Letter

Visible-Light-Mediated (*sp*^{3})C*α*−H Functionalization of Ethers Enabled by Electron Donor−Acceptor Complex

Sourav Roy and Indranil Chatterjee*

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A synthetically beneficial visible-light-mediated protocol has been disclosed to achieve C−H amination of readily available feedstocks cyclic and acyclic ethers. A rarely identified *N*-bromosuccinamide−tetrahydrofuran electron donor−acceptor complex served as an initiator to functionalize both *α*-diazoketones and dialkyl azodicarboxylates. This developed methodology gives an alternative and milder way to construct the C−N bond and can be explored for the formation of C−C bond to perform arylation and allylation reactions.

- Selective (sp^3)C-H functionalization
- Metal-free
- Light-promoted
- Newly identified EDA complex-guided
- Versatile reaction

29 examples upto 91%

KEYWORDS: (*sp*^{3})C*α*−H amination, ethers, N-bromosuccinamide, EDA complex, hydrazonation, radical chain process
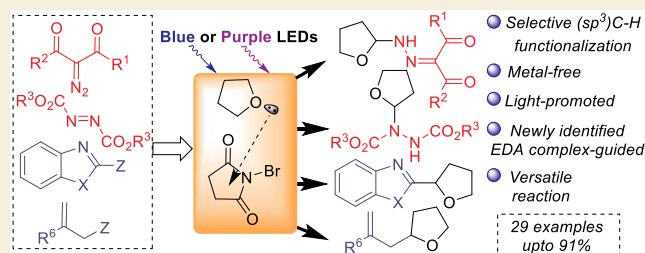
■ INTRODUCTION

Visible light has served as a robust tool in sustainable synthesis, operative via radical pathways under metal or metal-free conditions, enriching the chemistry of radical-based transformations.[1,2] Photoinduced excitation of organic molecules can drive remarkable transformation, generally inaccessible via conventional thermal routes. Among light-driven protocols, one of the most valuable techniques is the electron donor−acceptor (EDA) complex strategy due to its economic and synthetic utilities in modern-day chemistry.[3−5] The photoexcited EDA complex can break into a radical anion and radical cation, leading to various C−H and C−X bond functionalization.

Likewise, selective (*sp*^{3})C*α*−H functionalization of ethers has also gained tremendous attention in recent years. Traditionally, functionalization of (*sp*^{3})C*α*−H bonds requires external catalysts, additives, elevated temperature, extended reaction time, or excess synthetic oxidant, possessing low functional group tolerability and selectivity, and affords the product moderately.[6−13] Readily available feedstocks like cyclic and acyclic ethers are widely used to form *α*-oxyalkyl C-radicals that can be trapped by various acceptors. This strategy can be applied over the construction of eminent C−N bonds, offering an elegant synthetic approach to forge N-functionalized molecules.[14−16]

Over the years, diazo compounds remained as the prime building block in synthetic chemistry. Several methodologies have been developed by using these compounds as carbene precursors, C-nucleophiles, and 1,3-dipoles in the presence of metal or under photochemical conditions.[17−22] However, we are interested to use the diazo compound as the N-terminal electrophile to forge the C−N bond. The typical example for this type of reactivity is the Japp−Klingemann reaction, where

β-ketoesters or acids were allowed to react with aryldiazonium salts, forging the hydrazone moiety.[23] In 2006, the Takamura and Zhao groups reported the use of Grignard reagents as a nucleophile with diazo esters.[24−26] Following this, some valuable reports came into the picture, giving novel access to various hydrazonation reactions.[27−31]

In contrast, Nikolaev et al. demonstrate photosensitizer guided and UV-light mediated insertion of *α*-C−H bond of tetrahydrofuran (THF) into the terminal N-atom of the diazo group, suffering from a mixture of products with limited substrate scope (Scheme 1a).[32,33] In recent years, seminal work was done by the Yu and Xu groups individually with photoredox catalysis. Concurrently, two reports from the Lu group demonstrate the exploitation of aryl diazoacetates to synthesize hydrazone moieties under cobalt catalysis.[34−36]

Similar to diazo compounds, dialkyl azodicarboxylates were also employed for radical-based amination reactions.[37−41] In 2020, the Chudasama and Kokotos groups individually reported HFIP mediated and CFL lamp-promoted C−H amination, respectively (Scheme 1a).[42,43] Very recently, Laulhé et al. were able to functionalize the (*sp*^{3})C*α*−H bond of aliphatic cyclic ethers in the presence of visible light and traces of oxygen (Scheme 1a).[44]

Despite the previous methods mentioned above, there is still considerable room to develop new radical-based C−H amination techniques in an eco-friendly and atom-economical

Scheme 1. Metal-Free Radical-Based C−H Amination Reactions Using Diazo Compounds and Azodicarboxylates

a) Photoinduced and Metal-free C-H Amination of Ethers Using Diazo Compounds

b) This Protocol

Table 1. Optimization Study and Reaction Setup[a]

entry	2a (M)	NBS (mol %)	light source	time	yield %[b]
1[c]	0.5	0	450 nm	16 h	0
2	0.5	100	450 nm	16 h	72
3	0.25	100	450 nm	16 h	75
4	0.05	100	450 nm	16 h	62
5	0.1	100	450 nm	16 h	85
6	**0.1**	**20**	**450 nm**	**16 h**	**82 (78)**[g]
7	0.1	20	450 nm	24 h	77
8	0.1	20	450 nm	10 h	55
9	0.1	20	420 nm	16 h	60
10	0.1	20	405 nm	16 h	51
11	0.1	20	365 nm	16 h	32
12[d]	0.1	20	450 nm	16 h	48
13[e]	0.1	20	450 nm	16 h	75
14	0.1	20	in dark	16 h	0
15[f]	0.1	20	in dark	16 h	0

[a]Unless specified, reactions were performed on a 0.1 mmol scale under argon atmosphere by taking freshly distilled and deoxygenated THF. [b]Measured by ^{1}H NMR analysis of the crude reaction mixture using dibromomethane as an internal standard. Isolated yield in parentheses. [c]Reaction was performed under aerobic conditions. [d]Reaction was carried out at 10 °C. [e]Reaction was performed at 45 °C. [f]Reaction was performed at 60 °C. [g]Reaction performed on a 2.0 mmol scale gives 62% (360 mg) isolated yield of 3a.

fashion, excluded from any strong oxidants, bases, or metal catalysts, and in a cheaper way with sound potential importance. Our literature survey did not offer any report that dealt with EDA-guided, metal-free, photosensitizer, or photocatalyst-free conditions to functionalize $(sp^3)C\alpha$−H bonds of ethers by utilizing diazo compounds and dialkyl azodicarboxylates as radical acceptor under visible light irradiation.

On our ongoing interest in seeking different reactivities of diazo compounds under photochemical conditions, herein, we devised a catalytic amount of N-bromosuccinamide (NBS) as an inexpensive and efficient promoter in $(sp^3)C\alpha$−H bond functionalization of ethers. This resulted in synthesizing a wide range of hemiaminal ethers where α-diazoketones and dialkyl azodicarboxylates served as an amination reagent (Scheme 1b) guided by catalytic EDA system.[45,46]

RESULTS AND DISCUSSION

Based on the previous literature,[32,33] we hypothesized that an α-diazo-β-keto compound might act as a good N-terminal acceptor. Therefore, we geared our investigation by choosing α-diazo-β-keto ester 1a as a model substrate in THF (0.5 M) 2a at room temperature to commence the visible-light promoted C−H amination protocol. Here, THF can serve as both the solvent and α-oxyalkyl C-radical precursor under aerobic conditions (Table 1, entry 1). However, the formation of no product indicates that a radical initiator is required to trigger this process. Next, we screened several radical initiators (see the Supporting Information (SI) for more information, section 4.1) and NBS (1.0 equiv) gives the best result to furnish aminated product 3a in 72% yield (Table 1, entry 2). Variation in the solvent concentration was also checked, suggesting 0.1 (M) THF to be the best-fitted concentration for
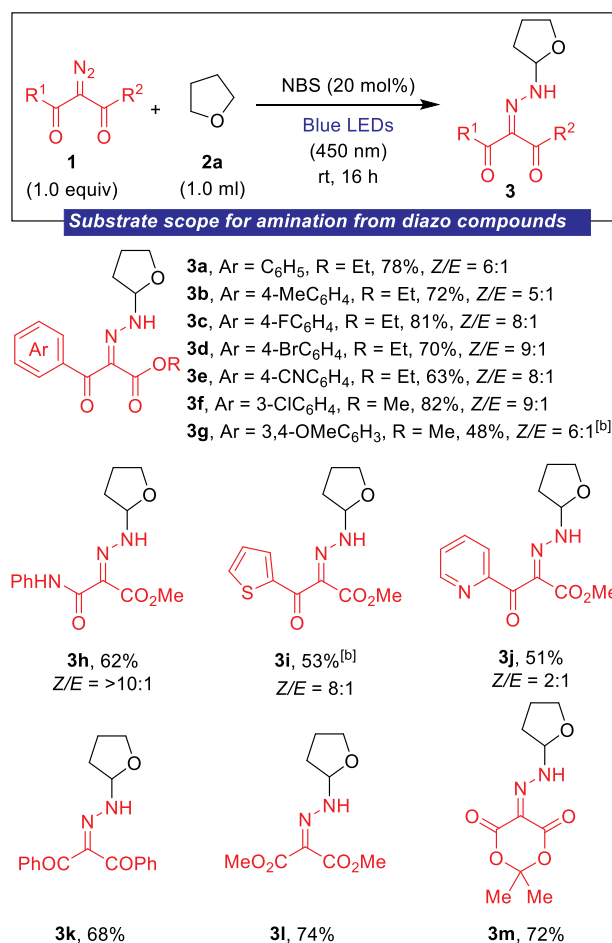
this transformation (Table 1, entries 2−5). We were pleased to find that using a catalytic amount of NBS (20 mol %) instead of a stoichiometric one does not alter the reaction yield significantly (Table 1, entry 6). Reaction times and other light source screenings indicate that blue-LEDs (450 nm) irradiation for 16 h remained more potent over others (Table 1, entries 7−11). In comparison, a decrease or increase in the reaction temperatures led to a decrease in the yield of 3a (Table 1, entries 12 and 13). No conversion for the reaction in the dark at room temperature and at high temperature (60 °C) suggests that the light source is essential for this reaction (Table 1, entries 14 and 15).
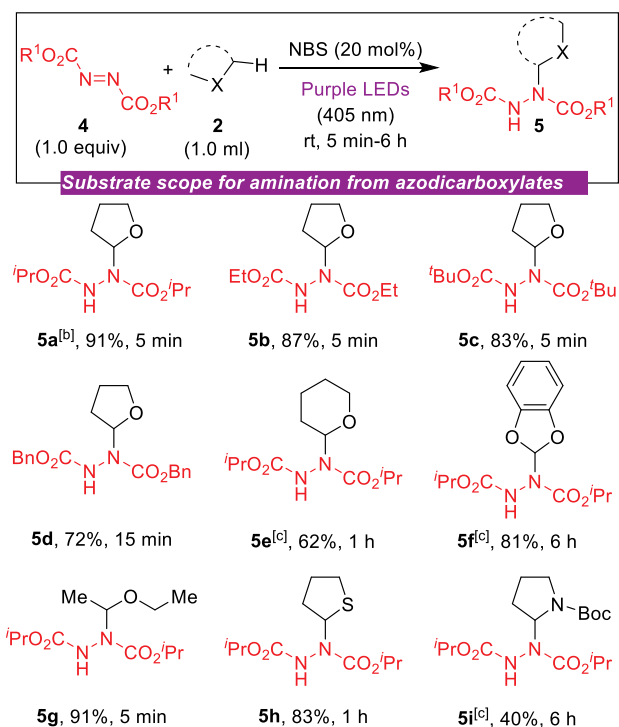
After establishing the optimal reaction conditions (Table 1, entry 6), we investigated the generality of this C−H amination protocol between α-diazo-β-keto compound 1 and THF 2a (Scheme 2). Under visible light, the electron-donating substituent and electron-withdrawing substitutions on the aryl ring, such as methyl, halogen, and cyano groups with *meta*- and *para*-substituted ones, smoothly furnished the product (Scheme 2, entries 3b−3f) with moderate to good yield and moderate Z/E isomeric ratio. Moreover, an aryl ring containing two methoxy substitutions at the *meta*- and *para*-positions delivered the desired product 3g in a 48% yield. Next, amide and heterocycle substituted diazo compounds were investigated, which form the corresponding hydrazones 3h−3j, with moderate yields. Symmetrical acyclic and cyclic α-diazo-β-keto compounds also lead to a facile transformation to achieve compounds 3j−3l in good yield. Although acceptor/acceptor−diazo compounds react well under these reaction conditions, donor/acceptor−diazo compounds such as α-aryldiazoacetates

Scheme 2. Substrate Scope for Amination from Diazo Compounds[a]

Substrate scope for amination from diazo compounds

3a, Ar = C₆H₅, R = Et, 78%, Z/E = 6:1
3b, Ar = 4-MeC₆H₄, R = Et, 72%, Z/E = 5:1
3c, Ar = 4-FC₆H₄, R = Et, 81%, Z/E = 8:1
3d, Ar = 4-BrC₆H₄, R = Et, 70%, Z/E = 9:1
3e, Ar = 4-CNC₆H₄, R = Et, 63%, Z/E = 8:1
3f, Ar = 3-ClC₆H₄, R = Me, 82%, Z/E = 9:1
3g, Ar = 3,4-OMeC₆H₃, R = Me, 48%, Z/E = 6:1[b]

3h, 62%
Z/E = >10:1

3i, 53%[b]
Z/E = 8:1

3j, 51%
Z/E = 2:1

3k, 68%

3l, 74%

3m, 72%

[a]Unless specified, reactions were performed on a 0.1 mmol scale under argon atmosphere by taking freshly distilled and deoxygenated THF. Yields refer to isolated ones. Z/E ratio was measured by ¹H NMR analysis of the crude reaction mixture using dibromomethane as an internal standard. [b]Reactions carried out for 10 h.

and α-aryldiazoketones remained incompatible. We reasoned this might be due to, under blue LEDs, α-aryldiazoacetates being prone to undergo dinitrogen extrusion to generate the carbene intermediate, which cannot take part in the reaction.[19−21] Next, several cyclic and acyclic ethers (**2b−2f**; see SI section 3.3) were tested as α-oxyalkyl C-radical precursors, but unfortunately, they also remained unreactive under this reaction condition.

To check the versatility of the developed protocol, we envisioned whether dialkyl azodicarboxylates could act as a radical acceptor to forge the C−N bond.[37−44] To our delight, THF radical was successfully trapped by diisopropylazodicarboxylate (**4a**, see SI) under blue LEDs irradiation to deliver amine product with moderate yield. A series of light sources and reaction times were then screened to check the best-fitted one (See SI for the optimization table, section 4.4). We found purple LEDs are the most efficient to promote this reaction, which gives 91% yield of **5a**. Here, azodicarboxylates substituted with different alkyl partners furnished the corresponding amines with good yield (Scheme 3, entries **5a-5d**). Subsequently, a range of cyclic and acyclic ethers participated in this transformation (Scheme 3, entries **5e-5g**).

Scheme 3. Substrate Scope for Amination from Azodicarboxylates[a]

Substrate scope for amination from azodicarboxylates

5a[b], 91%, 5 min

5b, 87%, 5 min

5c, 83%, 5 min

5d, 72%, 15 min

5e[c], 62%, 1 h

5f[c], 81%, 6 h

5g, 91%, 5 min

5h, 83%, 1 h

5i[c], 40%, 6 h

[a]Unless specified reactions were performed on a 0.1 mmol scale under argon atmosphere by taking **4** (1.0 equiv) and **2** (1.0 mL). Yields refer to isolated ones. [b]Reaction performed on a 2.0 mmol scale gives 80% (440 mg) isolated yield of **5a**. [c]10.0 equiv of **2** was used in 0.1 mL of benzene.

In addition, S-heterocycle and N-heterocycle were also successfully employed with high efficiency (Scheme 3, entries **5h** and **5i**).

We executed several control experiments to shed light on the plausible reaction pathways of this visible-light-driven transformation. The reaction between **1a** and dry-deoxygenated THF **2a** without NBS, under blue LEDs irradiation and oxygen atmosphere, delivered no product **3a** (Scheme 4a). Reaction under aerobic conditions and use of AR grade THF **2a** (Scheme 4b) did not provide the desired product. The yield of **3a** drops significantly when performing the reaction between **1a** and AR grade THF **2a** in the presence of NBS, under argon atmosphere, or aerobic conditions in the presence of blue LEDs (Scheme 4c, d). Moreover, reactions under dark conditions did not offer any product formation (Scheme 4e). These results suggest that NBS, blue LED irradiation, and entirely inert conditions are necessary to facilitate this transformation. Next, when diisopropyl azodicarboxylate **4a** was allowed to react with dry-deoxygenated THF **2a** under purple LED irradiation and oxygen atmosphere in the absence of NBS, the reaction gives traces amount of **5a**. However, on increasing the reaction time (5 min to 24 h), a considerable amount of product **5a** (45%) was obtained. Reactions performed by taking AR grade THF **2a** without NBS under aerobic condition and argon atmosphere led to the formation of 22% and 25% of **5a**, respectively (reaction time 24 h). Similarly, the experiment in the dark suggested the importance of the light source (see the SI for the control experiments, section 6.1).

Scheme 4. Control Experiments
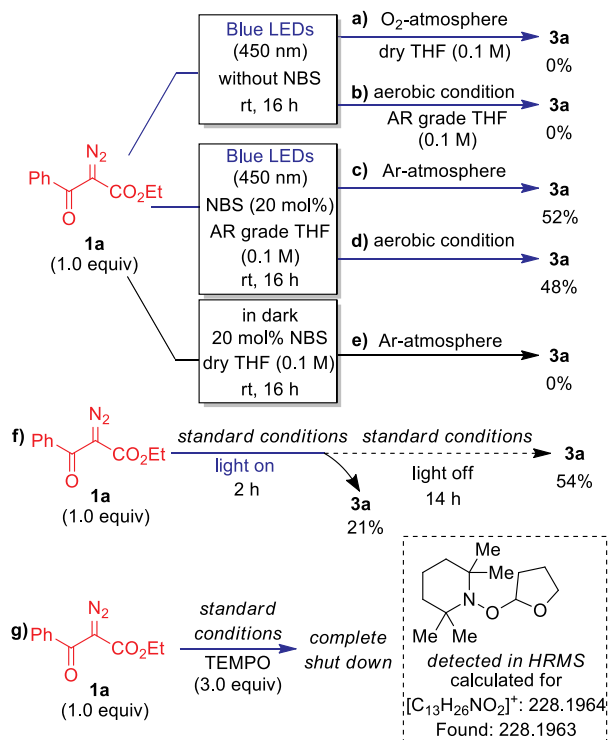
The colored solution of the reaction mixtures encouraged us to check ultraviolet−visible (UV/vis) spectra. A mixture of diazo compound **1a** and THF **2a** gives an absorbance band near the UV region. Pleasingly, a combination of NBS and THF (dry and deoxygenated) developed a yellow-colored solution. This solution shows a bathochromic shift in the visible spectral region in its optical absorption spectrum, diagnostic of an EDA complex (samples need to prepare in the glovebox to avoid oxygen). In contrast, NBS in acetonitrile does not show any colored solution, and its absorption falls near the UV region. Therefore, a catalytic amount of NBS can act as an acceptor in this system and THF acts as a donor to form the NBS-THF EDA complex (see SI section 6.2, for the UV−visible data).

Next, the existence of a radical intermediate was tested by adding (2,2,6,6-tetramethylpiperidin-1-yl)oxy (TEMPO) as a radical scavenger to the reaction mixture where THF radical **VII** was successfully trapped (detected in HRMS, Scheme 4g) and the reaction was completely stopped.

To validate whether the reaction proceeds via a radical chain process, we performed a '"light-on/light-off"' experiment. Irradiating the reaction mixture under blue LEDs for 2 h and then stirring the reaction in the dark for 14 h resulted in 54% of **3a** formation (Scheme 4f). A tool to better corroborate the chain process is to measure the reaction's quantum yield (ϕ) (λ = 405 and 450 nm, using potassium ferrioxalate as the actinometer).[47] We performed this measurement for both the amination reactions and found very high quantum yields (ϕ = 142.97 and 902.41 for the synthesis of **3a** and **5a**, respectively; see SI section 6.4, for the quantum yield calculations).

The above results offer compelling evidence to rationalize the mechanism. Based on the mechanistic experiments and literature precedence,[48] we envisioned that the reaction initiated by forming an activated colored NBS-THF EDA complex **I**. Irradiation of this EDA complex **I** by visible light

(blue or purple LEDs) facilitates the generation of radical cation **II** and radical anion **III**. Elimination of bromine radical **IV** leads to the formation of anionic species **V**. Intermediate **V** then abstracts one proton from intermediate **II** to deliver the THF radical **VII**. Consequently, the generation of succinimide **VI** also takes place via path a. This crucial radical intermediate **VII** then adds to substrate **1** or **4** to forge the C−N bond and fabricate their respective intermediates **VIII** and **IX**, respectively. Now, intermediate **VIII** and **IX** abstracts a hydrogen atom (HAT) from **2a** to facilitate the radical chain process and furnishes the aminated products (**3** or **5**) as well (Scheme 5). However, as this a radical chain process paths a′,

Scheme 5. Mechanistic Proposal for C−H Amination
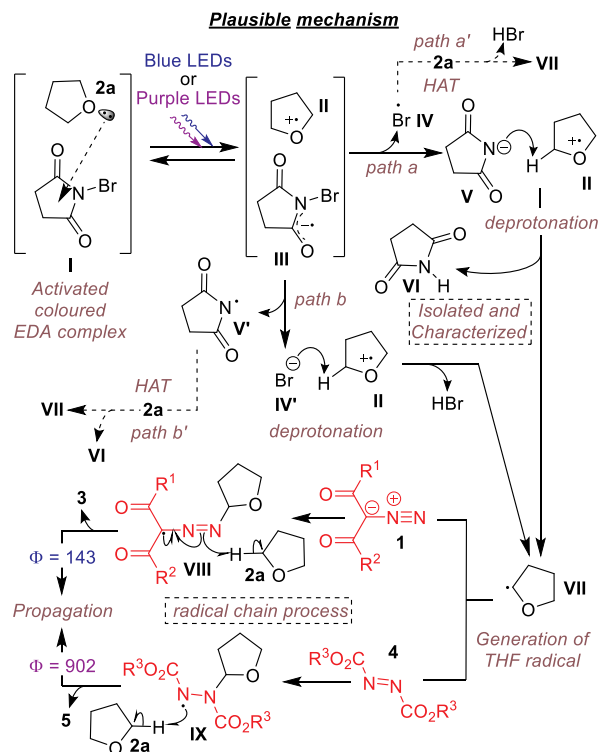
b, and b′, as described in Scheme 5, cannot be discarded as an alternative pathway for the generation of THF radical **VII**. Here, path b represents the formation of bromide ion **IV′** and radical intermediate **V′** from intermediate **III**. Intermediate **IV′** undergoes a deprotonation step with intermediate **II** to generate THF radical **VII**. Similarly, a HAT process between intermediate **V′** or **IV** with **2a** leads to the THF radical **VII** formation via path a′ and path b′, respectively.

The general applicability of any developed protocol showcases its usefulness. Gratifyingly, the catalytic NBS-THF EDA system also remained potent over some arylation and allylation reactions (Scheme 6). These reactions proceed via a similar mechanism described in Scheme 5 to generate the key THF radical **VII**. This carbon-centered radical **VII** then adds to various aryl and allyl sulfones to give the desired THF incorporated product via desulfonylation (Scheme 6, entries **8a**, **9a**−**9d**). Additionally, the aryl ring substituted with a halogen atom (e.g., *N*-Boc 2-chlorobenzimidazole **6b**, 2-chlorobenzoxazole **6c**; see SI section 3.5) as a leaving group instead of sulfones efficiently provides their corresponding products (Scheme 6, entries **8b** and **8c**). Here sodium acetate is used as an additive to neutralize in situ generated

Scheme 6. Substrate Scope for Arylation and Allylation Reactions[a]
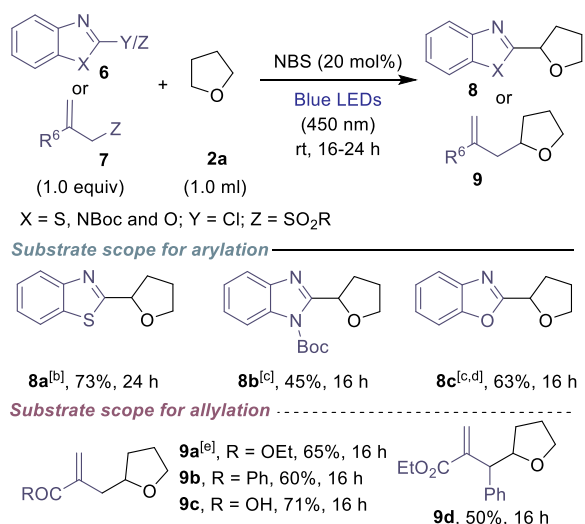
[a]Unless specified, reactions were performed on a 0.1 mmol scale under argon atmosphere by taking **4** (1.0 equiv), freshly distilled and deoxygenated THF. Yields refer to isolated ones. [b]Reaction performed on a 2.0 mmol scale gives 59% (240 mg) isolated yield of **8a**. [c]1.0 equiv NaOAc was used as an additive. [d]Purple LEDs were used instead of blue LEDs. [e]Reaction performed on a 2.0 mmol scale gives 54% (200 mg) isolated yield of **9a**.

hydrochloric acid, increasing the reaction yield.[49] This desulfonylation process follows an activated nucleophilic substitution reaction via an addition−elimination pathway. The calculated quantum yield (ϕ) for these reactions is 97.58 (for the synthesis of **8a**) and 99.85 (for the synthesis of **9a**), respectively, which supports the radical chain pathway (see SI section 6.4 for the quantum yield calculations).

CONCLUSIONS

In summary, the developed protocol provides a modular method to render a series of amine, $C(sp^2)$−H, and $C(sp^3)$−H alkylating products with various ethers. Visible lights were utilized to carry out this metal-free, oxidant-free C−N and C−C bond-forming event. The generation and identification of the catalytic NBS-THF electron donor−acceptor (EDA) complex were crucial, permitting direct and selective (sp^3)-Cα−H bond functionalization. A radical chain mechanism is proposed based on the literature and our experimental evidence. It is noteworthy that the developed methodology overcomes significant disadvantages like long reaction time and harsh reaction conditions associated with previous (sp^3)Cα−H bond functionalization techniques.

EXPERIMENTAL DETAILS

General Procedure for Amination

In an argon filled glovebox, to an oven-dried vial equipped with a Teflon-coated stir bar, **1** or **4** (0.1 mmol, 1.0 equiv) and *N*-bromosuccinamide (NBS) (0.02 mmol, 0.2 equiv) were added. Then ether **2** (0.1 M, 1.0 mL) was added to the reaction mixture and sealed. The vial was taken out from the glovebox and then irradiated under blue/purple LEDs for 5 min to 16 h at room temperature. The crude reaction mixture was used to measure the *Z/E* ratio by ¹H NMR if required after completion of the reaction. The solvent was evaporated under reduced pressure. Analytically pure products were obtained by

column chromatography on silica gel using petroleum ether and ethyl acetate as eluents.

ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsorginorgau.2c00008.

Experimental procedures, mechanistic evidence, and spectral data for the newly synthesized products (PDF)

AUTHOR INFORMATION

Corresponding Author

Indranil Chatterjee − *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India;* Ⓞ orcid.org/0000-0001-8957-5182; Email: indranil.chatterjee@iitrpr.ac.in

Author

Sourav Roy − *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsorginorgau.2c00008

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Xuan, J.; He, X.-K.; Xiao, W.-J. Visible light-promoted ring-opening functionalization of three-membered carbo-and heterocycle. *Chem. Soc. Rev.* **2020**, *49*, 2546−2556.

(2) Yu, X.-Y.; Chen, J.-R.; Xiao, W.-J. Visible Light-Driven Radical-Mediated C−C Bond Cleavage/Functionalization in Organic Synthesis. *Chem. Rev.* **2021**, *121*, 506−561.

(3) Yuan, Y.-Q.; Majumder, S.; Yang, M.-H.; Guo, S.-R. Recent advances in catalyst-free photochemical reactions via electron donor-acceptor (EDA) complex process. *Tetrahedron. Lett.* **2020**, *61*, 151506.

(4) Yang, Z.; Liu, Y.; Cao, K.; Zhang, X.; Jiang, H.; Li, J. Synthetic reactions driven by electron-donor−acceptor (EDA) complexes. *Beilstein J. Org. Chem.* **2021**, *17*, 771−799.

(5) Crisenza, G. E. M.; Mazzarella, D.; Melchiorre, P. Synthetic Methods Driven by the Photoactivity of Electron Donor−Acceptor Complexes. Acceptor Complexes. *J. Am. Chem. Soc.* **2020**, *142*, 5461−5476.

(6) Qvortrup, K.; Rankic, D. A.; MacMillan, D. W. C. A General Strategy for Organocatalytic Activation of C−H Bonds via Photoredox Catalysis: Direct Arylation of Benzylic Ethers. *J. Am. Chem. Soc.* **2014**, *136*, 626−629.

(7) Jin, J.; MacMillan, D. W. C. Direct α-Arylation of Ethers through the Combination of Photoredox-Mediated C−H Functionalization and the Minisci Reaction. *Angew. Chem., Int. Ed.* **2015**, *54*, 1565−1569.

(8) Bhakat, M.; Biswas, P.; Dey, J.; Guin, J. Heteroarylation of Ethers, Amides, and Alcohols with Light and O2. *Org. Lett.* **2021**, *23*, 6886−6890.

(9) Huang, X.-J.; Qin, F.-H.; Liu, Y.; Wu, S.-P.; Li, Q.; Wei, W.-T. Acylation/cyclization of 1,6-dienes with ethers under catalyst- and base-free conditions. *Green Chem.* **2020**, *22*, 3952−3955.

(10) Wang, X.; Lei, J.; Guo, S.; Zhang, Y.; Ye, Y.; Tang, S.; Sun, K. Radical selenation of C(sp^3)−H bonds to asymmetric selenides and mechanistic study. *Chem. Commun.* **2022**, *58*, 1526−1529.

(11) Batra, A.; Singh, P.; Singh, K. N. Recent Advances in Functionalization of α-C(sp^3)−H Centres in Inactivated Ethers through Cross Dehydrogenative Coupling. *Eur. J. Org. Chem.* **2017**, *2017*, 3739−3762.

(12) Faisca Phillips, A. M.; Pombeiro, A. J. L. Recent Developments in Transition Metal-Catalyzed Cross-Dehydrogenative Coupling Reactions of Ethers and Thioethers. *ChemCatChem.* **2018**, *10*, 3354−3383.

(13) Batra, A.; Singh, K. N. Recent Developments in Transition Metal-Free Cross-Dehydrogenative Coupling Reactions for C−C Bond Formation. *Eur. J. Org. Chem.* **2020**, *2020*, 6676−6703.

(14) Chen, J.-Y.; Wu, W.; Li, Q.; Wei, W.-T. Visible-Light Induced C(sp^3)−H Functionalization for the Formation of C−N Bonds under Metal Catalyst-Free Conditions. *Adv. Synth. Catal.* **2020**, *362*, 2770−2777.

(15) Wang, H.-Z.; Li, J.-Z.; Guo, Z.; Zheng, H.; Wei, W.-T. Visible-Light-Catalyzed N-Radical-Enabled Cyclization of Alkenes for the Synthesis of Five-Membered N-Heterocycles. *ChemSusChem* **2021**, *14*, 4658−4670.

(16) Zheng, Y.-N.; Zheng, H.; Li, T.; Wei, W.-T. Recent Advances in Copper-Catalyzed C−N Bond Formation Involving N-Centered Radicals. *ChemSusChem* **2021**, *14*, 5340−5358.

(17) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic carbene insertion into C−H bonds. *Chem. Rev.* **2010**, *110*, 704.

(18) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. Modern Organic Synthesis with α-Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115*, 9981.

(19) Ciszewski, Ł. W.; Rybicka-Jasińska, K.; Gryko, D. Recent developments in photochemical reactions of diazo compounds. *Org. Biomol. Chem.* **2019**, *17*, 432−448.

(20) Yang, Z.; Stivanin, M. L.; Jurberg, I. D.; Koenigs, R. M. Visible light-promoted reactions with diazo compounds: a mild and practical strategy towards free carbene intermediates. *Chem. Soc. Rev.* **2020**, *49*, 6833−6847.

(21) Durka, J.; Turkowska, J.; Gryko, D. Lightening Diazo Compounds? *ACS Sustainable Chem. Eng.* **2021**, *9*, 8895−8918.

(22) Dasgupta, A.; Richards, E.; Melen, R. L. Triarylborane Catalyzed Carbene Transfer Reactions Using Diazo Precursors. *ACS Catal.* **2022**, *12*, 442−452.

(23) Yao, H. C.; Resnick, P. Azo-Hydrazone Conversion. I. The Japp-Klingemann Reaction. *J. Am. Chem. Soc.* **1962**, *84*, 3514.

(24) Yasui, E.; Wada, M.; Takamura, N. Novel approach to arylhydrazones, the precursor for Fischer indole synthesis, via diazo esters derived from α-amino acid esters. *Tetrahedron Lett.* **2006**, *47*, 743.

(25) Yasui, E.; Wada, M.; Takamura, N. Novel method for synthesis of aryl hydrazones from α-diazo esters: scope and limitations of nucleophiles. *Tetrahedron* **2009**, *65*, 461.

(26) Zhang, L.; Meng, X.-H.; Liu, P.; Chen, J.; Zhao, Y.-L. *t*BuLi-Promoted Intermolecular Regioselective Nucleophilic Addition of Arenes to Diazo Compounds as N-Terminal Electrophiles: Efficient Synthesis of Hydrazine Derivatives. *Eur. J. Org. Chem.* **2017**, *2017*, 6137.

(27) Li, W.; Liu, X.; Hao, X.; Hu, X.; Chu, Y.; Cao, W.; Qin, S.; Hu, C.; Lin, L.; Feng, X. New Electrophilic Addition of α-Diazoesters with Ketones for Enantioselective C−N Bond Formation. *J. Am. Chem. Soc.* **2011**, *133*, 15268.

(28) Li, L.; Chen, J.-J.; Li, Y.-J.; Bu, X.-B.; Liu, Q.; Zhao, Y.-L. Activation of α-Diazocarbonyls by Organic Catalysts: Diazo Group Acting as a Strong N-Terminal Electrophile. *Angew. Chem., Int. Ed.* **2015**, *54*, 12107.

(29) Zheng, J.; Qi, J.; Cui, S. Fe-Catalyzed Olefin Hydroamination with Diazo Compounds for Hydrazone Synthesis. *Org. Lett.* **2016**, *18*, 128.

(30) Huo, J.; Xue, Y.; Wang, J. Regioselective copper-catalyzed aminoborylation of styrenes with bis(pinacolato)diboron and diazo compounds. *Chem. Commun.* **2018**, *54*, 12266.

(31) Yao, D.; Zhang, J.; Xu, L. C−N Coupling Reactions between Benzophenone Hydrazone and Aryl Chlorides and Boronic Acids. *Chin. J. Org. Chem.* **2020**, *40*, 1673−1679.

(32) Rodina, L. L.; Galkina, O. S.; Maas, G.; Platz, M. S.; Nikolaev, V. A. A New Method for C−H Functionalization of Aliphatic Compounds by an Unusual Photochemical Reaction of Diazoketones without Elimination of Nitrogen. *Asian J. Org. Chem.* **2016**, *5*, 691.

(33) Rodina, L. L.; Azarova, X. V.; Medvedev, J. J.; Semenok, D. V.; Nikolaev, V. A. Novel photochemical reactions of carbocyclic diazodiketones without elimination of nitrogen - a suitable way to N-hydrazonation of C−H-bonds. *Beilstein J. Org. Chem.* **2018**, *14*, 2250.

(34) Chan, C.-M.; Xing, Q.; Chow, Y.-C.; Hung, S.-F.; Yu, W.-Y. Photoredox Decarboxylative C(sp^3)−N Coupling of α-Diazoacetates with Alkyl N-Hydroxyphthalimide Esters for Diversified Synthesis of Functionalized N-Alkyl Hydrazones. *Org. Lett.* **2019**, *21*, 8037−8043.

(35) Wu, X.; Zheng, P.; Li, W.; Xu, T. Reductive cross-coupling to access C−N bonds from aryl halides and diazoesters under dual nickel/photoredox-catalyzed conditions. *Org. Chem. Front.* **2021**, *8*, 4118−4123.

(36) Shen, X.; Chen, X.; Chen, J.; Sun, Y.; Cheng, Z.; Lu, Z. Ligand-promoted cobalt-catalyzed radical hydroamination of alkenes. *Nat. Commun.* **2020**, *11*, 783.

(37) Chen, J.; Shen, X.; Lu, Z. Cobalt-Catalyzed Markovnikov Selective Sequential Hydrogenation/Hydrohydrazidation of Aliphatic Terminal Alkynes. *J. Am. Chem. Soc.* **2020**, *142*, 14455−14460.

(38) Lee, D.; Otte, R. D. Transition-Metal-Catalyzed Aldehydic C-H Activation by Azodicarboxylates. *J. Org. Chem.* **2004**, *69*, 3569−3571.

(39) Ryu, I.; Tani, A.; Fukuyama, T.; Ravelli, D.; Montanaro, S.; Fagnoni, M. Efficient C−H/C−N and C−H/C−CO−N Conversion via Decatungstate-Photoinduced Alkylation of Diisopropyl Azodicar-boxylate. *Org. Lett.* **2013**, *15*, 2554−2557.

(40) Bonassi, F.; Ravelli, D.; Protti, S.; Fagnoni, M. Decatungstate Photocatalyzed Acylations and Alkylations in Flow via Hydrogen Atom Transfer. *Adv. Synth. Catal.* **2015**, *357*, 3687−3695.

(41) Jin, Y.; Zhang, Q.; Wang, L.; Wang, X.; Meng, C.; Duan, C. Convenient C(sp^3)−H bond functionalisation of light alkanes and other compounds by iron photocatalysis. *Green Chem.* **2021**, *23*, 6984.

(42) Shamsabadi, A.; Maruani, A.; Ahmed, N.; Chudasama, V. Aerobically-initiated C(sp^3)−H bond amination through the use of activated azodicarboxylates. *Org. Biomol. Chem.* **2020**, *18*, 6258−6264.

(43) Papadopoulos, G. N.; Kokotou, M. G.; Spiliopoulou, N.; Nikitas, N. F.; Voutyritsa, E.; Tzaras, D. I.; Kaplaneris, N.; Kokotos, C. G. Phenylglyoxylic Acid: An Efficient Initiator for the Photochemical Hydrogen Atom Transfer C−H Functionalization of Heterocycles. *ChemSusChem* **2020**, *13*, 5934−5944.

(44) Niu, B.; Blackburn, B. G.; Sachidanandan, K.; Cooke, M. V.; Laulhé, S. Metal-free visible-light-promoted C(sp^3)−H functionalization of aliphatic cyclic ethers using trace O$_2$. *Green Chem.* **2021**, *23*, 9454−9459.

(45) Arceo, E.; Jurberg, I. D.; Álvarez-Fernández, A.; Melchiorre, P. Photochemical activity of a key donor−acceptor complex can drive stereoselective catalytic a-alkylation of aldehydes. *Nature Chem.* **2013**, *5*, 750−756.

(46) Cao, Z.-Y.; Ghosh, T.; Melchiorre, P. Enantioselective radical conjugate additions driven by a photoactive intramolecular iminium-ion-based EDA complex. *Nat. Commun.* **2018**, *9*, 3274.

(47) Cismesia, M. A.; Yoon, T. P. Characterizing chain processes in visible light photoredox catalysis. *Chem. Sci.* **2015**, *6*, 5426−5434.

(48) El-Habeeb, A. A.; Refat, M. S. Spectroscopic Studies on the Utility of Charge Transfer Interactions for Determination of Phenytoin Sodium. *Russ J. Gen Chem.* **2015**, *85*, 939−950.

(49) Lipp, A.; Lahm, G.; Opatz, T. Light Induced C−C Coupling of 2-Chlorobenzazoles with Carbamates, Alcohols, and Ethers. *J. Org. Chem.* **2016**, *81*, 4890−4897.