Alkene Difunctionalization Directed by Free Amines: Diamine Synthesis via Nickel-Catalyzed 1,2-Carboamination

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Abstract: A versatile method to access differentially substituted 1,3- and 1,4-diamines via a nickel-catalyzed three-component 1,2-carboamination of alkenyl amines with aryl/alkenylboronic ester nucleophiles and N–O electrophiles is reported. The reaction proceeds efficiently with free primary and secondary amines without needing a directing auxiliary or protecting group, and is enabled by fine-tuning the leaving group on the N–O reagent. The transformation is highly regioselective and compatible with a wide range of coupling partners and alkenyl amine substrates, all performed at room temperature. A series of kinetic studies support a mechanism in which alkene coordination to the nickel catalyst is turnover-limiting.

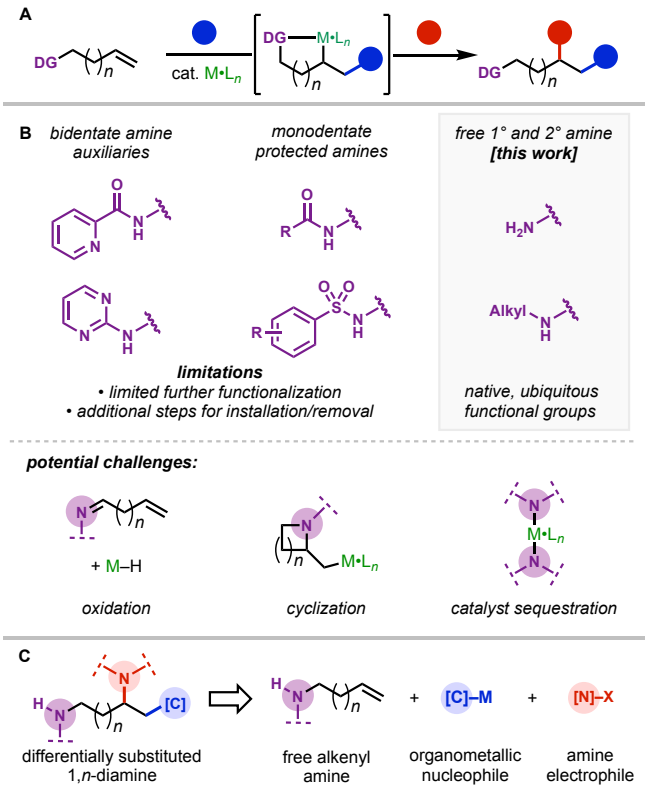
Amines are a key functional group in organic synthesis and medicinal chemistry. Free amines and nitrogen heterocycles are prevalent in numerous biologically active small molecules.[1] In addition, owing to their nucleophilic character, free amines are commonly used as chemical inputs in organic synthesis, including in a number of well-developed reactions, such as S_N2 addition, reductive amination, amide coupling, and Buchwald–Hartwig amination.[2–4] Diamines constitute an especially prized subclass, given their unique applications as pharmaceuticals, ligands and organocatalysts.[5] Thus, novel strategies for preparing structurally complex and differentially substituted diamines from simple starting materials are valuable in both academia and industry. In this context, we sought to develop methodology to directly convert a wide variety of simple alkenyl amines (primary or secondary), a family of readily available starting materials, into differentially functionalized diamines, where the preexisting amine directs the installation of a second amine through catalytic aminative 1,2-difunctionalization.

In recent years, directed three-component alkene difunctionalization has emerged as an effective strategy for selective synthesis of highly substituted, multifunctional, and stereochemically defined products from simple chemical inputs (Scheme 1A). In this context, successful amine-based directing groups have included those based on bidentate directing auxiliaries.[6–8] and monodentate protecting groups (e.g., amides and sulfonamides) (Scheme 1B).[9] In these cases, attachment of an electron-withdrawing group to the amine is critical as it attenuates Brønsted and Lewis basicity, diminishing its ability to interfere with catalysis. Although this methodology is valuable in its own right, when the corresponding free amine products are desired, two additional steps for protection and deprotection are needed. Moreover, with rare exception,[9h] these directing groups cannot directly undergo *N*-functionalization, requiring further manipulations to install desired *N*-alkyl or *N*-aryl substituents. Hence, these limitations significantly diminish the synthetic utility of this family of methods.

The goal of the present study was thus to achieve three-component catalytic alkene difunctionalization directed by native free amines. At the outset, we were aware of several potential challenges with using free amines as directing groups. First, free amines are prone to undesired oxidation to the corresponding imines by various transition metals.[10] In addition, the nucleophilic nature of free amines can lead to intramolecular cyclization on the alkene or direct coupling with the electrophile.[11] Furthermore, free amines often bind strongly to the transition metal catalyst and sequester it off cycle.[12] While important precedents have demonstrated the ability of free amines to direct catalytic hydrofunctionalization,[13,14] Heck-type coupling,[15] and homodiarylation,[16] three-component functionalization of free amines remains unknown to the best of our knowledge.

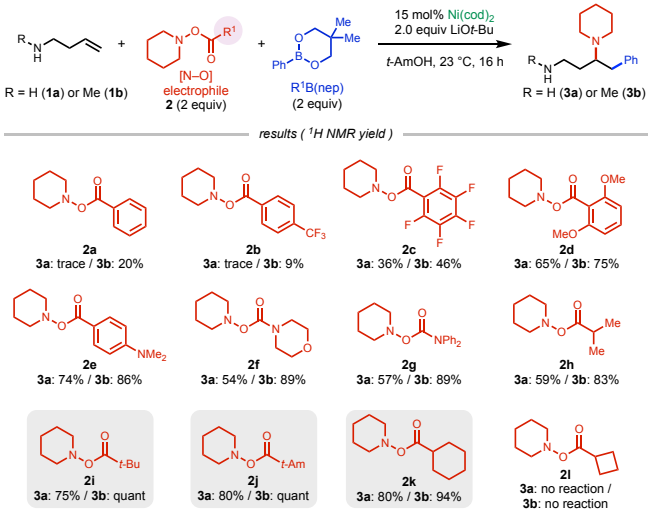
In order to gain entry to differentially substituted diamine products, we focused on catalytic three-component 1,2-carboamination, as developed by our group and others (Scheme 1C).[6d, 17–21] We recently demonstrated that native hydroxyl groups can efficiently direct 1,2-carboamination of alkenes.[19, 20] Enabling this advance was the discovery that a sterically and electronically tuned 2,6-dimethoxybenzoyl activating group on the N–O reagent prevented undesired β-hydride elimination and transesterification pathways, thereby promoting high product selectivity. Based on this precedent, we envisioned that 1,2-carboamination of free alkenyl amines could be enabled by

careful tailoring of the amine electrophile and optimization of the reaction conditions.



Scheme 1. Background and synopsis of current work.

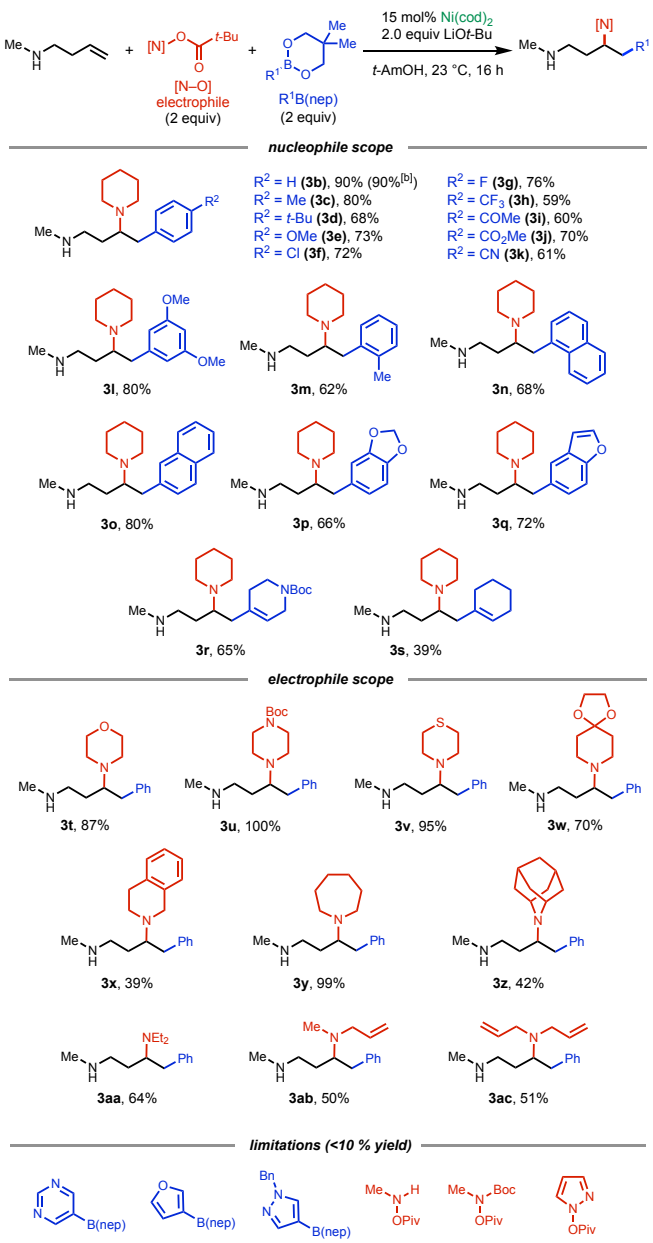
Initial experiments revealed that simply applying previously published carboamination conditions from our group (for free alkenyl alcohols)[19] and from the Wang group (for alkenyl picolinamides)[6d] to free alkenyl amine substrates led to unsatisfactory results (<40% yield, see SI). After extensive screening, we identified tractable conditions using phenylboronic acid neopentylglycol ester (PhB(nep)) as the nucleophilic coupling partner, LiO*t*-Bu as base, $Ni(cod)_2$ as precatalyst and *t*-AmOH as the solvent. We then tested various N–O reagents having different activating groups with both primary and secondary alkenyl amine substrates, 3-butene-1-amine (**1a**) and *N*-methyl 3-butene-1-amine (**1b**). *O*-Benzoylhydroxylamines with electron-neutral or -withdrawing groups at the *para* position gave poor yields with both substrates (**2a** and **2b**). In contrast, the pentafluorobenzoyl activating group delivered decent yields (**2c**). More electron-rich benzoyl activating groups showed improved reactivity (**2d** and **2e**). Interestingly, carbamoyl activating groups also delivered the desired products in good yield, especially with the secondary amine substrate (**2g** and **2h**). We next tested leaving groups derived from aliphatic acids and were pleased to observe excellent yields for both substrates when using *tert*-butyl- (**2i**), *tert*-amyl- (**2j**), or cyclohexylcarbonyl-substituted N–O reagents (**2k**). Notably, a cyclobutylcarbonyl-substituted electrophile did not provide any desired product (**2l**) A DFT parameterization/correlation study revealed that the highest yields were obtained with N–O electrophiles possessing LUMO energies within a narrow range (1.02–1.06 eV) (see SI). Finally, we selected *O*-pivaloylhydroxylamine (**2i**) as an optimal electrophilic coupling partner since it was the most general among **2i**–**2k** across different substrates and coupling partners (see SI). Additionally, **2i** is readily available from the corresponding free amine or hydroxylamine on large scale and is also compatible in several other types of transformations.[22]



Scheme 2. Optimization of the leaving group for the N–O electrophile. [a] Reaction conditions: **1a** or **1b** (0.1 mmol), Aryl/AlkenylB(nep) (0.2 mmol), N–O electrophile (0.2 mmol), LiO*t*-Bu (0.2 mmol), $Ni(cod)_2$ (0.015 mmol), *t*-AmOH (1 mL), 23 °C, 16 h.

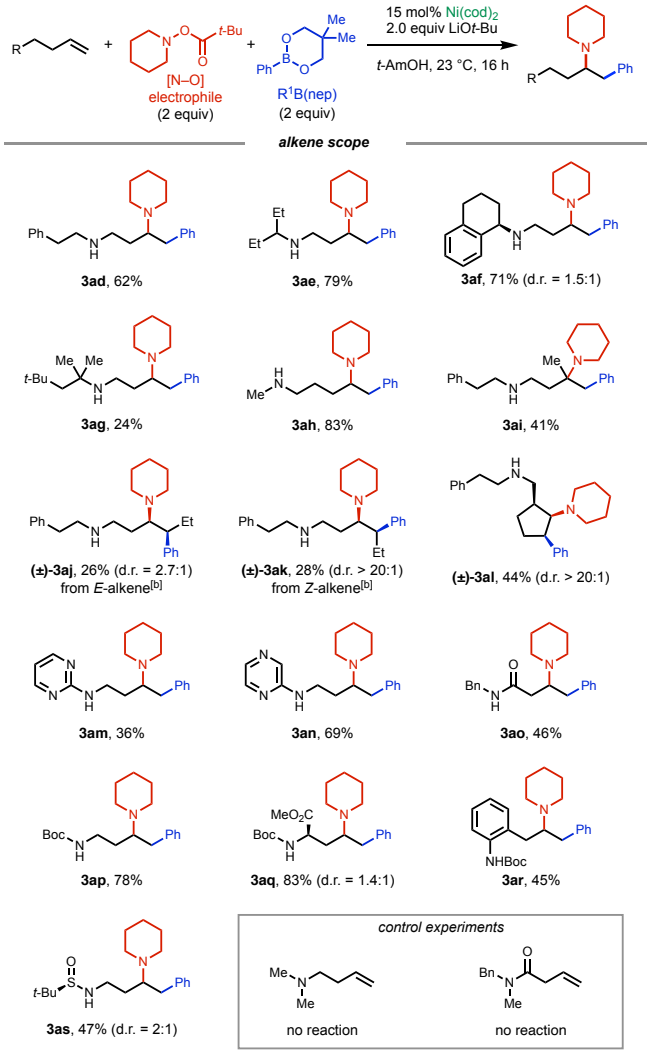
Having optimized the reaction conditions, we explored the scope with respect to the nucleophile. Arylboron reagents bearing electron-donating substituents in the *para*-position delivered good to excellent yields of the desired products (**3b**–**3f**). Interestingly, aryl nucleophiles containing electron-withdrawing groups, which gave poor yields in our previous alcohol-directed protocol,[19] showed significantly improved product yields (**3g**–**3k**). It is also notable that chloride (**3f**), ketone (**3i**), ester (**3j**), and nitrile (**3k**) functional groups on the aryl nucleophile were compatible under the reaction conditions, introducing handles for further product modification. Furthermore, *meta*- and *ortho*-substituted aryl nucleophiles and polycyclic groups performed well in this method (**3l**–**3q**). In addition, cyclic alkenylboronic ester nucleophiles gave the desired products in moderate yields (**3r** and **3s**).

Next, we examined the nitrogen electrophile scope using phenylboronic ester as the standard nucleophilic component. Six- and seven-membered azaheterocycle electrophiles delivered excellent yields (**3t**–**3y**). Notably, a comparatively lower yield was obtained for the tetrahydroisoquinoline-derived electrophile (**3x**). We observed 3,4-dihydroisoquinoline as a side product in this case, which implies decomposition of the electrophile, resulting in lower overall yield. We also investigated a sterically bulkier azaheterocycle (**3z**) and acyclic-amine-derived electrophiles (**3aa**–**3ac**), which were low-yielding in previous work (0–21% yield);[19] interestingly, we obtained substantially improved yields, including with mono- (**3ab**) and di-allyl amines (**3ac**), which can be readily deprotected and thus function as secondary and primary amine surrogates. On the other hand, NH, *N*-Boc, and heteroaromatic coupling partners were ineffective under the reaction conditions.



Scheme 3. Nucleophile and electrophile scope. [a] Reaction conditions: **1b** (0.1 mmol), Aryl/AlkenylB(nep) (0.2 mmol), N−O electrophile (0.2 mmol), LiO*t*-Bu (0.2 mmol), $Ni(cod)_2$ (0.015 mmol), *t*-AmOH (1 mL), 23 °C, 16 h. Percentages represent isolated yields. [b] ^{1}H NMR yield; reaction performed outside of the glovebox using $NiBr_2$•glyme instead of $Ni(cod)_2$.

3al). Notably, while cyclic and acyclic (*Z*)-alkenes yielded single (>20:1 d.r.) diastereomers (**3ak** and **3al**), we observed significant erosion of diastereoselectivity with an (*E*)-alkene (**3aj**), suggesting potential involvement of a competitive process involving reversible alkyl–Ni(III) homolysis to eject an alkyl radical and Ni(II).[23] Moving to *N*-aryl substrates, although we found an



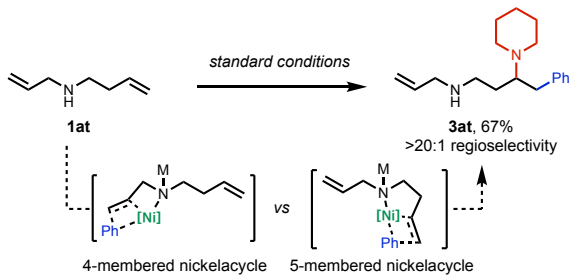
Scheme 4. Alkene scope. [a] Reaction conditions: alkene substrate (0.1 mmol), Aryl/AlkenylB(nep) (0.2 mmol), N−O electrophile (0.2 mmol), LiO*t*-Bu (0.2 mmol), $Ni(cod)_2$ (0.015 mmol), *t*-AmOH (1 mL), 23 °C, 16 h. Percentages represent isolated yields. [b] Unreacted starting materials remained, and no evidence of (*E*)/(*Z*) isomerization was observed in the crude reaction mixtures.

Turning our attention to the alkene scope, we first investigated secondary alkenyl amine substrates containing sterically differentiated *N*-substituents. Linear and α-branched alkyl groups provided good to excellent yields (**3ad**–**3af**), while α,α-disubstituted groups (i.e., *tert*-alkyl substituents) showed decreased reactivity (**3ag**). This clearly shows the importance of the coordinating interaction between the free amine group and the nickel catalyst in this directed carboamination reaction. We further tested a longer chain alkenyl amine and obtained an excellent yield of the 1,4-diamine product **3ah**. In addition, we were delighted to obtain the desired 1,2-carboaminated products from more sterically demanding 1,1- or 1,2-disubstituted alkenes (**3ai**–

alkene substrate with a simple *N*-phenyl group was low-yielding (<20% ^{1}H NMR yield), more electron-deficient *N*-pyrimidine and *N*-pyrazine substituted amine directing groups efficiently underwent 1,2-carboamination (**3am** and **3an**). Though the focus on this study was on free primary and secondary alkenyl amine substrates, the robustness of this method prompted us to consider substrates containing non-basic nitrogens as well. We found that a simple secondary amide was tolerated (**3ao**). Notably, an *N*-Boc-protected amine also proved compatible (**3ap**), which is significant given the operational ease of employing this type of protected amine substrate and its widespread in medicinal chemistry. Based on this success, we further tested *N*-Boc-

protected amino acid (**3aq**) and aniline substrates (**3ar**) and obtained excellent to good yields. Interestingly, Ellman's chiral sulfinamide[24] functioned as a directing group, delivering moderate yield and diastereoselectivity (**3as**), and the product mixture could be conveniently separated using preparative supercritical fluid chromatography (SFC). This result illustrates the potential of a sulfinamide-based chiral directing auxiliary in stereoselective alkene 1,2-difunctionalization. Control experiments with tertiary amine and amide substrates under standard conditions did not yield product, indicating that the presence of an N–H bond in the directing groups is essential.

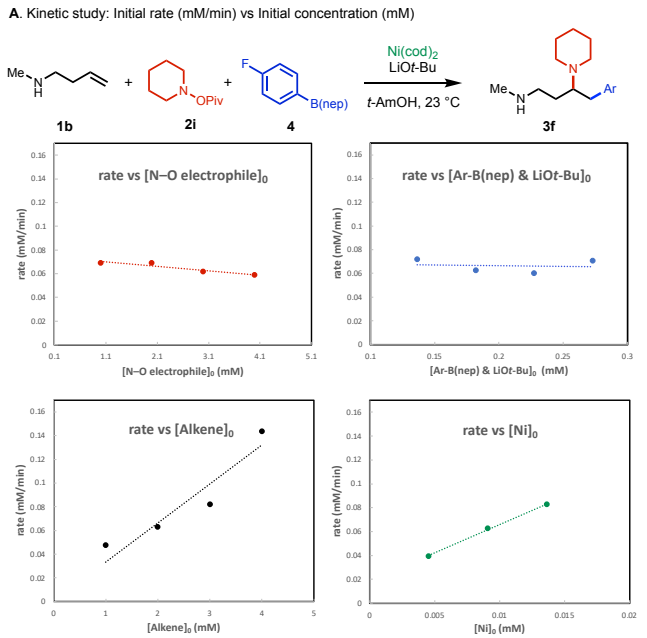
We next tested diene substrate **1at** that bears two potentially reactive terminal alkenes. Excitingly, the 1,4-diamine product **3at** was obtained exclusively, illustrating the excellent chemoselectivity of this method for the distal (homoallylic) alkene compared to the proximal (allylic) alkene. This unique chemoselectivity likely arises from preferrential formation of a 5-membered versus 4-membered nickelacycle intermediate. This result also highlights an advantage of this free-amine-directed method in distinguishing between two sterically and electronically similar terminal alkenes solely on the basis of tether length, which cannot be achieved with weaker directing groups or radical-insertion-based reactions.[9, 21a]

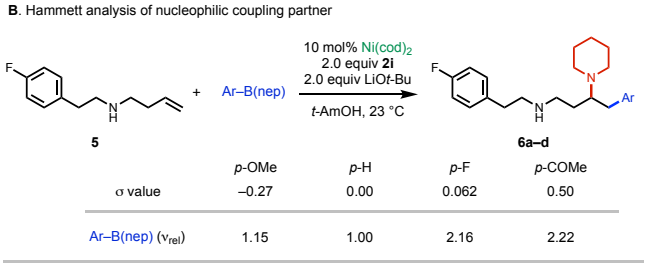


Scheme 5. [a] Reaction conditions: **1at** (0.1 mmol), Aryl/AlkenylB(nep) (0.2 mmol), N−O electrophile (0.2 mmol), LiO*t*-Bu (0.2 mmol), $Ni(cod)_2$ (0.015 mmol), *t*-AmOH (1 mL), 23 °C, 16 h. Percentages represent isolated yields. M = Li, H, or free lone pair (overall anionic complex).

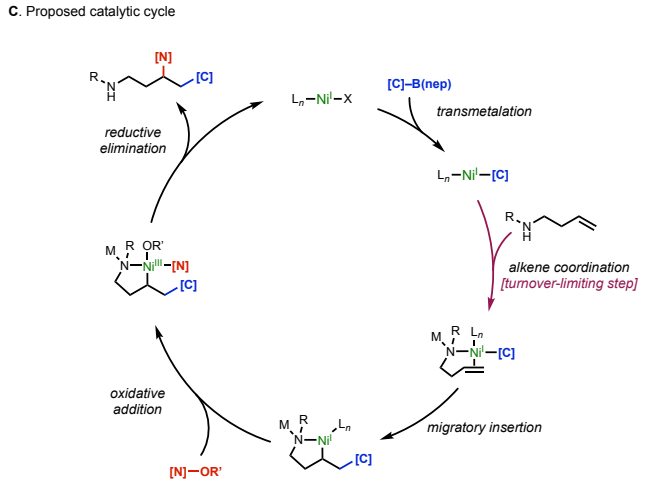
To gain insight into the reaction mechanism, we conducted a series of kinetic experiments. Using the method of initial rates, we examined the representative three-component coupling of **1b**, **2i**, and **4**. The reaction showed positive-order dependence on [**1b**] and $[Ni]_{total}$ and zero-order dependence on the other reagents (Scheme 6a). This result indicates involvement of the alkene and nickel catalyst in the turnover-limiting step. Two plausible scenarios are: (1) turnover-limiting associative ligand exchange of the alkene for a ligand on nickel or (2) reversible alkene coordination followed by turnover-limiting migratory insertion. To disambiguate between these two possibilities, we further investigated the initial reaction rates using four-electronically varied arylboronic ester nucleophiles with **5**. Interestingly, though there was not a clear linear correlation in the resulting Hammett plot (see SI), electron-deficient *p*-F- and *p*-COMe-substituted arylboronic esters led to faster reaction rates than electron-neutral and electron-rich aryl groups (Scheme 6b), which is the opposite trend that one would expect in turnover-limiting migratory insertion.[9a] Overall, the data is consistent with the first scenario, in which alkene coordination is turnover-limiting, though we cannot rule out an alternative explanation that the turnover-limiting step changes depending on the identity of the substrate and coupling partners.

Based on the kinetic data and literature precedents, we propose a plausible catalytic cycle in Scheme 6C.[19] As with our earlier work on alcohol-directed carboamination, we envision a Ni(I)/Ni(III) cycle involving successive transmetalation, migratory insertion, oxidative addition, and reductive elimination.





	p-OMe	*p*-H	*p*-F	*p*-COMe
σ value	–0.27	0.00	0.062	0.50
Ar–B(nep) (v_{rel})	1.15	1.00	2.16	2.22



Scheme 6. Initial rate experiments and proposed catalytic cycle. [a] Reactions were monitored by quantitative ^{19}F NMR using 1-fluoronaphthalene as internal standard. M = Li, H, or free lone pair (overall anionic complex).

In conclusion, we have demonstrated the free-amine-directed nickel-catalyzed 1,2-carboamination of unactivated alkenes. Through fine tuning of the leaving group on the amine electrophile, the reaction occurred efficiently and selectively at room temperature. Using this method, we have synthesized >40 examples of new complex diamine derivatives from ubiquitous alkenyl amine starting materials. Notably, several classes of coupling partners that were low-yielding in earlier work, including electron-deficient aryl nucleophiles and sterically bulky amine electrophiles, were compatible in this protocol. Kinetic experiments point to a catalytic cycle involving turnover-limiting alkene coordination.

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Keywords: Nickel Catalysis • Alkene Functionalization • Carboamination • Amine Electrophile • Diamine

[1] a) T. Henkel, R. M. Brunne, H. Müller, F. Reichel, *Angew. Chem.* **1999**, *111*, 688–691*; Angew. Chem. Int. Ed.* **1999**, *38*, 643–647; b) E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257–10274.

[2] O. I. Afanasyev, E. Kuchuk, D. L. Usanov, D. Chusov, *Chem. Rev.* **2019**, *119*, 11857–11911.

[3] J. R. Dunetz, J. Magano, G. A. Weisenburger, *Org. Process Res. Dev.* **2016**, *20*, 140–177.

[4] a) P. Ruiz-Castillo, S. L. Buchwald, *Chem. Rev.* **2016**, *116*, 12564–12649; b) R. Dorel, C. P. Grugel, A. M. Haydl, *Angew. Chem.* **2019**, *131*, 17276–17287; *Angew. Chem. Int. Ed.* **2019**, *58*, 17118–17129.

[5] a) X. Ji, H. Huang, *Org. Biomol. Chem.* **2016**, *14*, 10557–10566; b) J.-C. Kizirian, *Chem. Rev.* **2008**, *108*, 140–205; c) T. Hashimoto, K. Maruoka, *Org. Biomol. Chem.* **2008**, *6*, 829–835.

[6] a) T. Zeng, Z. Liu, M. A. Schmidt, M. D. Eastgate, K. M. Engle, *Org. Lett.* **2018**, *20*, 3853–3857; b) W. Li, J. K. Boon, Y. Zhao, *Chem. Sci.* **2018**, *9*, 600–607; c) Z. Liu, J. Chen, H.-X. Lu, X. Li, Y. Gao, J. R. Coombs, M. J. Goldfogel, K. M. Engle, *Angew. Chem.* **2019**, *131*, 17224–17229; *Angew. Chem. Int. Ed.* **2019**, *58*, 17068–17073; d) L. Xie, S. Wang, L. Zhang, L. Zhao, C. Luo, L. Mu, X. Wang, C. Wang, *Nat. Commun.* **2021**, *12*, 6280.

[7] For applications in alkene annulation and hydrofunctionalization, respectively, see: a) H.-Q. Ni, I. Kevlishvili, P. G. Bedekar, J. S. Barder, S. Yang, M. Tran-Dubé, A. M. Romine, H.-X. Lu, I. J. McAlpine, P. Liu, K. M. Engle, *Nat. Commun.* **2020**, *11*, 6432; b) J. Jeon, C. Lee, H. Seo, S. Hong, *J. Am. Chem. Soc.* **2020**, *142*, 20470–20480; c) C. Lee, H. Seo, J. Jeon, S. Hong, *Nat. Commun.* **2021**, *12*, 5657.

[8] For applications in C(alkenyl)–H activation, see: a) C. Wang, L. Zhang, C. Chen, J. Han, Y. Yao, Y. Zhao, *Chem. Sci.* **2015**, *6*, 4610–4614; b) Z. -L. Zang, S. Zhao, S. Karnakanti, C.-L. Liu, P.-L. Shao, Y. He, *Org. Lett.* **2016**, *18*, 5014–5017; c) H. M. F. Viart, A. Bachmann, W. Kayitare, R. Sarpong, *J. Am. Chem. Soc.* **2017**, *139*, 1325–1329; d) R. Parella, S. A. Babu, *J. Org. Chem.* **2017**, *82*, 6550–6567; e) M. Liu, P. Yang, M. K. Karunananda, Y. Wang, P. Liu, K. M. Engle, *J. Am. Chem. Soc.* **2018**, *140*, 5805–5813; f) Y.-C. Luo, C. Yang, S.-Q. Qiu, Q.-J. Liang, Y.-H. Xu, T.-P. Loh, *ACS Catal.* **2019**, *9*, 4271–4276; g) B. S. Schreib, E. M. Carreira, *J. Am. Chem. Soc.* **2019**, *141*, 8758–8763; h) B. S. Schreib, M. Fadel, E. M. Carreira, *Angew. Chem. Int. Ed.* **2020**, *59*, 7818–7822. For early work on C(sp^3)–H activation, see: i) V. G. Zaitsev, D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2005**, *127*, 13154–13155; j) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074–1086.

[9] Enamine derivatives: a) J.-W. Gu, Q.-Q. Min, L.-C. Yu, X. Zhang, *Angew. Chem.* **2016**, *128*, 12458–12462*; Angew. Chem. Int. Ed.* **2016**, *55*, 12270–12274; b) C. Xu, Z.-F. Yang, L. An, X. Zhang, *ACS Catal.* **2019**, *9*, 8224–8229; c) Z.-F. Yang, C. Xu, X. Zheng, X. Zhang, *Chem. Commun.* **2020**, *56*, 2642–2645; d) X. Wei, W. Shu, A. García-Domínguez, E. Merino, C. Nevado, *J. Am. Chem. Soc.* **2020**, *142*, 13515–13522; e) C. Xu, R. Cheng, Y.-C. Luo, M.-K. Wang, X. Zhang, *Angew. Chem.* **2020**, *132*, 18900–18906; *Angew. Chem. Int. Ed.* **2020**, *59*, 18741–18747. Allylamine derivatives: f) J. Derosa, R. Kleinmans, V. T. Tran, M. K. Karunananda, S. R. Wisniewski, M. D. Eastgate, K. M. Engle, *J. Am. Chem. Soc.* **2018**, *140*, 17878–17883; g) V. T. Tran, Z. Q. Li, T. J. Gallagher, J. Derosa, P. Liu, K. M. Engle, *Angew. Chem.* **2020**, *132*, 7095–7100; *Angew. Chem. Int. Ed.* **2020**, *59*, 7029–7034. Homoallyl- and bishomoallylamine derivatives: h) O. Apolinar, V. T. Tran, N. Kim, M. A. Schmidt, J. Derosa, K. M. Engle, *ACS Catal.* **2020**, *10*, 14234–14239. *ortho*-Vinylaniline derivatives: i) B. Shrestha, P. Basnet, R. K. Dhungana, S. KC, S. Thapa, J. M. Sears, R. Giri, *J. Am. Chem. Soc.* **2017**, *139*, 10653–10656.

[10] B. Chen, L, Wang, S, Gao, *ACS Catal.* **2015**, *5*, 5851–5876.

[11] a) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981–3019; b) D. M. Schultz, J. P. Wolfe, *Synthesis* **2012**, *3*, 351–361; b) Z. J. Garlets, D. R. White, J. P. Wolfe, *Asian J. Org. Chem.* **2017**, *6*, 636–653.

[12] a) P. Marcazzan, B. O. Patrick, B. R. James, *Organometallics* **2003**, *22*, 1177–1179; b) Y. Du, H. Chen, R. Chen, N. Xu, *Chem. Eng. J.* **2006**, *125*, 9–14; c) I. Aviv, Z. Gross, *Chem. Eur. J.* **2008**, *14*, 3995–4005; d) R. M. Stolley, M. T. Maczka, J. Louie, *Eur. J. Org. Chem.* **2011**, 3815–3824; e) J. Derosa, V. T. Tran, M. N. Boulous, J. S. Chen, K. M. Engle, *J. Am. Chem. Soc.* **2017**, *139*, 10657–10660.

[13] a) S. C. Ensign, E. P. Vanable, G. D. Kortman, L. J. Weir, K. L. Hull, *J. Am. Chem. Soc.* **2015**, *137*, 13748–13751; b) J. L. Kennemur, G. D. Kortman, K. L. Hull, *J. Am. Chem. Soc.* **2016**, *138*, 11914–11919; c) E. P. Vanable, J. L. Kennemur, L. A. Joyce, R. T. Ruck, D. M. Schultz, K. L. Hull, *J. Am. Chem. Soc.* **2019**, *141*, 739–742.

[14] For a transient directing group approach to hydroformylation of alkenyl amines, see: A. D. Worthy, C. L. Joe, T. E. Lightburn, K. L. Tan, *J. Am. Chem. Soc.* **2010**, *132*, 14757–14759.

[15] V. G. Landge, J. M. Maxwell, P. Chand-Thakuri, M. Kapoor, E. T. Diemler, M. C. Young, *JACS Au* **2021**, *1*, 13–22.

[16] V. G. Landge, A. J. Grant, Y. Fu, A. M. Rabon, J. L. Payton, M. C. Young, *J. Am. Chem. Soc.* **2021**, *143*, 10352–10360. For tertiary-amine-directed homodiarylation of vinyl ethers, see: A. Trejos, A. Fardost, S. Yahiaoui, M. Larhed, *Chem. Commun.* **2009**, *48*, 7587–7589.

[17] For two-component umpolung carboaminations, see: a) A. Faulkner, J.S. Scott, J. F. Bower, *J. Am. Chem. Soc.* **2015**, *137*, 7224–7230; b) X. Bao, Q. Wang, J. Zhu, *Angew. Chem.* **2017**, *129*, 9705–9709; *Angew. Chem. Int. Ed.* **2017**, *56*, 9577–9581; c) H.-B. Yang, S. R. Pathipati, N. Selander, *ACS Catal.* **2017**, *7*, 8441–8445.

[18] V. A. van der Puyl, J. Derosa, K. M. Engle, *ACS Catal.* **2019**, *9*, 224–229.

[19] T. Kang, N. Kim, P. T. Cheng, H. Zhang, K. Foo, K. M. Engle, *J. Am. Chem. Soc.* **2021**, *143*, 13962–13970.

[20] Ref. 19 also includes two alkenyl sulfonamide examples (54% and 56% yield).

[21] For other approaches to alkene carboamination, see: a) H. Jiang, A. Studer, *Chem. Soc. Rev.* **2020**, *49*, 1790−1811; b) F. Romanov-Michailidis, K. F. Sedillo, J. M. Neely, T. Rovis, *J. Am. Chem. Soc.* **2015**, *137*, 8892–8895; c) D. Zhao, S. Vásquez-Céspedes, F. Glorius, *Angew. Chem., Int. Ed.* **2015**, *54*, 1657–1661; d) T. Piou, T. Rovis, *Nature* **2015**, *527*, 86–90; e) Z. Liu, Y. Wang, Z. Wang, T. Zeng, P. Liu, K. M. Engle, *J. Am. Chem. Soc.* **2017**, *139*, 11261–11270. f) H. -M. Huang, M. Koy, E. Serrano, P.M. Pflüger, J. L. Schwarz, F. Glorius, *Nat. Catal.* **2020**, *3*, 393–400; g) S. Lee, T. Rovis, *ACS Catal.* **2021**, *11*, 8585–8590; h) S. N. Gockel, S. Lee, B. L. Gay, K. L. Hull, *ACS Catal.* **2021**, *11*, 5166–5171; i) Y. Kwon, W. Zhang, Q. Wang, *ACS Catal.* **2021**, *11*, 8807–8817.

[22] a) J. S. Bandar, M. T. Pirnot, S. L. Buchwald, *J. Am. Chem. Soc.* **2015**, *137*, 14812–14818; b) S. Ichikawa, S. Zhu, S. L. Buchwald. *Angew. Chem.* **2018**, *130*, 8850–8854; *Angew. Chem. Int. Ed.* **2018**, *57*, 8714–8718; c) E. Falk, S. Makai, T. Delcaillau, L. Gürtler, B. Morandi, *Angew. Chem.* **2020**, *132*, 21250–21257; *Angew. Chem. Int. Ed.* **2020**, *59*, 21064–21071.

[23] a) O. Gutierrez, J.C. Tellis, D. N. Primer, G. A. Molander, M. C. Kozlowski, *J. Am. Chem. Soc.* **2015**, *137*, 4896–4899; b) H. Yin, G. C. Fu, *J. Am. Chem. Soc.* **2019**, *141*, 15433–15440; c) D. Anthony, Q. Lin, J. Baudet, T. Diao, *Angew. Chem.* **2019**, *131*, 3230–3234; *Angew. Chem., Int. Ed.* **2019**, *58*, 3198–3202.

[24] M. T. Robak, M. A. Herbage, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 3600–3740.

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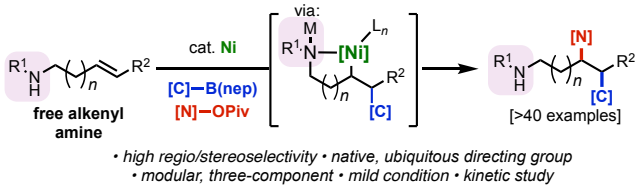

A nickel-catalyzed, free-amine-directed 1,2-carboamination of unactivated alkenes with aryl/alkenylboronic esters and O-pivaloyl hydroxylamine electrophiles is reported. This method enables synthesis of structurally complex diamines from the readily available alkenyl amine starting materials. Kinetic experiments indicate that alkene coordination step is turnover-limiting in the catalytic cycle.