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Iron-catalyzed three-component 1,2-azidoalkylation of conjugated dienes *via* activation of aliphatic C–H bonds†

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Azidoalkylation is an efficient strategy for the conversion of unsaturated precursors into nitrogen-containing structural motifs. Herein, we describe a convenient and highly regioselective iron-catalyzed 1,2-azidoalkylation of 1,3-dienes that employs TMSN_3 as a coupling partner with hydrocarbons that bear diverse C–H bonds. This chemistry is achieved through the direct functionalization of strong $\text{C}(\text{sp}^3)\text{--H}$ bonds and is facilitated by a combination of hydrogen atom transfer (HAT) and iron catalysis. Notably, the protocol operates with catalyst loadings as low as 0.2 mol% and furnishes access to versatile β -unsaturated azido products with high levels of site-, regio-, and stereoselectivities. Mechanistic studies suggest that the reaction proceeds *via* a radical pathway; depending on the electronic properties of the diene, the allylic radical intermediate may engage through either group transfer or a single electron oxidation process.

Introduction

The selective transformation of feedstock chemicals into value-added molecules is a key objective of modern synthetic chemistry, where the development of new methods offers significant potential to simplify synthetic routes and modify complex molecules through later-stage functionalization. Conjugated dienes are a readily available class of synthetic precursors that have emerged as a versatile platform for the efficient preparation of more elaborate building blocks.¹ Over the past few decades, extensive research has focused on transition metal-catalyzed difunctionalizations of 1,3-dienes.^{2–5} This process typically involves the generation of a metal–carbon species, followed by migratory insertion to form an allyl metal intermediate (Scheme 1A).^{6–18} The use of dienes as substrates introduces additional challenges that include the high reactivity of allylic intermediates generated from azidation of 1,3-dienes, as well as control over the site-, regio-, and *Z/E*-selectivities. Additionally, side reactions such as polymerization can further reduce the efficiency of the reaction. In prior work, we developed iron-catalyzed site- and regioselective 1,2-azidoamidations of 1,3-dienes, utilizing *N*-fluorobenzenesulfonimide (NFSI) as a dual oxidant and radical precursor to furnish versatile precursors to 1,2-diamines (Scheme 1B).¹⁹

The majority of the current methodologies for the carboazidation of alkenes require pre-functionalized radical

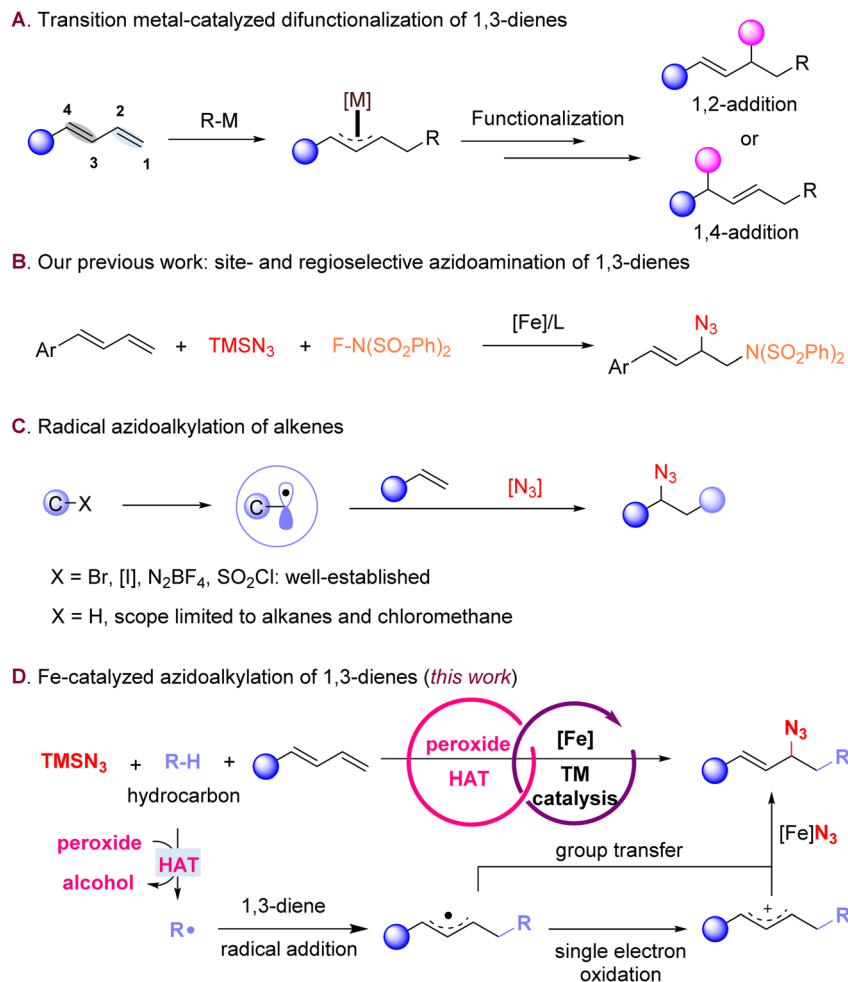
precursors, such as alkyl halides, alkyl sulfonyl chlorides, or Togni-type reagents; this need adds additional steps and reduces the overall efficiency of the process (Scheme 1C).^{20–27} The $\text{C}(\text{sp}^3)\text{--H}$ bonds of hydrocarbons are abundant chemical feedstocks, but display relatively high bond dissociation energies (BDEs) and low bond polarity, challenges that must be overcome to use them as radical precursors.^{28–31} Therefore, the development of carboazidation approaches that can directly activate a wide variety of simple hydrocarbons is highly desirable. In this context, hydrogen atom transfer (HAT) is an appealing strategy for the homolytic cleavage of diverse $\text{C}(\text{sp}^3)\text{--H}$ bonds.^{32–37}

Organic azides are an important class of molecules that are present in many natural products and bioactive molecules; in addition, the azide is a highly versatile handle for subsequent organic transformations.^{38–41} The Luo⁴² and Nishihara groups⁴³ reported the azidoalkylation of terminal styrenes using Fe or Cu catalysts, respectively; however, the C–H partners were limited to cycloalkanes, chloroalkanes, or cyclic ethers. More recently, Feng and coworkers described the asymmetric azidoalkylation of activated alkenes, but substrates were restricted to α -aryl-substituted aryl enones.⁴⁴ Although these reports advanced the state-of-the-art,^{22–24,42–47} carboazidations of 1,3-dienes *via* direct C–H activation is still underdeveloped, particularly in applications to more complex molecular scaffolds. There are only a few reported examples where the hydrocarbon coupling partner is limited to dichloromethane,⁴⁵ aldehydes^{48,49} and acetonitrile.⁵⁰

We envisioned that combining azidation with an HAT process that is compatible with diverse hydrocarbon coupling partners could provide efficient carboazidation of 1,3-dienes to

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Scheme 1 Radical azido-difunctionalization of alkenes and 1,3-dienes.

furnish allylic azides as useful precursors to amine building blocks for syntheses of bioactive and pharmaceutically relevant compounds (Scheme 1D).^{23–25,39–41} Herein, we describe the 1,2-azidoalkylation of diverse 1,3-dienes employing a broad array of inexpensive hydrocarbon chemical feedstocks. The chemistry proceeds through the direct and selective activation of the aliphatic C–H bonds and merges HAT with iron-catalyzed azidation. The reaction mechanism depends on the electronic features of the 1,3-diene precursor and proceeds *via* a single-electron transfer/HAT/radical addition through either group transfer or a single-electron oxidation process to construct the new C–C bond.

Results and discussion

Our study of the three-component azidoalkylation reaction commenced using 1-phenyl-1,3-butadiene **1a** as the model substrate, toluene as both the radical precursor and the solvent, di-*tert*-butyl peroxide (DTBP) as an oxidant and Fe(OTf)₂ as the catalyst. We found that the use of only a 0.5 mol% loading of the catalyst, coupled with vigorous stirring of the reaction mixture at 110 °C under nitrogen for 16 h, resulted in the desired adduct

1 in a yield of 70% (Table 1, entry 1). Next, different catalyst loadings were explored; results indicated that increasing the amount of catalyst increased the formation of unwanted diazidation products, while reducing the loading gave diminished reactivity (entries 2–5). A variety of other iron salts were investigated (entries 6–11); however, Fe(OTf)₂ proved to be the optimal catalyst. Control experiments underscored the necessity for both the iron salt and heat for the reaction to proceed (entries 12 and 13). Furthermore, substituting DTBP with either *tert*-butylperoxybenzoate (TBPB) or *tert*-butylhydroperoxide (TBHP) resulted in no detectable amount of 1,2-azido benzylation product **1** (entries 13, 14).

With the optimal reaction conditions in hand, the scope of the radical azidoalkylation reaction was investigated by evaluating an array of 1,3-dienes, as shown in Table 2. First, diverse 1-phenyl-1,3-butadienes, bearing both electron-donating and electron-withdrawing substituents at the *para*-, *meta*-, or *ortho*-positions of the phenyl group, were explored and found to be suitable substrates in this protocol. The corresponding azidoalkylation products **3–19** were obtained in good yields with high levels of regio-, site- and stereocontrol, largely favoring 1,2-over 1,4-addition and selectively installing the azide at the more

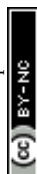
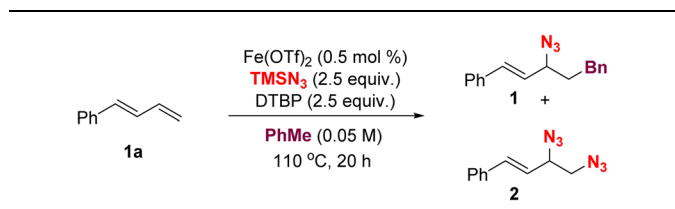
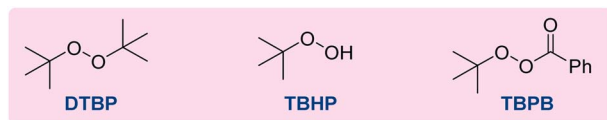


Table 1 Optimization of reaction conditions^a

Entry	Variation from standard conditions	Yield ^b (1/2)/%
1	None	70/<5
2	1 mol% of $\text{Fe}(\text{OTf})_2$	53/10
3	2 mol% of $\text{Fe}(\text{OTf})_2$	35/30
4	0.2 mol% of $\text{Fe}(\text{OTf})_2$	62/<5
5	0.1 mol% of $\text{Fe}(\text{OTf})_2$	24/<5
6	FeCl_2 instead of $\text{Fe}(\text{OTf})_2$	21/<5
7	FeBr_2 instead of $\text{Fe}(\text{OTf})_2$	41/<5
8	FeSO_4 instead of $\text{Fe}(\text{OTf})_2$	20/<5
9	FeCl_3 instead of $\text{Fe}(\text{OTf})_2$	44/<5
10	$\text{Fe}(\text{acac})_3$ instead of $\text{Fe}(\text{OTf})_2$	45/<5
11	$\text{Fe}(\text{OTf})_3$ instead of $\text{Fe}(\text{OTf})_2$	58/12
12	w/o $\text{Fe}(\text{OTf})_2$	<5
13	Conducted at room temperature	<5
14	TBPB instead of DTBP	<5
15	TBHP instead of DTBP	<5



^a Reaction conditions: **1** (0.10 mmol), TMSN_3 (0.25 mmol), DTBP (0.25 mmol), $\text{Fe}(\text{OTf})_2$ (0.5 mol%), toluene (2 mL), 20 h, under N_2 .

^b Determined by ^1H NMR analysis using 1,3,5-triacetylbenzene as an internal standard.

substituted C3 carbon of the diene. In general, electron-rich and electron-neutral 1-arylsubstituted dienes tended to give higher yields (3–7) as compared to those bearing electron-poor aryl substituents (8–14). Dienes bearing pharmaceutically important heteroaryl groups that include naphthalene, indole, benzofuran and thiophene effectively furnished the target azides **20–23** in moderate yields. Notably, introducing an additional alkyl substituent on the C1, C2 or C3 position of the 1-phenyl-1,3-butadiene gave smooth conversion to the corresponding products **24–26** in moderate-to-good yields and *E/Z* selectivity. The non-terminal 1,3-diene **27a** was also tolerated, delivering the corresponding adduct **27** in 36% yield and in a 1 : 1.1 diastereomeric ratio (dr). Additionally, alkyl-substituted 1,3-butadienes were effective in the azidoalkylation, affording the desired products **28** in 63% yield and **29** in 39% yield with 1 : 1.2 site-selectivity, respectively. Finally, 1,3-dienes tethered to bioactive molecules, including menthol, borneol, ibuprofen, citronellol, gemfibrozil, cholesterol and tocopherol, all reacted smoothly in the three-component coupling to deliver the target products **30–36** in moderate-to-good yield and excellent *Z/E* selectivities, showcasing the utility of this chemistry in more complex molecule settings.

The scope of aliphatic C–H coupling partners was examined next with a series of substituted 1-methylarenes (Table 3). Electron-donating and electron-withdrawing substituents at the *para* position of the phenyl group were well-tolerated to deliver the azides **37–46** with moderate-to-good yields. Compared with the C–H bond located α to oxygen, the benzylic position of 4-methylanisole proved more reactive to furnish **39** in 46% yield. In the case of 4-methylcumene, a 31% yield and 1 : 1.2 rr of **46** was observed. When substituents on the phenyl group were moved from the *p*- to *m*- or *o*-positions, the corresponding products **47–52** were afforded in good yield. A 3-methyl thiophene served as an alkylating agent to afford the heteroarene product **53**. Moreover, 2,3-dimethylbutane preferentially reacted at the tertiary C–H bonds to furnish **54** in 54% yield with a 6 : 1 rr and in 9 : 1 site-selectivity. Cycloalkanes of varying ring sizes (5-to-8 carbons) proceeded smoothly to provide the corresponding products **55–58** in moderate-to-good yields. Additionally, isopropyl ether, anisole and methyl *tert*-butyl ether displayed a preference for the α -oxy alkylated products **59–61**. *N,N*-dimethylamide gave a low yield of **62**, while a thiol ether **63a** and an acetal **64a** gave **63–64** in moderate yields. Unfortunately, the use of methanol as the source of the carbon-centered radical gave **65** in low yield. Both acetone and acetonitrile were capable of serving as the radical coupling partner to furnish the corresponding azides **66** and **67**. The tertiary C–H bonds of methyl isobutyrate engaged the diene to furnish azide **68** in 66% yield, with a 6 : 1 rr and in 20 : 1 site-selectivity. Notably, the C–H bond of an aldehyde group in **69a** and **70a** could be cleaved and added to the terminal carbon of the 1,3-diene to give the azido-carbonylation products **69** and **70** in moderate yields. However, alkyl aldehydes or formate resulted in decarbonylation and decarboxylation to yield **71** and **72**.

The synthetic utility of the azidoalkylation chemistry was demonstrated by carrying out selected post-functionalizations of azide **3** (Scheme 2). The reaction of **3a** was conducted on a larger scale employing slightly adjusted conditions to furnish **3** in 76% yield. Treatment of the azide **3** with $\text{P}(\text{OEt})_3$ yielded the phosphoramidate **73**. Compound **3** was readily reduced using $\text{PPh}_3/\text{H}_2\text{O}$ and subjected to amidation to give **74**, followed by subsequent ring-closing metathesis with Grubbs II at low concentrations to generate the target lactam **75**. The azide was readily transformed to the primary amine **76** via reduction of **3** with $\text{Pd}(\text{OH})_2/\text{C}$ and H_2 , while a copper-catalyzed Huisgen cycloaddition between azide **3** and phenylacetylene delivered the corresponding triazole **77** in a 93% yield. Treatment of the azides **66** and **68** with $\text{PPh}_3/\text{H}_2\text{O}$ furnished the subsequent imidization product **78** and lactam **79** in excellent yields of 92% and 98%, respectively.

To gain additional insights into the mechanism of this diene azidoalkylation reaction, we conducted a series of mechanistic probe experiments. The addition of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to the reaction of **3a** under the standard conditions completely inhibited the formation of the desired product **3**. The TEMPO-trapped adduct **81** was detected by high-resolution mass spectrometry, supporting the intermediacy of a benzylic radical likely generated from HAT from toluene by the *tert*-butoxyl radical (Scheme 3a, reaction 1).



Table 2 Substrate scope for 1,3-dienes^a

R OMe 3 80% yield ^b Me 4 69% yield ^b F 5 78% yield Cl 6 61% yield Br 7 72% yield	R OAc 8 45% yield OCF ₃ 9 63% yield CO ₂ Et 10 51% yield CF ₃ 11 49% yield SCF ₃ 12 52% yield
14 40% yield	13 37% yield
20 46% yield	21 45% yield
22 38% yield	23 44% yield
24 42% yield 3:1 E/Z	25 55% yield 8:1 E/Z
26 64% yield	27 36% yield 1:1.1 dr
28 63% yield	29 39% yield site-selectivity ^c = 1.2:1
30 , from menthol 50% yield	31 , from borneol 41% yield
32 , from ibuprofen 61% yield	33 , from citronellol 55% yield
34 , from gemfibrozil 50% yield	35 , from cholesterol 45% yield
36 , from tocopherol 39% yield	

^a Unless indicated, reactions were run with the 1,3-diene (0.1 mmol), TMSN₃ 2 (0.25 mmol), DTBP (0.25 mmol), Fe(OTf)₂ (0.0005 mmol), PhMe (2 mL), 110 °C, under N₂, 16 h. ^b 0.2 mol% of Fe(OTf)₂ was used. ^c Ratio of 1,2- and 1,4-addition.

Notably, when an electron-donating group (EDG) was present on the C1 phenyl ring in **3a**, the allylic radical-trapped product **80a** was not observed (Scheme 3a, reaction 1). However, with the introduction of an electron-withdrawing group (EWG) to the

phenyl ring of **10a**, **80b** was detected (Scheme 3a, reaction 2). As suggested by these experiments, the more electron-deficient allylic radical has a longer lifetime as compared to the more electron-rich allylic radical, indicating that a dual mechanistic

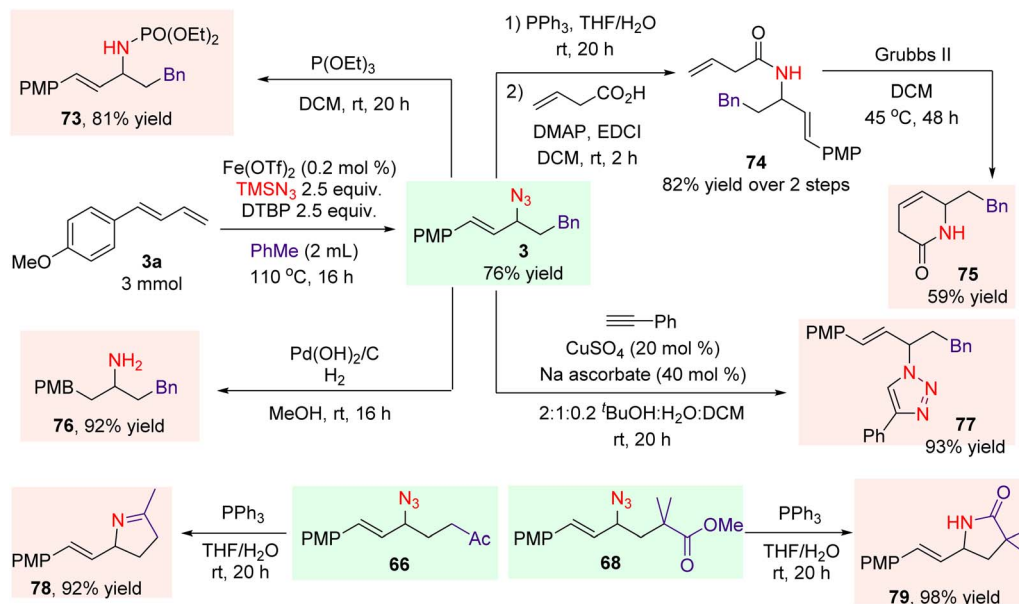
Table 3 Exploring the scope of aliphatic C–H coupling partners in the azidoalkylation of **3a**^a

		37	74% yield		
		38	55% yield		
		39	46% yield		
		40	56% yield		
		41	43% yield ^b		
		47	72% yield		
		49	61% yield		
		51	60% yield ^b		
		53	55% yield		
		55	57% yield ^b		
		57	48% yield ^b		
		59	31% yield ^b		
		61	35% yield ^b site-selectivity ^e = 20:1		
		63	65% yield ^b		
		65	15% yield		
		67	26% yield		
		69	34% yield ^c		
		71	59% yield ^d from <i>iso</i> -butyl aldehyde		
		72	36% yield site-selectivity ^e = 13:1 from <i>tert</i> -butyl formate		

^a Unless indicated, reactions were run with 1,3-diene (0.1 mmol), TMSN₃ (0.25 mmol), DTBP (0.25 mmol), Fe(OTf)₂ (0.0002 mmol), R–H (2 mL), 110 °C, under N₂, 16 h. ^b R–H/PhH = 1/1 (2 mL) as solvent. ^c R–H/MeCN = 1/1 (2 mL) as solvent. ^d 10 equiv. of R–H, PhH (2 mL) as solvent. ^e Ratio of 1,2- and 1,4-addition.

pathway might exist in this reaction. The reaction of the radical clock **82** also supported the existence of a radical pathway, as the ring-opened **83** was obtained in 34% yield in a 16:1 *E*:*Z* ratio, suggesting that the *in situ*-generated cyclopropylcarbonyl radical undergoes fast ring-opening to give an allylic radical, which is then rapidly trapped by the azide radical (Scheme 3b).

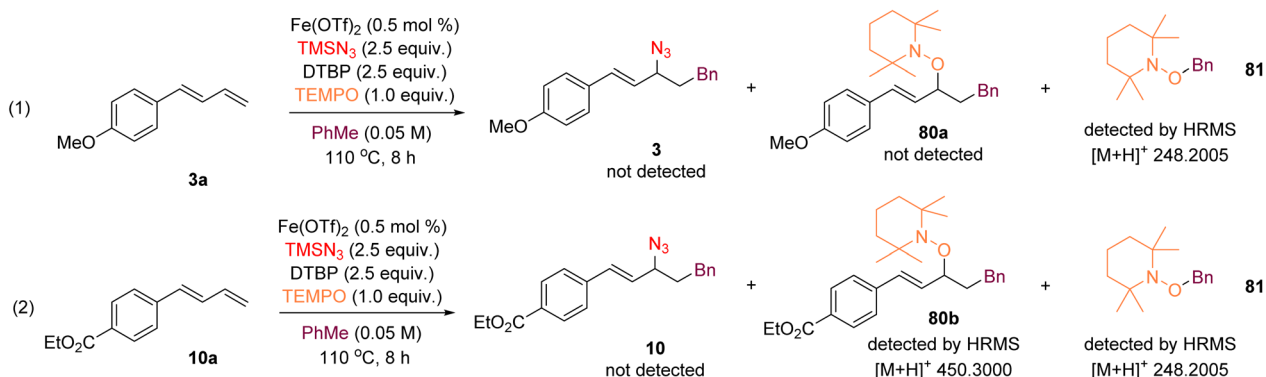
In addition, a kinetic isotope effect experiment clearly showed that such an effect was present, as a KIE of 3.03 (*k*_H/*k*_D) was observed for the reaction of diene **1a** in toluene and toluene-*d*₈ (Scheme 3c), suggesting that the aliphatic C–H bond cleavage might be involved in the rate-determining step of the reaction. We also conducted parallel KIE experiments and observed a KIE

Scheme 2 Derivatizations of the azidoalkylation product **3**.

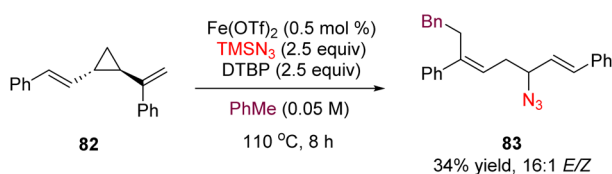
of 2.22 ($k_{\text{H}}/k_{\text{D}}$) (see the ESI† for details), also supporting the likelihood that C–H bond cleavage is involved in the rate-determining step of the reaction. Finally, we conducted

a series of Hammett studies (Scheme 3d). The negative slope of the Hammett plot indicated the possibility that allylic cation intermediates might be generated during the reaction.

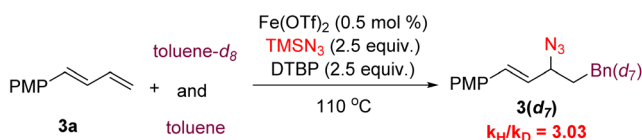
a Reaction in the presence of TEMPO



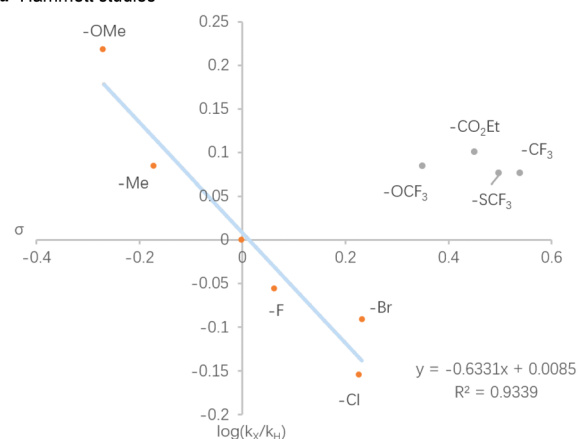
b Radical clock experiment



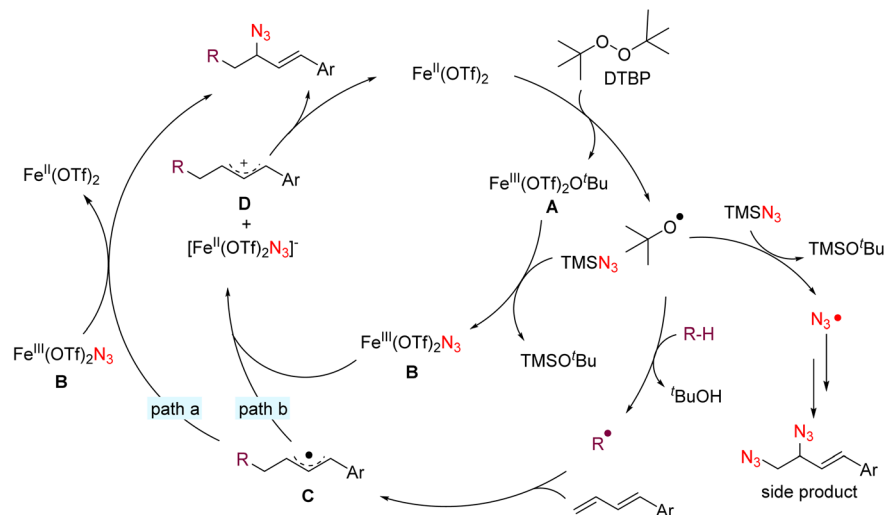
c Kinetic isotope effect experiment



d Hammett studies



Scheme 3 Mechanistic studies.



Scheme 4 Proposed catalytic cycle.

However, when electron-withdrawing groups (OCF_3 , CO_2Et , SCF_3 , CF_3) were introduced on the aryl group of the substrates, the expected negative trend was not observed (Scheme 3d), indicating that electron-deficient 1,3-dienes likely proceed through allylic radical intermediates, followed by a group transfer process to generate the final products.

Based on our mechanistic studies, a plausible mechanism for the Fe-catalyzed azidoalkylation of 1,3-dienes is proposed in Scheme 4. First, a single-electron oxidation process occurs through the reaction of the iron(II) trifluoromethanesulfonate complex with DTBP to produce an oxidized iron species A and a *tert*-butoxyl radical. Intermediate A then reacts with TMSN_3 to produce the iron(III) azide species B. The *tert*-butoxyl radical then selectively abstracts an H-atom from the coupling partner to generate the alkyl radical $\text{R}^\bullet$. This carbon-centered radical may add to the terminal carbon atom of the 1,3-diene to selectively generate the allylic radical C. This allylic radical intermediate is subsequently captured by B. In pathway a, electron-deficient dienes are more likely to be favored. A group transfer process leads to the formation of the final product and regenerates the active iron catalyst. In contrast, electron-rich dienes are expected to proceed *via* pathway b, where a single-electron transfer (SET) occurs first between the iron(III) azide B and C, which is then followed by nucleophilic attack by the azide species. In addition, the *tert*-butoxyl radical can potentially abstract the TMS group from TMSN_3 , which leads to the generation of a free azido radical ($\text{N}_3^\bullet$). A similar process may occur to furnish the undesired diazidation product from the 1,3-diene precursor, thereby reducing the overall conversion to the desired azidoalkylation product.

Conclusion

In conclusion, we have described a practical iron-catalyzed azidoalkylation of 1,3-dienes based on the direct and selective abstraction of aliphatic C–H bonds enabled by a HAT process. A wide array of commercially available hydrocarbons bearing

diverse C–H bonds were employed in the coupling to provide access to synthetically useful amines. Mechanistic studies indicated that the electronic properties of the precursor 1,3-dienes influence the mechanistic pathway of the transformation, with reaction proceeding *via* either group transfer for electron-deficient 1,3-dienes or sequential single-electron transfer and nucleophilic attack for electron-rich 1,3-dienes to furnish the azidoalkylation products.

Data availability

The data supporting this article have been included as part of the ESI.†

Author contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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References

- 1 X. Li, C. Pei and J. Gong, Shale Gas Revolution: Catalytic Conversion of C₁–C₃ Light Alkanes to Value-Added Chemicals, *Chem*, 2021, 7, 1755–1801.
- 2 X. Wu and L.-Z. Gong, Palladium(0)-Catalyzed Difunctionalization of 1,3-Dienes: From Racemic to Enantioselective, *Synthesis*, 2019, 51, 122–134.
- 3 Y. Xiong, Y. Sun and G. Zhang, Recent Advances on Catalytic Asymmetric Difunctionalization of 1,3-Dienes, *Tetrahedron Lett.*, 2018, 59, 347–355.
- 4 P.-Z. Wang, W.-J. Xiao and J.-R. Chen, Recent Advances in Radical-Mediated Transformations of 1,3-Dienes, *Chin. J. Catal.*, 2022, 43, 548–557.
- 5 E. McNeill and T. Ritter, 1,4-Functionalization of 1,3-Dienes With Low-Valent Iron Catalysts, *Acc. Chem. Res.*, 2015, 48, 2330–2343.
- 6 K. Chen, H. Zhu, S. Liu, J. Bai, Y. Guo, K. Ding, Q. Peng and X. Wang, Switch in Selectivities by Dinuclear Nickel Catalysis: 1,4-Hydroarylation of 1,3-Dienes to Z-Olefins, *J. Am. Chem. Soc.*, 2023, 145, 24877–24888.
- 7 H. Wang, R. Zhang and W. Zi, Synergistic Palladium/Copper-Catalyzed 1,4-Difunctionalization of 1,3-Dienes for Stereodivergent Construction of 1,5-Nonadjacent Stereocenters, *Angew. Chem., Int. Ed.*, 2024, 63, e202402843.
- 8 X.-Y. Ruan, D.-X. Wu, W.-A. Li, Z. Lin, M. Sayed, Z.-Y. Han and L.-Z. Gong, Photoinduced Pd-Catalyzed Enantioselective Carboamination of Dienes via Aliphatic C–H Bond Elaboration, *J. Am. Chem. Soc.*, 2024, 146, 12053–12062.
- 9 Y. Xiong and G. Zhang, Enantioselective 1,2-Difunctionalization of 1,3-Butadiene by Sequential Alkylation and Carbonyl Allylation, *J. Am. Chem. Soc.*, 2018, 140, 2735–2738.
- 10 Y. Li, Y. Dong, X. Wang, G. Li, H. Xue, W. Xin, Q. Zhang, W. Guan and J. Fu, Regio-, Site-, and Stereoselective Three-Component Aminofluorination of 1,3-Dienes via Cooperative Silver Salt and Copper Catalysis, *ACS Catal.*, 2023, 13, 2410–2421.
- 11 L.-F. Fan, R. Liu, X.-Y. Ruan, P.-S. Wang and L.-Z. Gong, Asymmetric 1,2-Oxidative Alkylation of Conjugated Dienes via Aliphatic C–H Bond Activation, *Nat. Synth.*, 2022, 1, 946–955.
- 12 N. H. Watkins, Y. Kwon and Q. Wang, Copper-Catalyzed 1,4-Aminohydroxylation and Aminothiolation of 1,3-Dienes by Carbonyl-Assisted Migration, *Chem Catal.*, 2024, 4, 101147.
- 13 S.-S. Chen, M.-S. Wu and Z.-Y. Han, Palladium-Catalyzed Cascade Sp² C–H Functionalization/Intramolecular Asymmetric Allylation: From Aryl Ureas and 1,3-Dienes to Chiral Indolines, *Angew. Chem., Int. Ed.*, 2017, 56, 6641–6645.
- 14 M. M. Parsutkar and T. V. RajanBabu, α - and β -Functionalized Ketones from 1,3-Dienes and Aldehydes: Control of Regio- and Enantioselectivity in Hydroacylation of 1,3-Dienes, *J. Am. Chem. Soc.*, 2021, 143, 12825–12835.
- 15 X. Pang, Z.-Z. Zhao, X.-X. Wei, L. Qi, G.-L. Xu, J. Duan, X.-Y. Liu and X.-Z. Shu, Regiocontrolled Reductive Vinylation of Aliphatic 1,3-Dienes with Vinyl Triflates by Nickel Catalysis, *J. Am. Chem. Soc.*, 2021, 143, 4536–4542.
- 16 X.-H. Yang and V. M. Dong, Rhodium-Catalyzed Hydrofunctionalization: Enantioselective Coupling of Indolines and 1,3-Dienes, *J. Am. Chem. Soc.*, 2017, 139, 1774–1777.
- 17 S. M. Thullen and T. Rovis, A Mild Hydroaminoalkylation of Conjugated Dienes Using a Unified Cobalt and Photoredox Catalytic System, *J. Am. Chem. Soc.*, 2017, 139, 15504–15508.
- 18 F. Burg and T. Rovis, Diastereoselective Three-Component 3,4-Amino Oxygenation of 1,3-Dienes Catalyzed by a Cationic Heptamethylindenyl Rhodium(III) Complex, *J. Am. Chem. Soc.*, 2021, 143, 17964–17969.
- 19 Z.-Y. Dai, I. A. Guzei and J. M. Schomaker, Iron-Catalyzed Site- and Regioselective 1,2-Azidoamidations of 1,3-Dienes, *Org. Lett.*, 2024, 26, 269–273.
- 20 F. Wang, X. Qi, Z. Liang, P. Chen and G. Liu, Copper-Catalyzed Intermolecular Trifluoromethylazidation of Alkenes: Convenient Access to CF₃-Containing Alkyl Azides, *Angew. Chem.*, 2014, 126, 1912–1917.
- 21 L. Xu, X.-Q. Mou, Z.-M. Chen and S.-H. Wang, Copper-Catalyzed Intermolecular Azidocyanation of Aryl Alkenes, *Chem. Commun.*, 2014, 50, 10676–10679.
- 22 L. Ge, H. Zhou, M.-F. Chiou, H. Jiang, W. Jian, C. Ye, X. Li, X. Zhu, H. Xiong, Y. Li, L. Song, X. Zhang and H. Bao, Iron-Catalysed Asymmetric Carboazidation of Styrenes, *Nature Catal.*, 2020, 4, 28–35.
- 23 W. Liu, M. Pu, J. He, T. Zhang, S. Dong, X. Liu, Y.-D. Wu and X. Feng, Iron-Catalyzed Enantioselective Radical Carboazidation and Diazidation of α,β -Unsaturated Carbonyl Compounds, *J. Am. Chem. Soc.*, 2021, 143, 11856–11863.
- 24 Y.-A. Yuan, D.-F. Lu, Y.-R. Chen and H. Xu, Iron-Catalyzed Direct Diazidation for a Broad Range of Olefins, *Angew. Chem.*, 2016, 128, 544–548.
- 25 L. Wu, Z. Zhang, D. Wu, F. Wang, P. Chen, Z. Lin and G. Liu, Anionic Bisoxazoline Ligands Enable Copper-Catalyzed Asymmetric Radical Azidation of Acrylamides, *Angew. Chem., Int. Ed.*, 2021, 60, 6997–7001.
- 26 H. Xiong, N. Ramkumar, M.-F. Chiou, W. Jian, Y. Li, J.-H. Su, X. Zhang and H. Bao, Iron-Catalyzed Carboazidation of Alkenes and Alkynes, *Nat. Commun.*, 2019, 10, 122.
- 27 F. Wang, X. Qi, Z. Liang, P. Chen and G. Liu, Copper-Catalyzed Intermolecular Trifluoromethylazidation of Alkenes: Convenient Access to CF₃-Containing Alkyl Azides, *Angew. Chem., Int. Ed.*, 2014, 53, 1881–1886.
- 28 C. S. Day, A. Fawcett, R. Chatterjee and J. F. Hartwig, Mechanistic Investigation of the Iron-Catalyzed Azidation of Alkyl C(Sp³)–H Bonds with Zhdankin's Λ^3 -Azidoiodane, *J. Am. Chem. Soc.*, 2021, 143, 16184–16196.
- 29 Z.-Y. Dai, S.-Q. Zhang, X. Hong, P.-S. Wang and L.-Z. Gong, A Practical FeCl₃/HCl Photocatalyst for Versatile Aliphatic C–H Functionalization, *Chem Catal.*, 2022, 2, 1211–1222.



- 30 Y. Wang, P. Hu, J. Yang, Y.-A. Zhu and D. Chen, C–H Bond Activation in Light Alkanes: A Theoretical Perspective, *Chem. Soc. Rev.*, 2021, **50**, 4299–4358.
- 31 O. Baudoin, Multiple Catalytic C–H Bond Functionalization for Natural Product Synthesis, *Angew. Chem., Int. Ed.*, 2020, **59**, 17798–17809.
- 32 M. Rivas, V. Palchykov, X. Jia and V. Gevorgyan, Recent Advances in Visible Light-Induced C(Sp³)–N Bond Formation, *Nat. Rev. Chem.*, 2022, **6**, 544–561.
- 33 L. Capaldo, D. Ravelli and M. Fagnoni, Direct Photocatalyzed Hydrogen Atom Transfer (HAT) for Aliphatic C–H Bonds Elaboration, *Chem. Rev.*, 2022, **122**, 1875–1924.
- 34 J. Zhang and M. Rueping, Metallaphotoredox Catalysis for Sp³ C–H Functionalizations through Hydrogen Atom Transfer (HAT), *Chem. Soc. Rev.*, 2023, **52**, 4099–4120.
- 35 S. Zhang and M. Findlater, Electrochemically Driven Hydrogen Atom Transfer Catalysis: A Tool for C(Sp³)/Si–H Functionalization and Hydrofunctionalization of Alkenes, *ACS Catal.*, 2023, **13**, 8731–8751.
- 36 L.-C. Wang, Y. Yuan, Y. Zhang and X.-F. Wu, Cobalt-Catalyzed Aminoalkylative Carbonylation of Alkenes toward Direct Synthesis of γ -Amino Acid Derivatives and Peptides, *Nat. Commun.*, 2023, **14**, 7439.
- 37 D. L. Golden, S.-E. Suh and S. S. Stahl, Radical C(Sp³)–H Functionalization and Cross-Coupling Reactions, *Nat. Rev. Chem.*, 2022, **6**, 405–427.
- 38 S. Bräse, C. Gil, K. Knepper and V. Zimmermann, Organic Azides: An Exploding Diversity of a Unique Class of Compounds, *Angew. Chem., Int. Ed.*, 2005, **44**, 5188–5240.
- 39 M. Shee and N. D. Pradeep Singh, Chemical Versatility of Azide Radical: Journey from a Transient Species to Synthetic Accessibility in Organic Transformations, *Chem. Soc. Rev.*, 2022, **51**, 2255–2312.
- 40 K. Wu, Y. Liang and N. Jiao, Azidation in the Difunctionalization of Olefins, *Molecules*, 2016, **21**, 352.
- 41 M. Goswami and B. de Bruin, Metal-Catalysed Azidation of Organic Molecules, *Eur. J. Org. Chem.*, 2017, **8**, 1152–1176.
- 42 W.-Y. Li, C.-S. Wu, Z. Wang and Y. Luo, Fe-Catalyzed Three-Component Carboazidation of Alkenes with Alkanes and Trimethylsilyl Azide, *Chem. Commun.*, 2018, **54**, 11013–11016.
- 43 Y. Ikemoto, S. Chiba, Z. Li, Q. Chen, H. Mori and Y. Nishihara, Carboazidation of Terminal Alkenes with Trimethylsilyl Azide and Cyclic Ethers Catalyzed by Copper Powder under Oxidative Conditions, *J. Org. Chem.*, 2023, **88**, 4472–4480.
- 44 L. Ge, H. Wang, Y. Liu and X. Feng, Asymmetric Three-Component Radical Alkene Carboazidation by Direct Activation of Aliphatic C–H Bonds, *J. Am. Chem. Soc.*, 2024, **146**, 13347–13355.
- 45 L. Xu, J. Chen and L. Chu, Solvent-Tuned Chemoselective Carboazidation and Diazidation of Alkenes via Iron Catalysis, *Org. Chem. Front.*, 2019, **6**, 512–516.
- 46 P. Sivaguru, Y. Ning and X. Bi, New Strategies for the Synthesis of Aliphatic Azides, *Chem. Rev.*, 2021, **121**, 4253–4307.
- 47 P. Palamini, E. M. D. Allouche and J. Waser, Iron-Catalyzed Synthesis of α -Azido α -Amino Esters via the Alkylazidation of Alkenes, *Org. Lett.*, 2023, **25**, 6791–6795.
- 48 L. Ge, Y. Li and H. Bao, Iron-Catalyzed Radical Acyl-Azidation of Alkenes with Aldehydes: Synthesis of Unsymmetrical β -Azido Ketones, *Org. Lett.*, 2019, **21**, 256–260.
- 49 W.-Y. Li, Q.-Q. Wang and L. Yang, Fe-Catalyzed Radical-Type Difunctionalization of Styrenes with Aliphatic Aldehydes and Trimethylsilyl Azide via a Decarbonylative Alkylation–Azidation Cascade, *Org. Biomol. Chem.*, 2017, **15**, 9987–9991.
- 50 J.-W. Hu, Y. Zhong and R.-J. Song, Copper/Iron Controlled Regioselective 1,2-Carboazidation of 1,3-Dienes with Acetonitrile and Azidotrimethylsilane, *Org. Biomol. Chem.*, 2025, **23**, 1437–1442.

