

Catalytic Diamination of Olefins via N–N Bond Activation

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CONSPECTUS: Vicinal diamines are important structural motifs present in various biologically and chemically significant molecules. Direct diamination of olefins provides an effective approach to this class of compounds. Unlike well-established oxidation processes such as epoxidation, dihydroxylation, and aminohydroxylation, direct diamination of olefins had remained a long-standing challenge and had been less well developed.

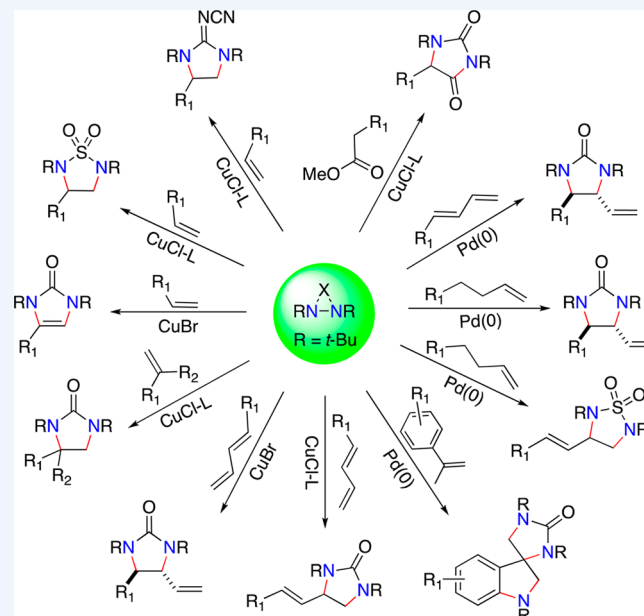
In this Account, we summarize our recent studies on Pd(0)- and Cu(I)-catalyzed diaminations of olefins using di-*tert*-butyldiaziridinone and its related analogues as nitrogen sources via N–N bond activation. A wide variety of imidazolidinones, cyclic sulfamides, indolines, imidazolinones, and cyclic guanidines can be obtained from conjugated dienes and terminal olefins. For conjugated dienes, the diamination proceeds regioselectively at the internal double bond with the Pd(0) catalyst. Mechanistic studies show that the diamination likely involves a four-membered Pd(II) species resulting from the insertion of Pd(0) into the N–N bond of di-*tert*-butyldiaziridinone. Interestingly, the Cu(I)-catalyzed process occurs regioselectively at either the terminal or internal double bond depending on the reaction conditions

via two mechanistically distinct pathways. The Cu(I) catalyst cleaves the N–N bond of di-*tert*-butyldiaziridinone to form a Cu(II) nitrogen radical and a four-membered Cu(III) species, which are likely in rapid equilibrium. The Cu(II) nitrogen radical and the four-membered Cu(III) species lead to the terminal and internal diamination, respectively.

Terminal olefins are effectively C–H diaminated at the allylic and homoallylic carbons with Pd(0) as catalyst and di-*tert*-butyldiaziridinone as nitrogen source, likely involving a diene intermediate generated in situ from the terminal olefin via formation of a π -allyl Pd complex and subsequent β -hydride elimination. When di-*tert*-butylthiadiaziridine 1,1-dioxide is used as nitrogen source, cyclic sulfamides are installed at the terminal carbons via a dehydrogenative diamination process. When α -methylstyrenes (lacking homoallylic hydrogens) react with Pd(0) and di-*tert*-butyldiaziridinone, spirocyclic indolines are formed with generation of four C–N bonds and one spiro quaternary carbon via allylic and aromatic C–H amination.

With Cu(I) catalysts, various terminal olefins can be effectively diaminated at the double bonds using di-*tert*-butyldiaziridinone, di-*tert*-butylthiadiaziridine 1,1-dioxide, and 1,2-di-*tert*-butyl-3-(cyanimino)-diaziridine as nitrogen sources, giving a variety of imidazolidinones, cyclic sulfamides, and cyclic guanidines in good yields, respectively. In the case of monosubstituted olefins using di-*tert*-butyldiaziridinone as nitrogen source, the resulting diamination products (imidazolidinones) are readily dehydrogenated under the reaction conditions, leading to the corresponding imidazolinones in good yields. Esters can also be diaminated to form the corresponding hydantoin with di-*tert*-butyldiaziridinone in the presence of a Cu(I) catalyst. A radical mechanism is likely to be operating in these Cu(I)-catalyzed reaction processes.

Asymmetric processes have also been developed for the Pd(0)- and Cu(I)-catalyzed diamination reactions. Biologically active compounds such as (+)-CP-99,994 and Sch 425078 have been synthesized via the diamination processes. The diamination reactions described herein provide efficient methods to access a wide variety of vicinal diamines from readily available olefins and show great potential for synthetic applications.



1. INTRODUCTION

Vicinal diamines are prevalent in a variety of biologically active molecules (Figure 1)^{1,2} and chiral catalysts.^{1b–d,3} Direct diamination of olefins presents an attractive strategy for the synthesis of vicinal diamines and has received considerable attention particularly in recent years. Significant progress has

been made for this challenging research topic,^{1b–e,4} including metal-mediated^{5,6} and -catalyzed^{6b,7–11} diamination processes. In our own studies, we have discovered that di-*tert*-

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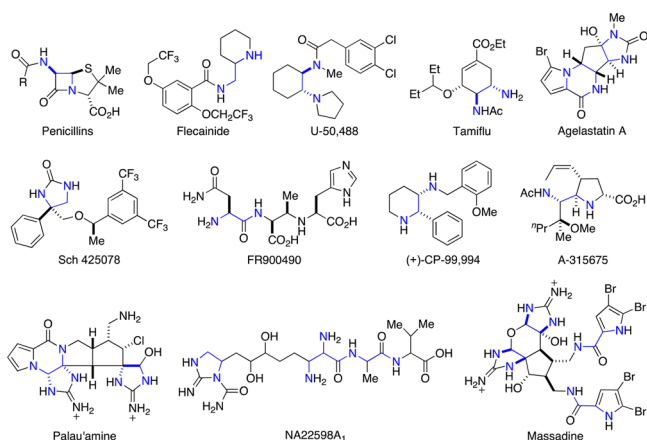


Figure 1. Selected examples of 1,2-diamine-containing biologically active molecules.

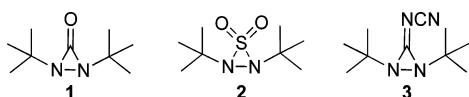


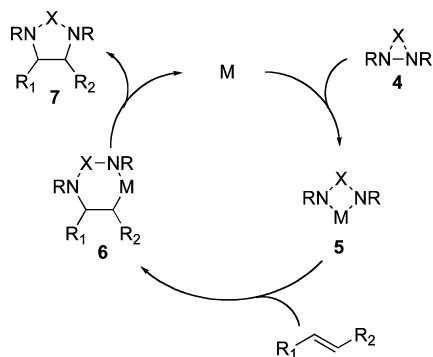
Figure 2. Di-*tert*-butyl diaziridinone (**1**) and its related analogues (**2** and **3**).

butyldiaziridinone (**1**) and its related analogues (Figure 2) are highly effective agents for the diamination of olefins in the presence of Pd(0) or Cu(I) catalyst. This account summarizes our studies on this subject.

2. Pd(0)-CATALYZED DIAMINATION VIA N–N BOND ACTIVATION

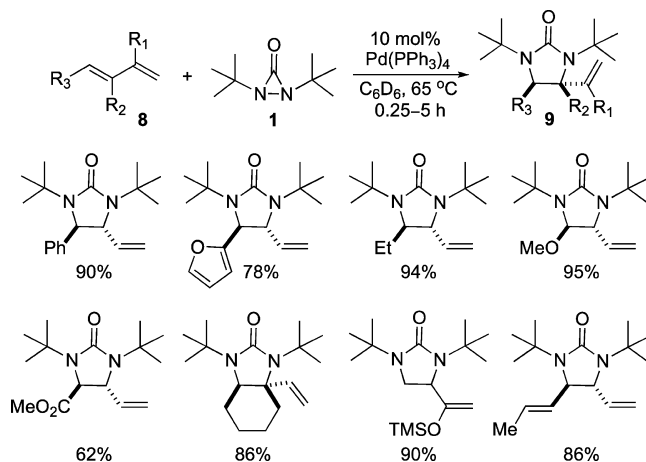
Inspired by our studies on the epoxidation of olefins via three-membered dioxiranes,¹² we have explored the possibility to

Scheme 1. Diamination of Olefins via N–N Bond Activation

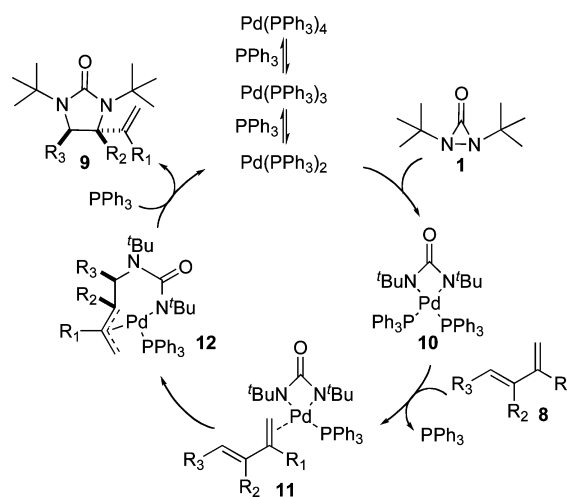


install nitrogen atom(s) onto C–C double bonds with related three-membered nitrogen analogues. It was envisioned that a metal could oxidatively add to the N–N bond of diaziridine **4** to form diamido species **5**, which could react with an olefin to give amination product **7** via migratory insertion to the double bond and subsequent reductive elimination (Scheme 1). Along this line, various metal catalysts, three-membered diaziridines, and olefin substrates were investigated. It was found that a variety of conjugated 1,3-dienes can be regio- and diastereoselectively diaminated at the internal double bond with Pd(0) as catalyst and di-*tert*-butyldiaziridinone (**1**) as nitrogen source, giving the corresponding imidazolidinones in high yields (Scheme 2).^{13,14} Both electron-rich and electron-

Scheme 2. Pd(0)-Catalyzed Diamination of Olefins Using **1**



Scheme 3. Proposed Catalytic Cycle for the Diamination of Olefins with **1**



deficient conjugated dienes were found to be effective substrates. When a conjugated triene was used, the diamination also occurred cleanly at the middle double bond. The amount of Pd(0) catalyst can be reduced from 10 to 1–2 mol % by slow addition of di-*tert*-butyldiaziridinone (**1**) under solvent-free conditions.^{15,14b} However, *cis*-dienes were not effective substrates under the current reaction conditions.

A plausible catalytic pathway for the diamination is outlined in Scheme 3 based on the NMR and kinetic studies.^{13,15} The Pd(0) first oxidatively inserts into the N–N bond of di-*tert*-butyldiaziridinone (**1**) to form four-membered Pd(II) species **10**, which undergoes a ligand exchange to give Pd(II) olefin complex **11**. Upon a migratory insertion, complex **11** is converted into π -allyl Pd species **12**, which undergoes a reductive elimination to form diamination product **9** and regenerate the Pd(0) catalyst. The symmetric four-membered Pd(II) intermediate (**10**) can be detected by ¹H NMR spectroscopy. It was formed when di-*tert*-butyldiaziridinone (**1**) was treated with Pd(PPh₃)₄ and gradually disappeared upon addition of (*E*)-1-phenylbutadiene (**8a**) (Figure 3).¹⁵ In addition, the four-membered Pd(II) species (**10**), generated from Pd(OAc)₂–PPh₃ (1:2) and dilithium salt of di-*tert*-butylurea (**14**), also regioselectively diaminated (*E*)-1,3-pentadiene (**8b**) at the internal double bond to give the

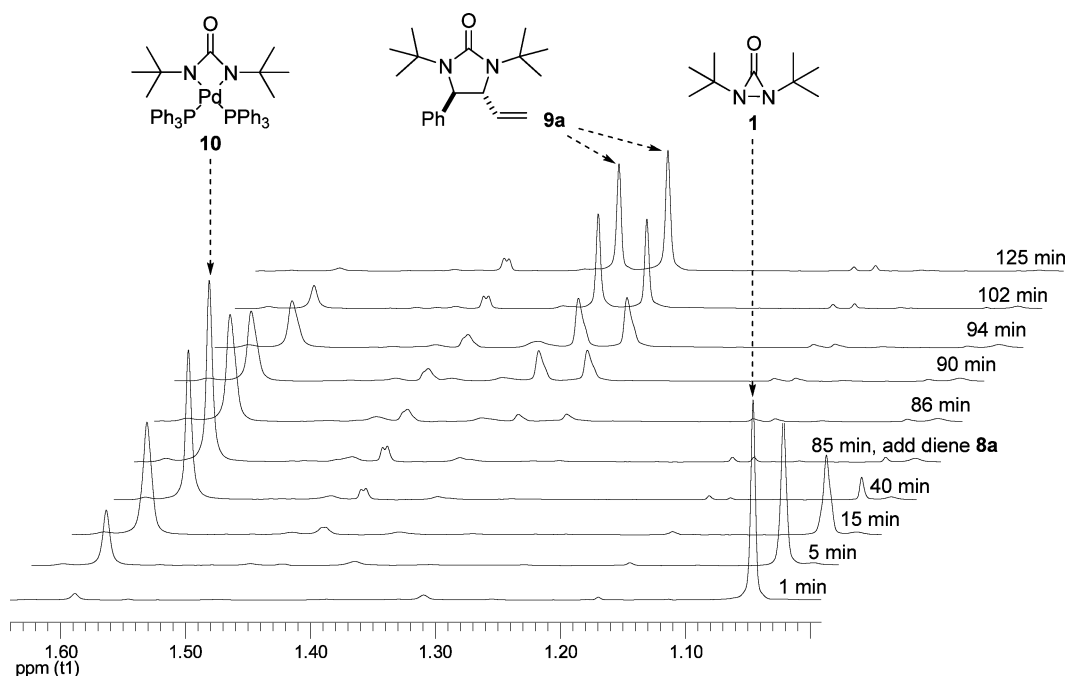
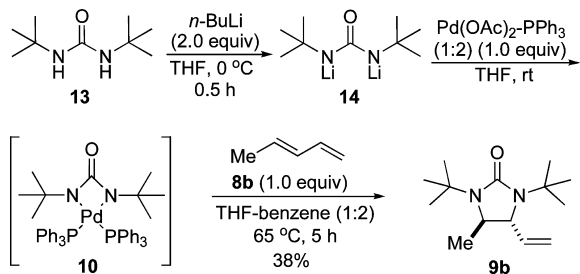


Figure 3. ^1H NMR monitoring of the reaction between di-*tert*-butyldiaziridinone (**1**) and $\text{Pd}(\text{PPh}_3)_4$, as well as the subsequent diamination of (*E*)-1-phenylbutadiene (**8a**).

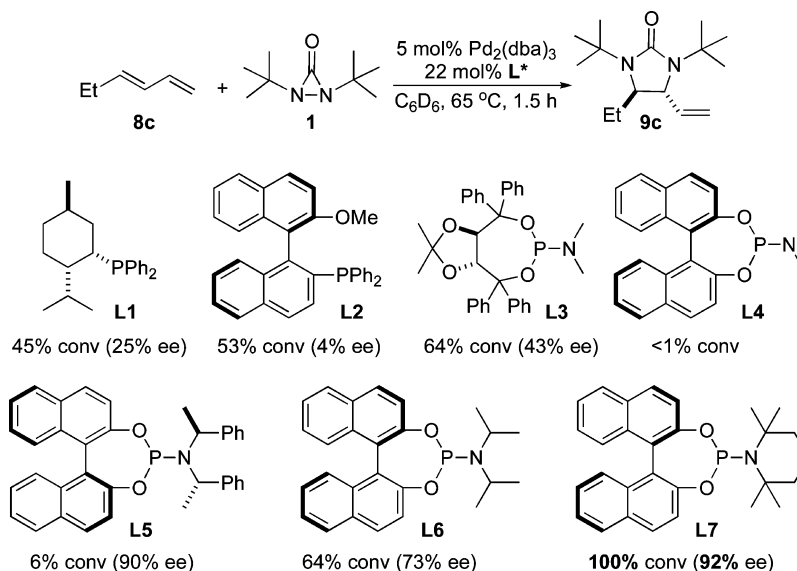
Scheme 4. Damination of (*E*)-1,3-Pentadiene with Four-Membered Pd(II) Species **10**



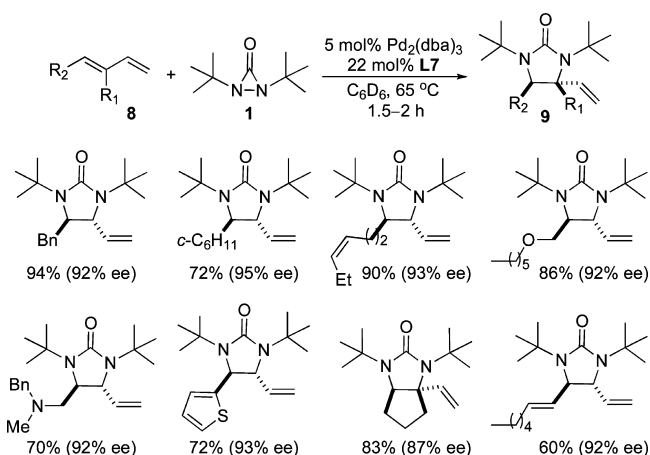
amination product in 38% yield (Scheme 4).¹⁵ These results support that four-membered Pd(II) species **10** is a likely intermediate for the diamination reaction.

Studies were subsequently carried out to develop an asymmetric version of the current diamination process. Various chiral ligands were examined with $\text{Pd}_2(\text{dba})_3$ and di-*tert*-butyldiaziridinone (**1**) using (*E*)-1,3-hexadiene (**8c**) as substrate (Scheme 5).¹⁶ The diamination reaction was found to be highly sensitive to the nature of the ligand used. As shown in the case of BINOL-based chiral phosphorus amidite ligands **L4–L7**, the nitrogen substituent had a profound impact on both reactivity and enantioselectivity for the diamination. To our delight, quantitative conversion and 92% ee were obtained with ligand **L7** containing a sterically bulky tetramethylpiper-

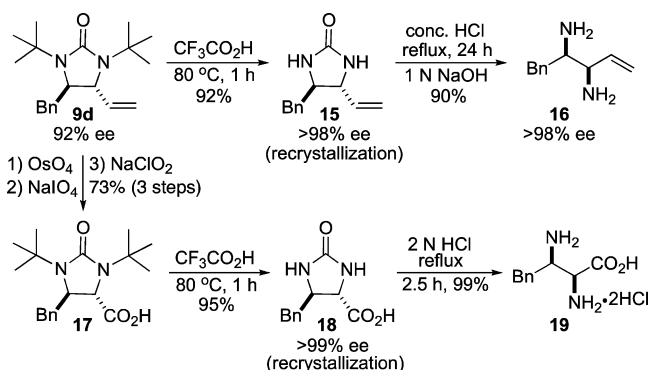
Scheme 5. Asymmetric Damination of 1,3-Hexadiene with Selected Ligands (L1–L7**)**



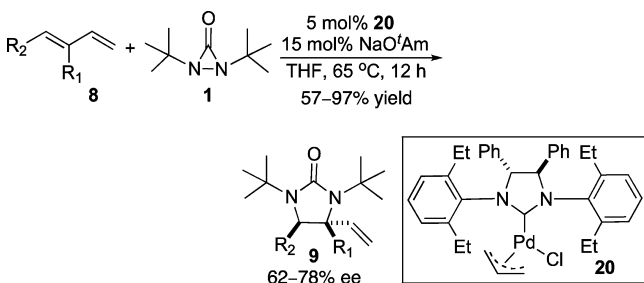
Scheme 6. Pd(0)-Catalyzed Asymmetric Diamination of Olefins with Diaziridinone 1



Scheme 7. Transformations of Optically Active Imidazolidinone 9d



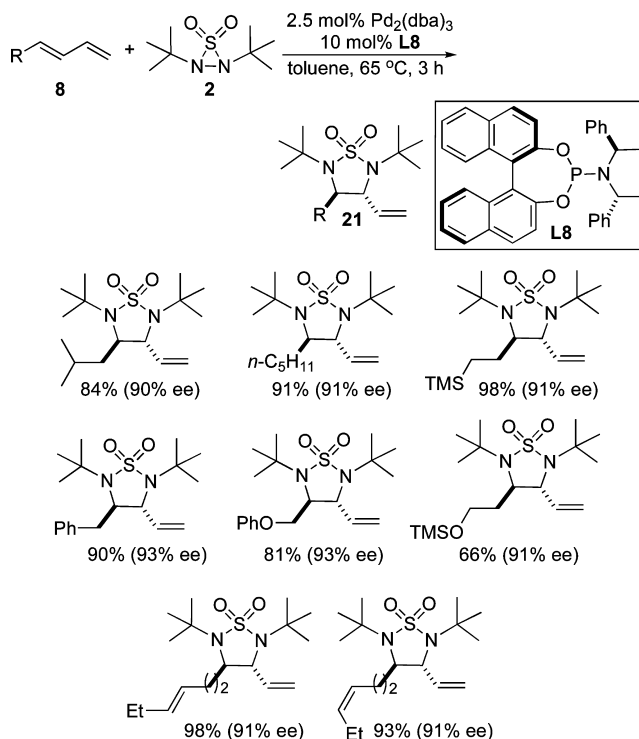
Scheme 8. NHC-Pd(0)-Catalyzed Asymmetric Diamination of Olefins Using 1



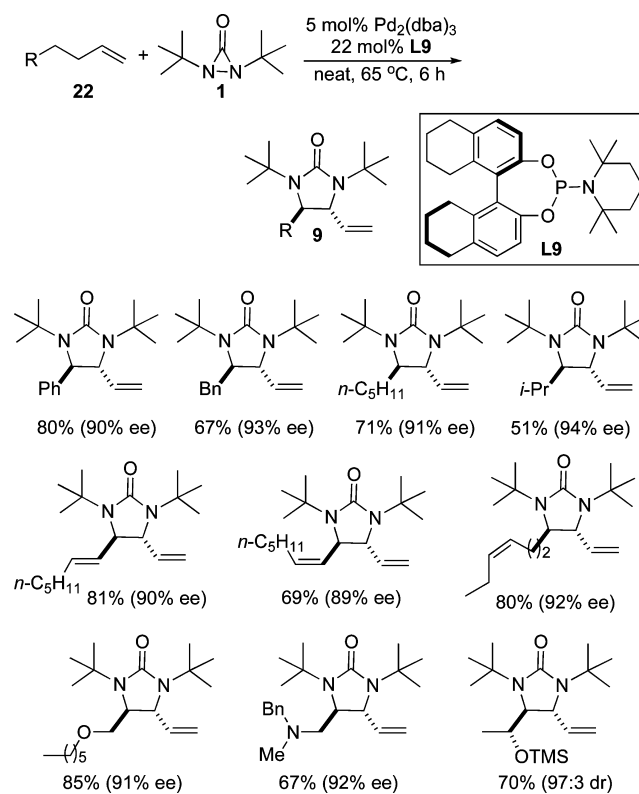
idine. A variety of conjugated dienes can be regioselectively diaminated at the internal double bond in good yields (62–95%) and high enantioselectivities (87–95% ee) (Scheme 6).¹⁶ With a conjugated triene substrate, the diamination regioselectively occurred at the middle double bond in high enantioselectivity. These results represent a breakthrough in catalytic asymmetric diamination of olefins,^{1d,4e} which had previously been a formidable challenge. As illustrated in Scheme 7, the resulting optically active imidazolidinone **9d** can be readily converted into other chiral compounds such as free diamine **16** and 2,3-diamino acid **19**.

Further studies showed that *N*-heterocyclic carbene–Pd(0) complexes were also effective catalysts for the diamination of olefins with di-*tert*-butyldiaziridinone (**1**).¹⁷ When chiral

Scheme 9. Pd(0)-Catalyzed Asymmetric Diamination of Olefins Using 2



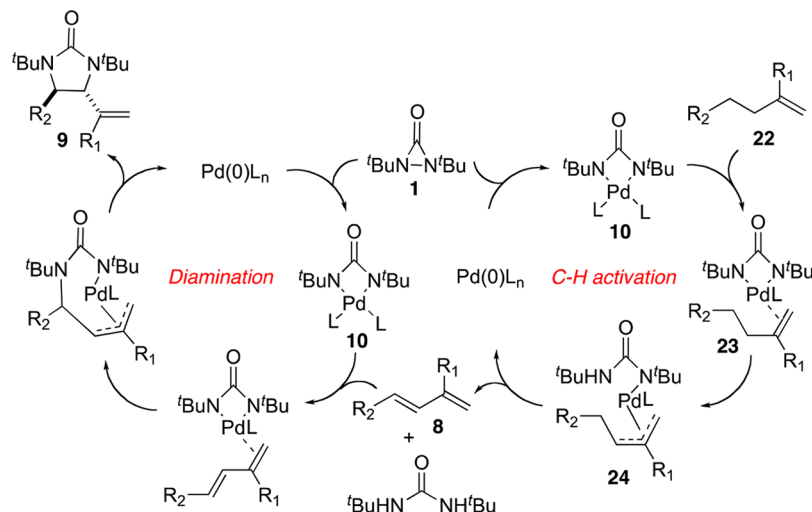
Scheme 10. Pd(0)-Catalyzed Asymmetric Allylic and Homoallylic C–H Diamination



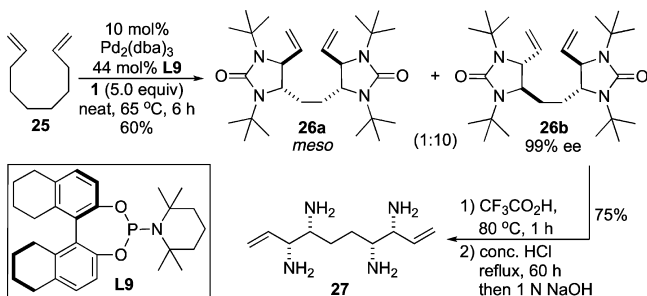
NHC–Pd(0) complex **20** was used as catalyst, the diamination products were obtained in 62–78% ee (Scheme 8).¹⁸

Cyclic sulfamides are important functional motifs contained in medicinally and biologically significant molecules. A variety

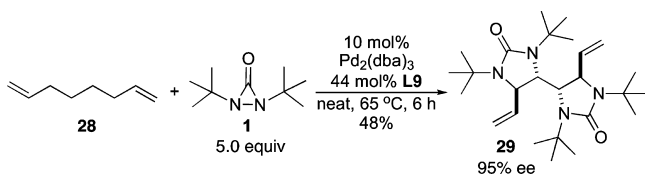
Scheme 11. Proposed Mechanism for the Pd(0)-Catalyzed C–H Diamination



Scheme 12. Asymmetric Bisdiamination of 1,9-Decadiene (25)



Scheme 13. Asymmetric Bisdiamination of 1,7-Octadiene (28)

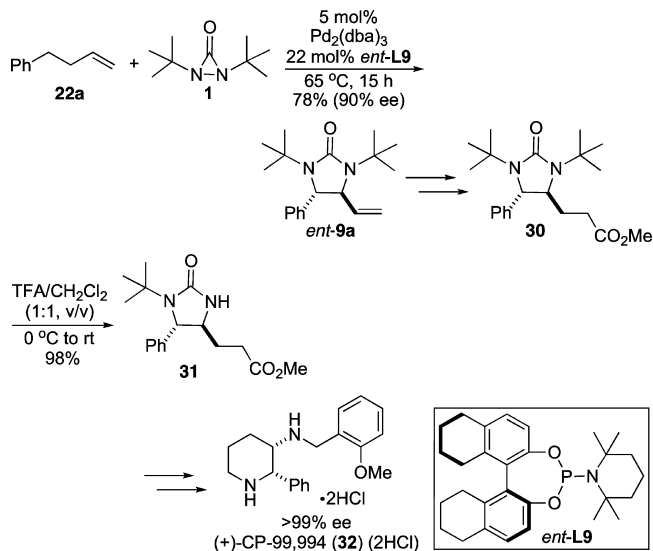
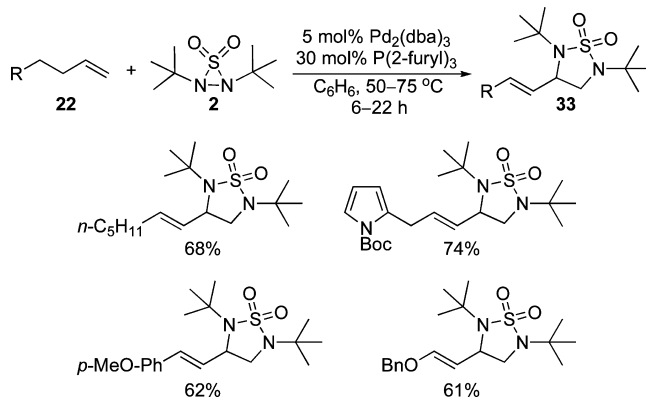


of optically active cyclic sulfamides can be obtained in 66–98% yield and 90–93% ee from conjugated 1,3-dienes with catalyst generated from $\text{Pd}_2(\text{dba})_3$ and chiral phosphoramidite **L8** using di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) as nitrogen source (Scheme 9).^{19,20} In this case, ligand **L8** was found to be more effective than tetramethylpiperidine-derived ligand **L7** for the diamination.

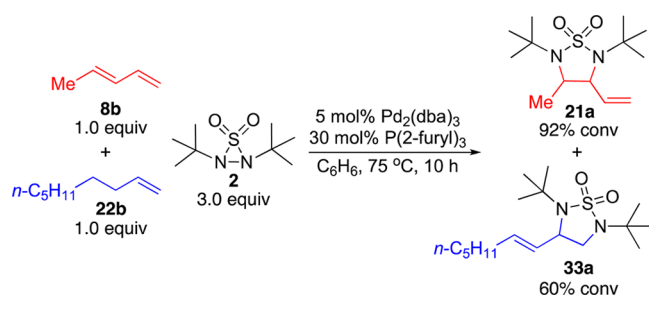
The diamination was also investigated for other olefin substrates. To our surprise, the diamination occurred at allylic and homoallylic carbons via C–H activation rather than at the double bond when terminal olefins were treated with $\text{Pd}(\text{PPh}_3)_4$ and di-*tert*-butylthiadiaziridinone (**1**) under solvent-free conditions.²¹ A catalytic asymmetric process was also achieved with a catalyst generated from $\text{Pd}_2(\text{dba})_3$ and H_8 -BINOL-derived phosphorus amidite ligand **L9** (Scheme 10).²² A variety of readily available terminal olefins can be efficiently C–H diaminated, giving the corresponding imidazolidinones in good yields with high diastereo- and enantioselectivities.

The C–H diamination likely proceeds via in situ formed diene intermediate **8** (Scheme 11).^{21,22} The terminal olefin

Scheme 14. Synthesis of (+)-CP-99,994 via Asymmetric C–H Diamination

Scheme 15. Pd(0)-Catalyzed Dehydrogenative Diamination Using **2**

coordinates with four-membered Pd(II) species **10**, resulting from the oxidative insertion of Pd(0) into the N–N bond of di-*tert*-butylthiadiaziridinone (**1**) to form complex **23**. π -Allyl Pd

Scheme 16. Diamination with a Mixture of (*E*)-1,3-Pentadiene (8b) and 1-Nonene (22b)

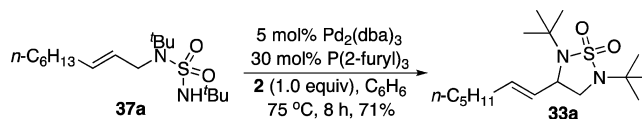
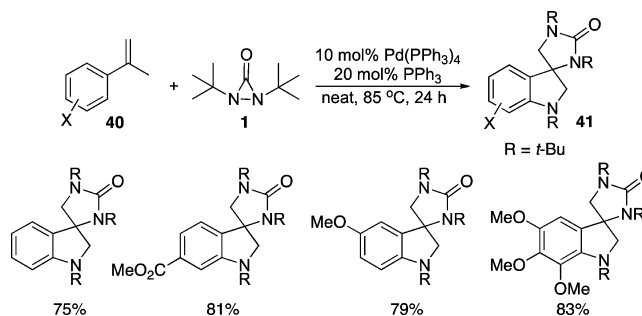
complex **24**, generated from **23** via allylic hydrogen abstraction, undergoes a β -H elimination to give diene **8** and regenerate the Pd(0) catalyst. The resulting diene is subsequently diaminated under the reaction conditions.

Bisdiamination can also be realized for substrates having two terminal double bonds, leading to stereoselective construction of four C–N bonds in one step with formal replacement of four sp^3 C–H bonds (Schemes 12 and 13).²² With the asymmetric C–H diamination process, potent and selective substance P receptor antagonist (+)-CP-99,994 (**32**) was synthesized in 20% overall yield and >99% ee from readily available 4-phenyl-1-butene (**22a**) (Scheme 14).²³ As illustrated in the case of imidazolidinone **30**, one of the *tert*-butyl groups could be selectively removed, allowing ready differentiation of the two nitrogens.

Interestingly, with di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) as the nitrogen source, the terminal olefin underwent a dehydrogenative diamination rather than the allylic and homoallylic C–H diamination, giving cyclic sulfamide **33** in good yield (Scheme 15).²⁴ When the diamination was carried out with a mixture of (*E*)-1,3-pentadiene (**8b**) and 1-nonene (**22b**), internal cyclic sulfamide **21a** and terminal cyclic sulfamide **33a**, respectively, were formed (Scheme 16), suggesting that the dehydrogenative diamination did not proceed via a diene intermediate as in the case of di-*tert*-butyldiaziridinone (**1**) (Scheme 11).

A plausible reaction mechanism is outlined in Scheme 17.²⁴ Four-membered Pd(II) species **34** is initially generated via the oxidative addition of Pd(0) to the N–N bond of di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**). The coordination of the

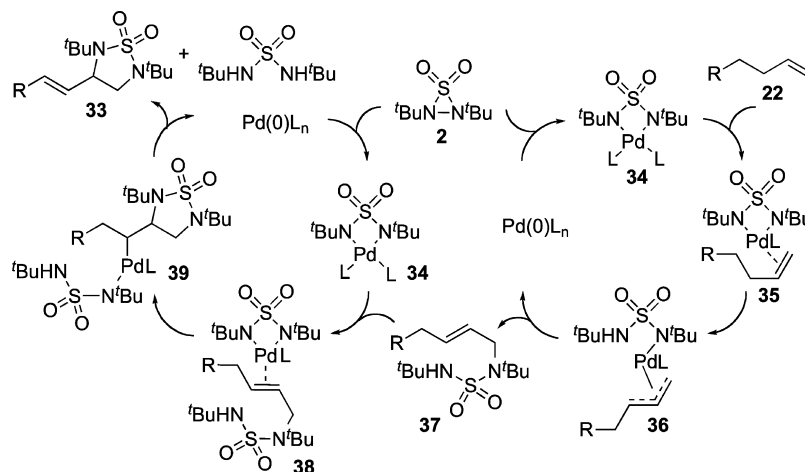
Scheme 18. Cyclization of Sulfamide 37a

Scheme 19. Pd(0)-Catalyzed Sequential Allylic and Aromatic C–H Aminations with **1**

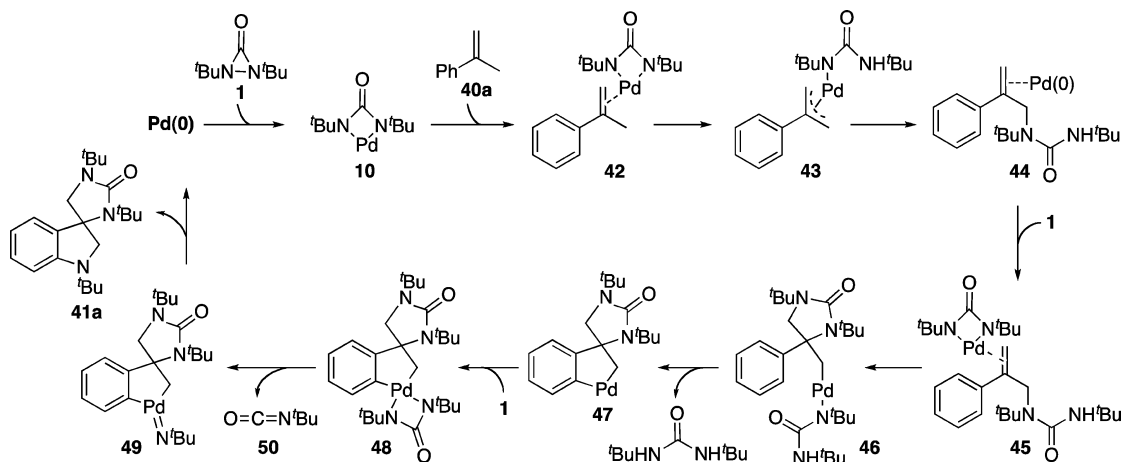
terminal olefin (**22**) to **34** forms complex **35**, which undergoes an allylic hydrogen abstraction to generate π -allyl Pd complex **36**. The reductive elimination of **36** gives allyl sulfamide **37** and regenerates the Pd(0) catalyst. Allyl sulfamide **37** undergoes a subsequent Pd(II)-catalyzed cyclization to form intermediate **39**, which is converted into sulfamide **33** with regeneration of the Pd(0) catalyst after a β -hydride elimination and reductive elimination. In this process, π -allyl Pd complex **36** preferentially undergoes a reductive elimination rather than a β -hydride elimination as in the case of intermediate **24** (Scheme 11), likely because the sulfamide group of **36** is more electron-deficient than the urea group of **24**. When preformed allyl sulfamide **37a** was subjected to the reaction conditions, cyclic sulfamide **33a** was indeed formed (Scheme 18),²⁴ further supporting the proposed mechanism.

Treating α -methylstyrenes with di-*tert*-butyldiaziridinone (**1**) and Pd(PPh₃)₄ led to a novel sequential allylic and aromatic C–H amination process, giving a variety of spirocyclic indolines **41** in good yields with creation of four C–N bonds and one spiro quaternary carbon in a single operation (Scheme 19).²⁵ A plausible catalytic pathway is proposed in Scheme 20.²⁵ π -Allyl Pd complex **43**, generated from four-membered Pd(II) species **10** and α -methylstyrene (**40a**), undergoes a

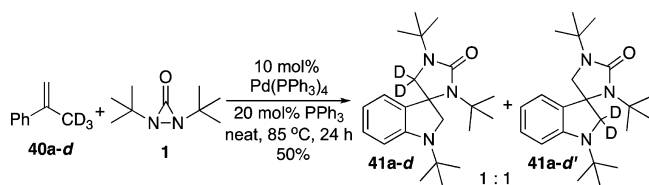
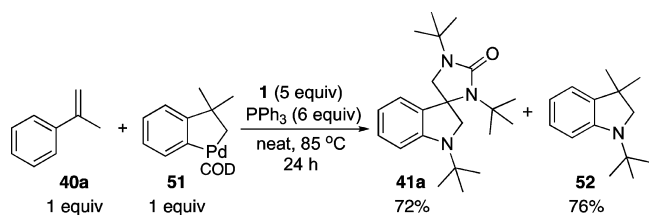
Scheme 17. Proposed Mechanism for Pd(0)-Catalyzed Dehydrogenative Diamination



Scheme 20. Proposed Mechanism for the Formation of Spirocyclic Indolines



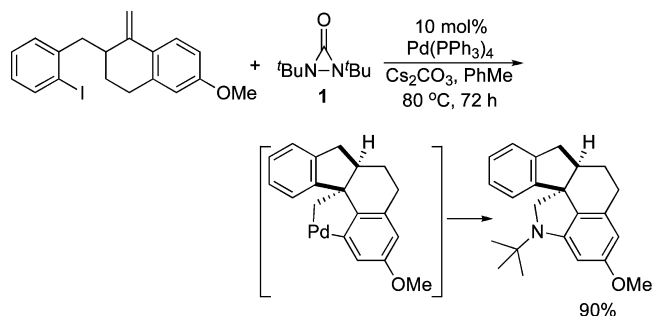
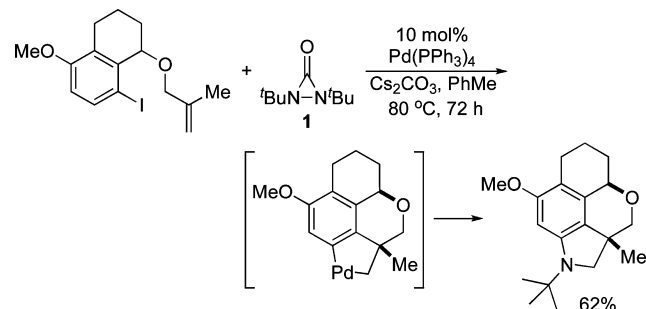
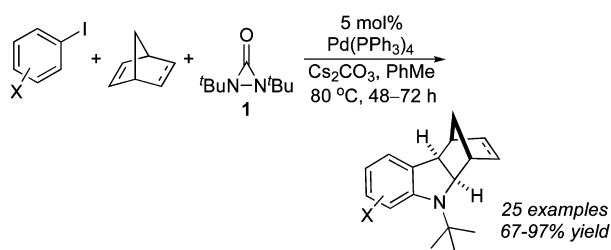
Scheme 21. Deuterium-Labeling Experiment

Scheme 22. Reaction of α -Methylstyrene (40a) with Pallada(II)cycle 51

reductive elimination to give allyl urea intermediate **44**, which is converted into intermediate **46** via a Pd(II)-catalyzed cyclization. Pallada(II)cycle **47** is subsequently formed from **46** via an intramolecular aromatic C–H activation. The oxidative insertion of **47** into the N–N bond of **1** gives pallada(IV)cycle **48**, which is transformed to Pd(IV)-nitrene **49** after release of a molecule of *tert*-butyl isocyanate (**50**). Two consecutive reductive eliminations of Pd(IV)-nitrene **49** form spirocyclic indoline product **41a** with regeneration of the Pd(0) catalyst.

The proposed reaction mechanism is also supported by additional experimental data.²⁵ For example, subjecting deuterium-labeled α -methylstyrene **40a-d** to the reaction conditions gave equal amounts of indoline products **41a-d** and **41a-d'** (Scheme 21), suggesting that π -allyl Pd complex **43** is an intermediate involved in this process. When α -methylstyrene (**40a**) was treated with preformed pallada(II)-cycle **51** and di-*tert*-butyldiaziridinone (**1**) (Scheme 22), indolines **41a** and **52** were isolated in 72% and 76% yield, respectively, supporting the intermediacy of pallada(II)cycle **47** in the catalytic cycle.

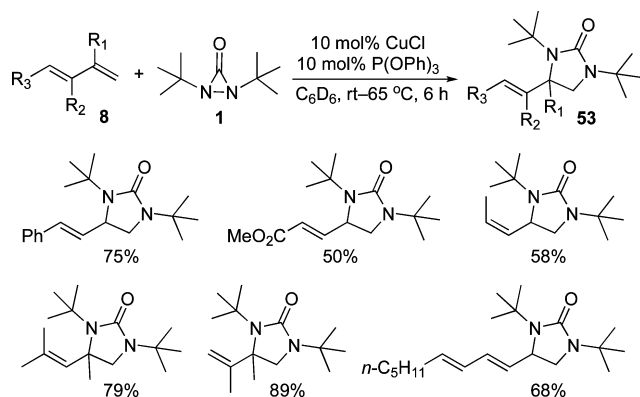
The observation that a pallada(II)cycle can be converted into an indoline with di-*tert*-butyldiaziridinone (**1**) via oxidative insertion and subsequent transformations opens up additional opportunities to develop new reaction processes. For example,

Scheme 23. Heck Reaction/C–H Activation/Amination Sequence with **1**

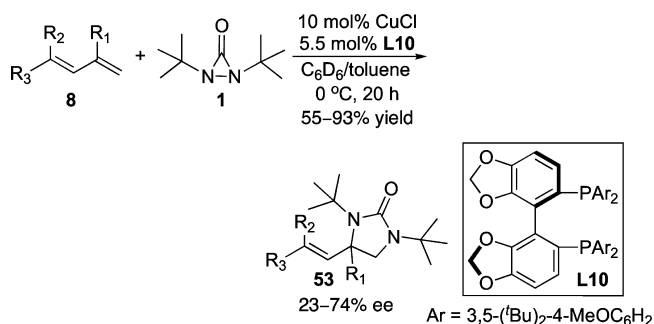
we have recently shown that a variety of polycyclic indolines can be obtained in good yields via a novel Pd(0)-catalyzed sequential Heck reaction/C–H activation/amination process (Scheme 23).²⁶

3. Cu(I)-CATALYZED DIAMINATION VIA N–N BOND ACTIVATION

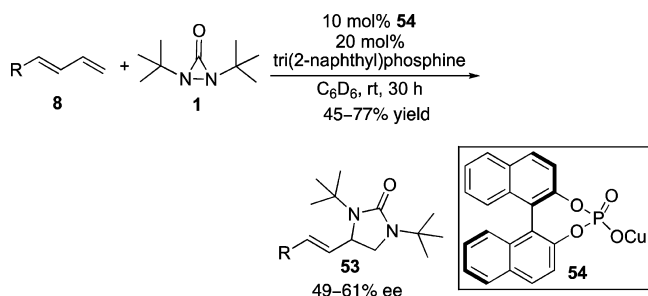
In search for complementary catalytic systems, it has been found that a variety of conjugated dienes and a triene can be effectively diaminated in good yields with CuCl–P(OPh)₃

Scheme 24. Cu(I)-Catalyzed Terminal Diamination of Dienes and Triene Using **1**

Scheme 25. Cu(I)-Catalyzed Asymmetric Terminal Diamination of Dienes and Triene

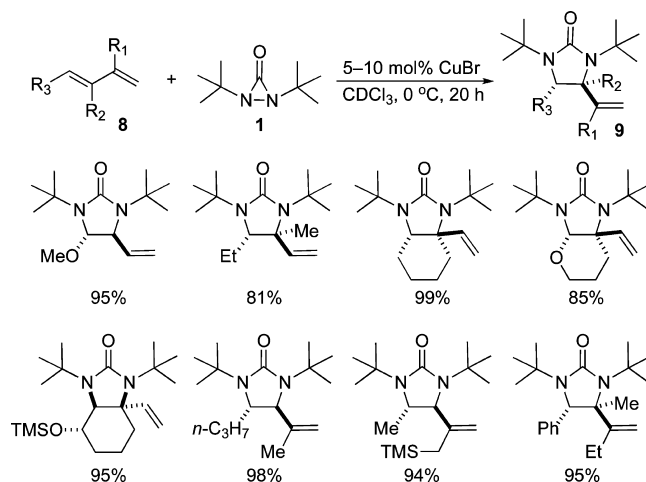
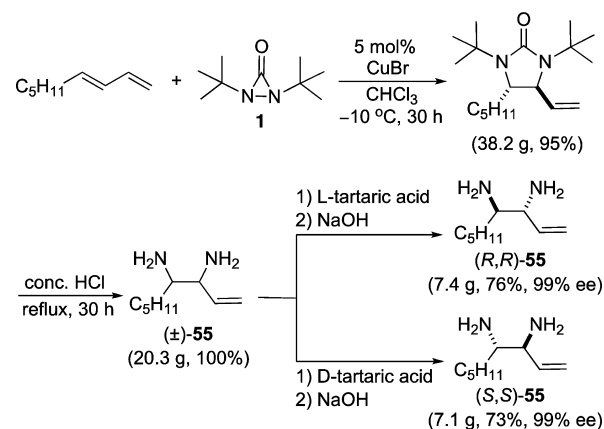


Scheme 26. Cu(I)-Catalyzed Asymmetric Terminal Diamination of Dienes and Triene

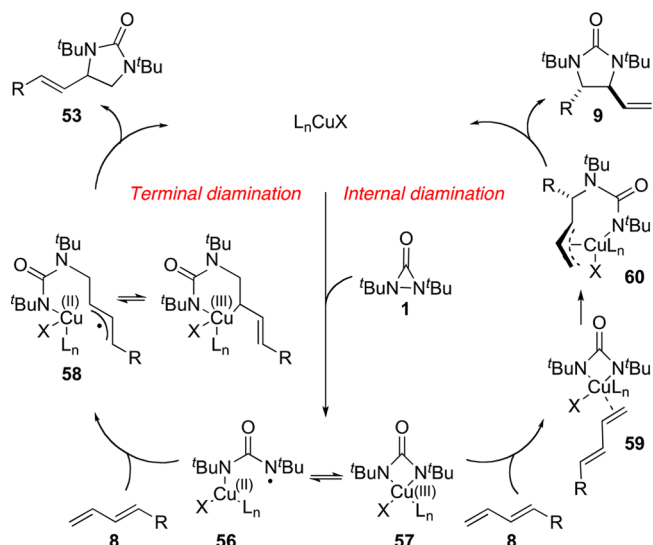
Table 1. Effect of Reaction Conditions on the Regioselectivity of Cu(I)-Catalyzed Diamination of (*E*)-1,3-Pentadiene (**8b**)

entry	catalyst	solvent	conv (%) ^a	53a/9b ^c
1	CuCl–P(OPh) ₃ (1:1.2)	C ₆ D ₆	92	34:66
2	CuCl–PCy ₃ (1:1.2)	C ₆ D ₆	61	78:22
3	CuCl–PCy ₃ (1:1.5)	C ₆ D ₆	100 (53%) ^b	97:3
4	CuCl	CDCl ₃	100	17:83
5	CuBr	CDCl ₃	100 (99%) ^b	1:99

^aThe conversion was determined by ¹H NMR analysis of the crude reaction mixture. ^bIsolated yield. ^cThe ratio of **53a** to **9b** was determined by ¹H NMR analysis of the crude reaction mixture.

Scheme 27. CuBr-Catalyzed Internal Diamination of Conjugated Dienes Using **1**Scheme 28. Gram-Scale Synthesis of Optically Active Diamine **55**

Scheme 29. Two Distinct Pathways for the Cu(I)-Catalyzed Regioselective Diamination of Conjugated Dienes



(1:1) and di-*tert*-butyldiaziridinone (**1**) under mild reaction conditions (Scheme 24).²⁷ In contrast to the Pd(0)-catalyzed process (Scheme 2), the Cu(I)-catalyzed diamination occurred

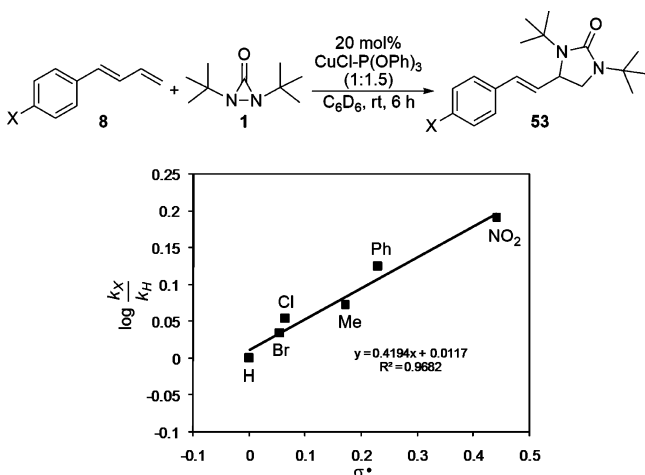
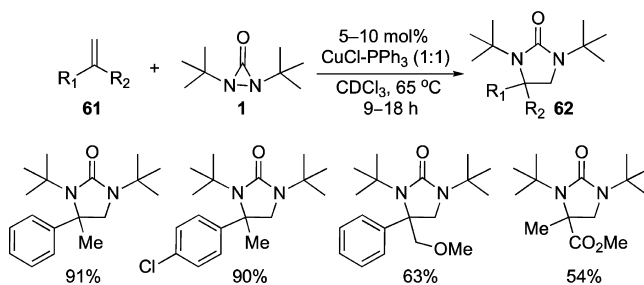


Figure 4. Hammett plot with radical substituent constant (σ^*) for the terminal diamination of *para*-substituted (*E*)-1-phenylbutadienes **8** with CuCl–P(OPh)₃ and di-*tert*-butyldiaziridinone (**1**).

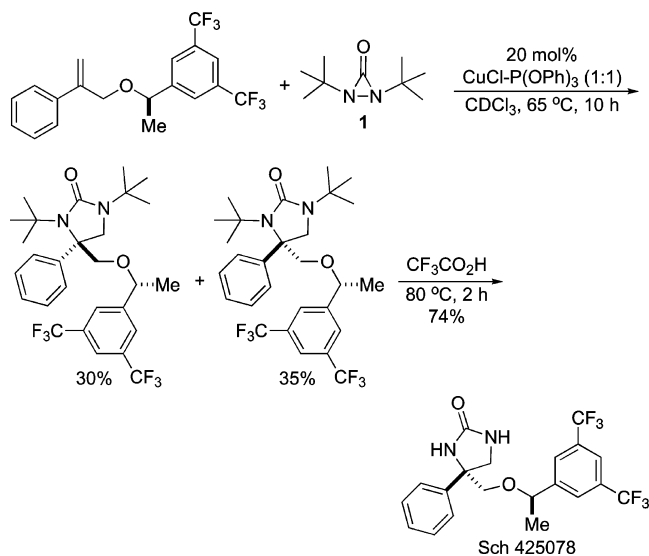
mostly at the terminal double bond of dienes with generally high regioselectivities (Scheme 24). The diamination reaction likely proceeds via a radical mechanism (*vide infra*), which is mechanistically distinct from the Pd(0)-catalyzed process. While the radical process presents a challenge for asymmetric control, the Cu(I)-catalyzed asymmetric diamination has been found to be feasible. For example, up to 74% ee was obtained with CuCl and (*R*)-DTBM-SEGPHOS (**L10**) (Scheme 25).²⁸ Asymmetric diamination with chiral Cu(I) phosphate catalyst has also been shown to be viable, while more effective systems need to be developed (Scheme 26).²⁹

The regioselectivity for the Cu(I)-catalyzed diamination of dienes with di-*tert*-butyldiaziridinone (**1**) can be switched by changing the reaction conditions.^{30,31} For example, while the diamination of (*E*)-1,3-pentadiene (**8b**) occurred predominantly on the terminal double bond with CuCl–PCy₃ (1:1.5) (Table 1, entry 3), essentially only internal diamination product **9b** was formed with CuBr (Table 1, entry 5).³⁰ Various conjugated dienes can be efficiently diaminated at the internal double bond with 5–10 mol % CuBr, giving the corresponding products **9** in high yields (81–99%) and high regioselectivities

Scheme 31. Cu(I)-Catalyzed Diamination of 1,1-Disubstituted Terminal Olefins



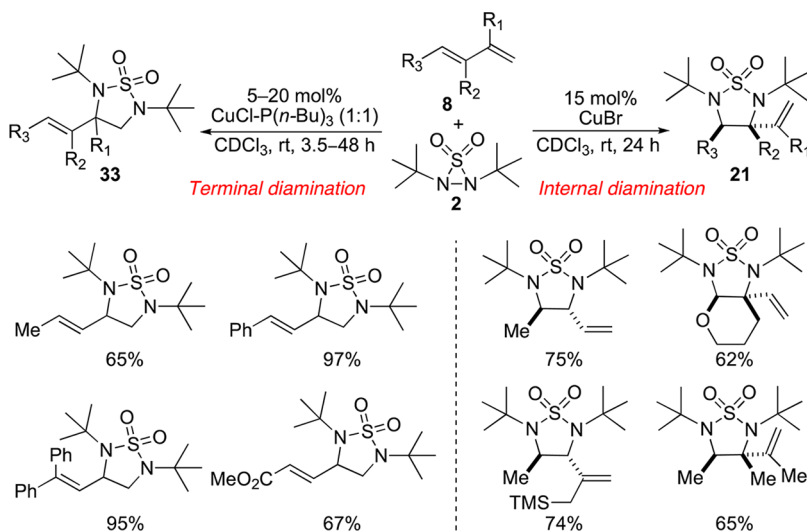
Scheme 32. Synthesis of Potent NK₁ Antagonist Sch 425078



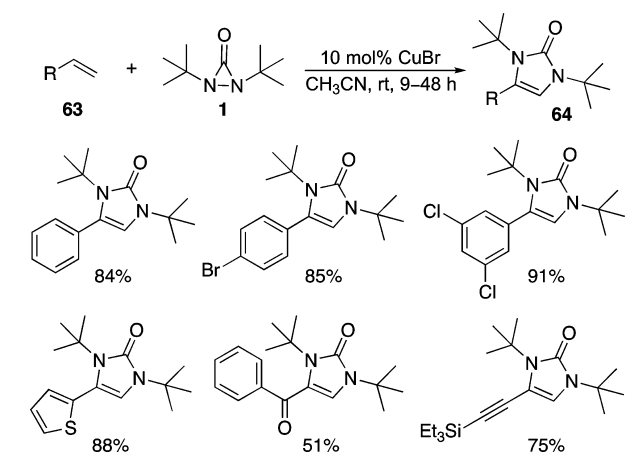
(Scheme 27).^{30,31} The internal diamination process can be conducted on relatively large scale with 5 mol % CuBr in high yield, and the resulting imidazolidinone was readily converted into optically active diamines via deprotection and simple resolution with tartaric acids (Scheme 28).³⁰

Studies show that the terminal diamination and internal diamination likely arise from two distinct and competing

Scheme 30. Cu(I)-Catalyzed Regioselective Diamination of Dienes Using **2**



Scheme 33. Sequential Diamination and Dehydrogenation of Terminal Olefins



mechanistic pathways involving Cu(II) and Cu(III) species, respectively (Scheme 29).^{30,31,27} The reductive cleavage of the N–N bond of di-*tert*-butyldiaziridinone (**1**) by the Cu(I) catalyst results in Cu(II) nitrogen radical **56** (detected by EPR spectroscopy) and four-membered Cu(III) species **57**. It is likely that these two species are in equilibrium, and nitrogen radical **56** is favored by the addition of a ligand such as PCy₃. The addition of the nitrogen radical to the terminal double bond of the diene leads to Cu(II) allyl radical species **58**, which is subsequently transformed to the terminal diamination product **53** with regeneration of the Cu(I) catalyst. The steric hindrance and the formation of a relatively more stable allyl radical **58** are likely contributing factors for the preferential addition of nitrogen radical **56** to the terminal double bond. Substrates with radical stabilizing groups such as (*E*)-1-phenylbutadiene further stabilize radical **58**, thus favoring the terminal diamination. The radical mechanism for the terminal diamination is also supported by the Hammett plot (Figure 4).³¹ The internal diamination likely proceeds via four-membered Cu(III) species **57** in a manner similar to the Pd(0)-catalyzed diamination.^{13,15} The absence of a ligand likely facilitates the formation of four-membered Cu(III) species **57** and/or its coordination with diene **8** to form complex **59**, which undergoes a migratory insertion to give π -allyl species **60**. Upon reductive elimination, **60** is converted into internal diamination product **9** with regeneration of the Cu(I) catalyst (Scheme 29).^{30,31} The regioselectivity for the diamination is also significantly affected by the counteranion of the Cu(I) catalyst. CuBr is more effective for the internal diamination than CuCl.

With di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) as nitrogen source, a variety of conjugated dienes can be regioselectively diaminated at the terminal double bond using CuCl–P(*n*-Bu)₃ and at the internal double bond using CuBr, giving the corresponding cyclic sulfamides in good yields (Scheme 30).³² The diamination also likely proceeds via a Cu(II) nitrogen

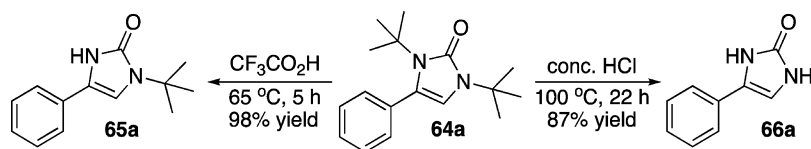
radical or a four-membered Cu(III) species analogous to the Cu(I)-catalyzed diamination with di-*tert*-butyldiaziridinone (**1**) (Scheme 29). The regioselectivity is highly dependent on the Cu(I) catalyst and the nature of the diene.³²

The Cu(I)-catalyzed diamination can also be extended to various terminal olefins. As shown in Scheme 31, a variety of activated 1,1-disubstituted terminal olefins were efficiently diaminated with 5–10 mol % CuCl–PPh₃ (1:1) and di-*tert*-butyldiaziridinone (**1**), giving the corresponding 4,4-disubstituted 2-imidazolinones (**62**) in good yields (Scheme 31).³³ With the diamination process, potent NK₁ antagonist Sch 425078 was readily synthesized in 20% overall yield (Scheme 32).³³

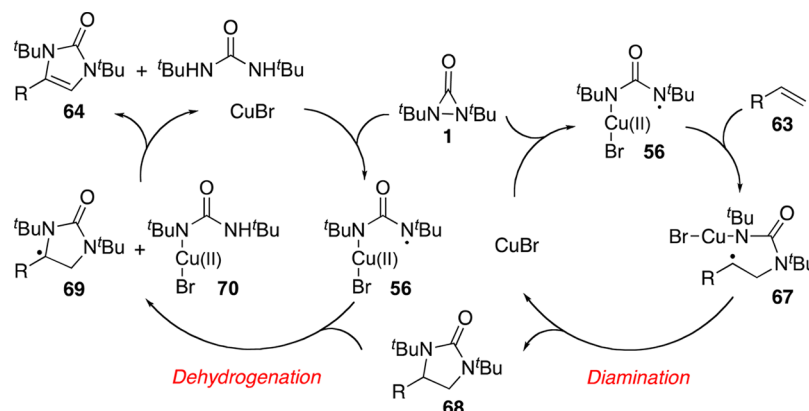
A sequential diamination/dehydrogenation process was observed when monosubstituted olefins **63** were treated with CuBr catalyst and di-*tert*-butyldiaziridinone (**1**) in CH₃CN. A variety of imidazolinones **64** can be easily obtained in good yields (Scheme 33).³⁴ The resulting imidazolinone **64a** could be selectively and completely deprotected with CF₃CO₂H and concentrated HCl, respectively (Scheme 34). In this diamination/dehydrogenation process, the terminal olefin is initially diaminated to form imidazolidinone **68**, which is converted into imidazolinone **64** via hydrogen abstraction by radical species **56** under the reaction conditions (Scheme 35).³⁴ Under similar conditions, no dehydrogenation products were observed when di-*tert*-butylthiadiaziridine 1,1-dioxide (**2**) was used. Various terminal olefins were efficiently diaminated to give the corresponding cyclic sulfamides in good yields (Scheme 36).³⁵

1,2-Di-*tert*-butyl-3-(cyanimino)-diaziridine (**3**) has also been found to be an effective nitrogen source for the Cu(I)-catalyzed diamination. A variety of conjugated dienes, trienes, and terminal olefins can be effectively diaminated using 10 mol % CuCl–PPh₃ (1:2), providing the corresponding cyclic guanidines **72** in good yields (Scheme 37).³⁶ A radical mechanism is also likely involved in this cycloguanidination. The diamination of dienes and trienes occurs regioselectively at the terminal double bond. Free cyclic guanidine **73a** can be obtained in high yield by removal of both the *t*-Bu and the cyano groups with HCl (Scheme 38).³⁶ Cyclic guanidines are present in many biologically active molecules. The current cycloguanidination process provides a ready access to this class of compounds

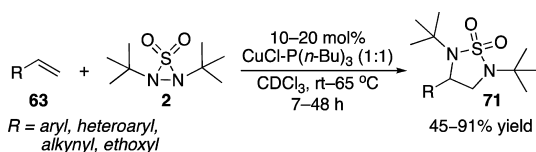
As a versatile reagent, di-*tert*-butyldiaziridinone (**1**) has also displayed interesting reactivity toward carbonyl compounds in the presence of a Cu(I) catalyst.^{37,38} For example, a variety of methyl arylacetates and β,γ -unsaturated methyl esters can be α -aminated with 5 mol % CuCl–P(*n*-Bu)₃ (1:1) and di-*tert*-butyldiaziridinone (**1**) to give the corresponding hydantoins in good yields (Scheme 39).³⁷ Selective or complete removal of the *t*-butyl group can be achieved with CH₃SO₃H in hexane (1:10, v/v) at rt or 65 °C, respectively (Scheme 40). This α -amination process allows rapid access to various hydantoins, which are present in various biologically active molecules and are versatile synthetic intermediates. The reaction process likely

Scheme 34. Deprotection of Imidazolinone **64a**

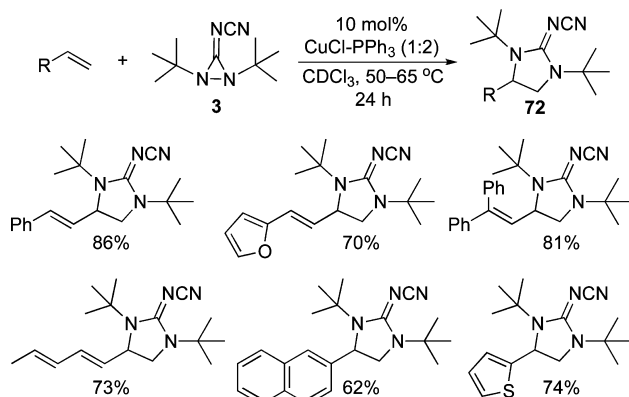
Scheme 35. Proposed Catalytic Cycle for the Diamination/Dehydrogenation Sequence



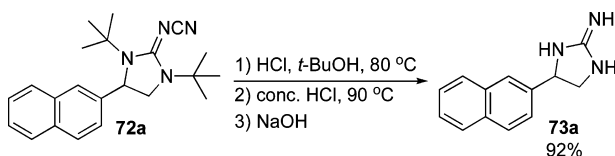
Scheme 36. Cu(I)-Catalyzed Diamination of Terminal Olefins Using 2



Scheme 37. Cu(I)-Catalyzed Diamination of Olefins Using 3



Scheme 38. Deprotection of Cyclic Guanidine 72a

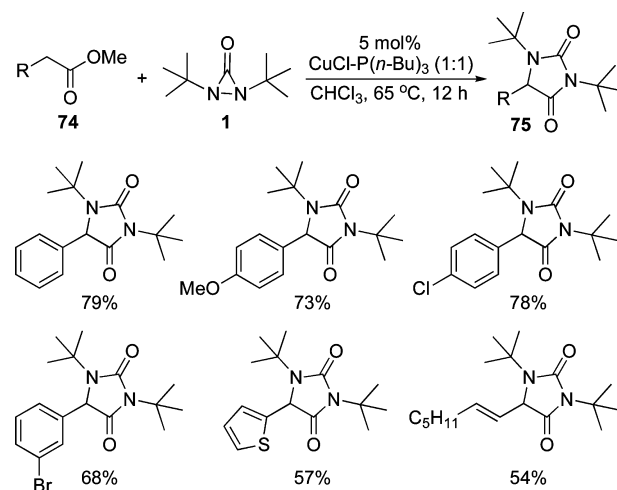


proceeds via a hydrogen abstraction or deprotonation of the ester (74) by Cu(II) nitrogen radical **56** or four-membered Cu(III) species **57** to form **78**, which undergoes a reductive elimination to amino ester **79** with regeneration of the Cu(I) catalyst. The cyclization of compound **79** gives the hydantoin (**75**) (Scheme 41).³⁷

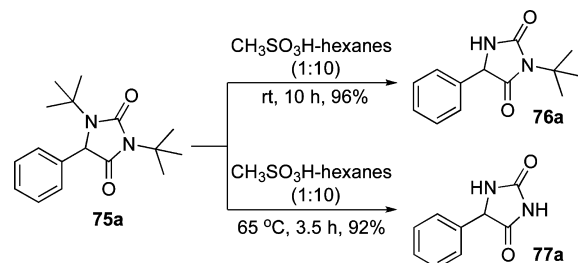
4. CONCLUSIONS AND OUTLOOK

Direct diamination of olefins provides a straightforward approach to vicinal diamines, which are important functional and structural moieties present in a variety of biologically active molecules and chiral catalysts. As summarized in this Account, we have developed a number of Pd(0)- and Cu(I)-catalyzed

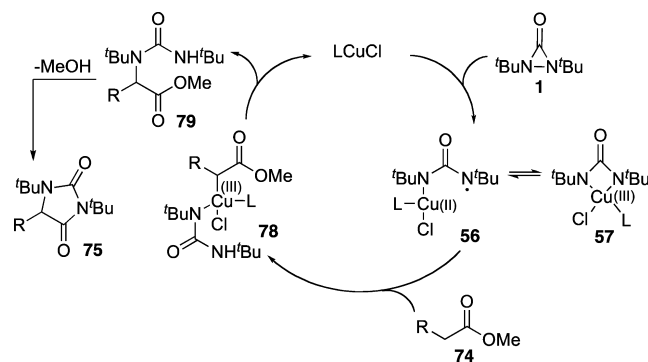
Scheme 39. Cu(I)-Catalyzed Diamination of Esters



Scheme 40. Deprotection of Hydantoin 75a



Scheme 41. Proposed Mechanism for Cu(I)-Catalyzed Diamination of Esters



diamination processes for olefins with di-*tert*-butyldiaziridinone (1), di-*tert*-butylthiadiaziridine 1,1-dioxide (2), and 1,2-di-*tert*-butyl-3-(cyanimino)-diaziridine (3) as nitrogen sources via N–N bond activation, allowing direct installation of two nitrogens onto a C–C double bond. The Pd(0)-catalyzed diamination of conjugated dienes occurs regioselectively at the internal double bond with di-*tert*-butyldiaziridinone (1) or di-*tert*-butylthiadiaziridine 1,1-dioxide (2), likely involving a four-membered Pd(II) species. The asymmetric diamination process has also been achieved, providing imidazolidinones and cyclic sulfamides in high ee's. The Pd(0)-catalyzed diamination of terminal olefins occurs at the allylic and homoallylic carbons with di-*tert*-butyldiaziridinone (1) as nitrogen source via an in situ generated diene intermediate. A highly enantioselective process has also been developed for this C–H diamination reaction. With di-*tert*-butylthiadiaziridine 1,1-dioxide (2) as nitrogen source, the two nitrogens are introduced onto the terminal carbons via a dehydrogenative diamination process. Complementary diamination processes have also been developed with Cu(I) catalysts. The Cu(I)-catalyzed diamination of conjugated dienes occurs regioselectively at either the terminal or internal double bond depending on the reaction conditions, likely involving a Cu(II) nitrogen radical or a four-membered Cu(III) species, respectively, via two mechanistically distinct pathways. Encouraging ee's have been obtained for the Cu(I)-catalyzed terminal diamination. The Cu(I)-catalyzed diamination can also be extended to various terminal olefins with nitrogen sources 1–3 via a radical mechanism, providing ready access to a variety of imidazolidinones, cyclic sulfamides, and cyclic guanidines in good yields.

The Pd(0)- and Cu(I)-catalyzed diaminations described herein exhibit a few favorable features: (1) In general, the diamination proceeds cleanly in high regio- and diastereoselectivity with a broad substrate scope. (2) Highly enantioselective catalytic diamination processes have been developed, which had previously been extremely challenging. (3) The diamination generally proceeds under mild conditions with no stoichiometric external oxidants required. (4) The reactions are operationally simple, amenable to gram scale, and potentially applicable to the synthesis of biologically active vicinal diamine-containing molecules. The diaziridinone and related compounds have been shown to be highly effective agents for the diamination reactions. Their unique and versatile reactivity would provide great opportunities for the development of new reaction processes.

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Notes

The authors declare no competing financial interest.

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