CHEMICAL REVIEWS

Review

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Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis

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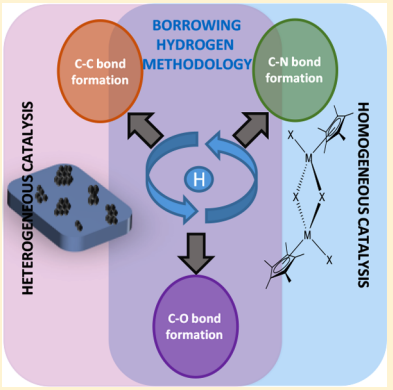
ABSTRACT: The borrowing hydrogen (BH) principle, also called hydrogen auto-transfer, is a powerful approach which combines transfer hydrogenation (avoiding the direct use of molecular hydrogen) with one or more intermediate reactions to synthesize more complex molecules without the need for tedious separation or isolation processes. The strategy which usually relies on three steps, (i) dehydrogenation, (ii) intermediate reaction, and (iii) hydrogenation, is an excellent and well-recognized process from the synthetic, economic, and environmental point of view. In this context, the objective of the present review is to give a global overview on the topic starting from those contributions published prior to the emergence of the BH concept to the most recent and current research under the term of BH catalysis. Two main subareas of the topic (homogeneous and heterogeneous catalysis) have been identified, from which three subheadings based on the source of the electrophile (alkanes, alcohols, and amines) have been considered. Then the type of bond being formed (carbon−carbon and carbon heteroatom) has been taken into account to end-up with the intermediate reaction working in tandem with the metal-catalyzed hydrogenation/dehydrogenation step. The review has been completed with the more recent advances in asymmetric catalysis using the BH strategy.



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1. INTRODUCTION

The borrowing hydrogen (BH) principle also called hydrogen auto-transfer is a powerful strategy which combines transfer hydrogenation (avoiding the direct use of molecular hydrogen) with one or more intermediate reactions to form more complex molecules without the need for tedious separation or isolation processes.

The key to this concept is that the hydrogen from a donor molecule will be stored by a catalytic metal fragment to be released in a final hydrogenation step, hence the reaction name. Following the above, the development of catalytic systems in borrowing hydrogen catalysis involves metal complexes or stabilized metal particles in which H_2 dissociation and recombination is simple, preferably without requiring severe reaction conditions. Unfortunately most of the metal hydrides that may form during hydrogen activation processes are too stable to easily give back the activated hydrogen, being therefore inactive for the BH methodology.[1,2] For example, ruthenium (Ru),[3,4] iridium (Ir),[5] and rhodium (Rh)[6]

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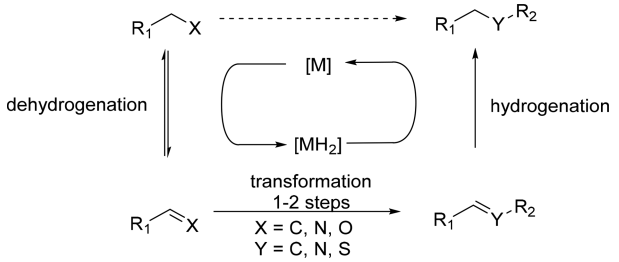
complexes, among others, are typical homogeneous complexes that have been reported for these reactions.

The borrowing hydrogen strategy begins with a metal-catalyzed dehydrogenation, by virtue of which a usually less reactive donor molecule is temporarily converted into a more reactive substrate (e.g., an alkane transforms into an alkene, an alcohol into an aldehyde, or a ketone and an amine into an imine). The more activated intermediate can undergo further transformations to give an unsaturated compound that will be reduced with the intervention of the metal hydrides generated during the first dehydrogenation step. A basic scheme of this concept is depicted in Scheme 1.

Scheme 1. Basic Scheme of the BH Methodology



In accordance with Scheme 1, the strategy typically relies on three steps: (i) dehydrogenation, (ii) intermediate reaction, and (iii) hydrogenation. Taking into account that the intermediate reaction step is a common organic reaction involving the dehydrogenated substrate (e.g., an aldehyde), the participation of the metal at this point is not absolutely essential, although this assumption may not necessarily hold since an electrophilic metal component of the catalyst can, for instance, increase the electrophilic nature of the C═O bond and thus enhance its reactivity.

An interesting feature of this method is that the hydrogenation step is usually thermodynamically favored, and this shifts the global process completely to the products, resulting in a very low E-factor. In essence, the irreversibility of the third step in Scheme 1 drives the first dehydrogenation step to near-completion. In this case, the same function can catalyze the dehydrogenation of the reactant and the hydrogenation of the intermediate product with the metal hydrides produced in the first step. It appears then that borrowing hydrogen catalysis is an excellent process from the synthetic, economic, and environmental point of view. Therefore, not surprisingly, the BH reactions have received much attention in the past few years.

In this respect, it is necessary to indicate that there are few examples that despite not strictly following the basic reaction sequence detailed in the Scheme 1 (dehydrogenation/intermediate reaction/hydrogenacion), they fulfill the philosophy of the BH strategy in the sense that the dehydrogenation product is not a waste any more.[7,8] As an example during the synthesis of pyrroles from 1,4-alkynediols[7] catalyzed by different ruthenium complexes, the hydrogenation reaction will occur immediately after the dehydrogenation step (and not at the end) on the resulting 1,4-alkynediketone followed by *N*-heterocyclization.[7]

Although early studies on heterogeneous systems reported more than three decades ago are the origin of this strategy, the real development of BH catalysis was paralleled by the design of homogeneous transition metal complexes in the search for more active catalysts.

Nonetheless it is well-known that homogeneous metal catalysts generally require the use of additives (ligands, acids, or bases), a fact that decreases the atom economy, whereas a wide variety of heterogeneous catalysts can be active under additive free conditions, also being true within the context of borrowing hydrogen catalysis.

Another key concept when using solid catalysts for borrowing hydrogen reactions is the possibility to prepare multifunctional catalysts. This has been achieved by preparing metal-loaded acidic and/or basic oxides, in which one of the acidic or basic sites selectively catalyzes the intermediate reaction, whereas the metallic component will catalyze both the dehydrogenation and hydrogenation steps.[9]

Due to its lack of a formal name, the BH concept has been passed by as it is extremely difficult to encounter, especially in early research. For this reason, the present report aims to rectify this situation for future or existing research by giving a global overview on the topic starting with those contributions published prior to the emergence of the BH concept to the most up-to-date research under the term of BH catalysis.

In this sense, it is important to note that most related review articles collect developments and/or improvements in the field albeit giving a partial overview on the topic.[9−20] In this regard, here we have also included other aspects that have not been sufficiently emphasized so far within the field of BH catalysis, such as alkane metathesis, a challenging reaction that has not been included in any of the most recent reviews on the topic.

Thus, first, we have identified the main two subareas of the topic (homogeneous and heterogeneous catalysis), from which we have considered three main subheadings based on the source of the electrophile (alkanes, alcohols, and amines). Then the type of bond being formed (carbon−carbon, carbon heteroatom) has been taken into account to end-up with the intermediate reaction working in tandem with the metal-catalyzed hydrogenation/dehydrogenation step. This classification is very comprehensive and whenever possible we will try to illustrate each of these sections with recent examples of bibliography. The review has been completed with the more recent advances in asymmetric catalysis using the BH strategy. So far the number of publications on this subject is scarce, as a result of the challenging conditions needed to perform enantioselective transformations within the context of borrowing hydrogen catalysis. Nonetheless, given that this issue has been successfully addressed with different homogeneous catalysts (e.g., by decreasing reaction temperatures below 40 °C), a representative number of reports on the enantioselective variant of BH will also be included here.[13]

Nonetheless, BH methodology as a tool for racemisation as well as dynamic kinetic resolution (DKR) of different substrates (e.g., secondary alcohols) is a topic that is out of the scope of this literature review.

2. BORROWING HYDROGEN METHODOLOGY IN HOMOGENEOUS CATALYSIS

2.1. Activation of Alkanes

The C−C bond is one of the strongest, more stable bonds, and for this reason it is of high importance to activate such covalent sigma link. One way to do this is by dehydrogenation to produce an olefin which may in principle undergo transformations such as metathesis as a route to longer alkanes.

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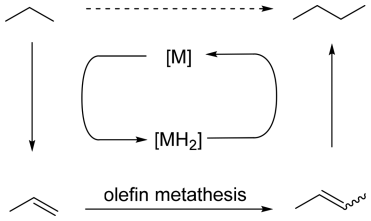
Obviously, alkane dehydrogenation integrated within the context of borrowing hydrogen catalysis can be an efficient and powerful route to activate alkanes.

2.1.1. Formation of C−C Bonds. *2.1.1.1. Olefin Metathesis.* Metathesis of alkenes working in tandem with dehydrogenation/hydrogenation reactions is a powerful BH strategy to form new alkanes known as alkane metathesis. Globally, alkane metathesis is a chemical reaction in which alkanes are rearranged to give longer alkanes as final products. It is similar to olefin metathesis,[21−23] except that olefin metathesis cleaves and forms new carbon−carbon double bonds, while alkane metathesis operates on carbon−carbon single bonds. Thus, alkane metathesis has been conceived on the bases of a tandem operational combination of alkane dehydrogenation/hydrogenation and olefin metathesis reactions[24] as depicted in Scheme 2.

Scheme 2. Borrowing Hydrogen and Olefin Metathesis Working in Tandem



One of the first homogeneous catalytic systems for converting a specific alkane into a higher homologue by means of BH methodology consisted of combining one iridium complex (e.g., complexes **1**−**3**, Figure 1) as dehydrogenation/

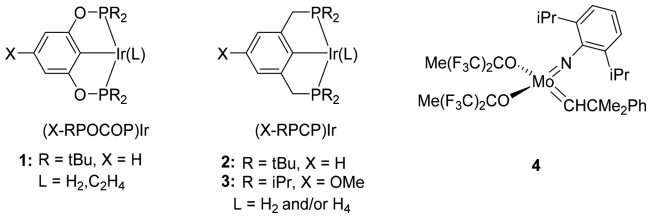


Figure 1. Structure of complexes **1**−**4** designed by Brookhart and Goldman for alkane metathesis reactions. Adapted with permission from ref 26. Copyright 2006 AAAS.

hydrogenation catalyst[25] and the Schroks molybdenium imido olefin catalyst **4**, being reported in 2006 by Goldman et al.[26,27]. The process was able to transform *n*-hexane into a range of C_{12} to C_{15} *n*-alkanes.

In Figure 1, the structure of catalysts **1**−**4** reported by Brookhart and Goldman for performing the dehydrogenation/metathesis/hydrogenation step is shown.

Other bisphosphine- and biphosphinite-based iridium complexes [(tBu_4PCP)Ir and (tBu_4POCOP)Ir] combined with a Mo complex (MoF12) were also able to catalyze transfer hydrogenation and olefin-metathesis reactions under alkane metathesis conditions.[28]

In this context, and in search for an efficient alkane metathesis system, an improved homogeneous dual catalytic system was developed by Schrock et al.[29] In this case, over 40 molybdenum and tungsten catalysts were tested in combination with an Ir-pincer-based complex as dehydrogenation/hydrogenation catalyst. With this dual system, the product yield decreased at temperatures higher than 125 °C surely due to the instability of the catalyst under the experimental conditions, albeit interestingly some of these catalysts could be synthesized in situ.[29]

For example, the catalytic results collected in Table 1[29] were obtained by using the iridium catalyst **1** together with different

Table 1. Concentration of Final Products When Reacting Iridium Catalyst 1 (10 mM) and Diverse Mo and W Alkylidene Complexes (16 mM) at 125 °C in *n*-Octane after 4 Days[a]

entry	catalyst	total product (mM)
1	Mo(NAr)(CHR)(pyr)$_2$	15
2	Mo(NAd)(CHR)(pyr)$_2$	25
3	W(NAr)(CHR)[OCMe(C$_6$F$_5$)$_2$]$_2$	25
4	Mo(NAr)(CHR)[OCMe(C$_6$F$_5$)$_2$]$_2$	33
5	Mo(NAr^{CF3})(CHR)[OCMe(CF$_3$)$_2$]$_2$	41
6	W(NAr)(CHR)(pyr)$_2$	81
7	Mo(NAr)(CHR)(CH$_2$−tBu)$_2$	89
8	W(NAr)(CHR)(CH$_2$−tBu)$_2$	122
9	Mo(NAr^{CF3})(CHR)(pyr)$_2$	130
10	W(NAr)(CHR)(OAr)$_2$	141
11	Mo(NAr)(CHR)(O-1-PhCy)(pyr)	152, 162
12	Mo(NAr)(CHR)(OTBS)$_2$	159
13	Mo(NAr)(CHR)(BIPHEN)	184
14	Mo(NAr)(CHR)[OC(CF$_3$)$_3$]$_2$	242
15	Mo(NAd)(CHR)[OCMe(CF$_3$)$_2$)$_2$	334, 358
16	Mo(NAr)(CHR)(BINAP$_{m\text{-}CF3}$)	359
17	W(NAr″)(CHR)[OCMe(CF$_3$)$_2$]$_2$	419
18	Mo(NAr)(CHR)[OSi(O-tBu)$_3$](pyr)	480
19	Mo(NAr)(CHR)(BINAP-TBS)$_2$	486, 593
20	Mo(NAr)(CHR)[OCMe(CF$_3$)$_2$](pyr)	746, 794
21	Mo(NAr)(CHR)(OAr)$_2$	759
22	Mo(NAr)(CHR)(OCMe$_2$CF$_3$)$_2$	808
23	Mo(NAr)(CHR)(OAr)(pyr)	963, 1120
24	W(NAr)(CHR)(OAr)(pyr)	1040
25	W(NAr)(CHR)(OCMe$_2$CF$_3$)$_2$	1200
26	Mo(NAr)(CHR)[OCMe(CF$_3$)$_2$]$_2$	1430, 1640
27	W(NAr)(CHR)[OC(CF$_3$)$_3$](pyr)	1550
28	W(NAr)(CHR)(BINAP-TBS)$_2$	1580
29	W(NAr)(CHR)[OCMe(CF$_3$)$_2$](pyr)	1670
30	Mo(NAr)(CHR)(OSiPh$_3$)(pyr)	1800
31	W(NAr)(CHR)[OC(CF$_3$)$_3$]$_2$[b]	1890
32	Mo(NAr)(CHR)(OSiPh$_3$)$_2$	1970
33	W(NAr)(CHR)[OCMe(CF$_3$)$_2$]$_2$	2030
34	W(NAr)(C$_3$H$_6$)[OC(CF$_3$)$_3$]$_2$	2210
35	W(NAr′)(CHR)[OCMe(CF$_3$)$_2$]$_2$	2230
36	W(NAr)(CHR)[OC(CF$_3$)$_3$]$_2$[c]	2310
37	W(NAr)(CHR)(OSiPh$_3$)(pyr)	2380
38	W(NAr)(CHR)[OC(CF$_3$)$_3$]$_2$	2760
39	W(NAr)(CHR)(OSiPh$_3$)$_2$	3380
40	W(NAr)(CHR)[OC(CF$_3$)$_3$]$_2$[d]	3015

[a]Reproduced from ref 29. Copyright 2009 American Chemical Society. Legend: CHR═CHCMe$_2$Ph; Ar = 2,6-diisopropylphenyl; Ar′ = 2,6-dimethylphenyl; Ar″ = 2,6-dichlorophenyl; Ar^{CF3} = 2-(trifluoromethyl)phenyl; Ad = 1-adamantyl; pyr = 2,5-dimethylpyrrolide; BIPHEN = 3,3′-di-*tert*-butyl-5,5′,6,6′-tetramethyl-1,1′-biphenyl-2,2′-diolate; BINAP$_{m\text{-}CF3}$ = 3,3′-bis(3,5-bis(trifluoromethyl)phenyl-BINOL; BINAP-TBS = 2′-(*tert*-butyldimethylsilyl)oxy)-1,1′-binaphtyl-2-olate. Repeated run values are given in some instances. [b]Reaction at 175 °C. [c]Reaction at 150 °C. [d]Reaction at 100 °C, maximizing after 14 days.

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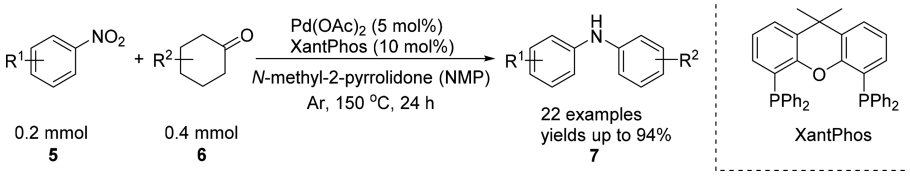
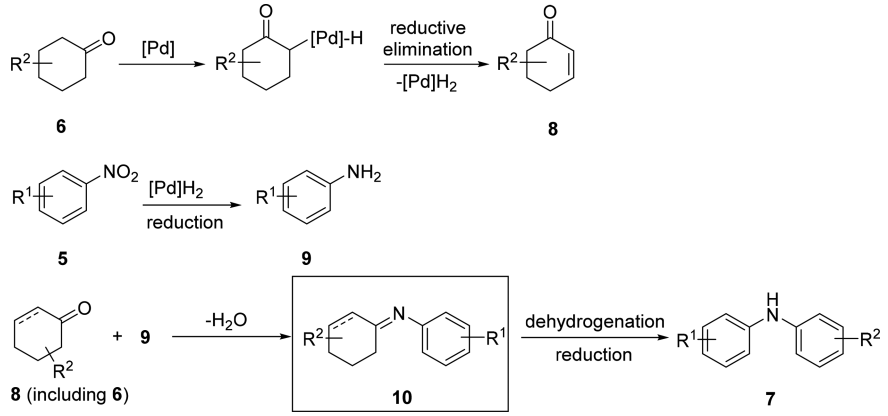
Scheme 3. Diarylamines (7) Formation from Nitroarenes (5) and Cyclohexanone Derivatives (6) on Pd Catalysts Using Borrowing Hydrogen Methods[a]



[a]Reproduced from ref 51. Copyright 2012 American Chemical Society.

Scheme 4. Proposed Reaction Pathway[a]



[a]Reproduced from ref 51. Copyright 2012 American Chemical Society.

molybdenum and tungsten complexes. The *n*-octane metathesis was used as a model reaction, giving a final product concentration that varied from 15 to 3380 mM. The catalytic experiments were carried out by using a 10 mM solution of **1** together with the W or Mo catalyst (16 mM) in *n*-octane as solvent with mesitylene (28 mM) as the internal standard.

Probably one of the most important conclusions that can be drawn from Table 1 is the higher performance of W catalysts among all the catalysts studied. In fact, at least 13 W-based catalysts were identified as the most active ones. As an example, the highest concentration of *n*-octane metathesis product (3380 mM) was obtained with catalyst $W(NAr)(CHR)(OSiPh_3)_2$ (entry 39, Table 1), a catalytic system that contains W and two triphenylsiloxide ligands (one of the most typical auxiliary ligands in this type of chemistry).[29] Such marked differences between these two series of Mo and W complexes can be related to a greater reluctance of tungsten compounds to be reduced (either by rearrangement of different metallacyclobutane intermediates or by decomposition of the respective alkylidene complexes). In fact, there are several examples of tungstacyclobutane complexes but the parent molybdacyclobutanes have only been observed spectroscopically.[30−33]

Another interesting conclusion is that the electrophilicity of the metal will play an important role in catalysis. Indeed as the electro-withdrawing effect of the alkoxide directly bound to W increases from trifluoro- to nonafluoro- *tert*-butoxide, the concentration of the metathesis product also increases (from 1200 to 2760 mM), though this trend is not held for the series of Mo complexes (entries 25, 38; Table 1).

It is interesting to note that similar high oxidation state Mo and W complexes have also been applied in classical olefin metathesis processes (organic synthesis and polymer chemistry), being the W complexes rather less explored in this context than Mo catalysts.[34−36] Another remarkable feature regarding the use of different metals in these processes is the involvement of Ru catalysts just in classical olefin metathesis processes and not in BH methodology.[37−39] This fact is surprising if we take into account that Ru complexes can be a catalyst of choice in those cases where Mo complexes are sensitive to water, molecular oxygen, and certain protic functionalities. In any case, the remaining challenges, both in classical metathesis processes and BH methodology, will include increasing the TON by slowing or preventing the decomposition of the metathesis catalyst.

In this regard, it is interesting to indicate that diverse scandium, yttrium, and lutetium-based complexes for methane metathesis reaction have also been studied.[40] The complexes were formed by ansa-indenyl ligands with different methylation degrees. In this case, the effect of the methylene-bridged ansa ligand on the complex geometries and activation enthalpies was quantified.

Thus, it appears that so far homogeneous catalysts have not given satisfactory turnover numbers when applied in alkane metathesis processes due to various challenges that still remain to be solved. In particular, the activation of methane in order to synthesize longer alkanes in the range of high quality diesel and jet fuel; a fact that with certainty would help to solve current and future energy problems.

2.1.2. Formation of C−N Bonds. Amines are important compounds for the chemical industry as intermediate products in the preparation of dyes, polymers, as well as for the synthesis of new pharmaceuticals, food additives, etc.[41,42] The amine-type functionality is also included in compounds with biological or pharmacological activity (e.g., nucleotides, amino acids, alkaloids, etc.).

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At this point, besides the traditional alkylation methods to get amines,[43] the development of improved catalytic processes for the synthesis of amines is still an active topic of research. For example, during the past decade, various catalytic aminations, such as palladium- and copper-catalyzed aminations of aryl halides,[44,45] hydroaminations,[46,47] hydroaminomethylations,[48] or reductive aminations[49,50] have received increased attention due to the high levels of conversion and yields of the corresponding amines. However, a re-examination of the above processes from an environmental point of view (utilization of hazardous chemicals and solvents) shows that BH processes are definitely superior. Therefore, unsurprisingly, certain industries are now investing and trying to implement this BH strategy for manufacturing amines.

Thus, within the context of forming amines through catalysis by borrowing hydrogen, the activation of C−C bonds (upon dehydrogenation) has been combined with ulterior successive reactions (see reported results below).

2.1.2.1. Condensation (N-Arylation). There is only an example of reaction initiated by alkane activation within the context of BH catalysis affording *N*-arylations which has been included in a recent literature review.[10] Since there has not been further examples on this issue, this reference will be described below so it does not pass unnoticed by the reader.

N-Arylation reactions involve the participation of cyclohexanone derivatives (acting simultaneously as hydrogen donors and aryl sources) with nitroarenes behaving as a source of nitrogen for forming diarylamines (Scheme 3).[51]

Mechanistically, nitroarenes (**5**) are reduced to amines (**9**) using hydrogen generated from an initial cyclohexanone derivative (**6**) dehydrogenation step (Scheme 4).[51]

Then, the resulting cyclic enone (**8**) will react with the aromatic amine **9** through a condensation reaction for forming initially an imine intermediate (**10**) that will be transformed into a diarylamine (**7**) through BH catalysis (Scheme 4).

All the reactions involved (nitro reduction, cyclohexanone dehydrogenation, imine formation, and dehydrogenation) were carried out in a cascade mode, and a variety of groups (alkyl, alkoxy, ester, as well as an acetyl function) were well-tolerated.

To summarize this section, alkane metathesis is one of the most promising reactions involving the activation of C−C bonds due to its enormous potential in transforming both renewable and fossil feedstocks to alkanes (in particular in the range of high quality diesel and jet fuel). However, despite great progress in the area of alkane metathesis there are still problems to overcome. Among them, the dehydrogenation catalysts which give acceptable rates only at temperatures at which the alkylidene-based olefin-metathesis catalysts tend to decompose. Thus, there is a real need to develop olefin metathesis catalysts that are more robust at higher temperatures, together with more regioselective dehydrogenation catalysts able to operate at moderated temperatures.

In general, processes in which alkanes are activated should be exploited not only for forming carbon−carbon bonds but also for forming carbon-heteroatom bonds. This will result in new and unexpected reaction pathways that will contribute to the expansion of the number of transformations in the context of hydrogen autotransfer processes. At the moment, this possibility has hardly been explored.

2.2. Activation of Alcohols

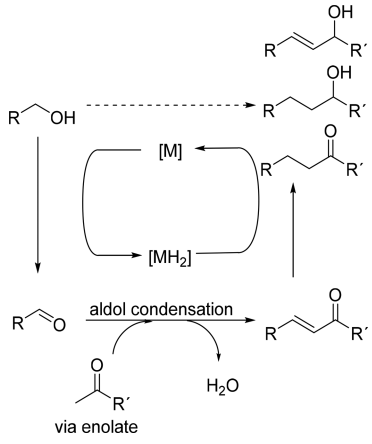
The reactivity of alcohols expands enormously when we consider their activation. For instance, the addition of a base will afford nucleophilic alkoxides, albeit the incorporation of an acid will give rise to electrophilic species.[52,53] Nonetheless, alcohols are generally poor electrophiles for alkylation reactions, requiring activation of the hydroxyl group into a suitable leaving group in order to facilitate the nucleophilic substitution.[54] A different approach to activate alcohols involves the removal of hydrogen from the alcohol to form an aldehyde, something that is usually carried out by dehydrogenation reactions in hydrogen autotransfer processes. In this case, the temporary transformation of alcohols into aldehydes or ketones has been exploited, for instance, for forming alkenes or imines (or enamines) followed by subsequent reduction to a C−C or a C−N bond.[10,11,14,16,19,55−57]

The activation of alcohols in hydrogen autotransfer has also been extensively studied in recent years in the form of a varied combination of BH reactions. In this sense, few references are out of specific bibliography reviews that have appeared on the subject in the last years. Nevertheless, we will try to illustrate this section with examples that have not been cited in previous specific revisions (either for forming C−C or C−N bonds), but when this is not possible, we will describe just significant examples ensuring that this Review does not lose its main structure.

2.2.1. Formation of C−C Bonds. There are numerous examples in which carbonyl compounds formed originally from an alcohol are involved in ulterior C−C forming reactions by virtue of borrowing hydrogen methods to give the corresponding alkenes. Then the resulting olefins will be hydrogenated in situ to afford saturated alkanes through a net alkylation process.[11,17,18]

2.2.1.1. Aldol Condensation. Aldol condensation is a well-known reaction in classic organic synthesis when it comes to the formation of C−C bonds by reacting aldehydes and/or ketones. In this respect, two different mechanisms have traditionally been established depending on the acid or basic nature of the catalyst.[58,59] At this point, it is possible to integrate this reaction within the BH strategy allowing access to more complex structures starting from simple alcohols. In this case, the hydroxylic compound would dehydrogenate into the corresponding aldehyde or ketone hence initiating the global reaction (Scheme 5). Once the corresponding carbonyl compound is formed, the aldol condensation takes place yielding the corresponding α,β-unsaturated compound through

Scheme 5. Schematic Representation of the BH Methodology Involving an Aldol Condensation as the Intermediate Reaction



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an enol or enolate intermediate. Finally, metal hydrides formed in the first step would reduce the unsaturated compound to the corresponding alcohol (Scheme 5).

Given that either one or both reactants can be alcohols, different combinations based on the nature of the starting reactants can be distinguished a priori in order to address a variety of BH reactions (Figure 2).

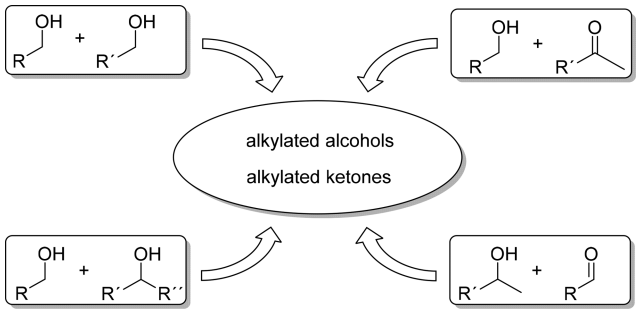


Figure 2. Schematic representation of the different approaches for the indirect aldol condensation through the BH strategy.

Briefly, three different reaction routes can take place in hydrogen autotransfer processes involving the aldolic reaction depending on the starting reagent (Figure 2): (a) α-alkylation of carbonyl compounds with alcohols, (b) β-alkylation of secondary alcohols to give β-alkylated alcohols or β−alkylated ketones, and (c) β-alkylation of primary alcohols with primary alcohols to yield β-alkylated alcohols.

These possibilities have been addressed in relatively recent studies and a collection of representative catalysts which were successfully applied in these C−C forming reactions have been included in diverse reviews.[11,16−18] Among them, the use of ruthenium and iridium complexes must be highlighted. For example, ruthenium-based complexes have been widely applied for the α-alkylation of ketones[60−64] or amides[65] with primary alcohols (Figure 2). Similarly, iridium complexes have attracted much attention in α-alkylations starting from ketones[66−71] and esters.[72,73]

In this context, one interesting contribution which appeared recently, introduced the possibility of performing an intensive process consisting of combining the BH-aldol condensation with another different reaction. Basically, α-alkylation of ketones (**14**) could be integrated together with the hydration reaction of alkynes within the context of BH methodology as depicted in Scheme 6.[74]

In this case, in the presence of (iPr)AuCl (**15**), silver triflate (AgOTf), and water, a series of alkynes (**11**) were first hydrated to give the corresponding methyl ketones (**12**), which in turn were α-alkylated by adding the iridium complex $[Cp^*IrCl_2]_2$ (**16**), KOtBu, and alcohols to the reaction mixture.[74] This reaction is highly attractive due to the availability of starting materials, the undeniable atom efficiency, the good to outstanding yields, and the low consumption of chemicals and energy.

Rhodium catalysts, though they are less frequently applied in borrowing hydrogen methods than ruthenium or iridium, have also catalyzed the α-alkylation of ketones (**13**) using methanol as well as other primary alcohols as methylating agents.[75,76]

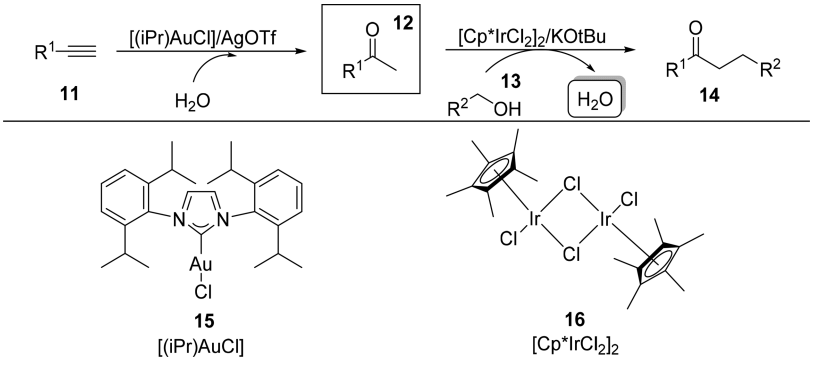
The same statement is applied to iron, which is considered as a valuable alternative to the use of precious transition metals in terms of sustainability and economy. For this reason, in the past decade the use of iron catalysts have increasingly been applied in C−C bond forming reactions. An interesting example within the context of BH strategies has been reported on iron-catalyzed α-alkylation of ketones with primary alcohols in the presence of a Knölberg-type iron complex (**19**) (Scheme 7).[77]

Knölberg-type complexes are stable precursors that have been successfully used in hydrogenations and hydrogen transfer reactions as well as for selective oxidations of alcohols.[14] In this case, the iron complex catalyzed the α-alkylation of ketones in the presence of catalytic amounts a base. Furthermore, an optimized system (**22**/PPh_3) catalyzed the Friedlander annulation reaction starting from an amino benzyl alcohol derivative (**13b**) and a ketone (**20**) to give quinolones (**21**) (Scheme 8).[77]

In general the low stability of the 2-aminobenzaldehyde compound is one of the challenges of this reaction. But under BH conditions the use of the more stable 2-aminobenzyl alcohol (**13b**) in the presence of catalytic amounts of tBuOK resulted in a truly advantageous alternative to carry out this reaction.

Other alternatives concerning the use of alcohols as starting reagents in BH processes involve the use of primary and secondary alcohols to yield the corresponding β-alkylated products (Figure 2). As in the previous case, ruthenium and iridium catalysts have been again extensively applied in these BH processes.[78−86] For example, a ruthenium compound containing a triazoledicarbene ligand was prepared and characterized as a tetraruthenium species **25** showing an

Scheme 6. Strategy for the Synthesis of α-Alkylated Ketones (14) Starting from Alkynes (11) and Alcohols (12)[a]



[a]Adapted with permission from ref 74. Copyright 2014 Wiley-VCH.

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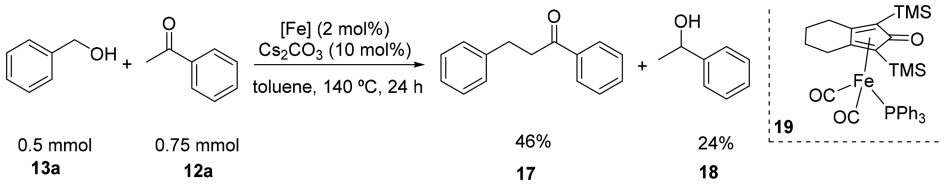
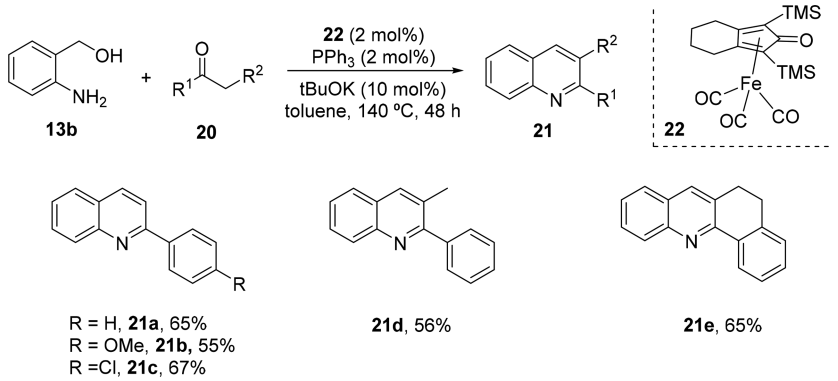
Chem. Rev. 2018, 118, 1410−1459

Scheme 7. α-Alkylation of Acetophenone with Benzyl Alcohol Catalyzed by a Knölberg Iron Complex (19)[a]



[a]Adapted with permission from ref 77. Copyright 2015 Wiley-VCH.

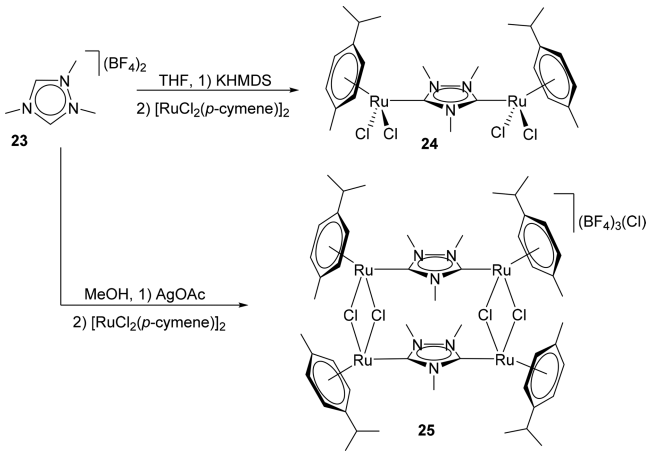
Scheme 8. Example of Friedlander Annulation Reaction Using Catalytic Amounts of tBuOK and the Iron Complex 22[a]



[a]Adapted with permission from ref 77. Copyright 2015 Wiley-VCH.

excellent catalytic activity in the β-alkylation of secondary alcohols with primary alcohols (Scheme 9).[78]

Scheme 9. Schematic Preparation of Dinuclear (24) and Tetranuclear Ruthenium Complexes (25) Coordinated to Triazolediylidene Ligands[a]



[a]Reproduced from ref 78. Copyright 2007 American Chemical Society.

In principle, the triazolediylidene ligand had been previously employed in the synthesis of dinuclear homoheterometallic species of Rh and Ir,[87] where it was shown that the connection of two catalytically active metal fragments provided a synergistic effect that accounted for a high catalytic performance. On this basis, the corresponding ruthenium analogues were prepared being applied in the β-alkylation of secondary alcohols with primary alcohols in a one-pot process under BH conditions (Scheme 10).[78]

It is important to emphasize that both complexes were active regardless of whether the alcohols were aliphatic or aromatic.

A second recent example on Ru(III) catalyzed β-alkylation of secondary alcohols with primary alcohols was reported by Wang et al. In this case, the catalyst was prepared by mixing $RuCl_3$ and the ligand **28** in refluxing ethanol to give the catalyst **29** (Scheme 11).[85]

The complex was characterized by HRMS, elemental analysis, and IR. Indeed the HRMS analysis showed a peak assigned to the fragment ($[M - Cl]^+$), whereas the IR spectrum showed a stretching vibration that shifted from 1580 cm^{-1} from the original ligand to 1609 cm^{-1} due to the coordination effect with the metal cation. The complex was active in a wide variety of examples going from primary to secondary alcohols. Scheme 12[85] shows selected examples obtained with this catalytic system to show the generality of the reaction.

A different representative example for the β-alkylation involved the participation of two different Ru complexes (Figure 2). In this context, Beller et al. reported the successful combination of two ruthenium catalysts [Ru-MACHO (**30**) and Shvo's catalyst (**31**)] for the selective cross-coupling of methanol and 2-arylethanols (Figure 3).[88]

The key point to this contribution was the access to products that alternatively have to be prepared by hydroformylation-reduction sequences (Scheme 13).[88]

Besides this, other obvious advantages to the present straightforward approach are the avoidance of toxic CO and extra hydrogen, as well as the need for high pressure equipment. Mechanistically, the combination of these two different ruthenium catalysts accounted for the occurrence of two different dehydrogenation reactions, a selective aldol reaction, subsequent dehydration, and a final hydrogenation step (Scheme 13).

The use of iridium complexes has also been a recurrent issue in β-alkylations of alcohols under BH catalysis. For example, recent approaches[89−91] for forming functionalized ketones have

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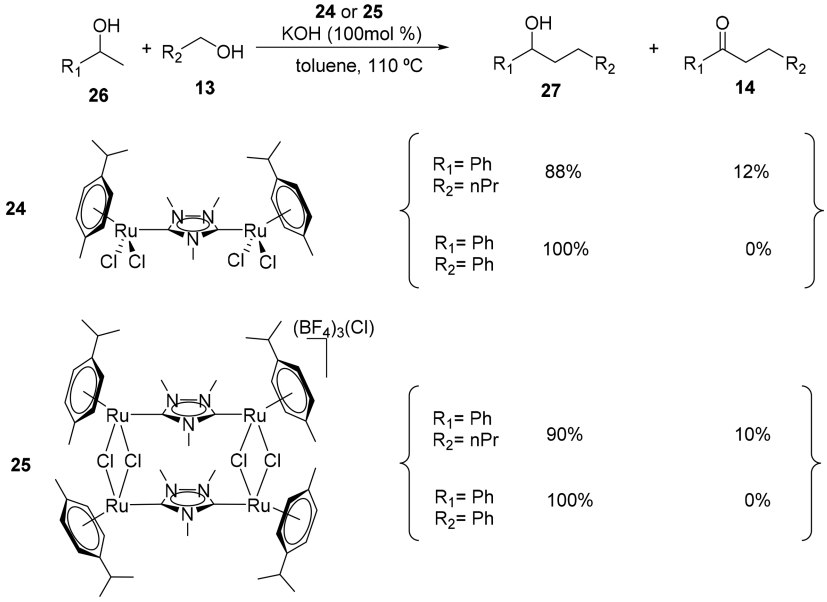
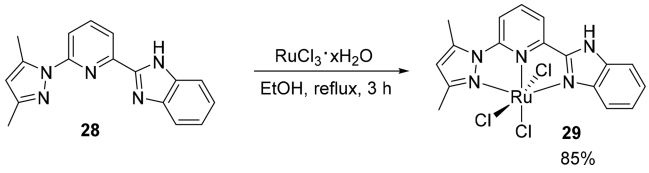
Chem. Rev. 2018, 118, 1410−1459

Scheme 10. β-Alkylation of Secondary Alcohols with Primary Alcohols Catalyzed by Dinuclear and Tetranuclear Ruthenium Complexes 24 and 25[a]



[a]Reproduced from ref 78. Copyright 2007 American Chemical Society.

Scheme 11. Schematic Preparation of Ru(III) Complex 29 Obtained by Wang[a]



[a]Reproduced from ref 85. Copyright 2016 American Chemical Society.

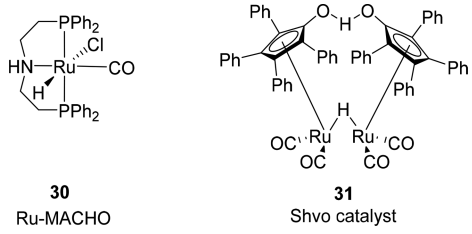
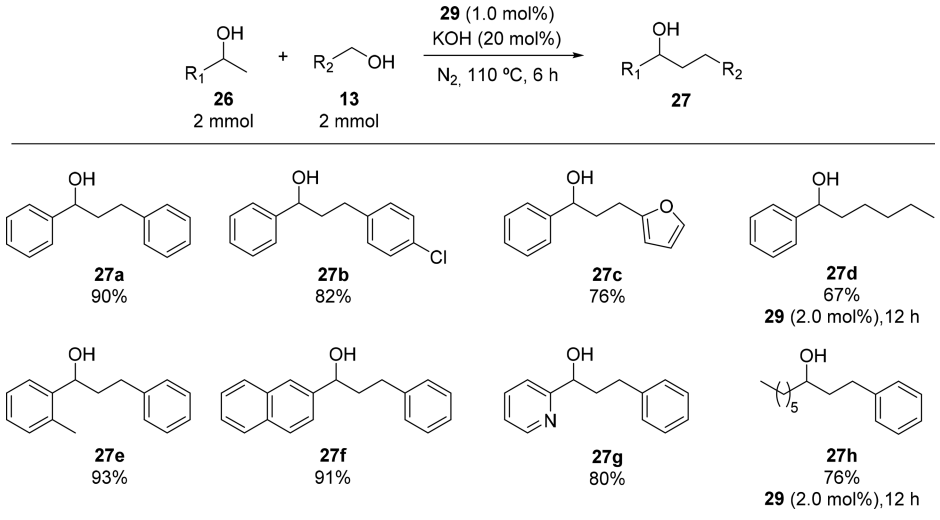


Figure 3. Structure of ruthenium catalysts Ru-MACHO **30** and Shvo's catalyst **31**. Adapted with permission from ref 88. Copyright 2014 Royal Society of Chemistry.

been described through the cross-coupling of primary and secondary alcohols with neutral (**32**–**35**) and cationic iridium (**36**–**39**) catalysts (Scheme 14).[91]

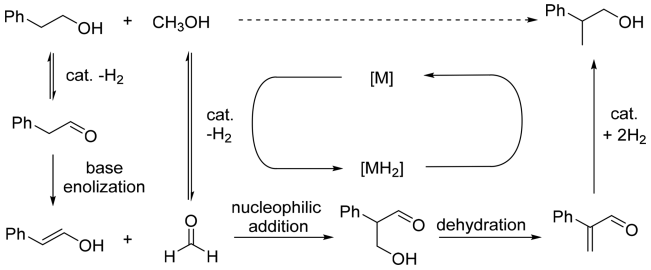
In this particular case, the iridium(I) complexes containing hemilabile O- and N-donor-functionalized ligands were synthesized by means of deprotonation of functionalized

Scheme 12. Scope of primary and secondary alcohols obtained with Ru(III) complex 29. Reproduced from ref 85. Copyright 2016 American Chemical Society



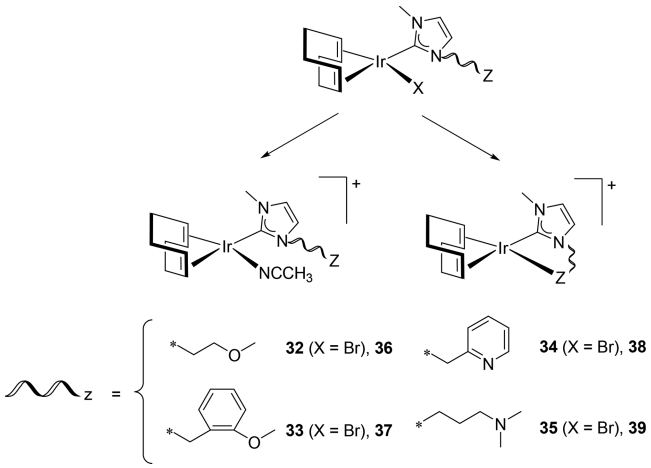
DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410–1459

Scheme 13. Plausible Reaction Scheme for the β-Alkylation Involving Two Primary Alcohols[a]



[a]Adapted with permission from ref 88. Copyright 2014 Royal Society of Chemistry.

Scheme 14. Examples of Cationic and Neutral Iridium(I) Complexes (36−39 and 32−35 Compounds, Respectively) with Functionalized NHC Ligands[a]



[a]Adapted with permission from ref 91. Copyright 2015 Wiley-VCH.

imidazolium salts. The catalysts were successfully applied in the β-alkylation reaction of 1-phenylethanol with benzyl alcohol as a model reaction. Besides, the catalysts yielded a mixture of β-alkylated alcohols and α-alkylated ketones starting from different alcohols. Some selected examples are given in Table 2.[91]

Finally, it is important to highlight the case of an iridium-based complex which was successfully applied for the formation of α,ω-diarylalkanes from primary alcohols by combining a Guerbet reaction (β-alkylation of alcohols) with other transformations (Scheme 15).[92]

In this case, the alkylated alcohol initially formed experienced a clean route to α,ω-diarylalkanes through a successive dehydrogenation/deoxidative addition (to the Ir catalyst), followed by CO extrusion with β-hydrogen elimination as well as a final reduction step of the intermediate compound **28**, as depicted in the Scheme 15.[92]

Palladium has also been used as a catalyst in cross-coupling reactions of primary and both secondary and primary alcohols to give β-alkylated alcohols as described by different groups.[93,94] As an example, in the presence of a pincer-type NHC/PdBr complex, the reaction (under either Ar or H_2 gas) showed a broad substrate scope as well as a high alcohol product selectivity.[93]

Other uncommon metals that have been reported to be catalytically active for this reaction are for instance $Cu(OAc)_2 \cdot H_2O$, which has also been used as a catalyst for forming new branched alcohols starting from primary and secondary alcohols,[95] albeit with a controversial reaction mechanism. The reference which has been included in a specific review on C-alkylation of ketones through BH methodology[11] brings with it reasonable doubt which arises due to the acceleration of the reaction under air atmosphere. In this respect, the authors point to a plausible transfer hydrogenation via a six-membered cyclic Meerwein-Pondorf-Verley type transition state instead of a BH strategy, although none of the two mechanisms can be discarded. The following figure shows the proposed reaction scheme for the Cu-catalyzed aerobic C-alkylation reaction (Scheme 16).[95]

In this case, the alcohol activation has been accomplished with ligand-free copper catalysts. These catalysts were superior than other metals in forming new C−C bonds in the form of secondary alcohols and ketones.

2.2.1.2. Knoevenagel Reaction. The modified aldol reaction known as the Knoevenagel reaction has also been used for monoalkylating C−H acid methylene compounds in combination with BH (Scheme 17). In the Knoevenagel reaction, a nucleophilic attack of an active carbanion takes place on a carbonyl group and then a dehydration reaction occurs (hence condensation) giving an α or β conjugated enone.

Grigg and co-workers described one of the first homogeneous transition metal catalyzed alkylations using the Knoevenagel reaction.[96] In this case, an in situ prepared rhodium catalyst ($RhCl_3$ and PPh_3) catalyzed the transformation of a series of arylacetonitrile derivatives into monoalkylated arylacetonitriles, the latter being applied as intermediate products for the synthesis of acids, amides, and heterocycles as well as biological active substrates.

Curiously, aromatic acetonitriles and primary alcohols were reacted in the presence of a rhodium complex in combination with triphenylphosphine and KOH for the synthesis of α-arylacetamides under microwave-assisted conditions.[97]

Nonetheless, as in previous sections, Ru and Ir-based complexes have shown again much higher reactivity for this reaction as compared to the in situ prepared rhodium catalyst above-mentioned.[96] Indeed, the Grigg's group reported a practical alkylation reaction of nitriles catalyzed by an iridium catalyst through an indirect Knoevenagel reaction using in some cases microwave activation.[98] In this case, a wide range of nitriles and alcohols, including indole and pyridine derivatives, could be selectively converted into the desired products in very high yields. For example, the alcohol derivative and 3-pyridylacetonitrile were reacted to yield the corresponding monoalkylated nitrile with a striking shortening of reaction time (from 17 h to 10 min) when the reaction was assisted by microwave (MW) radiation.

The same catalyst, as well as related iridium complexes, were applied for the alkylation of 1,3-dimethylbarbituric acid (highly important molecule in the synthesis of pharmaceuticals) and alkyl cyanoester derivatives.[99−102] For example, the microwave assisted indirect monoalkylation of 1,3-dimethylbarbituric acid (**40**) with alcohols was carried out in the presence of a bimetallic Ir(III)/Pd(0) catalyst to give the corresponding monoalkylated products (**41**) and by extension the spirocyclic barbiturates (**42**) in one-pot (Scheme 18).[99]

The use of both transition metal elements was compatible. In this approach, Ir(III) catalyzed the monoalkylation reaction at the 5 position of the dimethyl barbituric acid derivative using benzyl and aliphatic alcohols. In a particular case, the oxidative

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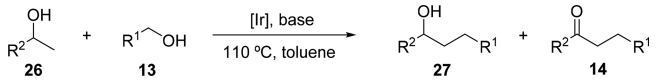
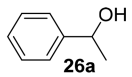
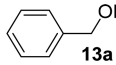
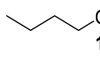
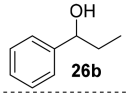
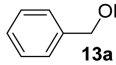
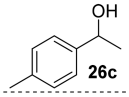
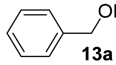
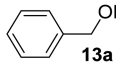
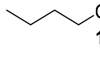
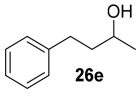
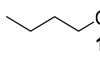
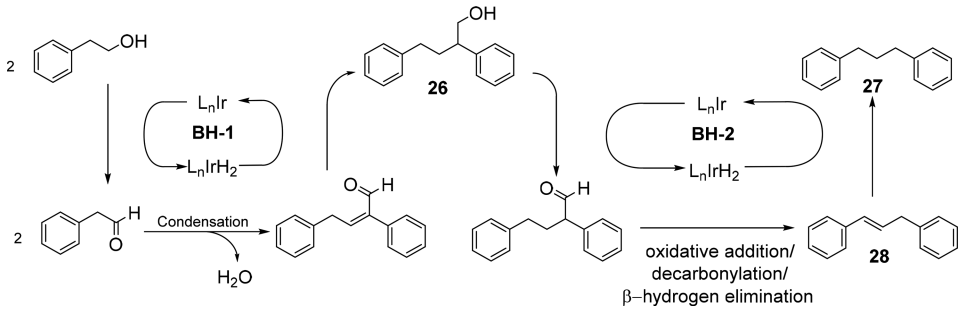
Table 2. β-Alkylation of Secondary Alcohols with Primary Alcohols Catalyzed by Iridium(I) Complexes 33 and 37 Having an NHC Ligand with a 2-Methoxybenzyl Substituent[a,b]



1			**33**[c]	9	97	99:1 (81%)[d]
2			**37**	7	93	86:14
3			**33**[c]	11	92	98:2 (78%)[d]
4			**37**	10	92	64:36
5			**33**	12	89	65:35
6			**33**	12	99	99:1 (83%)[d]
7			**33**	10	94	62:38
8			**37**	9	92	66:34
9			**37**	10	92	54:46
10			**37**[c]	10	94	99:1 (69%)[d]
11			**37**[c]	18	92	98:2 (85%)[d]

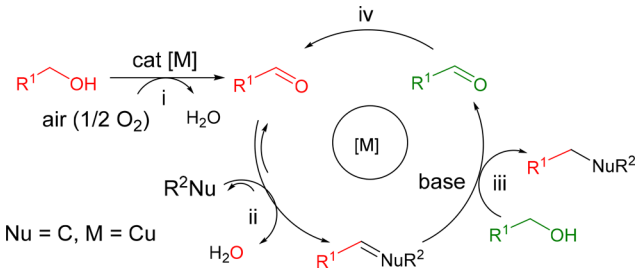
[a]Adapted with permission from ref 91. Copyright 2015 Wiley-VCH. Reaction conditions: catalyst (0.003 mmol, 1 mol %), catalyst/secondary alcohol/Cs_2CO_3 ratio 1:100:100 and primary alcohols (3.6 mmol), in toluene (0.3 mL) at 110 °C for 3 h. [b]Determined by GC analysis based on the secondary alcohol by using mesitylene as internal standard. [c]Catalyst/base ratio of 1:150. [d]Yield of the isolated β-alkylated alcohol product **27**.

Scheme 15. Plausible Reaction Pathway for the Formation of 1,3-Diphenylpropane 27 Starting from Phenethyl Alcohol[a]



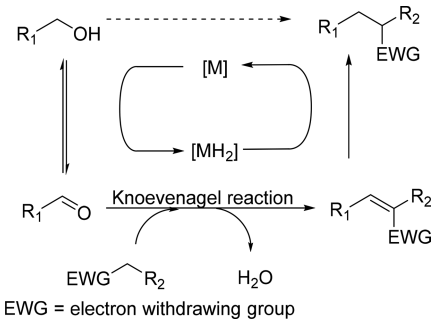
[a]Adapted with permission from ref 92. Copyright 2011 Wiley-VCH.

Scheme 16. Proposed Reaction Scheme or the Cu-Catalyzed C-Alkylation of Alcohols with Alcohols[a]



[a]Reproduced with permission from ref 95. Copyright 2012 Royal Society of Chemistry.

Scheme 17. Hydrogen Autotransfer Combined with Knoevenagel Reaction



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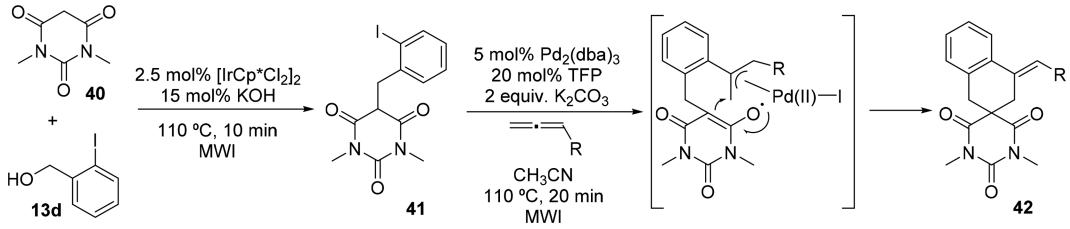
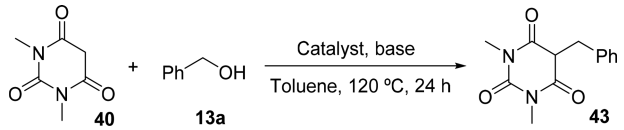
Chem. Rev. 2018, 118, 1410−1459

Scheme 18. Microwave Assisted One-Pot Synthesis of Monoalkylated 1,3-Dimethylbarbituric Acid 41 Followed By Spirocyclization to Give Compound 42 in the Presence of a Dual Ir(III)/Pd(0) Catalytic System[a]



[a]Reproduced with permission from ref 99. Copyright 2006 Royal Society of Chemistry.

Table 3. Optimization of Reaction Conditions[a]



entry	catalyst (mol % metal)	base (mol %)	**13a** (eq)	yield (%)[b]	TOF (h^{-1})[c]
1	$[Cp^*IrCl_2]_2$ (1)	KOH (20)	2	78	25
2	$Pd(OAc)_2$ (1)	KOH (20)	2	68	32
3	Pd/C (1)	KOH (20)	2	77	22
4	$[RuCl_2(p\text{-cymene})_2]_2$ (1)	KOH (20)	2	26	–
5	$[RuCl_2(p\text{-cymene})_2]_2$/2dppf (1)	KOH (20)	2	88	37
6	$RuCl_2(p\text{-cymene})_2$	KOH (20)	2	84	51
7	$RuCl_2(PPh_3)_3$ (1)	KOH (20)	2	96	53
8	$RuCl_2(PPh_3)_3$ (1)	K_2CO_3 (20)	2	98	–
9	$RuCl_2(PPh_3)_3$ (0.5)	K_2CO_3 (20)	2	42	–
10	$RuCl_2(PPh_3)_3$ (1)	K_2CO_3 (5)	2	99	–
11	$RuCl_2(PPh_3)_3$ (1)	–	2	30	–
12	$RuCl_2(PPh_3)_3$ (1)	K_2CO_3 (5)	1.2	99	–
13[d]	$RuCl_2(PPh_3)_3$ (1)	K_2CO_3 (5)	1.2	95	–

[a]Reproduced with permission from ref 104. Copyright 2017 Elsevier. Reaction conditions: mixture of **1a** (1 mmol), **13a** (1.2 or 2 equiv), catalyst (1 mol % metal), and base were heated at 120 °C in toluene for 24 h. [b]Determined by ^1H NMR. [c]Determined at initial conversion points after 30 min. [d]For 8 h.

addition of Pd(0) to one aryl iodide derivative followed by allene insertion would generate a π-allyl Pd(II) complex. This species would undergo a regio and setereoselective intramolecular nucleophilic attack of the C_5 barbiturate carbanion at the least hindered sp_2-carbon giving the E-alkene (Scheme 18).[99]

The importance of this approach relies in the fact that there is not a straightforward synthetic procedure for the synthesis of 5-monoalkylated barbituric acid derivatives. Therefore, for forming such important intermediates the direct alkylation with alcohols by means of BH strategies is an attractive alternative.

Other iridium-catalyzed C-alkylations using alcohols and nitroalkanes (nitroaldole reaction), as well as 1,3-diketones, ketonitriles, and malonates[103] should be highlighted.

With respect to ruthenium catalysts, it is important to indicate that $[RuH_2(PPh_3)_3(CO)]$/Xantphos catalyzed the C-alkylation of ketonitriles with benzylic alcohols with much lower metal loading (0.5 mol %) and giving the alkylated products in high yields, whereas the catalyst $RuCl_2(PPh_3)_3$[104] successfully monoalkylated barbituric acid.

In this particular case, 1,3-dimethylbarbituric acid **40** was monoalkylated with benzyl alcohols and heteroaromatic alcohols giving from good-to-excellent yields of the corresponding alkylated barbituric derivatives (**43**) in the presence of diverse ruthenium complexes and catalytic amounts of a base (Table 3).[104]

The catalytic system was also active using aliphatic alcohols, whereas different substituents on the nitrogen atom of the molecule were well-tolerated. This ruthenium-based catalytic system was applied to the synthesis of acid-fused benzopyrane derivatives **45** through the alkylation of barbituric derivative **40** with salicylic alcohols (**44a–44c**) followed by treatment with a strong Brönsted acid in one-pot (Scheme 19).[104]

It is interesting to note that the synthesis of γ-butyrolactone derivatives (**48**) has also been recently reported to take place using the BH strategy though integrated in an intensive sequential-type approach. This strategy combined a Knoevenagel reaction with an intramolecular cyclization, by reacting malonate derivatives (**47**) and 1,2-diols (**46**) in the presence of a Ru complex as catalyst as depicted in the scheme (Scheme 20).[105]

Besides the traditional ruthenium and iridium complexes, other uncommon transition elements such as cobalt and osmium have been exceptionally applied in this type of reaction.[106,107] For example, it is necessary to highlight the alkylation (**50a–l**) of amides (**49**) and esters with alcohols (**13**) through BH methods by using the Knoevenagel reaction as intermediate reaction and cobalt complexes stabilized with pincer ligands (**51**). One of the most interesting features of this approach is that the Co(II) complex can be prepared on a

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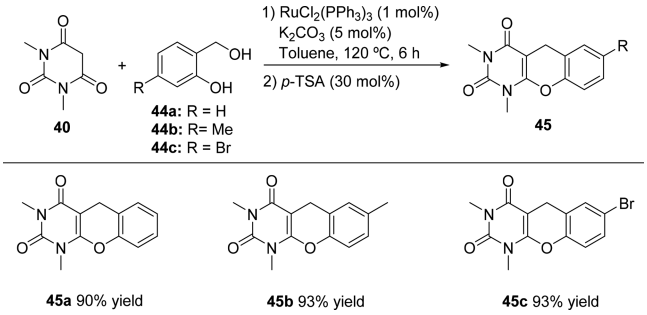
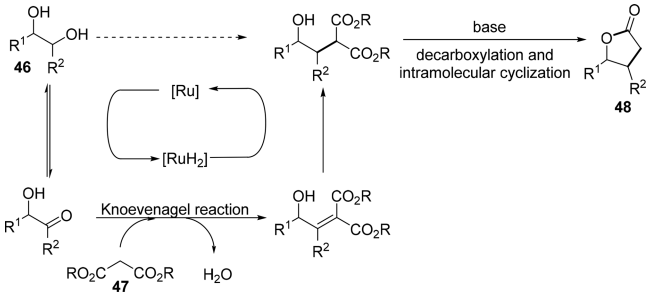
Scheme 19. Examples of One-Pot Synthesis of Fused-Benzopyrans 45a–45c Starting from 1,3-Dimethylbarbituric Acid (40) and Salicylic Alcohol Derivatives 44a–44c[a]



[a]Adapted with permission from ref 104. Copyright 2017 Elsevier.

Scheme 20. Schematic Transformation Involved during the Synthesis of Lactone Derivatives[a]



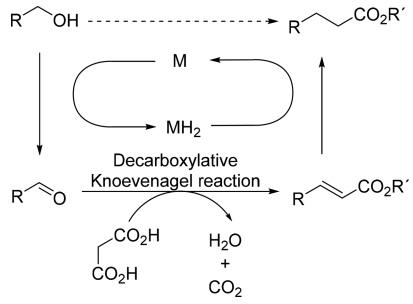
[a]Adapted with permission from ref 105. Copyright 2015 Royal Society of Chemistry.

multigram scale and can be activated under basic conditions (Scheme 21).[106]

In order to finalize this section we will refer to arylacetonitriles[107] that were also recently alkylated with primary alcohols (**13**) in the presence of an uncommon osmium catalyst, being included in a previous specific review on BH catalysis.

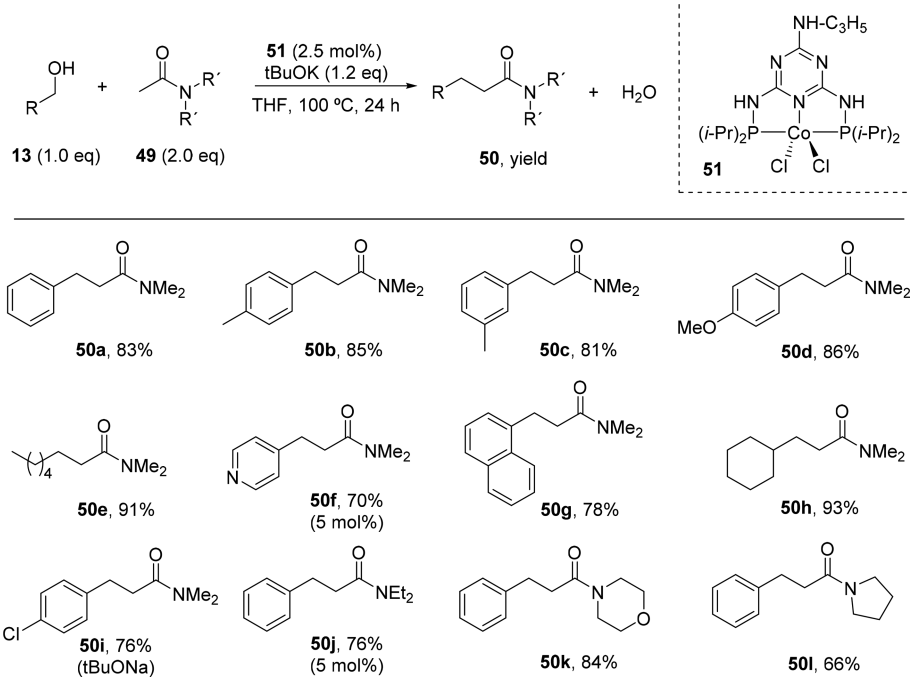
2.2.1.3. Decarboxylative Knoevenagel Reaction. Another interesting route involving the use of malonate half esters for alkylation reactions has also been considered according to the pathway outlined in Scheme 22.[108]

Scheme 22. Hydrogen Autotransfer Combined with a Decarboxylative Knoevenagel Reaction



In this work the temporary removal of hydrogen from the alcohol generates an aldehyde that undergoes a decarboxylative Knoevenagel reaction with malonate half ester giving the α,β-unsaturated ester. Finally, a last hydrogenation step yields the desired ester. The decarboxylative Knoevenagel reaction of aldehydes is a well-known process, which is usually catalyzed by a suitable amine.[109] Indeed, in one of the pioneering works pyrrolidine was chosen as the organocatalyst on its ability to carry out the decarboxylative Knoevenagel process,[109] in the presence of a $Ru(PPh_3)_3Cl_2$ catalyst. Since the only byproducts formed in this case were water and carbon dioxide, this process

Scheme 21. Product Scope for Amide Alkylation with Cobalt Complex 51[a]



[a]Reproduced from ref 106. Copyright 2016 American Chemical Society.

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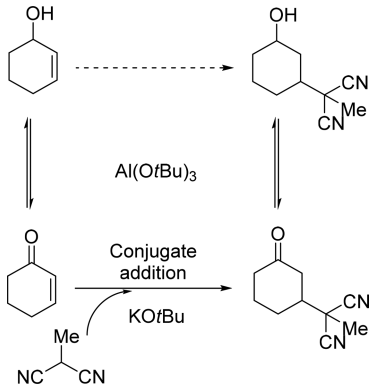
provides a useful alternative to the Wittig reaction for the conversion of aldehydes into α,β-unsaturated esters.[110]

2.2.1.4. Conjugate Addition. Only one example of conjugate addition as intermediate reaction in BH strategies has been found in literature, being a reference treated in previous reviews. Given that no more examples have been published to date, we will then describe this example to illustrate the importance of such intermediate reaction in the context of BH processes.

This study consists of an indirect nucleophilic addition of methylmalonitrile and benzylmalonitrile to different cycloalkenols to give the corresponding addition products.[111] The plausible reaction pathway when the allylic alcohol cyclohexen-1-ol was put in contact with methylmalonitrile is depicted in the following scheme (Scheme 23):[111]

Scheme 23. Catalytic Activation of Cyclohexen-1-ol Allows the Conjugate Addition and Subsequent Reduction[a]



[a]Adapted with permission from ref 111. Copyright 2001 Wiley-VCH.

The utility of this strategy relies on the fact that the catalytic electronic activation of the substrate makes possible the addition of the nucleophile to an allylic alcohol contrary to what could be expected.

2.2.1.5. C_3-Alkylation. Some years ago, Grigg and coworkers reported the synthesis of alkylated indoles using alcohols as hydrogen donors,[112] and more recently pyrrole and indole (**52**) molecules were alkylated with methanol using the same iridium complex as catalyst affording the corresponding methylated derivatives in high yields (**53**) (Scheme 24).[113]

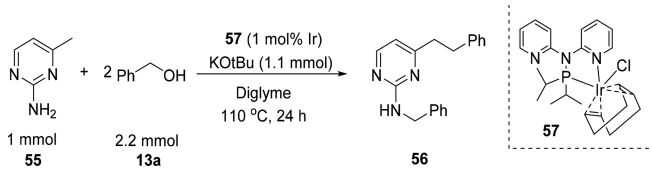
The scope or generality of the alkylation of indoles was studied under optimized conditions, and the results showed that indole derivatives with electron-donating or electron-withdrawing groups on the phenyl ring took place smoothly. Moreover, the halide substituents (fluoro-, chloro-, and bromo-indole derivatives) were well-tolerated under the experimental conditions, giving the corresponding alkylated indoles in good yields. Curiously, the nitro group at the indolic ring was easily reduced in the presence of methanol and the same iridium catalyst. The cyano indole derivative was alkylated to give the corresponding alkylated cyano indole derivative. Consistent with previous observations *N*-methylindole failed to afford methylation. This observation points to an anion intermediate as the key compound involved in the reaction mechanism.

The detection of bisindolylmethane (**54**) as secondary product formed through the Michael addition of indole **52** to the intermediate product **53** gives strong support to this reaction route.

Other examples refer to interesting applications with different Ir catalysts. These studies describe the synthesis of a series of monoamine alkaloids derived from tryptamine through the C_3-alkylation of indole, as well as the C_3-alkylation of oxindole (2-indolone).[114] In this last case, the reaction could be carried out under neat conditions under thermal or even microwave conditions.[114−116]

There is another particular case with iridium-based complexes, which slightly deviates from the general established reaction scheme and describes the C-alkylation of *N*-heteroaromatics.[117,118] This study describes the *C*- and *N*-alkylation of pyrimidinyl amine derivative **55** using simple alcohols (**13a**) in the presence of an iridium complex (**57**) (Scheme 25).[117]

Scheme 25. Observed C- and *N*-Alkylation of a Pyrimidinyl Amine Derivative 55 with Benzyl Alcohol 13a[a]



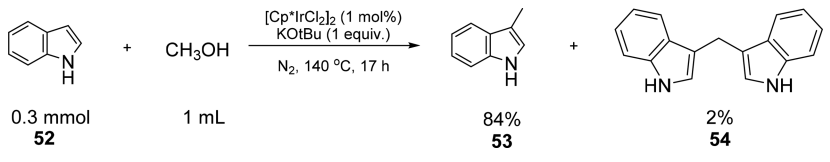
[a]Reproduced from ref 117. Copyright 2010 American Chemical Society.

In this case, the dehydrogenation of the alcohol and subsequent reaction of the resulting aldehyde with a heteroaromatic substrate (beforehand deprotonated by stoichiometric amounts of a strong base) led to the aldol product. The latter rapidly eliminated water at elevated temperatures giving an olefinic substrate onto which the borrowed hydrogen equivalents were incorporated to yield the final alkylated product (**56**).

As expected, this catalytic reaction has also been examined with ruthenium complexes, in particular, new (arene)-ruthenium(II) complexes featuring phosphinosulfonate ligands. These complexes catalyzed the alkylation of cyclic amines with alcohols using camphor sulfonic acid as an additive.[119]

2.2.1.6. Wittig Reaction. Ketones and aldehydes can also be involved in Wittig reactions to afford new carbon−carbon double bonds. Hence, by means of the BH strategy, hydroxyl groups can be transformed into aldehydes, which can undergo

Scheme 24. Iridium-Catalyzed Methylation of Indole (52) with Methanol[a]



[a]Adapted with permission from ref 113. Copyright 2015 Royal Society of Chemistry.

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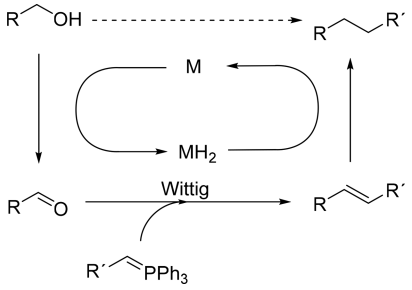
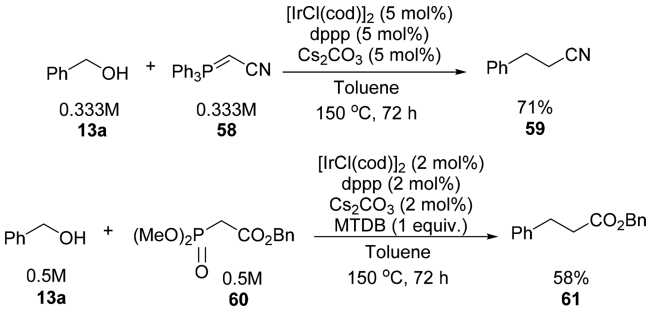
Wittig type reactions to give new alkenes (Scheme 26). Then, the metal hydride will hydrogenate the double bond giving the corresponding saturated compound.

Scheme 26. Indirect Wittig Reaction Using Alcohols



In this sense, Williams et al. reported a set of indirect Wittig type reactions, such as the iridium-catalyzed indirect Horner-Wadsworth-Emmons reaction of benzyl alcohol (**13a**) with phosphonates (**60**)[120] or Wittig reactions with cyano ylides (**58**)[121] to get the corresponding dihydrocinnamate (**59**) and propionitrile derivatives (**61**) (Scheme 27). Both references

Scheme 27. Examples of Indirect Wittig As Well As Horner-Wadsworth-Emmons Reaction Using Benzyl Alcohol 13a[a]



[a]Adapted with permission from ref 120. Copyright 2002 Wiley-VCH. Adapted with permission from ref 121. Copyright 2006 Wiley-VCH.

were cited in specific reviews, but given that no further examples have been reported since then, these two examples will be described below in order not to lose the perspective of the variety of intermediate reactions that can take part in BH processes.

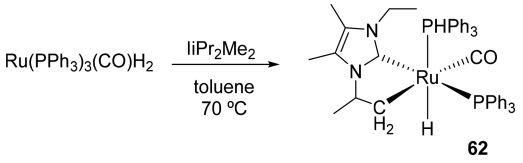
For example, in the present scheme the general indirect Wittig as well as Horner-Wadsworth Emmons reactions using benzyl alcohol in the presence of the same iridium complex and base Cs_2CO_3 are depicted (Scheme 27).[120,121]

The catalysts showed a high tolerance and compatibility with a wide variety of functional groups.

The same happened to the series of ruthenium catalysts that have been applied in this reaction. For example, the ruthenium carbene complex (**62**), synthesized upon heating $Ru(PPh_3)_3(CO)H_2$ with 4 equiv of $IiPr_2Me_2$ (Scheme 28),[122] was also described as a catalyst for the indirect Wittig reaction of alcohols with phosphorane ester ylides and cyano ylides.

This generation of ruthenium complexes was very active at lower temperature, although a hydrosilylation additive (vinyltrimethylsilane) was necessary to activate the catalyst. Under these experimental conditions, high yields of the final products could be achieved.[123]

Scheme 28. Synthesis of Ruthenium Complex 62 Reported by Burling et al.[a]



[a]Reproduced from ref 122. Copyright 2007 American Chemical Society.

2.2.1.7. Diene-Ketone Reductive Coupling. Details on the evolution of carbonyl addition chemistry have been given in an recent excellent review by Krische et al.[124] The same authors have described examples on the catalyzed diene-ketone reductive coupling via hydrogen autotransfer in a few and significant examples that will be described below.[125,126] These studies have been carried out with ruthenium catalysts which enabled the reductive coupling of activated ketones and dienes (**64**) from secondary alcohols (**65**).

Mechanistic studies revealed that there is a diene-carbonyl (**63**, **64**) oxidative coupling to give an oxaruthenacycle. Then a hydrogen transfer from the alcohol would afford the metalacycle hydrogenolysis, from which the C−C coupling product (**66**) would be released, regenerating the ketone and closing the catalytic cycle (Scheme 29).[126]

Besides α-hydroxyesters[125] and heteroaryl substituted secondary alcohols,[126] the process also applies to 3-hydroxy-2-indoles.[127]

2.2.2. Formation of C−N Bonds. *2.2.2.1. Aza-Wittig Reaction.* Examples of aza-Wittig reaction going in tandem with dehydrogenation/hydrogenation reactions have been described also in recent literature reviews. Given that there are no further examples on this intermediate reaction, we will describe these same examples to illustrate this section.

In this case, the nitrogen analogue of a Wittig olefination reaction (aza-Wittig reaction) involved in a BH strategy has been reported to give remarkable yields of the corresponding secondary amines (up to 91%) in the presence of an in situ generated Ir complex under moderate reaction conditions.[128]

Besides a similar process can take place with palladium(II) acetate as catalyst and a strong base as depicted in the following scheme (Scheme 30).[129]

In this case, and in an analogous manner to phosphorus ylides in the Wittig reaction, phosphazenes or iminophosphoranes (**67**) reacted with carbonyl compounds formed in situ through a dehydrogenation reaction from an alcohol (**13a**), being the product converted immediately after, to the corresponding secondary amine (**68a**). Modest yields (25%) were obtained by adding potassium carbonate, although this yield could be increased up to 94% when a stronger base such as cesium hydroxide was incorporated in the reaction media. Borrowing hydrogen catalysis was in this case a good strategy for forming C−N bonds, albeit the substrate scope was restricted to primary alcohols. Another important disadvantage was the need for large amounts of base as an additive.

Similarly, benzyl alcohol (**13a**) and phosphazene (**67**) reacted in the presence of the base tBuOK to give the expected amine with good yields in the presence of $Cu(OAc)_2$ as catalyst.[130]

2.2.2.2. Condensation. 2.2.2.2.a. N-Alkylation of Ammonia (Amination of Alcohols with Ammonia). Besides the Aza-

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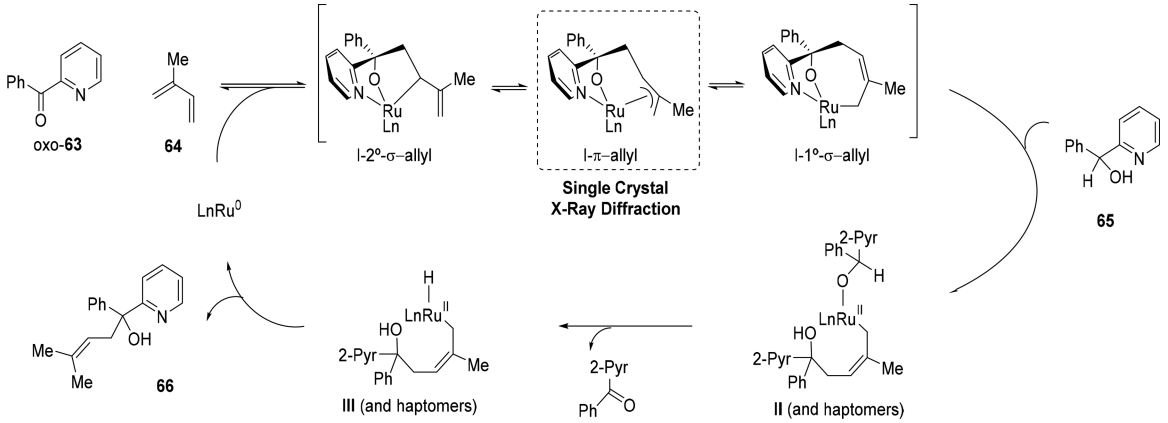
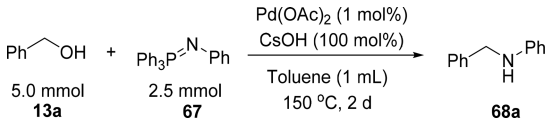
Scheme 29. Postulated Hypothetical Mechanism through a Stable Oxaruthenacycle (Framed in a Box) Involving Diene-Carbonyl Oxidative Coupling[a]



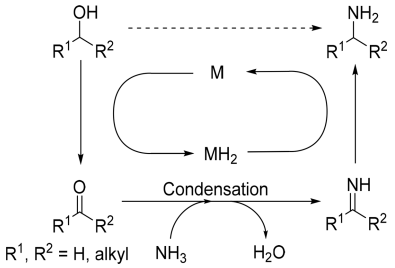
[a]Reproduced from ref 126. Copyright 2013 American Chemical Society.

Scheme 30. Example of an Indirect Aza-Wittig Reaction between the Iminophophorane Derivative 67 and Benzyl Alcohol (13a)[a]



[a]Adapted with permission from ref 129. Copyright 2011 Thieme.

Scheme 31. Catalytic BH Process for the Amination of Alcohols with Ammonia



Wittig reaction, there are other synthetic well-known procedures to synthesize amines. Among them the classical reductive amination which is of special industrial importance as it constitutes one of the most common methods to produce lower alkyl amines.[14,41] The main reason for the large scale use of this reaction is, on one hand, the availability of aldehydes from the respective alcohol precursor. Indeed, the latter are obtained through important industrial processes such as hydration of olefins, hydroformylation/reduction of alkenes, fermentation of sugars or direct production from synthesis gas.[131] On the other hand, ammonia is cheap and can be used with very high atom efficiency in the synthesis of structurally different amines, so that several million tons of amines can be produced annually.[41]

In close connection to this, it is possible to address the reductive amination through the N-alkylation of alcohols with ammonia by following the BH methodology. In accordance with this methodology, there is an initial common alcohol oxidation step to the corresponding aldehyde or ketone. The latter will react with ammonia through a condensation reaction giving an imine and water as the only secondary byproduct; something which is obviously far less problematic than the generation of inorganic salts formed in several amination reactions (e.g., using alkyl or aryl halides).The imine will be hydrogenated in the last step by the metal hydrides formed in the initial dehydrogenation reaction (Scheme 31).

Nonetheless, one important advantage of the BH methodology should be emphasized against the classic reductive amination. This advantage refers to side reactions that can easily occur in classic reductive aminations due to the high concentration of the electrophilic aldehyde (e.g., aldol condensation), and that can not take place in the BH strategy, since the aldehyde formed by dehydrogenation in BH strategies is only present in small amounts since it is formed and consumed continuously in situ.

Another important issue in the context of aminations of alcohols is the identification of the real mechanism, through acid-, base-catalyzed reaction or by the BH methodology (which is the object of this chapter). In this sense, the detection of intermediates such as imines or ketones is a clear indication of oxidation and strongly suggests a BH mechanism.

One of the first groups that studied the preparation of primary amines using inexpensive ammonia was the Milstein's group by using ruthenium coordinated to a hemilabile PNP acridine ligand.[132] Later on, the mechanism of the amination reaction of alcohols with ammonia catalyzed by ruthenium coordinated to structurally more common ligands [(e.g., diphosphine (oxidi-2,1-phenylene)-bis(diphenylphosphine) (DPEphos)] was proposed by Baumann et al.[133,134]

Almost in parallel, attempts to get primary amines from secondary alcohols and ammonia in the presence of $[Ru_3(CO)_{12}]$ and commercially available CataCXium PCy were independently reported by two groups.[135,136]

Similarly a broad screening of ruthenium catalysts, reaction conditions, and ligands were tested in different reactions with ammonia leading to the amination of alcohols for the synthesis of diamines, aminoesters,[137] α-amino acid amides[138] (important structures in different bioactive compounds) and the amination of bioalcohols.[139] For example, on the basis of the previously mentioned $Ru_3(CO)_{12}$/CataCXiumPCy system, a variety of ligands (**69**–**76**) were screened in order to find a more robust catalytic system. The authors found that compound **72** exhibited a high activity for transforming a series of primary

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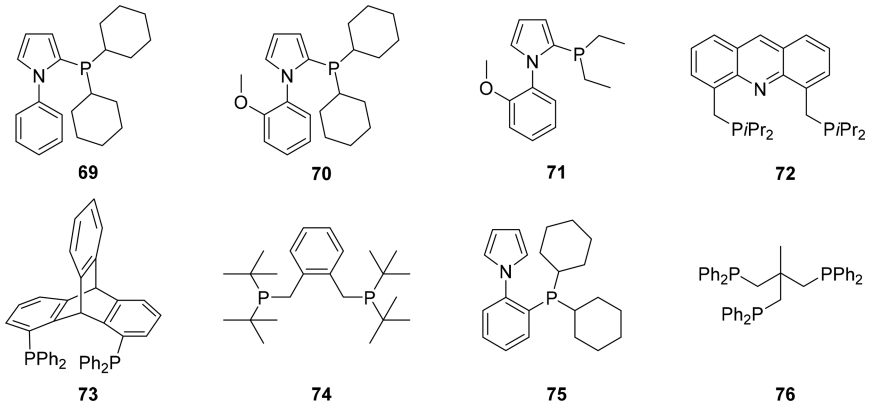


Figure 4. Collection of ligands tested in the amination reaction of cyclohexanol as model alcohol. Adapted with permission from ref 139. Copyright 2013 Wiley-VCH.

and secondary bio monoalcohols and bioderived diols into primary amines (Figure 4).[139]

Interestingly, the Ru/P ratio employed had a strong effect on the reaction rate, so that a 1:1 ratio appeared to be the optimal, whereas a higher ratio (Ru/P = 1:0.66) showed a similar activity initially but led to deactivation of the catalyst as the reaction was evolving with time.

The following table includes the most interesting results obtained in the secondary bioalcohol amination with the system $Ru(CO)_{12}$/**72** at different temperatures (Table 4).[139]

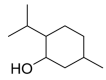
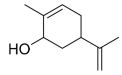
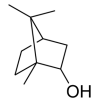
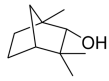
Examples of *N*-alkylations with ammonium salts and aqueous ammonia as an alternative to ammonia gas are scarce. In fact, only one example of each type has been reported in the literature that have been already included in previous specific reviews. Nonetheless, given their importance they will be quoted below describing their advantages and disadvantages for the information on readers.

For example, an interesting study reported the use of ammonium acetate as precursor for the in situ generation of ammonia in the amination of alcohols (using classical iridium catalyst ($[Cp^*IrCl_2]_2$)).[140] This strategy led to the obtention of trialkylamines.

However, though a priori the unnecessity of a pressure equipment turns a reaction into a more practical process; a problem in this case arises because the use of ammonium salts generate stoichiometric amounts of waste salts. An alternative would be the use of aqueous ammonia as shown in the hexanol and cyclohexanol amination to give tertiary and secondary amines reported by Fujita et al.[141] Notably the catalyst could be recycled and reused up to three times by adding a solvent followed by a phase separation.

It is important to emphasize that the use of ruthenium and iridium complexes has been extensively reported for the synthesis of amines, aminoesters, aminoalcohols, and diamines in the patent literature in parallel to academic reports which have used similar or closely related metal-based complexes. This highlights the importance of these two elements to academic and industrial practice.[137,142−148] Nonetheless, along with ruthenium and iridium, other less usual elements such as platinum have been reported to produce allylamines (**78**, **79**) from the corresponding allylic alcohols (**77**) and ammonia.[149] In this new protocol, a variety of primary allylamines (**78a−h**) were obtained in a straightforward fashion from the respective allylic alcohol in aqueous ammonia (28%). Unexpectedly, in this case the reaction with ammonia excess afforded a lower yield because of the partial deactivation of platinum. However, under optimized conditions, the allylic alcohol amination catalyzed by this metal was rather general. A collection of the most interesting results are included in the following table (Table 5).[149]

Table 4. Secondary Bioalcohol Amination with $[Ru_3(CO)_{12}]$/72 at 150 and 170 °C[a]

Substrate	t [h]	T [%]	Conversion[b] [%]	Selectivity[c,d] [%]	Ketones [%]
Menthol	21	150	25.3	18.0	82
	21	170	31.6	70.8	29.2
	63	150	32.7	24.3	75.7
Carveol	21	150	67.3	74.7	
	21	170	99.1	55.2	
	65.5	150	82.0	56	
	42	170	99.3	50.4	
Verbenol	21	150	93.5	39.7	44.2
	21	170	96.4	27.7	62.2
	63	170	98.8	25.0	47.7
Borneol	21	150	58.5	73.2	
	21	170	76.8	83.9	
	65.5	150	72.2	78.7	
	63	170	79.1	81.2	
Fenchol	21	150	50.6	0	34.8
	21	170	59.2	0	46.0
	63	150	54.5	0	38.2
	117	170	63.9	0	44.3

[a]Adapted with permission from ref 139. Copyright 2013 Wiley-VCH. Reaction conditions: $[Ru_3(CO)_{12}]$ (0.066 mmol), **72** (2 mmol), substrate (10 mmol), *tert*-amyl alcohol (13.3 mL), NH_3 (6 mL, 234 mmol), 150 and 170 °C. [b]Conversion determined form GC analysis on the basis of alcohol consumption and amine production. [c]Total of all primary amines. [d]Main byproducts are primary imines, amides, and ketones.

2.2.2.2.b. N-Alkylation of Primary and Secondary Amines (Amination of Alcohols with Primary and Secondary Amines). The amination of alcohols with primary amines by the BH methodology has the advantage of promoting the production of secondary amines because a primary amine can react more easily with the aldehyde. This fact contrasts sharply

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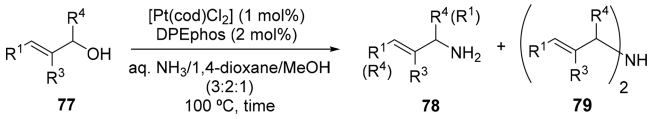
Table 5. Amination of Allylic Alcohols with Aqueous Ammonia Catalyzed by Pt(cod)Cl_2[a]



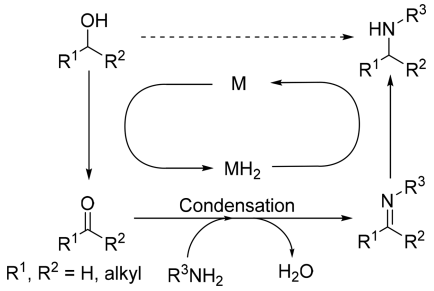
77 78 79

Entry	Product		t (h)	**78** Yield (%)[b]	**78**/**79**[b]
1	4-MeC_6H_4 NH_2	**78a**	24	76 (68)	93:7
2	4-$MeOC_6H_4$ NH_2	**78b**	48	78 (70)	91:9
3	1-naphtyl NH_2	**78c**	48	77 (70)	94:6
4	Ph NH_2	**78d**	24	77 (66)	91:9
5	3-FC_6H_4 NH_2	**78e**	24	77 (66)	93:7
6	Ph, Ph NH_2	**78f**	48	88 (78)	>99:1[c]
7[d]	NH_2	**78g**	64	78 (66)	>99:1[c]
8[d]	S NH_2	**78h**	48	72 (67)	92:8

[a]Adapted with permission from ref 149. Copyright 2012 Wiley-VCH. Reaction conditions: 77 (0.5 mmol), [Pt(cod)Cl_2] (1 mol %), DPEphos (2 mol %), 28% aq. NH_3, 1,4-dioxane and MeOH (3:2:1, total volume 6.0 mL), 100 °C in sealed tube. [b]Determined by ^{1}H NMR spectrum of the crude reaction mixture. The number in parentheses is the yield of the isolated product after Boc protection. [c]**79** was not detected by either ^{1}H NMR or CI-MS analysis of the crude reaction mixture. [d]3.0 mol % of catalyst was used.

with classical alkylation methods which tend to give over-alkylation products because the secondary amine is more reactive than the primary one toward the alkyl bromide. As in the previous case with ammonia, the BH methodology only generates water as byproduct and allows alcohols to replace more conventional but often toxic alkyl halides as alkylating agent.[150] The process occurs analogously through three in situ consecutive reactions: dehydrogenation, condensation, and hydrogenation (Scheme 32).

Scheme 32. Catalytic Condensation and Borrowing Hydrogen Methodology Going in Tandem for the *N*-Alkylation of Amines with Alcohols



The great potential of this reaction has stimulated a growing number of applications of BH chemistry on *N*-monoalkylations, so that the development of active homogeneous catalysts has greatly increased. The strategy for designing new catalysts has gone through the synthesis of new molecularly defined organometallic catalysts or the modification of other already existing ones. The result has been a wide collection of metal active complexes for the oxidative dehydrogenation of alcohols, condensation of the resulting carbonyl group to give imines, and the subsequent reduction of the latter to give amines, which are basically the demanded requirements for these catalytic systems.[10,12,14−17,19,57] Primary alcohols have mainly been used as hydrogen donors for the amination reactions, provided they were more reactive compared to secondary alcohols.

Looking back to the origins of this reaction we found that one of the first homogeneous catalysts for *N*-alkylation of amines with alcohols was introduced by Grigg et al.[151] and Watanabe et al.[152] in 1981. Grigg et al. reported the *N*-alkylation reaction of primary and secondary amines with primary alcohols, to give secondary as well as tertiary amines, being a rhodium catalyst [$RhH(PPh_3)_4$] the most active one.[151] In parallel, Watanabe and co-workers reported the ruthenium-catalyzed *N*-alkylation and *N*-heterocyclization of aniline with alcohols and aldehydes. In both reactions, only primary alcohols were applied as hydrogen donors.[152] From this background, *N*-alkylations for forming secondary amines (by reacting primary amines with alcohols)[5,153−170] and amino alcohols[171,172] have been extensively reported in the literature.

At this point, it is necessary to emphasize that iridium and ruthenium complexes have been again the dominant catalysts in these types of transformations. As an example, different types of anilines have been monoalkylated with benzyl as well as aliphatic alcohols in the presence of iridium coordinated to an anionic P,N ligand (**80** and **81** iridium complexes). The authors observed a nearly quantitative conversion under mild conditions (70 °C) and a very low iridium loading (0.05%) (Table 6).[157]

Some relatively recent applications that corroborate the interest that this reaction has awakened in large scale synthesis is the one kilogram scale application of this strategy for the synthesis of one inhibitor for the treatment of schizophrenia named PF-03463275. In particular, a GlyT1 inhibitor, which is prepared in the presence of $(Cp^*IrCl_2)_2$ under optimized conditions with catalyst loadings lower than 0.05 mol %, while requiring moderate reaction times.[173] Other interesting applications of Ir-based catalyst led to the *N*-alkylation of carbohydrate alcohols leading to *N*-substituted aminosugars with potential applications in the biochemical and pharmaceutical fields.[174]

Similarly, Fujita et al. reported that $[Cp^*IrCl_2]_2$ efficiently catalyzed the coupling between different amines and monoalcohols, or even vicinal diols for the synthesis of *N*-heterocycles,[175,176] whereas a related Ir compound $[Cp^*IrI_2]_2$ was also successfully applied in this reaction in a more benign aqueous media and without requiring the use of a base.[159] Besides, the synthesis of *N*-heterocycles through an intramolecular reaction of amines has also been described to take place in the presence of closely related Ir-based catalysts.[177] A related Cp* Ir half sandwich complex with amino acidato ligands has also been reported to catalyze the alkylation of amines with alcohols under milder conditions.[178]

Continuing with iridium, a cyclometalated iridium complex (**84**) has shown a similar substrate scope for the synthesis of secondary amines (**83**) (albeit its extraordinary activity was limited by a strong solvent effect) (Scheme 33).[179]

With regard to ruthenium, diverse ruthenium(II) carbonyl complexes bearing phosphine-functionalized hydrazine/thiosemicarbazone ligands and triphenylarsine ligands were prepared, being characterized by different techniques. In all these complexes, ruthenium(II) was coordinated with the ligand via

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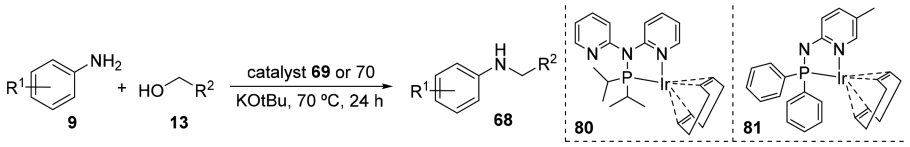
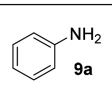
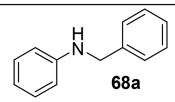
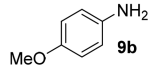
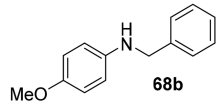
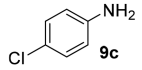
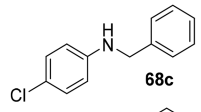
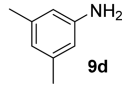
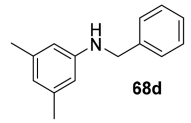
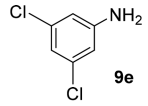
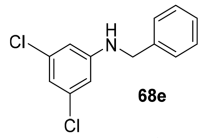
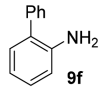
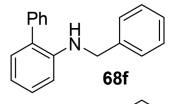
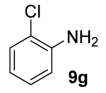
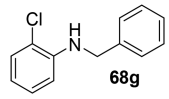
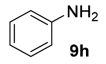
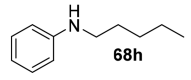
Table 6. Catalytic *N*-Alkylation of Anilines Derivatives with Primary Alcohols in the Presence of Iridium Catalysts 80 and 81[a]



Entry	Catalyst loading [mol%]	Amine	Product	Yield [%][b] Catalyst **80**	Yield [%][b] Catalyst **81**
1	0.1	 **9a**	 **68a**	38	92
2	0.2	 **9b**	 **68b**	29	92
3	0.05	 **9c**	 **68c**	75	98
4	0.2	 **9d**	 **68d**	33	81
5	0.2	 **9e**	 **68e**	54	98
6	0.4	 **9f**	 **68f**	48	91
7	0.2	 **9g**	 **68g**	73	97
8	0.2	 **9h**	 **68h**	52	98

[a]Adapted with permission from ref 157. Copyright 2010 Wiley-VCH. Reaction conditions: amine (1.0 mmol), benzyl alcohol (1.1 mmol), KOtBu (1.1 mmol), diglyme (0.2 mL), 70 °C, 24 h. [b]Yield determined by GC analysis with *n*-dodecane as the internal standard.

PNO/PNS donor atom being actives at very low catalyst loading. Figure 5 shows the structure of some of the ruthenium−phosphine-based catalysts (**84**−**88**) of this study.[180]

Another interesting sort of ruthenium complexes were prepared from readily available 1,3-dialkylbenzimidazolium salts, being characterized by X-ray diffraction. Interestingly, the RuNHC complexes (**92**−**94**) efficiently promoted the catalytic *N*-alkylation (**90**) as well as the N,C-dialkylation (**91**, see section 2.2.1.5) reaction of different cycloaliphatic amines like morpholine and pyrrolidine (**89**).[169] Table 7 shows some of the results obtained on the *N*-alkylation and C_3 alkylation of pyrrolidine with different benzylic alcohols.

Different ruthenium catalysts have also been prepared in situ by adding benzimidazolium sulfonate salts into the reaction mixture. The system $[RuCl_2(p\text{-cymene})]_2$/benzimidazolium sulfonate salt was active at 120 °C under neat conditions for the selective *N*-alkylation of primary aromatic amines (aniline) with benzyl alcohol into secondary amines. The following scheme (Scheme 34) shows the preparation of the benzimidazolium sulfonate salts (**96**) from benzimidazole (**95**) according to the synthetic method described in ref 181.

More recently a set of benzimidazolium sulfonate salts (**98**) have been incorporated as additives in $[RuCl_2(p\text{-cymene})]_2$ catalyzed reactions to give a very active complex for the obtention of secondary amines starting from aromatic primary amines. For example, the synthesis of amine **68a** starting from benzyl alcohol (**13a**) and aniline (**9a**) takes place with the incomplete hydrogenation of the corresponding imine **97** (Scheme 35).[181]

In another approach, a tunable amidation/amination reaction has been described to occur in the presence of a ruthenium NHC/phosphine complex. In accordance with these results, the amide derives from an acceptorless dehydrogenation process that involves the participation of a hemiaminal compound, meanwhile the "borrowing hydrogen" process takes place just for forming the amine (Scheme 36).[182]

The authors point out that the selectivity is based on the tuning of the *N*-proton transfer. This *N*-proton transfer can be easily tuned by changing the base and the solvent. The proton-to-hydrido transfer gives rise to amides; though the proton-to-

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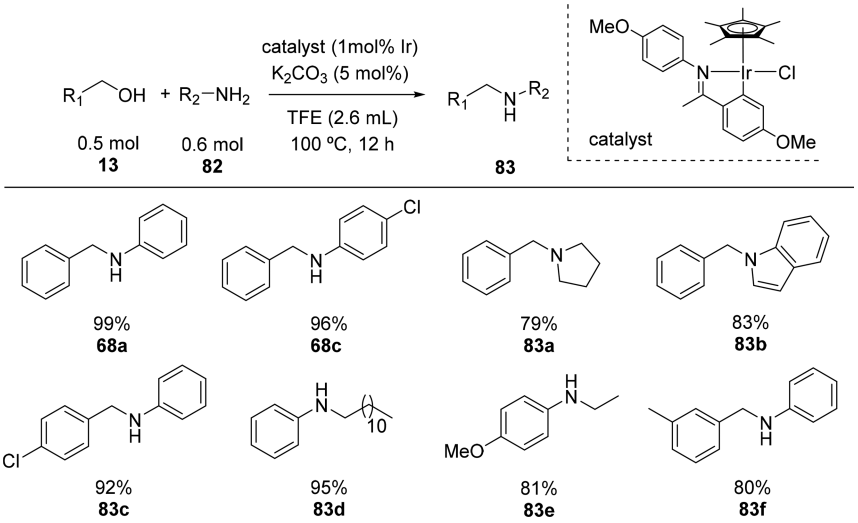
Scheme 33. Cyclometalated Iridium Complex Catalyzed *N*-Alkylation of Primary Amines (82) with Secondary Alcohols (13) Reported by Xiao and Coworkers[a]



[a]Adapted with permission from ref 179. Copyright 2015 Wiley-VCH.

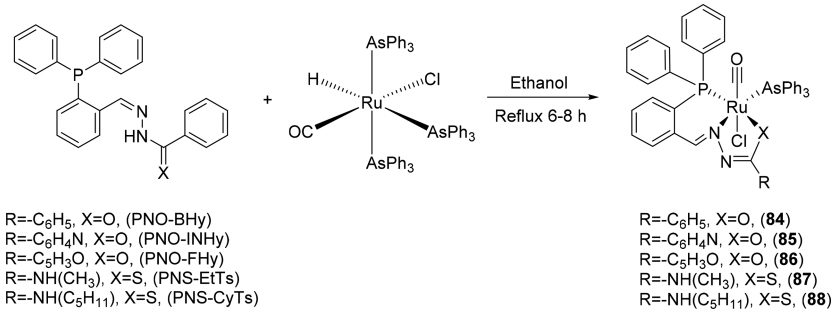


Figure 5. Collection of ruthenium-phosphine-based catalysts **84**−**88** for the amine synthesis from alcohols and schematic synthetic strategy for their preparation. Adapted with permission from ref 180. Copyright 2015 Elsevier.

alkoxide transfer will give an imine. The latter can be hydrogenated by the ruthenium hydride intermediate complex affording amines (Scheme 36).[182]

A novel ruthenium catalysts (**102**) was prepared and characterized by using the benzimidazolin-2-ylidene *N*-heterocyclic carbene as ligand.[183] This catalyst was successfully applied for the synthesis of *N*-alkylated amines such as cyclic amines (**101**) from amines (**100**) and diols (**99**) (Scheme 37).[183]

Previously, the homogeneously catalyzed *N*-alkylation of a poor nucleophile heterocycle such as indole (hence the importance of this reference) with alcohols,[184,185] the amination of 1,2-diols with anilines and secondary amines,[186] as well as the preparation of unsymmetrically tertiary amines from tertiary amines and primary alcohols in the presence of ruthenium complexes were reported.[187]

Another ruthenium(II) complex [Ru(COD)Cl_2] efficiently catalyzed the synthesis of trisubstituted 1,3,5-triazines (**105**) by reacting alcohols (**103**) and biguanides (**104**). The method had a broad scope, and a variety of functional groups showed high group tolerance. The Table 8 shows some interesting results for obtaining triazines.[188]

Another interesting application has to do with the transformation or upgrading of glycerol with primary and secondary amines. Indeed, isopropylideneglycerol (**106**) can be aminated in its primary position with [Ru(p-cymene)Cl_2] and a variety of secondary amines such as morpholine, piperidine, 1-phenylpiperazine, and 1-Boc piperazine (**107**) forming the corresponding aminated products (**108**) in up to 92% isolated yield. The synthesis of an antitussive molecule **109** in up to 86% yield from solketal showed the utility of this methodology (Scheme 38).[189]

Similarly, a variety of structurally complex Ru(II) catalysts (e.g., **113**) have also been described to have activity in the *N*-alkylation of sulfonamides as well as heterocyclic amines (e.g., **110**) in the presence of KOH (Scheme 39).[190]

Finally, we will refer to the possibility of synthesizing pyrrole far from those traditional routes suffering from harsh reaction conditions, nonavailability of raw materials, and poor functional tolerance, through a hydrogen autotransfer process. In this case (Scheme 40), iron-based complex catalyzed the amination of diols using primary amines.[191]

In light of these findings, it is fairly clear that mainly primary alcohols have been used as hydrogen donors for amination reactions over any other type of alcohol, provided that with few exceptions they are much more reactive compared to secondary alcohols.[153,159,160,192]

Nonetheless from now on, we will focus on studies about *N*-alkylation of amines through activation of secondary alcohols. In this context, the use of ruthenium complexes has attracted attention as catalysts for this strategy. Indeed, a few number of examples on the activation of secondary alcohols by ruthenium

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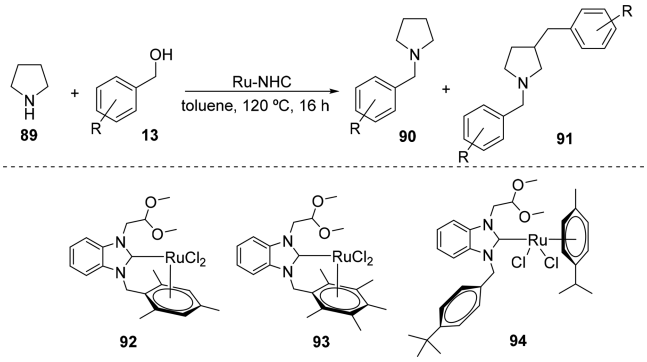
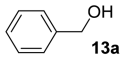
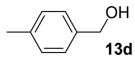
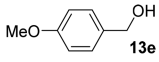
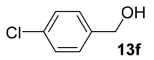
Table 7. *N*-Alkylation and N,C_3-Dialkylation of Pyrrolidine with Benzyl Alcohol Derivatives[a]



Entry	Alcohol	Ru-NHC	**90**(%)	**91**(%)
1		**92**	56	44
2		**93**	60	40
3		**94**	89	11
4		**92**	36	64
5		**93**	38	62
6		**94**	42	58
7		**92**	66	44
8		**93**	83	17
9		**92**	51	49
10		**93**	90	10

[a]Reproduced from ref 169. Copyright 2015 American Chemical Society. Reagents and conditions: pyrrolidine (1.0 mmol); alcohol (2.5 mmol); CSA (40 mol %); Ru-NHC (1 mol %); toluene (1 mL); 120 °C, 16 h. The yields of **90** and **91** were determined by GC using dodecane as an internal standard.

complexes have been found in the literature in the past decade giving from moderate to good yields of the respective secondary and tertiary amines.[193,194]

One recent contribution on the activation of secondary alcohols by Ru complexes (**119**) was described by Marichev et al.[195] In this case, the amination (**115**) of primary and secondary alcohols (**117a**) as well as diols yielded the corresponding secondary, tertiary, and *N*-heterocyclic amines (**116**, **118**) under relatively mild reaction conditions (Scheme 41).[195]

Several variants of inter- and intramolecular cyclizations were performed through BH catalysis giving rise to piperazines (**122**) and diazocines (Scheme 42).[195] In this regard, this scheme shows some of the most interesting structures obtained by reacting diamines (**120**) and diols (**121**) in the presence of a Ru(II) complex (**123**).

Although the majority of publications were focused on classic ruthenium and iridium complexes, there have been numerous attempts, at the academic level, to carry out the amination of alcohols by BH methodology using available and cheaper metals such as iron, copper, cobalt, palladium, silver, gold, and osmium.[196−202] Indeed, it is evident that the use of complexes based on nonprecious metals provides us with new opportunities in the *N*-monoalkylation of amines with alcohols. In this sense, Beller et al. have recently reported for the first time the use of a manganese pincer complex as catalyst for the *N*-alkylation of aromatic amines and primary alcohols (Scheme 43).[203]

The complexes (**124**−**127**) were highly stable being easily handled under air. In this case, it was possible to get high yields of the corresponding secondary amines, being the presence of different functional groups on the starting reactants well-tolerated under very mild conditions.[204,205]

Finally, a last example reported the excellent performance of an iron cyclopentadienone complex when a variety of alcohols and amines reacted to yield secondary amines and *N*-heterocycles.[206]

2.2.2.2.c. N-Alkylation of Amides and Sulfonamides. The same previous synthetic BH methodology can be applied to the *N*-alkylation of amides by alcohols. The reaction pathway depicted in Scheme 44 shows a close analogy to that described in previous sections.

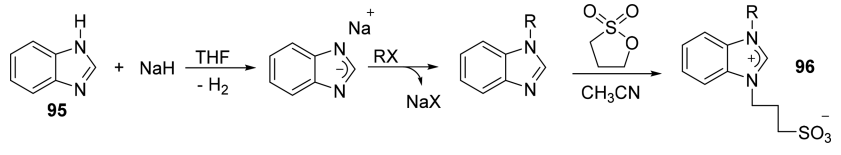
In a similar way to what was observed when using amines as substrates, different metal-based complexes were successfully applied as catalysts for the *N*-alkylation of amides, including iridium, ruthenium, palladium, as well as rhodium complexes.[207,208]

Nonetheless, we owe the early efforts on this issue to Watanabe, who described one of the first ruthenium-catalyzed formation of substituted amides through the *N*-alkylation of amides with alcohols.[209] Since then, only two studies on amide alkylation by means of BH methodology have appeared in the literature,[207,208] being already included in specific reviews. Given that further studies have not been published so far, these two previous references will be described below.

However, not only amines and amides are suitable candidates but sulfonamides are also good substrates to carry out alkylation reactions at the N position following the BH strategy.[207,208,210−213] Indeed, the interest of *N*-alkylated sulfonamides relies on their importance in agrochemical and pharmaceutical chemistry.[214−216] They are also relevant as protecting groups in synthetic chemistry since the sulfonyl group can be easily removed when bound to nitrogen, allowing the *N*-alkylated sulfonamides to be rapidly converted into the corresponding primary amines.[217] Typically, the classical processes for synthesizing *N*-alkylated sulfonamides are performed by reacting amines and sulfonyl halides or sulfonic acids activated by triphenylphosphine distriflate, as well as through the reductive amination of aldehydes.[218]

However, these previous processes have the inconveniences of giving secondary products and/or the need for sensitive substrates. Hence, the use of alcohols as alkylating reagents for

Scheme 34. Synthesis of Benzimidazolium Sulfonate Salts[a]



[a]Adapted with permission from ref 181. Copyright 2016 Elsevier.

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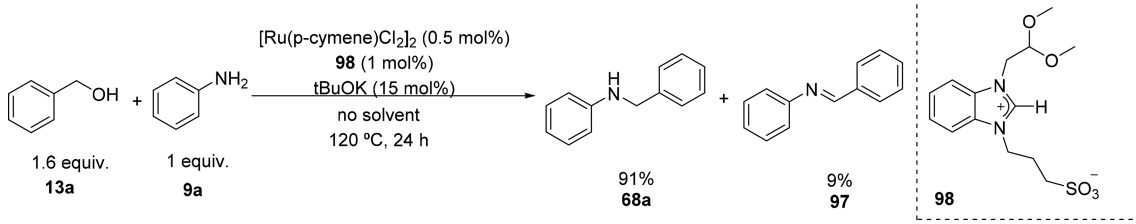
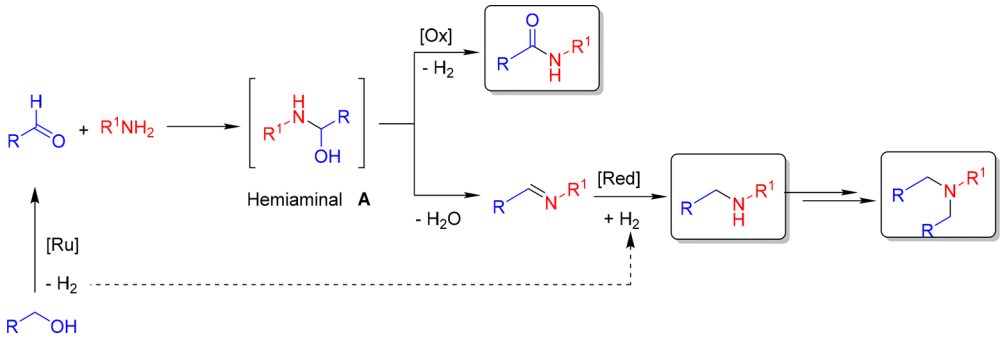
Chem. Rev. 2018, 118, 1410−1459

Scheme 35. Benzylation of Aniline (9a) with Benzyl Alcohol (13a) Catalyzed by a Ru Complex $[RuCl_2(p\text{-cymene})]_2$ and the Benzenosulfonate Salt 98 as Additive[a]



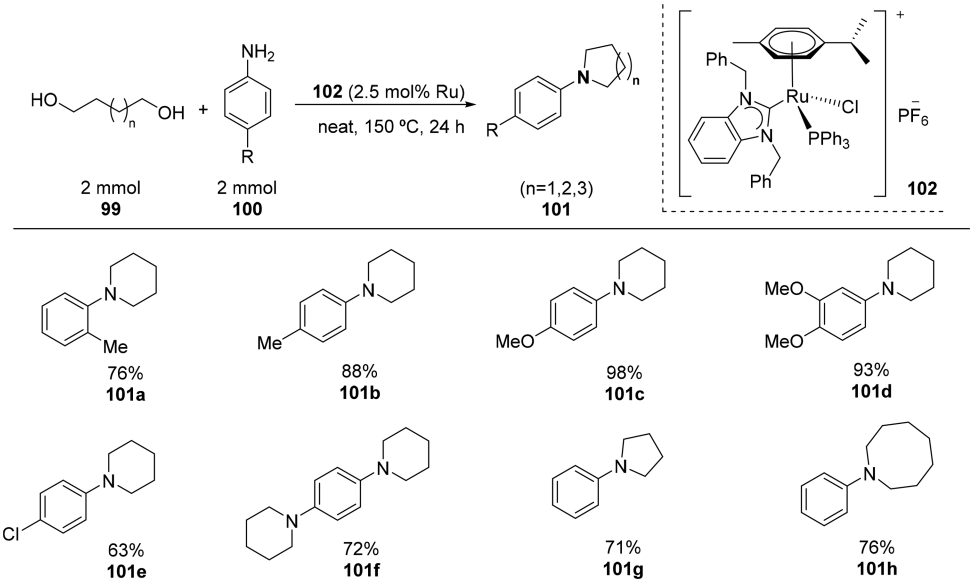
[a]Adapted with permission from ref 181. Copyright 2016 Elsevier.

Scheme 36. Proposed Reaction Pathways for the Formation of Secondary Amides and Alkylated Amines[a]



[a]Reproduced from ref 182. Copyright 2015 American Chemical Society.

Scheme 37. *N*-Alkylation of Aniline Derivatives (77) with Different Diols (76) Catalyzed by a Ru-NHC-Phosphine Complex (79)[a]



[a]Adapted with permission from ref 183. Copyright 2015 Royal Society of Chemistry.

N-alkylation through BH catalysis is an attractive strategy because it does not generate harmful or toxic byproducts. Besides, alcohols, are generally stable and are readily available compounds. Moreover most of these metal-catalyzed reactions for *N*-alkylating sulfonamides with alcohols can be successfully carried out with good activity and selectivity.

Indeed, under the optimized conditions, the scope of each particular protocol (with iron, ruthenium, palladium, iridium, rhodium, and copper complexes, etc.) has been well-demonstrated by a long list of different alkylation reactions performed with high yields of products (>90%).[129,130,219,220]

One of the few examples of iridium-catalyzed processes to alkylate sulfonamides has been described with the classical $[Cp^*IrCl_2]_2$ complex, which is very active for reacting primary and even secondary alcohols as alkylating agents[221] and Fe(II) complexes.[209] Interestingly, in this case, the existence of a possible mechanism involving a Fe(II)/Fe(0) catalytic cycle was suggested on the bases of XPS analysis.

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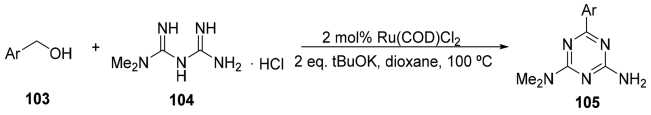
Chem. Rev. 2018, 118, 1410−1459

Table 8. Scope for the Synthesis of 1,3,5-Triazine Derivatives 105[a]



103 104 105

entry	Ar	alcohol	product	yield (%)
1	C_6H_5	**13a**	**105a**	74
2	4-MeC_6H_4	**13d**	**105b**	65
3[b]	4-$MeOC_6H_4$	**13e**	**105c**	71
4[b]	3-$MeOC_6H_4$	**103a**	**105d**	55
5[b]	2-$MeOC_6H_4$	**103b**	**105e**	70
6[b]	2,3-$(MeO)_2C_6H_3$	**103c**	**105f**	74
7	3,4-$(MeO)_2C_6H_3$	**103d**	**105g**	83
8	4-FC_6H_4	**103e**	**105h**	54
9	4-ClC_6H_4	**13f**	**105i**	63
10	4-BrC_6H_4	**103f**	**105j**	51
11[c]	2-furanyl	**103g**	**105k**	65
12[b]	2-thiophenyl	**103h**	**105l**	63

[a]Adapted with permission from ref 188. Copyright 2016 Royal Society of Chemistry. All reactions were performed with 1.0 mmol of **103** and 1.0 mmol of **104** using $Ru(COD)Cl_2$ (2 mol %), and dioxane (5 mL) at 100 °C for 14 h in a sealed reaction tube, isolated yields are shown. [b]20 h. [c]30 h.

A more recent contribution has reported the synthesis and characterization of a variety of ruthenium complexes bearing 2-(2-(diphenylphosphino)benzylidene)-*N*-ethylthiosemicarbazone (PNS-Et) ligands (**128**–**130**), which were revealed as very efficient catalysts in the *N*-alkylation of different sulfonamides with alcohols (Scheme 45).[190]

In order to explore the scope of the present method, the *N*-alkylation reaction (**132**) of a variety of primary sulphonamides (**131**) with benzylic and cycloaliphatic alcohols was tested by using the previously reported Ru(II) catalysts (Table 9).[190]

The authors observed that substituents on the aromatic ring of the primary sulphonamide or the benzyl alcohol had hardly influenced the alkylation reaction since the corresponding sulphonamides were obtained in very high yields (82–99%), no matter the electron-rich or electron-poor nature of the substituent (Table 9). In addition, the cycloaliphatic alcohol cyclohexanol gave the corresponding cyclohexyl sulphonamide derivative in moderate yield (entry 6, Table 9), whereas the monoalkylated methanesulphonamide was obtained with very low yields when using benzyl alcohol as a hydrogen donor (entry 7, Table 9).

2.2.2.3. Condensation/Deprotection. As previously stated, the development of synthetic methods for synthesizing primary amines is of current interest, and different experimental procedures inspired by the BH strategy have evolved in recent years. Among them, the incorporation of an ammonia equivalent in the form of a *N*-nucleophile followed by deprotection is an interesting approach.

Taking into account that the sulfonamide group can be easily removed as the protecting group,[217] different in situ deprotection protocols have been studied with the resulting sulfonamides and different catalysts. We will include an interesting and representative example that has been mentioned in a previous specific review. Given that this is the only example that has appeared on this particular reaction, we will describe it briefly below.

In this case, benzyl alcohol (**13a**) was readily transformed into benzylamine (**82a**) through an intensive process which combined a sort of reactions based on BH methods in the presence of a ruthenium-based catalytic system $[Ru(p\text{-cymene})Cl_2]_2$/DPEphos [DPEphos: oxidi-2,1-phenylene-bis-(diphenylphosphine)].[15,222] The initially formed *N*-alkylated sulfonamides obtained by borrowing hydrogen catalysis were submitted to an in situ deprotection treatment with CsF and DMF at 110 °C, or in certain cases with Mg/MeOH (Scheme 46).[222]

Nonetheless, even though these preparation methods gave very good yields of the desired amines, we would point out that the low atom efficiency is a common drawback to all these amination/deprotection processes.

2.2.2.4. Condensation/N-Heterocyclization. *N*-Heterocycles, which have attracted considerable attention due to their importance and prevalence in pharmaceuticals, materials chemistry, synthetic organic chemistry, and dyes have also been prepared through BH methods.

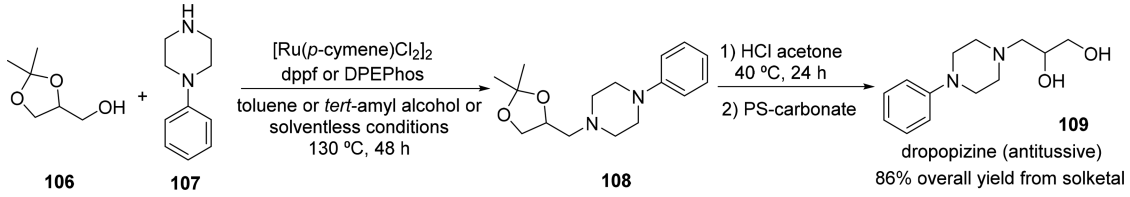
One interesting contribution from Fujita et al. described a cyclization reaction involving 2-aminophenethyl alcohols to indoles,[223] using $[Cp^*IrCl_2]_2$ as catalyst, whereas later on, Eary et al. reported the cyclization of anilino alcohols to get 1,2,3,4-tetrahydroquinoxalines and 2,3,4,5-tetra-1-H-benzo[b][1,4]-diazepines.[224] In this case, a higher catalyst loading (20 mol % $[Cp^*IrCl_2]_2$) and longer reaction times than in Fujita's work (2–5 days) were required.

More recently and in close connection to this, 2,3,4,5-tetrahydro-1H-1,4-benzodiazepine (**134**) was conveniently prepared through a one-pot ruthenium catalyzed reaction, encompassing two consecutive borrowing hydrogen cycles starting from 2-aminobenzyl alcohol (**13b**) and 1,2-amino-alcohol (**133**) (Scheme 47).[225]

Mechanistically, the starting benzylic amino alcohol derivative **13b** could undergo a dehydrogenation reaction resulting in the formation of the corresponding benzaldehyde derivative **135**, which would react with a second amino alcohol (**136**) giving a secondary amine (**137**) (Scheme 48).[225]

In a second borrowing, hydrogen process compound **137** may be dehydrogenated to give the intermediate compound **138**, the latter would undergo cyclization to yield compound

Scheme 38. Synthesis of the Antitussive Dropopizine 109[a]



106 107 108

[a]Reproduced from ref 189. Copyright 2016 American Chemical Society.

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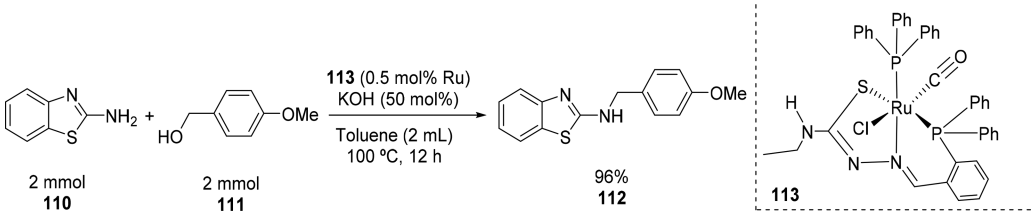
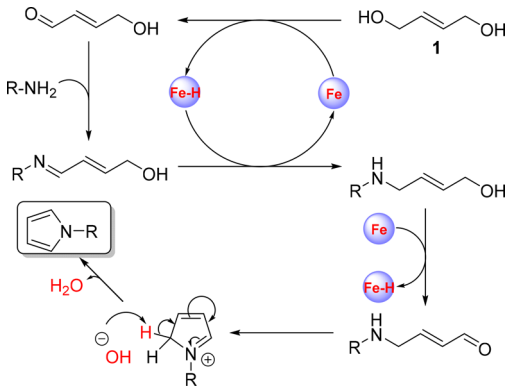
Scheme 39. [(PNS-Et)RuCl(CO)(PPh_3)] (113) Catalyzed Synthesis of the *N*-Alkylated Product 112 When Reacting 2-Aminobenzothiazole (110) with 4-Methoxybenzyl Alcohol (111)[a]



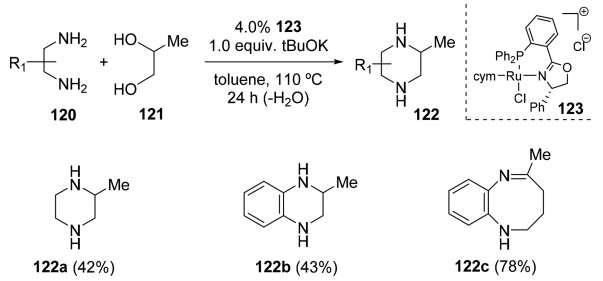
[a]Adapted with permission from ref 190. Copyright 2015 Royal Society of Chemistry.

Scheme 40. Plausible Catalytic Cycle for the Synthesis of Pyrrole[a]



[a]Reproduced from ref 191. Copyright 2017 American Chemical Society.

Scheme 42. Synthesis of Diazocines and Piperazines in the Presence of a Ru(II) Complex[a]



[a]Reproduced from ref 195. Copyright 2016 American Chemical Society.

139, and ulterior hydrogenation would give the benzodiazepine derivative **140** (Scheme 48).

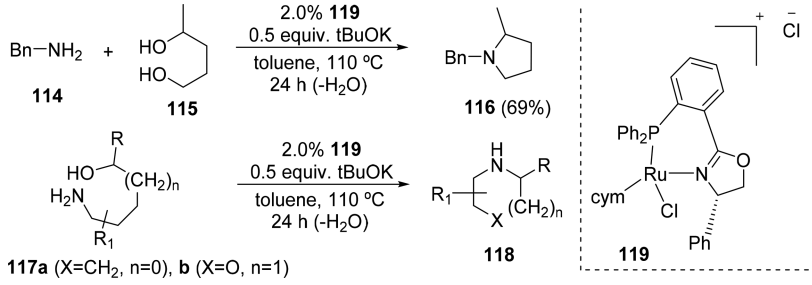
Interestingly the use of diols, butanediol and pentanediol, as alkylating agents gave the complete conversion to substituted pyrrolidines and piperidines at low temperature and low ruthenium catalyst loading.[226]

To summarize this section devoted to the activation of alcohols, we conclude that alcohols (especially the primary ones) are one of the most applied hydrogen donors in borrowing hydrogen strategies, with Ru and Ir complexes as homogeneous catalysts of preference involved in a wide variety of autotransfer processes. By virtue of this BH strategy, alcohols will transform into benign and versatile alkylating agents for different scaffolds. Therefore, showing that the method is not limited to the preparation of amines (C−N bonds), but it can also be extended to form C−C bonds. In light of these precedents, we may expect that the future research efforts will be focused on designing new and more active catalysts able to activate the less reactive secondary alcohols. These complexes will also extend the scope of the BH strategy to form new carbon-heteroatom bonds not described so far, as for instance the formation of C−O, C−S, C−Si, and C−P bonds among others.

2.3. Activation of Amines

Amines might be activated, a priori, as alcohols and alkanes by dehydrogenation to provide more reactive compounds such as imines and iminium cations or enamines. Effectively, imines are produced as intermediate compounds through the *N*-monoalkylation of amines with alcohols (see section 2.2.2) and can alternatively be prepared analogously to alcohols by direct oxidation of amines by hydrogen abstraction. Although this last transformation (*N*-alkylation of amines with amines) seems uncommon at first sight, there are many industries which are interested or involved in related transformations (see for instance transalkylation reactions) as can be deduced by the number of patents on this topic.[227−232]

Scheme 41. Synthesis of Five- and Six-Membered Cycloaliphatic Amines Catalyzed by a Ruthenium Complex 119[a]



[a]Reproduced from ref 195. Copyright 2016 American Chemical Society.

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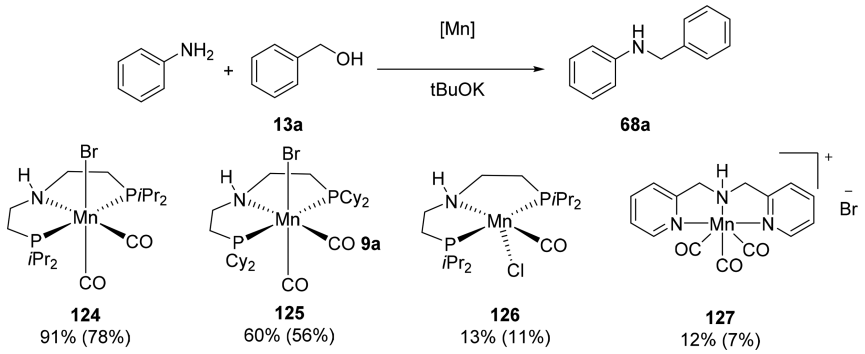
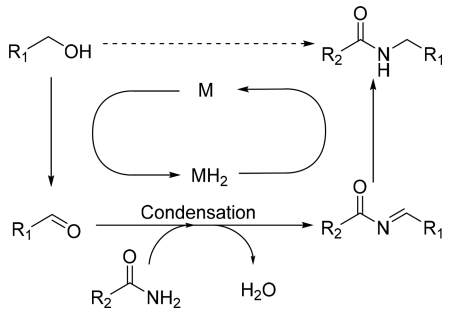
Chem. Rev. 2018, 118, 1410−1459

Scheme 43. Conversion and Yield of the *N*-Alkylation of Aniline with Benzyl Alcohol Catalysed by Different Mn Complexes[a]

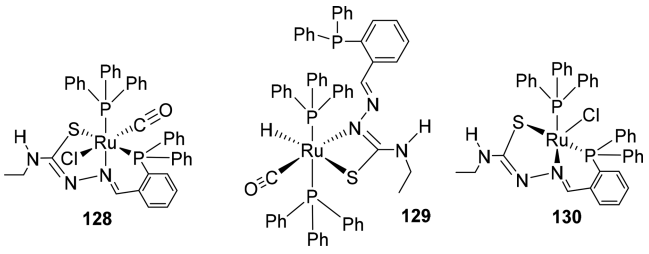


[a]Adapted from ref 203. Published by the Nature Publishing Group. This work is licensed under a Creative Commons Attribution 4.0 International License.

Scheme 44. Schematic Representation of the *N*-Alkylation of Amides

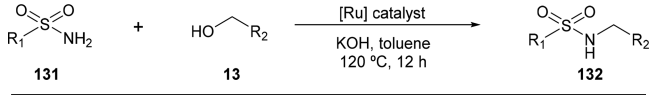


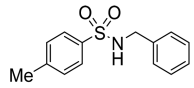
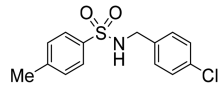
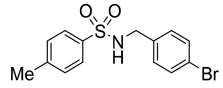
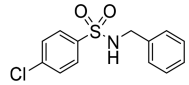
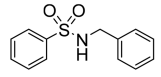
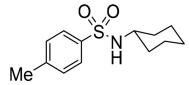
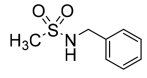
Scheme 45. Structure of Ruthenium(II) (128−130) Complexes Used As Catalysts in the *N*-Alkylation of Sulfonamides with Alcohols by Ramachandran et al.[a]



[a]Adapted with permission from ref 190. Copyright 2015 Royal Society of Chemistry.

Table 9. Results of the *N*-Alkylation of Sulfonamides with Ruthenium Catalysts 128−130.[a]



Entry	Product	Yield[b] (%)		
		128	129	130
1		82	91	84
2		95	99	85
3		86	94	82
4		93	97	89
5		88	92	87
6		62	74	71
7		21	54	46

[a]Adapted with permission from ref 190. Copyright 2015 Royal Society of Chemistry. Reaction conditions: 2.00 mmol of sulphonamides, 2.00 mmol of alcohol, KOH (50 mol %), catalyst (0.5 mol %) in 2 mL of toluene at 120 °C. [b]Yields were calculated after isolation of the pure *N*-alkylated amine through column chromatography using silica gel (100−200 mesh).

Hence, due to the interest in oxidizing amines to imines (analogously to alcohols) by a transition metal complex, a few reactions involving transfer hydrogenation processes with amines[233−236] and related reactions such as racemization of amines[237] soon appeared in the literature. In parallel, research studies showed that alkyl amines could also participate in BH processes for forming imines and/or iminium cations, so that they may undergo analogous reactions to aldehydes and ketones as it will be shown.

2.3.1. Formation of C−C Bonds. *2.3.1.1. α-Alkylation.* Cho et al. reported the α-alkylation of ketones with trialkylamines as hydrogen donors,[238] in which the alkyl group was transferred by the in situ prepared catalyst of ruthenium ($RuCl_3$ and PPh_3) to give the final product.

From these results, a variety of amines and ketones were reacted with this catalytic system. The reaction might take place presumably through an iminium intermediate that would react with the enolate derived from the ketone. The release of a secondary amine would lead to the alkylated ketone. This ruthenium-catalyzed reaction was regioselective and constituted the first example of alkyl-group transfer from trialkylamines (and imines) to the α-carbon atom of ketones.

Later on, the same group reported the regioselective alkyl moiety transfer from a primary amine (**82b**) to a ketone (**12a**), following this procedure (Scheme 49).[239]

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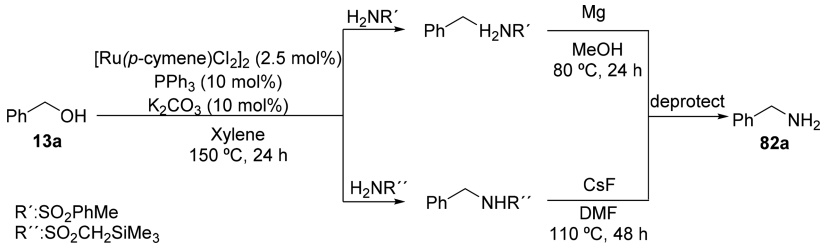
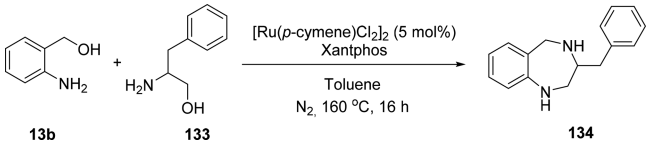
Chem. Rev. 2018, 118, 1410−1459

Scheme 46. Synthesis of Amine 82a by Borrowing Hydrogen Methodology through in Situ Sulfonamide Deprotection[a]



[a]Adapted with permission from ref 222. Copyright 2009 Elsevier.

Scheme 47. Ru Catalyzed Benzodiazepine Derivatives (93) Synthesis Reported by Taddei et al[a]



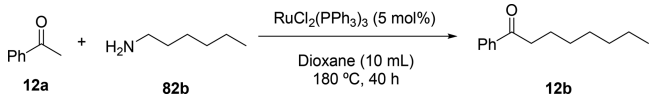
[a]Adapted with permission from ref 225. Copyright 2015 Wiley-VCH.

This new contribution has the advantage of allowing access to the same products obtained with trialkylamines but generating ammonia instead of secondary amines as by-products. The reaction pathway may undergo an analogous mechanism to that observed for alkyl transfer reactions with two different amines (see the following section 2.3.2.1).[240]

2.3.2. Formation of C−N Bonds. *2.3.2.1. Condensation. 2.3.2.1.a. N-Alkylation of Amines.* In close analogy to the *N*-alkylation of amines with alcohols (see section 2.2.2.2.b), amines are also suitable candidates for being dehydrogenated in a first reaction step. In this case, the metal catalyzes the oxidative dehydrogenation of the starting amine to give a new imine electrophile, which immediately reacts with a second amine molecule to form an unstable aminoaminal intermediate. The latter extrudes ammonia to form a new imine intermediate that is subsequently hydrogenated by the metal hydrides leading to the alkylated final amine (Scheme 50).

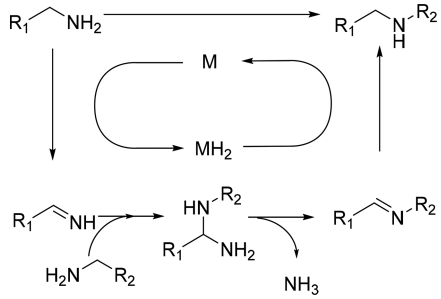
One of the numerous homogeneous catalysts reported for activating amines as hydrogen donors was described by Hollmann et al.[241] In this case, the reaction was carried out in the presence of the Shvo catalyst. In this case, a compilation of aniline derivatives and primary amines reacted smoothly to provide the corresponding aromatic amines in excellent yields. It is worth mentioning the ability of iridium catalyst [e.g., $\{Cp^*IrCl_2\}_2$ and alanine triazole iridium(III) complex],[242,243]

Scheme 49. α-Alkylation of Acetophenone with Hexylamine Catalyzed by a Ru Complex[a]



[a]Adapted with permission from ref 239. Copyright 2006 Elsevier.

Scheme 50. Primary Amine Alkylation Using Amines as Hydrogen Donors in BH Processes

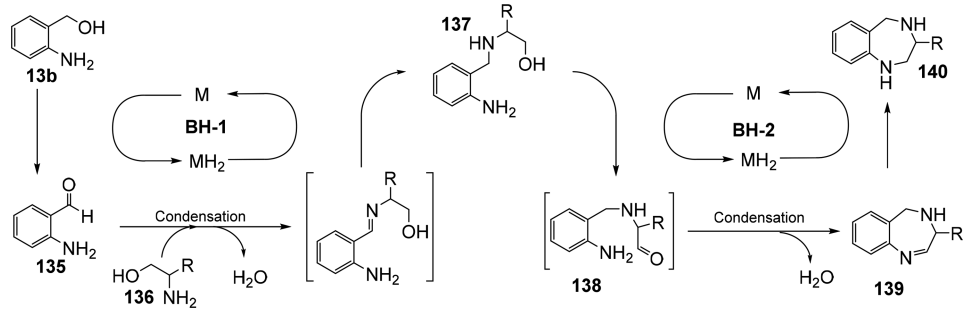


to couple two amines with excellent selectivity, even in the absence of bases. Indeed, amazingly even though both amines were exposed to undergo oxidation to the respective imine, only one of them behaved as a hydrogen source.[242]

For instance, one recent example described the cross-coupling of an alkyl amine and an aromatic amine using hydrogen autotransfer methodology. The catalyst was an alanine triazole iridium catalyst which efficiently promoted the C−N bond formation by reacting two different types of amines (Figure 6).[243]

Once the best catalytic conditions were identified, the BH method for forming amines was tested by using triethylamines as alkylating agent and the above-mentioned iridium catalyst. In

Scheme 48. Plausible Reaction Scheme for the Benzodiazepine Synthesis[a]



[a]Adapted with permission from ref 225. Copyright 2015 Wiley-VCH.

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Chem. Rev. 2018, 118, 1410−1459

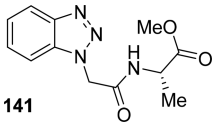


Figure 6. Alanine triazole compound (ATAs) (**141**) coordinatively bonded to $IrCl_3$ compound used as catalyst. Adapted with permission from ref 243. Copyright 2016 Elsevier.

this case, a wide range of functional groups was tolerated at different positions (methoxy, methyl, chloro, *tert*-butyl, etc.). The corresponding amines were obtained from moderate-to-good yields.

Alternatively, an interesting application of this strategy consisted of the catalytic *α,β*-H/D-exchange for tertiary amines in the presence of the Shvo's catalyst studied by the Beller's group.[244] This is the only study reported so far based on this particular strategy to accomplish the *α,β*-H/D exchange.

As has been highlighted previously, the replacement of classic ruthenium and iridium complexes by less expensive earth abundant elements is a major goal in synthetic chemistry. This has materialized in this case by using cobalt complexes in recent examples to synthesize amines. In this regard, it is interesting to remark a recent contribution by Yin and co-workers.[245] This group reported for the first time a series of cobalt pincer complexes (**142**−**147**) able to efficiently catalyze the synthesis of a broad range of aromatic, aliphatic, and cyclic sec-amines, with amines as starting materials. These Co-complexes showed similar activities to those which were observed with previous Ir and Ru complexes (Figure 7).[245]

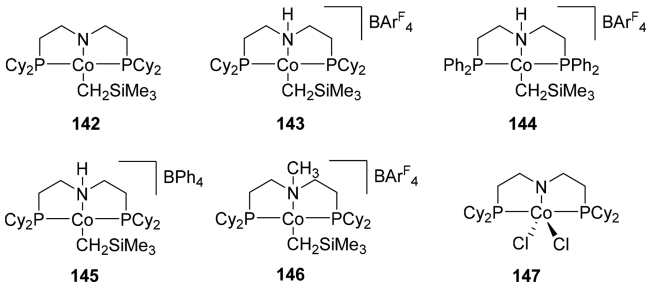


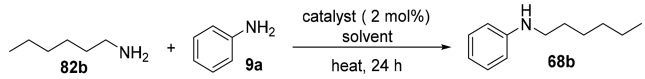
Figure 7. Cobalt pincer complexes (**142**−**147**) used as catalysts. Reproduced from ref 245. Copyright 2016 American Chemical Society.

Aniline (**9a**) and 1-hexylamine (**82b**) were reacted in the presence of these complexes as model reactions. In accordance with the results included in the following table, the neutral catalyst **1** was inactive. Fortunately the ionic cobalt(II) complex **143** was highly efficient, giving rise to the expected *N*-alkylated amine with almost quantitative yield (entries 1−2, Table 10).[245]

After a wide screening in order to find the best experimental conditions, the authors found that toluene was the best solvent at 120 °C (Table 10).

2.3.2.1.b. N-Alkyl Exchange (Transalkylation). The synthetic utility of transalkylation reactions is evident if we take into account that mixed alkyl amines are intermediates in important industrial synthetic processes ranging from biocides, phase transfer catalysts, surfactants, and polymerization catalysts.[246] Here the process by which the C−H bond is activated and the way that subsequent *N*-alkyl transfer takes place is closely related to reactions that are the subject of this review. Indeed, in agreement with isotopic labeling experiments, the metal inserts into a *α*-C−H bond, giving a metallazacyclopropane or metal-iminium complex. Then, the nucleophilic free amine will attack the catalyst, and rearrangement of the intermediate will take place to give the transalkylation products (Scheme 51).[247]

Table 10. Results of the Catalyzed Amination of Aniline with Hexylamine with Different Co(II) Catalysts and Different Experimental Conditions[a]



entry	catalyst	solvent	yield (%)[b]
1	1	toluene	0
2	2	toluene	98
3	3	toluene	86
4	4	toluene	<5
5	5	toluene	0
6	6	toluene	0
7	-	toluene	0
8	2	THF	43
9	2	hexane	25
10	2	benzene	90
11	2	1,4-dioxane	47
12[c]	2	toluene	42
13[d]	2	toluene	85

[a]Reproduced from ref 245. Copyright 2016 American Chemical Society. Conditions: 1-hexylamine (0.5 mmol), aniline (0.6 mmol), catalyst (2 mol % Co), and solvent (4 mL) are heated at 120 °C in a 100 mL Schlenk tube, 24 h. [b]Determined by GC analysis. [c]Reaction was run at 100 °C. [d]Reaction was run in a 50 mL Schlenk tube.

Examples of homogeneous catalysts known since 1980, which catalyze alkylation reaction exchange between tertiary amines are $Ru_3(CO)_{12}$, $Os_3(CO)_{12}$, and $Ir_4(CO)_{12}$.[248]

From these pioneering studies, and several years later Lee et al. reported the synthesis of indole derivatives (**149**) from aniline and trialkylamines (**148**) catalyzed by a ruthenium complex formed in situ from $RuCl_3{\cdot}nH_2O$ and PPh_3 (Scheme 52).[247]

The authors proposed an intermolecular alkyl group transfer between amines as a key step in the reaction mechanism on the bases of a previous work.[249]

The same Ru catalyst was applied for the synthesis of quinolines starting from aniline (**9a**) and 3-aminopropanol[250] or tris(3-hydroxypropylamine) (**152**),[251] respectively, where a *N*-alkyl exchange step was also involved (Scheme 53).[251]

The scheme shows that the reaction occurs involving an initial propanol transfer from tris(3-hydroxypropyl)amine to aniline (amine exchange reaction) to provide 3-anilino-1-propanol (**151**). *N*-Alkylation of aniline with **151** will form 1,3-dianilino propane (**150**) (cycle A, Scheme 53), followed by heteroannulation (cycle B, Scheme 53).

The reaction took place in the presence of $SnCl_2{\cdot}2H_2O$ as an additive, albeit its exact role is not completely understood. Curiously, despite a hydrogen acceptor molecule not being needed, the yield of the desired *N*-heterocycle (**153**) substantially improved when a ketone, an alkene, or an alkyne was added to the reaction mixture (Table 11).

This approach shows that synthesis of *N*-heterocycles is possible using transition metal catalyzed exchange reactions.

Similarly, another significant contribution of this group was the synthesis of quinolines starting from anilines and tertiary

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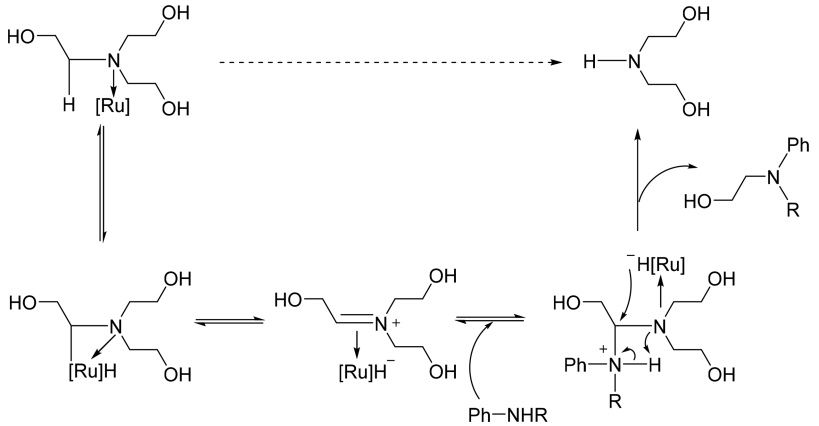
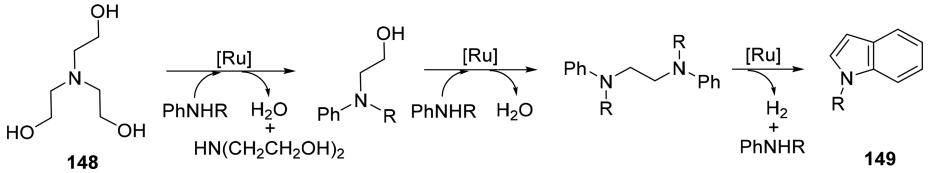
Scheme 51. Proposed Synthetic Sequence for Transalkylation Reaction[a]



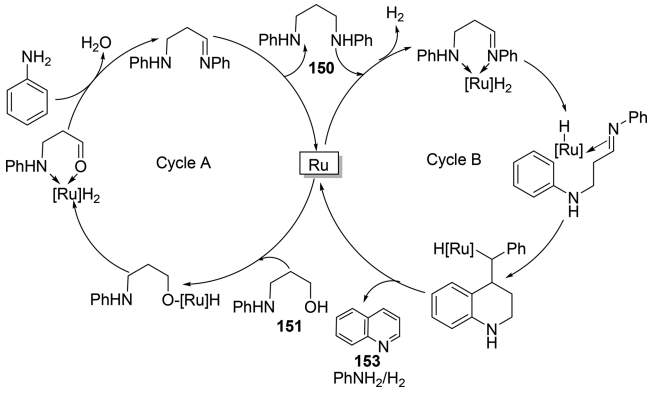
[a]Adapted with permission from ref 247. Copyright 1996 Korean Chemical Society.

Scheme 52. Indole Derivatives (149) Formation Path from Trialkylamines and Aniline Involving a Transalkylation First Step Reported by Cho et al[a]



[a]Adapted with permission from ref 247. Copyright 1996 Korean Chemical Society.

Scheme 53. Schematic Representation of the Synthesis of the *N*-Heterocycle Quinoline from Aniline and Tris(3-hydroxypropylamine) Catalyzed by $RuCl_3$[a]

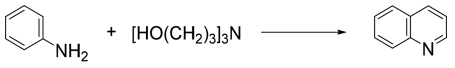


[a]Adapted with permission from ref 251. Copyright 2003 Korean Chemical Society.

amines, avoiding the use of aminoalcohols in the process. Particularly, they studied the alkyl transfer reaction of aniline and triallylamine to get quinolines in the presence of $RuCl_3 \cdot nH_2O$ and $SnCl_2 \cdot 2H_2O$ as an additive. The stannous(II) salt was indeed necessary to get an effective heteroannulation reaction. Furthermore, instead of trialkyl amines, the allylammonium chloride compound as well as 1-hexene (the latter as hydrogen acceptor) could be employed for the synthesis of quinolines.[252,253]

As previously stated, despite the fact that the role of stannous (II) chloride was not completely unraveled, the formation of imines during the first reaction stages appeared to be a decisive step. Ulterior steps appear to be followed by a Schiff-base

Table 11. Synthesis of Quinolones by $RuCl_3 \cdot nH_2O$ as Catalyst.[a]



entry	ruthenium catalyst	hydrogen acceptor	yield (%)[b]
1	$RuCl_3 \cdot nH_2O/3PPh_3$	acetone	60
2[c]	$RuCl_3 \cdot nH_2O/3PPh_3$	acetone	5
3	$RuCl_3 \cdot nH_2O/3PPh_3$	–	35
4	$RuCl_3 \cdot nH_2O/3PPh_3$	acetophenone	49
5	$RuCl_3 \cdot nH_2O/3PPh_3$	dodec-1-ene	45
6	$RuCl_3 \cdot nH_2O/3PPh_3$	oct-1-yne	26
7	$RuCl_2(PPh_3)_3$	acetone	33
8	$RuCl_2(=CHPh)(PCy_3)_2$	acetone	21
9	$Ru_3(CO)_{12}$	acetone	45
10	$RuH_2(PPh_3)_4$	acetone	9
11	$Cp^*RuCl_2(CO)$[d]	acetone	18

[a]Adapted with permission from ref 251. Copyright 2003 Korean Chemical Society. Reaction conditions: **9a** (4 mmol), **152** (1 mmol), hydrogen acceptor (10 mmol), ruthenium catalyst (0.05 mmol), $SnCl_2 \bullet 2H_2O$ (1 mmol), dioxane (10 mL), 180 °C, for 24 h, under argon. [b]GLC yield based on **152**. [c]In the absence of $SnCl_2 \cdot 2H_2O$. [d]$Cp^* = \eta^5\text{-}C_5Me_5$.

dimerization[254] as well as ruthenium-mediated heteroannulation, with the participation of 1-hexene.[255]

Continuing with the transalkylation reaction, previous studies by Cho et al. described the efficient *N*-monoalkylation of aromatic anilines (**9**) with tetraalkylammonium halides (**154**).[256] Both the ruthenium complex formed in situ (from $RuCl_3$ and PPh_3) as well as $[Ru_3(CO)_{12}]$ showed catalytic activity in the reaction. The incorporation of $SnCl_2$ was necessary for enlarging the yield of monoalkylated product

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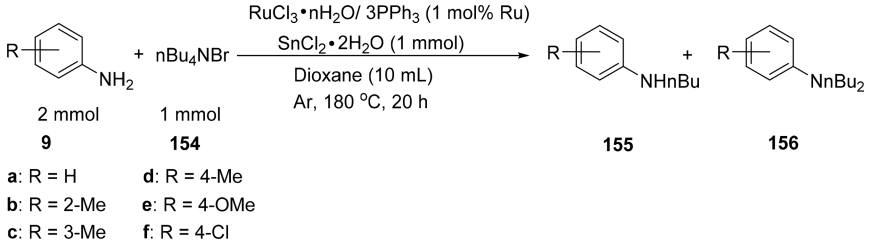
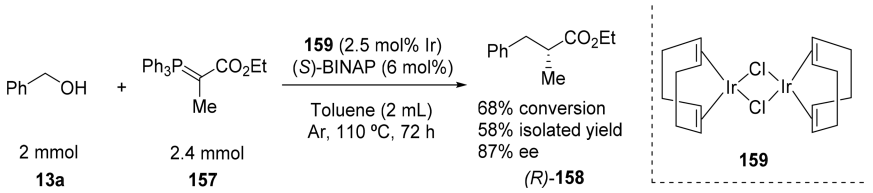
Scheme 54. *N*-Alkylation of anilines (9) with the Tetraalkylammonium Halide 154[a]



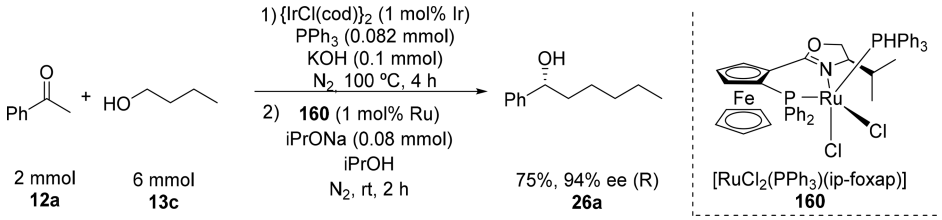
[a]Adapted with permission from ref 256. Copyright 2001 Taylor & Francis, Inc.

Scheme 55. Optimized Reaction Conditions for the Indirect Asymmetric Wittig Reaction with $[Ir(cod)Cl]_2$ /BINAP[a]



[a]Adapted with permission from ref 262. Copyright 2007 Elsevier.

Scheme 56. Reaction of Acetophenones with Butanol in the Presence of an Iridium and a Ruthenium Complex[a]



[a]Adapted with permission from ref 263. Copyright 2006 Wiley-VCH.

(**155**) compared to the dialkylated product (**156**). In this case, only a short number of aniline derivatives and tetraalkylammonium halides were transformed into moderate yields (Scheme 54).[256]

Trialkylamine can be considered as the true alkylating agent because it has been shown that quaternary ammonium salts can be transformed into tertiary amines by cleavage of the carbon−nitrogen bond in an aqueous medium.[257] Indeed, it was absolutely confirmed that the aromatic amine, aniline, reacted with tributylamine in the presence of a similar bifunctional tin−ruthenium catalyst to give **155** and **156**.[256]

More recent literature reports on the activity of several new bisbenzoxazolyl iridium(III) complexes pointed out that these complexes were excellent catalysts for C−N bond formation through the *N*-alkylation of *N*-arylamines with tertiary amines. Interestingly, all the substrates were completely transformed into the corresponding alkylated amines, while the addition of $AgNTf_2$ to the reaction mixture was comparatively more effective.[258] This may be because ionic complexes formed in situ upon addition of these silver salts can more easily coordinate with different substrates so they may have a better catalytic activity.

In summary, the use of amines as a source of H_2 has had much less impact when compared to alcohols, if we take into account the number of references and catalysts reported in the literature. This can be surely due to the inevitable loss of NH_3 in the reaction which makes amines less attractive as hydrogen donors from the operational and sustainability point of view. However, owing to the importance of catalytic transalkylation reactions as a potentially valuable strategy for the obtention of unsymmetrical tertiary amines, efforts have been focused on increasing the yields of these products by using cocatalysts and additives ($Sn(II)Cl_2$ or $AgNTf_2$) or by searching for other metals like palladium, hence highlighting it as one of the reactions that deserves to be studied in more detail.

2.4. Asymmetric Borrowing Hydrogen Catalysis

The most significant advances achieved in the stereoselective reduction of unsaturated organic functions (C═O, C═N, and C═C) through hydrogenation-transfer processes with homogeneous catalysts have been briefly reviewed.[259,260] In this context, asymmetric catalysis on the bases of the BH concept has also been explored. This powerful strategy that combines hydrogenation transfer with an intermediate reaction without requiring a separation process has been used to form asymmetric carbon−carbon and carbon−nitrogen bonds using alcohols as a hydrogen source.[13,261]

In accordance to this, few significant studies that appeared in the literature on asymmetric borrowing catalysis have been dealt with in a relatively recent microreview.[13]Nonetheless, we will include some of these references in this review in order to draw the readers attention to them since there have not been ulterior examples on the asymmetric reaction through BH methodology (Wittig type reaction and the chiral amination of alcohols approach).

Thus, significant studies on asymmetric catalysis will be included in the incoming sections.

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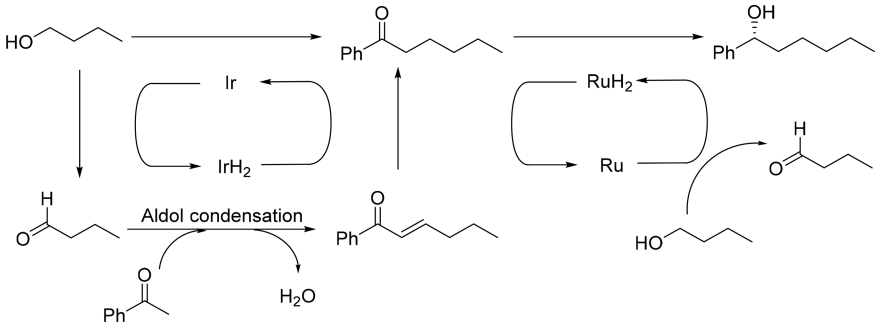
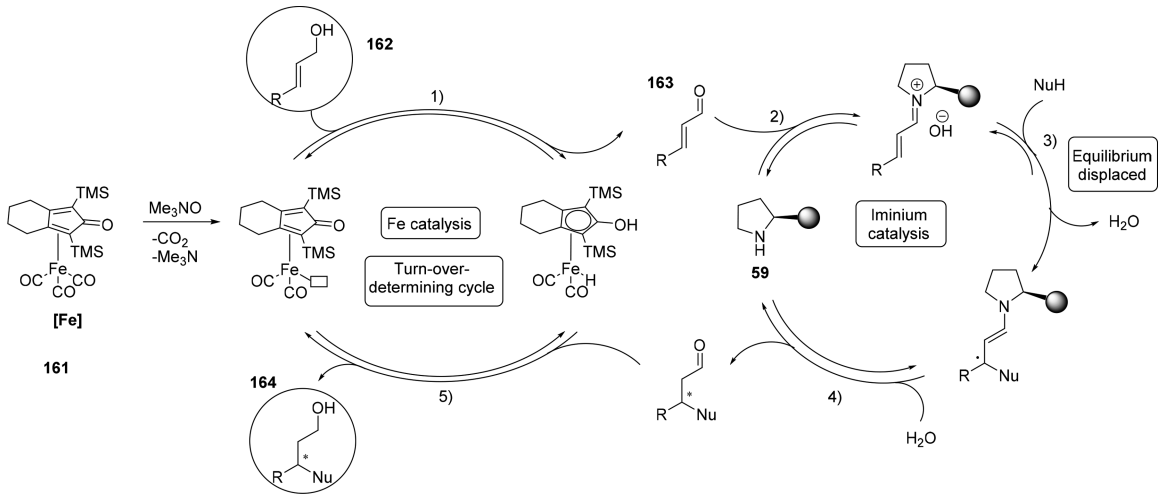
Scheme 57. Combination of α-Alkylation of Ketones As Well As Transfer Hydrogenation Reaction with Iridium and Ruthenium Complexes[a]



[a]Plausible reaction pathway. Adapted with permission from ref 263. Copyright 2006 Wiley-VCH.

Scheme 58. Schematic Representation of the Proposed Mechanism for the Iron/Amine Catalyzed Process (TMS = Trimethylsilyl)[a]



[a]Adapted with permission from ref 264. Copyright 2013 Wiley-VCH.

2.4.1. Activation of C−O Bonds (Alcohols). *2.4.1.1. Formation of C−C Bonds. 2.4.1.1.a. Wittig Reaction.* One of the first reports on Wittig type reactions with asymmetric variations was accomplished with the iridium precursor $[Ir(cod)Cl_2]_2$ (**159**) combined with different chiral ligands. The highest enantiomeric excess (ee) of the reduced Wittig product (**158**) was obtained using BINAP type ligands by reacting the Wittig reagent (**157**) and one alcohol (**13a**) (Scheme 55).[262] The shortening of the reaction time, as well as increasing ee and yield were clear challenges in this case.

2.4.1.1.b. Aldol Condensation. The occurrence of asymmetric α-alkylation reduction of a prochiral ketone (**12a**) with aliphatic alcohols (e.g., **13c**) has been reported to provide optically active alcohols (e.g., **26a**) with high levels of enantioselectivity in the presence of ruthenium (**160**) as well as iridium complexes (Scheme 56).[263]

In close similarity, an intensive process consisting of combining the α-alkylation of ketones with transfer hydrogenation in the presence of an iridium and a ruthenium complex to get asymmetric alcohols has been reported by Nishibayashi et al. The reaction sequence involved one iridium-catalyzed dehydrogenation of a primary alcohol, followed by a base-catalyzed aldol reaction to afford an α,β-unsaturated ketone. The latter was hydrogenated to give the α-alkylated product, which was asymmetrically reduced to optically pure alcohols (up to 98% ee) using a chiral ruthenium catalyst (Scheme 57).[263]

The compatibility between ruthenium and iridium complexes was crucial in obtaining optically active alcohols with high enantioselectivity as well as in the elongation of the carbon skeleton. For example, a mixture of acetophenone and 1-butanol were transformed into (*R*)-1-phenyl-1-hexanol with 75% yield and 94% ee using $[IrCl(COD)]_2$ and PPh_3, followed by incorporation of $[RuCl_2(PPh_3)(ip\text{-}foxap)]$.

2.4.1.1.c. Conjugate Addition. In a more recent approach an iron-catalyzed (**161**) hydrogen autotransfer process has been coupled to an organocatalytic cycle in a dual manner. The strategy relies on the combination of an organocatalytic Michael addition to unsaturated carbonyl compounds (**163**), formed in situ from the corresponding alcohol (**162**), with an aminocatalytic step. The resulting bicatalytic system enables the transformation of allylic alcohols into β-chiral alcohols (**164**) under mild conditions and with high enantioselectivity (up to 95:5 e.r).[264] The key to success was the insertion of the iminium cycle into the iron-catalyzed hydrogen autotransfer process (Scheme 58).[264]

2.4.1.2. Formation of C−N Bonds. Condensation. 2.4.1.2.a. N-Alkylation of Amines (Amination of Alcohols with Amines). As expected, the stereoselective synthesis of aminated alcohols (**167**) through a *N*-monoalkylation of

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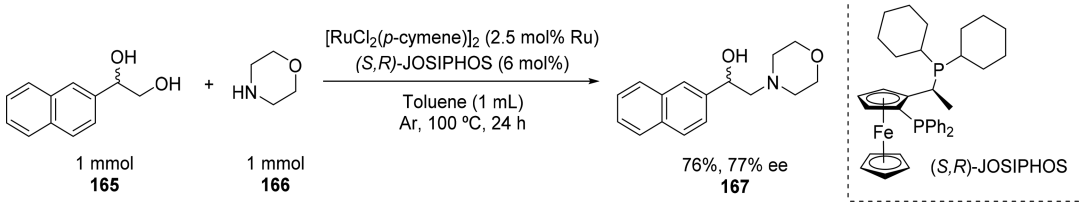
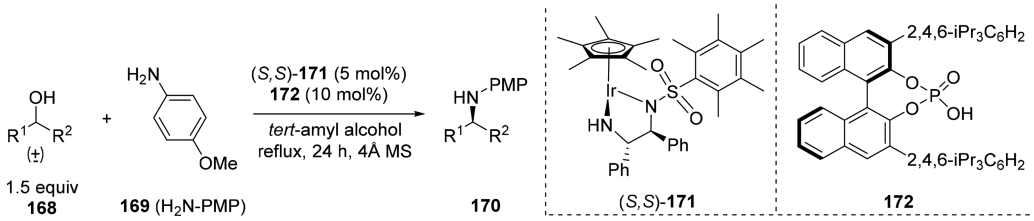
Scheme 59. N-Alkylation of Morpholine with 1-Phenyl-1,2-Ethanediol Carried out in the Presence of $[RuCl_2(p\text{-cymene})]_2$ and Chiral Ligand (S,R)-JOSIPHOS[a]



[a]Adapted with permission from ref 265. Copyright 2013 Wiley-VCH.

Table 12. Results on the Enantioselective Amination with Different Alcohols Using an Iridium Catalyst (171) and a Chiral Phosphoric Acid (172)[a]



entry	R^1	R^2	product	yield[b] (%)	ee (%)
1	*n*-hexyl	Me	**170a**	90	93
2[c]	nBu	Me	**170b**	90	92
3[d]	nPr	Me	**170c**	86	90
4	iPr	Me	**170d**	66	96
5	cyclohexyl	Me	**170e**	92	97
6	cylopropyl	Me	**170f**	93	91
7	$iPrCH_2$	Me	**170g**	75	82
8	$PhCH_2CH_2$	Me	**170h**	98	83
9	$BnO(CH_2)_3$	Me	**170i**	64	85
10	$TBSO(CH_2)_3$	Me	**170j**	95	91
11	Ph	Me	**170k**	81	91
12	$4\text{-}MeC_6H_4$	Me	**170l**	97	91
13	$4\text{-}MeOC_6H_4$	Me	**170m**	72	96
14	$4\text{-}BrC_6H_4$	Me	**170n**	69	83
15	$4\text{-}CF_3C_6H_4$	Me	**170o**	90 (40)[e]	70 (94)[e]
16	$3\text{-}MeC_6H_4$	Me	**170p**	83	94
17	1-naphtyl	Me	**170q**	80	94
18	$4\text{-}MeC_6H_4$	Et	**170r**	75	73
19	1-naphtyl	Et	**170s**	71	69
20[f]	iPr	Et	**170t**	80	75

[a]Adapted with permission from ref 266. Copyright 2014 Wiley-VCH. All reagents were used as received from the commercial supplier without purification. [b]Yield of isolated product. [c]3 equiv of the alcohol. [d]5 equiv of the alcohol. [e]Values in parentheses from reaction carried out at 80 °C for 48 h. [f]Reaction carried out in refluxing toluene for 24 h.

amines has also been addressed giving interesting optically active β-amino alcohols with high yields (76%) and moderate enantiomeric excess (77%). In the model reaction, 1,2-diols (**165**) will react with secondary amines (**166**) in the presence of a ruthenium catalyst coordinated to a chiral phosphine JOSIPHOS ligand (Scheme 59).[265]

In a much simpler example, the enantioselective amination of alcohols (**168**) with aromatic amines (**169**) for the synthesis of chiral amines (**170**) has been reported in the literature. In this case, diverse transition metal complexes formed by coordination with chiral ligands of preference for asymmetric hydrogenations were studied in combination with chiral Brönsted acids.[266] Table 12 shows the results obtained with a set of alcohol substrates and one iridium complex (**171**) and a chiral phosphoric acid (**172**).

2.4.1.2.b. N-Alkylation of Sulfonamides. Similarly, a ruthenium(II) PNP-type pincer catalyst (Ru-MACHO) (**173**) has been shown to catalyze the synthesis of α-chiral *tert*-butanesulfinylamines (**178**), from the Ellman's chiral *tert*-butanesulfonamide (**174**) and a sort of racemic secondary alcohols such as (**175**) via a BH strategy. This process involved the oxidation of the alcohol to a ketone (**176**), formation of the coupled intermediate (**177**), and a final reduction step.[267] The yield of α-chiral tert-butanesulfinylamines reached up to 89% with most reactions giving >95:5 dr.

The racemic alcohol (**175**) is oxidized by a Ru-pincer (**173**) complex to form a Ru-hydride and a ketone (**176**). The ketone would undergo condensation with the sulfonamide (**174**) to form the sulfinylimine (**177**). Finally, hydrogenation of the latter by the Ru-hydride complex would efficiently occur for

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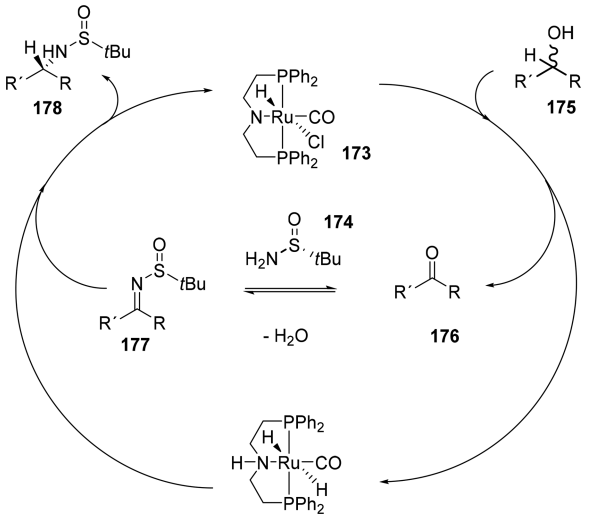
accessing the α-chiral sulfinylamine (**178**) with high diastereoselectivity (Scheme 60).[267]

Scheme 60. Mechanism for the Hydrogen Borrowing via a Ruthenium(II) Pincer Complex (Ru-MACHO). Reproduced from ref 267. Copyright 2014 American Chemical Society



One of the most interesting conclusions drawn from this section is that most of the enantioselective processes are still unapproachable through BH methodology because there are still high barrier processes to induce some kind of enantioselection. This justifies the scarce number of examples that have appeared in the literature on the topic. Thus, in the short/medium term there is a need for new catalysts that help to overcome this energy limitation. From another perspective, research into the synthesis of new chiral primary amines (from racemic alcohols and ammonia), enantiopure amines (through amination of racemic amines), or asymmetric functionalization of the β-position via enamines remain as the three main goals that should be undertaken.

3. BORROWING HYDROGEN METHODOLOGY IN HETEROGENEOUS CATALYSTS

Heterogeneous catalysis through BH methodology slowly started to develop driven by the advances in homogeneous catalysis. However, in recent years it seems that heterogeneous catalysis is starting to take off. Indeed, the progress in designing heterogeneous catalysts for a sustainable synthesis in autotransfer processes is a growing area of research due to the advantages in terms of efficiency and sustainability. In this context, a variety of approaches going from the most simple and classic processes to the most novel and original ones for separating, recovering, and recycling heterogeneous catalysts have been reported in BH transformations.[268,269]

In this section, we will summarize recent examples on the straightforward synthesis of chemicals by the BH methodology with heterogeneous catalysts that will complement two previous microreviews.[9,12] We will describe new examples according to the classification of this review. Exceptionally in the absence of new references, we will describe examples included in previous revisions so that readers do not miss out on the wide variety of different intermediate reactions catalyzed by heterogeneous catalysts (especially on the issue of activation of alcohols).

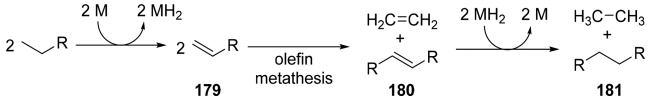
3.1. Activation of Alkanes

3.1.1. Formation of C–C Bonds. *3.1.1.1. Olefin Metathesis.* As previously stated in the section 2.1, alkane activation has been a target for research in the last century and is even more important today due to the finding of valuable reserves of natural gas.[270] At the same time, the olefin metathesis, a reaction which has been receiving increasing attention since its discovery, has led to the implementation of relevant industrial procedures such as the Lummus ABB process, which converts the ethylene into propylene using heterogeneous catalysts.[271]

Taking into account these precedents, the BH methodology allowed the combination of both processes toward the transformation of a specific alkane into its higher and lower counterparts as previously shown in section 2.1. This fact triggered intensive research on the set up of heterogeneous catalytic systems, leading to the discovery of one of the first industrial alkane metathesis processes.[272−274]

In general, the BH heterogeneous version follows the same reaction steps described with homogeneous catalysts (section 2.1), hence involving the dehydrogenation of the initial alkane into an alkene (**179**), followed by metathesis of the alkene and hydrogenation of the metathesis product (**180**) to yield a new alkane (**181**) (Scheme 61).[26,275]

Scheme 61. Alkane Metathesis via Transfer Hydrogenation-Olefin Metathesis[a]



[a]Adapted with permission from ref 26. Copyright 2006 AAAS.

For doing this, a combination of a dehydrogenation/hydrogenation catalysts, for instance Pt/Al_2O_3, and a metathesis catalyst such as WO_3 on silica was devised. Unfortunately, the dehydrogenation step was thermodynamically disfavored at low temperatures, and consequently, a temperature of 400 °C was required to get a high concentration of the olefin.

Similarly, a different dual catalytic system was developed using a partially heterogeneous catalytic system consisting of Re_2O_7/Al_2O_3 and different homogeneous iridium catalysts (**1**, **2**, **3**, **182**−**185**) deposited on γ-Al_2O_3 (Figure 8). The resulting catalysts were active in the metathesis of *n*-decane.[276]

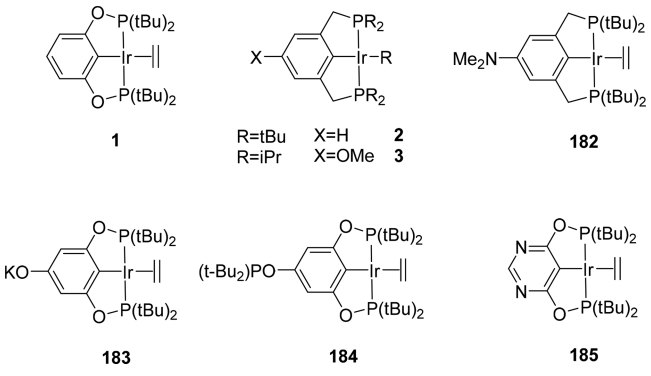


Figure 8. Iridium complexes **1**, **2**, **3**, **182**−**185** deposited onto γ-Al_2O_3. Adapted with permission from ref 276. Copyright 2010 Wiley-VCH.

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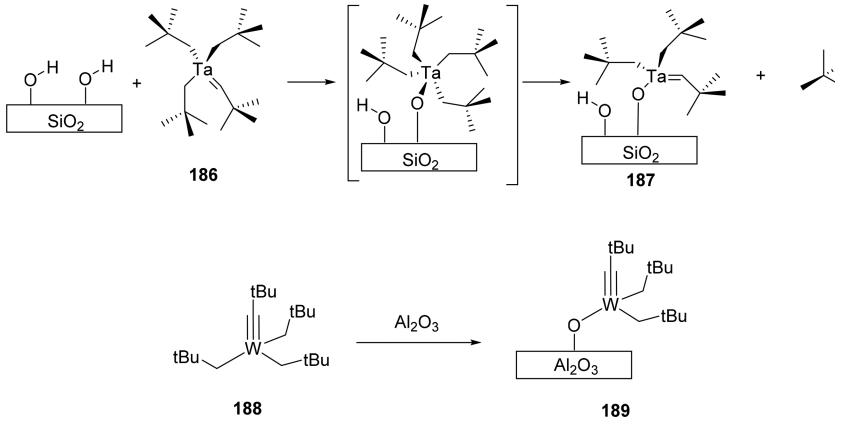
Scheme 62. Examples of Ta and W Complexes (186 and 188) Active for Alkane Metathesis and Their Heterogeneous Counterparts on SiO_2 and Al_2O_3 (187 and 189)[a]



[a]Adapted with permission from ref 279. Copyright 1999 Elsevier B.V. Adapted with permission from ref 287. Copyright 2005 Wiley-VCH.

Interestingly, the metathesis of *n*-decane by supported $Ir(C_2H_4)/Al_2O_3$ and Re_2O_7/Al_2O_3 [(molar ratio Ir:Re(1:2.5)] afforded a different distribution of alkanes.[276] Furthermore, the strong adsorption of the iridium pincer catalysts on γ-alumina apparently prevented the unfavorable interaction between the iridium species and Re_2O_7 responsible for decomposition.

Basset et al. reported a set of single site tantalum[277−286] or tungsten-derived heterogeneous catalysts[287,288] active for this reaction. Examples of some these grafted complexes (**186−189**) are displayed in the following scheme (Scheme 62).[279,287]

In this case, the alkane metathesis was conceived by using a single metal catalyst with dual activity (e.g., tantalum or tungsten).[289−297] Therefore, the active site would have all the required properties to complete the whole process. That is C−H activation, dehydrogenation, hydrogenation, and metathesis. These results were complemented by studies on the reaction mechanism by supported tantalum hydride complexes.[298−300]

In this regard, an interesting recent study by Basset et al. reported the influence of the support on the metathesis reaction of *n*-decane in the presence of WMe_5 on silica−alumina.[301] Indeed the importance of the metathesis catalyzed by tungsten systems has been reinforced by the expansion of this reaction in different hydrocarbon valorizations.[302]

In this line, the same group reported a highly efficient molybdenium imido complex (**190**) as precatalyst for alkane metathesis as well as a molybdenum/imido neopentyl (Np) neopentylidene (**191**) catalyst, both of them supported on silica (Figure 9).[303,304]

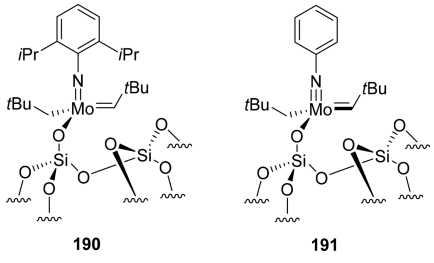


Figure 9. Structure of the molybdenum catalysts for alkane metathesis. Adapted with permission from ref 303. Copyright 2006 Wiley-VCH. Adapted with permission from ref 304. Copyright 2008 Wiley-VCH.

A fact that highlights the importance of this reaction is the number of patents and academic reports that have been published for manufacturing alkanes using alkane metathesis as well as the preparation of supported organometallic compounds as catalysts.[305−307]

In parallel, efforts have also focused on bifunctional catalysts on which the synergy between a supported bimetallic Zr/W catalyst has been studied taking the metathesis reaction of *n*-decane as a model reaction.[308] In this line, Zr-polyhydrides supported on SiO_2 or SiO_2/Al_2O_3 were also able to convert propane into lower and higher homologues, with 2-methylpropane being the major product.[309] Besides this, tantalum hydrides were also examined. For example, the Schrock tantalum alkylidene $Ta(=CHCMe_3)(CH_2CMe_3)_3$ was grafted onto partially dehydroxylated silica to generate a mixture of grafted complexes.[310] Besides, the synthesis and characterization of a Ta−H supported on tetrahedral $Zr(OH)_4$ was also accomplished [$TaHx/ZrO_2−SiO_2$].[311] With this catalyst, a much better reactivity and selectivity values were obtained for the alkane metathesis with respect to the original $TaHx/SiO_2$. For example, for the propane metathesis, the observed TON was 100 with [$TaHx/ZrO_2−SiO_2$] as catalyst compared to 58 for $TaHx/SiO_2$ at 150 °C after 120 h. The improved activity of [$TaHx/ZrO_2−SiO_2$] was attributed to its slower deactivation rate. Different supports for Ta-polyhydrides such as SiO_2/Al_2O_3 and Al_2O_3 were also employed as supports; although this time, similar results to those obtained with $Ta−H/SiO_2$ were achieved for the metathesis of propane in terms of activity and selectivity. This behavior contrasts sharply with the $ZrO_2−SiO_2$ system, which has a tetrahedral Zr atom that separates the tantalum center from the coordinating surface oxygens.

Other related supported hydrides such as WHx/SiO_2 were found to be less active for alkane metathesis than $TaHx/SiO_2$. The grafting of a Schrock precursor on alumina or silica/alumina was also studied leading to more stable supported polyhydrides [$WHx/SiO_2−Al_2O_3$] and [WHx/Al_2O_3].[288,312]

In close connection to the tungstene hydrides, the preparation of silica supported W-neopentylidene, alumina supported W-carbyne complexes, as well as silica supported WMe6 were reported.[313−316]

3.2. Activation of Alcohols

A compilation of heterogeneous C−C and C−N forming reactions through BH methodology using different intermedi-

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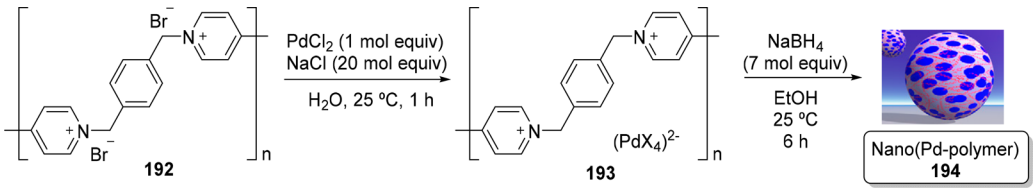
Scheme 63. Preparation of Solid Metal Nanoparticles of Pd Starting form $PdCl_2$ and the Non-Cross-Linked Viologen Polymer[a]



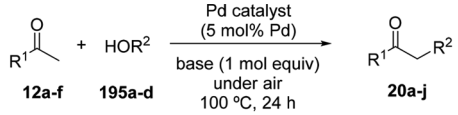
[a]Adapted with permission from ref 317. Copyright 2007 Elsevier.

ate reactions such as aldol condensation, C_3-alkylations, and Knoevenagel reactions among others have been described in specific literature revisions dealing with heterogeneous catalysis, albeit classified according to the type of global reaction.[9,11] Therefore, continuing with our classification, we will focus on the intermediate characteristic reaction in tandem with BH dehydrogenation/hydrogenation using alcohols as hydrogen source.

3.2.1. Formation of C–C Bonds. *3.2.1.1. Aldol Condensation.* Uozumi described a palladium nanocatalyst, composed of a mixture of palladium nanoparticles and a viologen polymer[317] (**194**), in combination with barium hydroxide ($Ba(OH)_2$), as a base for the α-alkylation of ketones. The Pd polymeric-based catalyst was prepared via a self-organization process of inorganic compounds and the non-cross-linked viologen polymer. In particular, anionic species $[PdX_4]^{2-}$ containing Pd self-assembled with the non-cross-linked cationic polymer (**192**) to give an ionic insoluble polymeric complex (**193**) which was reduced to afford nanoparticulated metal particles (Scheme 63).[317]

The solid catalyst **194** was characterized and applied to the α-alkylation of diverse ketones (**12a–j**) with alcohols under atmospheric conditions without using classic organic solvents (Scheme 64).[317]

Scheme 64. Examples of α-Alkylation of Ketones with Alcohols in the Presence of Nano-Pd-V catalyst[a]



12a, 20a, 20b, 20c	$R^1 = n\text{-}C_6H_{13}$	**195a, 20a**	$R^2 = n\text{-}C_8H_{17}$
12b, 20d	$R^1 = n\text{-}C_7H_{15}$	**195b, 20b**	$R^2 = n\text{-}C_{10}H_{21}$
12c, 20e	$R^1 = C_6H_5CH_2CH_2$	**195c, 20c-f, 20i-j**	$R^2 = C_6H_5CH_2$
12d, 20f, 20g	$R^1 = cyclo\text{-}C_6H_{11}$	**195d, 20g, 20h**	$R^2 = 4\text{-}CH_3OC_6H_4CH_2$
12e, 20h, 20i	$R^1 = C_6H_5$		
12f, 20j	$R^1 = 4\text{-}CH_3OC_6H_4$		

[a]Adapted with permission from ref 317. Copyright 2007 Elsevier Ltd.

The reactions proceed under mild conditions to afford moderate yields of the respective alkylated ketones (**20a–j**). The solid could be easily recovered and recycled to meet with the requirments of green chemistry. Interestingly, the same palladium catalyst was applied in the ring opening of cyclic diketones.[317]

Nickel, rhodium, and ruthenium deposited on diverse supports were also effective catalysts for the Guerbet reaction between CH_3OH and *n*-PrOH with complete selectivity toward the synthesis of isobutanol (^{i}BuOH). Besides, the presence of sodium methoxide as a basic component was necessary in this case to get catalytic activity.[318] Table 13 includes the most interesting results obtained with Ni-based supported catalysts as well as different bases and reaction conditions.

It is necessary to highlight an interesting result reported in the patent literature when palladium was supported on hydrotalcite derivatives (Pd/HT) and was used as catalysts for the Guerbet reaction. In particular, higher yields of *n*-butanol could be obtained when gallium was incorporated into the hydrotalcite structure. Besides, it was possible to carry out the process at lower temperatures.[319,320]

In a recent and interesting approach, the preparation of a DMF-stabilized iridium nanocluster as methylation catalyst has been described. The corresponding micrographs of HR-TEM showed that the small Ir clusters had an average diameter of 1–1.5 nm and were stabilized with DMF.[321] The characterization studies showed that DMF protected the Ir metal particles so that they started to have a weight loss at around 100 °C. Upon heating, it appears that a part of the protective DMF molecules were released, generating Ir nanoclusters with partially open sites that could act as active catalysts in the methylation reaction.

The stabilized metal nanoclusters were used as catalyst in the β-methylation (**196–197**) of alcohols with methanol (**26a**). The following table (Table 14) shows the screening of the reaction conditions.[321]

Onyestyak et al. reported two closely related studies on the α-alkylation of acetone with ethanol in vapor phase using a fixed-bed reactor and two metal-based catalysts with a great potential for achieving C-alkylations, such as Pd and Cu.[322,323]

In both cases, the authors moved from batch to a flow-through system trying to get closer to the systems that are most frequently used in the industry. Although a priori these results are not easy to compare with those obtained in batch, the authors reached promising results. In one of these studies,[322] a basic hydrotalcite support (HT) was used instead of the typically inert carbon in an attempt to avoid the use of bases. Then Pd was deposited onto this basic solid as a dehydrogenation/hydrogenation catalyst. The reaction model was the α-alkylation of acetone with different alcohols.

They found that the initial reaction rates were much higher with Pd than with Cu. Moreover, Pd/HT was highly efficient in the alkylating reaction both under inert atmosphere and under H_2. Besides, the selectivity and overall yield obtained with Pd were superior even when both metals were deposited on the basic carrier hydrotalcite HT (Pd 5 wt % and Cu 9 wt %).

The same group described the upgrading of biofuel derived from an alcohol-acetone feedstock, and again this study was carried out over a two-stage flow through catalytic system.[324]

Finally, examples of bimetallic catalysts should also be highlighted as they have also been described in recent studies on cross-coupling reactions of primary and secondary alcohols under BH conditions. For example, Cu–Ag/hydrotalcite has been applied as a catalyst for dehydrogenative cross-coupling of

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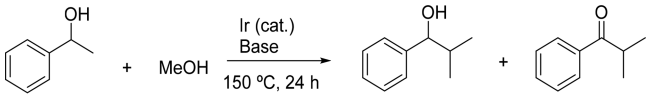
Table 13. Results Obtained on the Guerbet Reaction by Reacting Methanol and Propanol with Different Nickel-Supported Catalysts and Bases[a]

	Ni-catalyst[b]		basic component							iBuOH	
entry	type	mmol	type	mmol	B/Ni	time (h)	T (°C)	P_{H2} (atm)	P_{N2} (atm)	yield[c] (%)	TN[d] (h^{-1})
1[e]	Ni/k	2.56	MgO	80	31	6	200	30	–	0.8	0.05
2[e]	Ni/k	2.56	KOH	160	63	6	200	30	–	1.3	0.08
3[e]	Ni/k	2.56	MeONa	160	63	6	180	30	–	20.0	1.30
4[e]	Ni/k	0.97	MeONa	160	165	12	200	–	30	55.3	9.50
5[e]	Ni/k	0.20	MeONa	160	800	6	200	–	30	49.5	41.2
6[f]	Ni/k	0.20	MeONa	160	800	6	200	–	30	48.0	40.0
7[e]	Ni/Al_2O_3	0.45	MeONa	160	355	12	200	–	30	48.8	18.1
8[e]	Ni/Al_2O_3	0.20	MeONa	160	800	12	200	–	30	25.5	21.1
9[f]	Ni/Al_2O_3	0.20	MeONa	160	800	6	200	–	30	41.0	34.2
10[f]	$Ni/(OAc)_2$	0.125	MeONa	160	1280	6	200	–	30	31.3	41.7
11[f]	$NiCl_2(PiPr_3)_2$	0.098	MeONa	160	1633	6	200	–	30	38.6	65.6

[a]Adapted with permission from ref 318. Copyright 2003 Elsevier. Reaction conditions: MeOH (1250 mmol); MeOH/PrOH (12.5 mol/mol). [b]Ni/k represents a commercial catalyst (G49 from Girdler) containing 5 wt % of nickel on kieselguhr, whereas Ni/Al_2O_3 represents a commercial catalyst (3288 from Engelhard) containing 60 wt % of nickel on alumina. [c]Calculated with respect to PrOH. [d]Turnover number calculated after 6 h of reaction and expressed as mol ^{i}BuOH/(mol Ni × h). [e]Preactivated nickel catalysts were used. [f]No preactivation of the metal catalyst was performed.

Table 14. Screening of the Reaction Conditions[a]



26a 196 197

entry	[Ir]	base	Conv. (**26a**) [%]	total yield[b,c] [%] selectivity (**196**:**197**)[d]
1	Ir NCs	Cs_2CO_3	>99	68 (85:15)
2	$IrCl_3$	Cs_2CO_3	48	16 (46:54)
3[e]	$IrCl_3$	Cs_2CO_3	49	16 (33:67)
4[e]	$[IrCl(cod)]_2$	Cs_2CO_3	48	21 (28:72)
5[e,f]	$[IrCl(cod)]_2$/PPh_3	Cs_2CO_3	44	18 (–: >99)
6[e]	$[Cp^*IrCl_2]_2$	Cs_2CO_3	44	25 (25:75)
7	Ir NCs	KOH	>99	53 (87:13)
8	Ir NCs	KOtBu	>99	52 (87:13)
9	Ir NCs	K_2CO_3	59	31 (75:25)
10	Ir NCs	none	26	n.d.
11	none	Cs_2CO_3	30	n.d.
12	none	KOH	60	9 (>99: –)
13[g]	Ir NCs	Cs_2CO_3	11	3 (48:52)
14[h]	Ir NCs	Cs_2CO_3	>99	quant [87][c] (94:6)
15[h,i]	Ir NCs	Cs_2CO_3	57	24 (94:6)

[a]Adapted with permission from ref 321. Copyright 2017 Royal Society of Chemistry. Reaction conditions: **26a** (1 mmol) was allowed to react with methanol (2 mL), redissolved Ir NCs (0.1 mol %) and Cs_2CO_3 (1 mmol) at 150 °C for 24 h. [b]GC yields based on **26a** used. [c]Three numbers in the square bracket show isolated yields. [d]The numbers in parentheses show the selectivity for the alcohol and ketone products. [e]Ir catalyst (5 mol %) was used. [f]PPh_3 (10 mol %) was used. [g]At 100 °C. [h]Cs_2CO_3 (3 mmol) was used. [i]Ir NCs (0.001 mol %) for 48 h.

primary and secondary benzylic alcohols.[325] Besides, Pt–Sn deposited onto γ-Al_2O_3 catalyzed the β-alkylation of secondary alcohols with primary alcohols under solvent-free conditions.[326]

3.2.1.2. Knoevenagel Reaction. There are few examples on the Knoevenagel reaction as intermediate reaction in BH methodology using heterogeneous catalysts. One of them has to do with monoalkylation reactions of diverse C–H acid methylene compounds in the presence of a bifunctional metal-based catalyst.[327] In particular, Pd supported on basic MgO of high surface area (Pd/MgO) catalyzed the sequential reaction between benzyl alcohol (**13a**) and phenylacetonitrile (**199**), or diethylmalonate (**203**) or nitromethane, to give the respective α-monoakylated products (**201**, **204**, and **206**) without external supply of hydrogen. The process involved a three-step process taking place on two different catalytic surface sites.

First, the alcohol was oxidized to the corresponding aldehyde (**198**) with the simultaneous formation of a metal hydride, and then the aldehyde reacted with a methylene activated compound to give an alkene (**200**, **202**, and **205**), and finally hydrogen from the metal hydride was transferred to the alkene to give a new saturated C–C bond (Scheme 65).[327]

Kinetic studies showed that the rate-controlling step for the one-pot reaction sequence between benzylacetonitrile and benzyl alcohol was the hydrogen transfer reaction from the surface hydrides to the olefin, and more importantly, the global reaction rate improved when decreasing the size of the Pd metal nanoparticle (Scheme 65).

The alkylation of heterocyclic compounds with hydroxyl compounds has been also attempted recently with Pd/C and Ru/C.[104,320] The importance of this reaction relies on the fact that heterocyclic compounds are relevant structural motifs in molecules of biological and pharmaceutical importance (barbiturates, coumarins, etc.). Since such alkylated heterocyclic compounds are intermediates for the synthesis of useful molecules, the development of green and selective methods for alkylating heterocycles is a key matter in synthetic chemistry. For example, commercially available Pd/C was active in the alkylation of 4-hydroxycoumarin, 4-hydroxy-1-methylquinoline, and barbituric and oxoindole derivatives. The alkylation (**208**) of 1,3-dimethylbarbituric acid (**207**) was successfully scaled-up to one gram. Furthermore, the catalyst could be recycled up to five times with a negligible loss of efficiency (Figure 10).[320]

3.2.2. Formation of C–N Bonds. *3.2.2.1. Aza-Wittig Reaction.* Yus et al. reported in 2008 the Aza-Wittig reaction between different alcohols (**13a**) and *N*-(triphenylphosphoranilidene)aniline (**209**) in the presence of Ni nanoparticles.[328] The reaction was carried out in the absence of a base and under mild conditions. The main drawbacks were the moderate yields to the corresponding secondary amines (**68a**) and the amount of catalyst used (Scheme 66).[328]

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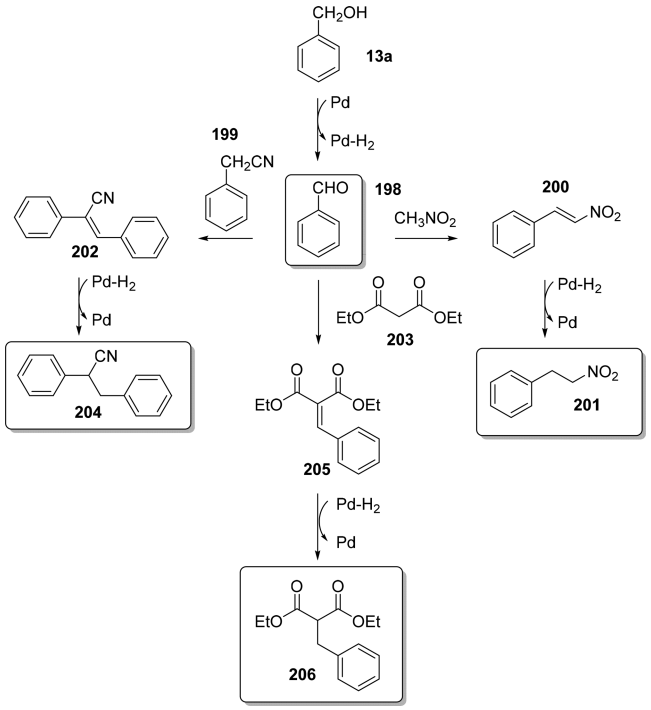
Scheme 65. Schematic Representation of the α-Monoalkylation Reaction of Phenylacetonitrile, Diethylmalonate, and Nitromethane with Benzyl Alcohol over Pd/MgO[a]



[a]Adapted with permission from ref 327. Copyright 2011 Elsevier.

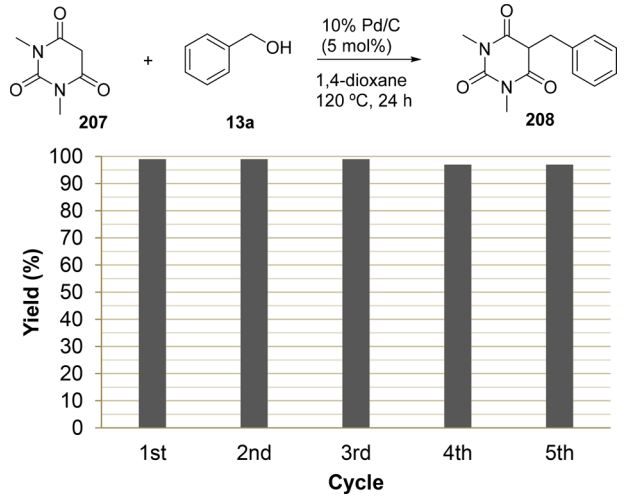
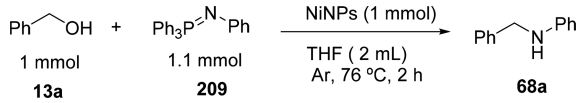


Figure 10. Graphic representation of the recycling of Pd/C by reacting the barbituric derivative **207** and alcohol **13a**. Adapted with permission from ref 320. Copyright 2015 Wiley-VCH.

Scheme 66. Indirect Aza-Wittig Reaction Catalyzed by NiNPs[a]



[a]Adapted with permission from ref 328. Copyright 2008 Wiley-VCH.

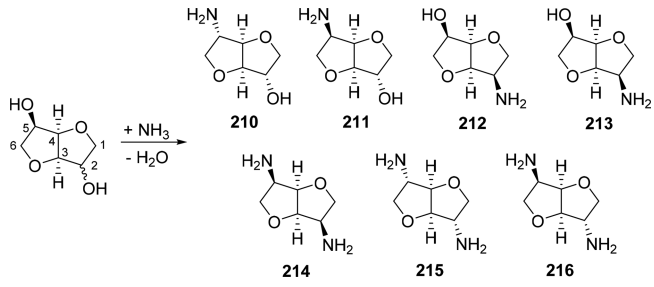
This is the first example reported in the literature on the activation of an alcohol to carry out the indirect aza-Wittig reaction in the presence of a heterogeneous catalyst. To the best of our knowledge, there are no further publications reporting improvements in this field.

3.2.2.2. Condensation. 3.2.2.2.a. N-Alkylation of Ammonia (Amination of Alcohols with Ammonia). The incorporation of ammonia as a nucleophile in the amination of alcohols is a long-standing goal when it comes to heterogeneous catalysis, as it happened with the homogeneous counterpart. In this context, experimental parameters such as the ammonia pressure and reaction temperature will significantly vary depending on the catalyst and the type of substrate. For example, methanol and ammonia will react together at 350−500 °C and 15−30 bar using aluminum-based heterogeneous catalysts in determined industrial processes.[329] It can be noticed that most heterogeneous catalysts active in amination of alcohols contain mainly tungsten, copper, iron, cobalt, nickel, and chromium as metallic elements, whereas it is known that the product distribution can be tuned by changing parameters such as the residence time and excess of ammonia.

In particular, using the catalytic BH strategy, it has been recently shown that small nickel nanoparticles supported on calcium silicate ($CaSiO_3$) by ion exchange followed hydrogenation of the calcined material afforded a $Ni/CaSiO_3$ material with high activity in the obtention of primary amines from NH_3 and alcohols. In this case, the catalytic active species is the metallic Ni(0) sites of about 3 nm particle size. It is important to indicate that the solid system was active in the alkylation of anilines as well as aliphatic amines with alcohols (aliphatic and benzyl alcohols) under neat conditions.[330]

One of the most recent examples of alkylation of ammonia using heterogeneous catalysts has to do with the amination of diverse biogenic isohexides which has been carried out with Ru/C in aqueous phase (Scheme 67).[331]

Scheme 67. Amination of Isohexides Yields Four Amino Alcohols and Three Diamines with Different Configuration (Endo/Exo) of the Hydroxyl and Amine Groups in Positions 2 and 5[a]



[a]Adapted with permission from ref 331. Copyright 2016 Wiley-VCH.

Isohexides are biogenic substrates that dissolve well only in polar solvents. For this reason, the amination of these molecules with alcohols was carried out in aqueous phase. The reaction was catalyzed with Ru/C in aqueous ammonia and using low pressures of H_2. The importance of this reaction relies in the fact that the catalyst is active in the transformation of secondary alcohols toward primary amines (**210**−**216**) in water through BH catalysis. This fact is striking if we take into account that water in principle would shift the equilibrium of the imine formation toward the nonfavored ketone so that the formation of amine would not be favored.

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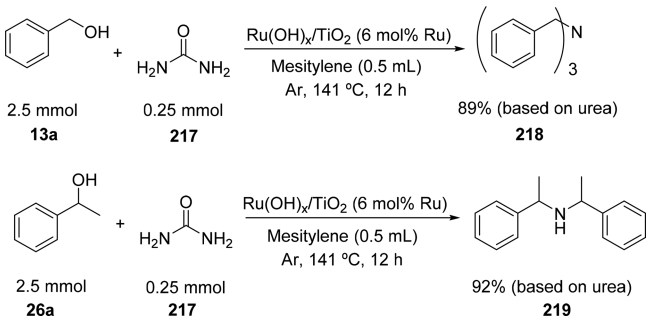
The synthesis of dodecylamine from dodecanol and ammonia has been recently reported to occur in the presence of metals such as platinum, palladium, ruthenium, iridium, and osmium supported on carbon. Interestingly, the authors found that the presence of an extra supply of hydrogen gas was beneficial to reach a high conversion as well as a high dodecylamine selectivity.[332]

As it has been already shown in the previous section devoted to homogeneous catalysis, ammonia has been successfully replaced in numerous examples by other alternative chemical sources, and these concerns have also reached to heterogeneous catalysis. In this case, one of the first examples reported by the group of Mizuno studied the synthesis of both secondary and tertiary amines (**218, 219**) from alcohols (**13a**, **26a**) and urea (**217**), albeit this time in the presence of a recoverable heterogeneous ruthenium catalyst.[333] The relatively wide scope of this catalytic system was evidenced by the transformation of primary alcohols into tertiary amines, whereas other more hindered alcohols (secondary alcohols) were converted into secondary amines (Scheme 68)[333] in both cases using an alcohol excess.

Scheme 68. Supported $Ru(OH)_x$ Catalyzed Formation of Secondary and Tertiary Amines from Benzylic Alcohols and Urea[a]



[a]Adapted with permission from ref 333. Copyright 2009 Wiley-VCH.

Another interesting approach studied the use of aqueous ammonia as an alternative to the need of a pressure equipment because of the ease of handling. From these results, it follows that the importance of primary amines both by themselves and as intermediates for further derivatization reactions pushed the researchers to undertake the development of efficient ways to prepare amines through BH methodology as an alternative to known classical synthetic procedures.[334,335]

So far, studies on bimetallic catalysts on this specific subject are scarce, albeit exceptionally the bibliography has described a bimetallic Rh−In/C catalyst which has been applied in aqueous medium with ammonia as the nucleophile for the amination of diverse C_3 alcohols (e.g., 1,3-propanediol). Among the screened activated carbons, the use of FAC-10 must be highlighted as the best support in terms of activity and resistance to metal leaching, giving a Rh−In alloy particle size of 3−4 nm, according to the TEM micrographs.[336]

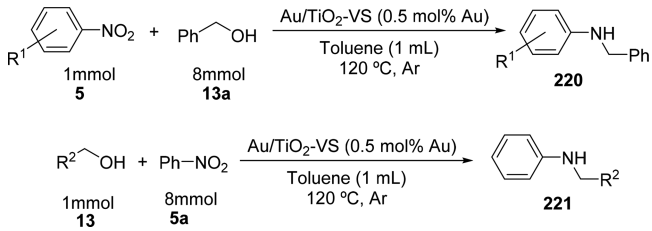
3.2.2.2.b. N-Alkylation of Primary and Secondary Amines with Alcohols. The use of solid catalysts for alcohol aminations is known from the first decades of the last century.[337,338] Nonetheless, the interest in the *N*-alkylation of amines using heterogeneous catalysts through BH methods derives from the success in the preparation of homogeneous complexes as has been indicated in section 2.2.2.2.b dealing with homogeneous catalysts.[339] In this context, several examples of industrial applications carried out with such amination processes have been described to take place in the presence of different heterogeneous catalysts (e.g., the *N*-alkylation of lower aliphatic amines with CH_3OH). In accordance to this, descriptions of these processes can be found with relative frequency in the patent literature.[329,340,341]

However, despite the fact that the amination of alcohols is a reaction of reference within the context of borrowing hydrogen, there is not a general catalytic method available for functionalized and/or sensitive or unstable compounds under milder reaction conditions (T < 100 °C). The problem has been temporarily solved in some cases by switching from heterogeneous to homogeneous phase working with organometallic catalysts (e.g., by immobilizing iridium complexes on siliceous supports),[342] albeit the search of more active solid catalysts has not stopped ever.

A very interesting contribution related to gold and silver nanoparticles as metal catalysts has to do with the reductive *N*-alkylation of nitroarenes using borrowing hydrogen methods.[343,344]

As an example, with the proper reaction conditions small gold nanoparticles (1.8 nm) deposited on TiO_2 (Au/TiO_2) were very active for the *N*-monoalkylation reaction or dialkylation of nitroarenes (**5**, **5a**) with alcohols (**13**, **13a**). The reaction involved the dehydrogenation reaction of the alcohol to form the aldehyde and concurrently the reduction of the nitroarene to give the respective amine (**220**, **221**). Notably other functional groups susceptible to be reduced, such as alkenes, ketones, or esters moieties, remained unreacted during the reductive *N*-monoalkylation reaction (Scheme 69).[343]

Scheme 69. Au/TiO_2-Catalyzed Reaction of Nitroarenes with Benzyl Alcohols and Nitrobenzene with Various Alcohols via BH Methodology[a]



[a]Adapted with permission from ref 343. Copyright 2011 Wiley-VCH.

The fact the Au−H complexes selectively reduce both the nitro group (as reactant) and the intermediate imine formed in situ to get another amine as final product shows the advantages of BH methodology for implementing intensive processes.

Secondary amines have also been obtained from alcohols and nitroarenes in the presence of Pd deposited on a semiconductor TiO_2 (Pd/TiO2) with the contribution of UV irradiation ($\lambda \geq$ 300 nm) and at room temperature (Scheme 70).[345]

Pd/TiO_2 catalyzed the one-pot synthesis of secondary amines from alcohols and nitroarenes under UV light, with a combination of photocatalytic and catalytic reactions consisting of (i) photocatalytic oxidation of the starting alcohol to the corresponding aldehyde and reduction of nitroarenes to afford the respective aniline compound; (ii) then condensation reaction of the formed carbonyl compounds and anilines and, (iii) photocatalyzed hydrogenation of the formed imines to give secondary amines.

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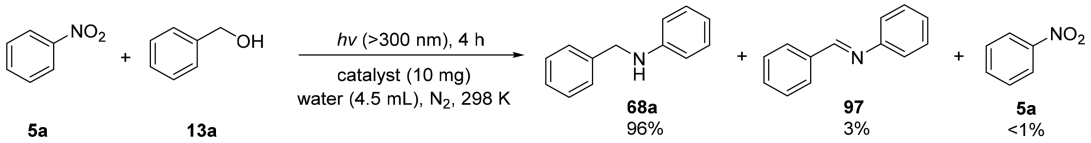
Scheme 70. Catalyst Properties and Results for One-Pot Synthesis of Secondary Amine from Nitrobenzene and Benzyl Alcohol under UV Irradiation[a]



[a]Adapted with permission from ref 345. Copyright 2015 Royal Society of Chemistry.

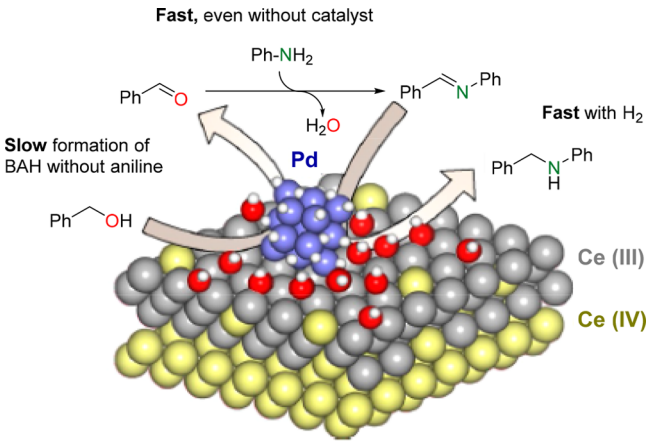
In principle, TiO_2 would oxidize the alcohol, producing aldehyde and protons (H^+). Then the photoexcited electrons would reduce H^+ on the Pd particles giving to afford H−Pd species. These metal hydride species may reduce nitroarene to give aniline. Catalytic condensation of the formed aniline and aldehyde by the Lewis acid sites on the surface of TiO_2 may produce the imine. This imine would be then hydrogenated by the H−Pd species to afford the corresponding amine.

Meanwhile, the one pot reaction between nitrobenzene and diverse alcohols to afford secondary amines and imines has also been catalyzed by bimetallic nanoalloys of gold−palladium and ruthenium−palladium supported on titania.[346] The metal-based catalysts were prepared by a modified impregation procedure. The authors found that bimetallic catalysts were far more active than the related monometallic ones due probably to a synergistic effect, following the order: Ru < Pd < Au ≪ Au−Pd < Ru−Pd.

In this regard, another bimetallic catalyst formed by different elements Pt−Sn/γ-Al_2O_3 has also been reported recently to catalyze the scalable synthesis of secondary and tertiary amines from amines and alcohols.[347]

Pd supported on CeO_2 (Pd/CeO_2) has been reported to behave as a reservoir and H_2-pump for the direct amination of alcohols (Scheme 71).[348]

Scheme 71. Hydrogen Transfer Pathway over Pd/CeO_2−HS for the Amination of Benzyl Alcohol with Aniline (And Ammonia)[a]



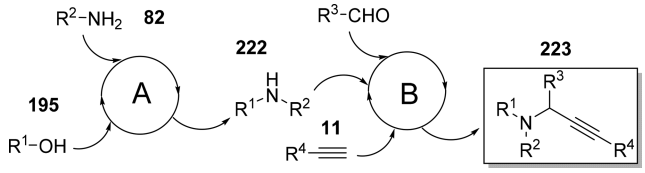
[a]For the sake of clarity, only a CeO_2(111) plane is represented. Adapted with permission from ref 348. Copyright 2016 Wiley-VCH.

In this case, a high surface CeO_2 material was pretreated at 500 °C, resulting in an abnormally highly active and selective catalyst for the *N*-monoalkylation of benzyl alcohol with ammonia and primary amines such as aniline as compared to the standard Pd/CeO_2 catalyst. In this case, a promoted H_2 transfer on high-surface Pd/CeO_2 was proposed to take place via back spillover phenomenon between Pd and the ceria support, being regarded as the main driver for amination under the hydrogen borrowing mechanism.

Other interesting material employed as support was cryptomelane-type manganese oxide octahedral molecular sieve (OMS-2), which was examined as a possible candidate for amination reactions. OMS-2 materials (also called K-hollandites or γ-MnO_2) are based on edge-shared MnO_6 octahedra, having both Mn(III) and Mn(IV) cations, and 2 × 2 1D microtunnels, having extra framework compensation ions (usually K^+).[349] This K-hollandite was Pd-substituted by the cation-exchanged method showing activity for the straightforward amination of alcohols with primary amines.[350] The model reaction using aniline and benzyl alcohol gave a *N*-benzylamine yield of 96% at 160 °C during 3 h with no formation of tertiary amine nor toluene. The good performance of this formulation was due to the formation of a highly active intermediate phase during the reaction which included the existence of a highly dispersed Pd(IV)/Pd(II) species near K and defective OH moieties, which favored the hydrogenation transfer.

In order to expand the scope of reactions catalyzed by gold taking place in one-pot through the borrowing hydrogen strategy, a nanoparticulated gold catalyst on CeO_2 (Au/CeO_2) was able to integrate the *N*-monoalkylation of amines with an additional catalytic cycle to access more complex structures such as propargylamines.[351] Indeed, Au/CeO_2 connected two catalytic cycles in a gold-catalyzed cascade mode (Scheme 72).[351]

Scheme 72. Two Multistep Catalytic Cycles for the One-Pot Synthesis of Propargylamines from Primary Amines and Alcohols with Au/CeO_2: Cycle A = *N*-Monoalkylation; Cycle B: A^3 Coupling Reaction[a]



[a]Adapted with permission from ref 351. Copyright 2012 Wiley-VCH.

In the first cycle (A, Scheme 72), gold atoms at the crystal corners promoted the *N*-monoalkylation of amines (**82**) with alcohols (**195**) to afford secondary amines (**222**) under hydrogenation transfer conditions. Then in a consecutive cycle (B, Scheme 72) 2-propinylamines (**223**) were formed through a multicomponent A^3 transformation, involving alkynes (**11**) and aldehydes, extending the applicability of Au/CeO_2 catalyst.[351]

The strategy led to the direct formation of C−C and C−N bonds through different consecutive transformations without interferences, a feature that resulted in a more intensive process

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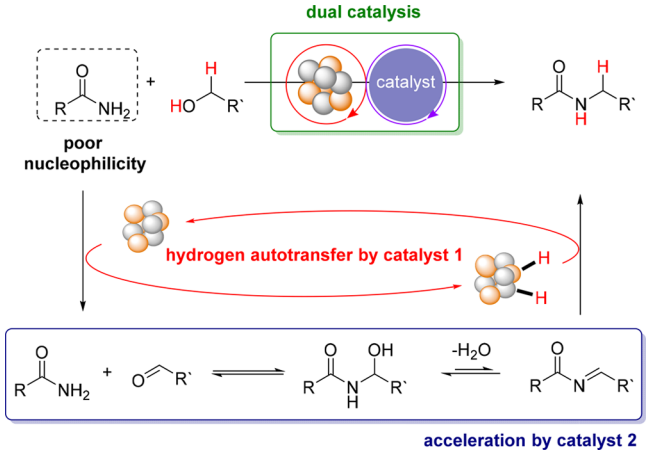
and higher product yield. In this case, because two different oxidation states of gold (Au^0 for the *N*-monoalkylation reaction and Au^{+n} for the A^3coupling) catalyzed two different reactions, the experimental conditions (temperature, metal loading, and preparation of catalyst) had to be optimized to avoid a sharp decrease of these oxidized gold active species as well as their sinterization. The strong interaction between different gold species on CeO_2 accounted for the observed high activity and stability of the catalytic species during the overall cascade reaction.[351]

3.2.2.2.c. N-Alkylation of Amides and Sulfonamides with Alcohols. Recently it has been described a synergistic cascade reaction catalyzed by Lewis acids and supported bimetallic Au/Pd as example of BH strategy[352] in the *N*-alkylation of amides (Scheme 73).[352]

Scheme 73. *N*-Alkylation of Primary Amides with Alcohols via Hydrogen Autotransfer in the Presence of a Dual Catalyst[a]



[a]Adapted from ref 352. This article is licensed under a Creative Commons Attribution 3.0 Unported License.

3.2.3. Formation of C–S Bonds. *3.2.3.1. Thioetherification (S-Alkylation).* Formation of C–S bonds has also been exceptionally achieved with a heterogeneous catalyst by means of borrowing hydrogen methods by reacting thiols and alcohols in the presence of Pd supported on a basic support (Pd/MgO).[353]

Effectively, bifunctional palladium-based catalyst (Pd/MgO) was able to form thioethers starting from thiols and aldehydes formed previously in situ from the respective alcohol under BH conditions. The reaction begun with a dehydrogenation of the alcohol (**13a**) to afford a palladium hydride intermediate and an aldehyde. The latter reacted with a thiol (**224**) involving most probably the intermediacy of a hemithioacetal (**225**) and a thionium ion RCH = S^+R, being reduced in situ by the metal hydrides to afford thioethers (**226a**) (Scheme 74).[353]

The reaction is a variation of the reductive thiolation of aldehydes by Pd–H species, in which both reactants were formed and reacted in situ on the metal surface to give thioethers. The reaction is general for thiols (**224**) as well as benzylic alcohols (**13a**), affording disulfides (**227**) along with the desired thioethers (**226a–d**) (Scheme 75).[353]

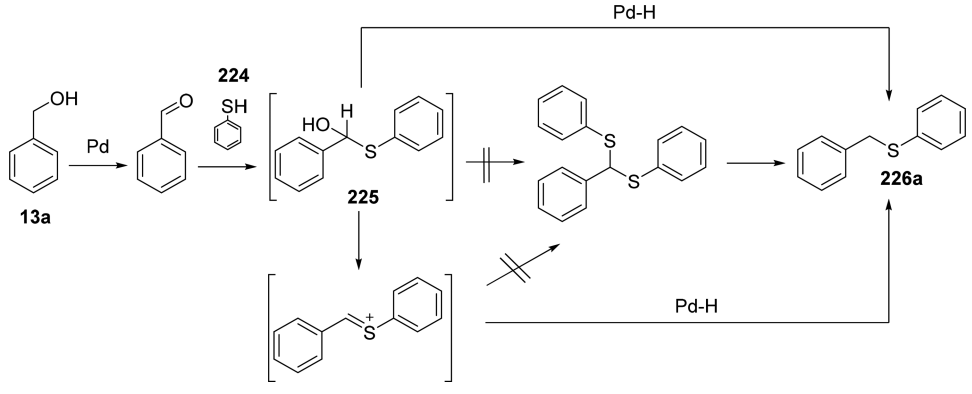
3.3. Activation of Amines

3.3.1. Formation of C–N Bonds. *3.3.1.1. Condensation (N-Alkylation).* The alkylation reaction of amines with amines is a well-known reaction. Diverse heterogeneous active catalysts were described in the literature a long time ago for the *N*-alkylation of amines with themselves acting as electrophiles analogously to alcohol molecules. For example, the synthesis of symmetrically substituted secondary amines was successfully carried out via the Cu/Al_2O_3 catalyzed self-condensation of primary amines.[354] Here diverse copper catalysts were screened for their activity in the self-coupling of the benzylamine as a model reaction against a series of different metal-loaded catalysts (e.g., Pd/Al_2O_3, Ru/Al_2O_3, and $AgAl_2O_3$). The following table (Table 15) includes some of the most significant results (**228–231**).[354]

Mechanistic studies were also carried out, and on the bases of different experimental observations the authors concluded that the reaction proceeded with the intervention of an intermediate Cu–H specie. This hydride species was formed after the initial dehydrogenation step, whereas hydrogen apparently was stored on the support through some kind of spillover effect. γ-Alumina or similar related phases were the most effective supports over the rest of the supports essayed.[354]

In a second example, a similar self-autocondensation of primary amines took place to give secondary amines using the same copper-based catalyst Cu/Al_2O_3, which was in turn

Scheme 74. Hypothetical Reaction Pathway for the One-Pot Synthesis of Thioethers with Pd/MgO Catalyst through a BH Strategy[a]



[a]Adapted with permission from ref 353. Copyright 2013 Wiley-VCH.

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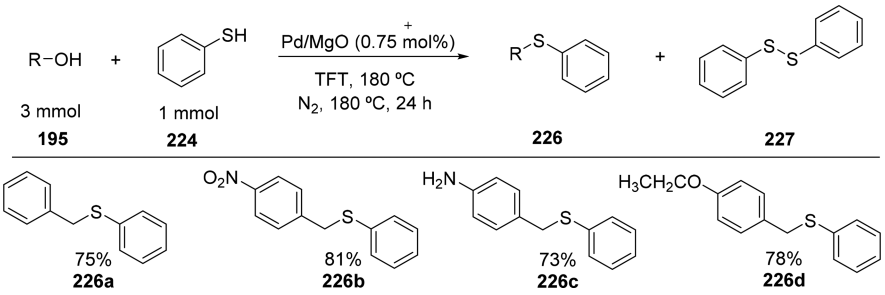
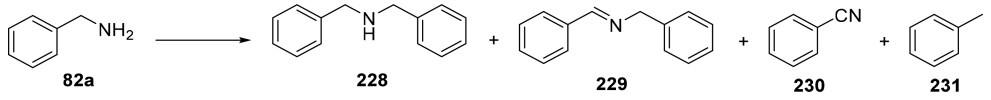
Scheme 75. Thioethers Obtained with This Methodology[a]



[a]Adapted with permission from ref 353. Copyright 2013 Wiley-VCH.

Table 15. Results on the Self *N*-Alkylation Reaction of Benzylamine in the Presence of Different Solid-Metal Catalysts[a]



				yield (%)			
entry	catalyst	solvent	time (h)	228	229	230	231
1	Cu/Al_2O_3	mesitylene	3	64	17	<1	<1
2	Cu/Al_2O_3	mesitylene	24	97	3	<1	<1
3	Cu/Al_2O_3	diglyme	3	31	11	<1	<1
4	Cu/Al_2O_3	*o*-dichlorobenzene	3	<1	16	<1	<1
5[b]	Cu/Al_2O_3	DMSO	3	<1	6	<1	35
6[c]	Cu/Al_2O_3	DMF	3	<1	<1	<1	<1
7	Cu/TiO_2	mesitylene	3	38	14	<1	<1
8	Cu/CeO_2	mesitylene	3	38	10	<1	<1
9	Cu/SiO_2	mesitylene	3	<1	<1	<1	<1
10	$Cu(OH)_x/Al_2O_3$	mesitylene	24	47	25	<1	<1
11	$CuCl_2/Al_2O_3$ (pretreated with H_2 at 180 °C)	mesitylene	24	<1	2	<1	<1
12	$Cu(OAc)_2/Al_2O_3$ (pretreated with H_2 at 180 °C)	mesitylene	24	<1	3	<1	<1
13[d]	Cu metal + Al_2O_3	mesitylene	24	<1	2	<1	<1
14	CuO	mesitylene	24	<1	3	<1	<1
15	$Cu(OH)_2$	mesitylene	24	<1	5	<1	<1
16	Cu_2O	mesitylene	24	<1	1	<1	<1
17	$CuCl_2 \cdot 2H_2O$	mesitylene	24	<1	9	<1	<1
18	$Cu(OAc)_2 \cdot 2H_2O$	mesitylene	24	<1	4	<1	<1
19	CuCl	mesitylene	24	<1	4	<1	<1
20	Ag/Al_2O_3	mesitylene	3	2	<1	<1	<1
21	Au/Al_2O_3	mesitylene	3	1	3	<1	<1
22	Ru/Al_2O_3	mesitylene	3	29	28	11	<1
23	Rh/Al_2O_3	mesitylene	3	<1	<1	58	24
24	Pd/Al_2O_3	mesitylene	3	2	16	47	18
25	Pt/Al_2O_3	mesitylene	3	29	21	27	7
26[d]	Al_2O_3	mesitylene	3	<1	<1	<1	<1
27	None	mesitylene	24	<1	<1	<1	<1

[a]Adapted with permission from ref 354. Copyright 2013 Royal Society of Chemistry. Reaction conditions: catalyst (metal: 5 mol %), **82a** (0.5 mmol), solvent (2 mL), 140 °C, in 1 atm of Ar. Yields were determined by GC. [b]*N*,*N*-Dimethylbenzylamine was formed as a byproduct (52%). [c]*N*-Benzylformamide was formed as a byproduct (51%). [d]Al_2O_3 (100 mg).

prepared from the precursor $Cu(OH)_x/Al_2O_3$.[355] In this case, diverse structurally primary amines going from benzylamine and picolylamine to aliphatic amine derivatives were selectively transformed into new secondary amines in moderate to very good yields without adding any cocatalyst or additive (base, ligands, ...).

By summarizing, there is not a currency in the use of a heterogeneous catalyst as it occurred in the homogeneous phase with Ir and Ru complexes. On the contrary, there is a wide variety of catalysts of different compositions just by varying the metal, while the support is used just to modulate the activity. Besides, the possibility of combining two metals with the ability to dehydrogenate, form metal hydrides, and release them opens the door to the synthesis of bimetallic-supported catalysts with increasing activity and selectivity as a function of the metal combination, the M1/M2 ratio, and the preparation. This fact will determine the way in which both species interact and thus will catalyze the reaction, hence making it possible to increase the number of BH studies in the

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short term (including the asymmetric reactions) under much greener conditions.

4. CONCLUSIONS AND FUTURE TRENDS

The advantages of oxidation and hydrogenation processes integrated within the BH methodology are logical. Therefore, the researchers will be able to drive the strategy further in search for new transformations for the synthesis of products. Right now, this is an active field of research.

There has been a rapid progress during the past decade within this area partly derived from the onset of favorable new factors to understand this methodology, such as the sustainable chemistry. This concept, has increased the significance of low-waste transformations hence making this strategy both acceptable and well-recognized. As noted earlier, these advances have been materialized in the high number of excellent results reported so far in the field of alkylation reactions (more specifically into *C*- and *N*-alkylation processes) both in the homogeneous and the heterogeneous phase. These results have been accompanied by the design of a great variety of catalysts, reaction conditions, and technical applications to the synthesis of molecules and derivatives, many of them having important functional groups.

It is important to remark that alkanes have not been fully exploited in the context of BH catalysis. This may be due to the greater stability of a C−H bond when belonging to an unfunctionalized alkane against alcohols and amines and, alternatively, simply because these studies appeared before the emergence of the BH concept, making many of these contributions pass completely unnoticed by the readers. Nonetheless, the ability of certain elements to transform low molecular weight alkanes into heavier alkanes is a challenging goal with important implications in the alkane manufacturing at the industrial level.

Similarly, the field of asymmetric catalysis has been less fruitful in BH as compared with other areas as a result of the challenging conditions needed to perform asymmetric catalysis within the context of BH catalysis.

For all these reasons and despite great progress in the design of efficient catalysts, major challenges remain. Although it is difficult to make predictions, a short vision into the future clearly shows that the main research lines in BH catalysis will be focused most likely on three basic points: (a) the activation of less reactive chemical bonds at low temperatures, a fact which passes through the necessary discovery of more potent and selective catalysts (ranging from mono to multifunctional catalysts); (b) the search for new reactivity paths in order to achieve different C−H transformations after this bond is cleaved; and (c) the improvement of the regioselectivity in dehydrogenation catalysts (especially in alkane metathesis transformations) as well as the stability of catalysts.

With respect to asymmetric catalysis, the challenge will be to design catalysts and experimental conditions in order to bring together the target transformation under milder conditions in order to get a maximum asymmetric induction effect. In doing so, more challenging reactions may become possible.

Finally, the development of more effective heterogeneous catalysts to improve the manufacturing efficiency of industrial BH processes together with the implementation of new ones on the large scale synthesis will be ideally some of the future challenges.

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Notes

The authors declare no competing financial interest.

Biographies

Avelino Corma, Professor and founder of the Instituto de Tecnología Química (CSIC-UPV) in Valencia (Spain), has been carrying out research in heterogeneous catalysis in academia and in collaboration with companies for nearly 35 years. He has worked on fundamental aspects of acid−base and redox catalysis with the aim of understanding the nature of the active sites and reaction mechanisms. With these bases, he has developed catalysts that are being used commercially in several industrial processes. He is an internationally recognized expert in solid acid and bifunctional catalysts for oil refining, petrochemistry, and chemical process, especially in the synthesis and application of zeolite catalysts. He has published more than 900 research papers and is an inventor on more than 130 patents. Corma earned his B.S. in Chemistry at Valencia University, Ph.D. at Madrid, and spent two years postdoc at Queen's University. He is a member of the Royal Academy of Engineering of Spain, a member of the Royal Academy of Exact Sciences, Physics and Natural Science of Spain, a foreign member of the National Academy of Engineering NAE (USA), a foreign member of French Academy of Sciences, and a foreign fellow of the Royal Society (UK) Member of Academia Europea, Chemical Science Section. He has received numerous scientific awards and holds 12 Doctorate Honorary Degrees.

Javier Navas was born in Castellón, Spain, in 1986. He obtained his degree in Chemistry from the Universidad Jaume I (Castellón) in 2009. He received a Ph.D. degree with honors by the Universidad Politècnica de Valencia in 2016, working at the Instituto de Tecnología Química (ITQ) under the supervision of Dr. María José Sabater, in the field of C−C, C−N, C−S, and S−S bond formation reaction catalyzed by supported metal nanoparticles. He is still working at the ITQ, and his current research involves the development of new supported nanoparticle-based catalytic systems for organic synthesis.

Maria Jose Sabater obtained her degree in Pharmacy from Universidad de Valencia (Spain) in 1987 and her Ph.D. in Organic Chemistry from the same University in 1991. After completing her doctorate, she joined the group of Prof. Waldemar Adam at the Würzburg University (Germany) as a postdoctoral fellow of the Alexander von Humboldt Foundation (Germany) (1993−1994) for completing studies on Photochemistry. Thereafter, she moved to Poitiers University (France) for a second postdoctoral stay under the supervision of Prof. Michel Guisnet (1995). This time her research interest focused on heterogeneous catalysis for Fine Chemistry. In early 1996, she returned to Spain at the Instituto de Tecnología Química (UPV-CSIC) at the Universitat Politècnica de València, where she was appointed Tenured Scientist from 2002. Since then, she pursued her research activities in the field of catalysis and synthesis of microporous and mesoporous materials.

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LIST OF ABBREVIATIONS

BH= borrowing hydrogen
Ru= ruthenium
Ir= iridium
Rh= rhodium
DKR= dynamic kinetic resolution
tBu= *tert*-butyl
iPr= isopropyl
Me= methyl
Mo= molybdenum
W= tungsten
Ph= phenyl
Si= silicon
mM= millimolar
TON= turnover number
Pd= palladium
Ar= argon
NMP= *N*-methyl-2-pyrrolidone
XantPhos= 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
Ag= silver
Au= gold
OTf= triflate
Cp*= 1,2,3,4,5-pentamethylcyclopentadiene
TMS= tetramethylsilane
Fe= iron
Cs= cesium
KHMDS= potassium bis(trimethylsilyl)amide
OAc= acetate
THF= tetrahydrofuran
Et= ethyl
HRMS= high-resolution mass spectrometry
IR= infrared spectroscopy
K= potassium
Ru-MACHO= carbonylchlorohydrido[bis(2-(diphenylphosphinoethyl)amino]ruthenium(II)
Shvo catalyst= 1-hydroxytetraphenylcyclopentadienyl-(tetraphenyl-2,4 cyclopentadien-1-one)-μ-hydrotetracarbonyldiruthenium(II)
Br= bromide
NHC= N-heterocyclic carbine
Cu= copper
M= metal
Nu= nucleophile
EWG= electron withdrawing group
MWI= microwave irradiation
dba= dibenzylideneacetone
TFP= tri(2-furyl)phosphine
dppf= 1,1′-bis(diphenylphosphino)ferrocene
Bn= benzyl
cod= 1,5-cyclooctadiene
dppp= 1,3-bis(diphenylphosphino)propane
MTDB= 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene
Pr= propyl
Ln= ligand
PNP= *para*-nitrophenol
DPEPhos= (oxydi-2,1-phenylene)bis(diphenylphosphine)
^{1}H NMR= proton nuclear magnetic resonance
CI-MS= chemical ionization-mass spectrometry
TFE= tetrafluoroethylene
PNO-BHy= (*Z*)-*N*′-(2-(diphenylphosphaneyl)benzylidene)-benzohydrazide
PNO-INHy= (*Z*)-*N*′-(2-(diphenylphosphaneyl)-benzylidene)nicotinohydrazide
(PNO-FHy)= (*Z*)-*N*′-(2-(diphenylphosphaneyl)-benzylidene)furan-2-carbohydrazide
(PNS-EtTs)= (*Z*)-2-(2-(diphenylphosphaneyl)benzylidene)-*N*-ethylhydrazine-1-carbothioamide
(PNS-CyTs)= (*Z*)-*N*-cyclohexyl-2-(2-(diphenylphosphaneyl)benzylidene)hydrazine-1-carbothioamide
PNS-Et= 2-(2-(diphenylphosphino)benzylidene)-*N*-ethylthiosemicarbazone
XPS= X-ray photoelectron spectroscopy
DMF= *N*,*N*-dimethylformamide
ATA= alanine triazole
Cy= cyclohexyl
$[BAR^F_4]^-$= tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
GC= gas chromatography
GLC= gas−liquid chromatography
Bu= butyl
BINAP= (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl)
Ip-foxap= chiral 2-(4-isopropyl-Δ^2-oxazolin-2-yl)ferrocenyl-(diphenyl)phosphine
TMS= trimethylsilyl
Nu= nucleophile
(S,R)-JOSIPHOS= (*S*)-1-[(1R)-2-(diphenylphosphino)-ferrocenyl]ethyldicyclohexylphosphine
TBS= *tert*-butyldimethylsilyl
Np= neopentyl
HT= hydrotalcite
HR-TEM= high-resolution transmission electron microscopy
NC= nanocluster
NP= nanoparticles
VS= very small
UV= ultraviolet
HS= high surface
OMS= octahedral molecular sieves
TFT= trifluorotoluene
DMSO= dimethyl sulfoxide

REFERENCES

(1) Mueller, W. M., B, J. P., Libowitz, G. G. *Metal Hydrides*; Academic Press Inc., 1968; p 119.
(2) Smithson, H.; Marianetti, C. A.; Morgan, D.; Van der Ven, A.; Predith, A.; Ceder, G. First-principles study of the stability and electronic structure of metal hydrides. *Phys. Rev. B* **2002**, *66*, 144107−144117.
(3) Chelucci, G. Ruthenium and osmium complexes in C-C bond-forming reactions by borrowing hydrogen catalysis. *Coord. Chem. Rev.* **2017**, *331*, 1−36.
(4) Slatford, P. A.; Whittlesey, M. K.; Williams, J. M. J. C-C Bond formation from alcohols using a Xantphos ruthenium complex. *Tetrahedron Lett.* **2006**, *47*, 6787−6789.
(5) Saidi, O.; Blacker, A. J.; Lamb, G. W.; Marsden, S. P.; Taylor, J. E.; Williams, J. M. J. Borrowing Hydrogen in Water and Ionic Liquids: Iridium-Catalyzed Alkylation of Amines with Alcohols. *Org. Process Res. Dev.* **2010**, *14*, 1046−1049.
(6) Fernandez, F. E.; Puerta, M. C.; Valerga, P. Ruthenium(II) Picolyl-NHC Complexes: Synthesis, Characterization, and Catalytic Activity in Amine *N*-alkylation and Transfer Hydrogenation Reactions. *Organometallics* **2012**, *31*, 6868−6879.
(7) Pridmore, S. J.; Slatford, P. A.; Daniel, A.; Whittlesey, M. K.; Williams, J. M. J. Ruthenium-catalysed conversion of 1,4-alkynediols into pyrroles. *Tetrahedron Lett.* **2007**, *48*, 5115−5120.

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

(8) Ji, J. G.; Lu, X. Y. Facile synthesis of 2,5-disubstituted furans via palladium complex and perfluorinated resinsulfonic acid-catalyzed isomerization dehydration of alkynediols. *J. Chem. Soc., Chem. Commun.* **1993**, 764−765.
(9) Shimizu, K.-i. Heterogeneous catalysis for the direct synthesis of chemicals by borrowing hydrogen methodology. *Catal. Sci. Technol.* **2015**, *5*, 1412−1427.
(10) Yang, Q.; Wang, Q.; Yu, Z. Substitution of alcohols by N-nucleophiles via transition metal-catalyzed dehydrogenation. *Chem. Soc. Rev.* **2015**, *44*, 2305−2329.
(11) Huang, F.; Liu, Z.; Yu, Z. C-Alkylation of ketones and related compounds by alcohols: Transition-metal-catalyzed dehydrogenation. *Angew. Chem., Int. Ed.* **2016**, *55*, 862−875.
(12) Muzart, J. Pd-catalyzed Hydrogen-Transfer reactions from alcohols to C═C, C═O, and C═N bonds. *Eur. J. Org. Chem.* **2015**, *2015*, 5693−5707.
(13) Hollmann, D. Advances in asymmetric Borrowing Hydrogen catalysis. *ChemSusChem* **2014**, *7*, 2411−2413.
(14) Baehn, S.; Imm, S.; Neubert, L.; Zhang, M.; Neumann, H.; Beller, M. The Catalytic Amination of Alcohols. *ChemCatChem* **2011**, *3*, 1853−1864.
(15) Guillena, G.; Ramon, D. J.; Yus, M. Hydrogen Autotransfer in the *N*-Alkylation of Amines and Related Compounds using Alcohols and Amines as Electrophiles. *Chem. Rev.* **2010**, *110*, 1611−1641.
(16) Nixon, T. D.; Whittlesey, M. K.; Williams, J. M. J. Transition metal catalysed reactions of alcohols using borrowing hydrogen methodology. *Dalton Trans.* **2009**, 753−762.
(17) Hamid, M. H. S. A.; Slatford, P. A.; Williams, J. M. J. Borrowing hydrogen in the activation of alcohols. *Adv. Synth. Catal.* **2007**, *349*, 1555−1575.
(18) Guillena, G.; Ramon, D. J.; Yus, M. Alcohols as electrophiles in C-C bond-forming reactions: The hydrogen autotransfer process. *Angew. Chem., Int. Ed.* **2007**, *46*, 2358−2364.
(19) Ma, X.; Su, C.; Xu, Q. *N*-Alkylation by Hydrogen Autotransfer reactions. *Top. Curr. Chem.* **2016**, *374*, 27.
(20) Obora, Y. C-alkylation by Hydrogen Autotransfer Reactions. *Top. Curr. Chem.* **2016**, *374*, 11.
(21) Grubbs, R. H.; Burk, P. L.; Carr, D. D. Consideration of mechanism of olefin metathesis reaction. *J. Am. Chem. Soc.* **1975**, *97*, 3265−3267.
(22) Katz, T. J.; McGinnis, J. Mechanism of olefin metathesis reaction. *J. Am. Chem. Soc.* **1975**, *97*, 1592−1594.
(23) Zielinski, G. K.; Grela, K. Tandem catalysis utilizing olefin metathesis reactions. *Chem. - Eur. J.* **2016**, *22*, 9440−9454.
(24) Haibach, M. C.; Kundu, S.; Brookhart, M.; Goldman, A. S. Alkane Metathesis by Tandem Alkane-Dehydrogenation-Olefin-Metathesis Catalysis and Related Chemistry. *Acc. Chem. Res.* **2012**, *45*, 947−958.
(25) Gupta, M.; Hagen, C.; Flesher, R. J.; Kaska, W. C.; Jensen, C. M. A highly active alkane dehydrogenation catalyst: Stabilization of dihydrido rhodium and iridium complexes by a P-C-P pincer-ligand. *Chem. Commun.* **1996**, 2083−2084.
(26) Goldman, A. S.; Roy, A. H.; Huang, Z.; Ahuja, R.; Schinski, W.; Brookhart, M. Catalytic alkane metathesis by tandem alkane dehydrogenation olefin metathesis. *Science* **2006**, *312*, 257−261.
(27) Goldman, A. S.; Brookhart, M.; MacArthur, A. R.; Ahuja, R.; Huang, Z. *A dual catalyst system for alkane metathesis*. International Patent PCT/US2006/026808, 2007.
(28) Nawara-Hultzsch, A. J.; Hackenberg, J. D.; Punji, B.; Supplee, C.; Emge, T. J.; Bailey, B. C.; Schrock, R. R.; Brookhart, M.; Goldman, A. S. Rational Design of Highly Active "Hybrid" Phosphine−Phosphinite Pincer Iridium Catalysts for Alkane Metathesis. *ACS Catal.* **2013**, *3*, 2505−2514.
(29) Bailey, B. C.; Schrock, R. R.; Kundu, S.; Goldman, A. S.; Huang, Z.; Brookhart, M. Evaluation of Molybdenum and Tungsten Metathesis Catalysts for Homogeneous Tandem Alkane Metathesis. *Organometallics* **2009**, *28*, 355−360.
(30) Tsang, W. C. P.; Hultzsch, K. C.; Alexander, J. B.; Bonitatebus, P. J.; Schrock, R. R.; Hoveyda, A. H. Alkylidene and metalacyclic complexes of tungsten that contain a chiral biphenoxide ligand. Synthesis, asymmetric ring-closing metathesis, and mechanistic investigations. *J. Am. Chem. Soc.* **2003**, *125*, 2652−2666.
(31) Schrock, R. R.; Depue, R. T.; Feldman, J.; Schaverien, C. J.; Dewan, J. C.; Liu, A. H. Preparation and reactivity of several alkylidene complexes of the type W(CHR′)(N-2,6-C_6H_3-i-PR_2)$(OR)_2$ and related tungstacyclobutane complexes - controlling metathesis activity through the choice of alkoxide ligand. *J. Am. Chem. Soc.* **1988**, *110*, 1423−1435.
(32) Feldman, J.; Davis, W. M.; Schrock, R. R. Trigonal-bipyramidal and square-pyramidal tungstacyclobutane intermediates are both present in systems in which olefins are metathesized by complexes of the type W(CHR′)(N-2,6-C_6H_3-i-PR_2)$(OR)_2$. *Organometallics* **1989**, *8*, 2266−2268.
(33) Feldman, J.; Davis, W. M.; Thomas, J. K.; Schrock, R. R. Preparation and reactivity of tungsten(VI) metallacyclobutane complexes - square pyramids versus trigonal bipyramids. *Organometallics* **1990**, *9*, 2535−2548.
(34) Schrock, R. R.; Czekelius, C. Recent advances in the syntheses and applications of molybdenum and tungsten alkylidene and alkylidyne catalysts for the metathesis of alkenes and alkynes. *Adv. Synth. Catal.* **2007**, *349*, 55−77.
(35) Schrock, R. R. Multiple metal-carbon bonds for catalytic metathesis reactions (Nobel lecture 2005). *Adv. Synth. Catal.* **2007**, *349*, 41−53.
(36) Schrock, R. R. High oxidation state multiple metal-carbon bonds. *Chem. Rev.* **2002**, *102*, 145−179.
(37) Chatterjee, A. K.; Grubbs, R. H. Synthesis of trisubstituted alkenes via olefin cross-metathesis. *Org. Lett.* **1999**, *1*, 1751−1753.
(38) Nolan, S. P.; Clavier, H. Chemoselective olefin metathesis transformations mediated by ruthenium complexes. *Chem. Soc. Rev.* **2010**, *39*, 3305−3316.
(39) Williams, M. J.; Kong, J.; Chung, C. *Ruthenium-based metathesis pre-catalyst compounds*. International Patent PCT/US2015/065142, 2016.
(40) Lewin, J. L.; Woodrum, N. L.; Cramer, C. J. Density Functional Characterization of Methane Metathesis in *ansa*-[Bis(η^5-2-indenyl)-methane]ML Complexes [M = Sc, Y, Lu; L = CH_3, $CH_2C(CH_3)_3$]. *Organometallics* **2006**, *25*, 5906−5912.
(41) Lawrence, S. A. *Amines: Synthesis, Properties and Applications*; Cambridge University Press, 2004; p 269.
(42) Hartwig, J. F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; John Wiley & Sons, Inc., 2003; pp 1051−1096.
(43) Salvatore, R. N.; Yoon, C. H.; Jung, K. W. Synthesis of secondary amines. *Tetrahedron* **2001**, *57*, 7785−7811.
(44) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. A Highly Active Catalyst for Palladium-Catalyzed Cross-Coupling Reactions: Room-Temperature Suzuki Couplings and Amination of Unactivated Aryl Chlorides. *J. Am. Chem. Soc.* **1998**, *120*, 9722−9723.
(45) Kwong, F. Y.; Buchwald, S. L. Mild and Efficient Copper-Catalyzed Amination of Aryl Bromides with Primary Alkylamines. *Org. Lett.* **2003**, *5*, 793−796.
(46) Alex, K.; Tillack, A.; Schwarz, N.; Beller, M. General zinc-catalyzed intermolecular hydroamination of terminal alkynes. *ChemSusChem* **2008**, *1*, 333−338.
(47) Brunet, J.-J.; Chu, N.-C.; Rodriguez-Zubiri, M. Platinum-catalyzed intermolecular hydroamination of alkenes: Halide-anion-promoted catalysis. *Eur. J. Inorg. Chem.* **2007**, *2007*, 4711−4722.
(48) Ahmed, M.; Buch, C.; Routaboul, L.; Jackstell, R.; Klein, H.; Spannenberg, A.; Beller, M. Hydroaminomethylation with novel rhodium-carbene complexes: An efficient catalytic approach to pharmaceuticals. *Chem. - Eur. J.* **2007**, *13*, 1594−1601.
(49) Malkov, A. V.; Stoncius, S.; Kocovsky, P. Enantioselective synthesis of 1,2-diarylaziridines by the organocatalytic reductive amination of alpha-chloroketones. *Angew. Chem., Int. Ed.* **2007**, *46*, 3722−3724.
(50) Hughes, G.; Devine, P. N.; Naber, J. R.; O'Shea, P. D.; Foster, B. S.; McKay, D. J.; Volante, R. P. Diastereoselective reductive Amination

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

of aryl trifluoromethyl ketones and alpha-amino esters. *Angew. Chem., Int. Ed.* **2007**, *46*, 1839−1842.
(51) Xie, Y.; Liu, S.; Liu, Y.; Wen, Y.; Deng, G.-J. Palladium-Catalyzed One-Pot Diarylamine Formation from Nitroarenes and Cyclohexanones. *Org. Lett.* **2012**, *14*, 1692−1695.
(52) Bradley, D.; Mehrotra, R. C.; Rothwell, I.; Singh, A. *Alkoxo and Aryloxo Derivatives of Metals*; Elsevier Science, 2001; p 383.
(53) Turova, N. Y.; Turevskaya, E. P.; Kessler, V. G.; Yanovskaya, M. I. *The Chemistry of Metal Alkoxides*; Springer: New York, 2006; p 11.
(54) March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*; John Wiley & Sons, Inc., Hoboken, NJ, 2007; p 496.
(55) Pan, S.; Shibata, T. Recent Advances in Iridium-Catalyzed Alkylation of C-H and N-H Bonds. *ACS Catal.* **2013**, *3*, 704−712.
(56) Obora, Y. Recent advances in alpha-alkylation reactions using alcohols with Hydrogen Borrowing methodologies. *ACS Catal.* **2014**, *4*, 3972−3981.
(57) Dobereiner, G. E.; Crabtree, R. H. Dehydrogenation as a Substrate-Activating Strategy in Homogeneous Transition-Metal Catalysis. *Chem. Rev.* **2010**, *110*, 681−703.
(58) Nielsen, A. T.; Houlihan, W. J. The Aldol Condensation. In *Organic Reactions*; John Wiley & Sons, Inc., 2004; p 25.
(59) Clayden, J.; Greeves, N.; Warren, S. *Organic Chemistry*; OUP: Oxford, 2012; pp 614−654.
(60) Yan, F.-X.; Zhang, M.; Wang, X.-T.; Xie, F.; Chen, M.-M.; Jiang, H. Efficient ruthenium-catalyzed alpha-alkylation of ketones using pyridyl methanols. *Tetrahedron* **2014**, *70*, 1193−1198.
(61) Kovalenko, O. O.; Lundberg, H.; Huebner, D.; Adolfsson, H. Tandem alpha-alkylation/asymmetric transfer hydrogenation of acetophenones with primary alcohols. *Eur. J. Org. Chem.* **2014**, *2014*, 6639−6642.
(62) Martinez, R.; Ramon, D. J.; Yus, M. Easy α-alkylation of ketones with alcohols through a hydrogen autotransfer process catalyzed by $RuCl_2(DMSO)_4$. *Tetrahedron* **2006**, *62*, 8988−9001.
(63) Martinez, R.; Brand, G. J.; Ramon, D. J.; Yus, M. $[Ru(DMSO)]_4Cl_2$ catalyzes the α-alkylation of ketones by alcohols. *Tetrahedron Lett.* **2005**, *46*, 3683−3686.
(64) Cho, C. S.; Kim, B. T.; Kim, T. J.; Shim, S. C. An unusual type of ruthenium-catalyzed transfer hydrogenation of ketones with alcohols accompanied by C-C coupling. *J. Org. Chem.* **2001**, *66*, 9020−9022.
(65) Kuwahara, T.; Fukuyama, T.; Ryu, I. Ruthenium hydride/nitrogen tridentate ligand-catalyzed α-alkylation of acetamides with primary alcohols. *RSC Adv.* **2013**, *3*, 13702−13704.
(66) Rueping, M.; Phapale, V. B. Effective synthesis of 2,5-disubstituted tetrahydrofurans from glycerol by catalytic alkylation of ketones. *Green Chem.* **2012**, *14*, 55−57.
(67) Quan, X.; Kerdphon, S.; Andersson, P. G. C-C coupling of ketones with methanol catalyzed by a N-heterocyclic carbene-phosphine iridium complex. *Chem. - Eur. J.* **2015**, *21*, 3576−3579.
(68) Ogawa, S.; Obora, Y. Iridium-catalyzed selective α-methylation of ketones with methanol. *Chem. Commun.* **2014**, *50*, 2491−2493.
(69) Taguchi, K.; Nakagawa, H.; Hirabayashi, T.; Sakaguchi, S.; Ishii, Y. An efficient direct α-alkylation of ketones with primary alcohols catalyzed by $Ir(cod)Cl_2/PPh_3$/KOH system without solvent. *J. Am. Chem. Soc.* **2004**, *126*, 72−73.
(70) Shen, D.; Poole, D. L.; Shotton, C. C.; Kornahrens, A. F.; Healy, M. P.; Donohoe, T. J. Hydrogen-borrowing and interrupted-hydrogen-borrowing reactions of ketones and methanol catalyzed by iridium. *Angew. Chem., Int. Ed.* **2015**, *54*, 1642−1645.
(71) Wang, D.; Zhao, K.; Ma, P.; Xu, C.; Ding, Y. Direct α-alkylation of ketones with primary alcohols catalyzed by iridium-CNP complex. *Tetrahedron Lett.* **2014**, *55*, 7233−7235.
(72) Iuchi, Y.; Obora, Y.; Ishii, Y. Iridium-Catalyzed α-Alkylation of Acetates with Primary Alcohols and Diols. *J. Am. Chem. Soc.* **2010**, *132*, 2536−2537.
(73) Guo, L.; Ma, X.; Fang, H.; Jia, X.; Huang, Z. A general and mild catalytic α-alkylation of unactivated esters using alcohols. *Angew. Chem., Int. Ed.* **2015**, *54*, 4023−4027.
(74) Ma, J.; Wang, N.; Li, F. One-pot sequential catalytic hydration of alkynes and α-alkylation with alcohols for the synthesis of α-alkylated ketones. *Asian J. Org. Chem.* **2014**, *3*, 940−947.
(75) Chan, L. K. M.; Poole, D. L.; Shen, D.; Healy, M. P.; Donohoe, T. J. Rhodium-catalyzed ketone methylation using methanol under mild conditions: Formation of α-branched products. *Angew. Chem., Int. Ed.* **2014**, *53*, 761−765.
(76) Satyanarayana, P.; Reddy, G. M.; Maheswaran, H.; Kantam, M. L. Tris(acetylacetonato)rhodium(III)-Catalyzed α-Alkylation of Ketones, β-Alkylation of Secondary Alcohols and Alkylation of Amines with Primary Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 1859−1867.
(77) Elangovan, S.; Sortais, J.-B.; Beller, M.; Darcel, C. Iron-catalyzed α-alkylation of ketones with alcohols. *Angew. Chem., Int. Ed.* **2015**, *54*, 14483−14486.
(78) Viciano, M.; Sanau, M.; Peris, E. Ruthenium Janus-head complexes with a triazolediylidene ligand. structural features and catalytic applications. *Organometallics* **2007**, *26*, 6050−6054.
(79) Gnanamgari, D.; Leung, C. H.; Schley, N. D.; Hilton, S. T.; Crabtree, R. H. Alcohol cross-coupling reactions catalyzed by Ru and Ir terpyridine complexes. *Org. Biomol. Chem.* **2008**, *6*, 4442−4445.
(80) Martinez, R.; Ramon, D. J.; Yus, M. $RuCl_2(DMSO)_4$ catalyzes the β-alkylation of secondary alcohols with primary alcohols through a hydrogen autotransfer process. *Tetrahedron* **2006**, *62*, 8982−8987.
(81) Cho, C. S.; Kim, B. T.; Kim, H. S.; Kim, T. J.; Shim, S. C. Ruthenium-catalyzed one-pot β-alkylation of secondary alcohols with primary alcohols. *Organometallics* **2003**, *22*, 3608−3610.
(82) Prades, A.; Viciano, M.; Sanau, M.; Peris, E. Preparation of a series of "Ru(*p*-cymene)" complexes with different N-heterocyclic carbene ligands for the catalytic β-alkylation of secondary alcohols and dimerization of phenylacetylene. *Organometallics* **2008**, *27*, 4254−4259.
(83) Bai, W.; Jia, G. Ruthenium-catalyzed β-alkylation of secondary alcohols with primary alcohols. *Inorg. Chim. Acta* **2015**, *431*, 234−241.
(84) Musa, S.; Ackermann, L.; Gelman, D. Dehydrogenative Cross-Coupling of Primary and Secondary Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 3077−3080.
(85) Wang, Q.; Wu, K.; Yu, Z. Ruthenium(III)-catalyzed β-alkylation of secondary alcohols with primary alcohols. *Organometallics* **2016**, *35*, 1251−1256.
(86) Dowson, G. R. M.; Haddow, M. F.; Lee, J.; Wingad, R. L.; Wass, D. F. Catalytic Conversion of Ethanol into an Advanced Biofuel: Unprecedented Selectivity for n-Butanol. *Angew. Chem., Int. Ed.* **2013**, *52*, 9005−9008.
(87) Mas-Marza, E.; Mata, J. A.; Peris, E. Triazolediylidenes: A versatile class of ligands for the preparation of discrete molecules of homo- and hetero-binuclear complexes for improved catalytic applications. *Angew. Chem., Int. Ed.* **2007**, *46*, 3729−3731.
(88) Li, Y.; Li, H.; Junge, H.; Beller, M. Selective ruthenium-catalyzed methylation of 2-arylethanols using methanol as C1 feedstock. *Chem. Commun.* **2014**, *50*, 14991−14994.
(89) Wang, D.; Zhao, K.; Yu, X.; Miao, H.; Ding, Y. Iridium-CNP complex catalyzed cross-coupling of primary alcohols and secondary alcohols by a borrowing hydrogen strategy. *RSC Adv.* **2014**, *4*, 42924−42929.
(90) Gong, X.; Zhang, H.; Li, X. Iridium phosphine abnormal N-heterocyclic carbene complexes in catalytic hydrogen transfer reactions. *Tetrahedron Lett.* **2011**, *52*, 5596−5600.
(91) Victoria Jiménez, M.; Fernandez-Tornos, J.; Javier Modrego, F.; Perez-Torrente, J. J.; Oro, L. A. Oxidation and β-alkylation of alcohols catalysed by iridium(I) complexes with functionalised N-heterocyclic carbene ligands. *Chem. - Eur. J.* **2015**, *21*, 17877−17889.
(92) Obora, Y.; Anno, Y.; Okamoto, R.; Matsu-ura, T.; Ishii, Y. Iridium-Catalyzed Reactions of ω-Arylalkanols to α,ω-Diarylalkanes. *Angew. Chem., Int. Ed.* **2011**, *50*, 8618−8622.
(93) Kose, O.; Saito, S. Cross-coupling reaction of alcohols for carbon-carbon bond formation using pincer-type NHC/palladium catalysts. *Org. Biomol. Chem.* **2010**, *8*, 896−900.
(94) Carlini, C.; Di Girolamo, M.; Macinai, A.; Marchionna, M.; Noviello, M.; Galletti, A. M. R.; Sbrana, G. Synthesis of isobutanol by

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

the Guerbet condensation of methanol with n-propanol in the presence of heterogeneous and homogeneous palladium-based catalytic systems. *J. Mol. Catal. A: Chem.* **2003**, *204−205*, 721−728.
(95) Liao, S.; Yu, K.; Li, Q.; Tian, H.; Zhang, Z.; Yu, X.; Xu, Q. Copper-catalyzed C-alkylation of secondary alcohols and methyl ketones with alcohols employing the aerobic relay race methodology. *Org. Biomol. Chem.* **2012**, *10*, 2973−2978.
(96) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. Oxidation of alcohols by transition-metal complexes 0.5. Selective catalytic monoalkylation of arylacetonitriles by alcohols. *Tetrahedron Lett.* **1981**, *22*, 4107−4110.
(97) Li, F.; Zou, X.; Wang, N. Direct coupling of arylacetonitriles and primary alcohols to α-alkylated arylacetamides with complete atom economy catalyzed by a rhodium complex-triphenylphosphine-potassium hydroxide system. *Adv. Synth. Catal.* **2015**, *357*, 1405−1415.
(98) Lofberg, C.; Grigg, R.; Whittaker, M. A.; Keep, A.; Derrick, A. Efficient solvent-free selective monoalkylation of arylacetonitriles with mono-, bis-, and tris-primary alcohols catalyzed by a Cp*Ir complex. *J. Org. Chem.* **2006**, *71*, 8023−8027.
(99) Lofberg, C.; Grigg, R.; Keep, A.; Derrick, A.; Sridharan, V.; Kilner, C. Sequential one-pot bimetallic Ir(III)/Pd(0) catalysed mono-/bis-alkylation and spirocyclisation processes of 1,3-dimethyl-barbituric acid and allenes. *Chem. Commun.* **2006**, 5000−5002.
(100) Grigg, R.; Lofberg, C.; Whitney, S.; Sridharan, V.; Keep, A.; Derrick, A. Iridium catalysed alkylation of *tert*-butyl cyanoacetate with alcohols under solvent free conditions. *Tetrahedron* **2009**, *65*, 849−854.
(101) Iuchi, Y.; Hyotanishi, M.; Miller, B. E.; Maeda, K.; Obora, Y.; Ishii, Y. Synthesis of ω-Hydroxy Carboxylic Acids and α,ω-Dimethyl Ketones Using α,ω-Diols As Alkylating Agents. *J. Org. Chem.* **2010**, *75*, 1803−1806.
(102) Morita, M.; Obora, Y.; Ishii, Y. Alkylation of active methylene compounds with alcohols catalyzed by an iridium complex. *Chem. Commun.* **2007**, 2850−2852.
(103) Black, P. J.; Cami-Kobeci, G.; Edwards, M. G.; Slatford, P. A.; Whittlesey, M. K.; Williams, J. M. J. Borrowing hydrogen: iridium-catalysed reactions for the formation of C-C bonds from alcohols. *Org. Biomol. Chem.* **2006**, *4*, 116−125.
(104) Putra, A. E.; Oe, Y.; Ohta, T. Ruthenium-catalyzed selective synthesis of monoalkylated barbituric acids through "borrowing hydrogen" methodology. *Tetrahedron Lett.* **2017**, *58*, 1098−1101.
(105) Pena-Lopez, M.; Neumann, H.; Beller, M. Ruthenium pincer-catalyzed synthesis of substituted γ-butyrolactones using hydrogen autotransfer methodology. *Chem. Commun.* **2015**, *51*, 13082−13085.
(106) Deibl, N.; Kempe, R. General and mild cobalt-catalyzed C-alkylation of unactivated amides and esters with alcohols. *J. Am. Chem. Soc.* **2016**, *138*, 10786−10789.
(107) Buil, M. L.; Esteruelas, M. A.; Herrero, J.; Izquierdo, S.; Pastor, I. M.; Yus, M. Osmium Catalyst for the Borrowing Hydrogen Methodology: α-Alkylation of Arylacetonitriles and Methyl Ketones. *ACS Catal.* **2013**, *3*, 2072−2075.
(108) Pridmore, S. J.; Williams, J. M. J. C-C bond formation from alcohols and malonate half esters using borrowing hydrogen methodology. *Tetrahedron Lett.* **2008**, *49*, 7413−7415.
(109) Klein, J.; Bergmann, E. D. The reaction of acetals with malonic acid and its derivatives - A contribution to the knowledge of the Knoevenagel-Doebner reaction. *J. Am. Chem. Soc.* **1957**, *79*, 3452−3454.
(110) List, B.; Doehring, A.; Fonseca, M. T. H.; Job, A.; Torres, R. R. A practical, efficient, and atom economic alternative to the Wittig and Horner-Wadsworth-Emmons reactions for the synthesis of (*E*)-α,β-unsaturated esters from aldehydes. *Tetrahedron* **2006**, *62*, 476−482.
(111) Black, P. J.; Harris, W.; Williams, J. M. J. Catalytic electronic activation: Indirect addition of nucleophiles to an allylic alcohol. *Angew. Chem., Int. Ed.* **2001**, *40*, 4475−4476.
(112) Whitney, S.; Grigg, R.; Derrick, A.; Keep, A. $[Cp^*IrCl_2]_2$-Catalyzed indirect functionalization of alcohols: Novel strategies for the synthesis of substituted indoles. *Org. Lett.* **2007**, *9*, 3299−3302.
(113) Chen, S.-J.; Lu, G.-P.; Cai, C. Iridium-catalyzed methylation of indoles and pyrroles using methanol as feedstock. *RSC Adv.* **2015**, *5*, 70329−70332.
(114) Bartolucci, S.; Mari, M.; Bedini, A.; Piersanti, G.; Spadoni, G. Iridium-catalyzed direct synthesis of tryptamine derivatives from indoles: exploiting N-protected β-amino alcohols as alkylating agents. *J. Org. Chem.* **2015**, *80*, 3217−3222.
(115) Jensen, T.; Madsen, R. Ruthenium-Catalyzed Alkylation of Oxindole with Alcohols. *J. Org. Chem.* **2009**, *74*, 3990−3992.
(116) Grigg, R.; Whitney, S.; Sridharan, V.; Keep, A.; Derrick, A. Iridium catalysed C-3 alkylation of oxindole with alcohols under solvent free thermal or microwave conditions. *Tetrahedron* **2009**, *65*, 4375−4383.
(117) Blank, B.; Kempe, R. Catalytic Alkylation of Methyl-N-Heteroaromatics with Alcohols. *J. Am. Chem. Soc.* **2010**, *132*, 924−925.
(118) Obora, Y.; Ogawa, S.; Yamamoto, N. Iridium-Catalyzed Alkylation of Methylquinolines with Alcohols. *J. Org. Chem.* **2012**, *77*, 9429−9433.
(119) Sundararaju, B.; Tang, Z.; Achard, M.; Sharma, G. V. M; Toupet, L.; Bruneau, C. Ruthenium-Catalyzed Cascade N- and C(3)-Dialkylation of Cyclic Amines with Alcohols Involving Hydrogen Autotransfer Processes. *Adv. Synth. Catal.* **2010**, *352*, 3141−3146.
(120) Edwards, M. G.; Williams, J. M. J. Catalytic electronic activation: Indirect "Wittig" reaction of alcohols. *Angew. Chem., Int. Ed.* **2002**, *41*, 4740−4743.
(121) Black, P. J.; Edwards, M. G.; Williams, J. M. J. Borrowing hydrogen: Indirect "Wittig" olerination for the formation of C-C bonds from alcohols. *Eur. J. Org. Chem.* **2006**, *2006*, 4367−4378.
(122) Burling, S.; Paine, B. M.; Nama, D.; Brown, V. S.; Mahon, M. F.; Prior, T. J.; Pregosin, P. S.; Whittlesey, M. K.; Williams, J. M. J. C-H activation reactions of ruthenium N-heterocyclic carbene complexes: Application in a catalytic tandem reaction involving C-C bond formation from alcohols. *J. Am. Chem. Soc.* **2007**, *129*, 1987−1995.
(123) Edwards, M. G.; Jazzar, R. F. R.; Paine, B. M.; Shermer, D. J.; Whittlesey, M. K.; Williams, J. M. J.; Edney, D. D. Borrowing hydrogen: a catalytic route to C-C bond formation from alcohols. *Chem. Commun.* **2004**, 90−91.
(124) Nguyen, K. D.; Park, B. Y.; Luong, T.; Sato, H.; Garza, V. J.; Krische, M. J. Metal-catalyzed reductive coupling of olefin-derived nucleophiles: Reinventing carbonyl addition. *Science* **2016**, *354*, 300.
(125) Leung, J. C.; Geary, L. M.; Chen, T.-Y.; Zbieg, J. R.; Krische, M. J. Direct, Redox-Neutral Prenylation and Geranylation of Secondary Carbinol C−H Bonds: C4-Regioselectivity in Ruthenium-Catalyzed C−C Couplings of Dienes to α-Hydroxy Esters. *J. Am. Chem. Soc.* **2012**, *134*, 15700−15703.
(126) Park, B. Y.; Montgomery, T. P.; Garza, V. J.; Krische, M. J. Ruthenium Catalyzed Hydrohydroxyalkylation of Isoprene with Heteroaromatic Secondary Alcohols: Isolation and Reversible Formation of the Putative Metallacycle Intermediate. *J. Am. Chem. Soc.* **2013**, *135*, 16320−16323.
(127) Chen, T.-Y.; Krische, M. J. Regioselective Ruthenium Catalyzed Hydrohydroxyalkylation of Dienes with 3-Hydroxy-2-oxindoles: Prenylation, Geranylation, and Beyond. *Org. Lett.* **2013**, *15*, 2994−2997.
(128) Cami-Kobeci, G.; Williams, J. M. J. Conversion of alcohols into *N*-alkyl anilines via an indirect aza-Wittig reaction. *Chem. Commun.* **2004**, 1072−1073.
(129) Martinez-Asencio, A.; Yus, M.; Ramon, D. J. Palladium(II) acetate as catalyst for the *N*-alkylation of aromatic amines, sulfonamides, and related nitrogenated compounds with alcohols by a hydrogen autotransfer process. *Synthesis* **2011**, *2011*, 3730−3740.
(130) Martinez-Asencio, A.; Ramon, D. J.; Yus, M. *N*-Alkylation of poor nucleophilic amines and derivatives with alcohols by a hydrogen autotransfer process catalyzed by copper(II) acetate: scope and mechanistic considerations. *Tetrahedron* **2011**, *67*, 3140−3149.
(131) Kunjapur, A. M.; Prather, K. L. J. Microbial engineering for aldehyde synthesis. *Appl. Environ. Microbiol.* **2015**, *81*, 1892−1901.

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

(132) Gunanathan, C.; Milstein, D. Metal-Ligand Cooperation by Aromatization-Dearomatization: A New Paradigm in Bond Activation and "Green" Catalysis. *Acc. Chem. Res.* **2011**, *44*, 588−602.
(133) Baumann, W.; Spannenberg, A.; Pfeffer, J.; Haas, T.; Koeckritz, A.; Martin, A.; Deutsch, J. Utilization of Common Ligands for the Ruthenium-Catalyzed Amination of Alcohols. *Chem. - Eur. J.* **2013**, *19*, 17702−17706.
(134) Walther, G.; Deutsch, J.; Martin, A.; Baumann, F. E.; Fridag, D.; Franke, R.; Kockritz, A. α,ω-Functionalized C19 Monomers. *ChemSusChem* **2011**, *4*, 1052−1054.
(135) Imm, S.; Bähn, S.; Neubert, L.; Neumann, H.; Beller, M. An Efficient and General Synthesis of Primary Amines by Ruthenium-Catalyzed Amination of Secondary Alcohols with Ammonia. *Angew. Chem., Int. Ed.* **2010**, *49*, 8126−8129.
(136) Pingen, D.; Muller, C.; Vogt, D. Direct Amination of Secondary Alcohols Using Ammonia. *Angew. Chem., Int. Ed.* **2010**, *49*, 8130−8133.
(137) Imm, S.; Baehn, S.; Zhang, M.; Neubert, L.; Neumann, H.; Klasovsky, F.; Pfeffer, J.; Haas, T.; Beller, M. Improved Ruthenium-Catalyzed Amination of Alcohols with Ammonia: Synthesis of Diamines and Amino Esters. *Angew. Chem., Int. Ed.* **2011**, *50*, 7599−7603.
(138) Zhang, M.; Imm, S.; Baehn, S.; Neumann, H.; Beller, M. Synthesis of a-Amino Acid Amides: Ruthenium-Catalyzed Amination of a-Hydroxy Amides. *Angew. Chem., Int. Ed.* **2011**, *50*, 11197−11201.
(139) Pingen, D.; Diebolt, O.; Vogt, D. Direct Amination of Bio-Alcohols Using Ammonia. *ChemCatChem* **2013**, *5*, 2905−2912.
(140) Yamaguchi, R.; Mingwen, Z.; Kawagoe, S.; Asai, C.; Fujita, K.-i A New Atom-Economical and Selective Synthesis of Secondary and Tertiary Alkylamines by Means of Cp*Iridium Complex Catalyzed Multiple *N*-Alkylation of Ammonium Salts with Alcohols without Solvent. *Synthesis* **2009**, *2009*, 1220−1223.
(141) Kawahara, R.; Fujita, K.-i.; Yamaguchi, R. Multialkylation of Aqueous Ammonia with Alcohols Catalyzed by Water-Soluble Cp*Ir−Ammine Complexes. *J. Am. Chem. Soc.* **2010**, *132*, 15108−15111.
(142) Schaub, T.; Buschhaus, B.; Brinks, M. K.; Schelwies, M.; Paciello, R.; Melder, J.-P.; Merger, M. *Method for producing primary amines obtained by homogeneously catalyzed alcohol amination*. Germany Patent WO 2012119927A1, 2012.
(143) Schaub, T.; Buschhaus, B.; Brinks, M. K.; Schelwies, M.; Paciello, R.; Melder, J.-P.; Merger, M. *Method for producing alkanol amines obtained by homogeneously catalyzed alcohol amination*. Germany Patent WO 2012119928A1, 2012.
(144) Schaub, T.; Buschhaus, B.; Brinks, M. K.; Schelwies, M.; Paciello, R.; Melder, J.-P.; Merger, M. *Process for the preparation of primary amines by homogeneously catalyzed alcohol amination*. U.S. Patent US 20120232309A1, 2012.
(145) Klasovsky, F.; Tacke, T.; Pfeffer, J. C.; Haas, T.; Beller, M.; Martin, A.; Deutsch, J.; Koeckritz, A.; Imm, S.; Haberland, J. *Process for the direct amination of alcohols using ammonia to form primary amines by means of a xantphos catalyst system*. Germany Patent WO 2012113475A1, 2012.
(146) Nakagawa, N.; Derrah, E. J.; Schelwies, M.; Rominger, F.; Trapp, O.; Schaub, T. Triphos derivatives and diphosphines as ligands in the ruthenium-catalysed alcohol amination with NH3. *Dalton Trans.* **2016**, *45*, 6856−6865.
(147) Derrah, E. J.; Hanauer, M.; Plessow, P. N.; Schelwies, M.; da Silva, M. K.; Schaub, T. Ru(II)-triphos catalyzed amination of alcohols with ammonia via ionic species. *Organometallics* **2015**, *34*, 1872−1881.
(148) Balaraman, E.; Srimani, D.; Diskin-Posner, Y.; Milstein, D. Direct synthesis of secondary amines from alcohols and ammonia catalyzed by a ruthenium pincer complex. *Catal. Lett.* **2015**, *145*, 139−144.
(149) Das, K.; Shibuya, R.; Nakahara, Y.; Germain, N.; Ohshima, T.; Mashima, K. Platinum-Catalyzed Direct Amination of Allylic Alcohols with Aqueous Ammonia: Selective Synthesis of Primary Allylamines. *Angew. Chem., Int. Ed.* **2012**, *51*, 150−154.
(150) Crabtree, R. H. An Organometallic Future in Green and Energy Chemistry? *Organometallics* **2011**, *30*, 17−19.
(151) Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S.; Tongpenyai, N. Transition metal-catalyzed *N*-alkylation of amines by alcohols. *J. Chem. Soc., Chem. Commun.* **1981**, 611−612.
(152) Watanabe, Y.; Tsuji, Y.; Ohsugi, Y. The ruthenium catalyzed *N*-alkylation and *N*-heterocyclization of aniline using alcohols and aldehydes. *Tetrahedron Lett.* **1981**, *22*, 2667−2670.
(153) Bartoszewicz, A.; Marcos, R.; Sahoo, S.; Inge, A. K.; Zou, X.; Martin-Matute, B. A Highly Active Bifunctional Iridium Complex with an Alcohol/Alkoxide-Tethered N-Heterocyclic Carbene for Alkylation of Amines with Alcohols. *Chem. - Eur. J.* **2012**, *18*, 14510−14519.
(154) Ruch, S.; Irrgang, T.; Kempe, R. New Iridium Catalysts for the Selective Alkylation of Amines by Alcohols under Mild Conditions and for the Synthesis of Quinolines by Acceptor-less Dehydrogenative Condensation. *Chem. - Eur. J.* **2014**, *20*, 13279−13285.
(155) Fernandez, F. E.; Carmen Puerta, M.; Valerga, P. Ruthenium-(II) Picolyl-NHC Complexes: Synthesis, Characterization, and Catalytic Activity in Amine *N*-alkylation and Transfer Hydrogenation Reactions. *Organometallics* **2012**, *31*, 6868−6879.
(156) Agrawal, S.; Lenormand, M.; Martin-Matute, B. Selective Alkylation of (Hetero)Aromatic Amines with Alcohols Catalyzed by a Ruthenium Pincer Complex. *Org. Lett.* **2012**, *14*, 1456−1459.
(157) Michlik, S.; Kempe, R. New Iridium Catalysts for the Efficient Alkylation of Anilines by Alcohols under Mild Conditions. *Chem. - Eur. J.* **2010**, *16*, 13193−13198.
(158) Tuan Thanh, D.; Ramalingam, B.; Shan, S. P.; Seayad, A. M. An efficient palladium-catalyzed *N*-alkylation of amines using primary and secondary alcohols. *ACS Catal.* **2013**, *3*, 2536−2540.
(159) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. J. Iridium-catalysed amine alkylation with alcohols in water. *Chem. Commun.* **2010**, *46*, 1541−1543.
(160) Kawahara, R.; Fujita, K.-i.; Yamaguchi, R. *N*-Alkylation of Amines with Alcohols Catalyzed by a Water-Soluble Cp*Iridium Complex: An Efficient Method for the Synthesis of Amines in Aqueous Media. *Adv. Synth. Catal.* **2011**, *353*, 1161−1168.
(161) Jumde, V. R.; Gonsalvi, L.; Guerriero, A.; Peruzzini, M.; Taddei, M. A Ruthenium-based catalytic system for a mild Borrowing-Hydrogen process. *Eur. J. Org. Chem.* **2015**, *2015*, 1829−1833.
(162) Yan, T.; Feringa, B. L.; Barta, K. Benzylamines via iron-catalyzed direct amination of benzyl alcohols. *ACS Catal.* **2016**, *6*, 381−388.
(163) Zhan, L.-W.; Han, L.; Xing, P.; Jiang, B. Copper N-heterocyclic carbene: A catalyst for aerobic oxidation or reduction reactions. *Org. Lett.* **2015**, *17*, 5990−5993.
(164) Leonard, J.; Blacker, A. J.; Marsden, S. P.; Jones, M. F.; Mulholland, K. R.; Newton, R. A survey of the Borrowing Hydrogen approach to the synthesis of some pharmaceutically relevant intermediates. *Org. Process Res. Dev.* **2015**, *19*, 1400−1410.
(165) Prakash, G.; Nirmala, M.; Ramachandran, R.; Viswanathamurthi, P.; Malecki, J. G.; Sanmartin, J. Heteroleptic binuclear copper(I) complexes bearing bis(salicylidene)hydrazone ligands: Synthesis, crystal structure and application in catalytic *N*-alkylation of amines. *Polyhedron* **2015**, *89*, 62−69.
(166) Rawlings, A. J.; Diorazio, L. J.; Wills, M. C-N Bond formation between alcohols and amines using an iron cyclopentadienone catalyst. *Org. Lett.* **2015**, *17*, 1086−1089.
(167) Pan, H.-J.; Ng, T. W.; Zhao, Y. Iron-catalyzed amination of alcohols assisted by Lewis acid. *Chem. Commun.* **2015**, *51*, 11907−11910.
(168) Midya, S. P.; Mondal, A.; Begum, A.; Balaraman, E. A Simple Cobalt(II) Chloride Catalyzed *N*-Alkylation of Amines with Alcohols. *Synthesis* **2017**, *49*, 3957−3961.
(169) Sahin, Z.; Gurbuz, N.; Ozdemir, I.; Sahin, O.; Buyukgungor, O.; Achard, M.; Bruneau, C. *N*-Alkylation and N,C-dialkylation of amines with alcohols in the presence of ruthenium catalysts with chelating *N*-heterocyclic carbene ligands. *Organometallics* **2015**, *34*, 2296−2304.
(170) Minakawa, M.; Okubo, M.; Kawatsura, M. Selective direct *N*-alkylation of amines with alcohols using iron(III) phthalocyanine

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

chloride under solvent-free conditions. *Bull. Chem. Soc. Jpn.* **2015**, *88*, 1680−1682.
(171) Michlik, S.; Hille, T.; Kempe, R. The Iridium-Catalyzed Synthesis of Symmetrically and Unsymmetrically Alkylated Diamines under Mild Reaction Conditions. *Adv. Synth. Catal.* **2012**, *354*, 847−862.
(172) Andrushko, N.; Andrushko, V.; Roose, P.; Moonen, K.; Boerner, A. Amination of Aliphatic Alcohols and Diols with an Iridium Pincer Catalyst. *ChemCatChem* **2010**, *2*, 640−643.
(173) Berliner, M. A.; Dubant, S. P. A.; Makowski, T.; Ng, K.; Sitter, B.; Wager, C.; Zhang, Y. Use of an Iridium-Catalyzed Redox-Neutral Alcohol-Amine Coupling on Kilogram Scale for the Synthesis of a GlyT1 Inhibitor. *Org. Process Res. Dev.* **2011**, *15*, 1052−1062.
(174) Cumpstey, I.; Agrawal, S.; Borbas, K. E.; Martin-Matute, B. Iridium-catalysed condensation of alcohols and amines as a method for aminosugar synthesis. *Chem. Commun.* **2011**, *47*, 7827−7829.
(175) Fujita, K.-i.; Enoki, Y.; Yamaguchi, R. Cp*Ir-catalyzed *N*-alkylation of amines with alcohols. A versatile and atom economical method for the synthesis of amines. *Tetrahedron* **2008**, *64*, 1943−1954.
(176) Lorentz-Petersen, L. L. R.; Nordstrom, L. U.; Madsen, R. Iridium-Catalyzed Condensation of Amines and Vicinal Diols to Substituted Piperazines. *Eur. J. Org. Chem.* **2012**, *2012*, 6752−6759.
(177) Yamaguchi, R.; Fujita, K.-i.; Zhu, M. Recent progress of new catalytic synthetic methods for nitrogen heterocycles based on hydrogen transfer reactions. *Heterocycles* **2010**, *81*, 1093−1140.
(178) Wetzel, A.; Wockel, S.; Schelwies, M.; Brinks, M. K.; Rominger, F.; Hofmann, P.; Limbach, M. Selective alkylation of amines with alcohols by Cp-star-Iridium(III) half-sandwich complexes. *Org. Lett.* **2013**, *15*, 266−269.
(179) Zou, Q.; Wang, C.; Smith, J.; Xue, D.; Xiao, J. Alkylation of amines with alcohols and amines by a single catalyst under mild conditions. *Chem. - Eur. J.* **2015**, *21*, 9656−9661.
(180) Ramachandran, R.; Prakash, G.; Nirmala, M.; Viswanathamurthi, P.; Malecki, J. G. Ruthenium(II) carbonyl complexes designed with arsine and PNO/PNS ligands as catalysts for *N*-alkylation of amines via hydrogen autotransfer process. *J. Organomet. Chem.* **2015**, *791*, 130−140.
(181) Kaloglu, N.; Ozdemir, I.; Gurbuz, N.; Achard, M.; Bruneau, C. Benzimidazolium sulfonate ligand precursors and application in ruthenium-catalyzed aromatic amine alkylation with alcohols. *Catal. Commun.* **2016**, *74*, 33−38.
(182) Xie, X.; Huynh, H. V. Tunable dehydrogenative amidation versus amination using a single ruthenium-NHC catalyst. *ACS Catal.* **2015**, *5*, 4143−4151.
(183) Shan, S. P.; Xiaoke, X.; Gnanaprakasam, B.; Dang, T. T.; Ramalingam, B.; Huynh, H. V.; Seayad, A. M. Benzimidazolin-2-ylidene *N*-heterocyclic carbene complexes of ruthenium as a simple catalyst for the *N*-alkylation of amines using alcohols and diols. *RSC Adv.* **2015**, *5*, 4434−4442.
(184) Baehn, S.; Imm, S.; Mevius, K.; Neubert, L.; Tillack, A.; Williams, J. M. J.; Beller, M. Selective Ruthenium-Catalyzed *N*-Alkylation of Indoles by Using Alcohols. *Chem. - Eur. J.* **2010**, *16*, 3590−3593.
(185) Plieninger, H.; Kraemer, H. P.; Roth, C. Note on *N*-alkylation of indolene. *Chem. Ber.* **1975**, *108*, 1776−1778.
(186) Baehn, S.; Tillack, A.; Imm, S.; Mevius, K.; Michalik, D.; Hollmann, D.; Neubert, L.; Beller, M. Ruthenium-catalyzed Selective Monoamination of Vicinal Diols. *ChemSusChem* **2009**, *2*, 551−557.
(187) Luo, J.; Wu, M.; Xiao, F.; Deng, G. Ruthenium-catalyzed direct amination of alcohols with tertiary amines. *Tetrahedron Lett.* **2011**, *52*, 2706−2709.
(188) Zeng, M.; Wang, T.; Cui, D.-M.; Zhang, C. Ruthenium-catalyzed synthesis of tri-substituted 1,3,5-triazines from alcohols and biguanides. *New J. Chem.* **2016**, *40*, 8225−8228.
(189) Stalsmeden, A. S.; Vazquez, J. L. B.; van Weerdenburg, K.; Rae, R.; Norrby, P.-O.; Kann, N. Glycerol upgrading via hydrogen borrowing: Direct ruthenium-catalyzed amination of the glycerol derivative Solketal. *ACS Sustainable Chem. Eng.* **2016**, *4*, 5730−5736.
(190) Ramachandran, R.; Prakash, G.; Selvamurugan, S.; Viswanathamurthi, P.; Malecki, J. G.; Linert, W.; Gusev, A. Ruthenium(II) complexes containing a phosphine-functionalized thiosemicarbazone ligand: synthesis, structures and catalytic C-N bond formation reactions via *N*-alkylation. *RSC Adv.* **2015**, *5*, 11405−11422.
(191) Emayavaramban, B.; Sen, M.; Sundararaju, B. Iron-catalyzed sustainable synthesis of pyrrole. *Org. Lett.* **2017**, *19*, 6−9.
(192) Fujita, K.; Li, Z. Z.; Ozeki, N.; Yamaguchi, R. *N*-Alkylation of amines with alcohols catalyzed by a Cp*Ir complex. *Tetrahedron Lett.* **2003**, *44*, 2687−2690.
(193) Hollmann, D.; Tillack, A.; Michalik, D.; Jackstell, R.; Beller, M. An improved ruthenium catalyst for the environmentally benign amination of primary and secondary alcohols. *Chem. - Asian J.* **2007**, *2*, 403−410.
(194) Hamid, M. H. S. A.; Allen, C. L.; Lamb, G. W.; Maxwell, A. C.; Maytum, H. C.; Watson, A. J. A.; Williams, J. M. J. Ruthenium-Catalyzed *N*-Alkylation of Amines and Sulfonamides Using Borrowing Hydrogen Methodology. *J. Am. Chem. Soc.* **2009**, *131*, 1766−1774.
(195) Marichev, K. O.; Takacs, J. M. Ruthenium-catalyzed amination of secondary alcohols using Borrowing Hydrogen methodology. *ACS Catal.* **2016**, *6*, 2205−2210.
(196) Gonzalez-Arellano, C.; Yoshida, K.; Luque, R.; Gai, P. L. Highly active and selective supported iron oxide nanoparticles in microwave-assisted *N*-alkylations of amines with alcohols. *Green Chem.* **2010**, *12*, 1281−1287.
(197) Li, F.; Shan, H.; Kang, Q.; Chen, L. Regioselective *N*-alkylation of 2-aminobenzothiazoles with benzylic alcohols. *Chem. Commun.* **2011**, *47*, 5058−5060.
(198) Shimizu, K.; Nishimura, M.; Satsuma, A. gamma-Alumina-Supported Silver Cluster for N-Benzylation of Anilines with Alcohols. *ChemCatChem* **2009**, *1*, 497−503.
(199) He, L.; Lou, X.-B.; Ni, J.; Liu, Y.-M.; Cao, Y.; He, H.-Y.; Fan, K.-N. Efficient and Clean Gold-Catalyzed One-Pot Selective *N*-Alkylation of Amines with Alcohols. *Chem. - Eur. J.* **2010**, *16*, 13965−13969.
(200) Ishida, T.; Kawakita, N.; Akita, T.; Haruta, M. One-pot *N*-alkylation of primary amines to secondary amines by gold clusters supported on porous coordination polymers. *Gold Bull.* **2009**, *42*, 267−274.
(201) Bertoli, M.; Choualeb, A.; Lough, A. J.; Moore, B.; Spasyuk, D.; Gusev, D. G. Osmium and Ruthenium Catalysts for Dehydrogenation of Alcohols. *Organometallics* **2011**, *30*, 3479−3482.
(202) Roesler, S.; Ertl, M.; Irrgang, T.; Kempe, R. Cobalt-catalyzed alkylation of aromatic amines by alcohols. *Angew. Chem., Int. Ed.* **2015**, *54*, 15046−15050.
(203) Elangovan, S.; Neumann, J.; Sortais, J.-B.; Junge, K.; Darcel, C.; Beller, M. Efficient and selective *N*-alkylation of amines with alcohols catalysed by manganese pincer complexes. *Nat. Commun.* **2016**, *7*, 12641.
(204) Werkmeister, S.; Neumann, J.; Junge, K.; Beller, M. Pincer-type complexes for catalytic (de)hydrogenation and transfer (de)-hydrogenation reactions: Recent progress. *Chem. - Eur. J.* **2015**, *21*, 12226−12250.
(205) Younus, H. A.; Su, W.; Ahmad, N.; Chen, S.; Verpoort, F. Ruthenium pincer complexes: Synthesis and catalytic applications. *Adv. Synth. Catal.* **2015**, *357*, 283−330.
(206) Yan, T.; Feringa, B. L.; Barta, K. Iron catalysed direct alkylation of amines with alcohols. *Nat. Commun.* **2014**, *5*, 5602.
(207) Yu, X.; Jiang, L.; Li, Q.; Xie, Y.; Xu, Q. Palladium-Catalyzed *N*-Alkylation of Amides and Amines with Alcohols Employing the Aerobic Relay Race Methodology. *Chin. J. Chem.* **2012**, *30*, 2322−2332.
(208) Liu, C.; Liao, S.; Li, Q.; Feng, S.; Sun, Q.; Yu, X.; Xu, Q. Discovery and Mechanistic Studies of a General Air-Promoted Metal-Catalyzed Aerobic *N*-Alkylation Reaction of Amides and Amines with Alcohols. *J. Org. Chem.* **2011**, *76*, 5759−5773.

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

(209) Watanabe, Y.; Ohta, T.; Tsuji, Y. The ruthenium catalyzed *N*-alkylation of amides with alcohols. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2647−2651.
(210) Cui, X.; Shi, F.; Zhang, Y.; Deng, Y. Fe(II)-catalyzed *N*-alkylation of sulfonamides with benzylic alcohols. *Tetrahedron Lett.* **2010**, *51*, 2048−2051.
(211) Watson, A. J. A.; Maxwell, A. C.; Williams, J. M. J. Borrowing Hydrogen Methodology for Amine Synthesis under Solvent-Free Microwave Conditions. *J. Org. Chem.* **2011**, *76*, 2328−2331.
(212) Cui, X.; Shi, F.; Tse, M. K.; Gördes, D.; Thurow, K.; Beller, M.; Deng, Y. Copper-Catalyzed *N*-Alkylation of Sulfonamides with Benzylic Alcohols: Catalysis and Mechanistic Studies. *Adv. Synth. Catal.* **2009**, *351*, 2949−2958.
(213) Qu, P.; Sun, C.; Ma, J.; Li, F. The *N*-alkylation of sulfonamides with alcohols in water catalyzed by the water-soluble iridium complex $\{Cp^*Ir[6,6'\text{-}(OH)_2bpy](H_2O)\}[OTf]_2$. *Adv. Synth. Catal.* **2014**, *356*, 447−459.
(214) Natarajan, A.; Guo, Y. H.; Harbinski, F.; Fan, Y. H.; Chen, H.; Luus, L.; Diercks, J.; Aktas, H.; Chorev, M.; Halperin, J. A. Novel arylsulfoanilide-oxindole hybrid as an anticancer agent that inhibits translation initiation. *J. Med. Chem.* **2004**, *47*, 4979−4982.
(215) Banerjee, M.; Poddar, A.; Mitra, G.; Surolia, A.; Owa, T.; Bhattacharyya, B. Sulfonamide drugs binding to the colchicine site of tubulin: Thermodynamic analysis of the drug-tubulin interactions by isothermal titration calorimetry. *J. Med. Chem.* **2005**, *48*, 547−555.
(216) Koehler, N. K. U.; Yang, C. Y.; Varady, J.; Lu, Y. P.; Wu, X. W.; Liu, M.; Yin, D. X.; Bartels, M.; Xu, B. Y.; Roller, P. P.; et al. Structure-based discovery of nonpeptidic small organic compounds to block the T cell response to myelin basic protein. *J. Med. Chem.* **2004**, *47*, 4989−4997.
(217) Quaal, K. S.; Ji, S.; Kim, Y. M.; Closson, W. D.; Zubieta, J. A. Substituent effects on reductive cleavage of N-methylarenesulfonanilides - Cleavage by odium anthracene and electrochemically at vitreous carbon electrode. *J. Org. Chem.* **1978**, *43*, 1311−1316.
(218) Caddick, S.; Wilden, J. D.; Judd, D. B. Direct synthesis of sulfonamides and activated sulfonate esters from sulfonic acids. *J. Am. Chem. Soc.* **2004**, *126*, 1024−1025.
(219) Zhu, M.; Fujita, K.-i.; Yamaguchi, R. Simple and Versatile Catalytic System for *N*-Alkylation of Sulfonamides with Various Alcohols. *Org. Lett.* **2010**, *12*, 1336−1339.
(220) Martinez-Asencio, A.; Ramon, D. J.; Yus, M. *N*-Alkylation of poor nucleophilic amine and sulfonamide derivatives with alcohols by a hydrogen autotransfer process catalyzed by copper(II) acetate. *Tetrahedron Lett.* **2010**, *51*, 325−327.
(221) Lu, L.; Ma, J.; Qu, P.; Li, F. Effective recognition of different types of amino groups: From aminobenzenesulfonamides to amino-(*N*-alkyl)benzenesulfonamides via iridium-catalyzed *N*-alkylation with alcohols. *Org. Lett.* **2015**, *17*, 2350−2353.
(222) Lamb, G. W.; Watson, A. J. A.; Jolley, K. E.; Maxwell, A. C.; Williams, J. M. J. Borrowing hydrogen methodology for the conversion of alcohols into N-protected primary amines and in situ deprotection. *Tetrahedron Lett.* **2009**, *50*, 3374−3377.
(223) Fujita, K.; Yamamoto, K.; Yamaguchi, R. Oxidative cyclization of amino alcohols catalyzed by a Cp*Ir complex. Synthesis of indoles, 1,2,3,4-tetrahydroquinolines, and 2,3,4,5-tetrahydro-1-benzazepine. *Org. Lett.* **2002**, *4*, 2691−2694.
(224) Eary, C. T.; Clausen, D. Preparation of substituted 1,2,3,4-tetrahydroquinoxalines and 2,3,4,5-tetrahydro-1*H*-benzo[*b*][1,4]-diazepines from catalytic Cp*Ir hydrogen transfer N-heterocyclization of anilino alcohols. *Tetrahedron Lett.* **2006**, *47*, 6899−6902.
(225) Jumde, V. R.; Cini, E.; Porcheddu, A.; Taddei, M. A metal-catalyzed tandem 1,4-benzodiazepine synthesis based on two Hydrogen-Transfer reactions. *Eur. J. Org. Chem.* **2015**, *2015*, 1068−1074.
(226) Enyong, A. B.; Moasser, B. Ruthenium-catalyzed *N*-alkylation of amines with alcohols under mild conditions using the Borrowing Hydrogen methodology. *J. Org. Chem.* **2014**, *79*, 7553−7563.
(227) Gerlach, T.; Evers, H.; Melder, J.-P. *Method for producing ethylene amines*. Germany Patent WO 2007036499A1, 2007.
(228) Melder, J.-P.; Krug, T. *Preparation of bis-((3-dimethylamino) propyl)amine, useful e.g. for synthesizing e.g. detergent additives, comprises continuous conversion of 3-(N,N-dimethylamino)propylamine in presence of heterogeneous catalysts in a reaction column*. Germany Patent DE 102005004853A1, 2006.
(229) Evers, H.; Melder, J.-P.; Benisch, C.; Frauenkron, M.; Gerlach, T.; Alba Perez, A.; Nouwen, J. *Method for increasing the space-time yield in a process used for the production of a symmetric secondary amine*. WO 2005061430A1, 2005.
(230) Frauenkron, M.; Krug, T.; Evers, H.; Melder, J.-P.; Roettger, R.; Siegert, M.; Gerlach, T.; Nouwen, J.; Dahlhoff, E.; Miller, C. *Method for producing ethylene-amines*. WO 2005012223A1, 2005.
(231) Qiao, X.; Zhang, J.; Cui, M.; Tang, J. *Method for preparing diphenylamine by aniline liquid phase condensation and denitrification coupling*. People's Republic of China CN 1629132A, 2005.
(232) Oikawa, S.; Ando, H. *Method for producing diarylamines*. Japan Patent JP 2003171353A, 2003.
(233) Samec, J. S. M.; Ell, A. H.; Backvall, J. E. Efficient ruthenium-catalyzed aerobic oxidation of amines by using a biomimetic coupled catalytic system. *Chem. - Eur. J.* **2005**, *11*, 2327−2334.
(234) Samec, J. S. M.; Ell, A. H.; Backvall, J. E. Mechanism of hydrogen transfer to imines from a hydroxycyclopentadienyl ruthenium hydride. Support for a stepwise mechanism. *Chem. Commun.* **2004**, 2748−2749.
(235) Ell, A. H.; Johnson, J. B.; Backvall, J. E. Mechanism of ruthenium-catalyzed hydrogen transfer reactions. Evidence for a stepwise transfer of CH and NH hydrogens from an amine to a (cyclopentadienone) ruthenium complex. *Chem. Commun.* **2003**, 1652−1653.
(236) Ell, A. H.; Samec, J. S. M.; Brasse, C.; Backvall, J. E. Dehydrogenation of aromatic amines to imines via ruthenium-catalyzed hydrogen transfer. *Chem. Commun.* **2002**, 1144−1145.
(237) Pamies, O.; Ell, A. H.; Samec, J. S. M.; Hermanns, N.; Backvall, J. E. An efficient and mild ruthenium-catalyzed racemization of amines: application to the synthesis of enantiomerically pure amines. *Tetrahedron Lett.* **2002**, *43*, 4699−4702.
(238) Cho, C. S.; Kim, B. T.; Lee, M. J.; Kim, T. J.; Shim, S. H. Ruthenium-catalyzed regioselective α-alkylation of ketones: The first alkyl-group transfer from trialkylamines to the α-C atom of ketones. *Angew. Chem., Int. Ed.* **2001**, *40*, 958−960.
(239) Cho, C. S. Ruthenium-catalyzed cross-coupling reactions between ketones and primary amines. *Catal. Commun.* **2006**, *7*, 1012−1014.
(240) Murahashi, S. I. Synthesis aspects of metal-catalyzed oxidations of amines and related reactions. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2443−2465.
(241) Hollmann, D.; Baehn, S.; Tillack, A.; Beller, M. A general ruthenium-catalyzed synthesis of aromatic Amines. *Angew. Chem., Int. Ed.* **2007**, *46*, 8291−8294.
(242) Saidi, O.; Blacker, A. J.; Farah, M. M.; Marsden, S. P.; Williams, J. M. J. Selective Amine Cross-Coupling Using Iridium-Catalyzed "Borrowing Hydrogen" Methodology. *Angew. Chem., Int. Ed.* **2009**, *48*, 7375−7378.
(243) Yu, X.; Zhao, R.; Wan, H.; Yang, Y.; Wang, D. Alanine triazole iridium-catalyzed C-N bond formation through borrowing hydrogen strategy. *Tetrahedron Lett.* **2016**, *57*, 4588−4591.
(244) Neubert, L.; Michalik, D.; Baehn, S.; Imm, S.; Neumann, H.; Atzrodt, J.; Derdau, V.; Holla, W.; Beller, M. Ruthenium-Catalyzed Selective α,β-Deuteration of Bioactive Amines. *J. Am. Chem. Soc.* **2012**, *134*, 12239−12244.
(245) Yin, Z.; Zeng, H.; Wu, J.; Zheng, S.; Zhang, G. Cobalt-catalyzed synthesis of aromatic, aliphatic, and cyclic secondary amines via a "Hydrogen-borrowing" strategy. *ACS Catal.* **2016**, *6*, 6546−6550.
(246) Roy, K.-M. In *Ullmann's Encyclopedia of Industrial Chemistry, Aliphatic Amines*; Wiley-VCH, 2000; p 8.
(247) Lee, D. Y.; Cho, C. S.; Kim, J. H.; Youn, Y. Z.; Shim, S. C.; Song, H. Ruthenium complex-catalyzed synthesis of indoles from N-substituted anilines and alkanolamines. *Bull. Korean Chem. Soc.* **1996**, *17*, 1132−1135.

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

(248) Shvo, Y.; Abed, M.; Blum, Y.; Laine, R. M. Homogeneous catalytic cleavage of saturated carbon-nitrogen bond. *Isr. J. Chem.* **1986**, *27*, 267−275.
(249) Tsuji, Y.; Huh, K. T.; Watanabe, Y. Ruthenium complex catalyzed N-heterocyclization - Syntheses of quinolines and indole-derivatives from aminoarenes and 1,3-propanediol of glycols. *J. Org. Chem.* **1987**, *52*, 1673−1680.
(250) Cho, C. S.; Oh, B. H.; Shim, S. C. Synthesis of quinolines by ruthenium-catalyzed heteroannulation of anilines with 3-amino-1-propanol. *J. Heterocycl. Chem.* **1999**, *36*, 1175−1178.
(251) Cho, C. S.; Kim, D. T.; Kim, T. J.; Shim, S. C. Ruthenium-catalyzed synthesis of quinolines from anilines and tris(3-hydroxypropyl)amine via amine exchange reaction. *Bull. Korean Chem. Soc.* **2003**, *24*, 1026−1028.
(252) Cho, C. S.; Oh, B. H.; Kim, J. S.; Kim, T. J.; Shim, S. C. Synthesis of quinolines via ruthenium-catalysed amine exchange reaction between anilines and trialkylamines. *Chem. Commun.* **2000**, 1885−1886.
(253) Cho, C. S.; Kim, T. K.; Choi, H. J.; Kim, T. J.; Shim, S. C. Ruthenium-catalyzed consecutive reduction and cyclization of nitro-arenes with tetraalkylammonium bromides leading to quinolines. *Bull. Korean Chem. Soc.* **2002**, *23*, 541−542.
(254) Kharasch, M. S.; Richlin, I.; Mayo, F. R. The condensation of butyraldehyde and aniline. *J. Am. Chem. Soc.* **1940**, *62*, 494−497.
(255) Watanabe, Y.; Tsuji, Y.; Ohsugi, Y.; Shida, J. The ruthenium complex catalyzed N-heterocyclization of aminoarenes to quinoline derivatives using allylic alcohols and aliphatic-aldehydes. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2452−2457.
(256) Cho, C. S.; Kim, J. S.; Kim, H. S.; Kim, T. J.; Shim, S. C. Ruthenium-catalysed selective N-monoalkylation of anilines with tetraalkylammonium halides. *Synth. Commun.* **2001**, *31*, 3791−3797.
(257) White, E. H.; Woodcock, D. J. In *The Amino Group (1968)*; John Wiley & Sons, Ltd., 2010; pp 407−497.
(258) Wang, D.; Zhao, K.; Xu, C.; Miao, H.; Ding, Y. Synthesis, structures of benzoxazolyl iridium(111) complexes, and applications on C-C and C-N bond formation reactions under solvent-free conditions: Catalytic activity enhanced by noncoordinating anion without silver effect. *ACS Catal.* **2014**, *4*, 3910−3918.
(259) Gladiali, S.; Alberico, E. Asymmetric transfer hydrogenation: chiral ligands and applications. *Chem. Soc. Rev.* **2006**, *35*, 226−236.
(260) Wang, C.; Wu, X.; Xiao, J. Broader, Greener, and More Efficient: Recent Advances in Asymmetric Transfer Hydrogenation. *Chem. - Asian J.* **2008**, *3*, 1750−1770.
(261) Ketcham, J. M.; Shin, I.; Montgomery, T. P.; Krische, M. J. Catalytic enantioselective C-H functionalization of alcohols by redox-triggered carbonyl addition: Borrowing Hydrogen, returning carbon. *Angew. Chem., Int. Ed.* **2014**, *53*, 9142−9150.
(262) Shermer, D. J.; Slatford, P. A.; Edney, D. D.; Williams, J. M. J. Borrowing hydrogen in an indirect asymmetric Wittig reaction. *Tetrahedron: Asymmetry* **2007**, *18*, 2845−2848.
(263) Onodera, G.; Nishibayashi, Y.; Uemura, S. Ir- and Ru-catalyzed sequential reactions: Asymmetric α-alkylative reduction of ketones with alcohols. *Angew. Chem., Int. Ed.* **2006**, *45*, 3819−3822.
(264) Quintard, A.; Constantieux, T.; Rodriguez, J. An Iron/Amine-Catalyzed Cascade Process for the Enantioselective Functionalization of Allylic Alcohols. *Angew. Chem., Int. Ed.* **2013**, *52*, 12883−12887.
(265) Putra, A. E.; Oe, Y.; Ohta, T. Ruthenium-Catalyzed Enantioselective Synthesis of β-Amino Alcohols from 1,2-Diols by "Borrowing Hydrogen". *Eur. J. Org. Chem.* **2013**, *2013*, 6146−6151.
(266) Zhang, Y.; Lim, C.-S.; Sim, D. S. B.; Pan, H.-J.; Zhao, Y. Catalytic enantioselective amination of alcohols by the use of Borrowing Hydrogen methodology: Cooperative catalysis by iridium and a chiral phosphoric acid. *Angew. Chem., Int. Ed.* **2014**, *53*, 1399−1403.
(267) Oldenhuis, N. J.; Dong, V. M.; Guan, Z. From racemic alcohols to enantiopure amines: Ru-catalyzed diastereoselective amination. *J. Am. Chem. Soc.* **2014**, *136*, 12548−12551.
(268) Baeza, A.; Guillena, G.; Ramon, D. J. Magnetite and metal-impregnated magnetite catalysts in organic synthesis: A very old concept with new promising perspectives. *ChemCatChem* **2016**, *8*, 49−67.
(269) Muller, J.-L.; Rickers, A.; Leitner, W. Raney Cobalt: An Effective and Recyclable Catalyst for the Pauson−Khand Reaction. *Adv. Synth. Catal.* **2007**, *349*, 287−291.
(270) Labinger, J. A.; Bercaw, J. E. Understanding and exploiting C-H bond activation. *Nature* **2002**, *417*, 507−514.
(271) Mol, J. C. Industrial applications of olefin metathesis. *J. Mol. Catal. A: Chem.* **2004**, *213*, 39−45.
(272) Heckelsberg, L. F.; Banks, R. L. *Combined dehydrogenation and disproportionation*. U.S. Patent US 3445541A, 1969.
(273) Hughes, T. R. *Catalytic disproportionation of saturated hydrocarbons*. France Patent FR 2075370A5, 1971.
(274) Burnett, R. L.; Hughes, T. R. Mechanism and poisoning of molecular redistribution reaction of alkanes with a dual-functional catalyst system. *J. Catal.* **1973**, *31*, 55−64.
(275) Deraedt, C.; d'Halluin, M.; Astruc, D. Metathesis Reactions: Recent Trends and Challenges. *Eur. J. Inorg. Chem.* **2013**, *2013*, 4881−4908.
(276) Huang, Z.; Rolfe, E.; Carson, E. C.; Brookhart, M.; Goldman, A. S.; El-Khalafy, S. H.; MacArthur, A. H. R. Efficient Heterogeneous Dual Catalyst Systems for Alkane Metathesis. *Adv. Synth. Catal.* **2010**, *352*, 125−135.
(277) Vidal, V.; Theolier, A.; ThivolleCazat, J.; Basset, J. M. Metathesis of alkanes catalyzed by silica-supported transition metal hydrides. *Science* **1997**, *276*, 99−102.
(278) Vidal, V.; Theolier, A.; Thivolle-Cazat, J.; Basset, J.-M. *Method of metathesis of alcanes and catalyst*. WO 9802244A1, 1998.
(279) Lefebvre, F.; Basset, J. M. Recent applications in catalysis of surface organometallic chemistry. *J. Mol. Catal. A: Chem.* **1999**, *146*, 3−12.
(280) Lefebvre, F.; Thivolle-Cazat, J.; Dufaud, V.; Niccolai, G. P.; Basset, J.-M. Oxide supported surface organometallic complexes as a new generation of catalysts for carbon-carbon bond activation. *Appl. Catal., A* **1999**, *182*, 1−8.
(281) Coperet, C.; Thivolle-Cazat, J.; Basset, J. M. In *Fine Chemicals through Heterogenous Catalysis*; Wiley-VCH, 2007; pp 553−561.
(282) Thieuleux, C.; Coperet, C.; Dufaud, V.; Marangelli, C.; Kuntz, E.; Basset, J. M. Heterogeneous well-defined catalysts for metathesis of inert and not so inert bonds. *J. Mol. Catal. A: Chem.* **2004**, *213*, 47−57.
(283) Thivolle-Cazat, J.; Coperet, C.; Soignier, S.; Taoufik, M.; Basset, J. M. Surface organometallic chemistry of tantalum: Application to the metathesis of alkanes catalyzed by a tantalum hydride supported on silica. *NATO Sci. Ser., II* **2005**, *191*, 107−123.
(284) Basset, J.-M.; Coperet, C.; Lefort, L.; Maunders, B. M.; Maury, O.; Saggio, G.; Thivolle-Cazat, J. *Process for manufacturing alkanes with methane*. WO2001004077A1, 2001.
(285) Le Roux, E. L.; Chabanas, M.; Baudouin, A.; de Mallmann, A.; Coperet, C.; Quadrelli, E. A.; Thivolle-Cazat, J.; Basset, J.-M.; Lukens, W.; Lesage, A.; et al. Detailed Structural Investigation of the Grafting of $[Ta(=CHtBu)(CH_2tBu)_3]$ and $[Cp^*TaMe_4]$ on Silica Partially Dehydroxylated at 700 °C and the Activity of the Grafted Complexes toward Alkane Metathesis. *J. Am. Chem. Soc.* **2004**, *126*, 13391−13399.
(286) Saggio, G.; Taoufik, M.; Basset, J.-M.; Thivolle-Cazat, J. Poisoning Experiments Aimed at Discriminating Active and Less-Active Sites of Silica-Supported Tantalum Hydride for Alkane Metathesis. *ChemCatChem* **2010**, *2*, 1594−1598.
(287) Le Roux, E.; Taoufik, M.; Coperet, C.; de Mallmann, A.; Thivolle-Cazat, J.; Basset, J. M.; Maunders, B. M.; Sunley, G. J. Development of tungsten-based heterogeneous alkane metathesis catalysts through a structure-activity relationship. *Angew. Chem., Int. Ed.* **2005**, *44*, 6755−6758.
(288) Taoufik, M.; Le Roux, E.; Thivolle-Cazat, J.; Coperet, C.; Basset, J.-M.; Maunders, B.; Sunley, G. J. Alumina supported tungsten hydrides, new efficient catalysts for alkane metathesis. *Top. Catal.* **2006**, *40*, 65−70.
(289) Merle, N.; Stoffelbach, F.; Taoufik, M.; Le Roux, E.; Thivolle-Cazat, J.; Basset, J.-M. Selective and unexpected transformations of 2-methylpropane to 2,3-dimethylbutane and 2-methylpropene to 2,3-

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

dimethylbutene catalyzed by an alumina-supported tungsten hydride. *Chem. Commun.* **2009**, 2523−2525.
(290) Coperet, C.; Maury, O.; Thivolle-Cazat, J.; Basset, J.-M. σ-Bond metathesis of alkanes on a silica-supported tantalum(V) alkyl alkylidene complex: first evidence for alkane cross-metathesis. *Angew. Chem., Int. Ed.* **2001**, *40*, 2331−2334.
(291) Chen, Y.; Ould-Chikh, S.; Abou-Hamad, E.; Callens, E.; Mohandas, J. C.; Khalid, S.; Basset, J.-M. Facile and efficient synthesis of the surface tantalum hydride $(\equiv SiO)_2Ta^{III}H$ and tris-siloxy tantalum $(\equiv SiO)_3Ta^{III}$ starting from novel tantalum surface species $(\equiv SiO)TaMe_4$ and $(\equiv SiO)_2TaMe_3$. *Organometallics* **2014**, *33*, 1205−1211.
(292) Riache, N.; Callens, E.; Espinas, J.; Dery, A.; Samantaray, M. K.; Dey, R.; Basset, J. M. Striking difference between alkane and olefin metathesis using the well-defined precursor $[\equiv Si\text{-}O\text{-}WMe_5]$: indirect evidence in favor of a bifunctional catalyst W alkylidene-hydride. *Catal. Sci. Technol.* **2015**, *5*, 280−285.
(293) Basset, J.-M. M.; Callens, E.; Riache, N.; Samantaray, M. K.; Abou-Hamad, E. *Alkane metathesis catalyst, methods of use and the preparation thereof*. WO 2015079321A2, 2015.
(294) Maury, O.; Saggio, G.; Theolier, A.; Taoufik, M.; Vidal, V.; Thivolle-Cazat, J.; Basset, J.-M. New reactions of C-C bond cleavage and formation catalysed by silica-supported tantalum and tungsten hydrides. *C. R. Acad. Sci., Ser. IIc: Chim.* **2000**, *3*, 583−587.
(295) Basset, J.-M.; Coperet, C.; Soulivong, D.; Taoufik, M.; Thivolle Cazat, J. Metathesis of Alkanes and Related Reactions. *Acc. Chem. Res.* **2010**, *43*, 323−334.
(296) Rascon, F.; Coperet, C. Alkylidene and alkylidyne surface complexes: Precursors and intermediates in alkane conversion processes on supported single-site catalysts. *J. Organomet. Chem.* **2011**, *696*, 4121−4131.
(297) Szeto, K. C.; Hardou, L.; Merle, N.; Basset, J.-M.; Thivolle-Cazat, J.; Papaioannou, C.; Taoufik, M. Selective conversion of butane into liquid hydrocarbon fuels on alkane metathesis catalysts. *Catal. Sci. Technol.* **2012**, *2*, 1336−1339.
(298) Basset, J. M.; Coperet, C.; Lefort, L.; Maunders, B. M.; Maury, O.; Le Roux, E.; Saggio, G.; Soignier, S.; Soulivong, D.; Sunley, G. J.; et al. Primary Products and Mechanistic Considerations in Alkane Metathesis. *J. Am. Chem. Soc.* **2005**, *127*, 8604−8605.
(299) Schinzel, S.; Chermette, H.; Coperet, C.; Basset, J.-M. Evaluation of the Carbene Hydride Mechanism in the Carbon-Carbon Bond Formation Process of Alkane Metathesis through a DFT Study. *J. Am. Chem. Soc.* **2008**, *130*, 7984−7987.
(300) Mazar, M. N.; Al-Hashimi, S.; Bhan, A.; Cococcioni, M. Alkane Metathesis by Tantalum Metal Hydride on Ferrierite: A Computational Study. *J. Phys. Chem. C* **2011**, *115*, 10087−10096.
(301) Samantaray, M. K.; Dey, R.; Abou-Hamad, E.; Hamieh, A.; Basset, J.-M. Effect of support on metathesis of n-decane: Drastic improvement in alkane metathesis with WMe5 linked to silica-alumina. *Chem. - Eur. J.* **2015**, *21*, 6100−6106.
(302) Popoff, N.; Mazoyer, E.; Pelletier, J.; Gauvin, R. M.; Taoufik, M. Expanding the scope of metathesis: a survey of polyfunctional, single-site supported tungsten systems for hydrocarbon valorization. *Chem. Soc. Rev.* **2013**, *42*, 9035−9054.
(303) Blanc, F.; Coperet, C.; Thivolle-Cazat, J.; Basset, J.-M. Alkane metathesis catalyzed by a well-defined silica-supported mo imido alkylidene complex:$[(\equiv SiO)Mo(=NAr)(=CHtBu)(CH_2tBu)]$. *Angew. Chem., Int. Ed.* **2006**, *45*, 6201−6203.
(304) Blanc, F.; Thivolle-Cazat, J.; Basset, J.-M.; Coperet, C. Structure-reactivity relationship in alkane metathesis using well-defined silica-supported alkene metathesis catalyst precursors. *Chem. - Eur. J.* **2008**, *14*, 9030−9037.
(305) Basset, J.-m.; Coperet, C.; Lefort, L.; Maunders, B. M.; Maury, O.; Saggio, G.; Thivolle-cazat, J. *Process for manufacturing alkanes*. WO 2000027781A1, 2000.
(306) Basset, J.-M.; Coperet, C.; Pardy, R.; Soulivong, D.; Sunley, J. G.; Thivolle-Cazat, J. *Process for manufacturing alkanes by reacting other alkanes with methane*. WO 2003066552A1, 2003.
(307) Chen, Y.; Abou-hamad, E.; Hamieh, A.; Hamzaoui, B.; Emsley, L.; Basset, J.-M. Alkane metathesis with the tantalum methylidene $[(\equiv SiO)Ta(=CH_2)Me_2]/[(\equiv SiO)_2Ta(=CH_2)Me]$ generated from well-defined surface organometallic complex $[(\equiv SiO)Ta^{V}Me_4]$. *J. Am. Chem. Soc.* **2015**, *137*, 588−591.
(308) Samantaray, M. K.; Dey, R.; Kavitake, S.; Abou-Hamad, E.; Bendjeriou-Sedjerari, A.; Hamieh, A.; Basset, J.-M. Synergy between two metal catalysts: A highly active silica-supported bimetallic W/Zr catalyst for metathesis of n-decane. *J. Am. Chem. Soc.* **2016**, *138*, 8595−8602.
(309) Thieuleux, C.; Maraval, A.; Veyre, L.; Coperet, C.; Soulivong, D.; Basset, J.-M.; Sunley, G. J. Homologation of propane catalyzed by oxide-supported zirconium dihydride and dialkyl complexes. *Angew. Chem., Int. Ed.* **2007**, *46*, 2288−2290.
(310) Dufaud, V.; Niccolai, G. P.; Thivollecazat, J.; Basset, J. M. Surface organometallic chemistry of inorganic oxides - the synthesis and characterization of $(\equiv SiO)Ta(=CHC(CH_3)_3)(CH_2C(CH_3)_3)_2$ and $(\equiv SiO)_2Ta(=CHC(CH_3)_3)(CH_2C(CH_3)_3)$. *J. Am. Chem. Soc.* **1995**, *117*, 4288−4294.
(311) Rataboul, F.; Chabanas, M.; de Mallmann, A.; Coperet, C.; Thivolle-Cazat, J.; Basset, J. M. Hydrogenolysis of cycloalkanes on a tantalum hydride complex supported on silica and insight into the deactivation pathway by the combined use of ID solid-state NMR and EXAFS spectroscopies. *Chem. - Eur. J.* **2003**, *9*, 1426−1434.
(312) Le Roux, E.; Taoufik, M.; Baudouin, A.; Coperet, C.; Thivolle-Cazat, J.; Basset, J.-M.; Maunders, B. M.; Sunley, G. J. Silica-alumina-supported, tungsten-based heterogeneous alkane metathesis catalyst: Is it closer to a silica- or an alumina-supported system? *Adv. Synth. Catal.* **2007**, *349*, 231−237.
(313) Le Roux, E.; Taoufik, M.; Chabanas, M.; Alcor, D.; Baudouin, A.; Coperet, C.; Thivolle-Cazat, J.; Basset, J. M.; Lesage, A.; Hediger, S.; et al. Well-defined surface tungstenocarbyne complexes through the reaction of $[W(\equiv CtBu)(CH_2tBu)_3]$ with silica. *Organometallics* **2005**, *24*, 4274−4279.
(314) Mowat, W.; Smith, J.; Whan, D. A. Disproportionation of propene by a heterogeneous catalyst derived from hexamethyltungsten. *J. Chem. Soc., Chem. Commun.* **1974**, 34−35.
(315) Samantaray, M. K.; Callens, E.; Abou-Hamad, E.; Rossini, A. J.; Widdifield, C. M.; Dey, R.; Emsley, L.; Basset, J.-M. WMe_6 tamed by silica: $\equiv Si\text{-}O\text{-}WMe_5$ as an efficient, well-defined species for alkane metathesis, leading to the observation of a supported W-methyl/methylidyne species. *J. Am. Chem. Soc.* **2014**, *136*, 1054−1061.
(316) Joubert, J.; Delbecq, F.; Sautet, P. Alkane metathesis by a tungsten carbyne complex grafted on gamma alumina: Is there a direct chemical role of the support? *J. Catal.* **2007**, *251*, 507−513.
(317) Yamada, Y. M. A.; Uozumi, Y. Development of a convoluted polymeric nanopalladium catalyst: alpha-alkylation of ketones and ring-opening alkylation of cyclic 1,3-diketones with primary alcohols. *Tetrahedron* **2007**, *63*, 8492−8498.
(318) Carlini, C.; Macinai, A.; Marchionna, M.; Noviello, M.; Galletti, A. M. R.; Sbrana, G. Selective synthesis of isobutanol by means of the Guerbet reaction - Part 3: Methanol/n-propanol condensation by using bifunctional catalytic systems based on nickel, rhodium and ruthenium species with basic components. *J. Mol. Catal. A: Chem.* **2003**, *206*, 409−418.
(319) Arjona Antolin, R.; Sanz Yaguee, J. L.; Corma Canos, A.; Domine, M. E. *Catalyst for obtaining higher alcohols*. EP 2679303A1, 2014.
(320) Putra, A. E.; Oe, Y.; Ohta, T. Pd/C-catalyzed alkylation of heterocyclic nucleophiles with alcohols through the "Borrowing Hydrogen" process. *Eur. J. Org. Chem.* **2015**, *2015*, 7799−7805.
(321) Oikawa, K.; Itoh, S.; Yano, H.; Kawasaki, H.; Obora, Y. Preparation and use of DMF-stabilized iridium nanoclusters as methylation catalysts using methanol as the C1 source. *Chem. Commun.* **2017**, *53*, 1080−1083.
(322) Onyestyak, G.; Novodarszki, G.; Barthos, R.; Klebert, S.; Wellisch, A. F.; Pilbath, A. Acetone alkylation with ethanol over multifunctional catalysts by a borrowing hydrogen strategy. *RSC Adv.* **2015**, *5*, 99502−99509.

DOI: 10.1021/acs.chemrev.7b00340
Chem. Rev. 2018, 118, 1410−1459

(323) Novodarszki, G.; Onyestyak, G.; Farkas Wellisch, A.; Pilbath, A. Catalytic alkylation of acetone with ethanol over Pd/carbon catalysts in flow-through system via Borrowing Hydrogen route. *Acta Chim. Slov.* **2016**, *63*, 251−257.
(324) Onyestyak, G.; Novodarszki, G.; Farkas Wellisch, A.; Pilbath, A. Upgraded biofuel from alcohol-acetone feedstocks over a two-stage flow-through catalytic system. *Catal. Sci. Technol.* **2016**, *6*, 4516−4524.
(325) Xu, J.; Yue, H.; Liu, S.; Wang, H.; Du, Y.; Xu, C.; Dong, W.; Liu, C. Cu-Ag/hydrotalcite catalysts for dehydrogenative cross-coupling of primary and secondary benzylic alcohols. *RSC Adv.* **2016**, *6*, 24164−24174.
(326) Wu, K.; He, W.; Sun, C.; Yu, Z. Bimetallic Pt-Sn/γ-Al_2O_3 catalyzed beta-alkylation of secondary alcohols with primary alcohols under solvent-free conditions. *Tetrahedron Lett.* **2016**, *57*, 4017−4020.
(327) Corma, A.; Rodenas, T.; Sabater, M. J. Monoalkylations with alcohols by a cascade reaction on bifunctional solid catalysts: Reaction kinetics and mechanism. *J. Catal.* **2011**, *279*, 319−327.
(328) Alonso, F.; Riente, P.; Yus, M. Alcohols for the α-Alkylation of Methyl Ketones and Indirect Aza-Wittig Reaction Promoted by Nickel Nanoparticles. *Eur. J. Org. Chem.* **2008**, *2008*, 4908−4914.
(329) Weissermel, K.; Arpe, H. J. In *Industrial Organic Chemistry, Fourth Completely Revised ed.*; Wiley: Weinheim, 2003, 51.
(330) Shimizu, K.-i.; Kanno, S.; Kon, K.; Hakim Siddiki, S. M. A.; Tanaka, H.; Sakata, Y. *N*-alkylation of ammonia and amines with alcohols catalyzed by Ni-loaded $CaSiO_3$. *Catal. Today* **2014**, *232*, 134−138.
(331) Pfuetzenreuter, R.; Rose, M. Aqueous-phase amination of biogenic isohexides by using Ru/C as a solid catalyst. *ChemCatChem* **2016**, *8*, 251−255.
(332) Ruiz, D.; Aho, A.; Saloranta, T.; Eränen, K.; Wärnå, J.; Leino, R.; Murzin, D. Y. Direct amination of dodecanol with NH_3 over heterogeneous catalysts. Catalyst screening and kinetic modelling. *Chem. Eng. J.* **2017**, *307*, 739−749.
(333) He, J.; Kim, J. W.; Yamaguchi, K.; Mizuno, N. Efficient Catalytic Synthesis of Tertiary and Secondary Amines from Alcohols and Urea. *Angew. Chem., Int. Ed.* **2009**, *48*, 9888−9891.
(334) Krüger, K.; Tillack, A.; Beller, M. Recent Innovative Strategies for the Synthesis of Amines: From C-N Bond Formation to C-N Bond Activation. *ChemSusChem* **2009**, *2*, 715−717.
(335) Roesky, P. W. Catalytic Hydroaminoalkylation. *Angew. Chem., Int. Ed.* **2009**, *48*, 4892−4894.
(336) Tsukasa, T.; Yoshinao, N.; Keiichi, T. Amination of Alcohols with Ammonia in Water over Rh−In Catalyst. *Chem. Lett.* **2014**, *43*, 822−824.
(337) Guyot, A.; Fournier, M. Catalytic preparation of primary and secondary amines. *Bull. Soc. Chim. Fr.* **1930**, *47*, 203−210.
(338) Brown, A. B.; Reid, E. E. Catalytic alkylation of aniline. *J. Am. Chem. Soc.* **1924**, *46*, 1836−1839.
(339) Roundhill, D. M. Transition-metal and enzyme catalyzed-reactions involving reactions with ammonia and amines. *Chem. Rev.* **1992**, *92*, 1−27.
(340) Bosch, M.; Eberhardt, J.; Roettger, R.; Krug, T.; Melder, J.-P. *Method for the continuous synthesis of methylamines*. WO 2005123658A1, 2005.
(341) Fujita, T.; Ogura, K.; Niwa, K.; Fukatsu, M. *Production of methylamines*. EP0763519A2, 1997.
(342) Wang, D.; Guo, X.-Q.; Wang, C.-X.; Wang, Y.-N.; Zhong, R.; Zhu, X.-H.; Cai, L.-H.; Gao, Z.-W.; Hou, X.-F. An efficient and recyclable catalyst for *N*-alkylation of amines and β-alkylation of secondary alcohols with primary alcohols: SBA-15 supported *N*-heterocyclic carbene iridium complex. *Adv. Synth. Catal.* **2013**, *355*, 1117−1125.
(343) Tang, C.-H.; He, L.; Liu, Y.-M.; Cao, Y.; He, H.-Y.; Fan, K.-N. Direct One-Pot Reductive *N*-Alkylation of Nitroarenes by using Alcohols with Supported Gold Catalysts. *Chem. - Eur. J.* **2011**, *17*, 7172−7177.
(344) Liu, H.; Chuah, G. K.; Jaenicke, S. Alumina-entrapped Ag catalyzed nitro compounds coupled with alcohols using borrowing hydrogen methodology. *Phys. Chem. Chem. Phys.* **2015**, *17*, 15012−15018.
(345) Selvam, K.; Sakamoto, H.; Shiraishi, Y.; Hirai, T. One-pot synthesis of secondary amines from alcohols and nitroarenes on TiO_2 loaded with Pd nanoparticles under UV irradiation. *New J. Chem.* **2015**, *39*, 2467−2473.
(346) Sankar, M.; He, Q.; Dawson, S.; Nowicka, E.; Lu, L.; Bruijnincx, P. C. A.; Beale, A. M.; Kiely, C. J.; Weckhuysen, B. M. Supported bimetallic nano-alloys as highly active catalysts for the one-pot tandem synthesis of imines and secondary amines from nitrobenzene and alcohols. *Catal. Sci. Technol.* **2016**, *6*, 5473−5482.
(347) Wu, K.; He, W.; Sun, C.; Yu, Z. Scalable synthesis of secondary and tertiary amines by heterogeneous Pt-Sn/γ-Al_2O_3 catalyzed *N*-alkylation of amines with alcohols. *Tetrahedron* **2016**, *72*, 8516−8521.
(348) Yan, Z.; Tomer, A.; Perrussel, G.; Ousmane, M.; Katryniok, B.; Dumeignil, F.; Ponchel, A.; Liebens, A.; Pera-Titus, M. A Pd/CeO_2 "H_2 pump" for the direct amination of alcohols. *ChemCatChem* **2016**, *8*, 3347−3352.
(349) Suib, S. L. Porous manganese oxide octahedral molecular sieves and octahedral layered materials. *Acc. Chem. Res.* **2008**, *41*, 479−487.
(350) Ousmane, M.; Perrussel, G.; Yan, Z.; Clacens, J. M.; De Campo, F.; Pera-Titus, M. Highly selective direct amination of primary alcohols over a Pd/K-OMS-2 catalyst. *J. Catal.* **2014**, *309*, 439−452.
(351) Corma, A.; Navas, J.; Sabater, M. J. Coupling of Two Multistep Catalytic Cycles for the One-Pot Synthesis of Propargylamines from Alcohols and Primary Amines on a Nanoparticulated Gold Catalyst. *Chem. - Eur. J.* **2012**, *18*, 14150−14156.
(352) Choo, G. C. Y.; Miyamura, H.; Kobayashi, S. Synergistic cascade catalysis by metal nanoparticles and Lewis acids in hydrogen autotransfer. *Chem. Sci.* **2015**, *6*, 1719−1727.
(353) Corma, A.; Navas, J.; Rodenas, T.; Sabater, M. J. One-Pot Palladium-Catalyzed Borrowing Hydrogen Synthesis of Thioethers. *Chem. - Eur. J.* **2013**, *19*, 17464−17471.
(354) Kim, I.; Itagaki, S.; Jin, X.; Yamaguchi, K.; Mizuno, N. Heterogeneously catalyzed self-condensation of primary amines to secondary amines by supported copper catalysts. *Catal. Sci. Technol.* **2013**, *3*, 2397−2403.
(355) Liu, H.; Chuah, G.-K.; Jaenicke, S. Self-coupling of benzyl-amines over a highly active and selective supported copper catalyst to produce N-substituted amines by the borrowing hydrogen method. *J. Catal.* **2015**, *329*, 262−268.

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Chem. Rev. 2018, 118, 1410−1459