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Photochemical Organocatalytic Synthesis of Thioethers from Aryl Chlorides and Alcohols

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Supporting Information Placeholder

ABSTRACT: Thioethers, often found in pharmaceuticals and natural compounds, typically involve metal cross coupling reactions, high temperatures, and the use of disagreeable thiols for their synthesis. Here we present a straightforward, thiol-free, organocatalytic protocol that uses mild conditions to stitch together inexpensive alcohols and aryl chlorides, yielding a diverse array of aryl alkyl thioethers. Central to this approach was the discovery that tetramethylthiourea can serve as simple sulfur source upon intercepting photochemically generated aryl radicals. To form radicals, we used a readily available indole thiolate organocatalyst which, when excited with 405 nm light, gained a strongly reducing power, enabling the activation of typically unreactive aryl chlorides via single-electron transfer. Radical trapping by the thiourea, followed by an alcohol attack via a polar path, resulted in the formation of the thioether products.

Thioethers are prevalent in natural products and pharmaceuticals[1] with bioactivity against diseases like cancer, HIV, and Alzheimer's. Devising synthetic methods for their efficient preparation has therefore attracted substantial interest. A prominent strategy involves metal-catalyzed C-S cross-coupling of aryl halides and thiols (Figure 1a).[2-5] However, this approach is complicated by the tendency of thiolates, generated from thiols, to coordinate with transition-metal catalysts,[6] leading to the need of high catalyst loadings and specialized ligands. Generally, these processes also require elevated temperatures and strong bases,[2] limiting the functional group tolerance and the structural diversity of the thioether products. Recent progresses have introduced more effective cross-coupling protocols capable of activating not only highly reactive aryl bromides and iodides but also more cost-effective and readily available aryl chlorides.[7] These metal-based systems required suitable conditions to address the challenging oxidative addition to poorly reactive C-Cl bonds. Despite these advances, these cross-coupling strategies largely rely on thiols,[5] characterized by undesirable traits like unpleasant odor, air instability, and limited commercial variety.

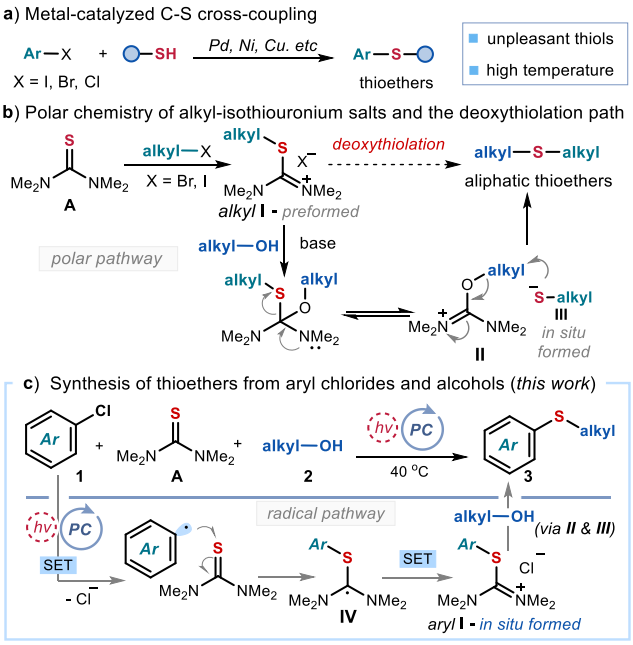
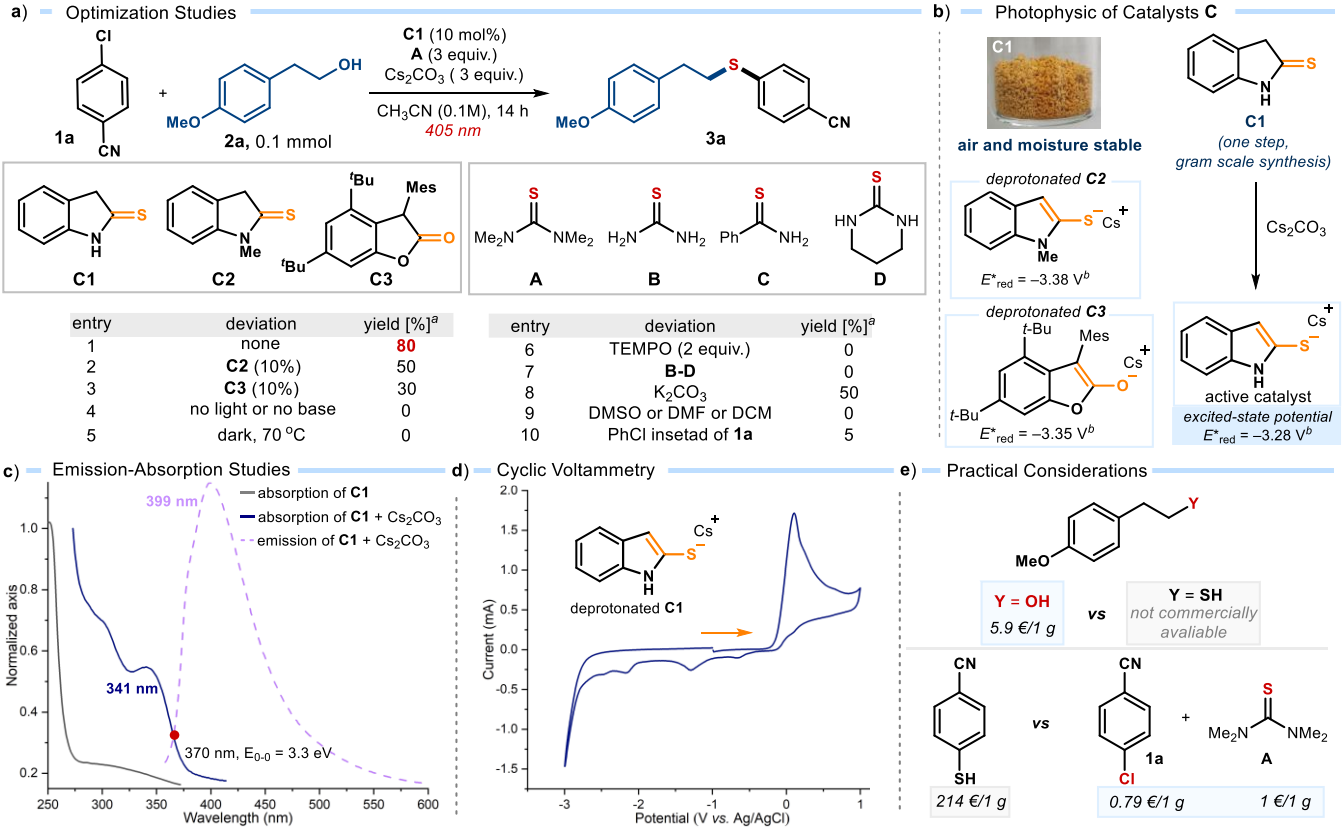


Figure 1. (**a**) Classical cross-coupling methods for synthesizing thioethers involve thiols and metal catalysts, often requiring elevated temperatures. (**b**) Synthesis of alkyl thioethers via deoxythiolation of alkyl alcohols and *preformed* alkyl isothiouronium salts **I**. (**c**) The present strategy uses a photocatalyst to generate, via SET reduction, an aryl radical from the parent chloride, which is trapped by tetramethylthiourea **A**; the *in situ formed* aryl isothiouronium **I** can then trigger the deoxythiolation path with alcohols leading to aryl-alkyl thioethers **3**. SET: single-electron transfer; PC: photoredox catalyst.

Another strategy is available for thioether synthesis that does not rely on thiols or metal catalysts but solely on widely accessible, inexpensive, and stable chemicals.[8] Specifically, alkyl-isothiouronium salts **I** are obtained via an S_N2 reaction between tetramethylthiourea **A** and alkyl electrophiles (Figure 1b). Subsequent nucleophilic addition of common alkyl alcohols to the preformed **I** generates a hemithioacetal, which is in equilibrium with isothiouronium salt **II** upon extrusion of thiolate **III**. Eventually, the transiently formed **III** reattacks intermediate **II**, following a deoxythiolation polar pathway that leads to the formation of the desired dialkyl thioethers. Although this metal- and thiol-free method uses readily available substrates, its scope is limited to the formation of aliphatic products.

Here, we disclose a simple method for synthesizing aryl-alkyl thioethers **3** that significantly expands the chemistry of isothiouronium salts **I**. The protocol requires low temperature (40 °C), visible light irradiation, an organic photocatalyst, and inexpensive, widely available substrates such as aryl chlorides **1** and aliphatic alcohols **2** (Figure 1c). Central to our reaction design was the discovery that tetramethylthiourea **A** can intercept photochemically generated aryl radicals, leading to the *in situ formation* of aryl isothiouronium salts **I** upon single-electron transfer (SET) oxidation of the resulting radical intermediate **IV**. The subsequent reaction of alcohols with **I** then follows the established polar deoxythiolation path depicted in Figure 1b to yield the desired aryl-alkyl thioether product **3**.

We started our investigations by using 1,1,3,3-tetramethylthiourea **A** as sulfur source and radical trap, 4-chlorobenzonitrile **1a** as the radical precursor [E (**1a**/**1a**$^{\cdot-}$) = -2.2 V vs Ag/AgCl], and 4-methoxyphenethyl alcohol **2a** as the nucleophile (Figure 2a). The experiments were performed in acetonitrile (CH_3CN) as the solvent under irradiation by a purple light-emitting-diode (LED, λ_{max} = 405 nm). Initially, we tested the highly reducing cyclic thioamide catalysts **C1** and **C2**, which we recently identified for their ability, upon deprotonation, to form indole thiolates.[9] These thiolates are capable of absorbing purple light and exhibiting strong reducing power in their excited state. This excited-state reactivity served to activate, by SET reduction, strong bonds in aromatic substrates, including C(sp^2)-Cl bonds. Performing the model reaction using 10 mol% of photocatalysts **C1** and **C2**, in the presence of Cs_2CO_3 (3 equiv.), afforded the target product **3a** in 80% and 50% yield, respectively (entries 1 and 2). We also tested a newly synthesized photoreductant **C3**, which displayed significantly reduced reactivity (entry 3). Control experiments established that the presence of photocatalyst **C1** and light was essential for reactivity (entries 4-5). When adding the radical scavenger TEMPO (2 equiv.) under the optimal conditions (entry 6), the reactivity was completely inhibited, which was congruent with a radical path being operative. Additional exploration of sulfur sources **B**-**D**, bases, and solvents resulted in lower product yields (entries 7-10).



entry	deviation	yield [%][a]
1	none	**80**
2	**C2** (10%)	50
3	**C3** (10%)	30
4	no light or no base	0
5	dark, 70 °C	0

entry	deviation	yield [%][a]
6	TEMPO (2 equiv.)	0
7	**B-D**	0
8	K_2CO_3	50
9	DMSO or DMF or DCM	0
10	PhCl insetad of **1a**	5

Figure 2. (**a**) Optimization studies and control experiments. Reactions performed on a 0.1 mmol scale for 14 h using 1 equiv. of **2a**, 3 equiv. of **1a** and 3 equiv. of **A** under illumination by a purple LED (*EvoluChem*) at 405 nm. (**b**) Deprotonation of **C1** and the estimated redox potential of the excited thiolates derived from catalysts **C1**-**C3**. (**c**) Emission of the excited thiolate (formed in situ treating **C1** with Cs_2CO_3) in CH_3CN upon irradiation at 350 nm and its intercept with the absorption spectrum at 373 nm, with a 0-0 transition energy ($E_{0,0}$) of 3.3 eV. (**d**) Cyclic voltammetry measurements of the deprotonated catalyst **C1** carried out in CH_3CN *vs.* Ag/AgCl. (**d**) Price comparisons between **1a**, **A** and thiols; data from Sigma-Aldrich, accessed in November 2023. [a]NMR yield using 1,3,5-trimethoxybenzene as internal standard. [b]Estimated redox potential *vs.* SCE in CH_3CN. Mes: mesityl.

To elucidate their mechanism of action, photocatalysts **C1**-**C3** underwent thorough characterization, detailed in Section D of the Supporting Information. NMR studies and absorption spectroscopic investigations established that the thiolate anions, generated upon catalyst deprotonation by Cs_2CO_3, can absorb visible light to access an electronically excited state (Figures 2b and 2c). Emission spectroscopic studies and cyclic voltammetry (Figure 2b and 2c,

see sections D4-6 in SI for full details) were used to estimate the redox potential of the excited thiolates (with E^* ranging from -3.28 to –3.38 V *vs* SCE in CH_3CN for deprotonated **C1-C3**), applying the Rehm-Weller formalism.[10] This confirmed that the anions of catalysts **C1-C3** acquire a strongly reducing power upon excitation. The practical benefits of our method compared to established protocols for thioether preparation (e.g. metal-catalyzed cross-coupling with thiols) can be appreciated when evaluating the starting substrate costs (Figure 2e). Current methods necessitate costly or non-commercially available thiols for the one-step synthesis of the target product **3a**. In contrast, our approach capitalizes on the affordability of a wide commercial assortment of aliphatic alcohols and aryl chlorides. Additionally, our organic photocatalysts are readily accessible. For instance, catalyst **C1** is an air-stable solid that can be synthesized on a gram-scale in a single step by oxygen-sulfur exchange of commercially available oxindole (see section B2 in SI for details).

Using the conditions described in Figure 2a entry 1, we then investigated the scope of the photochemical thioetherification (Figure 3).

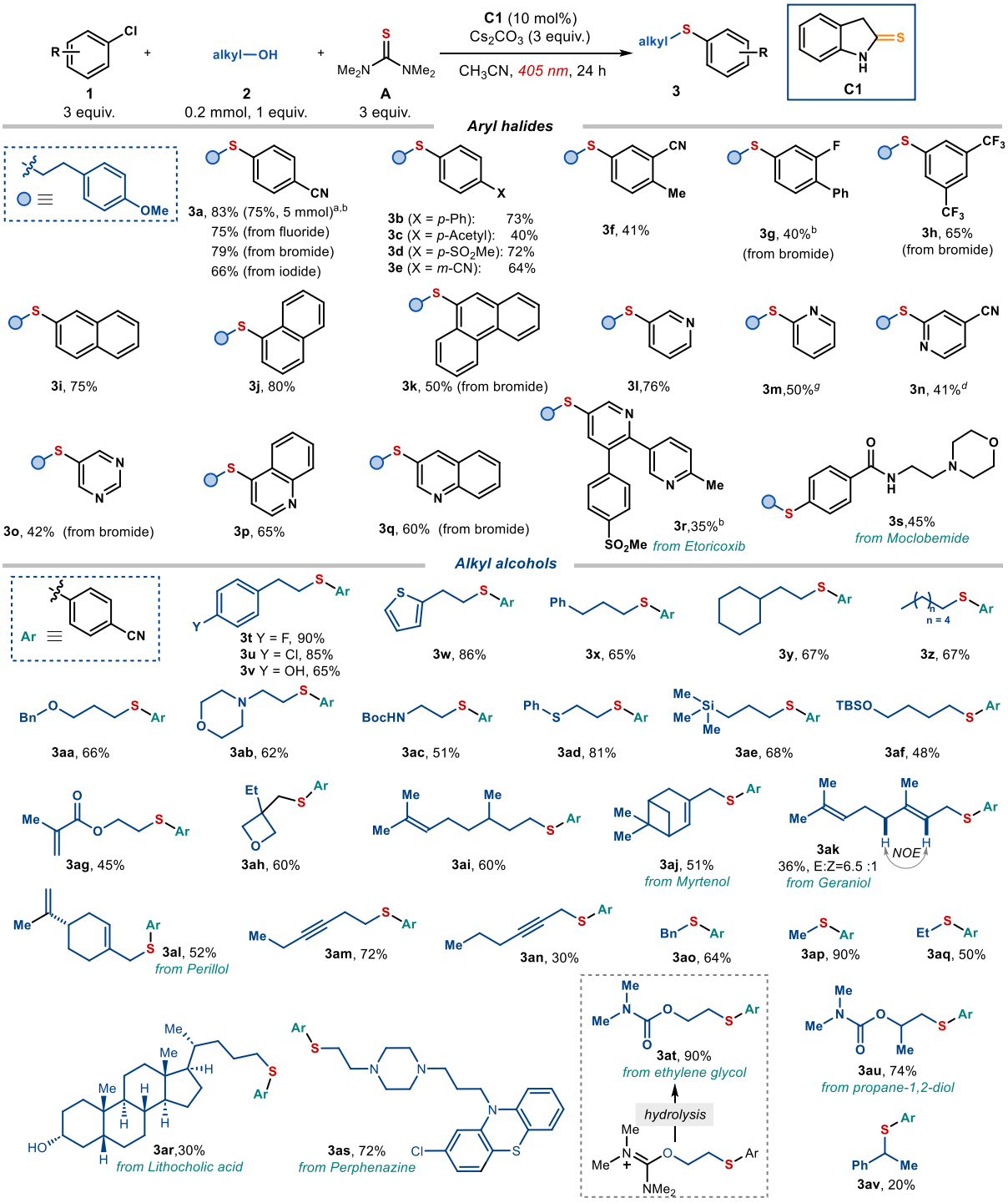


Figure 3. Photochemical organocatalytic synthesis of thioethers from aryl chlorides and alcohols. Reactions performed on a 0.2 mmol scale at 40 °C using photocatalyst **C1** (10 mol%), 3 equiv. of **1** and 3 equiv. of thiourea **A** under illumination by a purple LED (*EvoluChem*) at 405 nm. Yields refer to isolated products **3** after purification. Aryl chlorides were used as radical precursors, unless otherwise stated. [a]5 mmol scale reaction. [b]48 hour reaction time. Bn: benzyl, Boc: *tert*-butyloxycarbonyl, TBS: butyl(dimethyl)silyl.

We initially explored the reactivity of diverse aryl chlorides **1** as radical precursors, using 4-methoxyphenethyl alcohol **2a** as the nucleophile (Figure 3, upper panel). First, we demonstrated that the process was equally efficient on a 5 mmol scale, yielding 1.0 gram of product **3a** (75% yield). Compound **3a** could be synthesized not only by SET reduction of chloride **1a** but also upon activation of the corresponding fluoride, bromide, and iodide. Aryl chlorides with diverse substituents at various positions on the phenyl ring were tolerated well, yielding products **3b**-**3h** in high yield. The reaction proved compatible with substrates containing polycyclic aromatic structures (adducts **3i**-**3k**) and valuable *N*-heterocyclic frameworks, encompassing pyridines, pyrimidines, and quinolines (products **3l**-**3q**). Notably, late-stage modifications of chloride-containing drug molecules, such as the selective COX-2 inhibitor *Etoricoxib* (product **3r**) and the antidepressant *Moclobemide* (**3s**), were achieved, albeit in moderate yields.

We next examined the spectrum of alcohols compatible with this photochemical organocatalytic method (Figure 3, lower panel). Primary alcohols **2**, bearing potentially reactive aromatic systems such as phenol, thiophene, and halogen substituents, underwent smooth reactions, producing the respective thioethers **3t**-**3w**. A diverse array of functional groups was well-tolerated, including an ether (adduct **3aa**), tertiary amine (**3ab**), carbamate (**3ac**), and thioether (**3ad**). Sensitive functional moieties were effectively preserved, including trimethylsilane (**3ae**), silyl ether (**3af**), acrylate (**3ag**), and oxetane (**3ah**). Also alkenes and alkynes, susceptible to radical additions, showed compatibility (**3ai**-**3an**). Notably, straightforward thioetherification of simple benzyl alcohol, methanol, and ethanol was achieved (**3ao**-**3aq**). Complex substrates like natural products *myrtenol* (adduct **3aj**), *geraniol* (**3ak**), *perillol* (**3al**), *Lithocholic acid* derivative (**3ar**), and the pharmaceutical agent *Perphenazine* (**3as**) were efficiently functionalized. Interestingly, diols exhibited selective thioetherification of only one hydroxyl group, while the other alcohol moiety was converted into a carbamate (products **3at**-**3au**). This path likely arises from the hydrolysis of the isouronium intermediates. In these studies, aryl bromides were used when the corresponding chlorides were not commercially available.

As a limitation of the protocol, secondary alcohols, such as 1-phenylethanol, provided thioethers in moderate yield (**3av**), while phenol and tertiary alcohols remained completely unreactive, primarily due to their inability to undergo the substitution step (see Figures S3 and S5 in the SI for a comprehensive list of moderately reactive or non-reactive substrates). Another limitation concerned the lack of reactivity observed in electronically neutral or electron-rich aryl chlorides, which remained unreactive under the photoactivity of catalyst **C1**. Pleasingly, we found that the newly prepared dioxindole-based organocatalyst **C3** could act, upon deprotonation and excitation, as an effective photoreductant (E^*~-3.35 V *vs.* SCE) to activate these substrates (Figure 4, see Section D8 for a possible explanation of the better activity of **C3**). Consequently, we significantly broadened the range of aryl chlorides amenable to thioetherification. However, due to the relative instability of the catalyst, the protocol required the use of 40 mol% of **C3** along with 5 equivalents of aryl halides **1**.

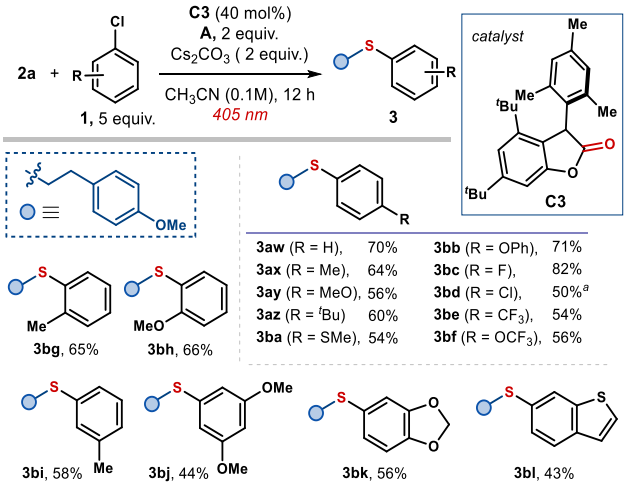


Figure 4. Thioetherification of electronically neutral or electron-rich aryl chlorides with alcohol **2a**. Reactions performed on a 0.2 mmol scale at 40 °C using 5 equiv. of **1** and 2 equiv. of **A** under illumination by a purple LED at 405 nm. Yields refer to isolated products **3** after purification. [a]Aryl bromides as radical precursors.

Electron-neutral aryl chlorides (product **3aw**) and substrates with electron-donating groups (**3ax**-**3bb**, **3bj**) underwent successful reactions. Additionally, other substituents, including halide (**3bc** and **3bd**), trifluoromethyl group (**3be**-**3bf**), and thiophene (**3bl**), were well-tolerated.

Figure 5a depicts the proposed mechanism for this process. Stern-Volmer quenching studies showed that the fluorescence of the deprotonated photocatalyst **C1**, excited by a laser at 350 nm, was effectively quenched by 4-chlorobenzonitrile **1a** (see section D4 in the SI for details). This observation is consonant with the ability of the excited deprotonated catalyst **C1** (E^*_{red} ~ −3.2 V *vs.* Ag/AgCl) to activate **1a** (E_{red}= -2.2 V *vs.* Ag/AgCl) through SET reduction. The resulting aryl radical is trapped by tetramethylthiourea **A**, forming radical **IV** (E (**I**/**IV**) ~ −1.6 V vs. Ag/AgCl) with the appropriate redox potential to reduce the sulfur-centered radical **V** (E (**V**/**C1**$^-$) ~ +0.1 V vs. Ag/AgCl) via SET, thus turning over catalyst **C1**. We also determined the quantum yield (Φ) of the process between **1a** and **2a**, which stood at a low value of 0.017, consistent with the proposed closed photoredox cycle.[11] Our suggested mechanism envisages a radical pathway leading to the in situ formation of the aryl isothiouronium ion **I**, with a follow-up polar deoxythiolation path involving alcohols **2** and yielding aryl alkyl thioethers **3**. The polar pattern was confirmed through an experiment using the preformed isothiouronium ion **4** (Figure 5b). Under dark conditions and in the presence of

Cs_2CO_3, stirring with alcohol **2a** resulted in the formation of product **3aw**. Additionally, subjecting the enantioenriched chiral alcohol **5** (97% ee) and phenyl chloride **6** to standard reaction conditions led to the corresponding chiral thioether product **7** in poor yield, but maintaining the same enantiopurity. Analysis of the absolute configuration via optical rotation[12] established that the process proceeded with complete stereoinversion, a signature of the stereospecific S_N2 ionic pathway.

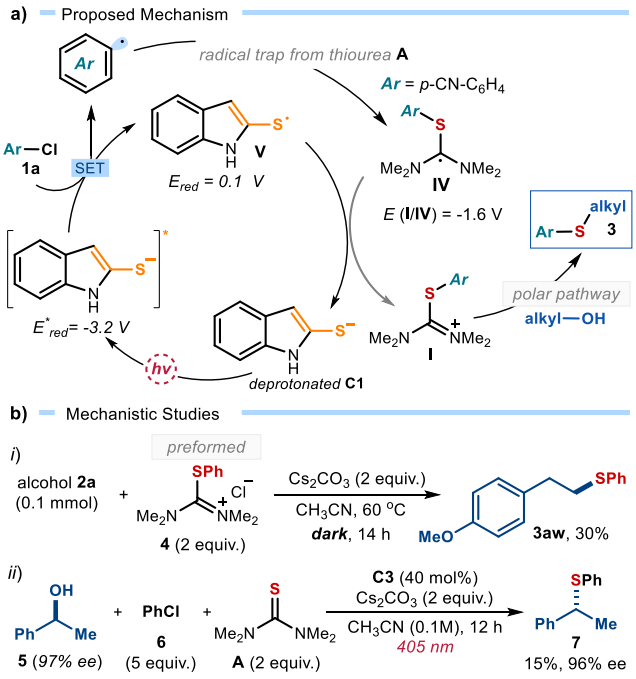


Figure 5. (**a**) Proposed mechanism and (**b**) mechanistic investigations: *i*) thioetherification from preformed phenyl isothiouronium salt **4**; *ii*) stereospecific thioetherification of optically active alcohol **5**.

In summary, we reported a photochemical catalytic protocol that enables the preparation of diverse alkyl aryl thioethers without thiol or transition metal involvement. The method operates under mild conditions using easily accessible substrates and catalysts. Its remarkable tolerance for functional groups allows for late-stage modifications of biorelevant compounds.

ASSOCIATED CONTENT

Supporting Information

Details of experimental procedures and full characterization data and copies of NMR spectra (PDF). The Supporting Information is available free of charge on the ACS Publications website.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Feng, M.; Tang, B.; Liang, S. H.; Jiang, X. Sulfur Containing Scaffolds in Drugs: Synthesis and Application in Medicinal Chemistry. *Curr. Top. Med. Chem.* **2016**, *16*, 1200–1216. (b) Scott, K. A.; Njardarson, J. T. Analysis of US FDA-Approved Drugs Containing Sulfur Atoms. *Top. Curr. Chem.* **2018**, *376*, 5. (c) Ilardi, E. A.; Vitaku, E; Njardarson, J. T. Data-Mining for Sulfur and Fluorine: An Evaluation of Pharmaceuticals to Reveal Opportunities for Drug Design and Discovery. *J. Med. Chem.* **2014**, *57*, 2832–2842. (d) Le Grand, B. L.; Pignier, C.; Létienne, R.; Cuisiat, F.; Rolland, F.; Mas, A.; Vacher, B. Sodium Late Current Blockers in Ischemia Reperfusion: Is the Bullet Magic? *J. Med. Chem.* **2008**, *51*, 3856–3866.

(2) For selected examples, see: (a) Kwong, F. Y.; Buchwald, S. L. A General, Efficient, and Inexpensive Catalyst System for the Coupling of Aryl Iodides and Thiols. *Org. Lett.* **2002**, *4*, 3517-3520. (b) Fernandez-Rodriguez, M. A.; Shen, Q. L.; Hartwig, J. F. A General and Long-Lived Catalyst for the Palladium-Catalyzed Coupling of Aryl Halides with Thiols. *J. Am. Chem. Soc.* **2006**, *128*, 2180–2181. (c) Uyeda, C.; Tan, Y.; Fu, G. C.; Peters, J. C. A New Family of Nucleophiles for Photoinduced, Copper-Catalyzed Cross-Couplings via Single-Electron Transfer: Reactions of Thiols with Aryl Halides Under Mild Conditions (o°C). *J. Am. Chem. Soc.* **2013**, *135*, 9548–9552. (d) Beletskaya, I. P.; Ananikov, V. P. Transition-Metal-Catalyzed C–S, C–Se, and C–Te Bond Formations via Cross-Coupling and Atom-Economic Addition Reactions. Achievements and Challenges. *Chem. Rev.* **2022**, *122*, 16110–16293, and references therein.

(3) For selected methods based on the combination of photoredox and transition metal catalysis, see: (a) Oderinde, M.S.; Frenette, M.; Robbins, D. W.; Aquila, B.; Johannes, J. W. Photoredox Mediated Nickel Catalyzed Cross-Coupling of Thiols with Aryl and Heteroaryl Iodides via Thiyl Radicals. *J. Am. Chem. Soc.* **2016**, *138*, 1760–1763. (b) Qin, Y.; Sun, R.; Gianoulis, N. P.; Nocera, D. G. Photoredox Nickel-Catalyzed C–S Cross-Coupling: Mechanism, Kinetics, and Generalization. *J. Am. Chem. Soc.* **2021**, *143*, 2005–2015. (c) Düker, J.; Ghosh, I.; König, B. Sequential One-Pot (Het)arene Thioetherification and Amination with Nickel and Visible Light. *ACS Catal.* **2023**, *13*, 13618–13625. (d) Ghosh, I.; Shlapakov, N.; Karl, T. A.; Düker, J.; Nikitin, M.; Burykina, J. V.; Ananikov, V. P.; König, B. General

cross-coupling reactions with adaptive dynamic homogeneous catalysis. *Nature* **2023**, *619*, 87–93.

(4) For other thioethers' preparation methods based on thiols, see: (a)Tyson, E. L.; Ament, M. S.; Yoon, T. P. Transition Metal Photoredox Catalysis of Radical Thiol-Ene Reactions. *J. Org. Chem.* **2013**, *78*, 2046–2050. (b) Das, A.K.; Thomas, R. J. Facile Thiol–Ene Click Protocol Using Benzil as Sensitizer and White LED as Light Source. *Eur. J. Org. Chem.* **2020**, 7214–7218. (c) Singh, M.; Yadav, A. K.; Yadav, L. D. S.; Singh, R. K. P. Visible Light Photocatalysis with Benzophenone for Radical Thiol-Ene Reactions. *Tetrahedron Lett.* **2017**, *58*, 2206–2208. (d) Sandfort, F.; Knecht, T.; Pinkert, T.; Daniliuc, C. G.; Glorius, F. Site-Selective Thiolation of (Multi)halogenated Heteroarenes. *J. Am. Chem. Soc.* **2020**, *142*, 6913–6919.

(5) For methods using sulfurating reagents other than thiols, see: (a) Qiao, Z.; Wei, J.; Jiang, X. Direct Cross-Coupling Access to Diverse Aromatic Sulfide: Palladium Catalyzed Double C–S Bond Construction Using $Na_2S_2O_3$ as a Sulfurating Reagent. *Org. Lett.* **2014**, *16*, 1212–1215. (b) Gholinejad, M. One-Pot Copper-Catalysed Thioetherification of Aryl Halides Using Alcohols and Lawesson's Reagent in Diglyme. *Eur. J. Org. Chem.* **2015**, 4162–4167. (c) Wang, M.; Qiao, Z.; Zhao, J.; Jiang, X. Palladium-Catalyzed Thiomethylation via a Three-Component-Cross-Coupling Strategy. *Org. Lett.* **2018**, *20*, 6193–6197.

(6) (a) Hegedus, L. L.; McCabe, R. W. Catalyst Poisoning. *Stud. Surf. Sci. Catal.* **1980**, *6*, 471–505. (b) Crabtree, R. H. *The Organometallic Chemistry of the Transition Metals*; John Wiley & Sons, Inc.: Hoboken, NJ, 2014.

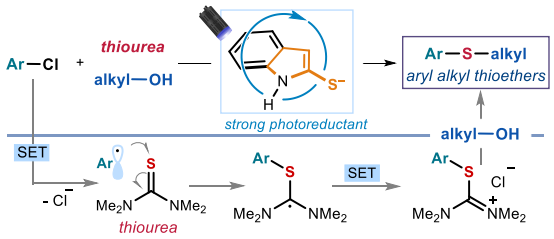
(7) For selected examples, see: (a) Li, G. Y. The First Phosphine Oxide Ligand Precursors for Transition Metal Catalyzed Cross Coupling Reactions: C-C, C-N, and C-S Bond Formation on Unactivated Aryl Chlorides. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513–1516. (b) Murata, M.; Buchwald, S. L. A General and Efficient Method for the Palladium-Catalyzed Cross-Coupling of Thiols and Secondary Phosphines. *Tetrahedron.* **2004**, *60*, 7397–7403. (c) Gehrtz, P. H.; Geiger, V.; Schmidt, T.; Srsan, L.; Fleischer, I. Cross-Coupling of Chloro(hetero)arenes with Thiolates Employing a Ni(0)-Precatalyst. *Org. Lett.* **2019**, *21*, 50–55. (d) Martín, M. T.; Marín, M.; Maya, C.; Prieto, A.; Nicasio, M. C. Ni(II) Precatalysts Enable Thioetherification of (Hetero)Aryl Halides and Tosylates and Tandem C-S/CN Couplings. *Chem. Eur. J.* **2021**, *27*, 12320–12326. (e) Oechsner, R. M.; Wagner, J. P.; Fleischer, I. Acetate Facilitated Nickel Catalyzed Coupling of Aryl Chlorides and Alkyl Thiols. *ACS Catal.* **2022**, *12*, 2233–2243.

(8) (a) Shizuo, F.; Isamu, F.; Yasumasa, N.; Shoji, K. A Facile One-pot Synthesis of Sulfides from Alkyl Halides and Alcohols Using Tetramethylthiourea. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2429–2430. (b) Aitken, R. A.; ali, K.; Mesher, S. T. E. Kinetic Resolution of Secondary Alcohols Using Proline-Derived Bicyclic Iminium Salts. *Tetrahedron Lett.* **1997**, *38*, 4179–4182; (c) Merad, J.; Matyasovsky, J.; Stopka, T.; Brutiu, B. R.; Pinto, A.; Dreschera, M.; Maulide, N. Stable and Easily Available Sulfide Surrogates Allow a Stereoselective Activation of Alcohols. *Chem. Sci.* **2021**, *12*, 7770–7774.

(9) Wu, S.; Schiel, F.; Melchiorre, P. A General Light-Driven Organocatalytic Platform for the Activation of Inert Substrates. *Angew. Chem., Int. Ed.* **2023**, *62*, e202306364.

(10) Farid, S.; Dinnocenzo, J. P.; Merkel, P. B.; Young, R. H.; Shukla, D.; Guirado, G. Reexamination of the Rehm–Weller Data Set Reveals Electron Transfer Quenching that Follows a Sandros–Boltzmann Dependence on Free Energy. *J. Am. Chem. Soc.* **2011**, *133*, 11580–11587.

(11) Buzzetti, L.; Crisenza, G. E. M.; Melchiorre, P. Mechanistic Studies in Photocatalysis. *Angew. Chem., Int. Ed.* **2019**, *58*, 3730–3747.

(12) Li, F.; Wang, D.; Chen, H.; He, Z.; Zhou, L.; Zeng, Q. Transition Metal-Free Coupling Reactions of Benzylic Trimethylammonium Salts with Di(hetero)aryl Disulfides and Diselenides. *Chem. Commun.* **2020**, *56*, 13029–13032.

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