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Catalysis Today 37 (1997) 155–165

CATALYSIS TODAY

Homogeneously catalyzed amination of alkenes

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Abstract

This review assesses the challenges facing the development of catalysts for the amination of alkenes. Short sections are included summarizing the use of both ammonium ion and amide ion as catalysts. The principal transition metal systems that have been used as homogeneous catalysts are discussed in terms of their mechanistic features. The use of organolanthanide complexes as amination catalysts is also discussed in terms of their reaction mechanism. The review also includes enzymic amination catalysts and the use of mercury photosensitization for alkene amination via hydrogen atom abstraction. A section covering allylic amination is also included.

1. Introduction

Ammonia and amines are reagents that are synthetic precursors for a wide range of commercially useful products. Among these products are amines, amides, ammonium and alkylammonium salts, ureas, carbamates, isocyanates and amino acids [1]. Ammonia and amines are moderate strength bases (pK_b about 5–6) and very weak acids (pK_a about 30–35) [2]. The N–H bond enthalpy in ammonia is 103.2 kcal/mol. The N–H enthalpies for primary amines range from 88 to 100 kcal/mol with those for secondary amines ranging from 87 to 92 kcal/mol [3]. The addition of an N–H bond to an alkene is a potentially useful chemical reaction because it leads to the formation of a C–N bond, and therefore to functionalization of the hydrocarbon. By changing the R group in amines such as RR′NH between hydrogen, alkyl, and aryl functionality's, the addition of the N–H bond to an alkene can be used to prepare a wide range of primary, secondary, and tertiary amines (Eq. (1)). If uncatalyzed this addition reaction is not a synthetically useful one and it

$$RR'NH + \text{alkene} \rightarrow \text{alkyl}NRR' \quad (1)$$

only occurs with activated alkenes [4,5]. Thermodynamic considerations indicate that the addition of an N–H bond to an alkene is approximately thermoneutral. This postulate is illustrated by the addition reactions of ammonia or dimethylamine to ethylene to give ethylamine and ethyldimethylamine, respectively (Eq. (2) and Eq. (3)). From the bond enthalpies in Table 1 it can be

$$C_2H_4 + NH_3 \rightarrow C_2H_5NH_2 \quad (2)$$

$$C_2H_4 + (CH_3)_2NH \rightarrow (CH_3)_2C_2H_5N \quad (3)$$

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PII S0920-5861(97)00008-4

Table 1
Bond dissociation energies for C–C, C=C, N–H and C–N

Bond	ΔH_f (kcal/mol)	Bond	ΔH_f° (kcal/mol)
H_2N–H	103.2	H_2C=CH_2	146
$(CH_3)_2N$–H	91.5	CH_3H_2C–NH_2	81.6
CH_3H_2C–H	98.2	$(CH_3)_2N$–C_2H_5	72.3
H_3C–CH_3	88		

concluded that reaction 2 is favored by approximately 18.6 kcal/mol and that reaction 3 by 21.0 kcal/mol [3,6,7].

For carbon–carbon triple bonds the addition of ammonia or an amine is more favorable, and the addition of an N–H bond to an alkyne can be used in the preparation of imines [8].

In the absence of a catalyst the rate of addition of an N–H bond to an alkene is slow, the yields of amine product are low, and multiple alkylation usually occurs to give mixtures of primary, secondary and tertiary amines.

2. Catalyzed addition of ammonia and amines to an alkene

2.1. *Ammonium ion as catalyst*

When isobutene and ammonia are reacted at 120°C in the presence of ammonium sulfate as catalyst the product is tertiary butylamine. The reaction requires the presence of water and it is likely that the reaction pathway involves the intermediate formation of tertiary butanol [9]. Ammonium halide catalysts have also been used for the conversion of C_{2-8} alkenes into amines by their reaction with ammonia or with primary or secondary amines [10].

2.2. *Amide ion as catalyst*

Alkali metal amides are homogeneous catalysts for the amination of alkenes with amines, but not with ammonia. The reaction of $(C_2H_5)_2NH$ with ethylene in the presence of $LiN(C_2H_5)_2$ gives $(C_2H_5)_3N$ (Eq. (4)) [11].

$$(C_2H_5)_2NH + C_2H_4 \rightarrow (C_2H_5)_3N \quad (4)$$

The reaction is carried out at temperatures of 70–90°C and pressures of 6–10 atm. The rate determining step is the addition of the diethylamide ion to the alkene.

Amide ions also catalyze the addition of amines to 1,3-butadiene to give enamines [12].

2.3. *Transition metal compounds as catalysts*

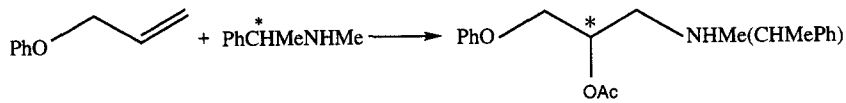
Transition metal compounds have been used as homogeneous catalysts for the amination of alkenes under photochemical conditions. Among the compounds used are Mo_8Cl_{12}, $Fe(CO)_5/P(OEt)_3$ and mercury [13]. Amination catalysts have also been prepared by anchoring discrete transition metal complexes onto zeolite supports [14]. The complexes used for anchoring are $RhCl(PPh_3)_3$, $RhCl_3{\cdot}3H_2O$, $[RhCl(cyclooctene)_2]_2$, $RhCl_3py_3$, $PdCl_2(PhCN)_2$ and $Pt(P(OPh)_3)_4$.

A mixture of ethylene and ammonia in the presence of a catalyst containing salts of palladium(II) and copper(II) gives principally pyridines as products that are substituted at the 2-position of the ring (Eq. (5)) [15]. These catalytic conditions that are employed are analogous to those

(5)

(n = 3, R = H; n = 4, R = C_2H_5)

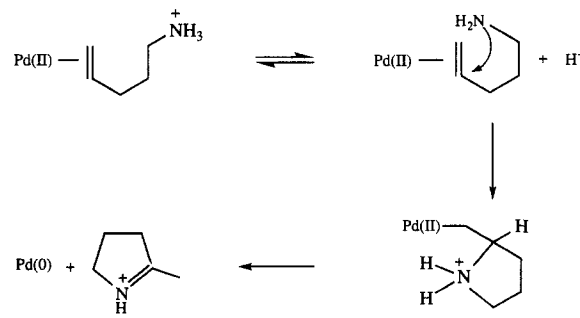
used in the Wacker catalyst, and the mechanism of the two reactions are analogous whereby the ethylene complexed to palladium undergoes initial nucleophilic attack by ammonia. As a result the palladium(II) is reduced to palladium(0), and subsequently re-oxidized back to the divalent state by copper(II) [16]. By a similar pathway (Scheme 1) primary aminoalkenes of type $CH_2{=}CH(CH_2)_nNH_2$ (n=3,4) cyclize to pyrrolines or piperdines in the presence of a mixture of $PdCl_2$ and $CuCl_2$. By contrast, aminoalkenes having a secondary amino group give the corresponding cyclic enamines, while tertiary aminoalkenes give aminoketones [17]. In the presence of palladium(II) complexes the compound $PhOCH_2CH(OAc)CH_2NMeCHMePh$ has been prepared from $PhOCH_2CH{=}CH_2$ and (*S*)-PhCHMeNHMe (Eq. (6)) [18].



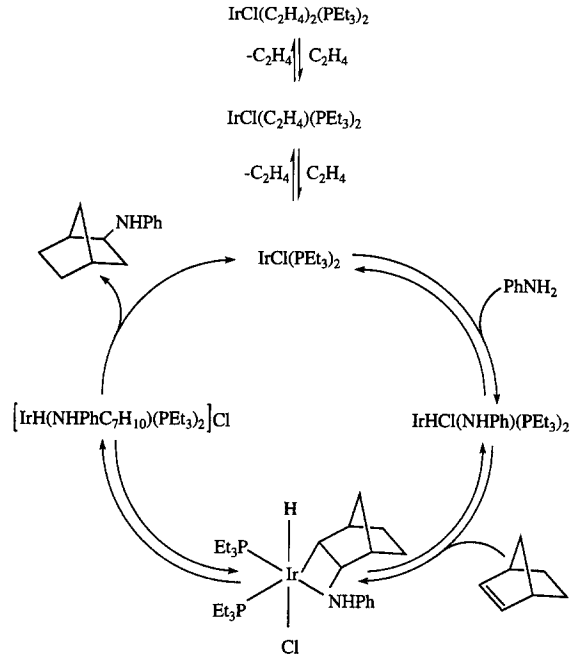
(6)

Low-valent transition metal compounds such as $Fe(CO)_5$ and $Ru_3(CO)_{12}$ have been used as catalysts for the addition of secondary amines to ethylene [19–21]. The reaction, which is carried out under hydroformylation conditions (CO and H_2), results in the formation of amine products that are homologated by one carbon. The reaction pathway likely involves an initial catalyzed hydroformylation of ethylene to the aldehyde. Subsequent reaction of the aldehyde with the amine to give a Schiff base, followed by hydrogenation of this second intermediate, leads to the final amine product. $Ru_3(CO)_{12}$ has also been used as a catalyst for the amination of styrene with diethylamine.

Another reaction pathway followed in the homogeneously catalyzed amination of alkenes involves the initial insertion of a low-valent metal complex into the N–H bond of ammonia or the amine. One such example is found in iridium(I) chemistry. This first successful demonstration of the amination of an alkene by a transition metal complex that likely involves initial N–H oxidative addition was accomplished using aniline as the amine and norbornylene as the alkene. In the catalytic reaction a mixture of $IrCl(C_2H_4)(PEt_3)_2$, $ZnCl_2$, aniline and norbornylene is refluxed for 48 h. The product is obtained in a catalytic yield of 6 turnovers based on the iridium complex [22]. A proposed pathway for the reaction is shown in Scheme 2. The complexes $Pd(SPh)_2bpy$ and



Scheme 1.

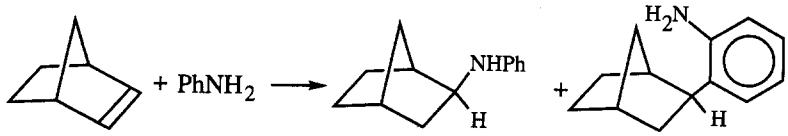


Scheme 2.

$Pd(SCN)_2(P(OPh)_3)_2$ have been used as catalysts for the addition of morpholine to 1-octene but no mechanistic details have been presented [23].

A consideration in developing catalytic cycles involving the insertion of a low-valent metal center into an N–H bond followed by insertion of an alkene into the metal–amide bond is the strength of this latter bond [6,7,24,25]. Within the second row transition metal series of elements a theoretical study has shown that the oxidative addition of ammonia is much more exothermic and has lower activation barriers for the transition metals that are to the left of the periodic table because of the attractive interaction between the ammonia lone-pair and the empty 4d orbitals. Half-empty 4d orbitals in the middle of the table are not sufficient for effective lone-pair donation [26].

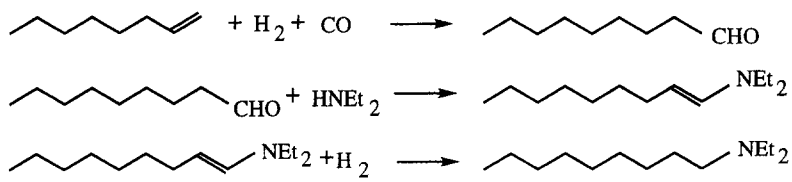
A catalytic system composed of $[RhCl(PEt_3)_2]_2$ and LiNHPh in aniline has been used for the hydroamination of norbornene. A second product involves addition of the *ortho* C–H bond (Eq. (7)) [27]. A rhodium anilide complex is likely involved as the catalytic species. A dimeric rhodium complex $[Rh(\mu\text{-}SBu_t)(CO)PPh_3]_2$ in the presence of a



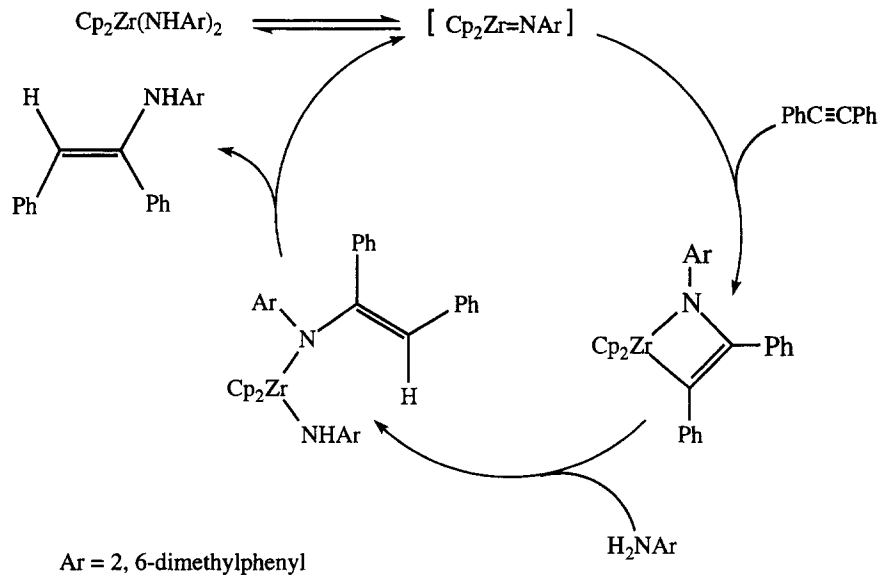
(7)

slight excess of triphenylphosphine catalyzes the aminomethylation of octene-1 [28]. The reaction pathway follows the sequence of reactions shown in Scheme 3 where the initial step involves hydroformylation of the terminal alkene, followed by Schiff base formation and hydrogenation of the imine.

A protonolysis approach has been used in the catalytic amination of alkenes with palladium(II) dialkyls [29]. The proposed pathway involves protonation of an alkyl group in the complexes PdR_2L_2 (R=alkyl, L_2=tertiary phosphine) to give the intermediate $PdRL_2^+$. In the addition of aniline to acrylonitrile this species can bind acrylonitrile and add the amine to give $PdRR'L_2$, where $R'=CH(CN)CH_2(NH_2Ph)^+$, which has been detected by NMR spectroscopy. Protonolysis completes the catalytic cycle.

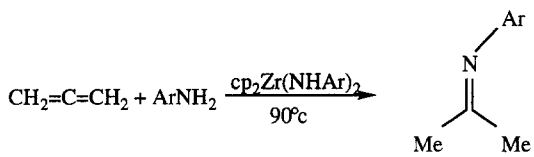


Scheme 3.



Scheme 4.

For the early transition metals, the bis amide complex $cp_2Zr(NHR)_2$ has been used to catalyze the hydroamination of alkynes and allene [30]. At 90°C allene can be catalytically hydroaminated with 2,6-dimethylaniline to give the anti-Markovnikov imine addition product (Eq. (8)). No mechanism has been proposed for the

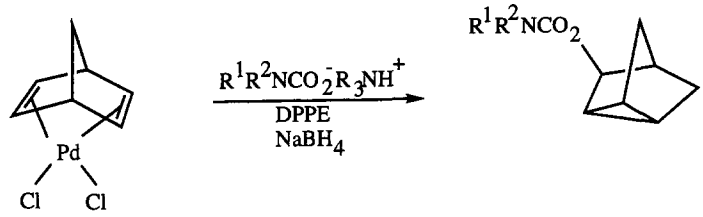


(8)

(Ar = 2, 6-dimethylphenyl)

hydroamination of allene. Nevertheless, for the hydroamination of the alkyne diphenylacetylene using the same catalyst system the pathway shown in Scheme 4 involving a metallocyclic intermediate has been proposed. This pathway has been supported by independently synthesizing some of the proposed intermediates and showing that they undergo the anticipated reaction steps.

Carbamate esters have been prepared by reaction of carbamate anions with a norbornadiene coordinated to palladium(II). A range of different groups R^1 and R^2 in $R^1R^2NCO_2^-$ (R^1=H, R^2=Bu^n; R^1=H, R^2=CH_2Ph; R^1=Me, R^2=CH_2Ph) have been used (Eq. (9)) [31].



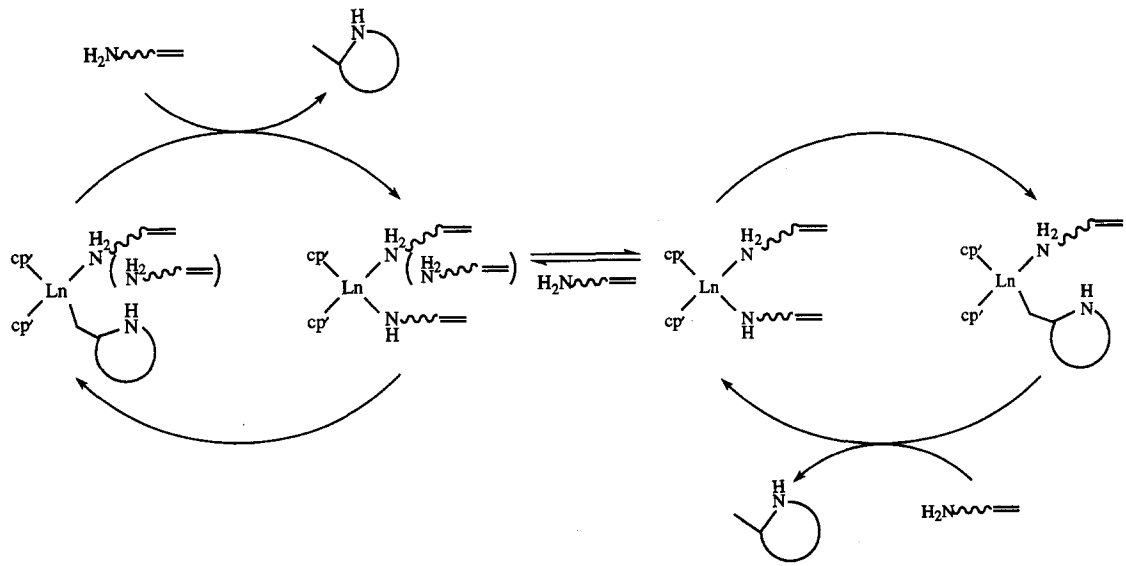
(9)

2.4. *Organolanthanides as catalysts*

The organolanthanide compounds $cp'_2LnR[cp'=\eta^5\text{-}C_5Me_5$; R=H, $CH(TMS)_2$, $\eta^3\text{-}C_3H_5$, $N(TMS)_2$; Ln=La, Nd, Sm, Y, Lu] catalyze the cyclization of the aminoalkenes $H_2NCHR^1R^2CH{=}CH_2$ give the corresponding heterocycles $HNCH(R^1)R^2CHCH_3$ (R^1=H, $R^2=(CH_2)_2$; R^1=H, $R^2=CMe_2CH_2$; R^1=H, $R^2=(CH_2)_3$; R^1=Me, $R^2=(CH_2)_2$; R^1=H, $R_2=CH(Me)CH_2$) [32]. The mechanistic pathway is shown in Scheme 5. This mechanism involves two parallel manifolds. The manifold that predominates at high amine concentrations show a high diastereoselectivity in the cyclization reaction. The second manifold that is the principal one at lower concentrations shows a lower diastereoselectivity. At high amine concentrations the catalyst is proposed to be a Ln(amino)$(amine)_2$ complex.

2.5. *Enzymes as catalysts*

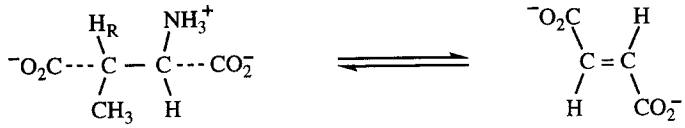
Enzymes have been isolated that will catalyze both the addition and elimination of N–H bonds with alkenes. These enzymes are classified as ammonia-lyases [33]. Examples of the reactions that are catalyzed by these enzymes are shown in Eq. (10)–(13). Isotope effects for the elimination of ammonium ion from aspartate suggest that the rate-determining step of the reaction is likely to be C–N cleavage, and the data imply that as the amino acid



Scheme 5.

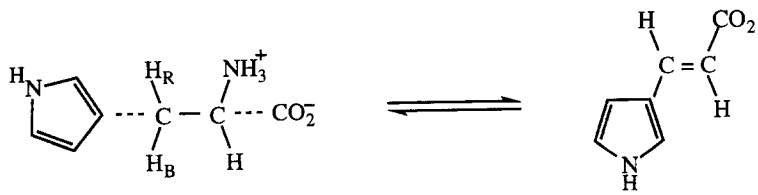
(10)

aspartate fumarate



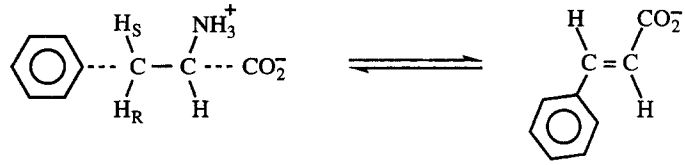
(11)

threo-3-methyl-L-aspartate mesaconate



(12)

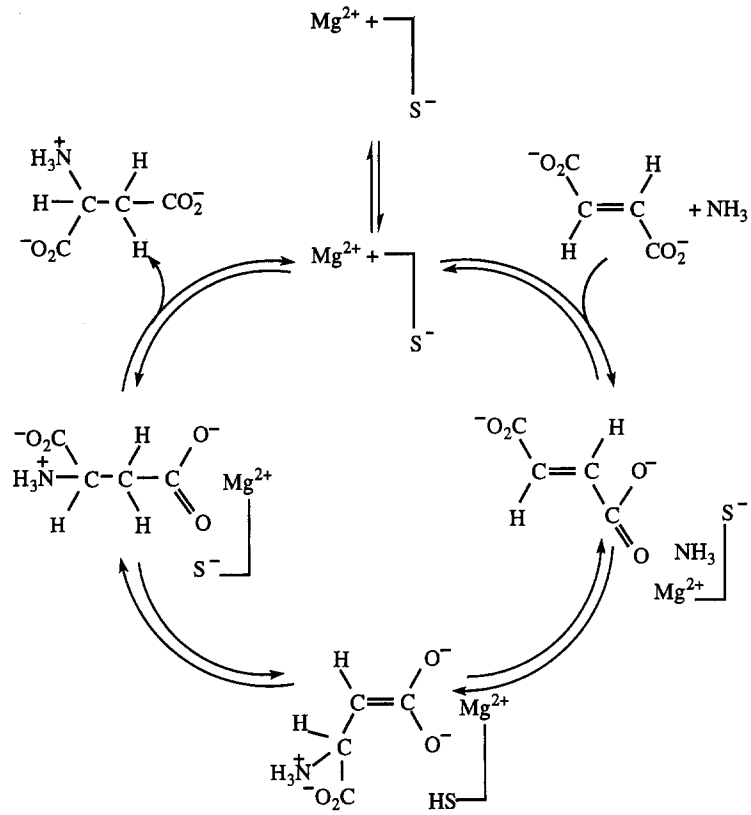
L-histidine uracanate



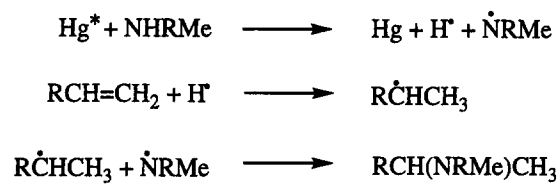
(13)

L-phenylalanine *trans*-cinnamate

group leaves the resulting intermediate is accompanied by considerable carbonium ion formation [34]. More recent secondary isotope data, however, suggest that a carbonionic mechanism is operable [35]. Kinetic data on the enzyme are consistent with the rapid addition of Mg^{2+} prior to that of aspartate, but random release of Mg^{2+}, NH_4^+ or fumarate. Monovalent cations such as Li^+, K^+, Cs^+ and Rb^+ are competitive against either aspartate or NH_4^+, but noncompetitive against fumarate. A pathway that explains many of the features of this enzyme is shown in Scheme 6. In this model the enzyme has a deprotonated sulfhydryl residue in close proximity to the active site. In the reversible formation of the C–N bond the sequential proton transfer that occurs involves this sulfhydryl residue. Although aspartate is activated by metal ions the requirement for a divalent metal ion is not specific. The binding stoichiometry corresponds to one metal ion per subunit with the metal ion binding at the activator site on L-aspartase rather than at the enzyme active site.



Scheme 6.



(R = H, Me)

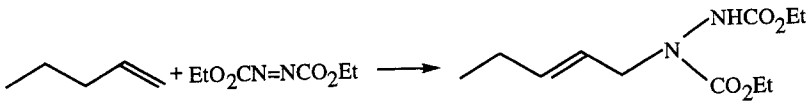
Scheme 7.

2.6. *Mercury photosensitized reactions*

Alkenes, like alkanes, can be aminated with amines upon photosenitization with mercury [36]. The reaction involves an initial homolysis of the N–H bond followed by attack of the alkene by hydrogen atoms to give alkyl radicals. Subsequent trapping of these radicals by the amine radical leads to alkene amination by an overall Markovnikov addition (Scheme 7). For 1-alkenes the H atom addition step usually occurs at the least substituted vinylic carbon, yielding mainly 2-functionalized products. A side product of the reaction is the alkane dimer, which is the major product when NH_3 is used as reactant instead of a substituted amine.

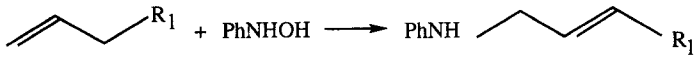
3. Allylic amination

Tin(IV) chloride has been used as a catalyst for the reaction of diethyl azodicarboxylates with alkenes to give allylic amines [37]. The example shown in Eq. (14) gives an *E*:*Z* ratio of 11:1.



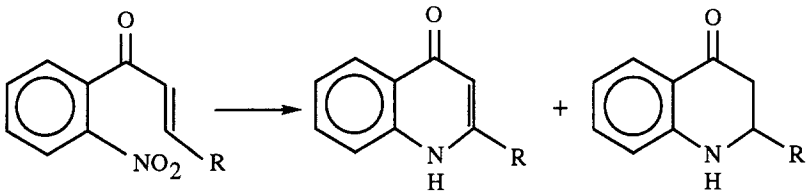
(14)

Transition metal complexes have been used for allylic amination reactions. In the presence of iron complexes, alkenes react with phenylhydroxylamine to give *N*-phenyl-*N*-allylamines [38]. The reaction shown in Eq. (15) is accompanied by the formation of azobenzene and azoxybenzene.



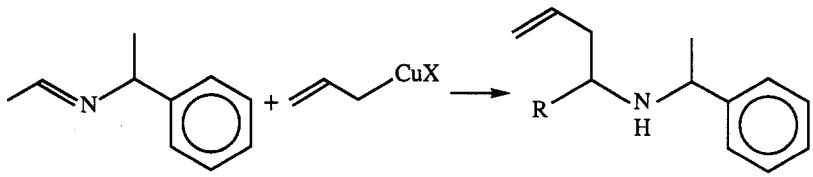
(15)

Iron phthalocyanines are particularly effective catalysts for this reaction [39]. These reactions likely involve the intermediacy of nitroso compounds, which are subsequently reduced by iron in its divalent state [40,41]. A similar-type reaction uses a mixture of $Ru_3(CO)_{12}$ and a diimine cocatalyst for the conversion of 2-nitrochalcones into quinolones and dihydroquinolones (Eq. (16)) [42].



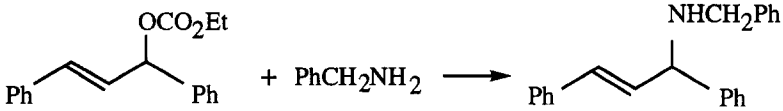
(16)

Allylic amines can also be prepared by the reaction between imines and allyl copper reagents (Eq. (17)) [43]. Dioxomolybdenum(VI) complexes also catalyze the allylic amination of alkenes



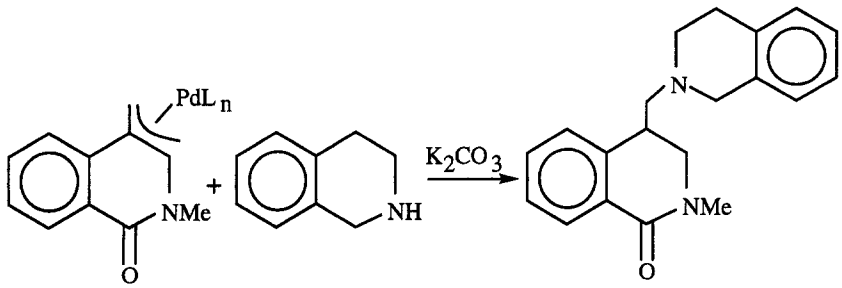
(17)

by phenylhydroxylamine [44]. Again, a nitroso intermediate is involved [45]. Palladium(0) compounds can also be used for the preparation of allylic amines from the reaction of allyl carbonates with benzylamine (Eq. (18)) [46].



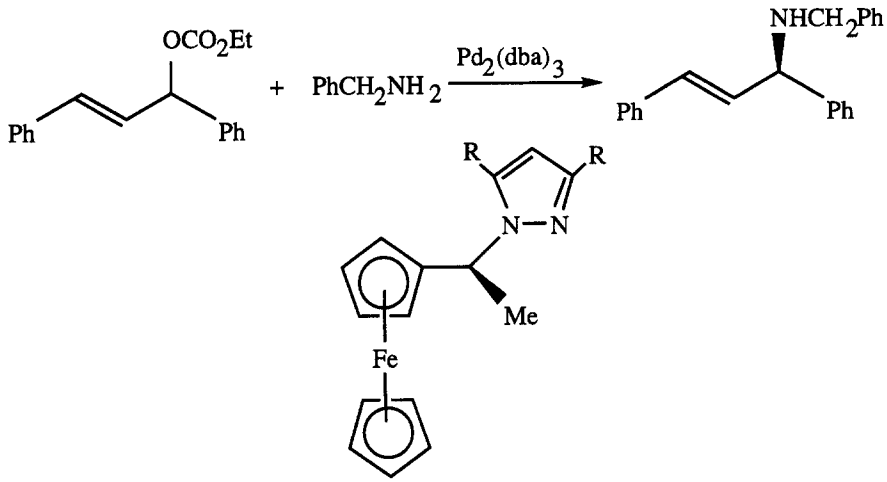
(18)

In a similar manner, palladium(0) complexes catalyze the cyclization–amination of allenes (Eq. (19)) [47].



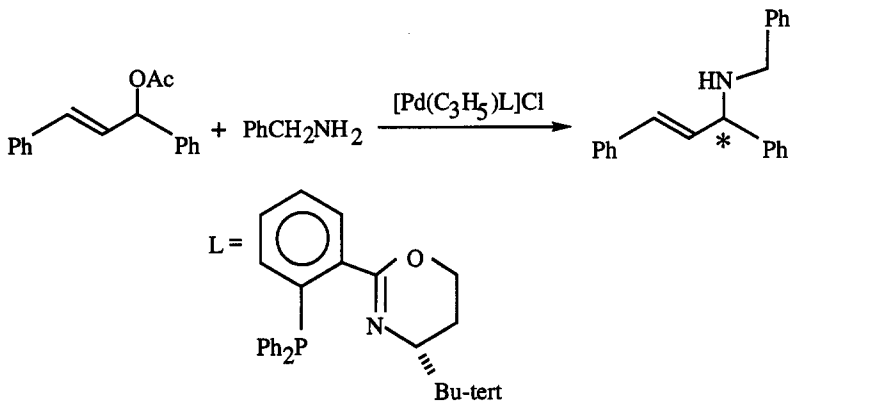
(19)

A symmetric allylic amination has been effected using a palladium complex containing a ferrocenyl *P, N* ligand [48–50]. The complex catalyzes the reaction of 1,3-diphenylallylethyl carbonate with benzylamine to give a secondary amine (Eq. (20)). Products having up to 96% ee have been obtained.



(20)

Chiral phosphinophenyl-oxazoline palladium(II) complexes are enantioselective catalysts for allylic amination reactions [51]. In the presence of the catalyst $[Pd(C_3H_5)L]Cl$, the reaction shown in Eq. (21) occurs with an enantioselective excess of 89%.



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Acknowledgements

We thank the National Science Foundation (USA) for support of our catalysis research.

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