Merging Cu(I) and Cu(II) Photocatalysis: Development of a Versatile Oxohalogenation Protocol for the Sequential Cu(II)/Cu(I)-Catalyzed Oxoallylation of Vinylarenes

Tirtha Mandal,[‡] Narenderreddy Katta,[‡] Hendrik Paps, and Oliver Reiser*

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sequential photocatalysis

- low catalyst loading
- highly regio- and chemoselective
- late-stage biomolecule functionalization
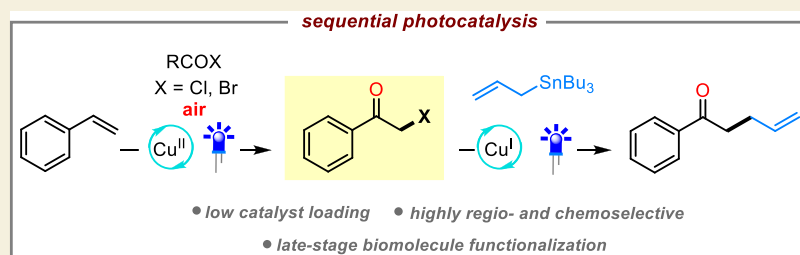
ABSTRACT: A sequential photocatalytic strategy is developed via the merger of Cu(II)/Cu(I)-catalytic cycles for the oxoallylation of vinyl arenes via α-haloketones. The initial Cu(II)-photocatalyzed oxohalogenation exploits ligand-to-metal charge transfer (LMCT) to generate halide radicals from acyl halides utilizing air as a terminal oxidant and can be employed for the late-stage modification of pharmaceuticals and agrochemicals. α-Bromoketones obtained this way can be subsequently subjected to a one-pot Cu(I)-photocatalyzed allylation. This sequential photocatalysis proceeds in a highly regio- and chemoselective fashion and is inconsequential to the electronic nature of styrenes.

KEYWORDS: α-Haloketones, Dissociative LMCT, Oxohalogenation, Oxoallylation, Photoredox catalysis, Sequential catalysis, Visible-light-induced homolysis

Earth-abundant copper complexes have become attractive photocatalysts, representing not only an economical alternative to commonly used metal complexes based on ruthenium or iridium, but also offering unique reaction modes within their inner coordination sphere.[1−5] Distinct processes have been developed utilizing either Cu(I) or Cu(II): Starting from Cu(I), radicals from a reducible precursor such as an organohalide or a sulfonyl chloride can be generated by single electron transfer (SET) and extrusion of an anionic leaving group (Scheme 1).[6,7] In turn, radicals can also be formed upon light-induced homolysis (LIH, dissociative LMCT[8,9]) of an oxidizable substrate bound to Cu(II), which has emerged as a versatile platform for engaging halides,[10−13] azides,[14] carboxylates,[15−19] and amines[20] as substrates in open-shell synthetic chemistry (Scheme 1). However, development of reaction pathways via sequential operation of Cu(I) and Cu(II) photocatalytic cycles is underexplored.

Based on our earlier work to engage α-haloketones in Cu(I)-photocatalyzed ATRA (atom transfer radical addition) reactions[21] and our development of Cu(II)-photocatalyzed oxoazidation of vinyl arenes,[14] we questioned whether an analogous Cu(II)-catalyzed oxohalogenation would allow a subsequent Cu(I)-catalyzed ATRA reaction. Our study commenced by developing a Cu(II)-photocatalyzed oxochlorination and oxobromination of vinyl arenes, which should also

make a useful contribution to the current methodology given that α-haloketones are fundamental building blocks in natural products and pharmaceuticals.[22,23] Traditional methods for the synthesis of α-haloketones often involve harsh reaction conditions, strong oxidants, and over stoichiometric amounts of inorganic salts as halogen sources.[24−26] Relevant to our work, the synthesis of α-haloketones by photocatalytic oxidative halogenation of olefins has emerged as an alternative (Scheme 2).[27−29] Wang et al. reported the synthesis of α-haloketones from styrenes using catalytic Ru(bpy)$_3$Cl$_2$ and PhI(OAc)$_2$ as terminal oxidant under visible-light irradiation.[30] The visible-light mediated FeX$_3$ (X = Cl, Br) catalyzed oxohalogenation protocol using inorganic salt (KX) and p-toluenesulfonic acid (TsOH) was developed by the Zhu group.[31]
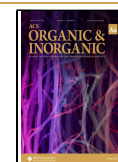
Recently, Cai et al. developed a visible-light mediated CuCl$_2$ catalyzed method for oxochlorination of vinylarenes calling for

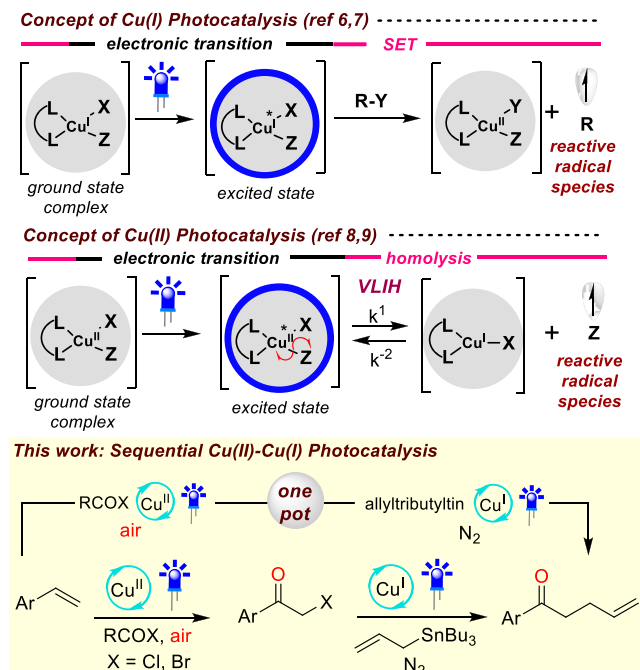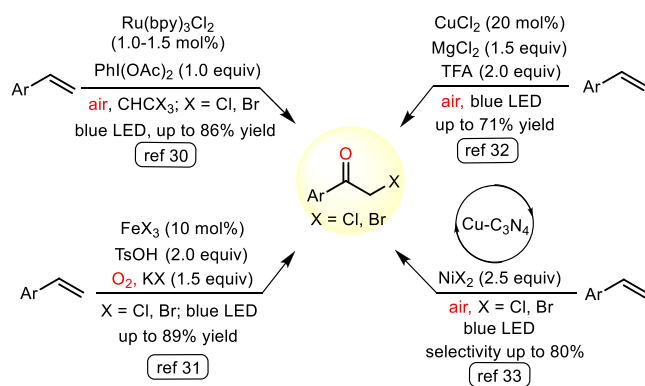## Scheme 1. Concepts of Cu-Photocatalysis and This Work

Scheme 2. Previous Reports on Photocatalytic Oxohalogenations of Styrenes

Table 1. Optimization of Reaction Conditions[a]

entry	deviation from standard conditions	% yield (3a)[b]
1	none	74
2	[Cu^I (dmp)$_2$]Cl (1 mol %)	76
3	[Cu^I (dap)$_2$]Cl (1 mol %)	78
4	[Cu^{II} (dap) Cl$_2$] (1 mol %)	76
5	Na$_2$CO$_3$ (1 equiv) is used as an additive	5
6	N$_2$ atmosphere instead of open air	nd
7[c]	[Cu^{II} (dmp)$_2$Cl]Cl (1 mol %)	nd
8	without [Cu^I (dmp)$_2$]Cl	nd
9	without irradiation	nd

[a]Reaction condition: **1a** (0.5 mmol, 1 equiv), **2a** (1.0 mmol, 2.0 equiv), [Cu^{II} (dmp)$_2$Cl]Cl (1 mol %), MeCN (0.25 M), blue LED, air, rt, 36 h. [b]Determined by NMR analysis using 1,1,2,2-tetrachloroethane. [c]**2a** not used. nd implies no desired product was detected.

anisylphenantrholine) and [Cu^{II} (dap) Cl$_2$], which are advantageous for some photocatalyzed processes,[34] did not perform significantly better (Table 1, entry 3 and 4), making [Cu^{II} (dmp)$_2$Cl]Cl and [Cu^I (dmp)$_2$]Cl the economic and operational catalyst of choice (Table 1, entry 1 and 2), since it can easily be prepared in gram quantities as a bench stable entity or prepared *in situ* by simply mixing CuCl and the commercial dmp ligand.[34] In contrast, no conversion was observed with other noncopper based photocatalysts (see the SI for details). Since the reaction is carried out under air atmosphere, benzaldehyde is formed as a byproduct in all cases (8−12%, see the SI) via the reaction of styrene **1a** with photocatalytically generated singlet oxygen. Considering the necessity to neutralize HCl as a potential catalyst poison that could be formed during the reaction,[6] stoichiometric amounts of Na$_2$CO$_3$ as an additive inhibited the transformation completely (Table 1, entry 5). Acetonitrile proved to be a critical component for the reaction, other solvents (Table S2) gave greatly inferior results. We speculate that acetonitrile can act as a stabilizing coligand in the catalytic cycles. Control experiments showed that no product formation was observed under N$_2$ atmosphere using either Cu(I) or Cu(II) photocatalysts (Table 1, entry 6), or in the absence of acetyl chloride **2a**, copper, or light (Table 1, entries 7−9).

With optimized conditions in hand, we investigated the scope of this transformation (Scheme 3). β-Alkyl substituted (**1u**; starting from both *cis-* and *trans*-isomer) and terminal styrenes gave the desired oxochlorinated products **3** in good yields, tolerating a wide range of electronically differentiated substituents in the arene moiety in ortho, meta, or para position. Of note is the smooth formation of oxochlorinated products **3j**, **3k**, **3o−3q**, given that the corresponding electron-rich styrenes are generally unsuitable alkenes in ATRA and ATRA-like reactions due to their ease of undergoing radical polymerizations.[6,35] Moreover, products that could have arisen from electrophilic substitutions with the arene moiety (acylation, chlorination) or radical substitutions with alkyl side chains were also not observed. On the other end of the electronic spectrum, *m*-NO$_2$, *p*-F, *p*-Cl, *p*-Br, *p*-CF$_3$, and *p*-CN were found to be compatible with the protocol (**3h**, **3l−3n**, **3r**,

20 mol % catalyst loading and the combination of MgCl$_2$ (1.5 equiv) and TFA (2 equiv).[32] A copper-modified graphite carbon nitride (Cu−C$_3$N$_4$) mediated heterogeneous photo-catalysis was also reported for the oxohalogenation of styrenes under visible-light irradiation, employing stoichiometric amounts of NiX$_2$ (X = Cl, Br) as the halide source.[33]

As an alternative, we envisioned the Cu(II)-catalyzed oxohalogenation of vinyl arenes in the presence of feedstock organic acyl halide sources whose photoactivation fosters the formation of halide radical via visible light-induced homolysis (dissociative LMCT).

Taking the oxochlorination of styrene **1a** as model reaction we found that acetyl chloride (**2a**) in the presence of only 1 mol % [Cu^{II} (dmp)$_2$Cl]Cl (dmp = 2,9-dimethylphenanthro-line) yielded the desired **3a** in 74% yield under blue LED irradiation and aerobic conditions (Table 1, entry 1; for further screening, details see the Supporting Information (SI)). When the corresponding Cu(I) photocatalyst (Table 1, entry 2) was used, **3a** could also be obtained in 76% yield in agreement that Cu(II) is easily formed in situ from Cu(I) under aerobic conditions. The Cu-complexes [Cu^I (dap)$_2$]Cl (dap = 2,9-di-p-
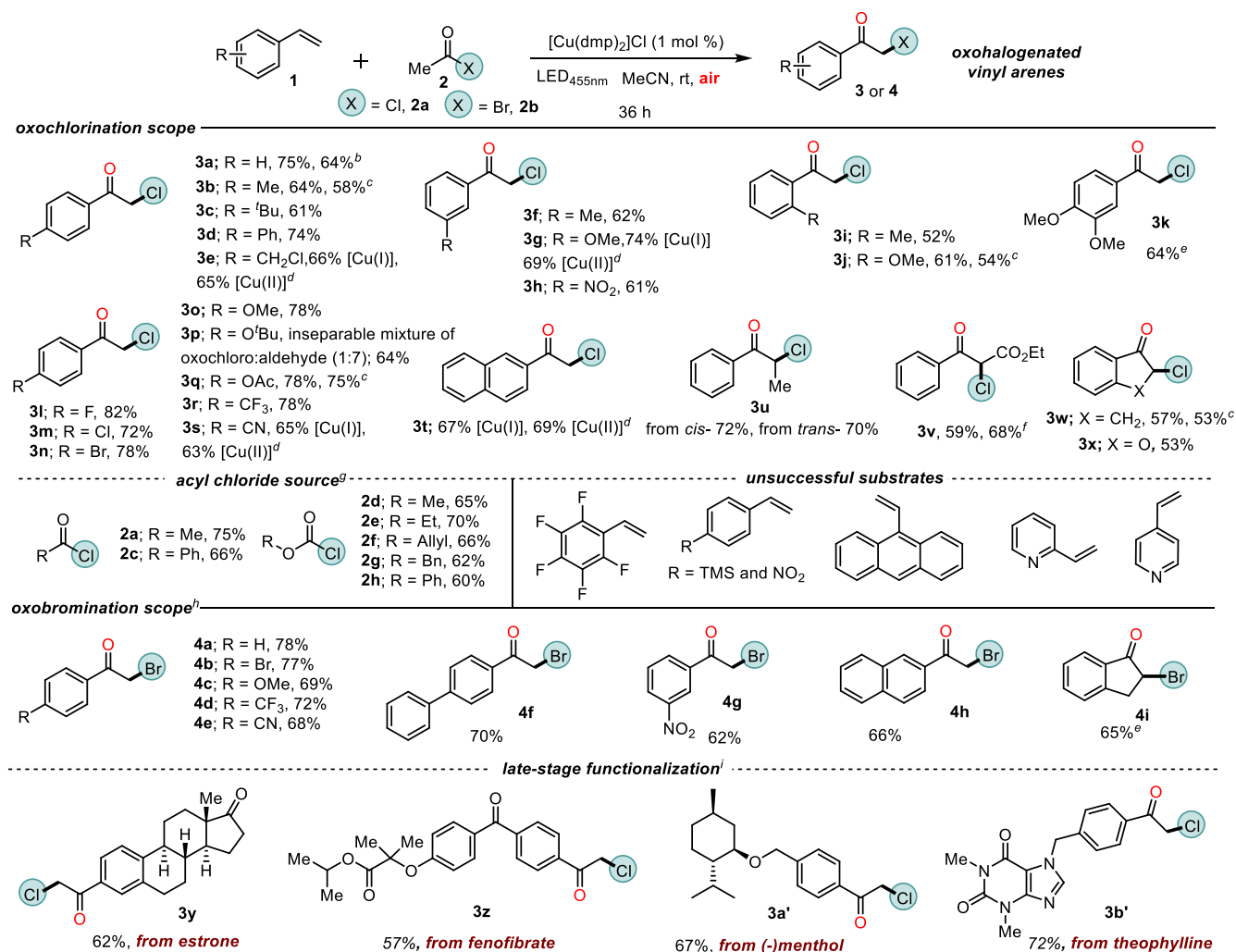
Scheme 3. Substrate Scope[a]

oxochlorination scope

3a; R = H, 75%, 64%[b]
3b; R = Me, 64%, 58%[c]
3c; R = tBu, 61%
3d; R = Ph, 74%
3e; R = CH₂Cl, 66% [Cu(I)], 65% [Cu(II)][d]

3f; R = Me, 62%
3g; R = OMe, 74% [Cu(I)] 69% [Cu(II)][d]
3h; R = NO₂, 61%

3i; R = Me, 52%
3j; R = OMe, 61%, 54%[c]

3k 64%[e]

3o; R = OMe, 78%
3p; R = OtBu, inseparable mixture of oxochloro:aldehyde (1:7); 64%
3q; R = OAc, 78%, 75%[c]
3r; R = CF₃, 78%
3s; R = CN, 65% [Cu(I)], 63% [Cu(II)][d]

3l; R = F, 82%
3m; R = Cl, 72%
3n; R = Br, 78%

3t; 67% [Cu(I)], 69% [Cu(II)][d]

3u from cis- 72%, from trans- 70%

3v, 59%, 68%[f]

3w; X = CH₂, 57%, 53%[c]
3x; X = O, 53%

acyl chloride source[g]

2a; R = Me, 75%
2c; R = Ph, 66%

2d; R = Me, 65%
2e; R = Et, 70%
2f; R = Allyl, 66%
2g; R = Bn, 62%
2h; R = Ph, 60%

unsuccessful substrates

R = TMS and NO₂

oxobromination scope[h]

4a; R = H, 78%
4b; R = Br, 77%
4c; R = OMe, 69%
4d; R = CF₃, 72%
4e; R = CN, 68%

4f 70%

4g 62%

4h 66%

4i 65%[e]

late-stage functionalization[i]

3y 62%, *from estrone*

3z 57%, *from fenofibrate*

3a' 67%, *from (-)menthol*

3b' 72%, *from theophylline*

[a]Reaction conditions: 1 (0.5 mmol, 1 equiv), 2 (1.0 mmol, 2 equiv), [Cu^I(dmp)₂]Cl (1 mol %), MeCN (0.25 M), blue LED (455 nm), air, rt, 36 h; 3c, 3f, 3k, 3n, and 4i were run in duplicate, yields differed ±2%. [b]1 (5.0 mmol), 2a (7.5 mmol, 1.5 equiv) is used, 48 h. [c]EtOCOCl is used as 2 (1.0 mmol, 2 equiv), reaction time 48 h. [d][Cu^{II}(dmp)₂Cl]Cl (1 mol %) is used. [e]92% purity for 3k and 90% purity for 4i. [f]2 mol % [Cu^I(dmp)₂] Cl is used. [g]1a (0.5 mmol, 1 equiv), 2 (1.0 mmol, 2 equiv) is used, yields are the isolated yields of 3a. [h]2b (0.75 mmol, 1.5 equiv) is used; reaction time 24 h. [i]1 (0.2 mmol), MeCN/DCM/CHCl₃ (1:1:1); Yields are of the isolated products.

Scheme 4. Chemoselective Oxohalogenation of Alkenes


3c' 47% (2e is used)

3d' 67%

4j 57%
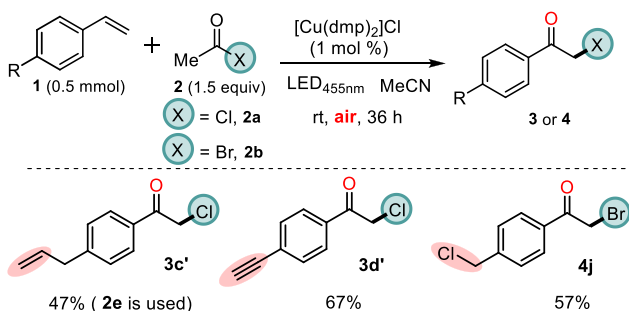
3s). A limitation is found with stronger electron withdrawing groups (pentafluoro, p-NO₂) that deactivate too severely the alkene for the attack of the electrophilic chlorine radical, and also with acid-sensitive functional groups (p-SiMe₃). Electron-deficient ethyl cinnamate provided the desired chloroaceto-phenone derivative 3v in good yield. Heteroaromatic benzofuran was efficiently converted to the corresponding

oxochloro derivative 3x in 53% yield. Finally, the oxochlori-nation performed well on a 5 mmol scale, affording product 3a in 64% yield (Scheme 4, see the SI for a detailed procedure). Besides acetyl chloride 2a, benzoyl chloride 2c and alkyl or aryl substituted chloroformates (2d–2h) can be effectively used as a chlorine source for this transformation (Scheme 3).

This Cu(II)-catalyzed photoactivation strategy proved to be effective also for the oxobromination of styrenes when acetyl bromide 2b was used as the bromide source. Along with styrenes bearing alkyl or aryl substituents, electron-donating and -withdrawing vinyl arenes including a five-membered indene moiety gave rise to diverse α-bromo acetophenone derivatives (4a-4i, 62–78% yield). In general, it should be noted that the α-haloketones, especially the bromoketones, are prone to hydrolysis, thus, the NMR spectra had to be taken immediately after sample preparation.

The mild conditions developed for this oxohalogenation process suggest that it can be used as a precision tool to perform late-stage modifications of complex biologically relevant scaffolds.[36] Vinyl arenes embedded in pharmaceuticals

Scheme 5. Photocatalytic Cu(II)−Cu(I) Promoted Sequential Oxobromination-Allylation
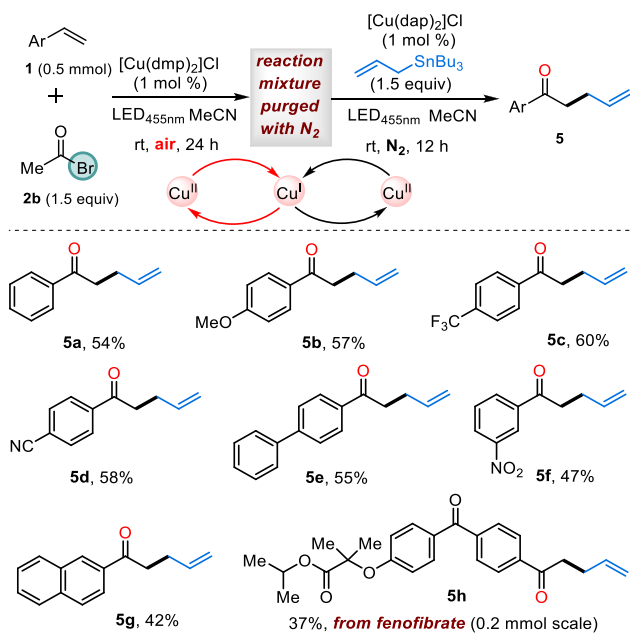
and natural products (Scheme 3) such as estrone (3y), fenofibrate (3z), (−)-menthol (3a'), and theophylline (3b') underwent successful oxochlorination to deliver the corresponding chloroacetophenone derivatives in good yields (57−72%).

A limitation of the protocol is found with unactivated olefins and alkynes, which showed no conversion in the title reaction. Hence, offering 4-vinyl allyl benzene to the established reaction conditions, only the activated double bond is selectively functionalized (Scheme 4, product 3c'). Likewise, when ethynyl-4-vinylbenzene is used as a substrate, the oxochlorination takes place chemoselectively only at the styrene double bond (product 3d'). Moreover, the oxobromination of 4-

benzyl chloride styrene selectively proceeds at the double bond to furnish 4j in 57% yield. No nucleophilic displacement or radical substitution product by the bromine radical at the benzylic position was observed.

We foresaw the possibility of applying our photocatalytic oxohalogenation strategy to develop a sequential photocatalysis protocol via a Cu(II)−Cu(I) catalytic shuttle. After the initial oxohalogenation reaction, the reaction vessel was sealed and purged under N_2 followed by adding a Cu(I)-photocatalyst and allyltributyltin[21] (Scheme 5). For the allylation step, we found out that α-bromoketones are more suitable precursors than α-chloroketones and $[Cu^I(dap)_2]Cl$ is more effective as photocatalyst than $[Cu^I(dmp)_2]Cl$ (see the SI for details). Notably, if the reaction sequence was started using $[Cu^I(dap)_2]Cl$ without refurnishing the catalyst for the second step, product 5 was still obtained, albeit in lower yields (see the SI). A selection of substituted styrenes- adorned with methoxy-, trifluoromethyl-, cyano-, nitro-functionalities as well as polyaromatic vinyl arenes, were submitted to the optimized sequence affording the corresponding ketones 5a−5g in moderate to good yields over two steps (42−60%, Scheme 5). Of note, vinyl arene derived from fenofibrate provided the ketone 5h in 37% yield following the developed oxobromination-oxoallylation sequence.

A plausible mechanism supported by quantum yield, TEMPO trapping and UV−vis experiments (see the SI) for the oxohalogenation involves a Cu(II)-complex like II as the catalytically active species[14] (Scheme 6). If $[Cu(dmp)_2]Cl$ is used as a precatalyst, the corresponding Cu(II) species should be easily obtainable by oxidation with dioxygen ($E_{Cu(II)/Cu(I)*} = -1.54$ V vs SCE; $E_{ox} = +0.33$ V for molecular oxygen). In the presence of acetyl halide 2, intermediate III is formed which could undergo ligand exchange to generate intermediate IV. Elemental steps from IV onward consist of a light-mediated homolytic dissociation to a Cu(I) species V and halide radical, forming a stabilized radical VI, which further reacts with oxygen to form VII. The peroxo radical VII can now combine with V forming a Cu(II) species VIII. Formation of product 3

Scheme 6. Plausible Mechanism and Mechanistic Studies
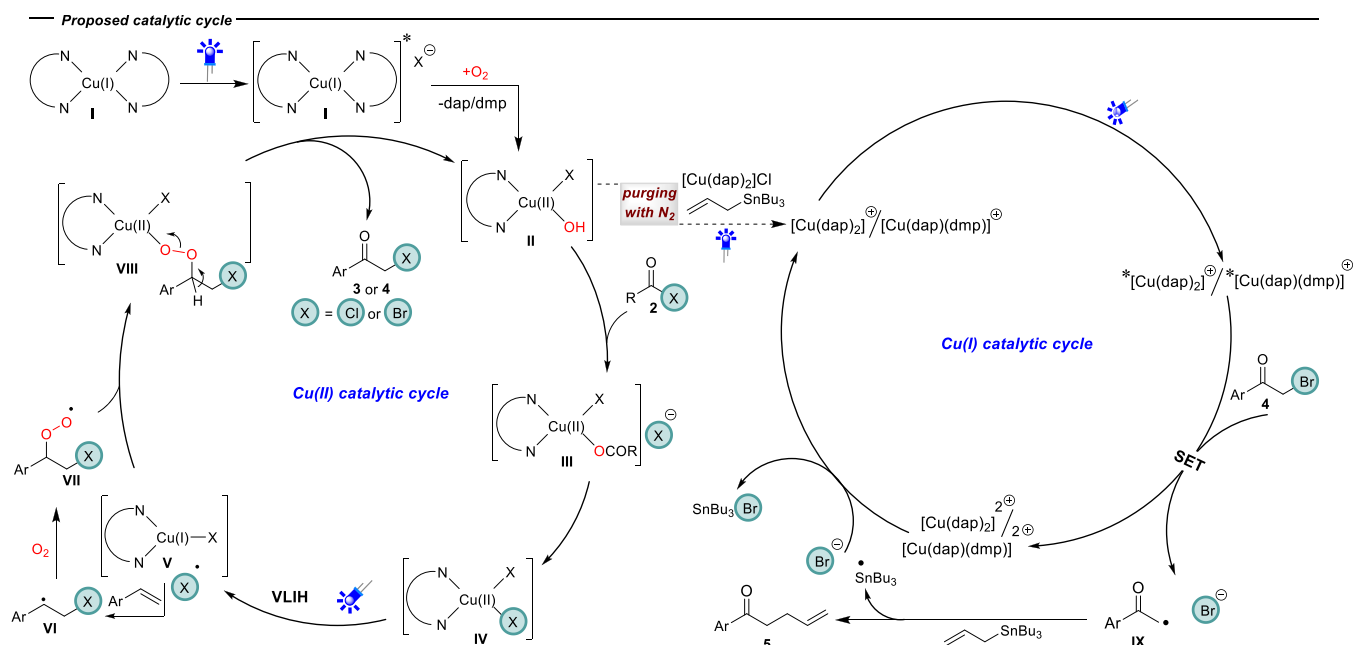
or **4** with concurrent elimination of **II** from **VIII** closes the catalytic cycle. In turn, Cu(I) activates the haloketone **4** via SET to form radical **IX**, which engages in an ATRA process following established lines.[21] However, involvement of a heteroleptic Cu(I)(dap)(dmp) complex is also possible for the Cu(I) photocatalyzed oxoallylation step as revealed by the ¹H NMR experiment (see the SI).

In conclusion, we have developed an efficient strategy using low-cost bulk chemical acetyl halides or haloformates for the visible-light-mediated Cu(II)-catalyzed synthesis of α-haloketones from vinyl arenes under aerobic conditions without the need for an additional oxidant. The protocol excels through high yields and environmentally benign reaction conditions, allowing the regio- and chemoselective vicinal difunctionalization of styrenes. Significantly, transformation opens the door for sequential photocatalysis via a merger of Cu(II)/Cu(I) catalytic cycles as demonstrated for oxohalogenation-allylation of styrenes. This modular approach allows the conversion of feedstock vinyl arenes to aromatic ketones bearing a terminal double bond with three-carbon extension in a one-pot manner. We envisage that the sequential photocatalytic strategy disclosed here will serve as a launchpad for developing new reaction pathways involving sequential Cu(II)/Cu(I) photo-catalysis or vice versa.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsorginorgau.3c00011.

> Additional experimental details, materials, and methods, including photographs of experimental setup, mechanistic studies, ¹H and ¹³C NMR spectra for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Oliver Reiser − Institut für Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany; ⓞ orcid.org/0000-0003-1430-573X; Email: oliver.reiser@chemie.uni-regensburg.de

Authors

Tirtha Mandal − Institut für Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany
Narenderreddy Katta − Institut für Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany; ⓞ orcid.org/0000-0002-3685-6703
Hendrik Paps − Institut für Organische Chemie, Universität Regensburg, 93053 Regensburg, Germany

Complete contact information is available at:
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Author Contributions

‡T.M. and N.K. contributed equally. CRediT: **Tirtha Mandal** conceptualization (equal), investigation (equal), methodology (equal), validation (equal), writing-original draft (equal), writing-review & editing (equal); **Narenderreddy Katta** investigation (equal); **Hendrik Paps** investigation (equal); **Oliver Reiser** conceptualization (equal), supervision (lead), writing-original draft (equal), writing-review & editing (equal).

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Hossain, A.; Bhattacharyya, A.; Reiser, O. Copper's rapid ascent in visible-light photoredox catalysis. *Science* **2019**, *364*, No. eaav9713.

(2) Engl, S.; Reiser, O. Copper-photocatalyzed ATRA reactions: concepts, applications, and opportunities. *Chem. Soc. Rev.* **2022**, *51*, 5287−5299.

(3) Zhong, M.; Pannecoucke, X.; Jubault, P.; Poisson, T. Recent advances in photocatalyzed reactions using well-defined copper(I) complexes. *Beilstein J. Org. Chem.* **2020**, *16*, 451−481.

(4) Zhang, Y.; Wang, Q.; Yan, Z.; Ma, D.; Zheng, Y. Visible-light-mediated copper photocatalysis for organic syntheses. *Beilstein J. Org. Chem.* **2021**, *17*, 2520−2542.

(5) Xiong, Y.; Li, S.; Xiao, H.; Zhang, G. Recent Advances in Visible-Light-Promoted Copper Catalysis in Organic Reactions. *Synthesis* **2021**, *53*, 4327−4340.

(6) Hossain, A.; Engl, S.; Lutsker, E.; Reiser, O. Visible-Light-Mediated Regioselective Chlorosulfonylation of Alkenes and Alkynes: Introducing the Cu(II) Complex [Cu(dap) Cl₂] to Photochemical ATRA Reactions. *ACS. Catal.* **2019**, *9*, 1103−1109.

(7) Engl, S.; Reiser, O. Copper Makes the Difference: Visible Light-Mediated Atom Transfer Radical Addition Reactions of Iodoform with Olefins. *ACS. Catal.* **2020**, *10*, 9899−9906.

(8) Abderrazak, Y.; Bhattacharyya, A.; Reiser, O. Visible-Light-Induced Homolysis of Earth-Abundant Metal-Substrate Complexes: A Complementary Activation Strategy in Photoredox Catalysis. *Angew. Chem., Int. Ed.* **2021**, *60*, 21100−21115.

(9) Juliá, F. Ligand-to-Metal Charge Transfer (LMCT) Photochemistry at 3d-Metal Complexes: An Emerging Tool for Sustainable Organic Synthesis. *ChemCatChem.* **2022**, *14*, No. e202200916.

(10) Kochi, J. K. Photolyses of Metal Compounds: Cupric Chloride in Organic Media. *J. Am. Chem. Soc.* **1962**, *84*, 2121−2127.

(11) Fayad, R.; Engl, S.; Danilov, E. O.; Hauke, C. E.; Reiser, O.; Castellano, F. N. Direct Evidence of Visible Light-Induced Homolysis in Chlorobis (2,9-dimethyl-1,10-phenanthroline) copper(II). *J. Phys. Chem. Lett.* **2020**, *11*, 5345−5349.

(12) Shields, B. J.; Doyle, A. G. Direct C(sp3)-H Cross Coupling Enabled by Catalytic Generation of Chlorine Radicals. *J. Am. Chem. Soc.* **2016**, *138*, 12719−12722.

(13) Treacy, S. M.; Rovis, T. Copper Catalyzed C(sp3)-H Bond Alkylation via Photoinduced Ligand-to-Metal Charge Transfer. *J. Am. Chem. Soc.* **2021**, *143*, 2729−2735.

(14) Hossain, A.; Vidyasagar, A.; Eichinger, C.; Lankes, C.; Phan, J.; Rehbein, J.; Reiser, O. Visible-Light-Accelerated Copper(II)-Catalyzed Regio- and Chemoselective Oxo-Azidation of Vinyl Arenes. *Angew. Chem., Int. Ed.* **2018**, *57*, 8288−8292.

(15) Morimoto, J. Y.; DeGraff, B. A. Photochemistry of the copper(II)-malonate system. Sensitized reaction. *J. Phys. Chem.* **1972**, *76*, 1387−1388.

(16) Natarajan, P.; Ferraudi, G. Photochemical properties of copper(II)-amino acid complexes. *Inorg. Chem.* **1981**, *20*, 3708−3712.

(17) Xu, P.; López-Rojas, P.; Ritter, T. Radical Decarboxylative Carbometalation of Benzoic Acids: A Solution to Aromatic

Decarboxylative Fluorination. *J. Am. Chem. Soc.* **2021**, *143*, 5349−5354.

(18) Li, Q. Y.; Gockel, S. N.; Lutovsky, G. A.; DeGlopper, K. S.; Baldwin, N. J.; Bundesmann, M. W.; Tucker, J. W.; Bagley, S. W.; Yoon, T. P. Decarboxylative cross-nucleophile coupling via ligand-to-metal charge transfer photoexcitation of Cu(II) carboxylates. *Nat. Chem.* **2022**, *14*, 94−99.

(19) Katta, N.; Zhao, Q.-Q.; Mandal, T.; Reiser, O. Divergent and Synergistic Photocatalysis: Hydro- and Oxoalkylation of Vinyl Arenes for the Stereoselective Synthesis of Cyclopentanols via a Formal [4 + 1]-Annulation of 1,3-Dicarbonyls. *ACS Catal.* **2022**, *12*, 14398−14407.

(20) Kumar, M.; Verma, S.; Mishra, V.; Reiser, O.; Verma, A. K. Visible-Light-Accelerated Copper-Catalyzed [3 + 2] Cycloaddition of N-Tosylcyclopropylamines with Alkynes/Alkenes. *J. Org. Chem.* **2022**, *87*, 6263−6272.

(21) Pirtsch, M.; Paria, S.; Matsuno, T.; Isobe, H.; Reiser, O. [Cu(dap)$_2$Cl] As an Efficient Visible-Light-Driven Photoredox Catalyst in Carbon-Carbon Bond-Forming Reactions. *Chem.—Eur. J.* **2012**, *18*, 7336−7340.

(22) Pchalek, K.; Jones, A. W.; Wekking, M. M. T.; Black, D. S. Synthesis of activated 3-substituted indoles: an optimized one-pot procedure. *Tetrahedron* **2005**, *61*, 77−82.

(23) Zhu, X.; Lin, Y.; San Martin, J.; Sun, Y.; Zhu, D.; Yan, Y. Lead halide perovskites for photocatalytic organic synthesis. *Nat. Commun.* **2019**, *10*, 2843.

(24) Erian, A. W.; Sherif, S. M.; Gaber, H. M. The Chemistry of α-Haloketones and Their Utility in Heterocyclic Synthesis. *Molecules.* **2003**, *8*, 793−865.

(25) Jiang, Q.; Sheng, W.; Guo, C. Synthesis of phenacyl bromides via K$_2$S$_2$O$_8$-mediated tandem hydroxybromination and oxidation of styrenes in water. *Green Chem.* **2013**, *15*, 2175−2179.

(26) Tian, S.; Jia, X.; Wang, L.; Li, B.; Liu, S.; Ma, L.; Gao, W.; Wei, Y.; Chen, J. The Mn-catalyzed paired electrochemical facile oxychlorination of styrenes via the oxygen reduction reaction. *Chem. Commun.* **2019**, *55*, 12104−12107.

(27) Itoh, A.; Nobuta, T.; Hirashima, S.-i.; Tada, N.; Miura, T. Facile Aerobic Photo-Oxidative Synthesis of Phenacyl Iodides and Bromides from Styrenes Using I2 or Aqueous HBr. *Synlett.* **2010**, *2010*, 2335−2339.

(28) Chen, Y. X.; He, J. T.; Wu, M. C.; Liu, Z. L.; Tang, K.; Xia, P. J.; Chen, K.; Xiang, H. Y.; Chen, X. Q.; Yang, H. Photochemical Organocatalytic Aerobic Cleavage of C = C Bonds Enabled by Charge-Transfer Complex Formation. *Org. Lett.* **2022**, *24*, 3920−3925.

(29) Li, S.; Tian, D.; Zhao, X.; Yin, Y.; Lee, R.; Jiang, Z. Visible light-driven copper(II) catalyzed aerobic oxidative cleavage of carbon-carbon bonds: a combined experimental and theoretical study. *Org. Chem. Front.* **2022**, *9*, 6229−6239.

(30) Wang, Z.; Wang, L.; Wang, Z.; Li, P.; Zhang, Y. A practical synthesis of α-bromo/iodo/chloroketones from olefins under visible light irradiation conditions. *Chin. Chem. Lett.* **2021**, *32*, 429−432.

(31) Luo, Z.; Meng, Y.; Gong, X.; Wu, J.; Zhang, Y.; Ye, L.-W.; Zhu, C. Facile Synthesis of α-Haloketones by Aerobic Oxidation of Olefins Using KX as Nonhazardous Halogen Source. *Chin. J. Chem.* **2020**, *38*, 173−177.

(32) He, X.-X.; Chang, H.-H.; Zhao, Y.-X.; Li, X.-J.; Liu, S.-A.; Zang, Z.-L.; Zhou, C.-H.; Cai, G.-X. CuCl2-Catalyzed α-Chloroketonation of Aromatic Alkenes via Visible-Light-Induced LMCT. *Chem.—Asian J.* **2023**, *18*, e202200954.

(33) Han, F.; Zhang, D.; Salli, S.; Ye, J.; Li, Y.; Rosei, F.; Wen, X.-D.; Niemantsverdriet, H.; Richards, E.; Su, R. Copper Cocatalyst Modulated Radical Generation for Selective Heterogeneous Photosynthesis of α-Haloketones. *ACS Catal.* **2023**, *13*, 248−255.

(34) Engl, S.; Reiser, O. Making Copper Photocatalysis Even More Robust and Economic: Photoredox Catalysis with [Cu^{II} (dmp)$_2$Cl]Cl. *Eur. J. Org. Chem.* **2020**, *2020*, 1523−1533.

(35) Matyjaszewski, K. From Atom Transfer Radical Addition to Atom Transfer Radical Polymerization. *Curr. Org. Chem.* **2002**, *6*, 67−82.

(36) Guillemard, L.; Kaplaneris, N.; Ackermann, L.; Johansson, M. J. Late-stage C-H functionalization offers new opportunities in drug discovery. *Nat. Rev. Chem.* **2021**, *5*, 522−545.