

C-H Activation: A Sustainable Approach for the Direct Functionalization of Quinolines [†]

Upendra Sharma ¹

¹ Chemical Technology Division, CSIR-IHBT, Palampur, India;

* Correspondence: upendraihbt@gmail.com (U.S.);

† Presented at Virtual International Conference on Physical Sciences (ICPS - 2021)

Received: 1.02.2021; Revised: 3.02.2021; Accepted: 4.02.2021; Published: 5.02.2021

Abstract: Quinoline is one of the most important heterocycles due to its occurrence in various natural products and pharmaceuticals. Obeying to its importance, tremendous progress has been made towards its synthesis and functionalization. Our group has synthesized various new quinolines derivatives via transition-metal catalyzed C-H activation and metal-free conditions [2, 3]. Most of these methods are applicable for C(sp²)-H functionalization at C8, C2, and C3 positions of quinolines under thermal conditions. We recently initiated work on the functionalization of quinolines under photocatalytic conditions where an efficient iridium-based photocatalyst is used to synthesize β -norbenzomorphan skeleton via unsymmetrical coupling of 2-methylquinolines under the blue LED light [4]. Regioselective methods have also been developed for C(sp³)-methylation, alkylation, and arylation of 8-methylquinolines [5]. Mild reaction conditions for the functionalization of quinolines through proper understanding of the reaction pathway is our long-lasting goal.

Keywords: C-H activation; functionalization of quinolines; LED light.

© 2021 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Funding

This research received no external funding.

Acknowledgments

This research has no acknowledgment.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. a) Sharma, R.; Thakur, K.; Kumar, R.; Kumar, I.; Sharma, U. Distant C-H Activation/Functionalization: A New Horizon of Selectivity Beyond Proximity. *Catalysis Reviews* **2015**, *57*, 345-405, <https://doi.org/10.1080/01614940.2015.1058623>. b) Sharma, R.; Sharma, U. Remote C-H bond activation/transformations: A continuous growing synthetic tool; Part II. *Catalysis Reviews* **2018**, *60*, 497-565, <https://doi.org/10.1080/01614940.2018.1474538>. (c) Sharma, U. et al., *Med. Chem.* **2019**, *15*, 1.
2. Sharma, R.; Kumar, R.; Kumar, I.; Sharma, U. RhIII-Catalyzed Dehydrogenative Coupling of Quinoline N-Oxides with Alkenes: N-Oxide as Traceless Directing Group for Remote C-H Activation. *Eur. J. Org. Chem* **2015**, *2015*, 7519-7528. b) Sharma, R.; Kumar, I.; Kumar, R.; Sharma, U. Rhodium-Catalyzed Remote C-8 Alkylation of Quinolines with Activated and Unactivated Olefins: Mechanistic Study and Total Synthesis of EP4 Agonist. *Advanced Synthesis & Catalysis* **2017**, *359*, 3022-3028,

- <https://doi.org/10.1002/adsc.201700542>. c) Sharma, R.; Kumar, R.; Kumar, R.; Upadhyay, P.; Sahal, D.; Sharma, U. Rh(III)-Catalyzed C(8)-H Functionalization of Quinolines via Simultaneous C-C and C-O Bond Formation: Direct Synthesis of Quinoline Derivatives with Antiplasmodial Potential. *The Journal of Organic Chemistry* **2018**, *83*, 12702-12710, <https://doi.org/10.1021/acs.joc.8b02042>. d) Dhiman, A.K.; Gupta, S.S.; Sharma, R.; Kumar, R.; Sharma, U. Rh(III)-Catalyzed C(8)-H Activation of Quinoline N-Oxides: Regioselective C-Br and C-N Bond Formation. *The Journal of Organic Chemistry* **2019**, *84*, 12871-12880, <https://doi.org/10.1021/acs.joc.9b01538>. e) Sharma, R.; Kumar, R.; Sharma, U. Rh/O₂-Catalyzed C8 Olefination of Quinoline N-Oxides with Activated and Unactivated Olefins. *The Journal of Organic Chemistry* **2019**, *84*, 2786-2797, <https://doi.org/10.1021/acs.joc.8b03176>. f) Dhiman, A.K.; Thakur, A.; Kumar, R.; Sharma, U. Rhodium-Catalyzed Selective C-H Bond Functionalization of Quinolines. *Asian Journal of Organic Chemistry* **2020**, *9*, 1502-1518, <https://doi.org/10.1002/ajoc.202000341>. g) Dhiman, A.K.; Thakur, A.; Kumar, I.; Kumar, R.; Sharma, U. Co(III)-Catalyzed C-H Amidation of Nitrogen-Containing Heterocycles with Dioxazolones under Mild Conditions. *The Journal of Organic Chemistry* **2020**, *85*, 9244-9254, <https://doi.org/10.1021/acs.joc.0c01237>. h) Gupta, S.S.; Kumar, R.; Sharma, U. Regioselective Arylation of Quinoline N-Oxides (C8), Indolines (C7) and N-tert-Butylbenzamide with Arylboronic Acids. *ACS Omega* **2020**, *5*, 904-913, <https://doi.org/10.1021/acs.omega.9b03884>.
3. a) Kumar, R.; Kumar, I.; Sharma, R.; Sharma, U. Catalyst and solvent-free alkylation of quinoline N-oxides with olefins: A direct access to quinoline-substituted α -hydroxy carboxylic derivatives. *Organic & Biomolecular Chemistry* **2016**, *14*, 2613-2617, <https://doi.org/10.1039/C5OB02600H>. b) Dhiman, A.K.; Kumar, R.; Kumar, R.; Sharma, U. Metal-Free Synthesis of 2-Substituted 3-(2-Hydroxyaryl)quinolines and 4-(2-Hydroxyaryl)acridines via Benzyne Chemistry. *The Journal of Organic Chemistry* **2017**, *82*, 12307-12317, <https://doi.org/10.1021/acs.joc.7b02149>. c) Kumar, R.; Kumar, R.; Dhiman, A.K.; Sharma, U. Regioselective Metal-Free C2-H Arylation of Quinoline N-Oxides with Aryldiazonium Salts/Anilines under Ambient Conditions. *Asian Journal of Organic Chemistry* **2017**, *6*, 1043-1053, <https://doi.org/10.1002/ajoc.201700267>. d) Kumar, R.; Chaudhary, S.; Kumar, R.; Upadhyay, P.; Sahal, D.; Sharma, U. Catalyst and Additive-Free Diastereoselective 1,3-Dipolar Cycloaddition of Quinolinium Imides with Olefins, Maleimides, and Benzyne: Direct Access to Fused N,N'-Heterocycles with Promising Activity against a Drug-Resistant Malaria Parasite. *The Journal of Organic Chemistry* **2018**, *83*, 11552-11570, <https://doi.org/10.1021/acs.joc.8b01520>. e) Dhiman, A.K.; Chandra, D.; Kumar, R.; Sharma, U. Catalyst-Free Synthesis of 2-Anilinoquinolines and 3-Hydroxyquinolines via Three-Component Reaction of Quinoline N-Oxides, Aryldiazonium Salts, and Acetonitrile. *The Journal of Organic Chemistry* **2019**, *84*, 6962-6969, <https://doi.org/10.1021/acs.joc.9b00739>. f) Chandra, D.; Dhiman, A.K.; Kumar, R.; Sharma, U. Microwave-Assisted Metal-Free Rapid Synthesis of C4-Arylated Quinolines via Povarov Type Multicomponent Reaction. *European Journal of Organic Chemistry* **2019**, *2019*, 2753-2758, <https://doi.org/10.1002/ejoc.201900325>.
4. Kumar, I.; Gupta, S.S.; Kumar, R.; Kumar, R.; Agrawal, P.; Sahal, D.; Sharma, U. Photocatalytic Unsymmetrical Coupling of 2-Substituted Quinolines: Synthesis and Evaluation of the Antiplasmodial Potential of β -Norbenzomorphan Frameworks. *ACS Sustainable Chemistry & Engineering* **2020**, *8*, 12902-12910, <https://doi.org/10.1021/acssuschemeng.0c03415>.
5. a) Kumar, R.; Kumar, R.; Chandra, D.; Sharma, U. Cp*CoIII-Catalyzed Alkylation of Primary and Secondary C(sp³)-H Bonds of 8-Alkylquinolines with Maleimides. *The Journal of Organic Chemistry* **2019**, *84*, 1542-1552, <https://doi.org/10.1021/acs.joc.8b02974>. b) Kumar, R.; Sharma, R.; Kumar, R.; Sharma, U. Cp*Rh(III)-Catalyzed Regioselective C(sp³)-H Methylation of 8-Methylquinolines with Organoborons. *Organic Letters* **2020**, *22*, 305-309, <https://doi.org/10.1021/acs.orglett.9b04331>. c) Kumar, R.; Kumar, R.; Parmar, D.; Gupta, S.S.; Sharma, U. Ru(II)/Rh(III)-Catalyzed C(sp³)-C(sp³) Bond Formation through C(sp³)-H Activation: Selective Linear Alkylation of 8-Methylquinolines and Ketoximes with Olefins. *The Journal of Organic Chemistry* **2020**, *85*, 1181-1192, <https://doi.org/10.1021/acs.joc.9b03257>. d) Parmar, D.; Kumar, R.; Kumar, R.; Sharma, U. Ru(II)-Catalyzed Chemoselective C(sp³)-H Monoarylation of 8-Methyl Quinolines with Arylboronic Acids. *The Journal of Organic Chemistry* **2020**, *85*, 11844-11855, <https://doi.org/10.1021/acs.joc.0c01603>. e) Kumar, R.; Parmar, D.; Gupta, S.S.; Chandra, D.; Dhiman, A.K.; Sharma, U. Cp*Rh(III)-Catalyzed Sterically Controlled C(sp³)-H Selective Mono- and Diarylation of 8-Methylquinolines with Organoborons**. *Chemistry - A European Journal* **2020**, *26*, 4396-4402, <https://doi.org/10.1002/chem.201905591>.