 6-membered rings is found. When benzothiophenes are reduced under addition of **29e**, stereo- and regioselective hydrogenation of the 5-membered ring occurs with high *ee* (≥96%) for all examined substituents in 2-position [97]. An extension of the substrate scope to several 2,4- and 2,5-substituted furans proves the versatile applicability of **29e** for different substrate skeletons [99].

A further attempt to optimize the asymmetric hydrogenation with ruthenium(II) NHCs included the addition of a second ligand **L** to the reaction mixture besides the NHC (Scheme 9) [100]. The substrate 3-methylisocoumarin was reduced with good *ee*, yields differ slightly for the ligands **L1**–**L4** (Table 14).

Table 14 shows that the *ee* remains quite constant for the investigated ligands, both for electron-withdrawing and electron-donating substituents on the aromatic ring. When no ligand is

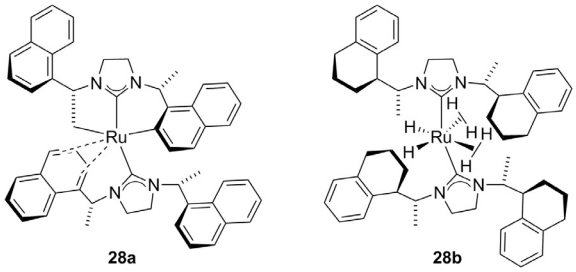


Fig. 15. Bis-NHCs **28a** and **28b**, formed by reaction of **27** with Ru(cod)(2-methylallyl)$_2$ and addition of KO^{t}Bu (**28a**), resp. under H_2 (**28b**) [96].

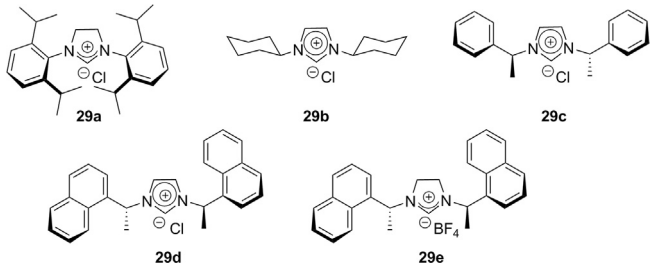
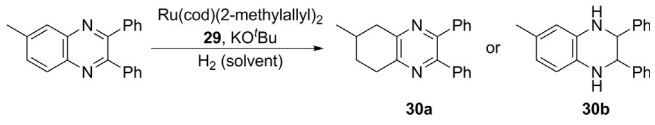
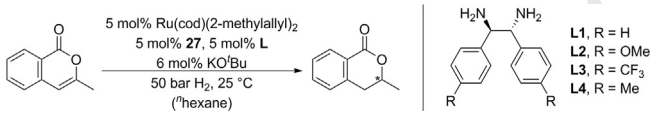


Fig. 16. Altering the wingtip substituent of NHCs for asymmetric hydrogenation [97].



Scheme 8. Reduction of 2,3-diphenylquinoline. Reaction conditions to obtain **30a**/**30b**: T = 60 °C/80 °C, p = 65 bar/55 bar H_2, solvent = hexane/toluene, B = 30 mol% KO^{t}Bu, 20 mol% NHC **29**, 10 mol% Ru(cod)(2-methylallyl)$_2$, t = 18 h [97,98].



Scheme 9. Addition of a second ligand **L** in the asymmetric hydrogenation of isocoumarins, t = 8–10 h [100].

added (entry 1), the opposite enantiomer is formed. Further examinations with secondary instead of primary amines inhibited the reaction and no product formation was observed. The best-performing ligand **L4** (entry 5) was used for the conversion of a variety of isocoumarin substrates, affording good yields and high *ee* (>93%) for almost all examined structures.

The described examples of asymmetric hydrogenation reactions of alkene substrates with ruthenium(II) NHCs underline the high potential of these complexes for asymmetric transformations. Their applicability in the synthesis of natural products reveals the pertinence not only for academia, but also as possible catalysts in the pharmaceutical industry.

4.2. Hydrogenation of ketones

The asymmetric hydrogenation of ketones catalyzed by ruthenium(II) NHCs has been sparingly described in the literature and only a few examples have been reported. Additional to the widely known ruthenium(II) hydride and phosphine hydrogenation catalysts prepared by this group [101–103], *Morris* et al. examined a

Table 14
Examination of different ligands **L** in the asymmetric hydrogenation of isocoumarins [100].

Entry	L	Time [h]	Yield [%]	*ee* [%]
1	–	10	69	-21
2	**L1**	10	79	92
3	**L2**	8	80	92
4	**L3**	19	51	89
5	**L4**	10	78	94

(Reaction conditions: T = 25 °C, p = 50 bar H_2, solvent = ^{n}hexane, B = 6 mol% KO^{t}Bu, 5 mol% catalyst loading, 5 mol% **27**, 5 mol% **L**.)

chiral ruthenium(II) NHC complex as catalyst for TH reactions. This half-sandwich complex **31** bears a pentamethylcyclopentadienyl (Cp*), an NHC and an acetonitrile ligand (Fig. 17) [104].

In contrast to the previously discussed monodentate NHCs (chapter 2.1), the cymene moiety is exchanged by the electron-rich Cp* anionic ligand. Consequently, the complex does not require an additional counterion and a higher catalytic activity is anticipated. In fact, **31** is very active in the hydrogenation of various ketones (Scheme 10 and Table 15) [104].

Albeit high TOFs up to 43,000 h^{-1}, only low enantioselectivity is observed for the examined substrates (Table 15). While alkyl- and aryl-ketones are fully converted to the corresponding alcohols within less than one hour, benzaldehyde and cyclohexanone-, furan- or styrene-derived substrates are not transformed.

The influence of the substrate itself on the reaction is furthermore shown by substitution of the phenyl ring in *ortho*-, *meta*- or *para*-position. The latter leads to a 3- to 5-fold increase of the TOF when chloride or methyl moieties are present. Substituents in *ortho*- or *meta*-position by contrast hamper the conversion.

To get additional insight in the role of the chiral NHC ligand and to improve enantioselectivities, mechanistic investigations were accomplished. NMR spectroscopy and DFT studies point to the existence of two possible enantiomers of an intermediate hydride species (Fig. 18).

The concurrent formation of both enantiomeric intermediates constitutes a plausible reason for the low *ee* observed in the hydrogenation of ketone substrates (Scheme 10 and Table 15). Another possibility for the low enantioselectivity of the catalyst is the racemization of the wingtip ligand under basic conditions.

A different approach for the improvement of chiral ruthenium (II) NHC catalysts was conducted by *Sakaguchi* et al., who described a series of chiral NHCs with different arene backbones (Fig. 19) [105].

The examination of these complexes as catalysts in the asymmetric TH of acetophenone (Table 16) reveals that the highest *ee* can be obtained with hexamethylbenzene as ligand (entry 3), albeit the overall yield is low. Better performance was observed with *p*-diisopropylbenzene (entry 5), reaching 56% conversion and an *ee* of 35%. Comparable results were obtained when using

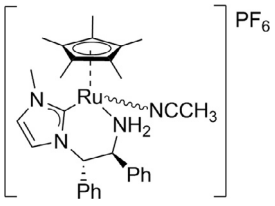
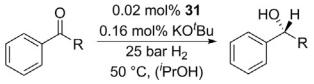


Fig. 17. Ruthenium(II) half-sandwich complex applied for the asymmetric HY of ketones [104].



Scheme 10. Hydrogenation of ketone substrates by **31**, **t** = 15–60 min [104].

Table 15
Hydrogenation of selected acetophenone-related substrates with **31** [104].

Entry	R	Time [min]	TOF [h^{-1}]	*ee* [%]
1	H	–	0	–
2	Me	15	31,000	5
3	Et	30	24,000	16
4	^{i}Pr	30	43,000	34
5	^{t}Bu	60	19,000	21[a]
6	Ph	15	40,000	–

(Reaction conditions: T = 50 °C, p = 25 bar H_2, solvent = ^{i}PrOH, B = 0.16 mol% KO^{t}Bu, 0.02 mol% catalyst loading. [a]The (*S*) enantiomer is formed.)

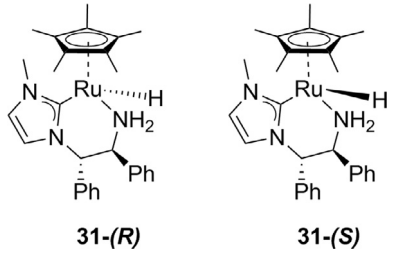


Fig. 18. Hydride intermediates formed from **31** in HY reactions [104].

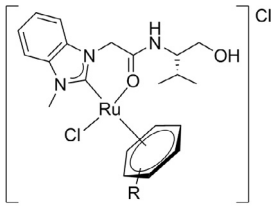


Fig. 19. Chiral ruthenium(II) NHCs for asymmetric TH reactions [105].

30 mol% ^{t}BuOK instead of KOH, albeit in 6 h reaction time. No experiment was performed that shows the influence of the amount of base used, however.

The discussed results show that asymmetric hydrogenation reactions of ketones can be performed reasonably well with chiral ruthenium(II) NHCs. Up to now, only moderate enantiomeric excess is achieved with the existing complexes. Further development should thus be directed towards an improvement of the enantioselectivity of the catalysts and the subsequent application in natural products chemistry.

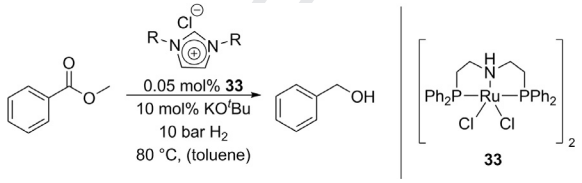
5. Reduction of esters, imines, nitriles and olefins by direct and transfer hydrogenation

Apart from the hydrogenation of ketones and aldehydes, several other functionalities can be hydrogenated with the help of ruthenium(II) NHCs. This review will be restricted to the reduction of esters, imines, nitriles and olefins as the most frequently investigated substrates in recent years. Reaction types involve direct hydrogenation under H_2 and transfer hydrogenation using ^{i}PrOH.

Table 16
Asymmetric TH of acetophenone to (*S*)-1-phenylethanol [105].

Entry	Arene	Yield [%]	ee [%]
1	*P*-Cymene	19	31
2	*p*-^{t}Bu-methylbenzene	27	27
3	Hexamethylbenzene	9	**41**
4	Benzene	4	9
5	*p*-Diisopropylbenzene	**56**	35
6	*m*-Diisopropylbenzene	6	25
7	1,3,5-Triisopropylbenzene	39	35

(Reaction conditions: T = RT, solvent = ^{i}PrOH, B = 30 mol% KOH, 4 mol% catalyst loading, t = 20 h.)



Scheme 11. Hydrogenation of methyl benzoate by **33** under addition of 0.1 mol% NHC, t = 5 h [107].

5.1. Ester hydrogenation

The hydrogenation of esters constitutes an important transformation in chemical and pharmaceutical industry, comprising for example the conversion of fatty acid esters or the formation of relevant intermediates to produce drugs [2,106]. Ruthenium(II) complexes represent an atom economic alternative to stoichiometric reduction processes performed by DIBAL-H, for instance. The NHCs that emerged therefore in the last years will be discussed, divided into monodentate, bidentate and pincer ligands.

As already mentioned for the hydrogenation of ketone substrates (chapters 2 and 3), different wingtip substituents of monodentate NHCs were examined likewise in ester hydrogenation [107]. Methyl benzoate was transformed to phenylmethanol by addition of the precatalyst $[RuCl_2(PNP)]_2$ **33** and the respective NHC under hydrogen pressure (Scheme 11).

A dependence of the product formation on the steric demand of the wingtip substituent can be observed (Table 17). Methyl moieties yield 85% of the alcohol within 5 h (entry 1), while very low yields are noted with ^{t}Bu or Mes substituents (entries 5 and 6). The bulkier a substituent, the less product is detected, possibly due to shielding of the free coordination site by the wingtips. Despite partly low yields with some of the examined substituents, a relatively low catalyst loading of 0.05 mol% was applied, compared to the most commonly observed 0.1–1.0 mol% catalyst loading (see previous examples). The TON therefore ranges from 100, as observed for monodentate NHCs (chapter 2.1) to 1700, calculated for instance for pincer complexes (chapter 2.2).

The anion of the NHC precursor further influences the reaction. Thus, the NHC with ^{i}Pr wingtip leads to 70% and 83% product yield when using Cl^- and BF_4^- as anion, respectively (entries 2 and 3). Since the hydrogenation of various substrates can be accomplished with the synthesized ruthenium(II) NHC complex **34** (Fig. 20), this property can be neglected in the following catalytic studies.

With **34**, several aromatic and two aliphatic esters were hydrogenated under ambient H_2 pressure (H_2 balloon), however with very low TOFs <10 h^{-1} [107]. Higher turnovers were obtained by *Beller* et al., who compared the activity of mono- and bidentate ruthenium(II) NHCs (Table 18) [108]. While the hydrogenation of methyl benzoate with a mesityl-substituted mono-NHC does not lead to a distinct alcohol formation after 6 h (entry 1), all investi-

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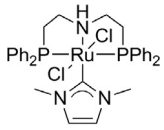
Table 17
Hydrogenation of methyl benzoate with different wingtip substituents on the NHC [107].

Entry	Wingtip R	Anion	Yield [%]	TON
1	Me	Cl^-	85	1700
2	^{i}Pr	Cl^-	70	1400
3	^{i}Pr	BF_4^-	83	1660
4	Cyclohexyl	BF_4^-	42	840
5	^{t}Bu	BF_4^-	11	220
6	Mes	Cl^-	5	100

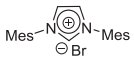
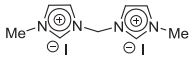
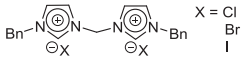
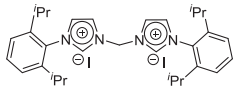
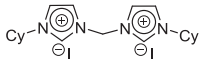
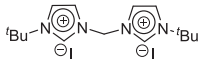
(Reaction conditions: T = 80 °C, p = 10 bar H_2, solvent = toluene, B = 10 mol% KO^{t}Bu, 0.05 mol% catalyst loading, t = 5 h.)



34

Fig. 20. Ruthenium(II) NHC **34** used for the hydrogenation of various esters [107].

Table 18
HY of methyl benzoate by addition of different mono- and bidentate NHCs [108].

Entry	NHC	Yield [%]
1		7
2		65
3		77 75 **82**
4		72
5		47
6		34

(Reaction conditions: T = 100 °C, p = 50 bar H_2, solvent = 1,4-dioxane, B = 30 mol% KO^{t}Bu, 0.5 mol% [(*p*-cymene)$RuCl_2$]$_2$, 2 mol% NHC, t = 6 h. Only selected NHCs depicted.)

gated bis-NHC compounds result in moderate (entries 5 and 6) to high (entries 2–4) yields.

The use of a high amount of base (30 mol% KO^{t}Bu) is attributed by the authors to incomplete conversion of substrate with smaller amounts, proved by a decrease of yield when applying 20 mol% KO^{t}Bu (77% instead of 88% yield). A remarkable influence of the wingtip substituents is observed in this case as well: bulky aliphatic moieties lead to modest yields (entries 5 and 6), aromatic substituents result in increased conversion (entries 3 and 4). The best catalytic effect is noticed for a benzyl-substituted bis-NHC (entry 3). With this ligand, the influence of the counterion was determined, showing iodide as the most effective, followed by chloride and bromide, respectively. Since no significant distinction between the yields is observed (up to 7% difference), no general conclusion can be drawn from these results, especially since only one of the NHC ligands was tested on the influence of the counterion.

The bis-NHC-chloride (entry 3) was further employed for the hydrogenation of various esters. More than 20 substrates, comprising aliphatic and aromatic skeletons, could be transformed successfully to their respective alcohols with up to 92% yield in 6 h (TOF = 31 h^{-1}). Unfortunately, double bonds present in selected aliphatic substrates were hydrogenated as well, discounting the chemoselectivity of the catalyst.

Though many different ester substrates can be hydrogenated by monodentate ruthenium(II) NHCs, the observed TOFs are comparably low. Bi- and tridentate carbenes were found to be more active, reaching turnovers of more than 4800 h^{-1}. Some examples for these complexes are depicted in Fig. 21 [109–111]. It is striking that also for the displayed catalysts, a wide range of aromatic and aliphatic esters is transformed to its respective alcohols.

A computational study for **35** ascertained an outer-sphere mechanism for the ester hydrogenation with this complex [111]. This bifunctional catalysis benefits from the aforementioned *NH effect* (chapter 2.4) which promotes the cleavage of dihydrogen and makes amine ligands popular for this type of catalysis [62,113,114]. Nevertheless, mechanistic considerations for the catalytic reduction of esters with ruthenium(II) NHC complexes have to take into account several parameters, such as the base strength [115], and no general mechanism can be proposed for this reaction.

The hydrogenation of esters is catalyzed by mono-, bi- and tridentate ruthenium(II) NHCs, generating TOFs up to 4830 h^{-1}. Despite partially lower activities of the catalysts for ester reduction in comparison with ketone substrates, the vast variety of transformed substrates is notable, as catalysts are active for aromatic and aliphatic esters.

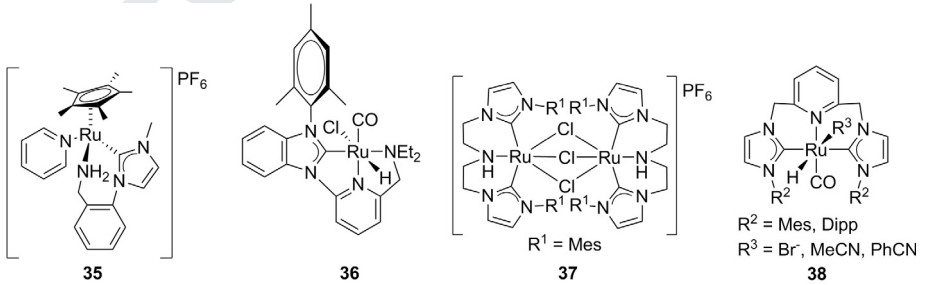


Fig. 21. Bi- and tridentate ruthenium(II) NHCs used for ester hydrogenation [109–112]. For **38**, Br^- was used as counterion when R^3 = MeCN, PhCN. Dipp = 2,6-diisopropylphenyl. TOFs are given for the substrate that afforded the highest values. Bases used: KO^{t}Bu (**35**, **37**), NaO^{t}Bu (**36**), KOMe (**38**).

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5.2. Imine and nitrile hydrogenation

The formation of amines by reduction of imines and nitriles receives attention in homogenous catalysis since the early 1970s. Pioneering work by *Wilkinson*, *Noyori* and *Buchwald* showed that transition metal complexes serve as efficient catalysts for these transformations [116–119]. Direct as well as transfer hydrogenation are employed and a variety of asymmetric reactions is carried out to date. An overview of the most recent examples of ruthenium NHCs used for HY and TH of imine and nitrile substrates is given in this chapter.

Frequently, a similar structure of the catalyst is applied for the hydrogenation of substrates with different functionalities. Thus, complexes **39a–d** (Fig. 22) were not only examined for ketone reduction (chapter 2.3), but also for the TH of imines with ^{i}PrOH [28].

N-Benzylideneaniline is transformed to its corresponding amine successfully, however resulting in low TOFs (Table 19). The best catalytic activity is still obtained with the pyrimidine backbone (entry 4). Despite the moderate outcome with ruthenium(II) NHCs **39a–d**, much higher conversions could be achieved than with the analogue iridium(III) and osmium(II) species.

The monodentate NHC complex **40** displays good activity in the transfer hydrogenation of nitrile substrates in ^{i}PrOH, resulting in the formation of ketimine derivatives as a result of the subsequent condensation with acetone (Scheme 12) [37].

Several aromatic and aliphatic nitriles can be transformed to their corresponding alkylated imines in good yields (Table 20). While aromatic substrates afford high yields in less than 3 h (entries 1–6), aliphatic starting material is converted quantitatively only after 48 h (entries 7–9). These results reveal a significant discrepancy for different substrate backbones, unlike in the hydrogenation of esters, for instance (chapter 5.1). The calculated TONs reach values between 64 and 198 and do not suggest a high stability of the catalyst, but catalytic trials were conducted only at one catalyst loading (0.5 mol%) and the focus lies rather on the broad substrate scope than on the stability of the catalyst.

Another interesting fact is the incomplete reduction of the C–N functionality, resulting in imines instead of amine products, which are usually observed [120–123]. Thus, *Bera* et al. found that several aromatic and aliphatic nitriles were converted selectively to their secondary amines under catalytic conditions (T = 80 °C, p = 60 bar H_2, solvent = ^{i}PrOH, 2 mol% Ru–NHC) and the reaction does not stop at the imine product [123]. The applied hydrogen pressure is presumably the reason for the reaction outcome, in a way that it leads to completely hydrogenated products, while TH halts at the imine.

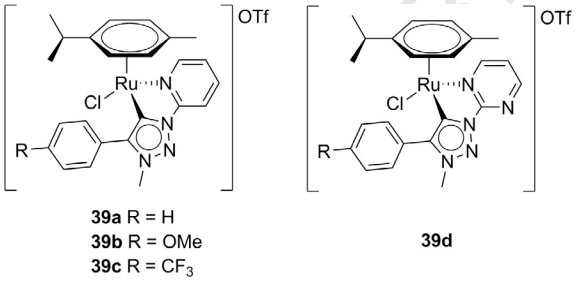
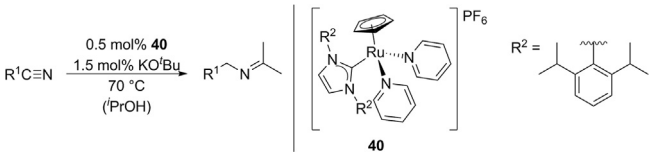


Fig. 22. Ruthenium(II) NHCs **39a–d** investigated for the TH of imines [28].

Table 19
TH of *N*-benzylideneaniline with catalysts **38** [28].

Entry	Catalyst	Conversion [%]	TOF [h^{-1}]
1	**39a**	71	7.9
2	**39b**	87	9.7
3	**39c**	60	6.7
4	**39d**	90	10.0

(Reaction conditions: T = 100 °C, solvent = ^{i}PrOH, B = 5 mol% K_2CO_3, 0.5 mol% catalyst loading, t = 18 h.)



Scheme 12. Monodentate ruthenium(II) NHC **40** used for the TH of nitriles [37].

Besides TH reactions of imines, the direct hydrogenation of those substrates has been carried out with the pincer NHC complexes **41a–d** (Fig. 23 and Scheme 13).

Depending on the electronic properties of the moieties R^1 and R^2 on the substrate, TOFs up to 167 h^{-1} (t = 6 h) could be achieved and a variety of electron-donating and -withdrawing substituents are tolerated. The turnover values are not among the best for ruthenium-catalyzed imine HY, but only few NHCs are known to facilitate this transformation [126–128].

Mechanistic studies, including NMR spectroscopy and DFT calculations, verified the analogy of the intermediate species with those found in the reduction of other substrates (e.g. ketones and esters). Similarly, dihydride formation via dissociation of the phosphine was observed and an outer-sphere mechanism was proposed for the hydrogenation of C=N groups [124].

Overall, TH and HY of nitriles and imines are useful tools for the synthesis of amines. Mostly asymmetric reactions are investigated and ruthenium NHCs are barely examined for these transformations. However, the considered complexes offer a broad substrate scope in most cases.

5.3. Olefin hydrogenation

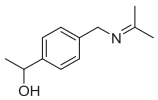
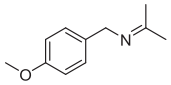
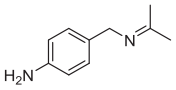
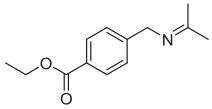
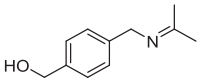
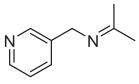
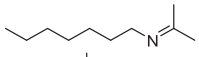
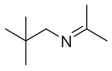
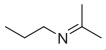
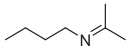
Compared to the previously described substrates, olefins are rather challenging functional groups for hydrogenation reactions due to their lack of polarity. Nevertheless a series of transition metal catalysts is known for this transformation, as the reaction is of importance in petrochemical industry [3]. Despite the general tendency to move to cheaper metals to catalyze the hydrogenation of alkenes [129–131], ruthenium NHCs still receive considerable attention within this field.

Direct hydrogenation and transfer hydrogenation can be applied likewise for the reduction of C=C double bonds. The following examples include both reaction types and provide mechanistic studies to evaluate ligand effects on the activity of the respective complexes in catalysis.

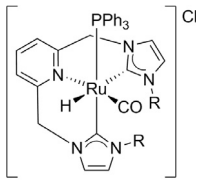
To extend the substrate scope of some previously mentioned catalysts (chapter 5.2) to several functionalities, complexes **39** and **40** (Fig. 22 and Scheme 12) were not only examined in the TH of amines and nitriles, but also of olefins. NHCs **39** (Fig. 22) hydrogenated *trans*-stilbene, *trans*-β-methylstyrene and *cis*-cyclooctene in reasonable yields (Table 21) [28]. Even if a relatively high amount of base was applied, only moderate turnovers could be obtained. In spite of the low TOFs, superior results than previously reported for similar catalysts were obtained [132], with better performances than those observed for corresponding iridium and osmium species. However, no selectivity towards the C=C double bond in presence of other functionalities was observed. When reacting cyclohexenone, both C=C and C=O bonds are reduced to yield cyclohexanol.

Both higher TOFs and better chemoselectivity were obtained with **40** (Scheme 12) [37]. Besides some cyclic and acyclic alkenes,

Table 20
TH of nitriles by **40** [37].

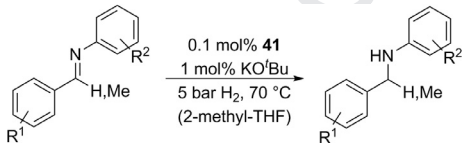
Entry	Product	Yield [%]	Time [min]	TOF [h^{-1}]	TON
1		97	45	259	194
2		98	50	235	196
3		87	90	116	174
4		90	195	55	180
5		97	120	97	194
6		95	165	69	190
7		59	48 h	3	118
8[a]		32	48 h	1	64
9[a]		98	48 h	4	196
10[a]		99	48 h	4	198

(Reaction conditions: T = 70 °C, solvent = ^{i}PrOH, B = 1.5 mol% KO^{t}Bu, 0.5 mol% catalyst loading. [a]Reaction at 90 °C.)



41a R = ^{i}Pr
41b R = hexyl
41c R = np[a]
41d R = 3,5-xilyl

Fig. 23. Pincer NHCs **41a–d** used for the HY of imines. [a]Bromide was used as anion [124,125].



Scheme 13. HY of imines by **41** [125].

several substrates with ester functionalities were reduced selectively (Scheme 14 and Table 22).

It must be noted that a transesterification from R^1 to ^{i}Pr occurs and that in some cases a considerable amount of the Michael adduct **M** is formed.

For most substrates, the major product is the hydrogenated alkene **HY** and only a low amount of **M** is formed. When the steric demand of R^1 increases from Me to Et or Ph, chemoselectivity drops significantly and up to 15% **M** is produced. A high substitution on the C=C double bond furthermore seems to enhance the chemoselective formation of **HY**, even though sterically hindered olefins are generally known as problematic starting material for hydrogenation reactions [133,134]. Similar to the behavior of **40** in nitrile hydrogenation, the substrate scope has priority over stability studies of the catalyst in the presented work, and only one catalyst loading (0.5 mol%) was examined, reaching TONs up to 198.

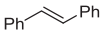
In addition to TH reactions, the direct hydrogenation of olefins with ruthenium(II) NHCs was examined. *Stephan* et al. found that several mono- and bis-NHCs are active in the HY of alkenes (Fig. 24) [135,136].

The depicted complexes **42**–**47** provided comparably low TOFs in first experiments (5 mol% catalyst loading, TOF <10 h^{-1}), but the high robustness of **43** was regarded as a promising prerequisite for further investigations. Since cyclic bent allenes are known to exhibit stronger σ- and π-basicity than their NHC analogues [137–139], one NHC ligand in **43** was exchanged for a cyclic bent allene to yield complex **48** (Fig. 25), which was then examined in the TH of olefins (Table 23) [140].

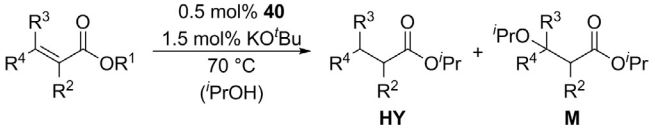
With 1-hexene, high TOFs of up to 112,800 h^{-1} could be achieved, showing that **48** is among the most active catalysts for olefin hydrogenation and much more efficient than previous examples [141,142]. Besides the high activity, a low catalyst loading of only 0.005 mol% is reached for certain substrates, evidencing the high stability of the complex in olefin HY. TONs of up to 19,400 are thus obtained, superior to all other presented examples.

In addition to linear alkenes (entries 1–7), aromatic compounds, such as styrene (entries 8–12), are reduced selectively at the aliphatic position. The more sterically hindered a substrate, the lower

Table 21
TH of olefins with catalysts **39** [28].

Entry	Substrate	Catalyst (loading [mol%])	Yield [%]	TOF [h^{-1}]
1		**39a** (1.0)	30	1.3
2		**39b** (1.0)	41	1.7
3		**39c** (1.0)	28	1.2
4		**39d** (1.0)	13	0.5
5		**39a** (1.0)	65	2.7
6		**39b** (1.0)	75	3.1
7		**39c** (1.0)	56	2.3
8		**39d** (1.0)	78	3.3
9		**39a** (0.5)	79	6.6
10		**39b** (0.5)	94	7.8
11		**39c** (0.5)	72	6.0
12		**39d** (0.5)	87	7.2

(Reaction conditions: T = 100 °C, solvent = ^{i}PrOH, B = 17 mol% KOH, t = 24 h.)



Scheme 14. TH of alkenes in the presence of ester groups with **40** [37].

Table 22
TH of alkenes in the presence of ester groups with **40** [37].

Entry	Substrate	Yield **HY**/**M** [%]	Time [h]	TOF[a] [h^{-1}]
1		80/20	8	20
2		95/5	8	24
3		85/15	8	21
4		89/11	8	22
5		89/11	16	11
6		98/0	48	4.1
7		93/7	16	12
8		99/0	72	3.0
9		No reaction	24	–

(Reaction conditions: T = 70 °C, solvent = ^{i}PrOH, B = 1.5 mol% KO^{t}Bu, 0.5 mol% catalyst loading. [a]TOFs calculated for **HY**.)

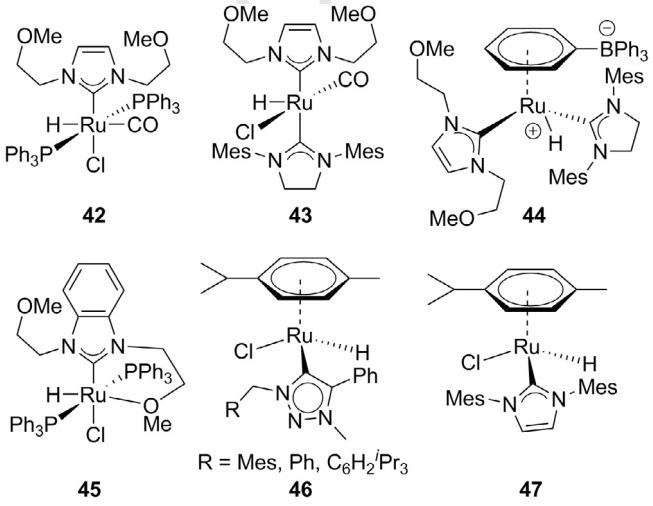


Fig. 24. Ruthenium(II) NHCs **42**–**47** for the HY of alkene substrates [135].

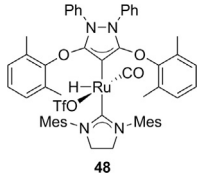


Fig. 25. Ruthenium(II) NHC **48** used for the TH of olefins [140].

turnovers are observed, however. A functionalization of the substrate with ketone, ester or nitrate groups retains the chemoselectivity of the catalyst and substrates like cyclohexenone are converted selectively into their alkane analogues.

DFT calculations for related ruthenium(II) NHC catalysts confirmed these experimental findings. The groups of *Liu* and *Houk* found that an increase of the substrate's steric demand leads to a significantly higher energy barrier for the hydride migration step [143]. This is due to the steric hindrance, resulting from the interaction of substrate and ligand moieties. High steric bulk on the NHC backbone by contrast results in a good stabilization of the complex and favors the reductive elimination and oxidative addition steps by lowering their reaction energy barrier. Consequently, both the substrate and the catalyst influence on the reaction must be considered.

In summary, a small number of ruthenium(II) NHCs for the HY and TH of olefins is established. Even if other substrates than ketones usually afford lower turnovers than their more profoundly investigated carbonyl counterparts, certain catalysts are known that exhibit TOFs up to 112,800 h^{-1} for the hydrogenation of olefins, with catalyst loadings as low as 0.005 mol%.

6. Conclusions

Ruthenium(II) NHCs are well-established catalysts for a series of hydrogenation reactions, namely the direct and transfer hydrogenation of aldehydes, ketones, olefins, esters, substrates with C–N functionalities, as well as the asymmetric hydrogenation to form chiral organic compounds. One of the most widely examined reactions is the transfer hydrogenation of ketone substrates, and a large

Table 23
HY of olefins with **48** [140].

Entry	Substrate	Ru [mol%]	Conv. [%] (Time [min])	TOF [h^{-1}]	TON
1	1-Hexene	0.01	100 (15)	40,000	10,000
2			68 (5)	81,600	6800
3		0.005	92 (15)	73,600	18,400
4			47 (5)	112,800	9400
5	Cyclohexene	0.01	93 (30)	18,600	9300
6	2-Methyl-2-butene	0.05	100 (120)	1000	2000
7			56 (30)	2240	1120
8	Styrene	0.005	97 (30)	38,800	19,400
9	2-Methylstyrene	0.02	95 (60)	4750	4750
10	1-Methylstyrene	0.05	95 (60)	1900	1900
11	Stilbene	0.05	100 (960)	125	2000
12	1-methylstilbene	0.5	98 (960)	12	196

(Reaction conditions: T = 25 °C, p = 20 bar H_2, solvent = dichloromethane, without base.)

number of ruthenium catalysts for this transformation were investigated, including mono-, bi-, tri- and tetradentate NHCs. Even if the obtained turnovers are not superior to those achieved for some ruthenium phosphines, the tunability of the NHC offers manifold possibilities to adjust the performance and selectivity to design task-specific catalysts. Direct hydrogenations, by contrast, are not in the field's center of attention, as its disadvantages prevail in comparison to hydrogen transfer from sources like ^{i}PrOH, formic acid or glycerol. Its application is largely limited to specific examples, such as hydrogenations in water. Since asymmetric reactions are of interest in industry, e.g. to produce pharmaceuticals, the stereoselective formation of alcohol derivatives has received growing interest in the last decades. An increasing number of ruthenium (II) NHCs are explored therefore, reaching good enantioselectivity for both the reduction of C=O and C=C bonds. An extension of the substrate scope of the catalysts to several functionalities, such as esters, imines, nitriles and olefins, was carried out successfully, with the development of chemoselective catalysts. Accordingly, ruthenium(II) NHCs complement phosphines as some of the most active homogenous catalysts for hydrogenation reactions. The possibility for modifications of NHCs offers high potential for the improvement of the catalytic properties and the substrate scope. Future work should exploit this ability to develop catalysts with both a high robustness and selectivity. A combination of the stability of NHC ligands with the considerable *trans*-effect of phosphines, for instance, displays an opportunity to exploit the beneficial features of both substituents. Mechanistic studies to support the rational design of task-specific catalysts are thereby ineviTable for a profound understanding of the catalytic processes.

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Declarations of interest

None.

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