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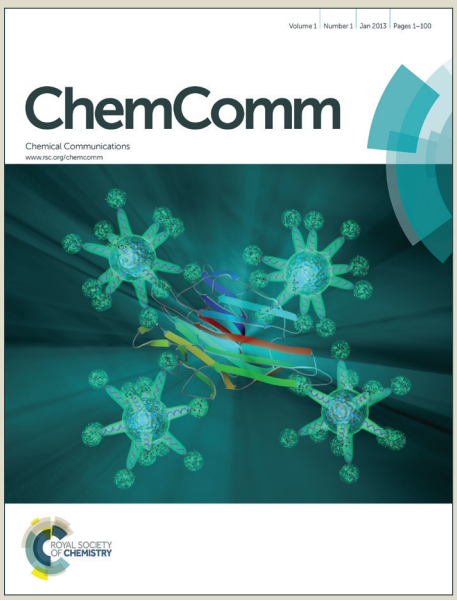

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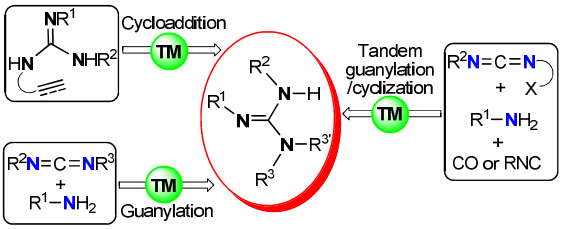

This article provides an overview of guanidine synthesis via transition metal catalyzed reactions including cycloaddition, guanylation and tandem guanylation/cyclization.

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FEATURE ARTICLE

Recent development on the synthetic methods of guanidines via transition metal catalysis

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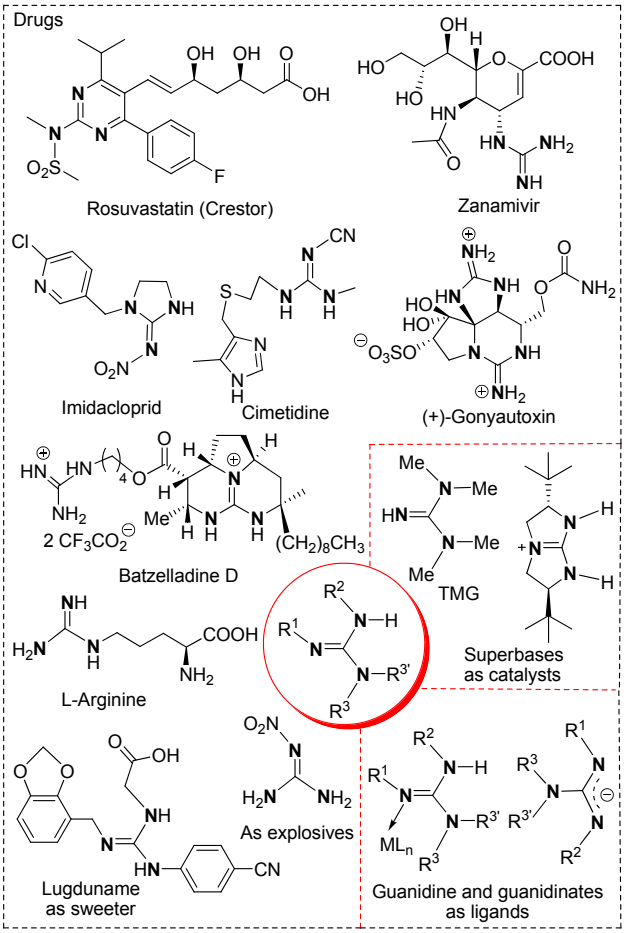
Multi-substituted guanidines have received much attention because of their important applications in many fields, such as pharmaceutics, organometallic and coordination chemistry, and organic synthesis. Although classical methods are available for the preparation of guanidines, the synthetic approaches to guanidines is still in great demand. In this review, we summarize recent development on the synthetic methods of guanidines via C–N bond formation. Three aspects are included: i) transition-metal-catalyzed guanidine synthesis based on classical methods; ii) catalytic guanylation reaction of amines with carbodiimides; and iii) tandem catalytic guanylation/cyclization reactions.

1 Introduction

Guanidine, $HN=C(NH_2)_2$, is an important 'CN_3'-core-containing molecule with a wide range of interesting properties since it was first prepared by oxidative degradation of guanine by Strecker in 1861.[1-3] The substituted guanidine derivatives, RN=C(NR'R")NHR'", have received more and more attention because of the tunable steric and electronic effect.[4-35] Guanidine derivatives have three characteristic applications in numerous fields. Firstly, they serve as building blocks in various drugs, natural products, agrochemicals, sweeters, explosives, etc. (Scheme 1).[5-10] For example, Rosuvastatin, a cholesterol biosynthesis inhibitor, ranked in third place in top 100 prescription drugs by sales in 2012.[11] L-Arginine, a guanidino group-containing basic amino acid, is involved in many important physiologically relevant processes.[12] Secondly, guanidine derivatives are organic superbases owing to the resonance stabilization of their conjugated acids and catalyze various types of organic reactions. *N,N,N′,N′*-Tetramethylguanidine (TMG) and its modified guanidines are typical guanidine compounds used in many kinds of base-catalyzed reactions.[13-16] Chiral guanidine catalysts have attracted much attention in asymmetric synthesis in the past few years,. They showed good enantioselectivity in Michael, Henry, Diels-Alder, Mannich reactions, etc.[17-21] Finally, neutral guanidines have found themselves as good supporting ligands in organometallic and coordination chemistry. More importantly, the highly versatile and readily available guanidinate anions play a critical role in stabilizing numerous complexes of various elements throughout the Periodic Table.[22-29]

Because of the importance of guanidine derivatives in various areas, about thirty reviews on guanidine chemistry have appeared in the literatures.[3-10,12-34] These reviews covered many aspects of guanidines, such as isolation, synthesis, reaction,



Scheme 1 Characteristic applications of guanidine derivatives.

catalytic application, coordination chemistry, biological activities, etc. In case of guanidine synthesis, reviews 13, 30-33 presented

the state-of-art routes for the preparation of various guanidine derivatives. They mainly concentrated on the development of guanylation reagents or derivatizing the 'CN_3' core. Very recently, a review entitled "Guanidines: from classical approaches to efficient catalytic syntheses" by Carrillo-Hermosilla *et al.* focused on two-component catalytic guanylation reaction for guanidine synthesis.[34]

Recently, metal catalyzed C–N bond formation has become a powerful tool for the construction of *N*-containing compounds.[35] In this review, we will present recent development on the synthetic methods of guanidines via C–N bond formation in the past ten years. Three aspects are included: i) transition-metal-catalyzed guanidine synthesis based on classical methods; ii) catalytic guanylation reaction of amines with carbodiimides; and iii) tandem catalytic guanylation/cyclization reactions.

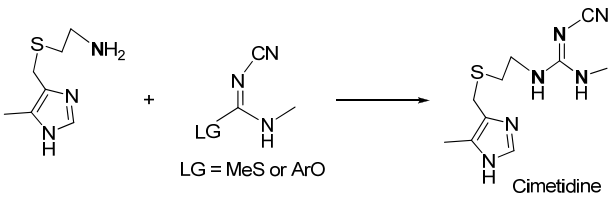
2 Guanidine synthesis via transition metal catalysis based on classical methods

2.1 Classical methods for guanidine synthesis.

Functionalization of a pre-existing guanidine core provides a typical method for the preparation of substituted guanidines. This has been widely used to synthesize alkyl, aryl or acyl guanidines. Protecting groups such as OTs, OTf or Boc are usually used for the prevention of over-substitutions and the sequential introduction of multiple functional groups.

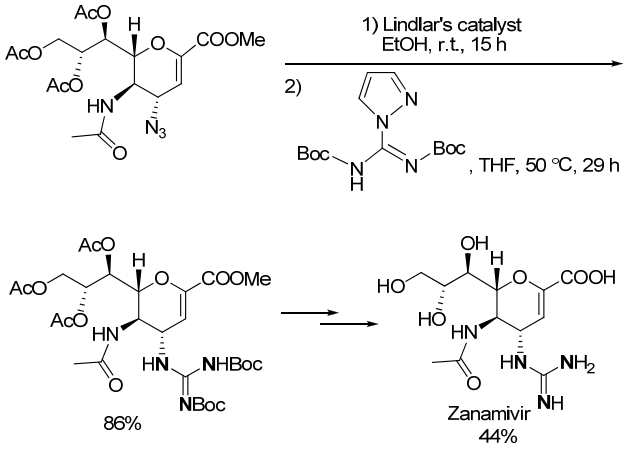
Di-, tri- or tetrasubstituted acyclic guanidines are generally prepared by the reaction of an amine compound with a suitable electrophilic guanylating reagent. Various guanylating reagents, including thioureas, isothioureas, aminoiminosulfonic acids, triflyl guanidines, pyrazole-1-carboximidamides, benzotriazole and imidazole-activated reagents, cyanamides, etc., are developed in order to obtain acyclic guanidines efficiently. In these guanylation of amines, guanylation reagents provide the corresponding CN_2-containing part. Their advantages and disadvantages in the stoichiometric guanylating reaction were described in the review.[31] The solid-phase synthesis of guanidines was also performed via anchoring thioureas and isothioureas or amines onto solid support.[36]

The reaction of an amine compound with a suitable electrophilic guanylating reagent provides a practical and efficient method for some important guanidine-containing drugs. Cimetidine, a H2-receptor antagonist, can be prepared from the corresponding amine by treatment with an isothiourea (LG = MeS). However, if this method is used as an industrial process, it would generate a large volume of CH_3SH by-product with very unpleasant odor.[37] When the alternative (LG = ArO) is used as a guanylating reagent, it becomes an environmentally friendly process (Scheme 2).[38]

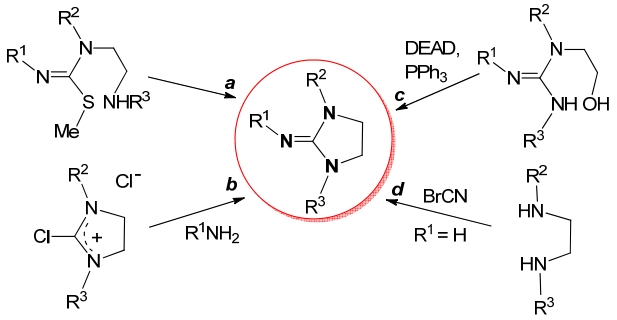


Scheme 2 Synthesis of Cimetidine.

Zanamivir, a potent neuraminidase inhibitor, can be enantioselectively synthesized from the simple starting materials. An important step in the process is the electrophilic guanylation of guanylating reagent pyrazole-1-carboximidamide with an amine which is in-situ generated by reduction of an azide (Scheme 3).[39]



Scheme 3 Synthesis of Zanamivir.

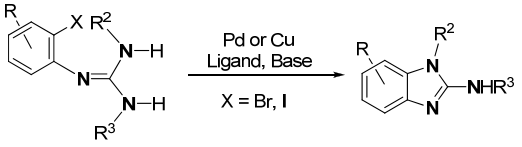


Scheme 4 Preparation of cyclic guanidines.

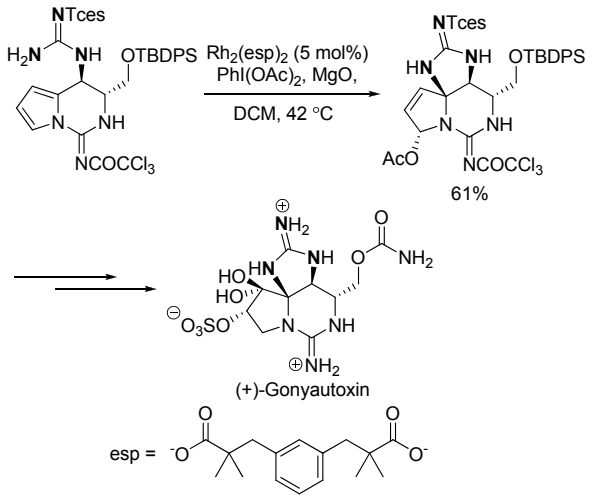
In addition to acyclic guanidines, cyclic guanidines are generally prepared by the intramolecular guanylation reaction of amines (Scheme 4***a***), amination of 2-chloro-1,3-imidazolium chloride (Scheme 4***b***), cyclization of guanidines bearing a hydroxyethyl group (Scheme 4***c***), or *N*-cyanation of amines with cyanogen bromide (Scheme 4***d***).[13]

2.2 Transition metal catalysis for guanidine synthesis.

Currently, many strategies have been developed to achieve various functionalized guanidines. Transition-metal-catalyzed *N*-arylation of guanidines is considered as an important way to construct cyclic guanidines (Scheme 5).[34] This has been reviewed by Maes *et al.*, so this topic is not covered here.



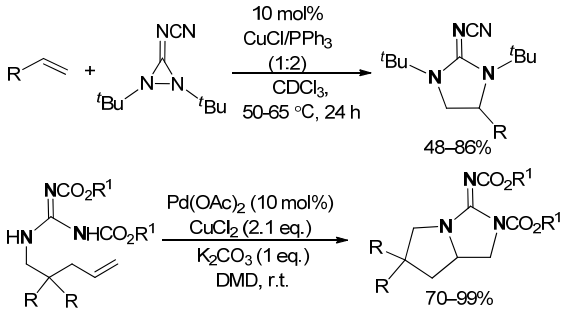
Scheme 5 Transition-metal catalyzed *N*-arylation of guanidines.



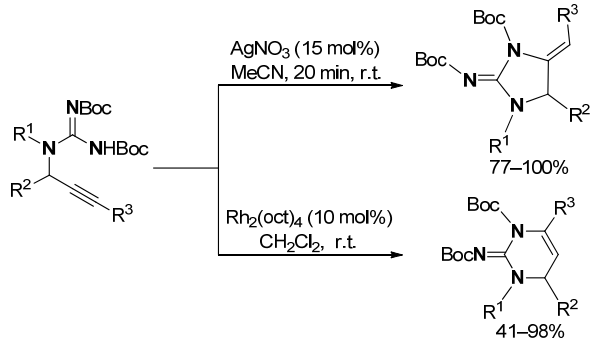
Scheme 6 Rh-catalyzed C–H amination and its application.

Transition-metal catalyzed C–H amination reaction has been established as a powerful tool for the synthesis of azaheterocycles. Recently, oxidative C–H amination of the electron-withdrawing 2,2,2-trichloroethoxysulfonyl (Tces) protected guanidines catalyzed by the commercial catalyst $Rh_2(esp)_2$ (esp: α,α,α′,α′-tetramethyl-1,3-benzenedipropionate) is reported to give 5-membered cyclic guanidines in high yield (Scheme 6). Furthermore, this protocol is applied to the total synthesis of polycyclic guanidine (+)-gonyautoxin.[40,41]

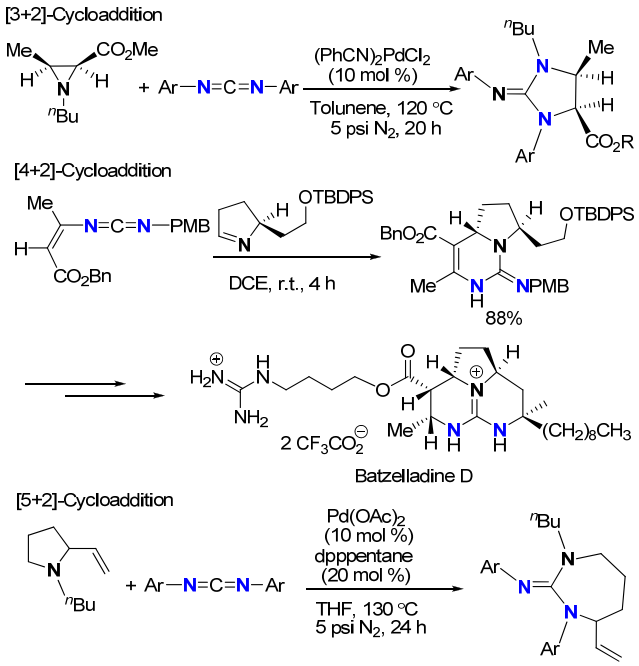
Transition-metal catalyzed cycloguanidination via alkene diamination represents an efficient and challenging transformation for the synthesis of cyclic guanidines. Shi *et al.* found the intermolecular Cu(I)-catalyzed cycloguanidination of terminal alkenes with diaziridinimines to provide various cyclic guanidines (Scheme 7). In case of dienes and trienes, the reaction proceeds regioselectively at the terminal double bond.[42] In addition, the intramolecular palladium(II)-catalyzed oxidative diamination was developed by Muñiz *et al.* to give bicyclic guanidines with complete selectivity and in high yield (Scheme 7).[43]



Scheme 7 Transition-metal catalyzed alkene diamination.



Scheme 8 Selective hydroaminations of progargylguanidines.



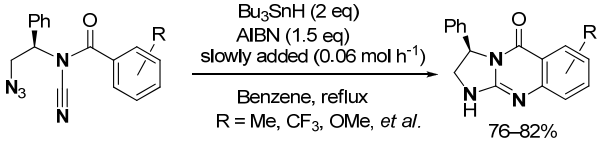
Scheme 9 Guanidines prepared by cycloaddition of carbodiimide.

Hydroaminations of progargylguanidines have been proven powerful for the preparation of cyclic guanidines. Recently, the Boc-protected propargylguanidines could be transformed into 2-iminoimidazolines via intramolecular π-philic Ag(I)-catalyzed 5-*exo*-dig heterocyclization. This method was successfully applied to the total synthesis of 2-aminoimidazole namine alkaloids.[44] In contrast, dirhodium(II) carboxylates can serve as highly 6-*endo*-dig selective hydroamination catalysts to give 6-membered cyclic guanidines (Scheme 8).[45]

In addition, cycloaddition reactions with carbodiimides provide the valuable routes for cyclic guanidines. For example, [3+2][46,47] cycloaddition reaction of aziridine with carbodiimide and [5+2][48] cycloaddition reaction of 2-vinylpyrrolidine with carbodiimide in the presence of palladium catalysts were reported by Alper *et al.* to afford 5 or 7-memebered cyclic guanidines, respectively (Scheme 9). Gin *et al.* applied [4+2][49] cycloaddition of imine with vinyl carbodiimide to prepare the 6-memebered cyclic guanidine, which was an important intermediate for the total synthesis of Batzelladine D (Scheme 9).

Furthermore, tricyclic guanidines could be efficiently

prepared via a radical domino process from *N*-acyl cyanamides (Scheme 10).[50]

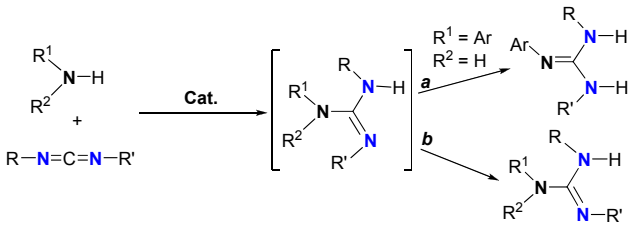


Scheme 10 Preparation of guanidines via a radical cyclization.

3 Guanidine synthesis via catalytic guanylation reaction of amines with carbodiimides

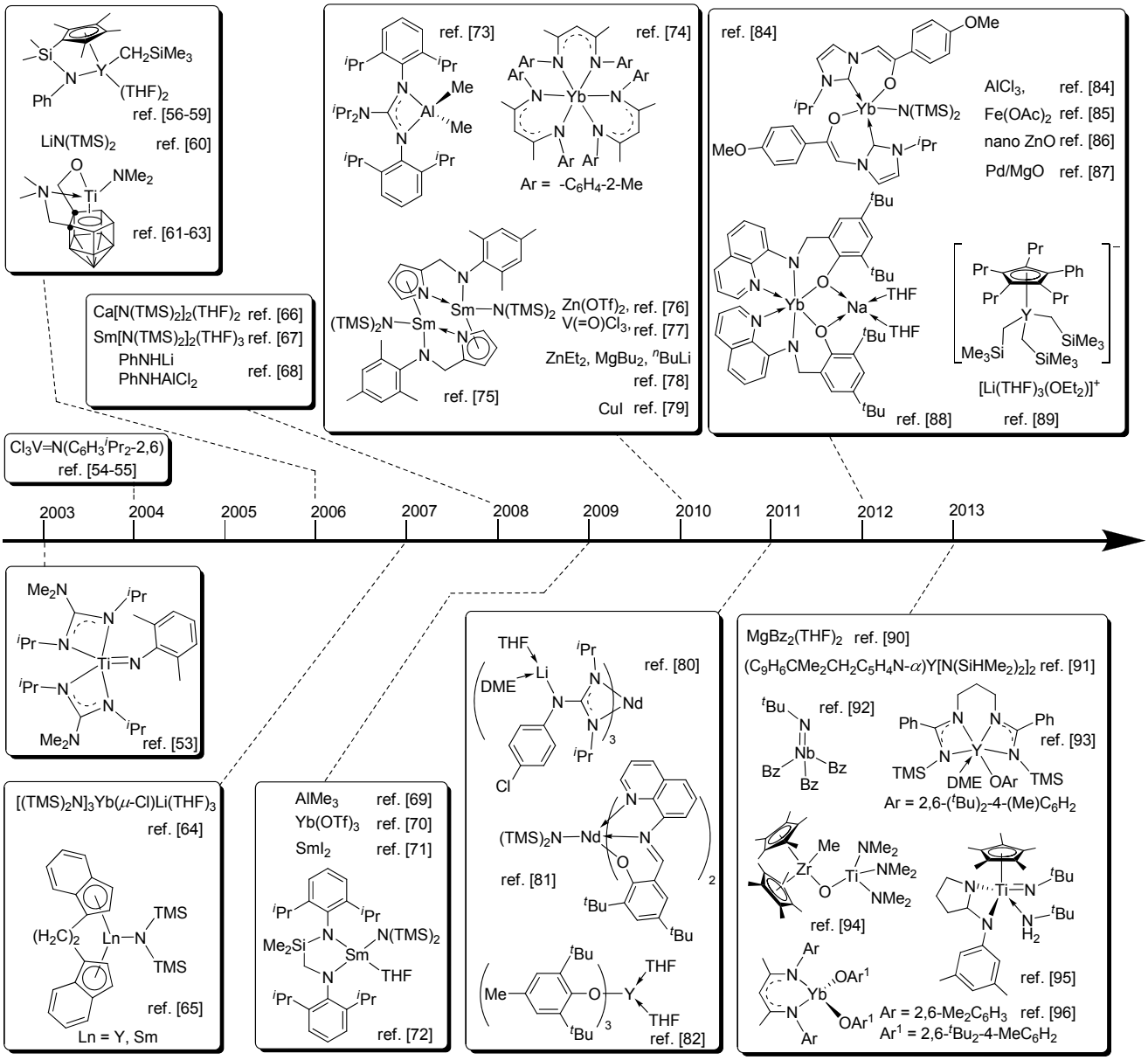
3.1 Discovery and development of catalytic guanylation reaction of amines with carbodiimides.

Under some circumstances in guanylation reaction of amines using thioureas and isothioureas as guanylation reagents, carbodiimides are often proposed as active intermediates for the synthesis of guanidines. As carbodiimides can be synthesized and isolated easily, direct addition of amine N–H bonds to carbodiimides which is also known as guanylation reaction of amines with carbodiimides or hydroamination of carbodiimides, is a straightforward and atom-economical route to guanidines. However, this guanylation reaction can only be applied to aliphatic amines in rather harsh condition without catalyst.[51] Due to the decreased nucleophilicity of aromatic amines or secondary amines, they hardly react with carbodiimides under the same or harsher conditions. Therefore, the invention and development of high efficient catalyst for this guanylation process is of great importance.

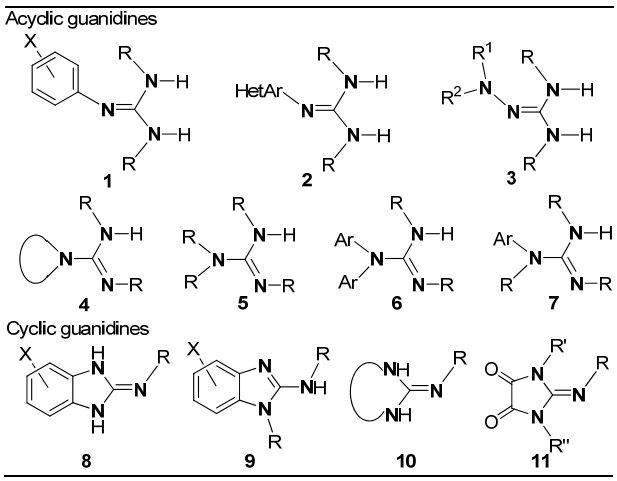


Scheme 11 Catalytic guanylation of amine with carbodiimide.

Tetrabutylammonium fluoride (TBAF) was used to promote this guanylation of some aromatic amines with the activated *N,N'*-diaryl substituted carbodiimides.[52] The dual activation effect of fluoride on both amines and carbodiimides leads to the formation of guanidines at room temperature. In 2003, the catalytic guanylation reaction of primary aromatic amines with unactivated carbodiimides was reported by Richeson *et al.* using titanium imido complexes (Scheme 11***a***).[53] The catalytic guanylation of secondary amines with carbodiimides was achieved by Hou *et al.* using a half-sandwich rare earth metal alkyl complex until 2006, (Scheme 11***b***).[54] Pioneered by these works, the catalytic guanylation of various amines with carbodiimides has received much current interest for the atom-economical preparation of guanidines. To date, more than forty catalysts including transition, main group and rare-earth metals have been designed and tested for the guanylation reaction.[53-97] Scheme 12 summarizes the discovery and development of various catalysts. Seven types of acyclic guanidines **1**-**7** and four types of cyclic guanidines **8**-**11** can be constructed by catalytic guanylation reaction as shown in Scheme 13. It is estimated that more than 260 guanidines with different substituted groups can be synthesized.



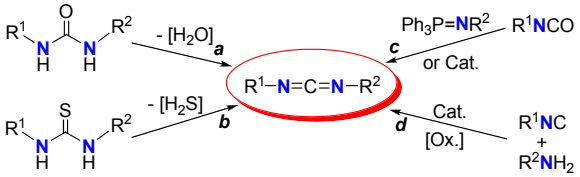
Scheme 12 Various catalysts found in the past ten years for guanylation reaction of amines with carbodiimides.



Scheme 13 The different types of acyclic and cyclic guanidines.

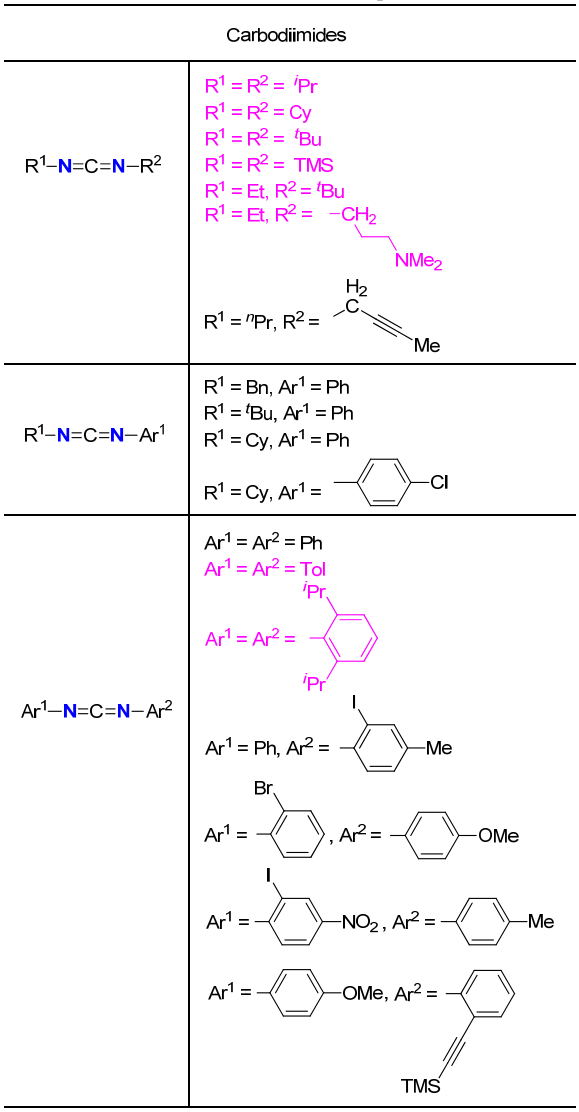
3.2 The summary of general synthetic routes of carbodiimides.

In two-component guanylation reaction, the carbodiimide is an important partner. The efficient preparation of various carbodiimides will accelerate the development of this area. Although several previous reviews on carbodiimide chemistry sporadically involved their synthetic methods,[98-100] the convenient and practical methods for carbodiimide synthesis are summarized in Scheme 14.



Scheme 14 The practical synthesis of carbodiimides.

The first efficient route (method ***a***) is dehydration of ureas to prepare corresponding carbodiimides. The strong dehydrators such as P_2O_5 or $POCl_3$ can be applied to the process.[101-104] In addition, due to the effect of the oxophilic phosphorus, $[Ph_3PBr]^+Br$, Ph_3P/CCl_4 or Ph_3P/CBr_4 can effect dehydration to afford carbodiimides from ureas in the presence of Et_3N.[105,106]



Scheme 15 Representative examples of carbodiimides.

The desulfurization of thioureas (method ***b***) provides the common method for the preparation of carbodiimide because *N,N'*-disubstituted thioureas can be efficiently synthesized by mixing isothiocyanate and amine. Therefore, a large amount of symmetric and asymmetric carbodiimides can be obtained by this method. The classical strategy to remove hydrogen sulfide usually utilizes heavy metal salt or oxide, such as $HgCl_2$ and HgO, which are toxic and harmful to environment.[107-109] Another strategy to remove hydrogen sulfide is to use oxidant/reducing agent. In the presence of Ph_3P, diethylazodicarboxylate (DEAD) can work as oxidant to accept two hydrogens of thiourea while the sulfur transfers to PPh_3 via the formation of $Ph_3P{=}S$.[110] This method has been widely used because of the good tolerance of functional group. Almost all carbodiimides with different substituents can be synthesized by this method. Nakazawa *et al.* developed a new strategy by using silanes as reducing agents under the presence of $CpFe(CO)_2Me$.[111]

The third efficient route (method ***c***) is condensation of isocyanate with the loss of CO_2. This reaction can be accelerated by many catalysts including metal carbonyls or compounds containing P=O moiety.[112-115] However, only symmetric carbodiimide can be prepared by condensation of isocyanate. Then, the aza-Wittig reaction between iminophosphoranes ($Ph_3P{=}NR$) and isocyanate is developed, in which iminophosphoranes are used as imino transfer reagents in the reaction with isocyanate. Thus unsymmetric carbodiimide is accessible by utilizing isocyanate as starting material. This strategy has also been widely used because of the easy availability of starting materials. Isocyanate is commercially available, and iminophosphoranes can be conveniently prepared by reaction of Ph_3P and azides.

Catalytic oxidative coupling of amine with isonitrile (method ***d***) is less utilized in the practical synthesis of carbodiimides. Initially, Ag_2O was applied as oxidant.[116] Then, I_2 and oxygen were developed to replace Ag_2O as cheaper oxidants.[117-119]

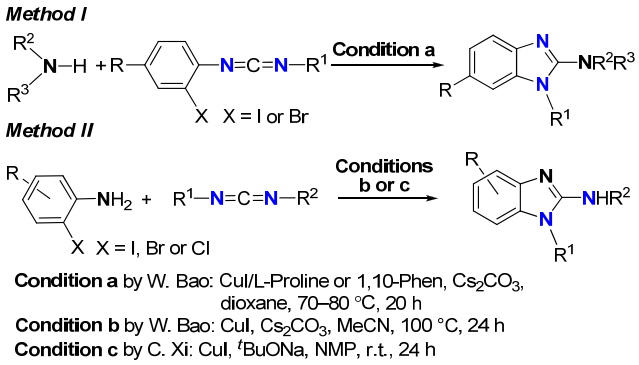
Based on the above practical synthetic routes, three types of molecules including *N,N'*-dialkyl-, *N*-alkyl,*N'*-aryl, *N,N'*-diaryl-substituted carbodiimides can be conveniently prepared (Scheme 15). Eight carbodiimides marked in pink are commercially available and often used in different reactions.

4 Guanidine synthesis via tandem catalytic guanylation/cyclization reaction

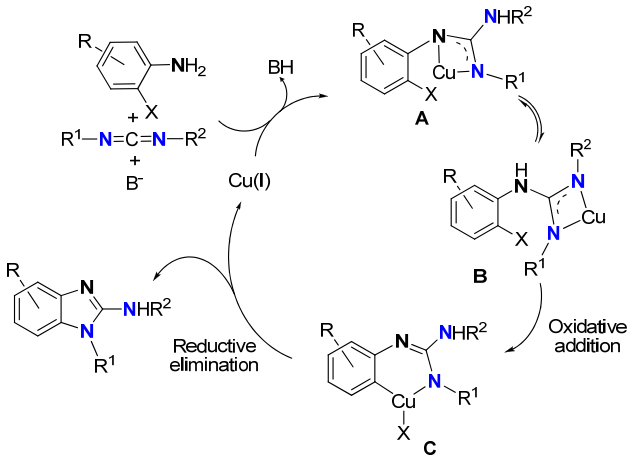
Catalytic guanylation reaction of amines with carbodiimides provides a straightforward and atom-economical preparation of substituted guanidines. These guanidines are multifunctional compounds with the active N–H, C–N and C=N bonds. If further transformation of N–H, C–N and C=N bonds of guanidines in one-pot tandem reaction is effected, it will become very useful for fast and efficient construction of some important *N*-containing compounds. Recently, a series of tandem guanylation/cyclization processes has been reported and these results are summarized.

4.1 Tandem guanylation/*N*-arylation cyclization

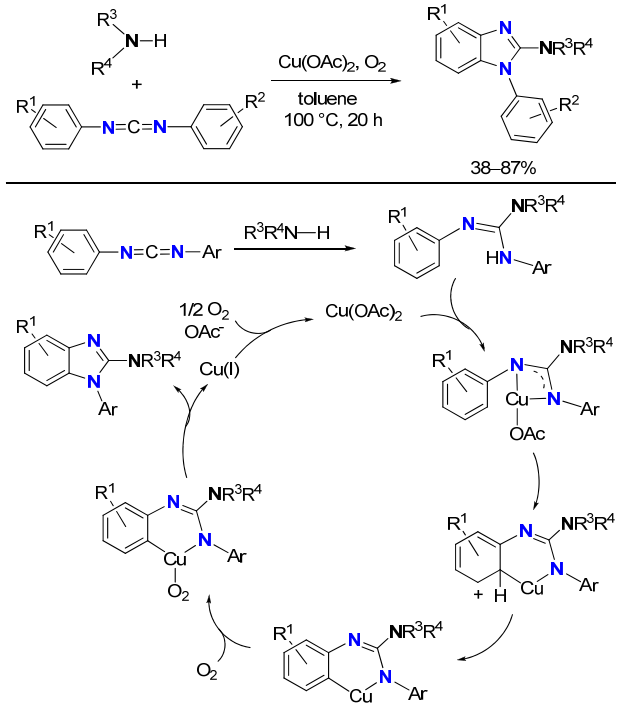
Two efficient strategies for the synthesis of a variety of 2-aminobenzimidazoles have been developed by Bao and Xi groups via Cu-catalyzed tandem guanylation/*N*-arylation cyclization: i) the coupling of amines or imidazoles with *o*-haloarylcarbodiimides;[120] ii) the coupling of *o*-haloanilines with carbodiimides (Scheme 16).[79,121] Many aliphatic amines including primary amines and cyclic or *n*-alkyl secondary amines were suitable *N*-nucleophiles for the synthesis of *N*-substituted 2-aminobenzimidazoles via method **I**. Method **II** provided a more convenient route to 2-aminobenzimidazoles than Method **I**. **Conditions b** and **c** were developed by Bao and Xi, respectively. **Condition c** provided a general and practical route to 2-aminobenzimidazoles, compared with **condition b** in which only *N,N'*-diphenylcarbodiimide can work. In the case of **condition c**, a wide range of *o*-haloanilines (X = I, Br and Cl) could be used. The symmetrical and unsymmetrical carbodiimides with aryl or alkyl substituents were suitable substrates. The good regioselectivity was observed when unsymmetrical carbodiimides were employed.



Scheme 16 Cu-catalyzed guanylation/*N*-arylation cyclization.



Scheme 17 Mechanism of Cu-catalyzed guanylation/*N*-arylation of *o*-haloanilines with carbodiimides.

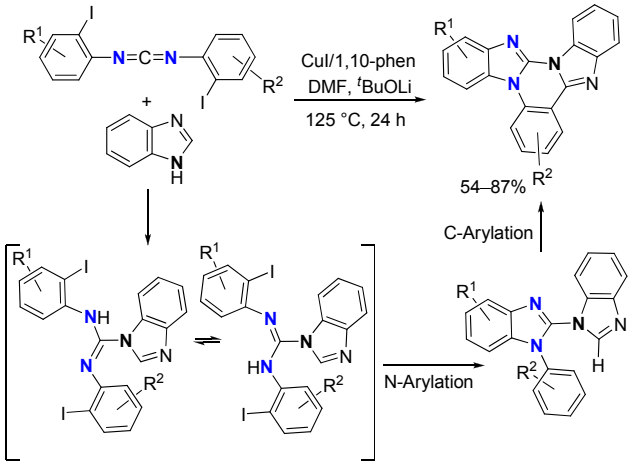


Scheme 18 Cu-catalyzed guanylation/*N*-arylation of amines with carbodiimides.

A possible mechanism for method **II** was proposed in Scheme 17. The intramolecular addition of anilines to carbodiimides under proper conditions should give Cu(I) guanidinate intermediate **A** or **B**. Then the Cu(III) intermediate **C** could be formed through the oxidative addition of C–X (X = Br, I) bond. Subsequent reductive elimination should give the final product and regenerate Cu(I) salt.

Interestingly, 2-aminobenzimidazoles could be synthesized directly by $Cu(OAc)_2/O_2$ catalyzed reaction of diarylcarbodiimide with amines.[122] This procedure proceeds a cascade additon/C–H activation/C–H functionalization process. The plausible mechanism of the cyclization is shown in Scheme 18. The Cu–N adducts with copper either in oxidation state II or III might be formed in cyclization process.

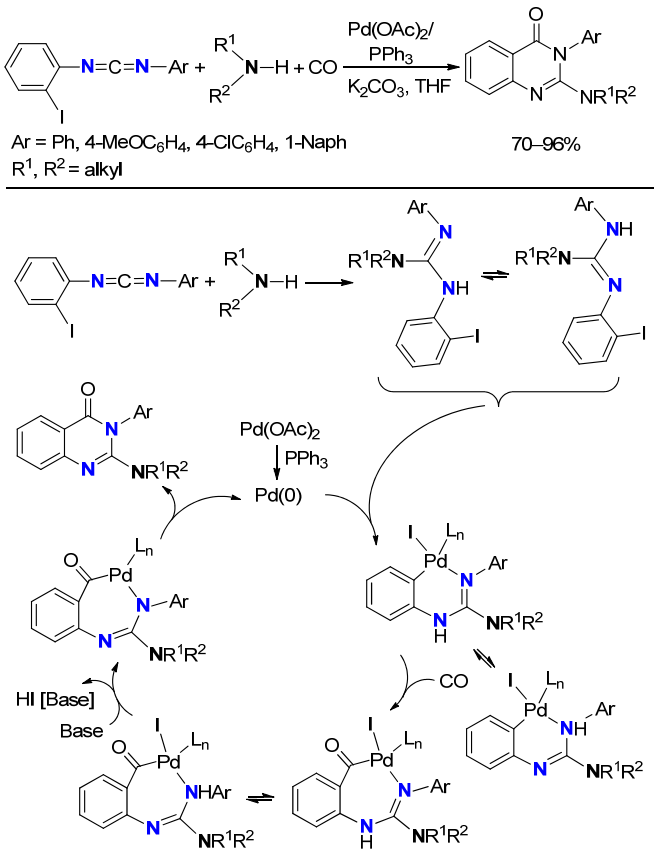
Very recently, an efficient method for the assembly of polycyclic benzimidazoles has been achieved via Cu-catalyzed tandem guanylation/*N*-arylation/*C*-arylation double cyclization from bis-(*o*-haloaryl)-carbodiimides and azoles (Scheme 19).[123] These azole-fused benzimidazoquinazolines could play important roles in medicinal chemistry and material science.



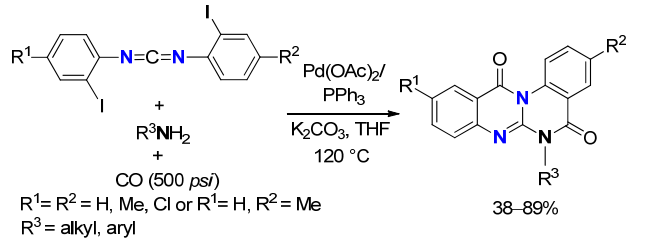
Scheme 19 Cu-catalyzed guanylation/*N*-arylation/*C*-arylation double cyclization.

4.2 Tandem guanylation/cyclocarbonylation cyclization

In 2010, Alper *et al.* reported an efficient method for the synthesis of 2-heteroquinazolin-4(*3H*)-ones by a palladium-catalyzed tandem guanylation addition/cyclocarbonylation reaction from *o*-haloarylcarbodiimides, amines and CO.[124] Various 2-heteroquinazolin-4(*3H*)-ones could be obtained in good to excellent yields under mild reaction conditions (80 °C, 100 psi). The reaction proceeds two stages: i) an intermolecular addition of amines to *o*-iodoarylcarbodiimides generating in situ guanidines, ii) palladium-catalyzed cyclocarbonylation through oxidative addition/CO insertion/intramolecular cyclization/reductive elimination (Scheme 20). Furthermore, the tandem guanylation addition/double cyclocarbonylation was developed in a single step by palladium-catalyzed reaction of bis-(*o*-haloaryl)-carbodiimides, amines and CO (Scheme 21).[125] The tandem reaction could efficiently provide the tetracyclic quinazolinones.



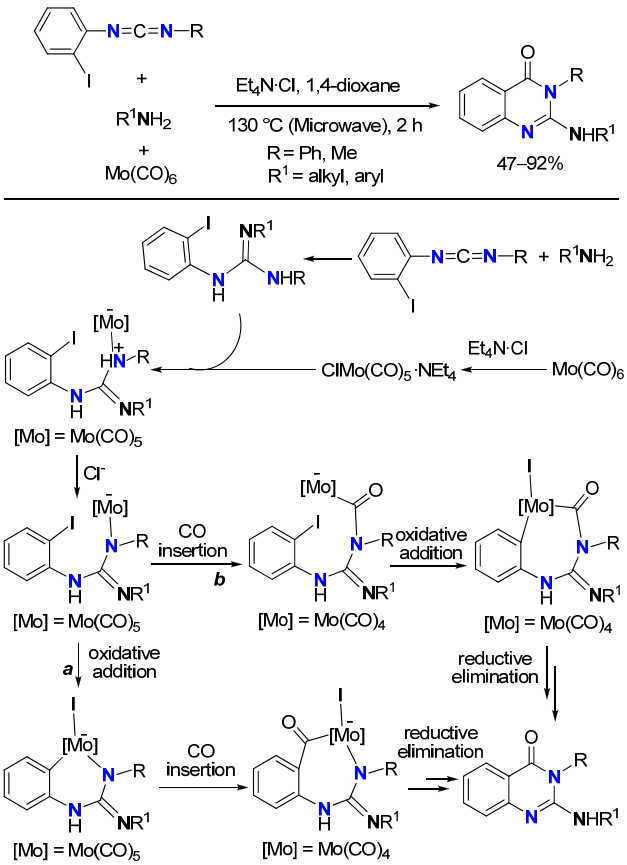
Scheme 20 Palladium-catalyzed guanylation/cyclocarbonylation.



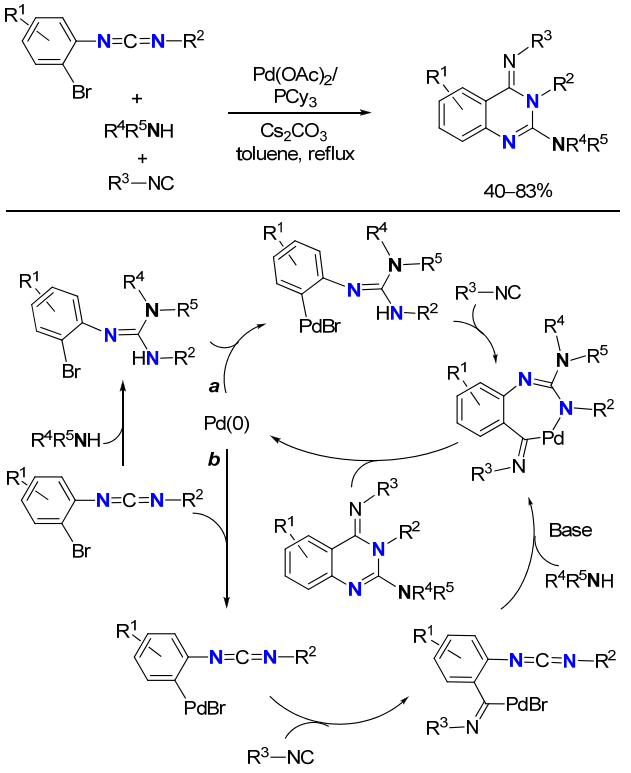
Scheme 21 Tandem guanylation/double cyclocarbonylation.

Without the need for gaseous CO, the $Mo(CO)_6$-mediated guanylation addition/cyclocarbonylation was developed for the synthesis of 2-heteroquinazolin-4(*3H*)-ones.[126] This reaction could proceed two pathways: a) nucleophilic addition/oxidative addition/CO insertion/reductive elimination, b) nucleophilic addition/CO insertion/oxidative addition/reductive elimination (Scheme 22).

The efficient method for the preparation of quinazolin-4(3*H*)-imines was developed by Wu *et al.* via a Pd-catalyzed three-component reaction of carbodiimides, isocyanides and amines (Scheme 23).[127] Two possible mechanisms were proposed: a) nucleophilic addition/oxidative addition/isocyanide insertion/reductive elimination, b) oxidative addition/isocyanide insertion/nucleophilic addition/reductive elimination. In this reaction process, the isocyanide insertion was believed to be the key step, which was similar to CO insertion proposed by Alper *et al.*



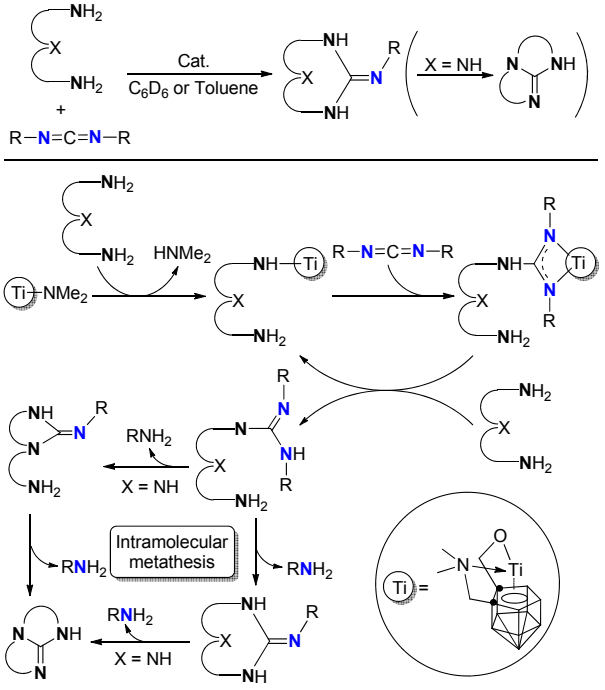
Scheme 22 $Mo(CO)_6$-mediated guanylation/cyclocarbonylation.



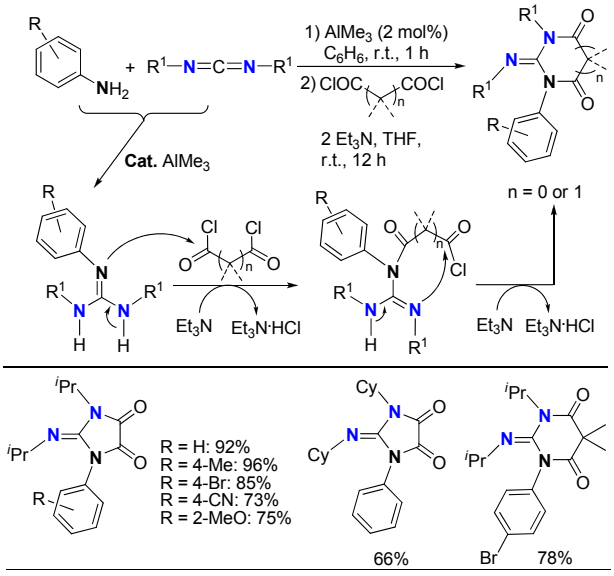
Scheme 23 Pd-catalyzed three-component reaction of carbodiimides, isocyanides and amines.

4.3 Tandem guanylation/metathesis cyclization

In 2006, Xie *et al.* reported that the titanium amido complex supported by the carboranyl–alkoxy ligand could catalyze the guanylation reaction of monoamines with carbodiimides yielding guanidines.[61] Then they found that mono/bicyclic guanidines could be constructed efficiently when diamine or triamine were allowed to react with carbodiimides (Scheme 24).[63] Based on the isolation and reaction of important intermediates, a possible mechanism is proposed. The reaction proceeds two important stages: guanylation via insertion/protonation pathway and intramolecular metathesis. When a triamine is used as the starting material (X = NH), twice intramolecular metathesis could occur to give bicyclic guanidines.



Scheme 24 Titanium amido complex catalyzed guanylation/ metathesis cyclization.



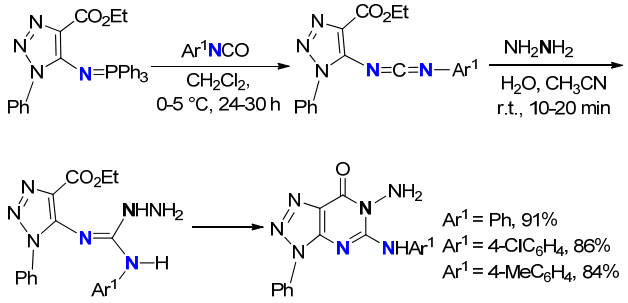
Scheme 25 Tandem guanylation/amidation.

4.4 Tandem guanylation/amidation cyclization

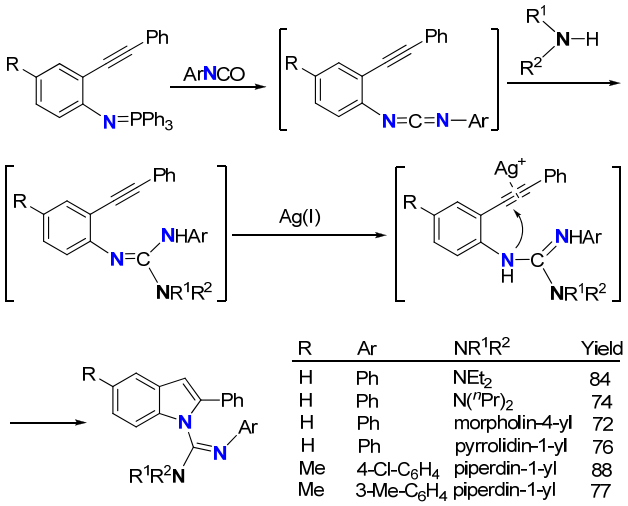
Our group demonstrated a sequential reaction by combining guanylation and amidation to give cyclic guanidines in 2012, (Scheme 25).[128] In the presence of $AlMe_3$, amines were added to carbodiimides to give guanidines, then the addition of oxalyl chloride with Et_3N as base led to the final products. $AlMe_3$ is critical in the process. If all of the reactants are mixed without $AlMe_3$, only an isomer of the cyclic guanidines can be achieved. The mechanism of this sequential process starts with the $AlMe_3$ catalyzed guanylation. Then twice addition-elimination gives the final products.

4.5 Tandem aza-Wittig/guanylation/nucleophilic addition cyclization

The aza-Wittig reaction of iminophosphorane have received much interest in the synthesis of aza-heterocyclic compounds. In some cases, carbodiimides which act as the active intermediates, can be generated in-situ by aza-Wittig reaction of iminophosphorane with aromatic isocyanates. For example, iminophosphorane-mediated synthesis of pyrimidinones could be obtained from iminophosphorane and aromatic isocyanates via aza-Wittig reaction/guanylation/amidation (Scheme 26).[129]



Scheme 26 Tandem aza-Wittig reaction/guanylation/amidation.



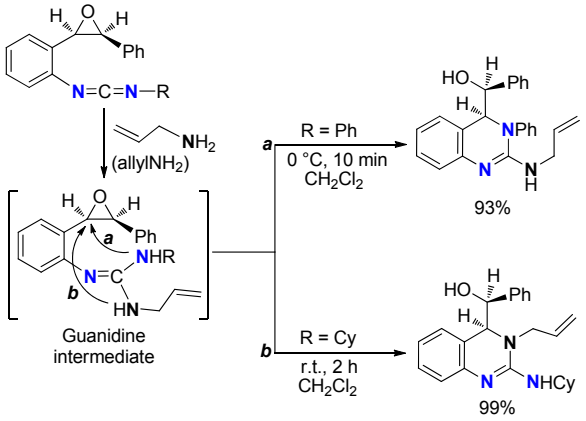
Scheme 27 Tandem aza-Wittig reaction/guanylation/ Ag(I)-catalyzed cyclization.

Interestingly, a sequential aza-Wittig reaction/guanylation/Ag(I)-catalyzed cyclization from iminophosphorane, aromatic isocyanates and amines was found to provide efficiently indole *N*-carboximidamides (Scheme 27).[130]

The one-pot approach has two features: high regioselectivity and mild reaction conditions.

4.6 Tandem guanylation/epoxy ring-opening cyclization

The oxiranylcarbodiimide-mediated guanylation/epoxy ring-opening cyclization was utilized in the synthesis of dihydroquinazolines (Scheme 28).[131] The reaction of oxiranylcarbodiimide (R = Ph) with allyl amine gives the corresponding dihydroquinazoline. The reaction proceeds the guanidine intermediate, in which an epoxy ring-opening cyclization occurs via pathway ***a***. In contrast, the reaction of oxiranylcarbodiimide bearing a bulky substituent (R = Cy) yields dihydroquinazoline via the alternative pathway ***b***.



Scheme 28 Tandem guanylation/epoxy ring-opening cyclization.

Conclusions and outlook

The classical methods for guanidine synthesis often have drawbacks such as the limited availability of starting materials, low yields, and the formation of undesired by-products. New synthetic approaches to guanidines are in great demand because of their important properties in many fields to meet the growing needs of guanidines. This review summarizes the recent synthetic methods to guanidines including: i) transition-metal-catalyzed guanidine synthesis based on classical methods; ii) catalytic guanylation reaction of amines with carbodiimides; and iii) tandem catalytic guanylation/cyclization reactions. As far as transition-metal-catalyzed syntheses of guanidines are concerned, functionalization of a pre-existing guanidine core via C–N bond formation and cycloaddition reactions are discovered to provide good routes for the preparation of substituted guanidines. Some methods have been successfully applied to the total synthesis of guanidine-containing natural products. In addition, the field of catalytic guanylation reaction has received increasing interest because of the efficiency in the preparation of guanidines. Although much progress has been made in the field of catalytic guanylation reaction, many issues remain to be addressed: the design and development of new homogeneous and heterogeneous catalysts, the activity of catalysts, the scope of substrates, the tolerance of functional groups, and the synthetic applications in important and complex guanidines.

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Notes and references

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