ORGANIC CHEMISTRY

Aminoalkyl radicals as halogen-atom transfer agents for activation of alkyl and aryl halides

Timothée Constantin[1], Margherita Zanini[1], Alessio Regni[1], Nadeem S. Sheikh[2], Fabio Juliá[1]*, Daniele Leonori[1]*

Organic halides are important building blocks in synthesis, but their use in (photo)redox chemistry is limited by their low reduction potentials. Halogen-atom transfer remains the most reliable approach to exploit these substrates in radical processes despite its requirement for hazardous reagents and initiators such as tributyltin hydride. In this study, we demonstrate that α-aminoalkyl radicals, easily accessible from simple amines, promote the homolytic activation of carbon-halogen bonds with a reactivity profile mirroring that of classical tin radicals. This strategy conveniently engages alkyl and aryl halides in a wide range of redox transformations to construct sp^3-sp^3, sp^3-sp^2, and sp^2-sp^2 carbon-carbon bonds under mild conditions with high chemoselectivity.

Carbon radicals are versatile synthetic intermediates central to the preparation of high-value compounds (*1*, *2*). The advent of visible-light photoredox catalysis (*3*) has offered a broadly applicable radical generation strategy, transforming a variety of redox-active precursors into open-shell intermediates by single-electron transfer (SET) and fragmentation (*4*–*6*). However, photoredox activation has thus far rarely extended to organic halides, one of the largest classes of building blocks available to organic chemists. The current synthetic gap is especially evident in the case of unactivated alkyl halides, for which only dehalogenation and intramolecular cyclization of iodides have been reported (*7*–*10*). The difficulties in engaging these feedstocks in redox chemistry arise from their highly negative reduction potentials [E_{red} < –2 V versus saturated calomel electrode (SCE) for unactivated alkyl and aryl iodides], which in turn necessitate the use of strongly reducing systems (*11*, *12*) (Fig. 1A). Furthermore, the mechanisms involved in photoredox reactions are often uncertain (*9*), displaying large redox mismatches (>1 V) for SET activation and thus thwarting the exploitation of the carbon radicals accessed in this manner.

This lack of synthetic applicability stands in stark contrast to the fundamental role alkyl and aryl halides have played in the development of radical chemistry. Methods based on tin or silicon reagents and trialkylborane–O_2 systems have proven to be highly reliable in accessing carbon radicals from organic halides, generating the open-shell intermediate by homolytic carbon-halogen bond cleavage via halogen-atom transfer (XAT) (*13*–*15*). However, the toxic, hazardous nature of these reagents and initiators is problematic and has been one of the main drivers toward the identification of alternative precursors and chemical strategies for carbon radical generation. Nevertheless, silicon radicals have been recently used in metallaphotoredox catalysis to overcome sluggish carbon-halogen oxidative additions with transition metals (*16*, *17*).

We questioned whether α-aminoalkyl radicals could serve as a distinct class of halogen-abstracting reagents (Fig. 1B). Our idea for this reactivity stemmed from the fact that although classical XAT processes benefit from the formation of strong halogen-tin or halogen-silicon bonds, it is the high degree of charge transfer in the transition state that facilitates halogen-atom abstraction by these nucleophilic radicals (*18*). We therefore reasoned that strongly nucleophilic α-aminoalkyl radicals might benefit from related kinetic polar effects and manifest the same reactivity. Such radicals can be easily generated from simple amines, a class of abundant and inexpensive reagents that would offer ample opportunity for fine steric and electronic tuning.

Here we report the successful realization of this concept and its implementation as part of a mild and general strategy for the engagement of unactivated alkyl and aryl halides in redox chemistry (Fig. 1C). Because α-aminoalkyl radicals display a reactivity profile similar to that of tin radicals, their capacity to abstract iodine and bromine atoms has enabled the development of deuteration, cross-electrophile coupling, Heck-type olefination, and aromatic C–H alkylation protocols.

We initiated our study by evaluating the iodine-atom transfer reaction from cyclohexyl iodide **2** to the α-aminoalkyl radical **I-a**, derived from triethylamine (Et_3N, **1a**) (Fig. 2A).

[1]Department of Chemistry, University of Manchester, Manchester M13 9PL, UK. [2]Department of Chemistry, College of Science, King Faisal University, Al-Ahsa 31982, Saudi Arabia. *Corresponding author. Email: fabio.juliahernandez@manchester.ac.uk (F.J.); daniele.leonori@manchester.ac.uk (D.L.)

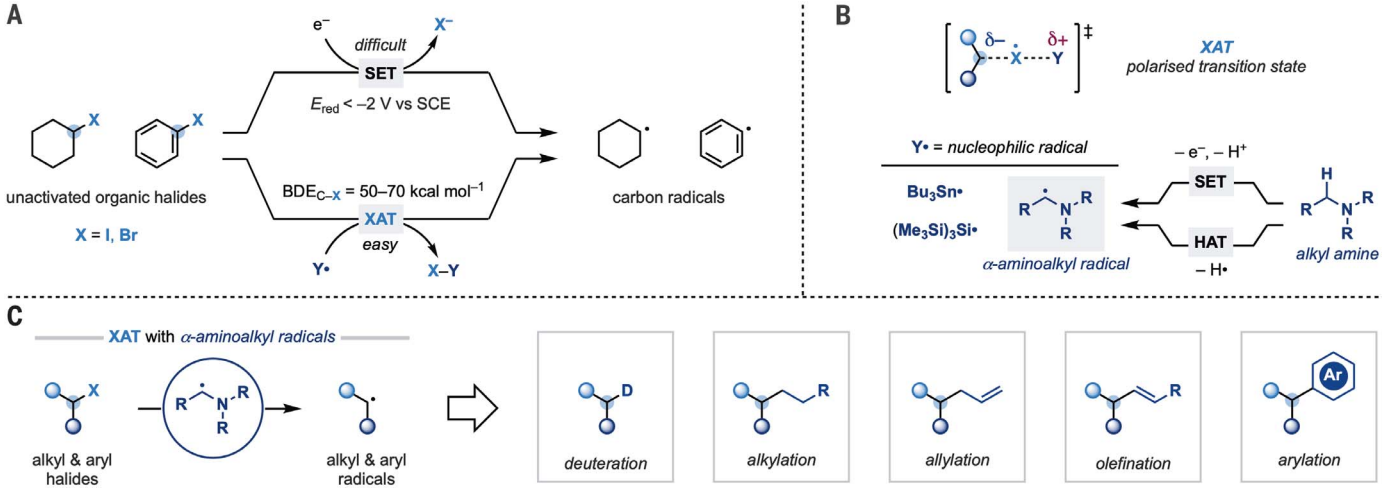

Fig. 1. Homolysis of carbon-halogen bonds by α-aminoalkyl radicals. (**A**) Activation modes for the generation of carbon radicals from alkyl and aryl halides. e⁻, electron. (**B**) Nucleophilic α-aminoalkyl radicals abstract halogen atoms (X) through polarized transition states, in analogy to tin and silicon radicals. Me, methyl; Bu, butyl; R, alkyl, aryl. (**C**) Outline of the transformations possible using alkyl and aryl halides activated via α-aminoalkyl radical-mediated XAT. Ar, aryl.

Density functional theory calculations predicted this XAT to be kinetically feasible, involving a polarized transition state with a notable charge-transfer character (δ^{TS} = 0.42), which supports the anticipated interplay of polar effects. Although the XAT is only slightly exothermic (*19*), the fast and irreversible dissociation of the resulting α-iodoamine **III-a** into the iminium iodide **IV-a** provides the thermodynamic driving force to the process. To gather direct experimental evidence, we generated and monitored **I-a** using laser flash photolysis (*20*, *21*) and observed a noticeable reactivity toward **2**. Data analysis provided a fast rate constant (k_{XAT} = 3.6 10^8 M^{-1} s^{-1}) that is only one order of magnitude slower than reported rates for I-abstraction by Bu_3Sn• and $(Me_3Si)_3Si$• (~10^9 M^{-1} s^{-1}) (*22*), showing promise for implementation in synthetic radical chemistry.

To explore the applicability of this strategy in radical reactions, we chose the dehalogenation of 4-iodo-*N*-Boc-piperidine **3**, using Et_3N as the XAT-agent precursor and methyl thioglycolate–H_2O as the H-atom donor (Fig. 2B). At the outset, we were particularly interested to evaluate whether the photochemical or thermal modes for α-aminoalkyl radical generation could be recruited for XAT reactivity. We therefore began by testing four known systems based on amine SET oxidation (Et_3N: E_{ox} = +0.77 V versus SCE) followed by deprotonation [i.e., photoredox catalysis (*23*), triplet benzophenone (*24*), and $SO_4^{\bullet-}$ (*25*)] or direct H-atom transfer (HAT) [Et_3N: α-N-C–H bond dissociation energy (BDE) = 91 kcal mol^{-1}] using *t*-BuO• (*26*). The desired product **4** was obtained in all cases in excellent to good yields, exemplifying the variety of conditions for α-aminoalkyl radical generation and ensuing XAT.

The proposed mechanism under photoredox conditions is depicted in Fig. 2C. Upon blue light irradiation, the excited organic photocatalyst 4CzIPN ($*E_{red}$ = +1.35 V versus SCE) oxidizes **1a**, which, after subsequent deprotonation, furnishes the key α-aminoalkyl radical **I-a**. This species undergoes XAT with **3**, and the resulting alkyl radical **V** provides the

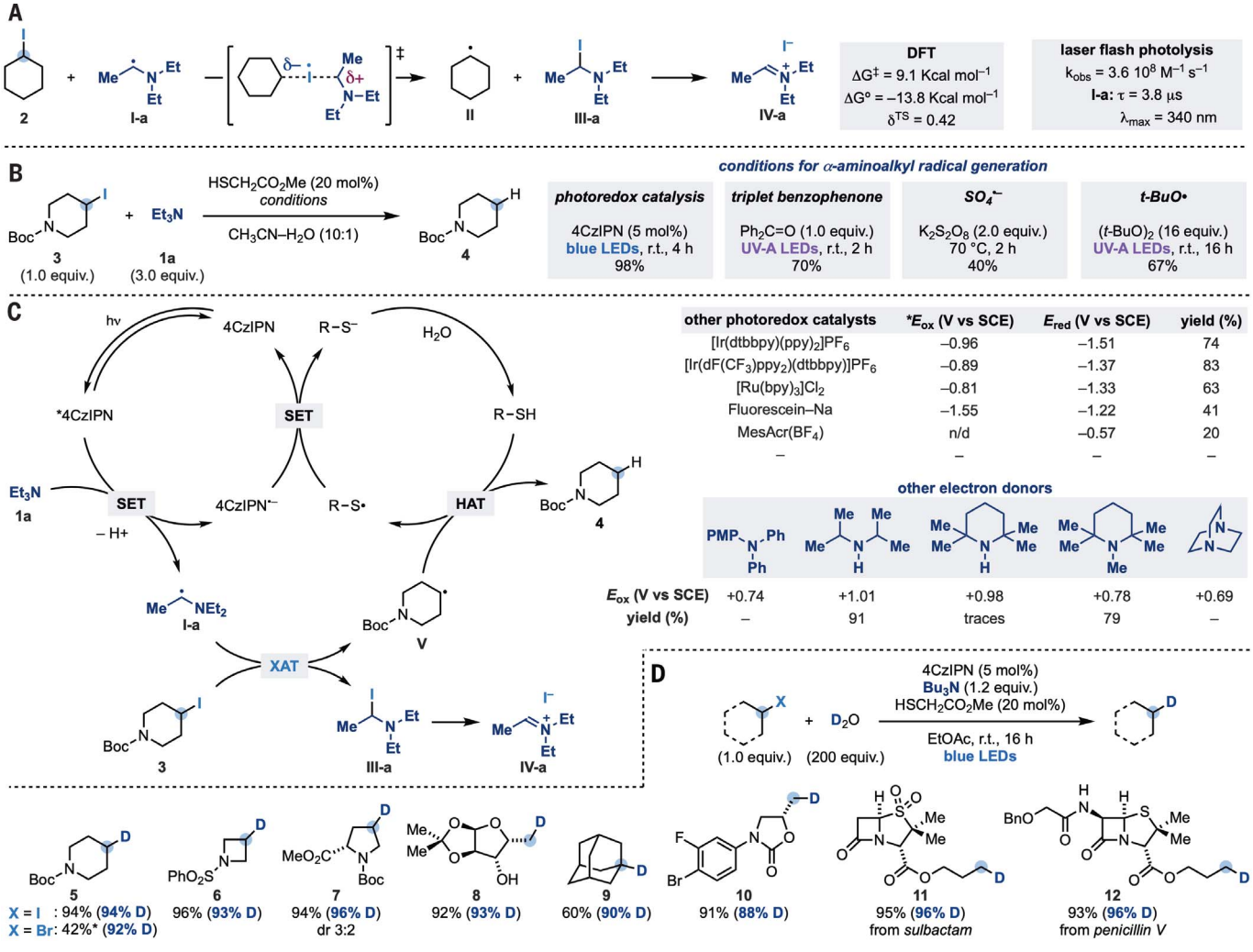

Fig. 2. Mechanistic analysis and application to dehalogenation and deuteration reactions. (**A**) Computational [B3LYP-D3/def2-TZVP] and laser flash photolysis studies on a model XAT reaction with an alkyl iodide. Et, ethyl; DFT, density functional theory; $\Delta G^{\ddagger}$, Gibbs energy of activation; $\Delta G°$, Gibbs free energy; λ_{max}, wavelength of maximum absorption. (**B**) Evaluation of photochemical and thermal strategies for α-aminoalkyl radical generation and their use in the dehalogenation of alkyl iodide **3**. Boc, *tert*-butoxycarbonyl; LEDs, light-emitting diodes; r.t., room temperature; Ph, phenyl; UV, ultraviolet; *t*-Bu, *tert*-butyl. (**C**) Proposed mechanism for the photoredox-based dehalogenation of alkyl iodide **3**. Mechanistic studies support the intermediacy of an α-aminoalkyl radical in the activation of the C–I bond. h, Planck's constant; ν, photon frequency; dtbbpy, 4,4′-di-*tert*-butyl-2,2′-dipyridyl; ppy, 2-phenylpyridyl; dF, difluoro; bpy, 2,2′-bipyridine; Mes, mesityl; Acr, acridinium; n/d, not determined. (**D**) Application of the XAT methodology in deuteration of alkyl halides. All yields are isolated. Deuteration was determined by gas chromatography–mass spectrometry/quantitative ^{13}C nuclear magnetic resonance spectroscopy. *Tribenzylamine **1b** was used as the amine. Ac, acetyl; Bn, benzyl; dr, diastereomeric ratio.

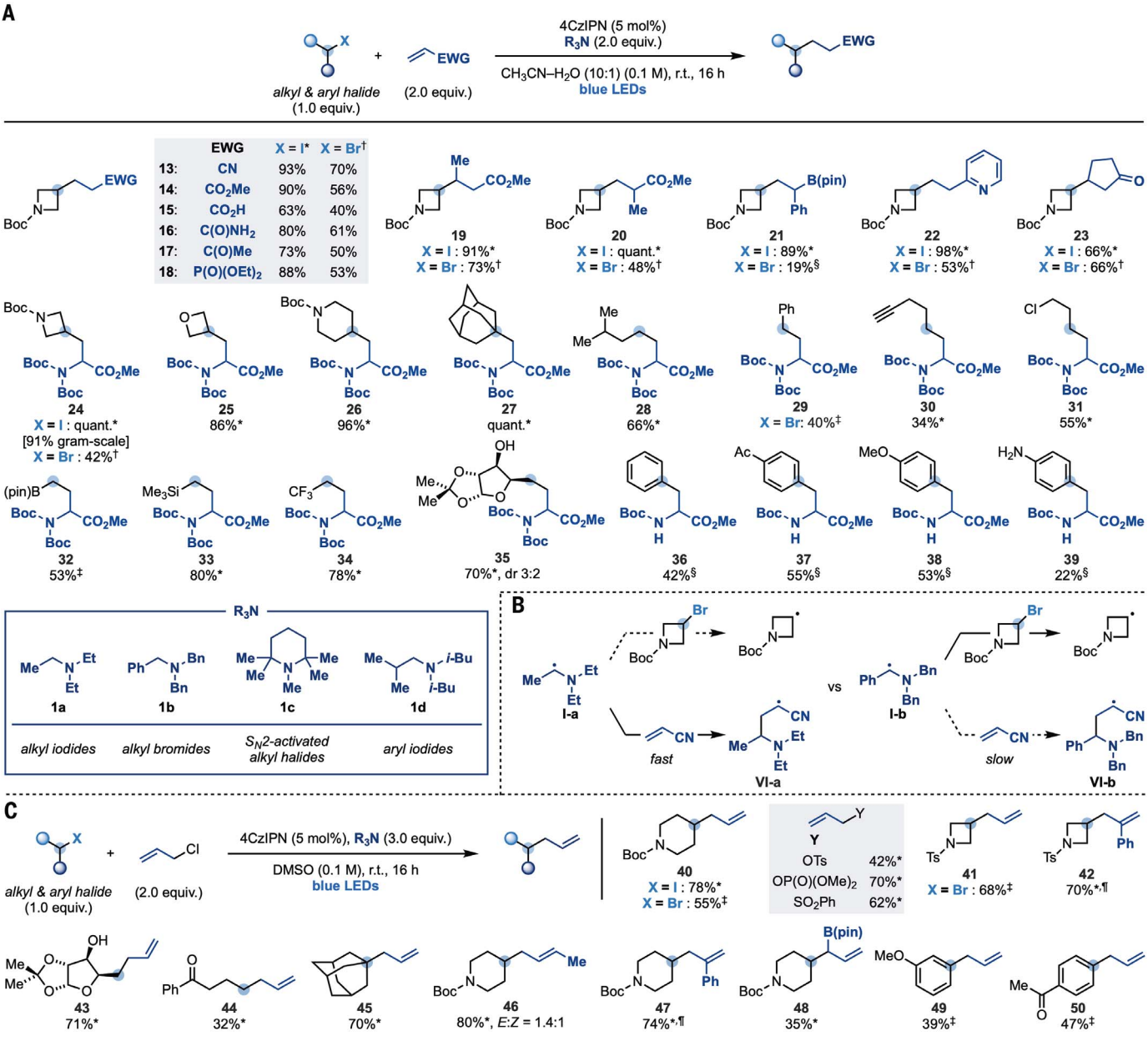

Fig. 3. Application to hydroalkylation and allylation. (**A**) Scope for the alkylation of alkyl iodides, alkyl bromides, and aryl iodides. *__1a__ was used as the amine. †__1b__ was used as the amine. ‡__1c__ was used as the amine. §__1d__ was used as the amine. EWG, electron withdrawing group; quant., quantitative; pin, pinacolato; Ac, acetyl; *i*-Bu, *iso*-butyl. (**B**) Tailoring XAT reactivity by modifying the α-aminoalkyl radical structure. (**C**) Scope for the allylation of alkyl iodides, alkyl bromides, and aryl iodides. All yields are isolated. ¶The corresponding allyl sulfone was used. Ts, tosyl.

product **4** by favorable HAT from methyl thioglycolate (S–H BDE = 87 kcal mol^{-1}). Lastly, SET between the thiyl radical and 4CzIPN$^{\bullet-}$, followed by protonation with H_2O, regenerates the thiol along with the ground-state photocatalyst. The choice of 4CzIPN and Et_3N is relevant to our mechanistic hypothesis because neither the excited nor the reduced state of the photocatalyst [$^*E_{ox}$ = −1.04 V; E_{red} = −1.21 V versus SCE (*27*)] or **I-a** [E_{ox} = −1.12 V versus SCE (*27*)] is strong enough to promote direct SET reduction of **3** (E_{red} = −2.35 V versus SCE). This means that the carbon radical generation is now dissected by the redox requirements of the system, and therefore the reductive ability of the photocatalyst is not crucial to the outcome of the reaction. Indeed, this process can be achieved with a diverse range of photocatalysts, including those of limited reductive power (e.g., Fukuzumi's acridinium; E_{red} = −0.57 V versus SCE). The replacement of Et_3N with other common electron donors [e.g., Ph_2N(PMP), sodium ascorbate, or Hantzsch ester] suppressed the reactivity, despite all compounds effectively quenching the excited photocatalyst (*19*). Moreover, other alkyl amines were tested, but only those able to generate an α-aminoalkyl radical promoted the desired reactivity (*19*). These results suggest that alkyl iodide activation via a reductive-quenching photoredox cycle is not operative and that the amine plays a fundamental role in the C–I bond cleavage that goes beyond its capacity to act as an electron donor.

The high yields obtained with the photoredox system, along with the use of H_2O as a stoichiometric H-atom source, prompted exploration of dehalogenation-deuteration reactions using D_2O (Fig. 2D). After optimization, we

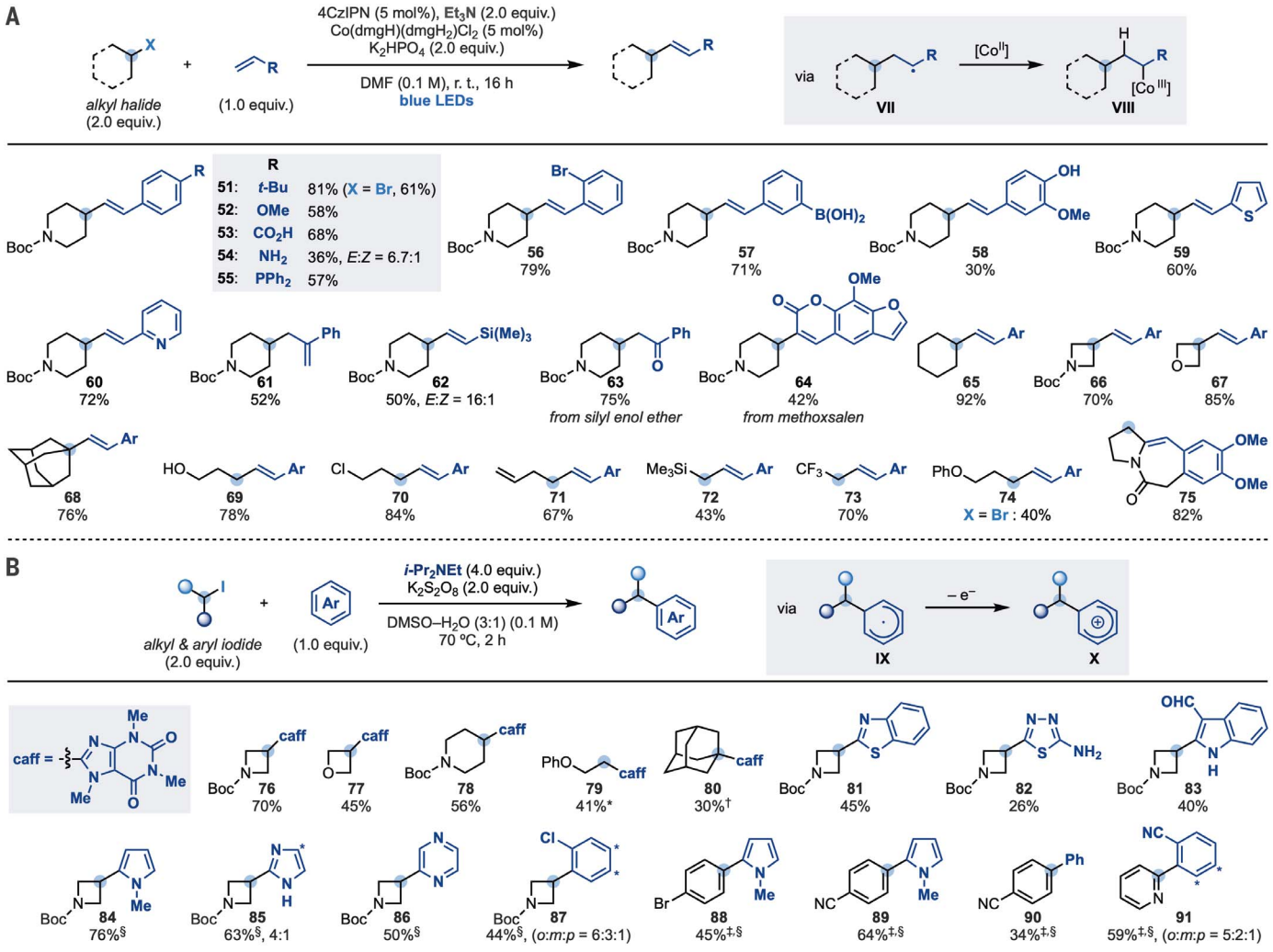

Fig. 4. Application to olefinations and arylations. (**A**) Scope for olefination of alkyl iodides and alkyl bromides. dmg, dimethylglyoximate; DMF, dimethylformamide. (**B**) Scope for the C–H alkylation and arylation of aromatics. All yields are isolated. *__1c__ was used as the amine. †Me_3N was used as the amine. ‡Bu_3N was used as the amine. §The reaction was run with 50 equiv of the arene. DMSO, dimethyl sulfoxide. Asterisks in structures indicate the position of the minor constitutional isomer.

achieved efficient deuteration of primary, secondary, and tertiary alkyl iodides in nearly quantitative yields (**5** to **12**). The mild reaction conditions tolerated multiple functional groups, showcasing the strong chemoselectivity of this XAT approach. Activation of alkyl bromides is still a challenging task in radical chemistry and is considered unfeasible using trialkylborane–O_2 systems (*28*). Our α-aminoalkyl radical–based XAT strategy is applicable to bromides, albeit in lower conversion compared with the results obtained for iodides.

The XAT strategy oxidatively generates carbon radicals from organic halides, representing an umpolung approach relative to the natural redox requirement for SET activation of these building blocks. We posited that the generated radicals could therefore be used in similar mechanistic scenarios to those involving carboxylic acids or potassium trifluoroborates, allowing their modular application in net reductive processes such as cross-electrophile couplings (*29*, *30*).

We explored this premise by developing Giese-type hydroalkylation of electron-poor olefins. Although these transformations have been performed with the aid of nickel catalysis, they typically require the use of stoichiometric metal reductants (e.g., Mn^0, Zn^0) or silane H-donors (*31*, *32*). In our case, because α-aminoalkyl radicals have been used as substrates in Giese additions (*33*), the success of this strategy hinged on their capacity to undergo XAT preferentially over their known reaction with the olefin. Exploration began with 3-iodo-*N*-Boc-azetidine in the presence of Et_3N and 4CzIPN under blue light irradiation (Fig. 3A; see fig. S10 for a proposed mechanism). A diverse range of electron-poor olefins were efficiently converted to the corresponding products in high to excellent yields (**13** to **23**). A variety of functionalities—including polar groups such as free carboxylic acid, primary amide, pyridine, and boronic ester—were readily accommodated. When the same reactions were attempted using 3-bromo-*N*-Boc-azetidine, no desired product was obtained and a substantial amount of the adduct arising from direct addition of **I-a** to the olefin acceptor was identified (Fig. 3B). In this case, XAT is slower owing to the stronger nature of the C–Br bond, thus rendering the direct Giese reaction of **I-a** with the acceptor competitive [observed rate constant k_{obs} ~ 10^7 M^{-1} s^{-1} (*21*)]. We therefore reasoned that the modulation of the electronic and steric properties of the α-aminoalkyl radical could be used to tune its reactivity. Indeed, we used tribenzylamine (**1b**) to restore XAT as the favored pathway for reactions of unactivated alkyl bromides in these hydroalkylations. Because the stabilized α-aminoalkyl

radical **I-b** was essentially unreactive toward electron-poor olefins [calculated rate constant $k_{calc} \sim 10^{-1}\ M^{-1}\ s^{-1}$ (*21*)], bromine abstraction became possible, providing the desired products in good yields.

We next explored the alkyl iodide scope by using Boc-protected dehydroalanine as an olefin acceptor, thus providing convenient access to unnatural amino acids (**24** to **35**). In this case, a variety of organyl groups bearing common functionalities (e.g., free alcohol, alkyl chloride, silane, and terminal alkyne) were compatible, reflecting the mildness of the reaction conditions. This protocol has also been carried out at gram scale without erosion in yield. The ability to generate primary alkyl radicals complements approaches that use oxalates and trifluoroborates, which are known to experience sluggish fragmentations (*34*, *35*). When alkyl halides activated toward S_N2 (second-order nucleophilic displacement) attack by Et_3N (e.g., **29** and **32**) were employed, the desired products were, unsurprisingly, obtained in low yields. This hurdle was addressed by adjusting the steric properties of the XAT reagent: Efficient couplings were achieved with the use of the bulkier amine 1,2,2,6,6-pentamethylpiperidine (PMP; **1c**). We have also been able to extend this methodology to unactivated aryl iodides by using the more hindered but less stabilized α-aminoalkyl radical derived from triisobutylamine (**1d**). These conditions enabled direct access to aryl radicals by sp^2 C–I bond cleavage and were applied to the one-pot transformation of tosylated serine into phenylalanine derivatives (**36** to **39**). Overall, these results illustrate how the large structural diversity of available tertiary amines facilitates the rational tailoring of the α-aminoalkyl radical reactivity to address different challenges in carbon-halogen bond activation.

The XAT strategy for cross-electrophile coupling is not restricted to electron-poor olefins. We also achieved efficient allylation of alkyl and aryl halides by using simple allyl chlorides and other pseudohalides (**40** to **50**) (Fig. 3C; see fig. S12 for a proposed mechanism). This approach bypasses the conventional conversion of one of the two coupling partners into a Grignard or organozinc reagent (*36*) and therefore tolerates functionalities, such as free alcohol and ketone, that are often troublesome with organometallics.

To further demonstrate the versatility of this activation mode, we sought to adapt it to target the use of alkyl halides in Heck-type olefinations, a long-standing challenge in conventional palladium catalysis, owing to undesired β-hydride elimination (*37*–*39*). Specifically, we questioned whether, after addition of alkyl radicals to suitable olefins (**VII**), a cobaloxime cocatalyst might trigger a dehydrogenation reaction (*40*), thus leading to sp^3-sp^2 C–C bond formation (via **VIII**) without the need for precious metals (see fig. S14 for a proposed mechanism). As shown in Fig. 4A, we found this dual XAT–[Co] protocol feasible, thus allowing direct olefination of primary, secondary, and tertiary alkyl iodides and bromides exclusively as the *E* isomers (**51** to **74**, with the exception of **54** and **62**). The broad functional group compatibility was demonstrated with the successful engagement of substrates containing phenol, aniline, and benzoic acid moieties, as well as aryl bromide, boronic acid, and phosphine groups that could limit application under transition metal catalysis. The olefination was also very effective in intramolecular settings, as showcased by the construction of tricyclic **75** in good yield. Couplings with aryl iodides were attempted but generally resulted in low yields.

In a final effort to establish the generality of this XAT strategy, we turned our attention to the direct aromatic C–H alkylation via radical intermediates (Fig. 4B; see fig. S15 for a proposed mechanism). Recently, the use of zinc alkylsulfinates has provided a powerful and effective solution to this synthetic challenge (*41*, *42*). Because these reagents are often prepared from the corresponding halides, a methodology that directly uses these building blocks would obviate multistep synthesis of any reactive intermediate. In this case, however, a photoredox system for α-aminoalkyl radical generation is difficult to implement, owing to the mechanistic requirement of a second oxidation after radical addition to the arene to allow rearomatization (**IX**→**X**). The broad set of reactivity modes for α-aminoalkyl radical generation enabled identification of simple thermal, net oxidative conditions for the direct alkylation of caffeine with alkyl iodides, without the need for light or catalysts (**76** to **80**). This manifold for aromatic C–H alkylation was compatible with the installation of primary, secondary, and tertiary alkyl groups and could be extended to other heteroarenes commonly found in bioactive molecules, such as indoles and azoles as well as benzenoids (*43*) (**81** to **87**). Furthermore, we demonstrated that aryl iodide activation and subsequent sp^2-sp^2 coupling (*44*) is also possible, as shown by the successful preparation of **88** to **91**.

The results presented here demonstrate that alkyl and aryl halides can be converted to carbon radicals by XAT using α-aminoalkyl radicals. We believe that the broad scope, functional group tolerance, and modularity of this approach for carbon-halogen bond activation will likely be of great utility to chemists in both academia and industry.

REFERENCES AND NOTES

1. J. M. Smith, S. J. Harwood, P. S. Baran, *Acc. Chem. Res.* **51**, 1807–1817 (2018).
2. S. P. Pitre, N. A. Weires, L. E. Overman, *J. Am. Chem. Soc.* **141**, 2800–2813 (2019).
3. C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **113**, 5322–5363 (2013).
4. J. Xuan, Z.-G. Zhang, W.-J. Xiao, *Angew. Chem. Int. Ed.* **54**, 15632–15641 (2015).
5. J. K. Matsui, S. B. Lang, D. R. Heitz, G. A. Molander, *ACS Catal.* **7**, 2563–2575 (2017).
6. A. Togni *et al.*, *Angew. Chem. Int. Ed.* 10.1002/anie.201911660 (2019).
7. J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.* **4**, 854–859 (2012).
8. H. Kim, C. Lee, *Angew. Chem. Int. Ed.* **51**, 12303–12306 (2012).
9. Y. Shen, J. Cornella, F. Juliá-Hernández, R. Martin, *ACS Catal.* **7**, 409–412 (2017).
10. D. Alpers, M. Gallhof, J. Witt, F. Hoffmann, M. Brasholz, *Angew. Chem. Int. Ed.* **56**, 1402–1406 (2017).
11. J. L. Kuo, C. Lorenc, J. M. Abuyuan, J. R. Norton, *J. Am. Chem. Soc.* **140**, 4512–4516 (2018).
12. G. Nocera *et al.*, *J. Am. Chem. Soc.* **140**, 9751–9757 (2018).
13. W. P. Neumann, *Synthesis* **1987**, 665–683 (1987).
14. C. Chatgilialoglu, C. Ferreri, Y. Landais, V. I. Timokhin, *Chem. Rev.* **118**, 6516–6572 (2018).
15. H. Yorimitsu, K. Oshima, in *Radicals in Organic Synthesis*, P. Renaud, M. P. Sibi, Eds. (Wiley, 2008), pp. 11–27.
16. C. Le, T. Q. Chen, T. Liang, P. Zhang, D. W. C. MacMillan, *Science* **360**, 1010–1014 (2018).
17. P. Zhang, C. C. Le, D. W. C. MacMillan, *J. Am. Chem. Soc.* **138**, 8084–8087 (2016).
18. W. H. Tamblyn, E. A. Vogler, J. K. Kochi, *J. Org. Chem.* **45**, 3912–3915 (1980).
19. See the supplementary materials for more information.
20. J. C. Scaiano, in *Reactive Intermediate Chemistry*, R. A. Moss, M. S. Platz, M. Jones, Eds. (Wiley, 2005), pp. 847–871.
21. J. Lalevée, B. Graff, X. Allonas, J. P. Fouassier, *J. Phys. Chem. A* **111**, 6991–6998 (2007).
22. K. U. Ingold, J. Lusztyk, J. C. Scaiano, *J. Am. Chem. Soc.* **106**, 343–348 (1984).
23. K. Nakajima, Y. Miyake, Y. Nishibayashi, *Acc. Chem. Res.* **49**, 1946–1956 (2016).
24. S. G. Cohen, A. Parola, G. H. Parsons, *Chem. Rev.* **73**, 141–161 (1973).
25. J. K. Laha, K. S. S. Tummalapalli, A. Nair, N. Patel, *J. Org. Chem.* **80**, 11351–11359 (2015).
26. D. D. M. Wayner, J. J. Dannenberg, D. Griller, *Chem. Phys. Lett.* **131**, 189–191 (1986).
27. J. Luo, J. Zhang, *ACS Catal.* **6**, 873–877 (2016).
28. V. Soulard, G. Villa, D. P. Vollmar, P. Renaud, *J. Am. Chem. Soc.* **140**, 155–158 (2018).
29. D. A. Everson, D. J. Weix, *J. Org. Chem.* **79**, 4793–4798 (2014).
30. E. Richmond, J. Moran, *Synthesis* **50**, 499–513 (2018).
31. K. M. M. Huihui, R. Shrestha, D. J. Weix, *Org. Lett.* **19**, 340–343 (2017).
32. F. Zhou, J. Zhu, Y. Zhang, S. Zhu, *Angew. Chem. Int. Ed.* **57**, 4058–4062 (2018).
33. R. A. Aycock, C. J. Pratt, N. T. Jui, *ACS Catal.* **8**, 9115–9119 (2018).
34. C. C. Nawrat, C. R. Jamison, Y. Slutskyy, D. W. C. MacMillan, L. E. Overman, *J. Am. Chem. Soc.* **137**, 11270–11273 (2015).
35. C. Lévêque, L. Chenneberg, V. Corcé, C. Ollivier, L. Fensterbank, *Chem. Commun.* **52**, 9877–9880 (2016).
36. H. Yorimitsu, K. Oshima, *Angew. Chem. Int. Ed.* **44**, 4435–4439 (2005).
37. M. R. Netherton, G. C. Fu, in *Palladium in Organic Synthesis*, J. Tsuji, Ed. (Springer, 2005), pp. 85–108.
38. G.-Z. Wang, R. Shang, W.-M. Cheng, Y. Fu, *J. Am. Chem. Soc.* **139**, 18307–18312 (2017).
39. D. Kurandina, M. Parasram, V. Gevorgyan, *Angew. Chem. Int. Ed.* **56**, 14212–14216 (2017).
40. X. Sun, J. Chen, T. Ritter, *Nat. Chem.* **10**, 1229–1233 (2018).
41. Y. Fujiwara *et al.*, *Nature* **492**, 95–99 (2012).
42. R. Gianatassio *et al.*, *Angew. Chem. Int. Ed.* **53**, 9851–9855 (2014).
43. Z. Jiao, L. H. Lim, H. Hirao, J. S. Zhou, *Angew. Chem. Int. Ed.* **57**, 6294–6298 (2018).
44. I. Ghosh, T. Ghosh, J. I. Bardagi, B. König, *Science* **346**, 725–728 (2014).

ACKNOWLEDGMENTS

We thank D. Heyes for help with laser flash photolysis studies. **Funding:** D.L. thanks EPSRC for a Fellowship (EP/P004997/1) and the European Research Council for a research grant (758427). **Author contributions:** F.J. and D.L. designed the project and wrote the manuscript. T.C., M.Z., A.R., and F.J. performed all experiments. N.S.S. performed the computational studies. All authors analyzed the results. **Competing interests:** The authors declare no competing interests. **Data and materials availability:** All data are available in the main text or the supplementary materials.

SUPPLEMENTARY MATERIALS

science.sciencemag.org/content/367/6481/1021/suppl/DC1
Materials and Methods
Figs. S1 to S24
Tables S1 to S16
NMR Spectra
References (*45–101*)

16 November 2019; accepted 31 January 2020
10.1126/science.aba2419

Aminoalkyl radicals as halogen-atom transfer agents for activation of alkyl and aryl halides

Timothée Constantin, Margherita Zanini, Alessio Regni, Nadeem S. Sheikh, Fabio Juliá and Daniele Leonori

Science **367** (6481), 1021-1026.
DOI: 10.1126/science.aba2419

Amines as a gateway to alkyl radicals

In recent years, photoredox catalysis driven by blue light has often been used to oxidize carbon centers adjacent to nitrogen. Constantin *et al.* now show that these aminoalkyl radicals can, in turn, conveniently strip iodine atoms from a variety of alkyl carbons. The new alkyl radicals that result readily undergo deuteration and couplings such as alkylation, allylation, and olefination. The upshot is that simple amines can replace more hazardous conventional reagents such as trialkyltin compounds in the homolytic activation and functionalization of halocarbons.

Science, this issue p. 1021