JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
pubs.acs.org/JACS
Communication

# Nickel-Catalyzed Branched Hydroalkylation of Alkenes with Diazo Compounds

Nikita Kvasovs,[#] Valeriia Iziumchenko,[#] Alistair J. Sterling, and Vladimir Gevorgyan*

Cite This: J. Am. Chem. Soc. 2025, 147, 8093−8100
Read Online

**ABSTRACT:** A nickel-catalyzed, branched-selective hydroalkylation of alkenes using diazo compounds has been developed. This protocol enables the functionalization of both activated and unactivated alkenes, in both directed and nondirected manners. Mono-, di-, and trisubstituted alkenes can be effectively transformed. Highly diastereoselective hydroalkylations have also been demonstrated. The method provides a novel approach for introducing an $\alpha$-carbonyl moiety to alkenes, which is currently inaccessible by existing methods. Preliminary mechanistic investigations suggest a carbene-type mechanism, which is unusual for nickel catalysis.

Versatile reactivity of $\alpha$-carbonyl diazo compounds made them an instrumental part of modern organic synthesis.[1] Particularly important are their reactions with alkenes, including cyclopropanation[2] (**I**) and allylic C−H insertion[3] (**II**) reactions (Scheme 1A).

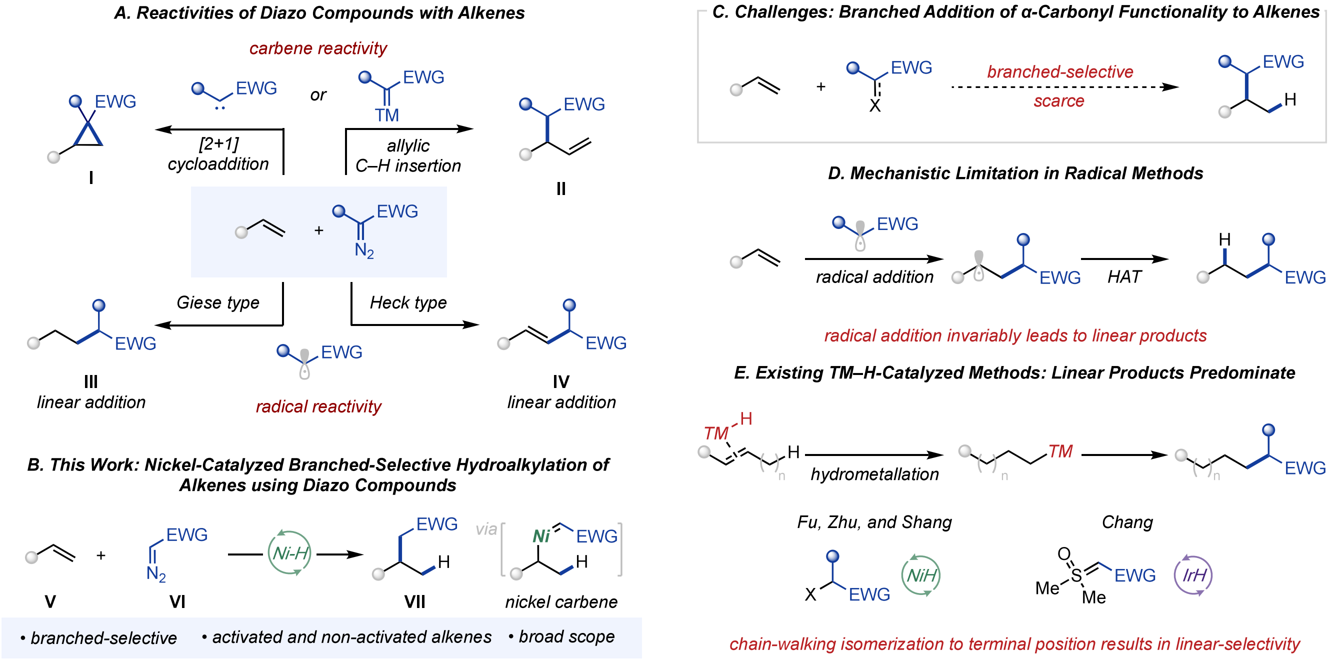
More recently, the radical reactivity of diazo compounds[4] with alkenes has been revitalized by Doyle and Qiu,[5] with the demonstration of robust catalytic methods for converting diazo compounds into C-centered radicals following by Giese-type addition (**III**). This discovery gave rise to a series of related works on the radical carbofunctionalization of alkenes using diazo compounds.[6] Beyond reductive additions, our group has recently reported a Heck-type C−H alkylation, allowing the preservation of a valuable alkene moiety (**IV**).[7] All of these methods further expanded the versatility of diazo compounds and added them as an alternative source to classical radical precursors. However, despite these advances, certain limitations remain. Particularly, in all radical approaches, the C−C bond between the alkene and the carbon of the diazo group is always formed at the terminal positions, such as in **III** and **IV**. Reactivity that would allow for the general synthesis of otherwise unattainable branched products from the same starting materials is currently absent in the literature. Herein, we report a mild, branched-selective (**VII**) nickel-catalyzed hydroalkylation protocol using diazo compounds as coupling partners (Scheme 1B). This methodology offers a unique route for functionalization of both activated and nonactivated alkenes **V** with diazo compounds **VI**, in a directed or nondirected manner. Preliminary investigation suggests an unusual mechanism for nickel catalysis involving metal-carbene[8] intermediates, which offer new synthetic opportunities.[9] Notably, the reaction can be promoted by simple nickel salts without the need for additional ligands.

General access to compounds with branched attachment of the $\alpha$-carbonyl moiety directly from alkenes is currently a significant challenge (Scheme 1C). The aforementioned intermolecular radical reactions inevitably lead to linear products due to the innate features of the addition step, where the C-centered radical species tend to add at the less hindered position (Scheme 1D). This limitation is not unique to the chemistry of diazo compounds, as analogous radicals generated from more classical radical precursors exhibit the same selectivity trend.[10]

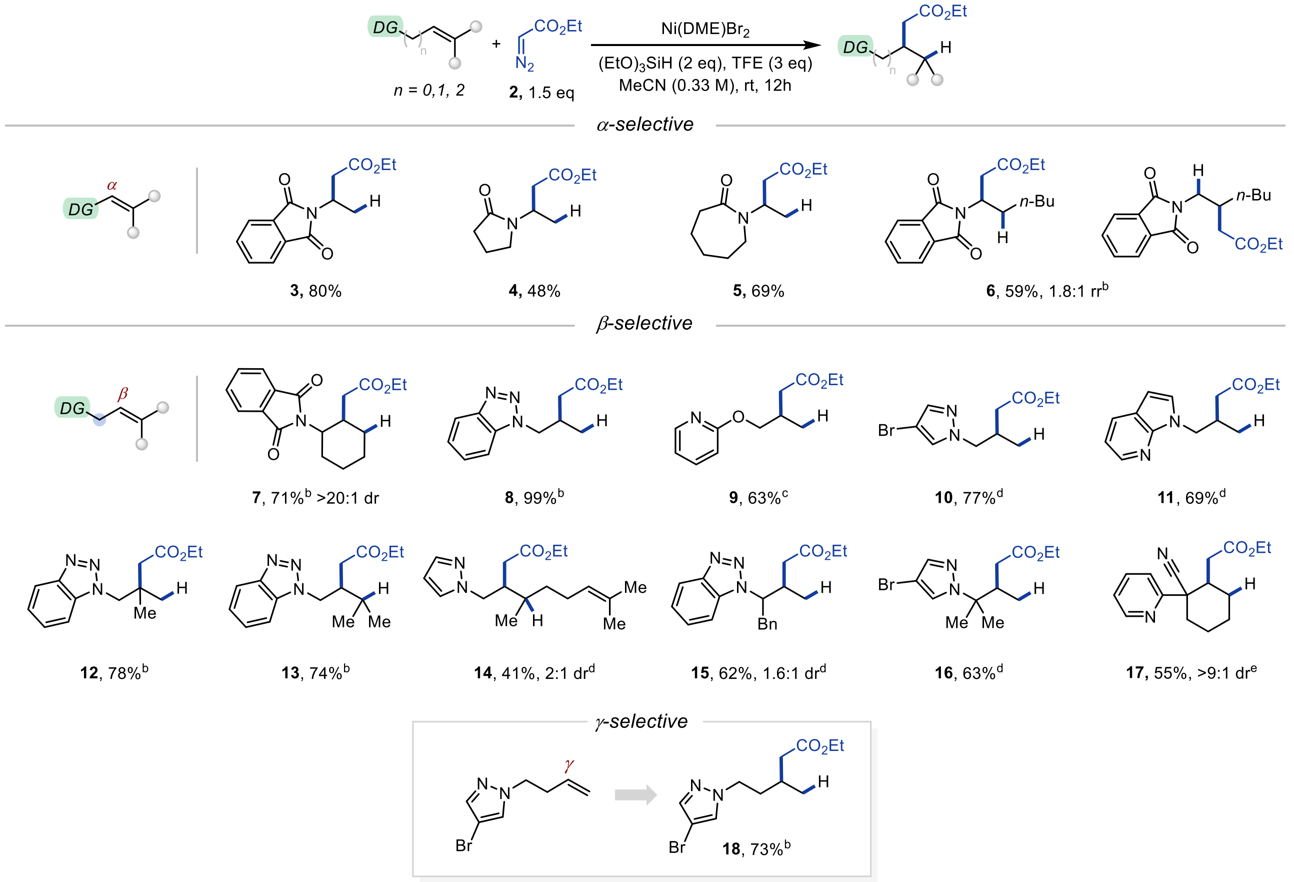
To this end, the chemistry of transition-metal hydrides is of interest, as the key hydrometalation step, depending on the system, may proceed with either branched or linear selectivity.[11,12] There are few notable reports in the context of reactions of alkenes with $\alpha$-carbonyl-containing precursors. Thus, Fu,[13] Zhu,[14] and Shang[15] employed the latter in the well-established nickel-catalyzed hydroalkylation process,[16] whereas Chang[17] accomplish hydroalkylation with sulfur ylides under iridium catalysis (Scheme 1E). In these reports, the chain-walking isomerization mechanism allows for the use of internal alkenes (and even mixtures of isomers) to perform terminal-selective C−C bond formation via a series of hydrometalations/$\beta$-hydride eliminations. This approach dramatically expands the scope of used alkenes compared to traditional radical methods. Moreover, the involvement of transition-metal intermediates provides an opportunity for stereoselective synthesis. However, the chain-walking in these particular reports almost always leads to the transition metal being attached to a terminal carbon, even though an alternative outcome is possible for both metals.[18,19] Thus, linear products are still the major outcome in these processes. Following our recent studies on the reactions of diazo compounds with alkenes,[7] we discovered that under certain conditions, nickel salts promoted the hydroalkylation of

**Received:** December 9, 2024
**Revised:** February 1, 2025
**Accepted:** February 19, 2025
**Published:** February 25, 2025

Scheme 1. Overview of Reactions of Diazo Compound with Alkenes and Approaches towards Branched-Selective Transformations

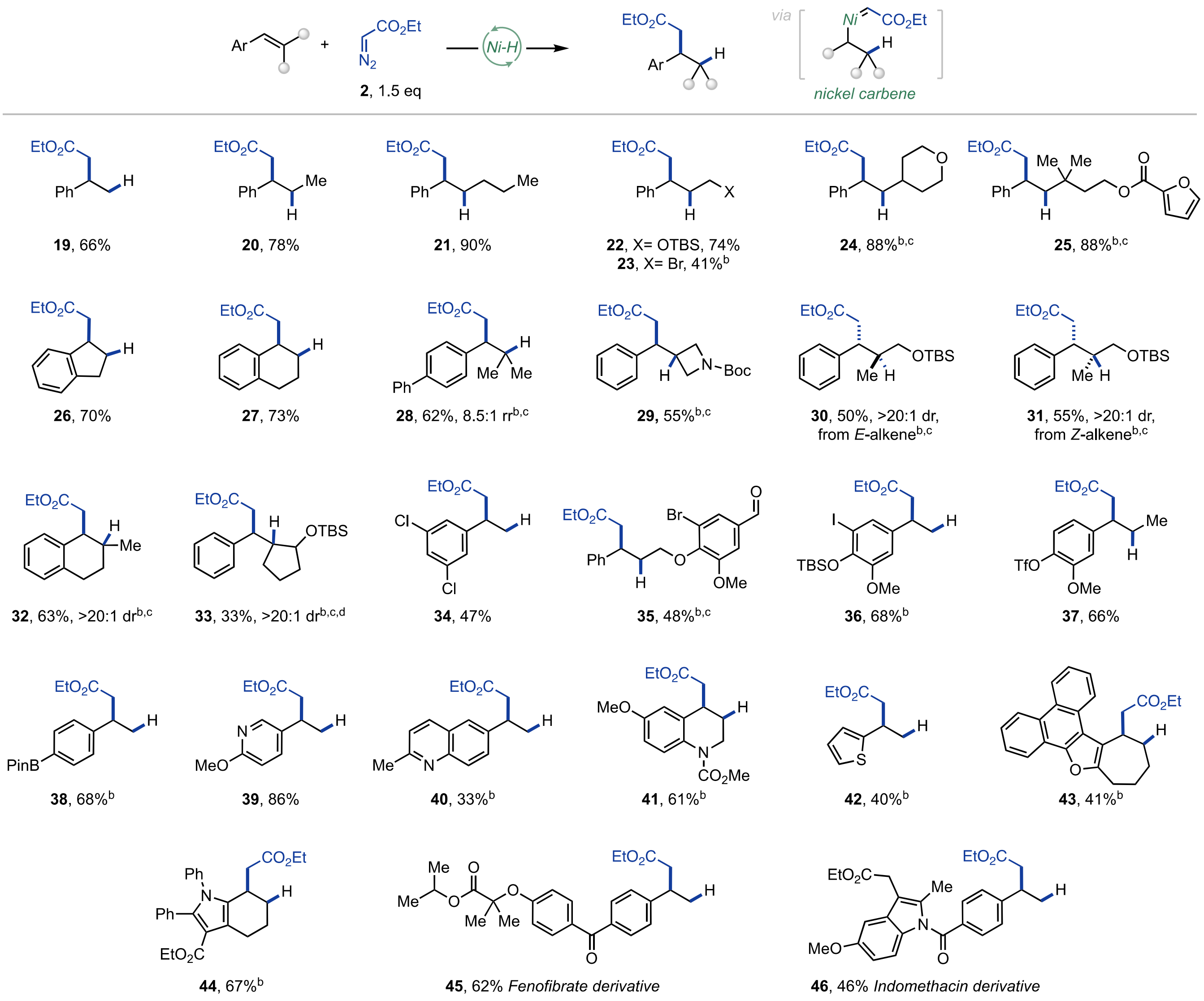


Scheme 2. Scope of Alkenes Bearing Directing Group[a]



[a]0.4 mmol scale. [b]MeCN/DCE solvent mixture (0.25 M, 1/3). [c]THF solvent (0.25 M). [d]MeCN/DMA solvent mixture (0.25 M, 1/3), HFIP (3 equiv) instead of TFE. [e]MeCN/DMA solvent mixture (0.25 M, 1/3).

**Scheme 3. Scope of Vinyl Arenes**[a]



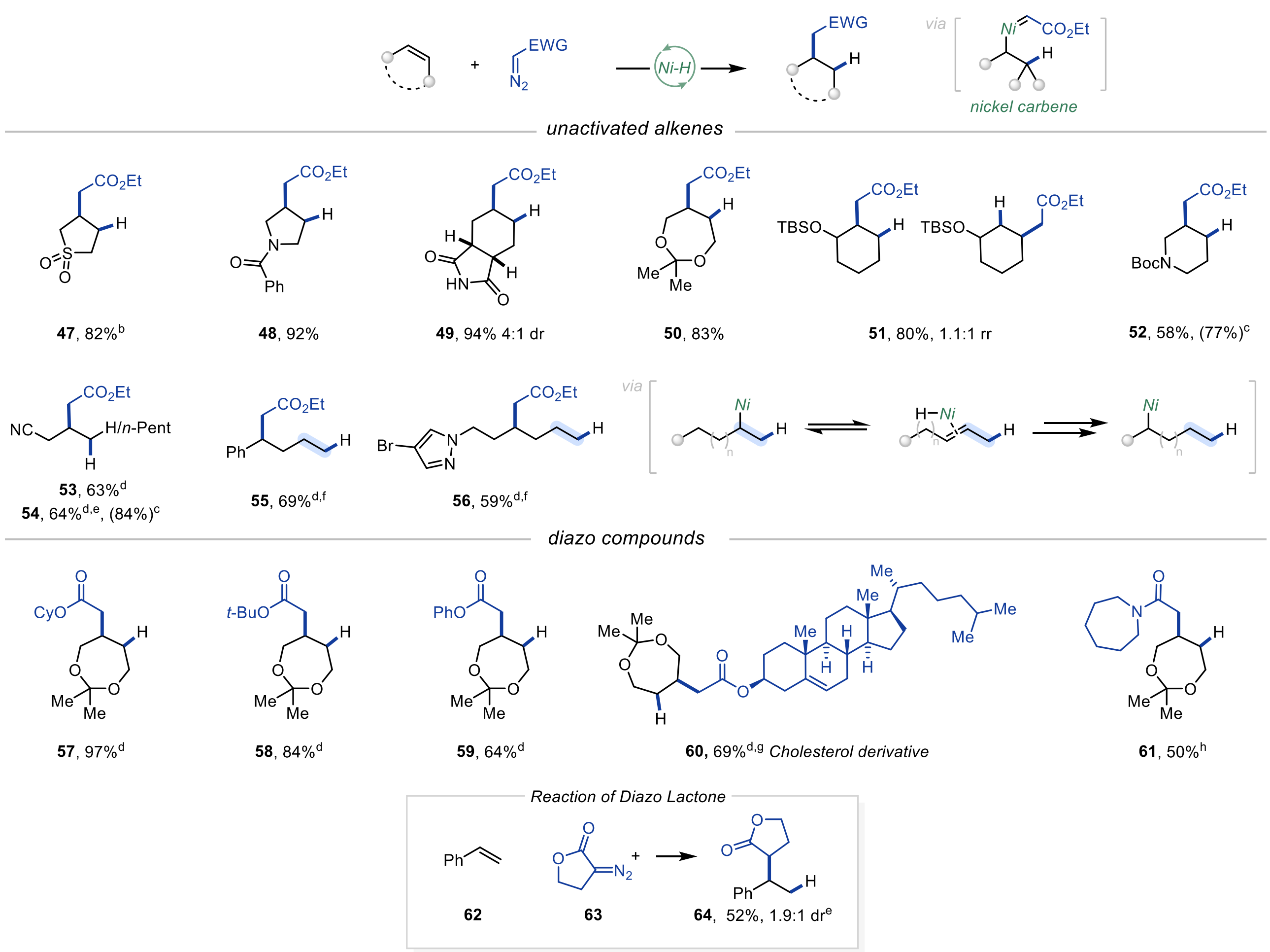
[a]Conditions: 0.3−0.4 mmol scale, Ni(DME)$Br_2$ (5 mol %), $PPh_3$ (5 mol %), $(EtO)_3SiH$ (2 equiv), TFE (1.5 equiv), MeCN/DCE (0.25 M, 1/3), rt, 12h. [b]Three equiv of TFE. [c]$AsPh_3$ (5 mol %) instead of $PPh_3$. [d]Yield after stirring with conc. $HCl_{aq}$ (See Supporting Information for details).

alkenes with diazo compounds. Initially, mixtures of branched and linear products were observed; however, upon further investigation, it was found that branched-selective hydrofunctionalization could be achieved for many classes of alkenes. Optimization studies identified conditions,[20] under which *N*-vinylphthalimide reacted with ethyl diazoacetate **2** in the presence of a simple nickel(II) salt, hydrosilane, and alcohol, to deliver product **3** as the sole isomer (Scheme 2). The observed regioselectivity was attributed to a directing effect of the amide group in the nickel-catalyzed hydroalkylation reactions.[21] The most important aspect of these conditions is the lack of a ligand. Surprisingly, it was found that common ligands suppressed the efficiency of this transformation. This observation contrasts with existing literature reports, where nitrogen-based ligands are prerequisite in promoting similar transformations.[16,22]

Like the phthalimide-containing product **3**, pyrrolidinone and caprolactam derivatives (**4** and **5**) could be synthesized with exclusive selectivity and moderate to good efficiency. However, employment of a 1,2-disubstituted *N*-alkenyl amide led to nonselective hydroalkylation (**6**). We found this result to be promising toward achieving $\beta$-selective functionalization. Indeed, the cyclohexene derivative bearing a phthalimide directing group yielded product **7** with excellent diastereo- and regiocontrol. It was also found that, in addition to phthalimide, various nitrogen-containing heterocycles promoted branched-selective transformations.[23] Thus, benzotriazole **8**, pyridine **9**, pyrazole **10**, and pyrollopyridine **11** derivatives could all be made with good to excellent efficiency and perfect regiocontrol. These heterocycles were proven to be the most effective at promoting the desired reaction, as even di- and trisubstituted alkenes could be functionalized in this manner (**12** and **13**). Unsymmetrical trisubstituted alkenes reacted with perfect regiocontrol, albeit with a modest diastereoselectivity (**14**). The chiral center $\alpha$-to-nitrogen in acyclic systems did not exhibit a substantial effect on diastereoselectivity of the reaction (**15**). In contrast, such substitution in the cyclic system led to good diastereocontrol (**17**). Initial studies proved that $\gamma$-selective functionalization could also be achieved with good efficiency (**18**).

https://doi.org/10.1021/jacs.4c17586
J. Am. Chem. Soc. 2025, 147, 8093−8100

**Scheme 4. Scope of Unactivated Alkenes and Diazo Compounds**[a]



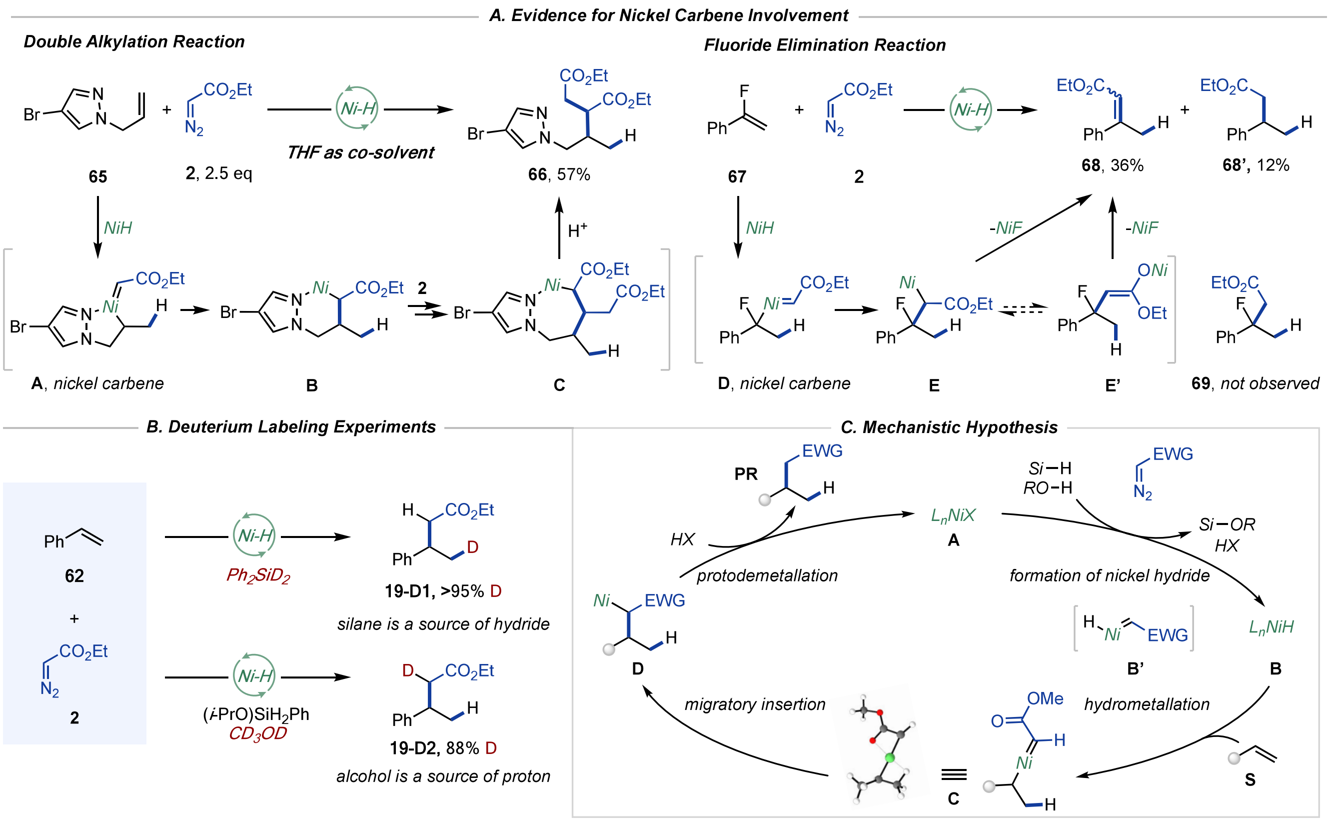
[a]Conditions: 0.4 mmol scale, 1 equiv of alkene, 1.5 equiv of EDA, Ni(DME)$Br_2$ (5 mol %), $(EtO)_3SiH$ (2 equiv), TFE (3 equiv), MeCN (0.33 M), rt, 12h. [b]1.1 equiv of EDA, 1.1 equiv of $(EtO)_3SiH$, 1.1 equiv of TFE. [c]Total yield with other regioisomers. [d]MeCN/DCE (0.25 M, 1/3). [e]$AsPh_3$ (5 mol %). [f]Tris(2-furyl)phosphine (0.05 equiv). [g]0.1 mmol scale, MeCN/DCE (0.125 M, 1/3). [h]0.23 mmol scale, MeCN/DMA (0.3 M, 1/1), 60h.

After establishing the scope of the directed transformation, the focus shifted toward the functionalization of alkenes which do not possess a directing group (Scheme 3). It was hypothesized that vinyl arenes could undergo a regioselective reaction due to the adjacency of the aryl group.[24] Indeed, the reaction demonstrated a high degree of regiocontrol; however, to obtain a single isomer, another round of optimization was necessary.[20] Triphenylphosphine was identified as a ligand, enabling the desired levels of efficacy and regioselectivity. Thus, products **19−22** were obtained in good to excellent yields as single regioisomers. Excitingly, even cinnamyl bromide underwent the desired transformation to deliver product **23** in a moderate yield. This is particularly surprising, considering that alkyl bromides are typically competent substrates in nickel-catalyzed hydroalkylation chemistry.[25]

The presence of a secondary or even tertiary carbon center adjacent to the vinyl group did not hinder reactivity, giving rise to products **24** and **25** in excellent yields. Cyclic alkenes also smoothly converted to products **26** and **27**. Markedly, trisubstituted alkenes (**28−33**) underwent the desired reaction in a highly regioselective manner. In contrast to the substrates containing directing groups (*vide supra*), unsymmetrical trisubstituted alkenes reacted highly diastereoselectively (**30−33**). The reaction appears to be stereospecific, as a particular alkene geometry led to particular diastereoisomers (**30** and **31**). Moreover, compound **33**, containing three contiguous stereocenters, was also synthesized as a single diastereoisomer, albeit in a lower yield. Next, different substituents at the arene were tested. Importantly, typical cross-coupling electrophiles, such as aryl chlorides (**34**), bromides (**35**), iodides (**36**), and triflates (**37**), as well aryl boron nucleophile (**38**), were all compatible with the reaction conditions. Different vinyl heteroarenes could be used as substrates with various degrees of efficiency (**39−44**), although several vinyl heteroarenes were reduced under the reaction conditions instead of undergoing the expected transformation.[20] The developed method was also applicable for the synthesis of drug derivatives such as **45** and **46**.

After developing an efficient and selective hydroalkylation of *activated alkenes* was developed, analogous reactions of the most challenging substrates, *unactivated alkenes*, were examined (Scheme 4). Excitingly, it was found that reactions with symmetrical cyclic alkenes worked with a high efficiency (**47−50**). It was also found that certain unsymmetrical alkenes reacted in a highly regioselective manner (**52-54**). Upon employment of terminal unactivated alkenes possessing an alkyl chain, formation of regioisomeric products beyond

**Scheme 5. Mechanistic Studies**



the alkene's position was observed. This pointed to the possibility of a chain-walking process. It was hypothesized that if a compound possessing a distant aromatic or directing group was employed, selective remote functionalization could potentially be achieved. Indeed, under slightly reoptimized conditions, products **55** and **56** could be synthesized *as sole regioisomers*. Importantly, these outcomes further confirm the involvement of nickel-hydride species in this hydroalkylation reaction.[22a,26] Lastly, the reactivity of different diazo compounds was evaluated (Scheme 4). For this purpose, the *cis*-buten-1,4-diol derivative was used as a standard alkene. Diazo esters derived from secondary or tertiary alcohols, as well as phenol, all engaged in the studied reaction, delivering the corresponding products **57**−**59** in good to excellent yields. Similarly, a cholesterol-derived diazo compound underwent the expected transformation (**60**). Preliminary results indicated that diazo amides also appeared to be capable alkylating agents; however, a significantly prolonged reaction time was required to obtain a reasonable amount of product (**61**). It was also found that diazo lactone **63** underwent a smooth reaction with styrene **62** delivering product **64** in moderate yield.

While the reaction scope was investigated, a few mechanistically relevant results were obtained (Scheme 5A). Next, in reactions of substrates containing nitrogen-based heterocycles as directing groups with ethyl diazoacetate **2**, a side double alkylation product sometimes was observed. It was found that the amount of this product could be enhanced by altering the reaction solvents.[20] For instance, the reaction of **65** in the MeCN/THF mixture selectively provided double alkylation product **66** (Scheme 5A), as opposed to the selective monoalkylation obtained in MeCN/DMA (**10**, Scheme 3). The formation of **66** could be rationalized via a migratory insertion of the nickel-carbene complex **A** to form intermediate **B**, which would undergo reaction with another 1 equiv of ethyl diazoacetate **2** in a similar manner. The resultant seven-membered nickelacycle **C** would yield the final product **66** upon protodemetalation. Another result that points to the possible intermediacy of a nickel-carbene bond is the reaction of $\alpha$-fluorostyrene **67**. Its reaction under the standard conditions produced an $\alpha,\beta$-unsaturated ester **68** alongside its reduced version **68′** instead of expected product **69**. Control experiments[20] confirmed that compounds **68** and **68′** did not form from **69**. Thus, the loss of fluoride could be explained by either an $\beta$-F elimination from intermediate **E** or an E1′ type elimination from enolate **E′**. The formation of these intermediates, in turn, may occur via a migratory insertion from the nickel-carbene complex **D**. Compound **68′** probably formed via reduction of **68** by a nickel hydride. Such reduction was indeed observed for Michael acceptors of analogues type under the conditions used.[20] To gain further insight into the potential mechanism for this hydroalkylation reaction, deuterium labeling experiments were performed (Scheme 5B). Thus, the reaction performed in the presence of a deuterated silane led to **19-D1** with exclusive deuterium incorporation at the terminal site. On the other hand, the reaction in the presence of methanol-$d_4$ provided **19-D2**, a product of D-incorporation $\alpha$ to the ester. These results point to silane being a hydride source, while alcohol is a proton source. Based on the experimental observations, as well as literature precedents,[9,16] the following plausible mechanism is proposed (Scheme 5C). Nickel salt undergoes reactions with silane and diazo compound to form nickel-hydride carbene complex **B**. Preliminary DFT calculations[20] suggest formation of nickel-carbene-hydride complex **B′** that is more favorably engages in a hydrometalation step with alkene **S** to give intermediate **C**, which upon a migratory insertion forms alkyl nickel-carbene species **D**. A subsequent protodemetalation would yield the product and recover the catalyst. Further detailed mechanistic investigation is necessary to establish an exact mechanistic pathway.

In summary, we developed a general protocol for the branched-selective hydroalkylation of activated and non-activated alkenes using diazo compounds as alkylating agents. This novel nickel-catalyzed method is efficient and selective for both directed and undirected hydroalkylation reactions. This methodology further expands the utility of diazo compounds and provides an alternative regioselectivity to the currently existing methods. Notably, the reaction appears to proceed through rare nickel-carbene intermediates, which may lead to new opportunities in the field of alkene functionalizations.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c17586.

Additional experimental details, materials, methods, and characterization data for all new compounds (PDF)

Results of calculations (ZIP)

## AUTHOR INFORMATION

### Corresponding Author

**Vladimir Gevorgyan** − *Department of Chemistry and Biochemistry, The University of Texas at Dallas, Richardson, Texas 75080-3021, United Sates;* orcid.org/0000-0002-7836-7596; Email: vlad@utdallas.edu

### Authors

**Nikita Kvasovs** − *Department of Chemistry and Biochemistry, The University of Texas at Dallas, Richardson, Texas 75080-3021, United Sates;* orcid.org/0009-0006-2265-6053

**Valeriia Iziumchenko** − *Department of Chemistry and Biochemistry, The University of Texas at Dallas, Richardson, Texas 75080-3021, United Sates;* orcid.org/0000-0002-0785-6448

**Alistair J. Sterling** − *Department of Chemistry and Biochemistry, The University of Texas at Dallas, Richardson, Texas 75080-3021, United Sates;* orcid.org/0000-0002-3571-1094

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.4c17586

### Author Contributions

[#]N.K. and V.I. contributed equally.

### Funding

This work was supported by the National Institutes of Health (GM120281) and Welch Foundation (Chair, AT-0041).

### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

We thank the High-Throughput Reaction Discovery & Synthesis (HT-RDS) Center at UTD. We also thank the UTSA Mass Spectrometry & Proteomics Core Facility.

## REFERENCES

(1) (a) Doyle, M.; McKervey, M.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; John Wiley & Sons, Inc., 1998. (b) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. Modern Organic Synthesis with $\alpha$-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981−10080. (c) Ciszewski, Ł. W.; Rybicka-Jasińska, K.; Gryko, D. Recent Developments in Photochemical Reactions of Diazo Compounds. *Org. Biomol. Chem.* **2019**, *17*, 432−448. (d) Qiu, D.; Wang, J. *Recent Developments of Diazo Compounds in Organic Synthesis*; World Scientific Publishing Company, 2020. (e) Wang, J. Diazo Compounds: Recent Applications in Synthetic Organic Chemistry and Beyond. *Tetrahedron Lett.* **2022**, *108*, No. 154135. (f) Zhang, Z.; Gevorgyan, V. Visible Light-Induced Reactions of Diazo Compounds and Their Precursors. *Chem. Rev.* **2024**, *124*, 7214−7261.

(2) (a) Doyle, M. P.; Forbes, D. C. Recent Advances in Asymmetric Catalytic Metal Carbene Transformations. *Chem. Rev.* **1998**, *98*, 911−936. (b) Maas, G. Ruthenium-Catalysed Carbenoid Cyclopropanation Reactions with Diazo Compounds. *Chem. Soc. Rev.* **2004**, *33*, 183−190. (c) Ebner, C.; Carreira, E. M. Cyclopropanation Strategies in Recent Total Syntheses. *Chem. Rev.* **2017**, *117*, 11651−11679. (d) Chen, Z.-L.; Xie, Y.; Xuan, J. Visible Light-Mediated Cyclopropanation: Recent Progress. *Eur. J. Org. Chem.* **2022**, *2022*, No. e202201066. (e) Simões, M. M. Q.; Cavaleiro, J. A. S.; Ferreira, V. F. Recent Synthetic Advances on the Use of Diazo Compounds Catalyzed by Metalloporphyrins. *Molecules* **2023**, *28*, 6683.

(3) (a) Davies, H. M. L.; Beckwith, R. E. J. Catalytic Enantioselective C−H Activation by Means of Metal−Carbenoid-Induced C−H Insertion. *Chem. Rev.* **2003**, *103*, 2861−2904. (b) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic Carbene Insertion into C−H Bonds. *Chem. Rev.* **2010**, *110*, 704−724. (c) He, Y.; Huang, Z.; Wu, K.; Ma, J.; Zhou, Y.-G.; Yu, Z. Recent Advances in Transition-Metal-Catalyzed Carbene Insertion to C−H Bonds. *Chem. Soc. Rev.* **2022**, *51*, 2759−2852.

(4) (a) Chen, Y.; Zhang, X. P. Vitamin $B_{12}$ Derivatives as Natural Asymmetric Catalysts: Enantioselective Cyclopropanation of Alkenes. *J. Org. Chem.* **2004**, *69*, 2431−2435. (b) Jiang, J.; Liu, J.; Yang, L.; Shao, Y.; Cheng, J.; Bao, X.; Wan, X. Cu-Based Carbene Involved in a Radical Process: A New Crossover Reaction to Construct $\gamma$-Peroxy Esters and 1,4-Dicarbonyl Compounds. *Chem. Commun.* **2015**, *51*, 14728−14731. (c) Giedyk, M.; Goliszewska, K.; ó Proinsias, K.; Gryko, D. Cobalt(I)-Catalysed CH-Alkylation of Terminal Olefins, and Beyond. *Chem. Commun.* **2016**, *52*, 1389−1392. (d) Huang, X.; Webster, R. D.; Harms, K.; Meggers, E. Asymmetric Catalysis with Organic Azides and Diazo Compounds Initiated by Photoinduced Electron Transfer. *J. Am. Chem. Soc.* **2016**, *138*, 12636−12642. (e) Li, P.; Zhao, J.; Shi, L.; Wang, J.; Shi, X.; Li, F. Iodine-Catalyzed Diazo Activation to Access Radical Reactivity. *Nat. Commun.* **2018**, *9*, 1972. (f) te Grotenhuis, C.; van den Heuvel, N.; van der Vlugt, J. I.; de Bruin, B. Catalytic Dibenzocyclooctene Synthesis via Cobalt(III)−Carbene Radical and *ortho*-Quinodimethane Intermediates. *Angew. Chem., Int. Ed.* **2018**, *57*, 140−145.

(5) Su, Y.-L.; Liu, G.-X.; Liu, J.-W.; Tram, L.; Qiu, H.; Doyle, M. P. Radical-Mediated Strategies for the Functionalization of Alkenes with Diazo Compounds. *J. Am. Chem. Soc.* **2020**, *142*, 13846−13855.

(6) (a) Ma, N.; Guo, L.; Qi, D.; Gao, F.; Yang, C.; Xia, W. Visible-Light-Induced Multicomponent Synthesis of $\gamma$-Amino Esters with Diazo Compounds. *Org. Lett.* **2021**, *23*, 6278−6282. (b) Fu, X.; Tang, J.; Hua, R.; Li, X.; Kang, Z.; Qiu, H.; Hu, W.

Functionalization of DNA-Tagged Alkenes with Diazo Compounds Via Photocatalysis. *Org. Lett.* **2022**, *24*, 2208−2213. (c) Li, F.; Zhu, S.; Koenigs, R. M. Photocatalytic 1,2-Oxo-Alkylation Reaction of Styrenes with Diazoacetates. *Chem. Commun.* **2022**, *58*, 7526−7529. (d) Liu, Y.; Zhu, K.; Zhao, J.; Li, P. Photocatalytic Regioselective Difunctionalization of Alkenes with Diazo Compounds and Tert-Butyl Nitrite: Access to γ-Oximino Esters. *Org. Lett.* **2022**, *24*, 6834−6838. (e) Su, Y.-L.; Liu, G.-X.; De Angelis, L.; He, R.; Al-Sayyed, A.; Schanze, K. S.; Hu, W.-H.; Qiu, H.; Doyle, M. P. Radical Cascade Multicomponent Minisci Reactions with Diazo Compounds. *ACS Catal.* **2022**, *12*, 1357−1363. (f) Zhang, B.; Qi, J.-Q.; Liu, Y.; Li, Z.; Wang, J. Visible-Light-Driven Bisfunctionalization of Unactivated Olefins Via the Merger of Proton-Coupled Electron Transfer and Carbene Catalysis. *Org. Lett.* **2022**, *24*, 279−283. (g) Datta, P.; Roy, D.; Jain, D.; Kumar, S.; Sil, S.; Bhunia, A.; Dasgupta, J.; Mandal, S. K. Uncovering the On-Pathway Reaction Intermediates for Metal-Free Atom Transfer Radical Addition to Olefins through Photogenerated Phenalenyl Radical Anion. *ACS Catal.* **2024**, *14*, 3420−3433. (h) Xie, Y.; Bao, Y.-P.; Zhuo, X.-Y.; Xuan, J. Photocatalytic Synthesis of Indanone, Pyrone, and Pyridinone Derivatives with Diazo Compounds as Radical Precursors. *Org. Lett.* **2024**, *26*, 1393−1398.

(7) Zhang, Z.; Kvasovs, N.; Dubrovina, A.; Gevorgyan, V. Visible Light Induced Brønsted Acid Assisted Pd-Catalyzed Alkyl Heck Reaction of Diazo Compounds and *N*-Tosylhydrazones. *Angew. Chem., Int. Ed* **2022**, *61*, No. e202110924.

(8) Xia, Y.; Qiu, D.; Wang, J. Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810−13889.

(9) During preparation of this manuscript, related work on hydroalkylation of allenes appeared: Karmakar, U.; Bae, J.; Kim, J. A.; Kim, S.; Yang, W.-G.; Cho, E. J. Nickel-Catalyzed Regio- and Stereoselective Hydroalkylation of Allenes: Exploiting the Unique Reactivity of Diazo Compounds as an Alkylating Source. *ACS Catal.* **2024**, *14*, 16570−16576.

(10) (a) Vogel, H.-H. Radical Addition of Carboxylic Acids and Carboxylic Acid Derivatives to Unsaturated Compounds as a Synthetic Method. *Synthesis* **1970**, *1970*, 99−140. (b) Lenardon, G. V. A.; Nicchio, L.; Fagnoni, M. Photogenerated Electrophilic Radicals for the Umpolung of Enolate Chemistry. *J. Photochem. Photobiol., C* **2021**, *46*, No. 100387. (c) Yamashita, Y.; Kobayashi, S. Efficient Radical-Mediated Intermolecular α-Alkylation Reactions of Carbonyl Compounds with Nonactivated Alkenes. *Chem.-Asian J.* **2024**, *19*, No. e202400319.

(11) (a) Franke, R.; Selent, D.; Börner, A. Applied Hydroformylation. *Chem. Rev.* **2012**, *112*, 5675−5732. (b) Wu, X.-F.; Fang, X.; Wu, L.; Jackstell, R.; Neumann, H.; Beller, M. Transition-Metal-Catalyzed Carbonylation Reactions of Olefins and Alkynes: A Personal Account. *Acc. Chem. Res.* **2014**, *47*, 1041−1053. (c) Ning, Y.; Ohwada, T.; Chen, F.-E. Transition Metal-Catalyzed Branch-Selective Hydroformylation of Olefins in Organic Synthesis. *Green Synth. Catal.* **2021**, *2*, 247−266. (d) Guo, J.; Cheng, Z.; Chen, J.; Chen, X.; Lu, Z. Iron- and Cobalt-Catalyzed Asymmetric Hydrofunctionalization of Alkenes and Alkynes. *Acc. Chem. Res.* **2021**, *54*, 2701−2716. (e) Chakrabortty, S.; Almasalma, A. A.; de Vries, J. G. Recent Developments in Asymmetric Hydroformylation. *Catal. Sci. Technol.* **2021**, *11*, 5388−5411.

(12) For hydrofunctionalization of alkenes proceeding via MHAT see: (a) Crossley, S. W. M.; Obradors, C.; Martinez, R. M.; Shenvi, R. A. Mn-, Fe-, and Co-Catalyzed Radical Hydrofunctionalizations of Olefins. *Chem. Rev.* **2016**, *116*, 8912−9000. (b) Shevick, S. L.; Wilson, C. V.; Kotesova, S.; Kim, D.; Holland, P. L.; Shenvi, R. A. Catalytic Hydrogen Atom Transfer to Alkenes: A Roadmap for Metal Hydrides and Radicals. *Chem. Sci.* **2020**, *11*, 12401−12422. (c) Wu, J.; Ma, Z. Metal-Hydride Hydrogen Atom Transfer (MHAT) Reactions in Natural Product Synthesis. *Org. Chem. Front.* **2021**, *8*, 7050−7076.

(13) Wang, Z.; Yin, H.; Fu, G. C. Catalytic Enantioconvergent Coupling of Secondary and Tertiary Electrophiles with Olefins. *Nature* **2018**, *563*, 379−383.

(14) Zhou, F.; Zhang, Y.; Xu, X.; Zhu, S. NiH-Catalyzed Remote Asymmetric Hydroalkylation of Alkenes with Racemic α-Bromo Amides. *Angew. Chem., Int. Ed.* **2019**, *58*, 1754−1758.

(15) Sun, S.-Z.; Cai, Y.-M.; Zhang, D.-L.; Wang, J.-B.; Yao, H.-Q.; Rui, X.-Y.; Martin, R.; Shang, M. Enantioselective Deaminative Alkylation of Amino Acid Derivatives with Unactivated Olefins. *J. Am. Chem. Soc.* **2022**, *144*, 1130−1137.

(16) (a) Zhang, Z.; Bera, S.; Fan, C.; Hu, X. Streamlined Alkylation Via Nickel-Hydride-Catalyzed Hydrocarbonation of Alkenes. *J. Am. Chem. Soc.* **2022**, *144*, 7015−7029. (b) Sun, X.-Y.; Yao, B.-Y.; Xuan, B.; Xiao, L.-J.; Zhou, Q.-L. Recent Advances in Nickel-Catalyzed Asymmetric Hydrofunctionalization of Alkenes. *Chem. Catal.* **2022**, *2*, 3140−3162. (c) Mirza, Y. K.; Bera, P. S.; Mohite, S. B.; Pandey, A. K.; Bera, M. Silanes as a Versatile Hydride Source for Ni−H Catalysis: A Promising Tool for π-Hydro Functionalization. *Org. Chem. Front.* **2024**, *11*, 4290−4317.

(17) Wang, Q.; Kweon, J.; Kim, D.; Chang, S. Remote Catalytic C(sp$^3$)−H Alkylation via Relayed Carbenoid Transfer upon Olefin Chain Walking. *J. Am. Chem. Soc.* **2024**, *146*, 31114−31123.

(18) (a) Yang, P.-F.; Zhu, L.; Liang, J.-X.; Zhao, H.-T.; Zhang, J.-X.; Zeng, X.-W.; Ouyang, Q.; Shu, W. Regio- and Enantioselective Hydroalkylations of Unactivated Olefins Enabled by Nickel Catalysis: Reaction Development and Mechanistic Insights. *ACS Catal.* **2022**, *12*, 5795−5805. (b) For the branched-selective hydroalkylation of alkenyl boranes see: Bera, S.; Fan, C.; Hu, X. Enantio- and Diastereoselective Construction of Vicinal C(sp$_3$) Centres Via Nickel-Catalysed Hydroalkylation of Alkenes. *Nat. Catal.* **2022**, *5*, 1180−1187.

(19) (a) Takeuchi, R.; Sagawa, J.; Fujii, M. Cationic Iridium Complex-Catalyzed Intermolecular Hydroalkylation of Unactivated Alkenes with 1,3-Diketones. *Org. Lett.* **2019**, *21*, 741−744. (b) Sawano, T.; Ogihara, K.; Sagawa, J.; Ono, M.; Takeuchi, R. Iridium-Catalyzed Hydroalkylation of Aliphatic Alkenes with β-Ketoesters: Formal Hydroalkylation with Methyl Ketones. *Org. Lett.* **2020**, *22*, 6187−6191. (c) Sawano, T.; Ono, M.; Iwasa, A.; Hayase, M.; Funatsuki, J.; Sugiyama, A.; Ishikawa, E.; Yoshikawa, T.; Sakata, K.; Takeuchi, R. Iridium-Catalyzed Branch-Selective Hydroalkylation of Simple Alkenes with Malonic Amides and Malonic Esters. *J. Org. Chem.* **2023**, *88*, 1545−1559.

(20) See the Supporting Information for details.

(21) (a) He, Y.; Song, H.; Chen, J.; Zhu, S. NiH-Catalyzed Asymmetric Hydroarylation of *N*-Acyl Enamines to Chiral Benzylamines. *Nat. Commun.* **2021**, *12*, 638. (b) Wang, J.-W.; Li, Y.; Nie, W.; Chang, Z.; Yu, Z.-A.; Zhao, Y.-F.; Lu, X.; Fu, Y. Catalytic Asymmetric Reductive Hydroalkylation of Enamides and Enecarbamates to Chiral Aliphatic Amines. *Nat. Commun.* **2021**, *12*, 1313. (c) Wang, S.; Zhang, J.-X.; Zhang, T.-Y.; Meng, H.; Chen, B.-H.; Shu, W. Enantioselective Access to Chiral Aliphatic Amines and Alcohols via Ni-Catalyzed Hydroalkylations. *Nat. Commun.* **2021**, *12*, 2771. (d) Cuesta-Galisteo, S.; Schörgenhumer, J.; Wei, X.; Merino, E.; Nevado, C. Nickel-Catalyzed Asymmetric Synthesis of α-Arylbenzamides. *Angew. Chem., Int. Ed.* **2021**, *60*, 1605−1609.

(22) (a) Romano, C.; Martin, R. Ni-Catalysed Remote C(sp$^3$)−H Functionalization Using Chain-Walking Strategies. *Nat. Rev. Chem.* **2024**, *8*, 833−850. (b) Velasco-Rubio, Á.; Martin, R. Recent Advances in Ni-Catalyzed 1,1-Difunctionalization of Unactivated Olefins. *Adv. Synth. Catal.* **2024**, *366*, 593−602.

(23) (a) Tran, V. T.; Li, Z.-Q.; Gallagher, T. J.; Derosa, J.; Liu, P.; Engle, K. M. Integrating Allyl Electrophiles into Nickel-Catalyzed Conjunctive Cross-Coupling. *Angew. Chem., Int. Ed.* **2020**, *59*, 7029−7034. (b) Cao, Y.; Li, Z.-Q.; Engle, K. M. Ni-Catalyzed 1,2-Diarylation of Unactivated Alkenes Directed by Diverse Azaheterocycles. *Tetrahedron Lett.* **2023**, *132*, No. 154764.

(24) (a) He, Y.; Cai, Y.; Zhu, S. Mild and Regioselective Benzylic C−H Functionalization: Ni-Catalyzed Reductive Arylation of Remote and Proximal Olefins. *J. Am. Chem. Soc.* **2017**, *139*,

1061−1064. (b) He, Y.; Liu, C.; Yu, L.; Zhu, S. Enantio- and Regioselective Nih-Catalyzed Reductive Hydroarylation of Vinylarenes with Aryl Iodides. *Angew. Chem., Int. Ed.* **2020**, *59*, 21530−21534. (c) Liu, C.-F.; Wang, Z.-C.; Luo, X.; Lu, J.; Ko, C. H. M.; Shi, S.-L.; Koh, M. J. Synthesis of Tri- and Tetrasubstituted Stereocentres by Nickel-Catalysed Enantioselective Olefin Cross-Couplings. *Nat. Catal.* **2022**, *5*, 934−942.

(25) (a) Lu, X.; Xiao, B.; Zhang, Z.; Gong, T.; Su, W.; Yi, J.; Fu, Y.; Liu, L. Practical Carbon−Carbon Bond Formation from Olefins through Nickel-Catalyzed Reductive Olefin Hydrocarbonation. *Nat. Commun.* **2016**, *7*, 11129. (b) Bera, S.; Hu, X. Nickel-Catalyzed Regioselective Hydroalkylation and Hydroarylation of Alkenyl Boronic Esters. *Angew. Chem., Int. Ed.* **2019**, *58*, 13854−13859.

(26) Sommer, H.; Juliá-Hernández, F.; Martin, R.; Marek, I. Walking Metals for Remote Functionalization. *ACS Cent. Sci.* **2018**, *4*, 153−165.

https://doi.org/10.1021/jacs.4c17586
J. Am. Chem. Soc. 2025, 147, 8093−8100