


 Cite this: *Chem. Commun.*, 2023, 59, 1637

 Received 29th November 2022,
Accepted 13th January 2023

DOI: 10.1039/d2cc06486c

rsc.li/chemcomm

Minisci reaction of heteroarenes and unactivated C(sp³)-H alkanes *via* a photogenerated chlorine radical†

 Zi-Tong Pan, Li-Miao Shen, Fentahun Wondu Dagnaw, Jian-Ji Zhong, 
Jing-Xin Jian * and Qing-Xiao Tong *

Here, an efficient Minisci reaction of heteroarenes and unactivated C(sp³)-H alkanes was achieved using an inexpensive FeCl₃ as a photocatalyst. The photogenerated chlorine radical contributed to the HAT of C-H and subsequently initiated this reaction. Surprisingly, salt water and even seawater can act as a chlorine radical source, which provided an enlightening idea for future organic synthesis methods.

N-heteroarenes, such as benzothiazole and quinoline, are key structural motifs of many natural products, bioactive compounds, and pharmaceuticals (Scheme 1a).¹ The derivatizations of the functionalization of benzothiazoles and quinolines have attracted the attention of many researchers because of their wide existence. The Minisci reaction, which involves the addition of carbon-centered radicals to basic heteroarenes followed by formal hydrogen atom loss,² has provided a robust tool for the late-stage alkylation of N-containing heteroarenes because of its high atomic economy.³ But the photocatalytic derivatization and functionalization of alkylating reagents to produce alkylated carbon radicals are confined to active C(sp³)-H compounds. To date, only a few inactive C(sp³)-H compounds have been used as alkyl reagents. Besides, equivalent oxidants including peroxides,⁴ iodine reagents,⁵ persulfate (S₂O₈²⁻)⁶ and Selectfluor⁷ are required to promote this type of reaction by activating the substrate.

Alkanes, the major constituents of petroleum and natural gas, are widely distributed in nature and are mainly used as fuels, but few are utilized as economical chemical feedstocks.⁸ Unlike the C-H bonds activated by heteroatoms, aldehydes, benzylic and allylic groups,⁹ the unactivated C(sp³)-H bonds in

samples of alkanes have great intrinsic inertness and uncontrollable chemoselectivity due to their high bond dissociation energies (BDEs) of >95 kcal mol⁻¹.^{9b} Therefore, the functionalization of non-activated C(sp³)-H bonds has always been a research hotspot in organic synthetic chemistry. In recent years, the photocatalytic system based on the intermolecular hydrogen atom transfer (HAT) process was developed,¹⁰ which could seize the hydrogen atoms of inactive C(sp³)-H. In addition, the selectivity of the HAT process depends not only on the activated C(sp³)-H bond of the substrate, but also on the electronic effects of the HAT reagent as well as on spatial effects. However, current strategies involving C(sp³)-H bond homolytic cleavage mainly rely on a HAT strategy with bromine, nitrogen, and oxygen as the central electrophilic heteroatom radicals, and strong reducing catalysts or oxidants are required under harsh experimental conditions.¹¹

The chlorine radical (Cl•) is an effective HAT reagent that can cleave various C(sp³)-H bonds.¹² Chlorine (Cl₂)¹³ and N-chlorosuccinimide (NCS) are the two conventional reagents that produce Cl•, which in turn can afford alkyl radicals *via* the HAT process.¹⁴ Consequently, the chlorine radical (Cl•) formed from chloride ions (Cl⁻) as the HAT reagents has a greater potential for C(sp³)-H bond functionalization (Scheme 1b). In previous reports, noble metal catalysts¹⁵ and strong chemical oxidants¹⁶ were usually required in this process. The direct oxidation of soluble chlorides to Cl• requires a high oxidation potential (+ 1.21 V vs. SCE),^{15c} which is intolerant to some of the easily oxidized substrates. On the other hand, photoinduced ligand-to-metal charge transfer (LMCT) can well contribute to the generation of HAT reagents in photocatalytic systems.^{15a,17} However, a mild photocatalytic system avoiding the commonly used strong chemical oxidants and noble metal catalysts is still a serious challenge and is highly required for unactivated C(sp³)-H substrates. In recent years, there have been some reports about photoinduced iron-catalysed Minisci reactions.¹⁸ Herein, we describe a Minisci alkylation reaction of unactivated alkanes catalysed by inexpensive ferric

College of Chemistry and Chemical Engineering, Key Laboratory for Preparation and Application of Ordered Structural Material of Guangdong Province, and Guangdong Provincial Key Laboratory of Marine Disaster Prediction and Prevention, Shantou University, Shantou, Guangdong, 515063, China.
E-mail: jxjian@stu.edu.cn, qxtong@stu.edu.cn

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d2cc06486c>

