16
Hydrogenation of Arenes and Heteroaromatics

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16.1
Introduction

The hydrogenation of arenes and heteroaromatics to partially or fully saturated cyclic hydrocarbons is a reaction of paramount industrial importance, typically catalyzed in heterogeneous phase by a number of transition metals [1]. Just to mention a few huge applications, each year a million tons of benzene are hydrogenated on Raney nickel to cyclohexane for the production of nylon *via* adipic acid [2], and much larger amounts of liquid fossil fuels are hydrotreated in refineries to remove sulfur, nitrogen, and oxygen from various heteroaromatics – the hydrodesulfurization (HDS), hydrodenitrogenation (HDN), and hydrodeoxygenation (HDO) processes [3]. The hydrogenation of aromatics and heteroaromatics will become increasingly important if coal, which contains a huge amount of such compounds, continues to be used for the production of petrochemicals.

Aromatic hydrogenation reactions in homogeneous phase are much less numerous, and also much less efficient than in heterogeneous phase, especially in terms of turnover frequencies and catalyst stability [4]. On the other hand, soluble metal complexes still provide a better regio- and stereo-control in the reduction of heteroaromatics, although this supremacy over heterogeneous catalysis is being threatened by the development of increasingly efficient chiral phase-transfer reagents and chiral auxiliaries adsorbed onto the support materials [5]. There is little doubt, however, that organometallic compounds will always play an irreplaceable role as models systems to gain insight into the mechanisms of substrate binding and activation as well as hydrogen adsorption, activation, and transfer. The origin of the chemo-, regio-, and stereoselectivity is another issue that can be better addressed at the molecular level than using a supported metal particle.

The scarce number of metal complexes capable of catalyzing the hydrogenation of arenes is a direct consequence of the tendency of these substrates to use all the available π-electrons for coordination, and hence to occupy three contigu-

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ous coordination sites [6]. Indeed, the barrier to disruption of the aromaticity is generally very high and other bonding modes, such as the η^2 and the η^4, which would allow a more facile metal coordination and a lower barrier to reduction (H_2 activation and transfer), are extremely difficult to accomplish, even with highly energetic metal fragments [7]. Just the presence of the heteroatom, with suitable lone pairs for σ-bonding to the metal, is the main reason for the relatively large number of homogeneous catalysts capable of hydrogenating sulfur-, oxygen-, and nitrogen-heteroaromatics [8]. The most effective molecular catalysts for the hydrogenation of arenes and heteroaromatics are complexes consisting of a central metal ion (generally ruthenium, rhodium, or iridium), one or more ligands, and anions. The ensemble of these three components is responsible for the activation of hydrogen (either heterolytic or homolytic) and its selective transfer to an acceptor substrate. Experience has shown that low-valent metal complexes stabilized by ligands with phosphorus and/or nitrogen donor atoms constitute the most active and versatile catalysts [2, 8, 9].

The aim of this chapter is to provide the reader with a survey of the molecular catalysts that are able to hydrogenate aromatics, and to demonstrate the advantages and limits of the homogeneous approach. This review includes hydrogenation reactions performed in aqueous-biphasic systems, while the many structural and mechanistic analogies between molecular catalysts and heterogenized single-site metal catalysts induced us to comment also about aromatic hydrogenation by metal complexes tethered to both inorganic and organic support materials.

Several excellent reviews on the selective hydrogenation of arenes and heteroaromatics by single-site metal catalysts have been published over the past few years [8–10]. Consequently, the reader is advised to become acquainted with these accounts in order to obtain a deeper insight into the subject.

16.2
Hydrogenation of Arenes

16.2.1
Molecular Catalysts in Different Phase-Variation Systems

Very few metal complexes have been reported to generate effective catalysts for the hydrogenation of carbocyclic aromatic rings in homogeneous phase. Moreover, even the reported cases are not completely convincing, as black metal often precipitates during the catalysis. In fact, the reduction of arenes is the domain of heterogeneous catalysts, especially those based on noble metals among which rhodium, ruthenium, and platinum generate the most active systems [11]. The chemoselectivity is generally low, as most of the functional groups are hydrogenated prior to the aromatic ring. In contrast, several regioselective examples of *cis* hydrogen addition have been reported [12], while no example of asymmetric hydrogenation of prochiral arenes in homogeneous phase has been reported so far.

Table 16.1 Homogeneous catalysts, tethered single-site catalysts, and biphase catalysts for the hydrogenation of aromatic hydrocarbons.

Catalyst	Substrate	*T* [°C]	pH_2 [bar]	Reference(s)
$M(OAr)(H)_3L_2$ (M = Ta, Nb; L = PM_2Ph, $PMePh_2$)	benzenes, polyaromatics	80–100	3–100	30
$[Ru(\eta^6\text{-}C_{10}H_{14})(\eta^2\text{-triphos})Cl]PF_6$	benzenes [a]	90	60	19
$RuH_2(H_2)_2(PCy_3)_2$	benzenes, polyaromatics	80	3–20	18
$[Ru_3(\eta^6\text{-}C_6Me_6)_2(\eta^6\text{-}C_6H_6)(\mu_3\text{-}O)(\mu_2\text{-}OH)(\mu_2\text{-}H)_2]BF_4$	benzenes [a]	20	40	22
$RuCl_2(PTA)(\eta^6\text{-}C_{10}H_{14})$; $RuCl(PTA)_2(\eta^6\text{-}C_{10}H_{14})$	benzenes	90	60	21
$Co(\eta^3\text{-}C_3H_5)\{P(OR_3)_3\}$	benzenes, polyaromatics	25	1	13
$Ni(\eta^6\text{-}CH_3C_6H_5)(C_6F_5)_2$	benzene		35	45
Metal alkoxides, acac, or carboxylates + AlR_3	benzenes, polyaromatics	150–210	70	34, 35
$Co(Cy_2PC_8H_{11})(\eta^5\text{-}C_8H_{13})$	benzene	25	1	46
$[Cp^*RhCl_2]_2$	benzenes, anthracene	50	50	25
$L_2RhH(\mu\text{-}H)_3RhL_2$ (L = $P(O^iPr)_3$)	benzenes	25	1	14
$Rh(acac)\{P(OPh)_3\}_2$	benzenes	80	10	47
$RhH\{P(NC_4H_4)_3\}_4$; $RhH(CO)\{P(NC_4H_4)_3\}_4$	benzenes	25	5	48
$[Rh(diphos)(MeOH)_2]BF_4$	anthracenes	50–75	1	17
$[RhCl(diene)]_2^+[NR_4]X$	benzenes [b], naphthalene	25	1	49
$Rh(cod)(sulphos)/Pd^0/SiO_2$	benzenes [c]	40	30	42
Rh or Pt complexes on SiO_2-supported metals (Pd, Pt, Ru)	benzenes, naphthalene [c]	40	1	38, 40
$Ru(\eta^6\text{-}C_6Me_6)(\eta^4\text{-}C_6Me_6)$	benzenes	90	2–3	50
$[Ru(\eta^6\text{-}C_6Me_6)_2(\mu\text{-}H)_2(\mu\text{-}Cl)]Cl_2$	benzenes	50	50	25
$Ru(H)_3(PPh_3)_3$; $Ru(H)_2(H_2)(PPh_3)_3$	anthracenes	50–100	5	23
$Ru_4H_4(\eta^6\text{-}C_6Me_6)$; $Ru_2Cl_4(\eta^6\text{-}C_6Me_6)$	benzenes [a]	90	60	20, 52
Fe, Co, Mn, Rh, Ru, W, Mo, Cr carbonyls	polyaromatics [d, e]	180	25	24
$Fe(CO)_5$ + ammonium salt	anthracene	150	35	51
Early metal complexes on oxides (Th, U, Nb, Ta, Zr)	benzenes, polyaromatics [c]	100–120	70–90	44
$Co_2(CO)_8$	polyaromatics [e]	135–185	230–270	36

a) Liquid biphasic catalysis.
b) Phase transfer catalysis.
c) Supported metal complexes.
d) CO/H_2O as reducing agent.
e) Syngas as reducing agent.

As a general trend in both homogeneous and heterogeneous phase, the hydrogenation of arenes requires higher H_2 pressures and higher temperature as compared to the hydrogenation of olefins. Naphthalenes are extremely difficult to reduce, while higher polynuclear arenes are hydrogenated more easily than benzenes, especially at the outer rings, the resonance-stabilization of which is not as efficacious as that of the inner benzene ring.

A list of the metal complexes that have been claimed to generate catalysts for the hydrogenation of carbocyclic aromatic rings is provided in Table 16.1. This list includes homogeneous catalysts, biphase catalysts, and tethered single-site catalysts.

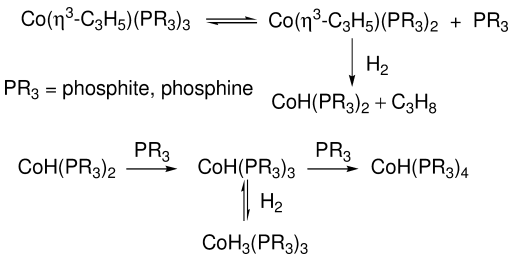
Ruthenium (Ru), rhodium (Rh), and cobalt (Co) form the most active and versatile catalysts, with a prevalence for Ru; effective catalysts have been reported also for other metals such as Ni, Pd, Pt, Cr, W, Mo, Mn, Nb, and Ta, some of which, however, are selective for the partial reduction of polynuclear aromatics.

The first well-documented case of homogeneous catalytic hydrogenation of a carbocyclic aromatic ring was reported by Muetterties and coworkers, who employed allyl cobalt complexes of the general formula (η^3-C_3H_5)$Co(PR_3)_3$ (PR_3 = phosphite, phosphine) to hydrogenate benzene, alkylbenzenes, anisole, naphthalene, anthracene, and phenanthrene under mild conditions (25 °C, 1–3 bar H_2) [13]. The catalytic activity was found to increase with the size of the phosphite/phosphine ligand in the order $P(OMe)_3 < P(OEt)_3 < PMe_3 < P(OiPr)_3$. Remarkably, the hydrogenation of benzene to cyclohexane could be achieved already at 25 °C and 1 bar H_2, yet only 25 turnovers were observed prior to catalyst deactivation. Alkyl substituents on the benzene ring were also found to inhibit the reduction. In contrast to what is generally observed in both homogeneous and heterogeneous phase, the cobalt catalysts proved more active for benzene than for polyaromatics. The monohydride Co^I fragment $CoH(PR_3)_2$, generated by hydrogenation of the precursor, was proposed as the catalytically active species. This unsaturated 14-electron fragment reacts with further phosphite/phosphine, yielding $CoH(PR_3)_n$ (n = 3, 4) and with H_2 yielding the trihydride $CoH_3(PR_3)_3$ (Scheme 16.1). As both these species are catalytically inactive, their unavoidable formation during the catalysis was suggested to be the main factor for catalyst deactivation.

Scheme 16.2 illustrates the catalytic mechanism proposed by Muetterties and coworkers [13]. Salient features of this mechanism are the coordination of benzene in the η^4-fashion, to give a transient $CoH(\eta^4\text{-}C_6H_6)(PR_3)_2$ complex, and the intramolecular hydride transfer to form the allylic intermediate $Co(\eta^3\text{-}C_3H_7)(PR_3)_2$. Hydrogen addition would give an η^4-1,3-cyclohexadiene complex that ultimately releases cyclohexane *via* H_2 addition/hydride migration steps. Complete *cis* stereoselectivity of hydrogen addition was demonstrated by replacing H_2 with D_2.

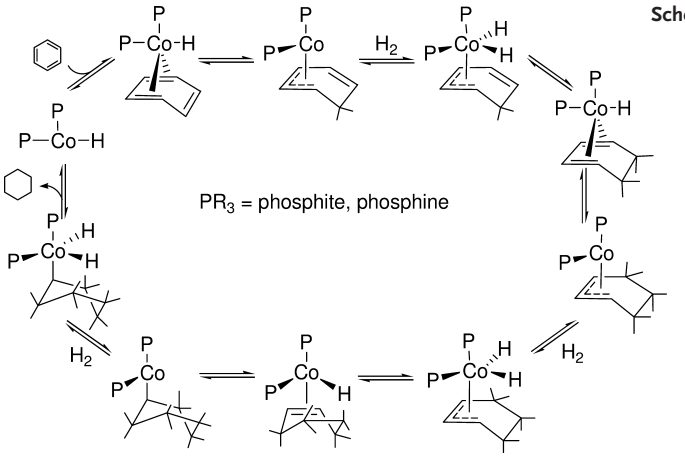
A mechanism similar to that shown in Scheme 16.2 has also been proposed to rationalize the arene hydrogenation activity of the triply-bridged dirhodium complex $L_2HRh(\mu\text{-}H_3)RhL_2$ (L = P(O*i*Pr)$_3$) [14].

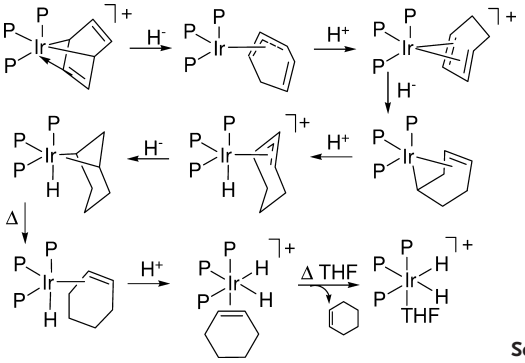
Some steps of the mechanism proposed by Muetterties have been proved experimentally by Bianchini and coworkers [15]. These authors synthesized the η^4-benzene Ir^I complex $[Ir(triphos)(\eta^4\text{-}C_6H_6)]^+$(triphos = $CH_3C(CH_2PPh_2)_3$), and studied



Scheme 16.1

Scheme 16.2



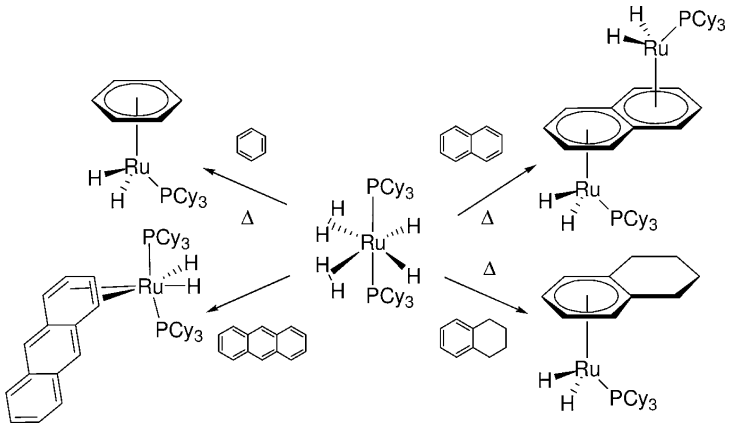


Scheme 16.3

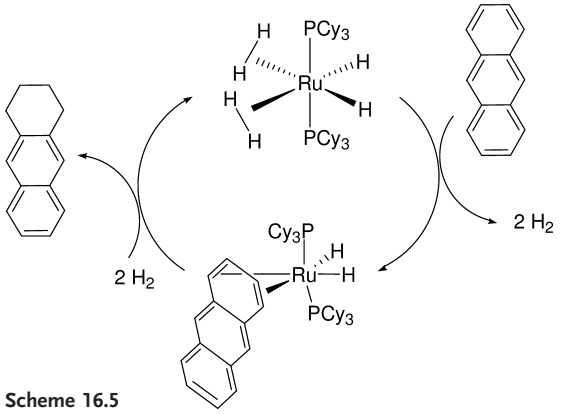
in detail each reduction step down to the conversion of benzene to cyclohexene by sequential addition of H^- and H^+. The overall reaction sequence is illustrated in Scheme 16.3. All the metal intermediates along the conversion of benzene to cyclohexene were unambiguously characterized and the region/stereochemistry of each "H" addition was determined.

It is noteworthy that the starting η^4-benzene complex was prepared by cyclotrimerization of acetylene by $IrCl(C_2H_4)$(triphos) [16]. All of the attempts to react the fragment $[Ir(triphos)]^+$ with benzene were unsuccessful, which reflects the difficulty met by a transition-metal fragment to overcome the energy barrier to η^4-benzene coordination.

The complex $[Rh(MeOH)_2(diphos)]^+$ (diphos = 1,2-bis(diphenylphosphino)ethane) has been reported to hydrogenate polynuclear aromatic hydrocarbons under mild conditions (60 °C, 1 bar H_2) [17]. A kinetic study of the hydrogenation of 9-CF_3CO-anthracene to the corresponding 1,2,3,4-tetrahydroanthracene was consistent with a rapid conversion of the precursor to $[Rh(\eta^6$-anthracene)(diphos)$]^+$ and a rate-determining step involving the reaction of the latter complex with H_2



Scheme 16.4



Scheme 16.5

to give 1,2-dihydroanthracene. A second-order rate kinetic law (–d[anthracene]/dt = k [Rh] [H_2]) was determined with $k(59.7\,^{\circ}C) = (9.0 \pm 1.0) \times 10^{-2}$ M^{-1} s^{-1}.

Whilst the metals of the cobalt group have provided valuable mechanistic information on the mechanism of homogeneous hydrogenation of arenes, there is little doubt that ruthenium forms the most active and versatile catalysts.

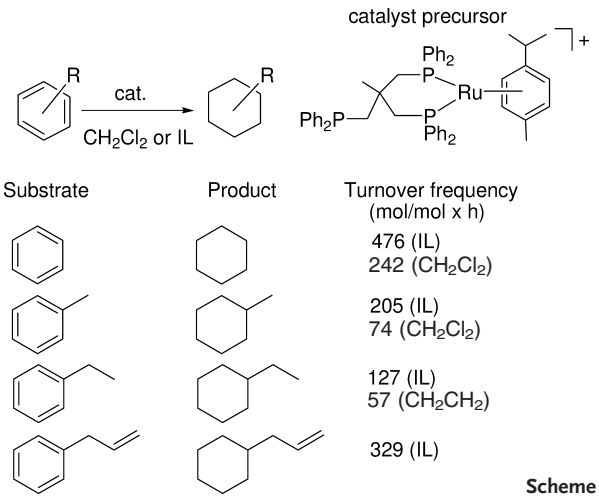
Borowski and coworkers have reported that benzene, naphthalene, and anthracene are reduced to cyclohexane, tetralin and a mixture of 1,2,3,4-tetrahydroanthracene (4H-An) and 1,2,3,4,5,6,7,8-octahydroanthracene (8H-An), respectively, in the presence of the dihydride bishydrogen complex $RuH_2(H_2)_2(PCy_3)_2$ (80 °C, 3–30 bar H_2) [18]. Notably, the latter was found to react at 80 °C with neat benzene or with cyclohexane solutions of naphthalene or tetralin to form the corresponding η^6-adducts (Scheme 16.4). These products were also isolated from the final catalytic mixtures.

Unlike the previous arenes, anthracene reacted with $RuH_2(H_2)_2(PCy_3)_2$ already at room temperature to form an η^4-anthracene adduct which was found to be an

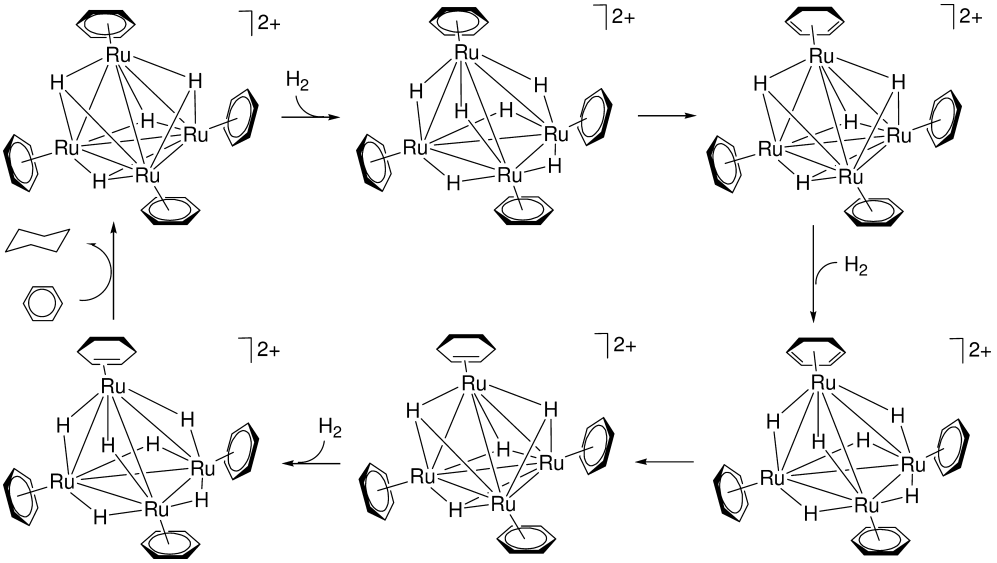
effective catalyst for anthracene hydrogenation. It was suggested, therefore, that all these arene adducts may have an active role in the catalytic cycle. A simplified cycle for the hydrogenation of anthracene to 4H-An by $RuH_2(H_2)_2(PCy_3)_2$ is shown in Scheme 16.5. This involves the preliminary dissociation of two H_2 molecules to generate a coordination vacancy for the incoming molecule that ultimately binds the metal in η^4 fashion. The occurrence of this step was supported by evidence that the reaction rate decreased by increasing the H_2 pressure. The reduction of the second external ring of 4H-An to 8H-An would follow a similar mechanism as it appreciably started only when most – if not all – anthracene was consumed. 9,10-Dihydroanthracene – a typical product of catalysis proceeding through a radical mechanism – was not detected.

It is worth noting, however, that the real homogeneous character of the reactions catalyzed by the hexahydride $RuH_2(H_2)_2(PCy_3)_2$ remains questionable, as elemental mercury was found to inhibit the hydrogenation reaction, which may indicate the formation of catalytically active ruthenium metal. In contrast, a truly homogeneous ruthenium catalyst for the hydrogenation of benzenes seems to be generated by the precursor [RuCl(η^2-triphos)(η^6-*p*-cymene)]PF_6, recently described by Dyson and coworkers (Scheme 16.6) [19]. The catalytic activity of this complex was evaluated at 90 °C and 60 bar H_2 either in dichloromethane or in a biphasic system comprising the substrate and 1-butyl-3-methylimidazolium tetrafluoroborate. Due to its solubility in the ionic liquid (IL), the catalyst could be recovered and recycled after use. Interestingly, 1-alkenyl-substituted arenes, such as styrene and 1,3-divinylbenzene, were not hydrogenated, whereas allylbenzene was selectively converted to allylcyclohexane with a turnover frequency (TOF; mol. product mol^{-1} catalyst h^{-1}) of 329 and complete regioselectivity.

The catalytic hydrogenation of various benzene derivatives by the ruthenium tetrahydride clusters $[Ru_4H_4(\eta^6\text{-}C_6H_6)_4]^{2+}$ was investigated by Süss-Fink in both



Scheme 16.6



Scheme 16.7

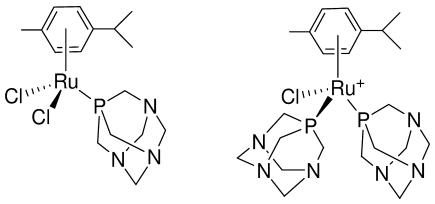
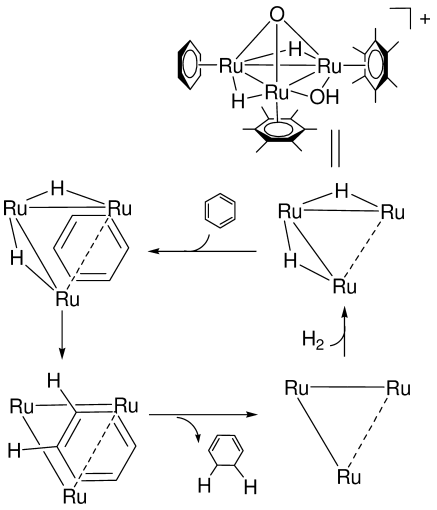


Fig. 16.1 Sketches of $Ru(PTA)Cl_2(\eta^6\text{-}C_{10}H_{14})$ and $[RuCl(PTA)_2(\eta^6\text{-}C_{10}H_{14})]^+$ (PTA = 1,3,5-triaza-7-phosphadamantane).

biphasic and aqueous systems [20]. Under aqueous biphasic conditions, cyclohexanes were produced with TOFs varying from 20 to 2000, depending on the substrate. On a quite speculative basis, a hydrogenation mechanism was proposed involving $\eta^6 \rightarrow \eta^4 \rightarrow \eta^2$ arene intermediates (Scheme 16.7). However, the only proven step was the hydrogenation of the starting $[Ru_4H_4(\eta^6\text{-}C_6H_6)_4]^{2+}$ cluster to $[Ru_4H_6(\eta^6\text{-}C_6H_6)_4]^{2+}$.

The ruthenium cluster $[Ru_4H_4(\eta^6\text{-}C_6H_6)_4]^{2+}$ was also employed for the hydrogenation of arenes in a biphasic water/1-butyl-3-methylimidazolium tetrafluoroborate biphasic system. At 90 °C and 60 bar H_2, benzene was reduced to cyclohexane with a TOF of 364.

The two water-soluble complexes $Ru(PTA)Cl_2(\eta^6\text{-}C_{10}H_{14})$ and $[RuCl(PTA)_2(\eta^6\text{-}C_{10}H_{14})]^+$ (PTA = 1,3,5-triaza-7-phosphadamantane) (Fig. 16.1) have been tested as catalyst precursors for the hydrogenation of benzenes at 90 °C and 60 bar H_2 [21]. After catalysis, the former complex was converted to a triruthenium cluster



Scheme 16.8

with no coordinated PTA (NMR and electrospray mass spectrometry). In contrast, the starting complex with two PTAs gave a termination-metal product containing these ligands.

It is worth highlighting a very particular case of arene hydrogenation involving a triruthenium cluster [22]. In contrast to any other previous report, the hydrogenation of benzene was suggested by Süss-Fink to involve a direct H-transfer without substrate coordination to the metal. The proposed mechanism is shown in Scheme 16.8. The salient feature of this mechanism is adsorption of the arene in the hydrophobic pocket formed by the three arene ligands of the trimetallic precursor. The lack of substrate exchange with the originally coordinated arenes and the mass-spectrometry detection of a benzene adduct of the starting cluster were brought forward as substantial evidence for the proposed mechanism.

Many other mononuclear and binuclear Ru^{II} complexes stabilized by phosphine, cyclopentadienyl or arene ligands – for example $Ru(H)_2(H_2)(PPh_3)_3$ [23], $RuCl_2(CO)_2(PPh_3)_3$ [24], $[Ru(\mu\text{-}H_2)(\mu\text{-}Cl)(\eta^6\text{-}C_6H_6)_2]Cl_2$ [25], $[Rh(\eta^5\text{-}C_5Me_5)Cl_2]_2$ [26], and $Ru(\eta^6\text{-}C_6Me_6)(O_2CMe)_2$ [27] – have been claimed to catalyze the hydrogenation of polynuclear aromatic hydrocarbons in homogeneous fashion. Later evidence has suggested and, in some cases proved, that most of these systems are heterogeneous [28]. A paradigmatic case is the binuclear complex $[Rh(\eta^5\text{-}C_5Me_5)Cl_2]_2$ that was reported to hydrogenate benzene and substituted benzenes to cyclohexanes under relatively mild conditions (50 °C, 50 bar H_2) in the presence of a base that would promote the heterolytic splitting of H_2 as well as tie up the evolved HCl. Based on light-scattering experiments and on the good *cis* stereospecificity of hydrogen addition (e.g., *o*-xylene gave *cis*- and *trans*-1,2-dimethylcyclohexanes in a 62:1 ratio and *m*-xylene gave 1,3-dimethylcyclohexanes in *cis*:*trans* 38:1 ratio), this catalyst was thought to be homogeneous. However, later studies suggested that the true catalyst is likely heterogeneous [29].

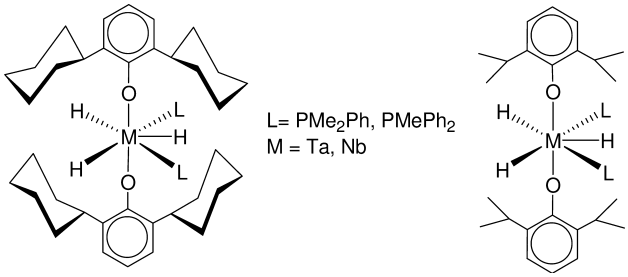


Fig. 16.2 The Nb^V and Ta^V hydride complexes containing bulky aryloxide ligands (as described by Rothwell).

Arene hydrogenation catalysts based on other metals than late transition ones are less numerous. Of particular relevance are the results reported by Rothwell, who found that Nb^V and Ta^V hydride complexes containing bulky aryloxide ligands (Fig. 16.2) are active for the homogeneous hydrogenation of arenes [30].

These catalytic systems demonstrated high regio- and stereoselectivity in the hydrogenation of benzene and of polynuclear aromatic hydrocarbons. For instance, the isolated tantalum trihydrides $Ta\{OC_6H_3(C_6H_{11})_2\text{-}2,6\}_2(H_3)(PMe_2Ph)_2$ and $Ta\{OC_6H_3\text{-}Pr^i_2\text{-}2,6)\}_2(H_3)(PMe_2Ph)_2$ catalyzed the hydrogenation of naphthalene and anthracene at 80 °C and 3–100 bar H_2. The former substrate was converted to tetralin, while anthracene was reduced to 1,2,3,4,5,6,7,8-octahydroanthracene *via* 1,2,3,4-tetrahydroanthracene. Since no trace of 9,10-dihydroanthracene was observed, the occurrence of either a radical reaction [31] or a Birch-type reduction was ruled out [32].

As shown in Scheme 16.9, the intermolecular hydrogenation of $[^2H_8]$toluene, $[^2H_{10}]$acenaphthene, $[^2H_8]$naphthalene, and $[^2H_{10}]$anthracene produced single isotopomers. The ^1H- and $^{13}C\{^1H\}$-NMR spectra confirmed a high selectivity: all-*cis* hydrogenation occurred without H/D scrambling between unreacted substrates and products. The all-*cis* nature of $[^2H_8]$tetralin was also proved using mass-spectrometry techniques. A unique characteristic of the niobium compound is its ability to rapidly hydrogenate arylphosphine ligands, thereby providing a new interesting procedure for the synthesis of cyclohexylphosphine ligands [33].

The only "homogeneous or substantially homogeneous" system which seems to offer a viable alternative to heterogeneous catalysis for the large-scale hydrogenation of arenes remains the IFP process [34]. This process utilizes Ziegler-type catalysts obtained by reacting at least two different metal salts (e.g., nickel and cobalt alkoxides, acetylacetonates or carboxylates), and a metal, selected among iron, zinc, and molybdenum, with trialkylaluminum as reducing agent. The hydrogenation of aromatic hydrocarbons is carried out under relatively mild conditions (155–180 °C, 10–30 bar H_2) in a solvent or in neat substrate. Bis-phenol A, phenol and benzene are hydrogenated to propane-dicyclohexanol, cyclohexanol and cyclohexane, respectively (Table 16.2).

cat = Ta or Nb trihydrides

Scheme 16.9

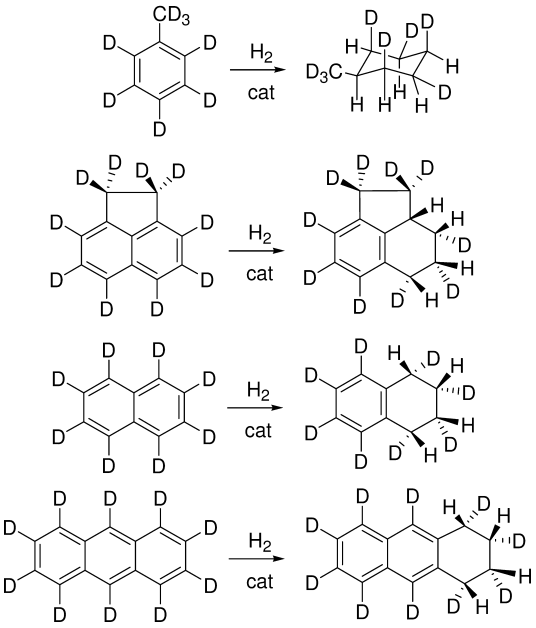


Table 16.2 Hydrogenation of aromatic hydrocarbons with the IFP process.[a)]

Catalyst	Substrate	Substrate/M ratio	% Conversion (TOF)[b)] product
1	bis-phenol A	250	99 (62) propane-dicyclohexanol
2	benzene	1829	99 (3621) cyclohexane
3	phenol	708	99 (2805) cyclohexanol

a) Experimental conditions: **1** (nickel octoate 0.35 mmol, iron octoate 0.35 mmol, triethylaluminum 5.6 mmol, solvent = 100 g cyclohexanol, 30 bar H_2, 4 h, 180 °C); **2** (cobalt stearate 2.2 mmol, iron stearate 0.2 mmol, triisobutylaluminum 2 mmol, 10 bar H_2, 30 min, 155 °C); **3** (nickel octoate 0.25 mmol, zinc octoate 0.25 mmol, triethylaluminum 2.1 mmol, 30 bar H_2, 15 min, 155 °C).

b) Mol of product (mol M × h)$^{-1}$.

Other examples of arene hydrogenation by Ziegler-type catalysts have been reported [35]. However, none of them is discussed at this point as they are generally poorly defined. Likewise, some hydrogenation catalytic systems in either oxo or water-gas-shift conditions are only reported in the list of references for sake of information [24, 36].

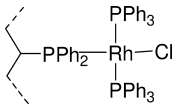


Fig. 16.3 Heterogenization of $RhCl(PPh_3)_2$ by grafting to a cross-linked phosphinated styrene/divinylbenzene resin.

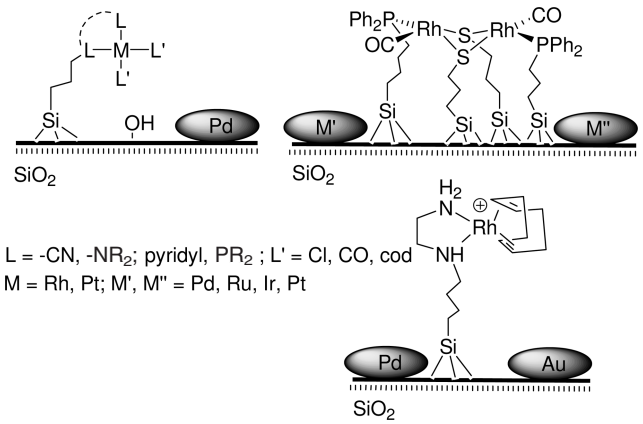


Fig. 16.4 Some examples of tethered complexes on supported metals (as described by Angelici).

16.2.2
Molecular Catalysts Immobilized on Support Materials

One of the very first attempts to hydrogenate aromatic compounds by means of a single-site metal catalyst was reported by Fish and coworkers, who were able to tether "$RhCl(PPh_3)_2$" moieties to a cross-linked phosphinated styrene/divinylbenzene (DVB) resin ($RhCl(PPh_3)_2$/P) (Fig. 16.3).

The resulting catalyst proved active for the hydrogenation of pyrene, tetralin, *p*-cresol, and methylnaphthalene [37]. A rate-enhancement effect was observed which was attributed to the ability of some substrates (especially *p*-cresol) to stabilize unsaturated rhodium species formed during the course of the catalysis. Since then, no remarkable progress in arene hydrogenation by single-site metal catalysts has been made, until a new class of catalysts emerged from the combination on the same support of both molecular complexes and metal particles. These systems, known under the name of tethered complexes on supported metals (TCSM), were introduced by Angelici [38a] and developed independently by Angelici [38b,c] and Bianchini [39].

Angelici's approach to heterogenization involves the functionalization of a ligand, either monodentate or bidentate, with a tail bearing a reactive group capable of forming covalent bonds to silica (e.g., alkyl-$Si(OR)_3$). Three TCSM catalysts, among several Rh/Pd, Pt/Pd and Rh/Pd : Au examples reported by Angelici, are shown in Figure 16.4 [38].

It has been found that the complexed metal and the supported metal(s) act synergistically, to provide enhanced results, superior to those of the component catalysts, in various reactions that include the hydrogenation of arenes. Typical tethered complexes contain Rh^I, while the silica-grafted ligands can be either monodentate with N and P donors or chelating with P-N and N-N donors (diamines, pyridylphosphines). Benzenes bearing a variety of functional groups (ester, ether, hydroxy, acyl, vinyl) have been hydrogenated with TOFs much higher than those of the single components which in some cases are completely inactive. To report one such example, the hydrogenation of phenol to cyclohexanol occurs with a TOF of 3400 with a Rh(N-N)/Pd-SiO_2 catalyst, whereas both Pd-SiO_2 and unsupported Rh(N-N) are inactive (N-N = bipyridyl) [40].

Angelici has proposed that the enhanced activity might be due to a hydrogen-spillover process, promoted by the supported metallic phase, that would enhance specifically the hydrogenation activity of the molecular catalyst [40]. A later study of the hydrogenation of arenes with a catalyst obtained by silica sol-gel co-entrapment of metallic palladium and $[Rh(cod)(\mu\text{-}Cl)]_2$ (cod = cyclohexa-1,5-diene) disagreed with the hydrogen spillover hypothesis and suggested that the action of both metals is caused by a type of synergistic effect [41]; however, no clear-cut explanation was provided.

A synergistic effect operating at the level of the first H_2 addition (e.g., conversion of benzene to cyclohexadiene) was demonstrated by Bianchini and coworkers for the hydrogenation of various benzenes to cyclohexanes by means of a different class of TCSM catalysts [42]. These differ substantially from Angelici's catalysts for the bonding interaction of the molecular complexes to the support material. The ligands of the molecular complexes were functionalized with sulfonate tails capable of forming robust hydrogen bonds to the isolated silanols of silica (Fig. 16.5 a) [42, 43].

For this reason, these catalysts are also known under the name of supported hydrogen-bonded (SHB) catalysts and, in conjunction with Pd^0 particles on the same support material, have contributed to generate active heterogeneous systems for the hydrogenation of benzenes in aprotic solvents. Irrespective of the substrate, the combined single-site/dispersed-metal catalyst Rh^I-Pd^0/SiO_2 shown in Figure 16.5 a was from four- to six-fold more active than supported palladium

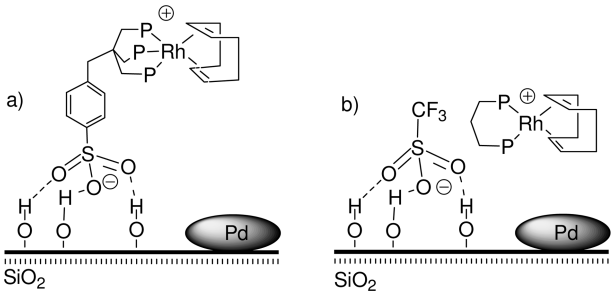


Fig. 16.5 Some examples of supported hydrogen-bonded catalysts (as described by Bianchini).

Table 16.3 Hydrogenation of benzenes with Pd^0/SiO_2, Rh^I/SiO_2 or Rh^I-Pd^0/SiO_2. [a)]

Catalyst	Temp. [°C]	Substrate	Substrate/M ratio	% Conversion [b)] (TOF, M) [c)] product
Pd^0/SiO_2	40	benzene	525	4 (11) cyclohexane
Rh^I/SiO_2	40	benzene	9200	0
Rh^I-Pd^0/SiO_2	40	benzene	525/9200	15 (39, Pd) cyclohexane
Pd^0/SiO_2 [d)]	40	toluene	426	4 (8) methylcyclohexane
Rh^I/SiO_2 [e)]	40	toluene	7520	0
Rh^I-Pd^0/SiO_2 [f)]	40	toluene	426/7520	16 (32, Pd) methylcyclohexane
Pd^0/SiO_2	60	styrene	400	97 (194) ethylbenzene; 3 (6) ethylcyclohexane
Rh^I/SiO_2	60	styrene	8750	98 (4287) ethylbenzene
Rh^I-Pd^0/SiO_2	60	styrene	400/8750	81 (162, Pd) ethylbenzene; 19 (38, Pd) ethylcyclohexane
Pd^0/SiO_2	60	ethylbenzene	400	3 (6) ethylcyclohexane
Rh^I/SiO_2	60	ethylbenzene	8750	0
Rh^I-Pd^0/SiO_2	60	ethylbenzene	400/8750	20 (40, Pd) ethylcyclohexane

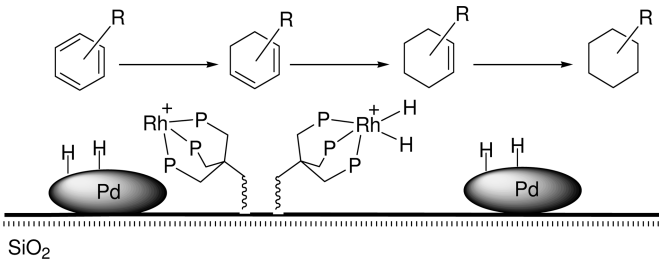
a) Experimental conditions: Pd^0/SiO_2 (9.86 wt.% Pd), 0.044 mmol Pd; Rh^I/SiO_2 (0.56 wt.% Rh), 0.0025 mmol Rh; Rh^I-Pd^0/SiO_2 (0.56 wt.% Rh, 9.86 wt.% Pd), 0.044 mmol Pd, 0.0025 mmol Rh; 30 bar H_2; 30 mL *n*-pentane, 2 h, 1500 rpm.
b) Average values over at least three runs.
c) Mol product (mol M × h)$^{-1}$ (M = Pd, Rh).
d) 0.088 mmol Pd.
e) 0.005 mmol Rh.
f) 0.088 mmol Pd, 0.005 mmol Rh.

alone (Pd^0/SiO_2), while the tethered Rh^I complex alone (Rh^I/SiO_2) proved to be totally inactive (Table 16.3).

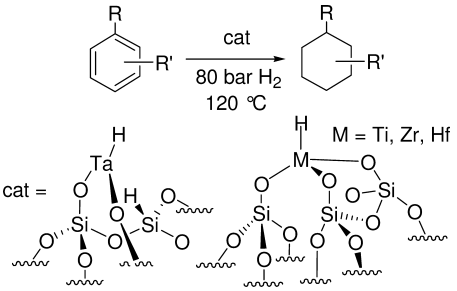
Separate experiments with cyclohexadienes and cyclohexenes showed that 1,3-cyclohexadienes are more rapidly reduced to cyclohexenes at rhodium, while the latter are predominantly reduced at palladium. It was also found that the 1,3-cyclohexadiene disproportionation, occurring on palladium, is inhibited by the grafted rhodium complex. Based on this information, as well as a number of experiments (including the isolation of relevant intermediates), the authors concluded that the enhanced activity of the Rh^I-Pd^0/SiO_2 catalyst is not due to hydrogen spillover, but to the fact that the rate-limiting hydrogenation of benzenes to cyclohexa-1,3-dienes is assisted by both palladium and rhodium, the concerted action of which, besides preventing the competitive diene disproportionation to benzene and cyclohexene, speeds up the reduction of the first double bond (Scheme 16.10).

The intimate mechanism by which the single rhodium sites and the neighboring palladium particles interact with benzene to accelerate its reduction to cyclohexadiene remains somewhat obscure.

A variation of the SHB technology to immobilize cationic molecular catalysts on silica is shown in Figure 16.5 b. This involves SHB immobilization of the counter-



Scheme 16.10



Scheme 16.11

anion, provided that the latter is capable of forming robust hydrogen bonds to the surface silanols, as is the case of the triflate counter-anion. Clearly, only aprotic solvents are viable for the successful use in catalysis of this SHB technique. It has been shown, using ^{31}P- and ^{19}F-NMR spectroscopy in CD_2Cl_2, that the metal cations reside close to the silica surface by electrostatic interaction with the SHB triflate. Therefore, only the counter-anions are truly immobilized on the support, whereas the cationic catalysts can interact freely with the substrate and H_2 as if they were in solution. Following this protocol, several chiral catalysts, for example [Rh((+)-DIOP)(nbd)](SO_3CF_3) and [Rh((*S*)-BINAP)(nbd)](SO_3CF_3) (nbd = norbornadiene), have been immobilized and successfully employed for the enantioselective hydrogenation of prochiral alkenes [39c]. Recently, this SHB approach was successfully extended to arene hydrogenation through the immobilization of cationic catalysts, such as [Rh(diphos)(cod)] (SO_3CF_3), on silica containing supported palladium particles [39c]. Enhanced conversions to saturated cyclic hydrocarbons, as compared to the single components, were observed for the hydrogenation of benzenes and anthracenes [43].

A distinct class of single-site metal catalysts for arene hydrogenation is known under the name of surface organometallics. The surface organometallic technique has been introduced and largely developed by Basset and Marks, and is currently utilized in a number of catalytic processes [44]. Silica- or alumina-supported Ta, Ti, Zr and Hf hydrides, generated *in situ* by hydrogenation of alkyl derivatives, have been found capable of catalyzing the reduction of benzene and alkyl-substituted benzenes with TOFs as high as 1000 (Scheme 16.11) [44b,c].

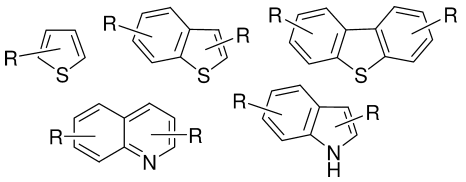


Fig. 16.6 Common *S*- and *N*-heterocycles contained in fossil fuels.

16.3 Hydrogenation of Heteroaromatics

16.3.1 Molecular Catalysts in Different Phase-Variation Systems

The number of homogeneous catalysts available for the hydrogenation of *N*-, *S*- and *O*-heteroaromatics is exceedingly greater than that of the catalysts for arenes. A crucial role in making the reduction of heteroaromatics easier than that of carbocyclic aromatic rings is just played by the heteroatom that possesses at least one σ-lone pair for occupying a coordination vacancy at the metal center. The heteroatom also has the effect of decreasing the overall aromatic character of the molecule, favoring the localization of electron density on the proximal X=C bond, hence allowing for the coordination of the substrate in the easily reducible olefin-like η^2-C-X mode (X=heteroatom) [8, 9].

A great impulse to design homogeneous catalysts for the hydrogenation heteroaromatics stems from the need to understand the mechanisms of the HDS, HDN, and HDO reactions [3]. These three processes form the heart of fossil fuels hydrotreatments, and have a vast commercial and environmental importance. It is not surprising, therefore, that most studies have been centered on the development of molecular catalysts for the hydrogenation of thiophenes, quinolines, and indoles (Fig. 16.6), as these substrates are largely abundant in crude oils and their degradation remains incomplete, even with the most efficient heterogeneous catalysts [3, 8, 9].

16.3.1.1 S-Heteroaromatics

The homogeneous hydrogenation of thiophenes and benzothiophenes to the corresponding cyclic thioethers is a reaction which is catalyzed, under relatively mild experimental conditions, by a number of metal complexes, generally comprising noble metals modified with phosphine ligands: $RuCl_2(PPh_3)_3$ [53], $RuHCl(CO)(PPh_3)_3$ [53], $RuH_2(\eta^2\text{-}H_2)(PCy_3)_2$ [54], $OsHCl(CO)(PPh_3)_3$ [53], $RhCl(PPh_3)_3$ [53], $[Rh(MeCN)_3(Cp^*)](BF_4)_2$ [55], $[Rh(PPh_3)_2(cod)]PF_6$ [53, 56], $[Ir(PPh_3)_2(cod)]PF_6$ [53, 57, 58], and $[Ru(MeCN)_3(triphos)](SO_3CF_3)_2$ [39b, 59, 60]. In contrast, no metal complex has been ever reported to hydrogenate diben-

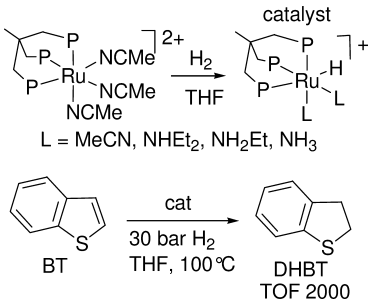
zo[*b,d*]thiophene (DBT) to either tetrahydrodibenzothiophenes or hexahydrodibenzothiophenes, which reflects the strong aromatic character of this substrate.

A common feature of all hydrogenation catalysts for thiophene (T) and benzo[*b*]thiophene (BT) is apparently a d^6 electronic configuration of the metal ion, which favors the η^2-*C,C* coordination of the thiophenic molecule over the alternative η^1-*S* bonding mode. The latter is more frequent for low-valent metal fragment and is precursor to C-S insertion, hence to hydrogenolysis rather than to hydrogenation [8, 9a]. As a general trend, the hydrogenation activity decreases in the order $Ru^{II} > Rh^{III} > Os^{II} > Ir^{III}$ as well as with increasing nucleophilicity of the solvent that may compete with the substrate for coordination.

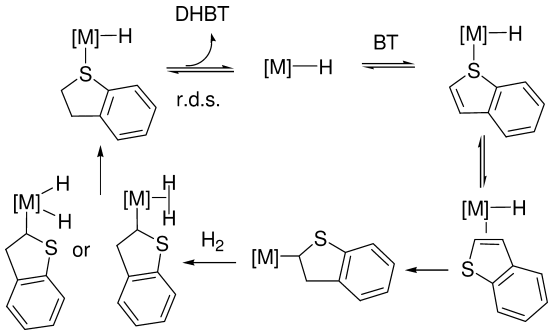
The highest activity for BT hydrogenation to dihydrobenzo[*b*]thiophene (DHBT) has been reported for the Ru^{II} catalyst $[(triphos)RuH]^+$ obtained by hydrogenation of the precursor $[Ru(NCMe)_3(triphos)](SO_3CF_3)_2$ in basic solvents capable of promoting the heterolytic splitting of H_2 (Scheme 16.12) [59]. Interestingly, the hydrogenation of $[Ru(NCMe)_3(triphos)](SO_3CF_3)_2$ in apolar or non-basic solvents (e.g., CH_2Cl_2) produced the 16-electron system $[Ru(H)_2(triphos)]^+$, which was slightly less active than the monohydride fragment (TOF = 1340) [39b, 60].

The hydrogenation mechanism of BT has been widely studied using a variety of techniques, including operando HP-NMR, kinetic studies, and deuterium labeling. A unique mechanism has been proposed, irrespective of the metal catalyst: η^2-*C,C* coordination of the substrate (eventually in equilibrium with η^1-*S* coordination), addition of H_2 in either oxidative $[M(H)_2]$ or intact form $[M(H_2)]$ (this step may also precede the previous one), hydride transfer to form dihydrobenzothienyl, and elimination of DHBT by hydride/dihydrobenzothienyl reductive coupling. Scheme 16.13 exemplifies this mechanism for a model catalyst bearing one hydride ligand, as is the case of the 14-electron fragment $[RuH(triphos)]^+$ [39b, 59, 60].

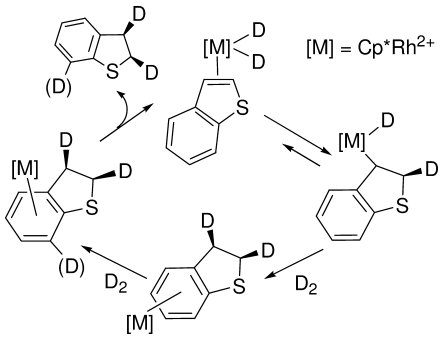
Kinetic studies of the hydrogenations of BT to DHBT catalyzed by $[Rh(PPh_3)_2(cod)]PF_6$ [56] and $[Ir(PPh_3)_2(cod)]PF_6$ [57] indicated the hydride migration yielding the dihydrobenzothienyl intermediate as the rate-determining step. In contrast, the rate-determining step of the reaction catalyzed by $[RuH(triphos)]^+$ was shown to be the reversible dissociation of DHBT from the metal center [59].



Scheme 16.12



Scheme 16.13

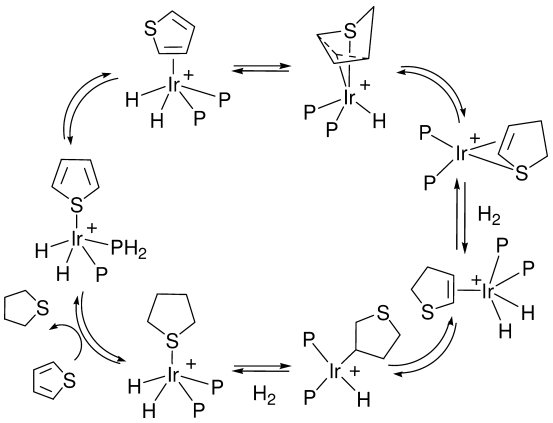


Scheme 16.14

Substituting deuterium for hydrogen gas in the reduction of BT to DHBT with the catalyst precursor $[Rh(NCMe)_3(Cp^*)](BF_4)_2$ has shown that the stereoselective *cis*-deuteration of the double bond is kinetically controlled by the η^2-*C,C* coordination of BT. The incorporation of deuterium in the 2- and 3-positions of unreacted substrate and in the 7-position of DHBT has been interpreted in terms of reversible double-bond reduction and arene-ring activation, respectively (Scheme 16.14) [55].

Overall, the hydrogenation of thiophene to tetrahydrothiophene (THT) is quite similar to that of BT, the only remarkable difference being the formation of a thioallyl complex via regio- and stereospecific hydride migration (*endo* migration). Scheme 16.15 shows the catalytic mechanism proposed for $IrH_2(\eta^1$-*S*-T$)(PPh_3)_2]PF_6$ [58]. Upon hydride addition, the thioallyl intermediate formed a 2,3-dihydrothiophene ligand which was then hydrogenated like any other alkene. The substitution of either 2,3- or 2,5-dihydrothiophene for thiophene showed that only the 2,3-isomer was hydrogenated to THT.

The use of water-soluble metal catalysts for the hydrogenation of thiophenes in aqueous biphasic systems has been primarily introduced by Sanchez-Delgado and coworkers at INTEVEP S.A. [61]. The precursors $RuHCl(TPPTS)_2(L_2)$ (TPPTS = triphenylphosphine trisulfonate; L = aniline, 1,2,3,4-tetrahydroquinoline) and $RuHCl(TPPMS)_2(L_2)$ (TPPMS = triphenylphosphine monosulfonate) were



Scheme 16.15

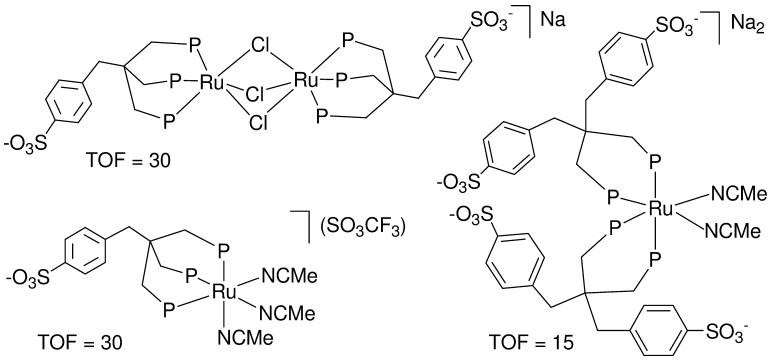


Fig. 16.7 Water-soluble polyphosphine metal catalysts used to hydrogenate thiophenes.

employed to hydrogenate BT to DHBT in water-decaline under relatively harsh experimental conditions (130–170 °C, 70–110 bar H_2). It was observed that nitrogen compounds did not inhibit the hydrogenation; on the contrary, a promoting effect was observed. Later, rhodium and ruthenium catalysts with the polydentate water-soluble ligands $(NaO_3S(C_6H_4)CH_2)_2C(CH_2PPh_2)_2$ (Na_2DPPPDS) [62] and $NaO_3S(C_6H_4)CH_2C(CH_2PPh_2)_3$ (Nasulphos) [63], which differ from traditional water-soluble phosphines for the presence of the hydrophilic groups in the ligand backbone were successfully employed to hydrogenate BT under biphasic conditions (Fig. 16.7) [39b, 59, 60, 64, 65].

The aqueous-biphase hydrogenation reactions of thiophenes to the corresponding cyclic thioethers have been shown to be mechanistically similar to those in truly homogenous phase.

16.3.1.2 *N*-Heteroaromatics

As a general trend, six-membered mononuclear *N*-heteroaromatics such as pyridine and derivatives are much less prone to undergo hydrogenation than bi- and trinuclear *N*-ring compounds (e.g., quinolines, benzoquinolines, acridines) due to their higher resonance stabilization energy.

The first examples of selective hydrogenation of pyridine to piperidine and of quinoline to 1,2,3,4-tetrahydroquinoline (THQ) by a homogeneous metal catalyst ($Rh(PY)_3Cl_3/NaBH_4$ in DMF under 1 bar H_2) were reported in 1970 by Jardine and McQuillin [66]. The first mechanistic studies appeared much later, when Fish employed the Rh^I and Ru^{II} precatalysts $RhCl(PPh_3)_3$ [67] and $RuHCl(PPh_3)_3$ [68] to hydrogenate various *N*-polyaromatics (85 °C, 20 bar H_2, benzene). The hydrogenation rates decreased in the order phenanthridine > acridine > quinoline > 5,6-benzoquinoline (5,6-BQ) > 7,8-BQ, which reflects the influence of both steric and electronic effects. All substrates were hydrogenated regioselectively at the heteroaromatic ring; only acridine was converted to a mixture of 9,10-dihydroacridine and 1,2,3,4-tetrahydroacridine. The hydrogenation of quinoline was found to be inhibited by the presence of pyridines and of THQ in the reaction mixture, due to competing coordination to the metal center, while all the other substrates had no appreciable effect on the hydrogenation rate.

The substitution of D_2 for H_2 in the reduction of quinoline catalyzed by either $RhCl(PPh_3)_3$ [67] or $RuHCl(PPh_3)_3$ [68] showed that: 1) hydrogenation of the C=N bond is reversible; 2) the C_3–C_4 double bond is irreversibly hydrogenated in stereoselective *cis* manner; and 3) the C_8–H bond in the carbocyclic ring is activated, likely *via* cyclometalation. Later, Fish studied the hydrogenation of 2-methylpyridine to 2-methylpiperidine catalyzed by $[Rh(NCMe)_3Cp^*]^{2+}$, again by means of deuterium labeling experiments [55]. The rate-limiting step of the reaction was identified as being the initial C=N bond hydrogenation, which actually disrupts the aromaticity of the molecule. It was also proposed that the reversible reduction of the C=N and C=C bonds was promoted by the allylic nature of the reduction product, NH-CH_2-C=C, which is highly activated toward re-aromatization of the N-ring.

The reduction of 1,2,5,6-tetrahydropyridine (THPY) with D_2 in the presence of $[Rh(NCMe)_3Cp^*]^{2+}$, yielding exclusive deuterium incorporation in the C_3 and C_4 carbon atoms, and the independent synthesis of $[Rh(\eta^1(N)\text{-THPY})(NCMe)_2Cp^*]^{2+}$ showed that: 1) η^1(N)-THPY complexes are not intermediate to piperidine production; and 2) partially hydrogenated N-heterocycles are easily dehydrogenated to their aromatic precursors [55].

Deuterium gas experiments, continuous NMR and GC/MS analysis, *in situ* high-pressure NMR spectra and the isolation of some intermediates provided Fish with sufficient information to propose the mechanism shown in Scheme 16.16 for the hydrogenation of quinoline to THQ, catalyzed by $[Rh(NCMe)_3Cp^*]^{2+}$ (40 °C, 33 bar H_2, CH_2Cl_2) [55].

The salient features of this mechanism are:

- η^1(N) bonding of quinoline to rhodium with loss of complexed MeCN, followed by the formation of a hydride.

- Reversible 1,2-N=C bond hydrogenation, likely *via* η^2(N,C) coordination.
- Migration of Cp*Rh from nitrogen to the C_3–C_4 double bond.
- Reversible C_3–C_4 double bond reduction.
- Cp*Rh complexation to the carbocyclic ring, followed by C_6–H and C_8–H bond activation.
- $\eta^6(\pi C)$ coordination of THQ, followed by ligand exchange with quinoline to continue the catalytic cycle.

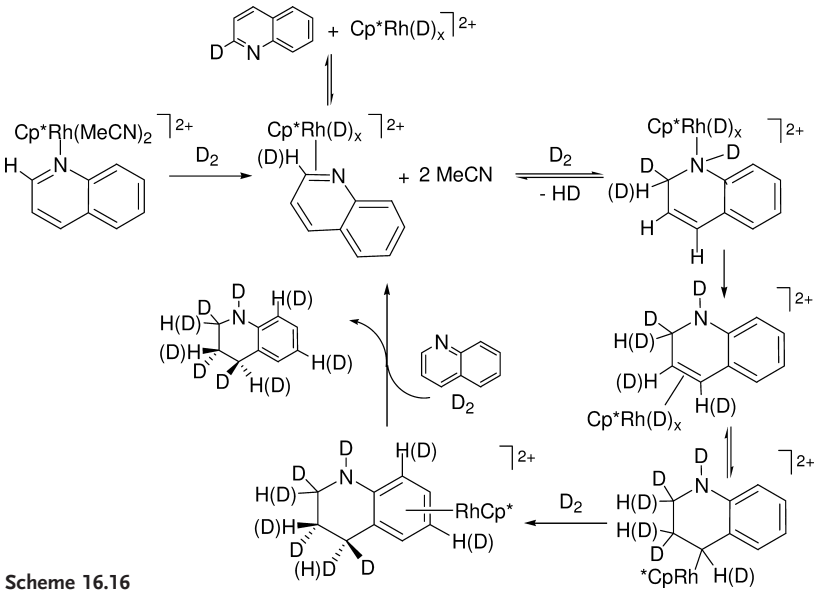
In this mechanistic picture, the rhodium center goes through the catalysis with the unusual III → V → III oxidation/reduction cycle.

Various late transition-metal carbonyls, alone or modified by phosphine ligands, have been found to hydrogenate pyridine and polyaromatic heterocycles such as quinoline, 5,6-BQ, 7,8-BQ, acridine, and isoquinoline (IQ) using either H_2 obtained from water-gas-shift (WGS) or syngas (SG) [69, 70]. Selective hydrogenation of the heterocyclic ring has been achieved with $Fe(CO)_5$, $Mn_2(CO)_8(PBu_3)_2$ and $Co_2(CO)_6(PPh_3)_2$ [24a]. The cobalt catalyst was the most active for the hydrogenation of both acridine to 9,10-dihydroacridine (TOF = 10) and quinoline to THQ (TOF = 14). The iron and manganese catalysts converted appreciably only acridine, with TOFs of 5 and 2 (or 10 under SG conditions), respectively. Under WGS conditions, $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_4H_4(CO)_{12}$ proved to be inactive due to competitive coordination of CO, while efficient regioselective hydrogenation of the substrate was achieved using H_2 gas ($TOF_{acridine/9,10\text{-}dihydroacridine} = TOF_{quinoline/THQ} = 5$) [24a]. In all cases, however, high temperatures (180–200 °C) were required for appreciable conversions.

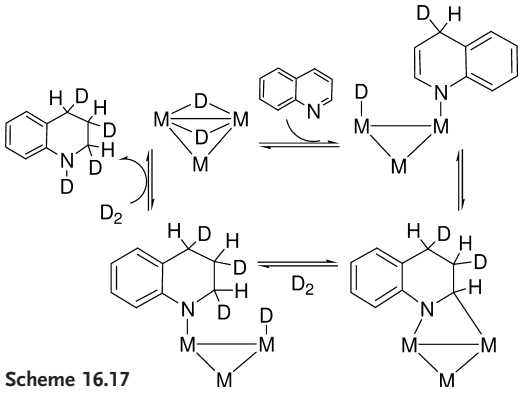
Using as catalyst precursors the clusters $Os_3H_2(CO)_{10}$ and $Os_3(CO)_{12}$ [71, 72], Laine and coworkers found a deuteration pattern of quinoline hydrogenation similar to that shown in Scheme 16.16, except for the presence of more deuterium in the 4-position and less in the 2-position, which has been interpreted in terms of the occurrence of oxidative addition of the osmium cluster to C–H bonds in quinoline, and also 1,4-hydrogenation (Scheme 16.17).

In an attempt to correlate the catalytic performance of comparable precursors with the nature of the metal center, Sánchez-Delgado and Gonzáles have investigated the selective hydrogenation of quinoline to THQ (150 °C, 30 bar H_2, toluene) by $RuCl_2(PPh_3)_3$ (TOF = 63), $RhCl(PPh_3)_3$ (TOF = 52), $RuHCl(CO)(PPh_3)_3$ (TOF = 29), $OsHCl(CO)(PPh_3)_3$ (TOF = 5), $[Rh(PPh_3)_2(cod)]^+$ (TOF = 199), and $[Ir(PPh_3)_2(cod)]^+$ (TOF = 17) [73]. The cationic rhodium complex was by far the most active.

Several ruthenium complexes have been found capable of hydrogenating *N*-heteroaromatics (acridine, quinoline, 5,6-BQ, 7,8-BQ, indole, IQ, for example: $[Ru(NCMe)_3(triphos)](SO_3CF_3)_2$ ($TOF_{indole/indoline} = 17$) in conjunction with protic acids [59, 65a, 74–76], $[RuH(CO)(NCMe)_2(PPh_3)_2]BF_4$ ($TOF_{quinoline/THQ} = 16$) [77,78], and $RuH_2(\eta^2\text{-}H_2)_2(PCy_3)_2$ ($TOF_{quinoline/5,6,7,8\text{-}THQ} = 2$; $TOF_{indole/indoline} < 1$) [79]. The latter complex also led to saturation of the aromatic ring, which has been proposed to involve the coordination of the substrate through the aromatic ring, in a manner similar to that reported for η^4-arene complexes (see Scheme



Scheme 16.16



Scheme 16.17

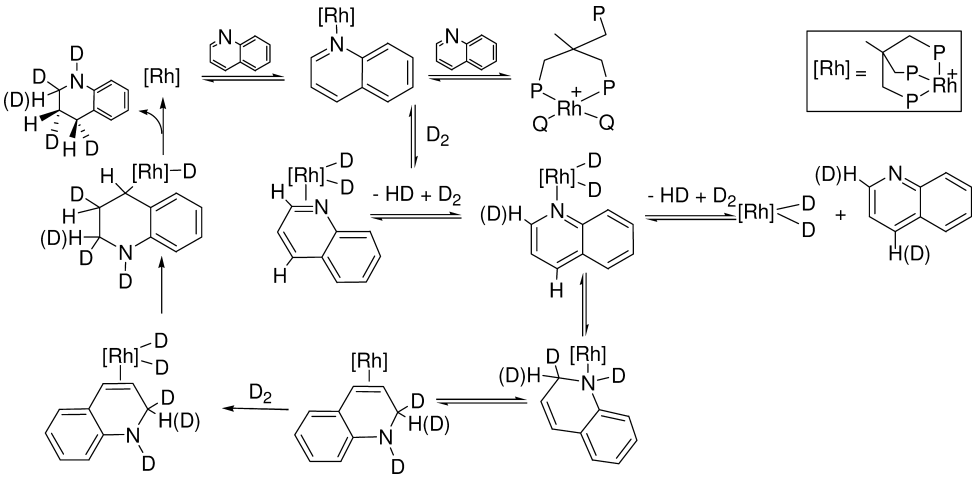
16.4). However, it must be remembered that the true homogeneous nature of this system remains a matter of debate.

Kinetic studies of the hydrogenation of *N*-heteroaromatics have been reported wherein quinoline is the most studied substrate. Sánchez-Delgado and co-workers have identified the experimental rate law $r_i = k_{cat}\,[Rh][H_2]^2$, with $k_{cat} = 50 \pm 6\ M^{-2}\ s^{-1}$ at 370 K for the hydrogenation of quinoline by $[Rh(PPh_3)_2(cod)]PF_6$ [80]. Kinetic studies for quinoline reduction to THQ have also been reported by Rosales for the reactions catalyzed by $[RuH(CO)(MeCN)(PPh_3)_2]BF_4$ [77]. At low hydrogen pressure, the experimental rate law was $r_i = k_{cat}\,[Ru_0][H_2]^2$ ($k_{cat} = 28.5\ M^{-2}\ s^{-1}$ at 398 K), while a first-order dependence of the reaction rate with respect to the hydrogen concentration was ob-

served at high H_2 pressure. The proposed mechanism involves a rapid and reversible partial hydrogenation of bonded quinoline, followed by a rate-determining second hydrogenation of dihydroquinoline.

A much more complex kinetic law has been reported by Bianchini and coworkers for the hydrogenation of quinoline catalyzed by the Rh^I complex [Rh(DMAD)(triphos)]PF_6 (DMAD = dimethyl acetylenedicarboxylate) [74, 75]. The rate was first order with respect to both H_2 in the pressure range from 4 to 30 bar, and in the catalyst concentration range from 36 to 110 mM, while the hydrogenation rate showed an inverse dependence with respect to quinoline concentration. The empiric rate law $r = k''$ [Rh][H_2][Q]^2, where $k'' = k$ (a + b[Q] + c[Q]^2)$^{-1}$, was proposed to account for the inhibiting effect of quinoline (Q) concentration and the experimental observation that the rate tends to be second order for very low quinoline concentrations (< 30 mM) and zero-order for very high quinoline concentrations (> 70 mM). On the basis of the kinetic study, deuterium labeling and high-pressure NMR experiments under catalytic conditions, as well as the identification of catalytically relevant intermediates, a mechanism was proposed (Scheme 6.18) which essentially differs from that proposed by Sánchez-Delgado for the rate-limiting step (i.e., reversible reduction of the C=N bond instead of the irreversible one of the C_3=C_4 bond). The overall hydrogenation of the C=N bond, which actually disrupts the aromaticity of quinoline, was proposed as the rate-determining step, which was consistent with the fact that 2,3-dihydroquinoline was reduced faster than quinoline, while the lack of deuterium incorporation into the carbocyclic ring of both THQ and quinoline ruled out the formation of η^6-quinoline or η^6-THQ intermediates [74, 75].

The reduction of acridine to 9,10-dihydroacridine by the precursor [RuH(CO)$(NCMe)_2(PPh_3)_2$]BF_4 has been found to occur with the experimental rate law $r = k_{cat}$ [Ru][H_2] and the postulated mechanism involves, as the determining



Scheme 16.18

step, the hydrogenation of coordinated acridine in $[RuH(CO)(\eta^1(N)\text{-AC})(NCMe)(PPh_3)_2]^+$ to yield 9,10-dihydroacridine and the coordinatively unsaturated complex $[RuH(CO)(NCMe)(PPh_3)_2]^+$ [78].

In homogeneous phase, indole is much more difficult to reduce than quinoline, as shown by the limited number of known catalysts (e.g., $RuHCl(PPh_3)_3$ [68] and $[RuH(CO)(NCMe)(PPh_3)_2]BF_4$ [78]) as well as their very scarce activity (TOFs ≤ 1). Indeed, the $\eta^1(N)$ coordination, which is critical for selective nitrogen ring reduction in quinoline, is virtually unknown for indole, which prefers to bind metal centers using the carbocyclic ring. In the latter coordination mode, the C=N bond is not activated and the many occupied coordination sites at the metal center make oxidative addition of H_2 very difficult to accomplish. Consistently, the hydrogenation of indole is generally inhibited when the reaction mixture contains basic substrates such as quinoline, THQ, and pyridine. The only catalysts that have proved able to regioselectively hydrogenate indole to indoline with an acceptable TOF are $[Rh(DMAD)(triphos)]PF_6$ and $[Ru(NCMe)_3(triphos)](SO_3CF_3)_2$, though on condition that a protic acid is added to the catalytic mixture [74, 76]. The rhodium catalyst was more efficient than the ruthenium catalyst, and allowed for hydrogenation of the substrate even at 60 °C and 30 bar H_2, with TOFs as high as 100. It was shown experimentally that indoline was actually formed by reduction of the protonated form of indole, the 3H-indolium cation which possesses a localized C=N bond.

The selective hydrogenation of N-heterocycles has been achieved with the use of water-soluble Ru^{II} catalysts prepared *in situ* by reacting an excess of either triphenylphosphine trisulfonate (TPPTS) or triphenylphosphine monosulfonate (TPPMS) with $RuCl_3 \cdot 3H_2O$. The resulting solutions were added to a hydrocarbon solution containing various N-heteroaromatics such as quinoline, acridine, and IQ. The biphasic reactions were performed under relatively drastic experimental conditions (130–170 °C, 70–110 bar H_2) and led to selective reduction of the heterocyclic ring [61, 81].

The regioselective reduction of quinoline to THQ in water/hydrocarbon has also been achieved with bidentate and tridentate water-soluble ligands. The Rh^I complex $[Rh(H_2O)_2(DPPPDS)]Na$ was employed in water/*n*-octane to hydrogenate 1:1 mixtures of quinoline and BT at high temperature (160 °C). Only the N-heterocycle was efficiently reduced (TOF = 50), with BT hydrogenation to DHBT being only marginal (TOF = 2) [8c]. A similar selectivity has been reported for the catalytic system $RuCl_3 \cdot H_2O/2Na_2DPPPDS$ prepared *in situ*. In contrast, the individual hydrogenation rates for quinoline and BT have been reported to be similar (TOF = 30 at 140 °C, 30 bar H_2, water/*n*-heptane) and independent of the presence of either substrate by using the binuclear precursor $Na[\{(sulphos)Ru\}_2(\mu\text{-}Cl)_3]$ $(sulphos = (PPh_2CH_2)_3CCH_2(C_6H_4)SO_3^-)$ [8c, 82].

Under biphasic conditions, the zwitterionic Rh^I complex Rh(cod)(sulphos) proved to be very efficient for the hydrogenation of quinoline to THQ (TOF = 20 at 160 °C, 30 bar H_2, water/*n*-heptane) [8c].

16.3.1.3 O-Heteroaromatics

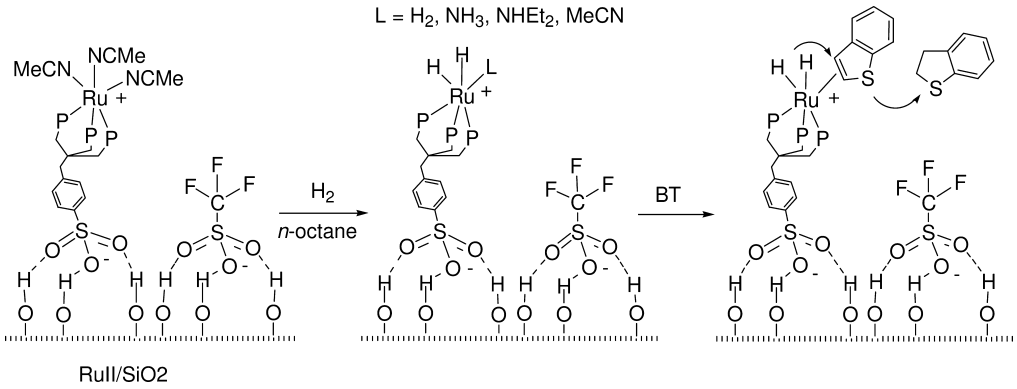
Very few examples of hydrogenation of O-heteroaromatics with molecular metal catalysts have appeared in the literature to date. Besides some cases of enantioselective catalysis (see Section 16.4), there is only one example reported by Fish dealing with the homogeneous hydrogenation of benzofuran to 2,3-dihydrobenzofuran using $[Rh(NCMe)_3(Cp^*)](BF_4)_2$ as the catalyst precursor [55]. As for the hydrogenation of BT performed by the same catalyst, the hydrogenation of benzofuran has been proposed to involve coordination of the substrate through the 2,3 double bond to a Rh–H species, followed by hydrogen transfer to yield 2,3-dihydrobenzofuran.

16.3.2 Molecular Catalysts Immobilized on Support Materials

$Rh(PPh_3)_3Cl$ tethered to 2% cross-linked phosphinated polystyrene-divinylbenzene was the first heterogenized single-site metal catalyst to be used in the hydrogenation of N- and S-heteroaromatics (see Fig. 16.3) [37]. This catalyst was able to hydrogenate quinoline, acridine, 5,6-BQ and 7,8-BQ in benzene solution (85 °C, 20 bar H_2) with an order of activity (acridine > quinoline > 5,6-BQ > 7,8-BQ) that is identical to that in homogeneous phase with the unsupported catalysts, except for the initial rates that were from 10- to 20-fold faster than in homogeneous phase [67]. This remarkable rate enhancement was attributed to steric requirements surrounding the active metal center in the tethered complex, which apparently would favor the coordination of the N-heterocycles by disfavoring that of PPh_3. The regioselectivity of hydrogenation was even higher than that in homogeneous phase as no formation of 1,2,3,4-tetrahydroacridine was observed. The deuteration pattern of the heteroaromatic ring after a catalytic reaction with D_2 was identical to that observed in homogeneous phase, except for the absence of deuterium incorporation at position 8 of the carbocyclic ring. The tethered catalyst proved able also to hydrogenate BT to DHBT (benzene, 85 °C, 20 bar H_2) with rates three-fold faster than those observed in homogeneous phase with the parent precursor $RhCl(PPh_3)_3$ [37].

The most active and fully recyclable single-site catalyst for the hydrogenation of thiophenes is still that generated by the SHB precursor $[Ru(NCMe)_3(sulphos)](OSO_2CF_3)/SiO_2$ (Ru^{II}/SiO_2), obtained by tethering $[Ru(NCMe)_3(sulphos)](OSO_2CF_3)$ to silica (Scheme 16.19). In this case, immobilization of the molecular catalyst involves the formation of hydrogen-bonds to the surface silanols by SO_3^- groups from both the sulphos ligand and the triflate counter-anion [39b]. Upon hydrogenation (30 bar H_2), Ru^{II}/SiO_2 has been found to generate a very active, recyclable and stable catalyst for the selective hydrogenation of BT to DHBT, with TOFs as high as 2000. The TOF with Ru^{II}/SiO_2 did not practically change even when a new feed containing 2000 equiv. BT in *n*-octane was injected into the reactor after 1 h reaction, which means that DHBT does not compete with BT for coordination to the Ru^{II} center.

All attempts to hydrogenate thiophenes by using TCSM catalysts of the types shown in Figures 16.4 and 16.5 have, so far, been unsuccessful. Rh^I-Pd^0/SiO_2



Scheme 16.19

was tested in the hydrogenation (30 bar H_2) of BT in *n*-octane under 30 bar at 100–170 °C, but the production of a DHBT was the same as that obtained with silica-supported Pd^0 nanoparticles alone (TOF = 8–10) [43]. Apparently, no synergistic effect between the isolated rhodium sites and the surface palladium atoms takes place for the hydrogenation of thiophenes. This was not totally unexpected, as neither silica-supported Rh(cod)(sulphos)/SiO_2 in *n*-octane [43] nor free Rh(cod)(sulphos) [83] in MeOH or [Rh(cod)(triphos)]PF_6 [83] in THF proved able to hydrogenate appreciably BT and thiophene below 150–170 °C. In fact, at these high temperatures hydrogenolysis to the corresponding thiol occurred [83 b, c]. In contrast, the SHB rhodium complexes Rh(cod)(sulphos)/SiO_2 and [Ru(NCMe)$_3$(sulphos)](SO$_3$CF$_3$)/SiO_2 have been used successfully to hydrogenate quinoline in *n*-octane (100 °C, 30 bar H_2), yielding selectively THQ with TOFs as high as 100 [43]. In line with the behavior of the Fish catalyst RhCl(PPh$_3$)$_3$/P [37], both Rh(cod)(sulphos)/SiO_2 and [(sulphos)Ru(NCMe)$_3$](SO$_3$CF$_3$)/SiO_2 have been found to be more efficient catalysts than the homogeneous and aqueous-biphasic counterparts with triphos or sulphos ligands. The rate enhancement observed for the heterogeneous reactions has been attributed to the fact that, unlike in fluid solution systems, the heterogenized complexes do not undergo dimerization to give catalytically inactive species.

The supported complex [Rh(cod)(POLYDIPHOS)]PF_6, obtained by stirring a CH_2Cl_2 solution of [RhCl(cod)]$_2$ and Bu_4NPF_6 in the presence of a diphenylphosphinopropane-like ligand tethered to a cross-linked styrene/divinylbenzene matrix (POLYDIPHOS), forms an effective catalyst for the hydrogenation of quinoline (Fig. 16.8) [84]. Under relatively mild experimental conditions (80 °C, 30 bar H_2), quinoline was mainly converted to THQ, though appreciable formation of both 5,6,7,8-THQ and decahydroquinoline also occurred (Scheme 16.20).

An effective catalyst recycling with no loss of catalytic activity was accomplished by removing the liquid phase via the liquid sampling valve and re-charging the autoclave with a solution containing the substrate. In all cases, no rhodium leaching occurred. Remarkably, the hydrogenation activity of the 1,3-bis-

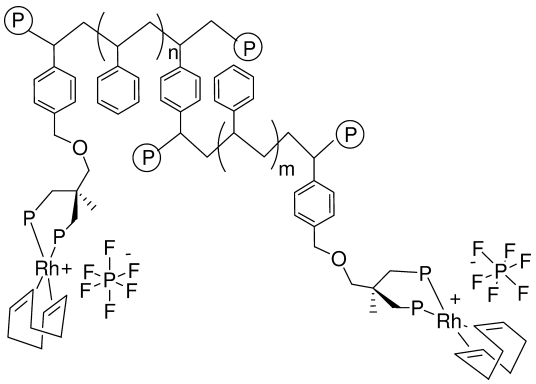
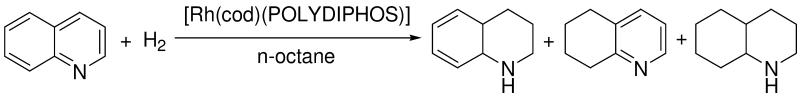


Fig. 16.8 Schematic of a diphosphine rhodium complex covalently tethered to a cross-linked styrene/divinylbenzene matrix, used for the hydrogenation of quinoline.



Scheme 16.20

diphenylphosphinopropane complex [Rh(dppp)(cod)]PF_6 in THF was much lower, as well as being selective, for THQ.

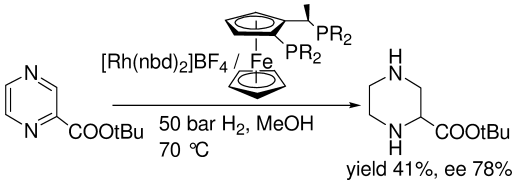
16.4 Stereoselective Hydrogenation of Prochiral Heteroaromatics

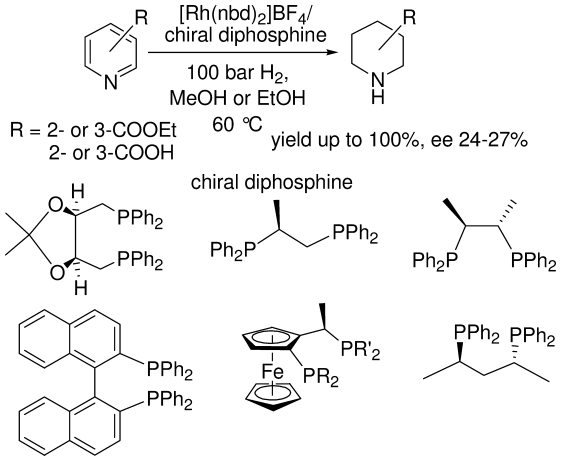
16.4.1 Molecular Catalysts in Homogeneous Phase

The enantioselective hydrogenation of prochiral heteroaromatics is of major relevance for the synthesis of biologically active compounds, some of which are difficult to access via stereoselective organic synthesis [4]. This is the case for substituted N-heterocycles such as piperazines, pyridines, indoles, and quinoxalines. The hydrogenation of these substrates by supported metal particles generally leads to diastereoselective products [4], while molecular catalysts turn out to be more efficient in enantioselective processes. Rhodium and chiral chelating diphosphines constitute the ingredients of the vast majority of the known molecular catalysts.

Relevant examples of enantioselective hydrogenation of aromatic N-heterocycles are given below. Scheme 16.21 shows the hydrogenation of a 2-ester substituted piperazine to the corresponding 2-substituted pyrazine with a catalyst

Scheme 16.21





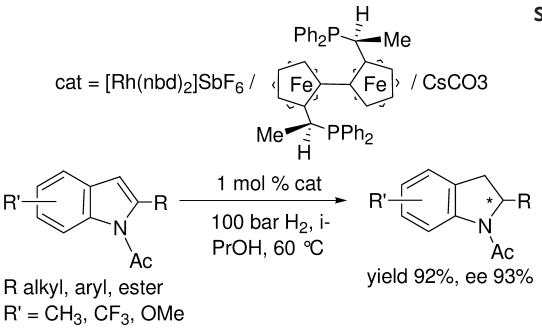
Scheme 16.22

prepared *in situ* by mixing $[Rh(nbd)_2Cl]_2$ with a *Josiphos*-type ferrocenyldiphosphine, preferentially 1-[1(*R*)-(dicyclohexylphosphino)ethyl]-2(*S*)-(diphenylphosphino)ferrocene [85]. Under relatively mild conditions, the conversions were low, but the ee-values were quite satisfactory.

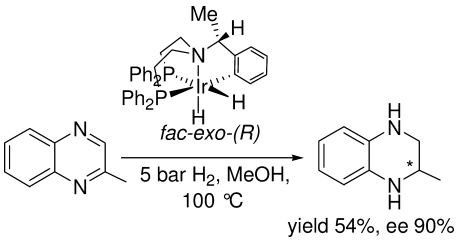
Josiphos-rhodium systems have been also used to hydrogenate 2- or 3-substituted pyridines and furans, yet both the activities (TOF = 1–2) and enantioselectivities were rather low (Scheme 16.22) [86, 87]. Comparable results were obtained with a number of chiral chelating diphosphines of various symmetries.

The diphosphines leading to the formation of six- or seven-membered metallarings have been found to give higher ee-values as compared to 1,2-diphosphines. With most ligands, the 2- or 3-substituted furans were hydrogenated with much lower enantioselectivity (ee 1–7%). Only the *Josiphos* ligand with R = *t*-Bu gave a significant ee (24%) for the reduction of substituted furans, yet the activity was almost negligible (3%) [85]. It is worth noting that black precipitates were observed in some experiments, which may indicate catalyst decomposition.

Excellent ee-values (up to 94%) have been obtained for the hydrogenation of various 2-substituted *N*-acetyl indoles with an *in-situ* prepared rhodium catalyst modified with the *trans*-chelating diphosphine (*S*,*S*)-(*R*,*R*)-2,2″-bis[1-(diphenylphosphino)ethyl]-1,1″-biferrocene (Scheme 16.23) [88]. A strong base was required as co-reagent to observe both high conversion (TOFs of 50–100) and en-



Scheme 16.23



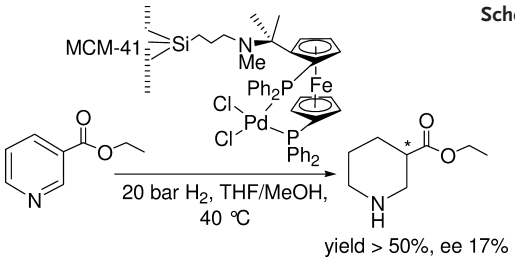
Scheme 16.24

antioselectivity. Best results were achieved with catalytic systems comprising $CsCO_3$ and $[Rh(nbd)_2]SbF_6$.

A quite different ligand system has been found to generate a selective iridium catalyst for the hydrogenation of 2-methylquinoxaline to (–)-(2*S*)-2-methyl-1,2,3,4-tetrahydroquinoxaline (Scheme 16.24) [89]. Unlike all previous examples of enantiomeric hydrogenation, an isolated catalyst precursor, namely the Ir^{III} *o*-metalated dihydride *fac-exo*-(*R*)-$[IrH_2\{C_6H_4C^*H(Me)N(CH_2CH_2PPh_2)_2\}]$, was employed. Under quite mild experimental conditions, ee-values of up to 90% were obtained at 50% conversion, while at 100% conversion the ee decreased to 75%. An *operando* high-pressure NMR study showed that the catalytically active species was generated by de-orthometalation rather than by H_2-reductive elimination. It was also shown that the two C=N moieties of 2-methylquinoxaline were reduced at comparable rates. Notably, the use of the *fac-exo*-(*S*) dihydride precursor gave the product with opposite configuration, that is (+)-(2*R*)-2-methyl-1,2,3,4-tetrahydroquinoxaline [89].

The only other example of enantioselective hydrogenation of 2-methylquinoxaline has been reported by Murata and coworkers, who used a [(+)-(DIOP)RhH] catalyst to produce 2-methyl-1,2,3,4-tetrahydroquinoxaline, albeit in 3% ee [90].

Scheme 16.25



16.4.2
Molecular Catalysts Immobilized on Support Materials

The enantioselective hydrogenation of ethyl nicotinate to ethyl nipecotinate is a difficult process of which only a few heterogeneous examples are known, generally catalyzed by Pd/C modified with supported chiral auxiliaries [91]. No example in homogeneous phase has been reported to date. Palladium(II) complexes with the chelating ligand (*S*)-1-[(*R*)-1,2′-bis(diphenylphosphino)ferrocene are equally inactive, but their immobilization onto the inner walls of MCM-41 has surprisingly generated an effective catalyst, albeit with a modest ee (Scheme 16.25) [92]. Nonetheless, this reaction deserves to be highlighted for the elegant approach to heterogenization as well as for developing the concept of catalyst confinement as an innovative method to magnify both the catalytic activity and the asymmetric induction [92, 93].

Abbreviations

4H-An	1,2,3,4-tetrahydroanthracene
8H-An	1,2,3,4,5,6,7,8-octahydroanthracene
BQ	benzoquinoline
BT	benzo[*b*]thiophene
DBT	dibenzo[*b*,*d*]thiophene
DHBT	dihydrobenzo[*b*]thiophene
DVB	divinylbenzene
ee	enantiomeric excess
HDN	hydrodenitrogenation
HDO	hydrodeoxygenation
HDS	hydrodesulfurization
IQ	isoquinoline
PTA	1,3,5-triaza-7-phosphadamantane
SG	syngas
SHB	supported hydrogen-bonded
TCSM	tethered complexes on supported metals
THPY	1,2,5,6-tetrahydropyridine

THQ	1,2,3,4-tetrahydroquinoline
THT	tetrahydrothiophene
TOF	turnover frequency
TPPMS	triphenylphosphine monosulfonate
TPPTS	triphenylphosphine trisulfonate
WGS	water-gas-shift

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