ORGANIC CHEMISTRY FRONTIERS

RESEARCH ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Org. Chem. Front.*, 2021, **8**, 6395

Radical heteroarylation of unactivated remote C(sp^3)–H bonds *via* intramolecular heteroaryl migration†

Zhu Cao,‡[a] Huihui Zhang,‡[a] Xinxin Wu,[a] Yahong Li *[a] and Chen Zhu *[a,b]

Received 12th August 2021,
Accepted 18th September 2021

DOI: 10.1039/d1qo01209f

rsc.li/frontiers-organic

The radical-mediated heteroarylation of unactivated remote C(sp^3)–H bonds *via* intramolecular heteroaryl migration is achieved, leading to a variety of heteroaryl-substituted aliphatic ketones. A library of O-/S-/N-containing heteroaryls such as benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, oxazolyl, and thiazolyl are amenable to the migration approach. The heteroaryl migration is triggered by an azido radical-mediated hydrogen atom abstraction from unactivated aliphatic C(sp^3)–H bonds. The transformation features mild C–C bond cleavage, good selectivity for tertiary C(sp^3)–H bonds, and broad functional group compatibility.

Introduction

Heteroarenes are important structural motifs widely existing in natural and pharmaceutical products, and materials science.[1] Over the past century, tremendous efforts from organic chemistry communities have been devoted to construct heteroarenes and investigate their transformations. Notwithstanding the great progress achieved in heterocyclic chemistry, our group has a long-term interest in developing ingenious approaches to incorporate heteroarenes to target molecules by radical-mediated functional group migration.[2–4] For instance, radical-mediated difunctionalization of alkenes *via* intramolecular heteroaryl migration provides an efficient tactic for the concomitant installation of a heteroaryl and another functional group in an alkene.[3] An upgraded docking-migration strategy significantly extends the compatibility of substrates, allowing the radical heteroarylation of more general alkenes.[4]

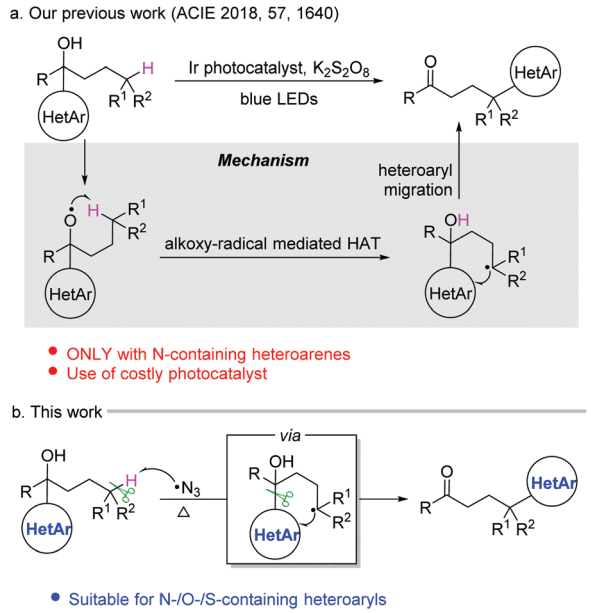
Direct functionalization of inert C(sp^3)–H bonds represents a powerful and atom-economical synthetic strategy.[5] As a complement to transition metal-catalyzed C(sp^3)–H activation, radical-mediated site-selective functionalization of C(sp^3)–H bonds has received rapidly increasing attention,[6,7] and many new reaction modes have been unveiled during the last decade. It should be noted that although remote radical C–H-functionalization has become a heavily investigated field of the chemical community, the remote C(sp^3)–H arylation as addressed herein is particularly challenging and only very few examples have been reported complementing transition-metal-catalyzed C(sp^3)–H arylation that only work for primary and secondary alkyl sites.[6h,i] In 2018, we disclosed a tertiary alcohol-directed radical heteroarylation of unactivated C(sp^3)–H bonds *via* remote heteroaryl migration under photochemical conditions (Scheme 1a).[8] In the presence of an Ir complex as a photocatalyst and potassium persulfate as an oxidant, the nascent alkoxy radical enabled the hydrogen atom transfer (HAT) and the ensuing heteroaryl migration. Although (benzo) thiazolyl and pyridyl were readily incorporated at the δ-position of alcohols, the substrates were limited to alcohols bearing N-containing heteroaryls. Despite the fact that O/S-containing heteroaryls have also showcased the migratory aptitude,[3h,i] they were not tolerated under strong oxidation conditions due to their high electron density, and thus failed to generate the desired products. To address this issue, we conceive an intermolecular HAT instead of the alkoxy radical-mediated intramolecular HAT to generate the alkyl radical, and meanwhile avoid the use of harsh conditions. Considering that the azido radical is a common HAT species easily accessible under mild conditions,[9] we envision that the azido radical-mediated HAT might be compatible with the following O-/S-containing heteroaryl migration, thus realizing the unprecedented O-/S-heteroarylation of unactivated C(sp^3)–H bonds by a functional group migration strategy (Scheme 1b).

Herein, we provide the proof of principle for the hypothesis. Compared to the previous protocol,[8] the current one provides

[a]*Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, 199 Ren-Ai Road, Suzhou, Jiangsu 215123, China. E-mail: chzhu@suda.edu.cn, liyahong@suda.edu.cn*
[b]*Key Laboratory of Synthetic Chemistry of Natural Substances, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China*

†Electronic supplementary information (ESI) available. See DOI: 10.1039/d1qo01209f

‡These authors have contributed equally to this paper.



Scheme 1 Radical-mediated heteroarylation of unactivated C(sp^3)–H bonds by means of functional group migration.

a broader substrate scope for the azido radical-mediated heteroarylation of C(sp^3)–H bonds. In addition to N-containing heteroaryls, O- and S-containing heteroaryls also readily migrate in the reaction, leading to heteroaryl-substituted aliphatic ketones in synthetically useful yields. The transformation features mild C–C bond cleavage, good selectivity for tertiary C(sp^3)–H bonds, and wide functional group compatibility.

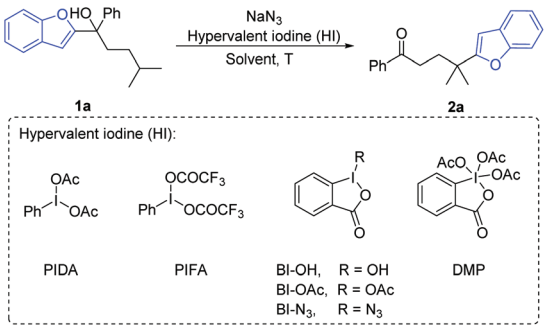
Results and discussion

We commenced the investigation with the benzofuryl-substituted tertiary alcohol **1a** as a model substrate and the combination of (diacetoxyiodo)benzene (PIDA) and sodium azide as the azido radical source (Table 1). Among the screened organic solvents, MeCN delivered the highest yield of the desired product **2a** (entries 1–7). Elevating the reaction temperature to 80 °C improved the isolated yield of **2a** to 53% (entry 8). It was found that changing the temperature to be higher or lower did not further increase the yield (entries 9 and 10). The amounts of PIDA and NaN_3 were then examined (entries 11–15), showing that the use of excess PIDA and NaN_3 was indeed beneficial for the reaction (entry 11). Slightly increasing the volume of MeCN to 2.5 mL resulted in a better yield (entry 16). The survey of hypervalent iodine (HI) reagents indicated that PIDA is still the most efficient reagent (entry 16, entries 18–22). Surprisingly, BI-N_3 capable of serving both as an oxidant and azido radical source did not provide the expected reactivity in the absence of NaN_3 (entry 23).

With the optimized reaction conditions in hand, the generality of the protocol was assessed (Scheme 2). A variety of tertiary alcohols bearing either an electron-rich or electron-deficient substituent were converted into the corresponding ketone products (**2a–2t**). The use of substrates with *para*-, *meta*-, or *ortho*-substitution resulted in comparable yields (**2b–2d**, **2e–2g**, and **2k–2m**), probably suggesting that the steric hindrance of tertiary alcohols did not affect the reaction yield much. The moderate yields of products **2b–2d** might be attributed to the competitive HAT with the benzylic C–H bonds of substrates.[10] Other tertiary C(sp^3)–H bonds, such as the cyclohexyl C–H bond (**2u**), and the C–H bond adjacent to the O-atom (**2v**) were also regioselectively functionalized. Not only aryl ketones but also some dialkyl ketones were generated, albeit with decreased yields (**2w–2y**). In addition to benzofuryl, other heteroaryls such as benzothienyl, benzothiazolyl, thiazolyl, benzoxazolyl, and oxazolyl also readily migrated in the reaction, leading to the desired products in synthetically useful yields (**2z–2af**).

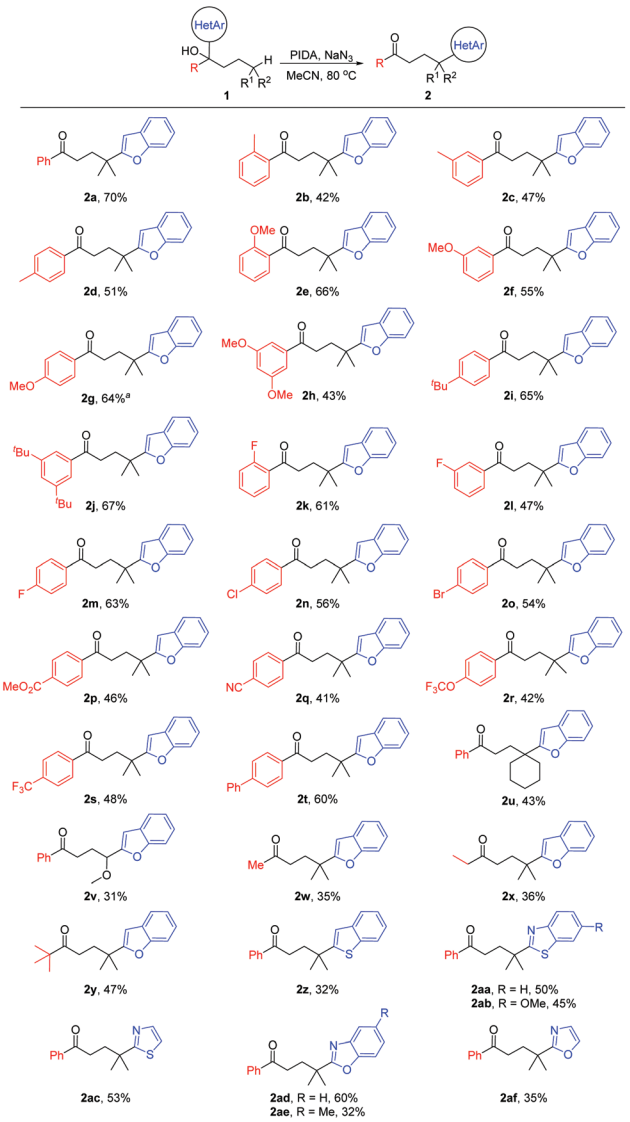
In order to illustrate the utility of the product, the transformations of **2a** were performed. Upon treating **2a** with

Table 1 Survey of reaction parameters[a]

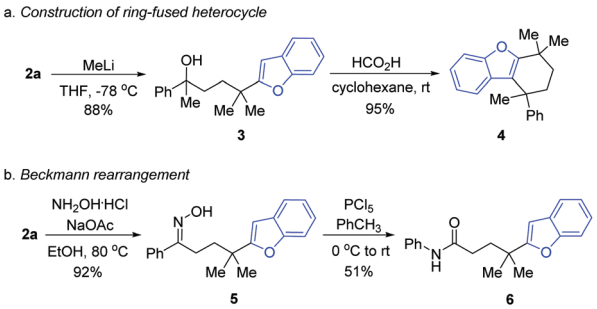


Entry	HI	Solvent (mL)	T (°C)	Yield[b] (%)
1[c]	PIDA	MeCN (2.0)	30	37
2[c]	PIDA	THF (2.0)	30	<10
3[c]	PIDA	$PhCF_3$ (2.0)	30	25
4[c]	PIDA	DMF (2.0)	30	<10
5[c]	PIDA	EA (2.0)	30	31
6[c]	PIDA	DCM (2.0)	30	35
7[c]	PIDA	^{t}BuCN (2.0)	30	<10
8[c]	PIDA	MeCN (2.0)	80	53
9[c]	PIDA	MeCN (2.0)	70	47
10[c]	PIDA	MeCN (2.0)	90	46
11	PIDA	MeCN (2.0)	80	60
12[d]	PIDA	MeCN (2.0)	80	58
13[e]	PIDA	MeCN (2.0)	80	58
14[f]	PIDA	MeCN (2.0)	80	44
15[g]	PIDA	MeCN (2.0)	80	36
16	PIDA	MeCN (2.5)	80	70
17	PIDA	MeCN (3.0)	80	65
18	PIFA	MeCN (2.5)	80	30
19	BI-OH	MeCN (2.5)	80	Trace
20	BI-OAc	MeCN (2.5)	80	53
21	BI-N_3	MeCN (2.5)	80	57
22	DMP	MeCN (2.5)	80	<10
23[h]	BI-N_3	MeCN (2.5)	80	Trace

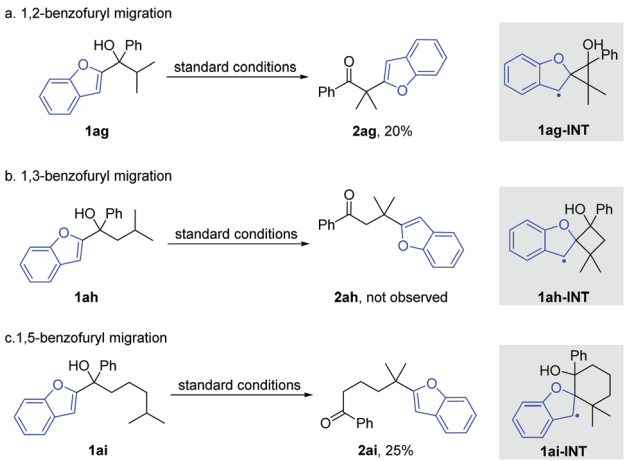
[a] Reaction conditions: **1a** (0.2 mmol), HI (4.0 equiv.), and NaN_3 (4.0 equiv.) in MeCN (2.5 mL), 80 °C for 12 h. [b] Isolated yield. [c] PIDA (2.5 equiv.), NaN_3 (2.5 equiv.). [d] PIDA (3.5 equiv.), NaN_3 (3.5 equiv.). [e] PIDA (4.5 equiv.), NaN_3 (4.5 equiv.). [f] PIDA (4.0 equiv.), NaN_3 (2.0 equiv.). [g] PIDA (2.0 equiv.), NaN_3 (4.0 equiv.). [h] Without NaN_3.



Scheme 2 Substrate scope. Reaction conditions: **1** (0.2 mmol), PIDA (4.0 equiv.), and NaN_3 (4.0 equiv.) in MeCN (2.5 mL), 80 °C for 12 h. Yields of the isolated products are given. [a]PIDA (6.0 equiv.) and NaN_3 (6.0 equiv.).



Scheme 3 Synthetic applications.

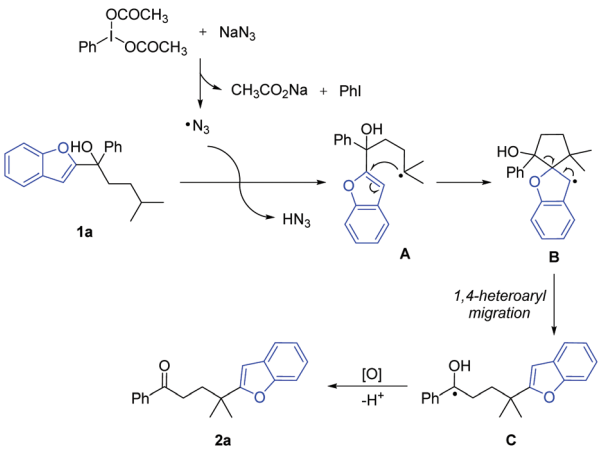


Scheme 4 Investigations on the preference of cyclic intermediates.

methyl lithium, the tertiary alcohol **3** was generated, which was then subjected to intramolecular annulation *via* dehydration in the presence of formic acid, leading to the valuable ring-fused heterocyclic product **4** in a high yield (Scheme 3a). Treating **2a** with hydroxylamine hydrochloride and sodium acetate generated the oxime **5**, which served as the precursor of Beckmann rearrangement to afford the corresponding amide **6** (Scheme 3b).

Afterwards, the migration distance was varied in the substrates to probe the transition states that might influence the heteroaryl migration (Scheme 4). In Scheme 2, all products were obtained *via* 1,4-heteroaryl migration, facilitated by a kinetically favoured five-membered cyclic intermediate. The 1,2-/1,5-benzofuryl migration *via* a three- or six-membered cyclic intermediate also proceeded, however, affording the corresponding products **2ag** and **2ai** in low yields (Scheme 4a and c). In sharp contrast, the 1,3-benzofuryl migration did not proceed owing to the disfavoured four-membered cyclic intermediate (Scheme 4b).

Based on the experimental results, a proposed mechanism is shown in Scheme 5. The interaction of PIDA with NaN_3 gen-



Scheme 5 Proposed mechanism.

erates an azido radical that regioselectively abstracts a hydrogen atom from the tertiary C(sp^3)–H bond with the lowest bond dissociation energy. The resulting alkyl radical intermediate **A** undergoes intramolecular cyclization to generate the spiro radical intermediate **B**. The subsequent 1,4-heteroaryl migration *via* a five-membered cyclic intermediate results in the metastable ketyl radical **C**. Finally, single-electron oxidation of **C** with PIDA followed by deprotonation furnishes the desired product **2a**.

Conclusions

In summary, a radical-mediated remote heteroarylation of unactivated C(sp^3)–H bonds of tertiary alcohols has been disclosed, leading to a variety of useful heteroaryl-substituted aliphatic ketones. The reaction proceeds *via* a cascade of azido radical-mediated HAT and intramolecular heteroaryl migration, in which an inert C–H bond and C–C bond are consecutively cleaved under mild conditions. A library of O-/S-/N-containing heteroaryls, such as benzofuryl, benzothiazolyl, benzothienyl, benzoxazolyl, oxazolyl, and thiazolyl, readily migrate in the reactions. Mechanistic studies reveal that the heteroaryl migration prefers a five-membered cyclic intermediate. Moreover, the transformation features broad functional group tolerance and good regioselectivity. This protocol offers an ingenious approach for selective functionalization of inert C(sp^3)–H bonds.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors are grateful for the financial support from the National Natural Science Foundation of China (grant no. 21971173, 22001185, 21772140), the Project of Scientific and Technologic Infrastructure of Suzhou (SZS201905), and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

Notes and references

1 (*a*) N. A. McGrath, M. Brichacek and J. T. Njardarson, A graphical journey of innovative organic architectures that have improved our lives, *J. Chem. Educ.*, 2010, **87**, 1348; (*b*) A. J. Waldman, T. L. Ng, P. Wang and E. P. Balskus, Heteroatom–heteroatom bond formation in natural product biosynthesis, *Chem. Rev.*, 2017, **117**, 5784; (*c*) M. Stępień, E. Gońka, M. Żyła and N. Sprutta, Heterocyclic nanographenes and other polycyclic heteroaromatic compounds: synthetic routes, properties, and applications, *Chem. Rev.*, 2017, **117**, 3479; (*d*) Z. Cai, M. A. Awais, N. Zhang and L. Yu, Exploration of syntheses and functions of higher ladder-type π-conjugated heteroacenes, *Chem*, 2018, **4**, 2538; (*e*) M. N. Peerzada, E. Hamel, R. Bai, C. T. Supuran and A. Azam, Deciphering the key heterocyclic scaffolds in targeting microtubules, kinases and carbonic anhydrases for cancer drug development, *Pharmacol. Ther.*, 2021, **225**, 107860.

2 For reviews on radical-mediated heteroaryl migration, see: (*a*) X. Wu and C. Zhu, Radical-mediated remote functional group migration, *Acc. Chem. Res.*, 2020, **53**, 1620; (*b*) X. Wu, S. Wu and C. Zhu, Radical-mediated difunctionalization of unactivated alkenes through distal migration of functional groups, *Tetrahedron Lett.*, 2018, **59**, 1328; (*c*) X. Wu, Z. Ma, T. Feng and C. Zhu, Radical-mediated rearrangements: past, present, and future, *Chem. Soc. Rev.*, 2021, DOI: 10.1039/d1cs00529d.

3 (*a*) Z. Wu, D. Wang, Y. Liu, L. Huan and C. Zhu, Chemo- and regioselective distal heteroaryl *ipso*-migration: a general protocol for heteroarylation of unactivated alkenes, *J. Am. Chem. Soc.*, 2017, **139**, 1388; (*b*) H. Zhang, X. Wu, Q. Zhao and C. Zhu, Copper-catalyzed heteroarylsilylation of unactivated olefins through distal heteroaryl migration, *Chem. – Asian J.*, 2018, **13**, 2453; (*c*) D. Chen, Z. Wu, Y. Yao and C. Zhu, Phosphinoyl-functionalization of unactivated alkenes through phosphinoyl radical-triggered distal functional group migration, *Org. Chem. Front.*, 2018, **5**, 2370; (*d*) M. Wang, Z. Wu, B. Zhang and C. Zhu, Azidoheteroarylation of unactivated olefins through distal heteroaryl migration, *Org. Chem. Front.*, 2018, **5**, 1896; (*e*) D. Chen, M. Ji, Y. Yao and C. Zhu, Difunctionalization of unactivated alkenes through SCF_3 radical-triggered distal functional group migration, *Acta Chim. Sin.*, 2018, **76**, 951; (*f*) J. Yu, D. Wang, Y. Xu, Z. Wu and C. Zhu, Distal functional group migration for visible-light induced carbo-difluoroalkylation/monofluoroalkylation of unactivated alkenes, *Adv. Synth. Catal.*, 2018, **360**, 744; (*g*) N. Tang, S. Yang, X. Wu and C. Zhu, Visible-light-induced carbosulfonylation of unactivated alkenes *via* remote heteroaryl and oximino migration, *Tetrahedron*, 2019, **75**, 1639; (*h*) H. Zhang, L. Kou, D. Chen, M. Ji, X. Bao, X. Wu and C. Zhu, Radical-mediated distal *ipso*-migration of O/S-containing heteroaryls and DFT studies for migratory aptitude, *Org. Lett.*, 2020, **22**, 5947; (*i*) H. Zhang, M. Ji, Y. Wei, H. Chen, X. Wu and C. Zhu, Radical-mediated hetaryl functionalization of nonactivated alkenes through distal *ipso*-migration of O- or S-hetaryls, *Synlett*, 2021, **32**, 401.

4 (*a*) J. Yu, Z. Wu and C. Zhu, Efficient docking-migration strategy for selective radical difluoromethylation of alkenes, *Angew. Chem., Int. Ed.*, 2018, **57**, 17156; (*b*) J. Liu, S. Wu, J. Yu, C. Lu, Z. Wu, X. Wu, X.-S. Xue and C. Zhu, Polarity umpolung strategy for the radical alkylation of alkenes, *Angew. Chem.*, 2020, **59**, 8195; (*c*) T. Niu, J. Liu, X. Wu and C. Zhu, Radical heteroarylalkylation of alkenes *via* three-component docking-migration thioetheri-fication cascade, *Chin. J. Chem.*, 2020, **38**, 803; (*d*) H. Zhang, M. Wang, X. Wu and C. Zhu, Designed heterocyclizing

reagents for rapid assembly of N-fused heteroarenes from alkenes, *Angew. Chem.*, 2021, **60**, 3714; (*e*) M. Ji, X. Wang, J. Liu, X. Wu and C. Zhu, Catalyst-free, radical-mediated intermolecular 1,2-arylheteroarylation of alkenes by cleaving inert C-C bond, *Sci. China: Chem.*, 2021, DOI: 10.1007/s11426-021-1077-4; (*f*) M. Ji, C. Chang, X. Wu and C. Zhu, Photocatalytic intermolecular carboarylation of alkenes by selective C–O bond cleavage of diarylethers, *Chem. Commun.*, 2021, **57**, 9240.

5 For selected reviews, see: (*a*) X. Chen, K. M. Engle, D. H. Wang and J.-Q. Yu, Palladium(II)-catalyzed C-H activation/C-C cross-coupling reactions: versatility and practicality, *Angew. Chem., Int. Ed.*, 2009, **48**, 5094; (*b*) J. Yamaguchi, A. D. Yamaguchi and K. Itami, C-H bond functionalization: emerging synthetic tools for natural products and pharmaceuticals, *Angew. Chem., Int. Ed.*, 2012, **51**, 8960; (*c*) S. A. Girard, T. Knauber and C.-J. Li, The cross-dehydrogenative coupling of C(sp^3)-H bonds: a versatile strategy for C-C bond formations, *Angew. Chem., Int. Ed.*, 2014, **53**, 74; (*d*) L. Yang and H. Huang, Transition-metal-catalyzed direct addition of unactivated C-H bonds to polar unsaturated bonds, *Chem. Rev.*, 2015, **115**, 3468; (*e*) K. Yang, M. Song, H. Liu and H. Ge, Palladium-catalyzed direct asymmetric C-H bond functionalization enabled by the directing group strategy, *Chem. Sci.*, 2020, **11**, 12616; (*f*) N. Y. S. Lam, K. Wu and J.-Q. Yu, Advancing the logic of chemical synthesis: C-H activation as strategic and tactical disconnections for C-C bond construction, *Angew. Chem.*, 2021, **60**, 15767; (*g*) D. Aynetdinova, M. C. Callens, H. B. Hicks, C. Y. X. Poh, B. D. A. Shennan, A. M. Boyd, Z. H. Lim, J. A. Leitch and D. J. Dixon, Installing the "magic methyl" - C-H methylation in synthesis, *Chem. Soc. Rev.*, 2021, **50**, 5517.

6 For selected examples, see: (*a*) J. C. K. Chu and T. Rovis, Complementary strategies for directed C(sp^3)-H functionalization: a comparison of transition-metal-catalyzed activation, hydrogen atom transfer, and carbene/nitrene transfer, *Angew. Chem., Int. Ed.*, 2018, **57**, 62; (*b*) S. Sarkar, K. P. S. Cheung and V. Gevorgyan, C-H functionalization reactions enabled by hydrogen atom transfer to carbon-centered radicals, *Chem. Sci.*, 2020, **11**, 12974; (*c*) W. Guo, Q. Wang and J. Zhu, Visible light photoredox-catalysed remote C–H functionalisation enabled by 1,5-hydrogen atom transfer (1,5-HAT), *Chem. Soc. Rev.*, 2021, **50**, 7359; (*d*) L. Capaldo, D. Ravelli and M. Fagnoni, Direct photocatalyzed hydrogen atom transfer (HAT) for aliphatic C-H bonds elaboration, *Chem. Rev.*, 2021, DOI: 10.1021/acs.chemrev.1c00263; (*e*) X.-Q. Hu, J.-R. Chen and W.-J. Xiao, Controllable remote C–H bond functionalization by visible-light photocatalysis, *Angew. Chem., Int. Ed.*, 2017, **56**, 1960; (*f*) X. Wu and C. Zhu, Radical functionalization of remote C(sp^3)-H bonds mediated by unprotected alcohols and amides, *CCS Chem.*, 2020, **2**, 813; (*g*) X. Wu and C. Zhu, Recent advances in alkoxy radical-promoted C-C and C-H bond functionalization starting from free alcohols, *Chem. Commun.*, 2019, **55**, 9747; (*h*) F. W. Friese, C. Mück-Lichtenfeld and A. Studer, Remote C-H functionalization using radical translocating arylating groups, *Nat. Commun.*, 2018, **9**, 2808; (*i*) N. Radhoff and A. Studer, Functionalization of α-C(sp^3)-H bonds in amides using radical translocating arylating groups, *Angew. Chem.*, 2021, **60**, 3561.

7 For selected examples from our group, see: (*a*) X. Wu, H. Zhang, N. Tang, Z. Wu, D. Wang, M. Ji, Y. Xu, M. Wang and C. Zhu, Metal-free alcohol-directed regioselective heteroarylation of remote unactivated C(sp^3)-H bonds, *Nat. Commun.*, 2018, **9**, 3343; (*b*) S. Wu, X. Wu, D. Wang and C. Zhu, Regioselective vinylation of remote unactivated C(sp^3)-H bonds: Access to complex fluoroalkylated alkenes, *Angew. Chem., Int. Ed.*, 2019, **58**, 1499; (*c*) N. Tang, X. Wu and C. Zhu, Practical, metal-free remote heteroarylation of amides *via* unactivated C(sp^3)-H bond functionalization, *Chem. Sci.*, 2019, **10**, 6915; (*d*) S. Yang, X. Wu, S. Wu and C. Zhu, Regioselective sulfonylvinylation of the unactivated C(sp^3)-H bond via a C-centered radical-mediated hydrogen atom transfer (HAT) process, *Org. Lett.*, 2019, **21**, 4837; (*e*) M. Wang, L. Huan and C. Zhu, Cyanohydrin-mediated cyanation of remote unactivated C(sp^3)-H bonds, *Org. Lett.*, 2019, **21**, 821; (*f*) S. Wu, X. Wu, Z. Wu and C. Zhu, Regioselective introduction of vinyl trifluoromethylthioether to remote unactivated C(sp^3)-H bonds via radical translocation cascade, *Sci. China: Chem.*, 2019, **62**, 1507; (*g*) X. Shao, X. Wu, S. Wu and C. Zhu, Metal-free radical-mediated C(sp^3)-H heteroarylation of alkanes, *Org. Lett.*, 2020, **22**, 7450; (*h*) T. Niu, S. Yang, X. Wu and C. Zhu, Remote C(sp^3)-H vinylation *via* radical-mediated consecutive fission of C-H and C-C bonds, *Org. Chem. Front.*, 2020, **7**, 2981.

8 X. Wu, M. Wang, L. Huan, D. Wang, J. Wang and C. Zhu, Tertiary-alcohol-directed functionalization of remote C(sp^3)-H bonds by sequential hydrogen atom and heteroaryl migrations, *Angew. Chem., Int. Ed.*, 2018, **57**, 1640.

9 For selected examples, see: (*a*) A. P. Antonchick and L. Burgmann, Direct selective oxidative cross-coupling of simple alkanes with heteroarenes, *Angew. Chem., Int. Ed.*, 2013, **52**, 3267; (*b*) Y. Wang, X. Hu, C. A. Morales-Rivera, G.-X. Li, X. Huang, G. He, P. Liu and G. Chen, Epimerization of tertiary carbon centers *via* reversible radical cleavage of unactivated C(sp^3)-H bonds, *J. Am. Chem. Soc.*, 2018, **140**, 9678; (*c*) A. S. H. Ryder, W. B. Cunningham, G. Ballantyne, T. Mules, A. G. Kinsella, J. Turner-Dore, C. M. Alder, L. J. Edwards, B. S. J. McKay, M. N. Grayson and A. J. Cresswell, Photocatalytic α-tertiary amine synthesis *via* C-H alkylation of unmasked primary amines, *Angew. Chem.*, 2020, **59**, 14986; (*d*) L. Niu, C. Jiang, Y. Liang, D. Liu, F. Bu, R. Shi, H. Chen, A. D. Chowdhury and A. Lei, Manganese-catalyzed oxidative azidation of C(sp^3)-H bonds under electrophotocatalytic conditions, *J. Am. Chem. Soc.*, 2020, **142**, 17693.

10 (*a*) Y. Zhang and C.-J. Li, DDQ-mediated direct cross-dehydrogenative coupling (CDC) between benzyl ethers and simple ketones, *J. Am. Chem. Soc.*, 2006, **128**, 4242; (*b*) Z. Li, Q. Wang and J. Zhu, Copper-catalyzed remote C(sp^3)-H arylation of carboxamides and sulfonamides, *Angew. Chem., Int. Ed.*, 2018, **57**, 13288.