Thioetherification via Photoredox/Nickel Dual Catalysis

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**Key to Abbreviated Terms:**

bpy: 2,2’-bipyridyl

CFL: Compact fluorescent light

LED: Light-emitting diode
dtbppy: 4,4’-di-tert-butyl-2,2’-dipyridyl

**General Considerations:**

**General:**
All chemical transformations requiring inert atmospheric conditions or vacuum distillation utilized Schlenk line techniques with a 4- or 5-port dual-bank manifold. Argon or nitrogen was used to provide such an atmosphere. NMR Spectra (1H, 13C, 19F) were performed at 298 K. 1H NMR spectra were referenced to residual non-deuterated chloroform (δ 7.26) in CDCl3, residual DMSO-d5 (δ 2.50) in DMSO-d6, acetone-d5 (δ 2.09) in acetone-d6, and residual MeCN-d3 (δ 1.94) in MeCN-d3. 13C NMR spectra were referenced to CDC13 (δ 77.30), DMSO-d6 (δ 39.52), the carbonyl carbon of acetone (δ 205.87), or the nitrile carbon of MeCN-d3 (δ 118.26), respectively. 19F NMR spectra were referenced to hexafluorobenzene (δ –164.9) as an internal standard.4 Reactions were monitored by HPLC, GC/MS, 1H NMR, and/or by TLC on silica gel plates (60 Å porosity, 250 µm thickness). TLC analysis was performed using hexanes/EtOAc as the eluant and visualized using permanganate stain, Seebach’s stain,6 ninhydrin stain, and/or UV light. Silica plugs utilized flash silica gel (60 Å porosity, 32-63 µm). Flash chromatography was accomplished using an automated system (visualizing at 254 nm, monitoring at 280 nm) with silica cartridges (60 Å porosity, 20-40 µm). Solvents were purified by use of drying cartridges through a solvent delivery system. Melting points (°C) are uncorrected. Optical rotations were recorded using a Jasco P-2000 polarimeter with concentration (c) is in g/100 mL.

**Chemicals:**
Deuterated NMR solvents were either used as purchased (DMSO-d6) or were stored over 4 Å molecular sieves and/or K2CO3 (CDCl3). Na2SO4, MgSO4, MeOH, CH2Cl2, CHCl3, MeCN, pentane, Et2O, and pyridine, were used as purchased. Et3N and i-Pr2NH, were purchased from commercial suppliers and distilled from CaH2 prior to use. THF was purchased and dried via a solvent delivery system. Catechol was purchased and recrystallized from refluxing hexanes or heptanes. DMF (99.8%, extra dry) was stored over 4 Å molecular sieves. [NiCl2(dme)] (min. 97%) and RuCl3•3H2O were purchased commercially. Aryl halides were purchased from commercial suppliers and used without further purification. [Ru(bpy)3](PF6)2 was prepared in-house by the procedure outlined here. New alkylsilicates were prepared according to the representative procedure outlined here from their corresponding alkyltrimethoxysilanes. Information (preparation protocols, characterization etc.) for silicates 2d, 2e, 2f, 2g, and 2h can be found in our previous report.3

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1 Ravikumar, I.; Saha, S.; Ghosh, P. Chem. Commun. 2011, 47, 4721.
2 Seebach, D.; Imwinkelried, R; Stucky, G. Helv. Chim. Acta 1987, 70, 448.
3 Jouffroy, M.; Primer, D.; Molander, G. A. J. Am. Chem. Soc., 2015, ASAP DOI: 10.1021/jacs.5b10963
Photochemistry:
Irradiation of reaction vessels was accomplished either using standard 26 W CFLs or LEDs (blue or white). The choice of light source did not seem to have any effect on reaction success. In most cases either CFL or blue LEDs were employed for irradiation. LEDs were configured as outlined in the Photochemical Reactor Design section. A fan was employed to ensure reactions remained at or near room temperature when using either CFLs or LEDs.

Information for LED-based Photoreactor Components:
- **Blue LEDs**: 39.4 inch strips, 470 nm blue light, 32918 mcd ft$^{-1}$
- **Natural White LEDs**: 39.4 inch strips, 380-700 nm, CCT rating: 4000K
- **Power Supply**: 12V DC CPS series Power Supply - 15 Watt
- **Connectors** (links power supply to LEDs): LC2 Locking Male Connector CPS Adapter Cable
- **Clip Fan**: 2-Speed Clip Fan, 6-Inch
- Pyrex crystallizing dishes (125 X 65 mm)
- Aluminum foil
- Duct tape
Photochemical Reactor Design (LEDs only)

Protocol for reactor setup
Remove the protective layer on the sticky side of the LED strip and carefully wrap the LED strips on the inside of a clean Pyrex dish.\(^4\) Four bands of LEDs can fit into a 125 X 65 mm Pyrex crystallizing dish.\(^5\) Once the LEDs are securely wrapped, place a layer of aluminium foil around the outside of the dish (including the bottom). Tape the connector wires as well as the foil with duct tape to secure both in place. For vial-scale reactions, cut a sample vial rack using a saw and place it inside. For larger vessels (e.g., round bottom flasks), simply lower the flask into the irradiation bay.\(^6\) Place the reactor on top of a stirring place. Position a fan about 6-12 inches above the reactor for cooling and set it to its maximum setting. Turn on the lights and fan. Allow 15 min to pass for temperature equilibration. Temperature should be monitored in real time using a temperature probe (or thermometer) to determine the ambient temperature within the reactor. Place a double layer of aluminum foil in front of the reactor to reflect light back into the reactor. **CAUTION:** Given the brightness of the reactor, it is recommended that impact-resistant sunglasses be used when working with the reactor for eye protection.

\(^4\) Starting from the bottom upward affords the easiest approach.
\(^5\) If smaller lengths of LED strips are used, they can be linked together. Most LED strips are able to be cut (at specified locations) and powered by either end. The appropriate connector is required (male or female) for each end.
\(^6\) This design can accommodate up to a 250 mL round bottom flask. However, if desired, a larger reactor can be assembled by using larger recrystallization dish and additional LEDs.
Synthesis of Alkylbis(catecholato)silicates
Preparation of Diisopropylammonium Bis(catecholato)(3-mercaptpropyl)silicate (1a)

To an oven-dried, 250 mL round bottom flask equipped with a stir bar, reflux condenser, and gas inlet adapter was added catechol\(^7\) (11.74 g, 106.6 mmol, 1.95 equiv) followed by anhyd THF (110 mL) and anhyd diisopropylamine\(^8\) (6.53 g, 9.08 mL, 64.6 mmol, 1.2 equiv). The mixture was placed under an argon atmosphere and was allowed to stir at rt for 5 min. The solution became a pale reddish brown. After this time, (3-mercaptopropyl)trimethoxysilane (10.57 g, 53.8 mmol, 1.0 equiv) was added. The solution immediately lightened to a golden yellow. The solution was then heated to reflux in an oil bath and allowed to stir at this temperature overnight.\(^9\) Once the reaction was judged to be complete by crude \(^1\)H NMR analysis,\(^10\) the solvent was removed \textit{in vacuo} by rotary evaporation. The resulting powder was collected via filtration through a medium porosity fritted funnel. The powder was washed with \(\text{Et}_2\text{O}\) (~100 mL). The solid was collected and dried further \textit{in vacuo} to give the alkylthiol silicate 1a containing 0.25 equiv of THF\(^11\) (21.90 g, 93%) as a powdery off-white solid (mp = 135 °C).

\(^1\)H NMR (MeCN-\(d_3\), 500 MHz) \(\delta\) 0.59 - 0.68 (m, 2H), 1.30 (d, \(J=6.4\) Hz, 12H), 1.33 - 1.41 (br s, 1H), 1.51 (dt, \(J=15.4, 7.7\) Hz, 2H), 2.35 (t, \(J=6.6\) Hz, 2H), 3.55 (spt, \(J=6.6\) Hz, 2H), 6.51 - 6.59 (m, 4H), 6.61 - 6.70 (m, 4H). \(^{13}\)C NMR (MeCN-\(d_3\), 125 MHz) \(\delta\) 17.6 (CH\(_2\)), 19.3 (CH\(_3\)), 28.3 (CH\(_2\)), 30.7 (CH\(_2\)), 49.3 (CH), 111.1 (C), 118.9 (CH), 151.2 (CH). \textbf{FT-IR} (cm\(^{-1}\), neat, ATR) 3045 (w, br), 2988 (w), 1484 (vs), 1237 (vs), 1013 (w), 811 (vs) 736 (s, br), 517 (w). \textbf{HRMS} (ES-) calcd for C\(_{15}\)H\(_{15}\)O\(_4\)SSi [M–Et\(_3\)NH]: 319.0460, found: 319.0467.

Diisopropylammonium Bis(catecholato)isobutylsilicate, 1b (4.86 g, 86%) was prepared according to the general procedure from isobutyltrimethoxysilane (2.50 g, 0.014 mol) \textit{with the following modification}: After reaction completion and solvent removal, the crude solid was dissolved in CH\(_2\)Cl\(_2\) (~60 mL), and a minimum amount of pentane (~10 mL) was added as an anti-solvent, resulting in precipitation of a fine white powder. The powder was washed with a

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\(^7\) Recrystallized from hexane or heptane prior to use.

\(^8\) A similar protocol can be used to prepare the more organic soluble triethylammonium salt. This salt works equally well for photoredox thioetherification.

\(^9\) Depending on the nature of the silicate and its solubility in THF, precipitation of the product would occur.

\(^10\) For DIPA silicates, it is advisable to use acetone-\(d_6\) or DMSO-\(d_6\) as the NMR solvent, as these silicates have poor solubility in most other deuterated solvents.

\(^11\) Presence of THF does not impede any photoredox process involving silicates, included thioetherification.
minimal amount of Et₂O (~100 mL), followed by a copious amount of pentane (~125 mL). The desired silicate 1b was isolated as a powdery white solid (mp = 216 °C).

**1H NMR** (DMSO-\(d_6\), 500 MHz) \(\delta\) 0.50 (d, \(J = 6.9\) Hz, 2H), 0.75 (d, \(J = 6.4\) Hz, 6H), 1.20 (d, \(J = 6.6\) Hz, 12H), 1.68 (sept, \(J = 6.6\) Hz, 1H), 3.35 (dt, \(J = 12.9, 6.4\) Hz, 2H), 6.39 - 6.45 (m, 4H), 6.47 - 6.55 (m, 4H), 8.02 (br s, 2H).

**13C NMR** (DMSO-\(d_6\), 125 MHz) \(\delta\) 18.8 (CH₃), 24.4 (CH), 26.3 (CH₃), 29.4 (CH₂), 46.4 (CH), 109.4 (C), 117.0 (CH), 150.6 (CH).

**FT-IR** (\(cm^{-1}\), neat, ATR) 3047 (w, br) 2948 (w) 1484 (vs) 1238 (vs) 1014 (w) 812 (w) 734 (vs) 498 (m).

**HRMS** (ES-) calcd for C\(_{16}\)H\(_{17}\)O\(_4\)Si [M – iPr\(_2\)NH\(_2\)]: 301.0896, found: 301.0899

**Diisopropylammonium Bis(catecholato)hexadecylsilicate, 1c** (5.86 g, 71 %) was prepared according to the general procedure for silicate synthesis from hexadecyltrimethoxysilane (5.00 g, 14.4 mmol). The desired silicate 1c was isolated as an off-white powdery solid (mp = 138 °C).

**1H NMR** (DMSO-\(d_6\), 500 MHz) \(\delta\) 0.42 - 0.53 (m, 2H), 0.85 (t, \(J = 6.9\) Hz, 3H), 1.05 - 1.31 (m, 40H), 3.35 (sept, \(J = 6.4\) Hz, 2H), 6.39 - 6.45 (m, 4H), 6.48 - 6.54 (m, 4H), 8.03 (br s, 2H).

**13C NMR** (DMSO-\(d_6\), 125 MHz) \(\delta\) 13.9 (CH₃), 18.3 (CH₂), 18.8 (CH₃), 22.1 (CH₂), 24.2 (CH₂), 28.7 (CH₂), 29.0 (CH₂ \(\times 9\)), 31.3 (CH₂), 32.8 (CH₂), 46.4 (CH), 109.4 (C), 116.9 (CH), 150.6 (CH).

**FT-IR** (\(cm^{-1}\), neat, ATR) 3048 (w, br), 2988 (m), 2924 (w), 1486 (vs), 1239 (vs), 813 (vs), 734 (s), 717 (s, br).

**HRMS** (ES-) calcd for C\(_{28}\)H\(_{41}\)O\(_4\)Si [M – Pr\(_2\)NH\(_2\)]: 469.2774, found: 469.2770.
This procedure is a modification of the procedure outlined by Wrighton.\textsuperscript{12} To a 500 mL round bottom flask equipped with a stir bar and reflux condenser was added 2,2’-bipyridyl (9.68 g, 62.0 mmol, 5.1 equiv) and RuCl\textsubscript{3}•3H\textsubscript{2}O (3.16 g, 12.1 mmol, 1.0 equiv). The system was sealed with a rubber septum and evacuated four times via an inlet needle and purged with N\textsubscript{2}. Freshly distilled and degassed EtOH (300 mL) was then added, and the solution was heated to reflux via an oil bath. The solution was allowed to stir at reflux for 16 h. The flask was then cooled to rt and NH\textsubscript{4}PF\textsubscript{6} (16.30 g, 100 mmol, 8.3 equiv) was added, resulting in the formation of a voluminous orange precipitate. The reflux condenser was removed, and the solution was heated 15 min at 40 °C. After this time, the solution was cooled to rt and then chilled in a refrigerator (≈ 5 °C) overnight. The precipitate was collected by vacuum filtration and washed thoroughly with H\textsubscript{2}O (~1 L), EtOH (~300 mL), and finally Et\textsubscript{2}O (~200 mL) to afford a bright red powder.\textsuperscript{13} \textsuperscript{1}H NMR analysis of the solid revealed the presence of a small amount of 2,2’-bipyridyl. To purify the photocatalyst further, the red solid was taken up in hot acetone (400 mL) and filtered through a pad of Celite\textsuperscript{®} (10 x 3 cm), eluting with hot acetone (~300 mL). The resulting pumpkin orange filtrate was concentrated in vacuo by rotary evaporation to ca. 400 mL, then reagent grade MeOH (~200 mL) was added. Rapidly, an orange solid formed, and addition of Et\textsubscript{2}O (~300 mL) further enhances precipitation of the solid. The precipitate was collected by vacuum filtration, and the pumpkin orange cake was washed thoroughly with EtOH (~300 mL) and finally Et\textsubscript{2}O (~200 mL) to afford the title compound as a fluffy powder (8.07 g, 78%). Characterization data for this compound matched that reported in the literature.\textsuperscript{25}

\textsuperscript{1}H NMR (acetone-\textit{d}_6, 500 MHz) \(\delta\) 7.57 - 7.66 (m, 6H), 8.10 (dd, \(J = 5.6, 0.5\) Hz, 6H), 8.25 (tt, \(J = 7.8, 1.2\) Hz, 6H), 8.86 (dd, \(J = 8.2, 0.6\) Hz, 6H). \textsuperscript{13}C NMR (acetone-\textit{d}_6, 125 MHz) \(\delta\) 125.0 (CH), 128.5 (CH), 138.6 (CH), 152.4 (CH), 157.8 (CH). \textsuperscript{19}F NMR (acetone-\textit{d}_6, 471 MHz) \(\delta\) -73.58 (s, 6F) -72.08 (s, 6F). \textsuperscript{31}P NMR (acetone-\textit{d}_6, 202 MHz) \(\delta\) -144.27 (quin, \(J = 704.60\) Hz).

\textsuperscript{12} Mabrouk, P. A.; Wrighton, M. S. \textit{Inorg. Chem.} 1986, 25, 526.

\textsuperscript{13} In some cases, NMR analysis of the intermediate brick red solid shows the presence of other complexes, namely [Ru(bpy)\textsubscript{3}]Cl\textsubscript{2} and [Ru(bpy)\textsubscript{3}](PF\textsubscript{6})Cl. In these cases, the solid was retaken up in H\textsubscript{2}O (~200 mL), and NH\textsubscript{4}PF\textsubscript{6} (~2 equiv) was added. The resulting suspension was sonicated at rt for 30 min then filtered, affording a brick red cake that was purified using the above mentioned procedure.
General Procedure for Thioetherification Using Thiolsilicate 1a

![Thioetherification Reaction Scheme]

[1,1'-Biphenyl]-4-yl(propyl)sulfane (2a)

To an 8 mL reaction vial equipped with an appropriately sized stir bar were added dtbbpy (6.7 mg, 0.025, 0.05 equiv) and [NiCl$_2$(dme)] (5.5 mg, 0.025 mmol, 0.05 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and placed under a N$_2$ atmosphere via an inlet needle. The vial was charged with ~1.5 mL of anhyd THF and the resulting suspension was heated briefly with a heat gun until a homogenous pale green solution was observed. The solution was cooled in an ice water bath, resulting in the immediate precipitation of an evergreen solid. The solution was then evaporated in vacuo to give the ligated nickel complex.$^{14}$ The cap was removed from the vial and alkylthiol silicate 1a (253 mg, 0.60 mmol, 1.2 equiv), 4-bromo-1,1'-biphenyl (117 mg, 0.50 mmol, 1 equiv),$^{15}$ and [Ru(bpy)$_3$](PF$_6$) (8.6 mg, 0.01 mmol, 0.02 equiv) were added. The vial was resealed and was evacuated three times via an inlet needle then purged with inert gas. The vial was then charged with dissolved in anhyd, degassed DMF (5 mL) via a syringe. The cap was sealed with Parafilm$^\text{®}$, and the now bright red solution was irradiated in the aforementioned LED reactor. The temperature of the reaction was maintained at approximately 27 °C via a fan. The solution was stirred vigorously while being irradiated. Reaction progress was monitored by HPLC and/or GC/MS. The now opaque, milky-brown solution was poured in a separatory funnel and diluted with saturated aqueous Na$_2$CO$_3$ (20 mL)$^{16}$ and Et$_2$O$^{17}$ (~20 mL). The layers were separated,$^{18}$ and the aqueous layer was extracted with Et$_2$O (3 × ~20 mL). The combined organic layers were washed with saturated aqueous Na$_2$CO$_3$ (2 × ~30 mL), deionized H$_2$O (~30 mL), and brine (~50 mL).$^{19}$ The organic layer was dried (MgSO$_4$), and the solvent was removed in vacuo by rotary evaporation. Further purification was accomplished by SiO$_2$ column chromatography (gradient hexane/EtOAc) to give the desired thioether 2a as a white powder (83 mg, 73%) (mp = 69 °C).

$^{14}$ We have performed the reaction with and without pre-ligation of the ligand. We found that there is no effect on the yield of cross couplings performed here. However, it was necessary for certain systems in our previous report, see Ref 3.

$^{15}$ Liquid bromides were added later as a solution in DMF.

$^{16}$ Alternatively 2 M NaOH may be used.

$^{17}$ EtOAc was used in place of Et$_2$O for the extractions when isolating products containing polar functional groups.

$^{18}$ Note that a precipitate will often form and rest at the interface between the organic and aqueous layers. It can be discarded during the washes without compromising yield.

$^{19}$ In certain cases, specifically when working with systems that did not contain basic moieties, an optionally four wash can be added. Following the saturated aqueous Na$_2$CO$_3$ (or 2 M NaOH) wash, a 2 M HCl (~30 mL) may be used. This will remove any residual dtbbpy.
1H NMR (CDCl3, 500 MHz) δ 1.08 (t, J = 7.3 Hz, 3H), 1.70 - 1.78 (m, 2H), 2.97 (t, J = 7.3 Hz, 2H), 7.36 (t, J = 7.3, 1.7 Hz, 1H), 7.40 - 7.48 (m, 4H), 7.54 (d, J = 8.6 Hz, 2H), 7.58 - 7.62 (m, 2H). 13C NMR (CDCl3, 125 MHz) δ 13.7 (CH3), 22.8 (CH2), 35.9 (CH2), 127.1 (CH), 127.5 (CH), 127.7 (CH), 129.1 (CH), 129.5 (CH), 136.4 (C), 138.9 (C), 140.8 (C). GC-MS (EI) 228 ([M]+, 100%), 199 (11%), 185 (62%), 166 (34%), 152 (30%), 141 (6%), 115 (8%) 102 (2%), 77 (3%), 63 (2%). FT-IR (cm⁻¹, neat, ATR) 3055 (vw), 3032 (vw), 2963 (w), 2932 (w), 2872 (vw), 1593 (w), 1477 (m), 1098 (m), 823 (m), 752 (vs), 685 (s). HRMS (Cl+) calcd for C15H16S [M]+: 228.0973, found: 228.0971.

(4-Benzylphenyl)(propyl)sulfane, 2b (118 mg, 97%) was prepared according to the general procedure for thioetherification from 1-benzyl-4-bromobenzene (123 mg, 0.5 mmol). The desired thioether was obtained as a clear, colorless oil.

1H NMR (CDCl3, 500 MHz) δ 1.06 (t, J = 7.3 Hz, 3H), 1.66 - 1.74 (m, 2H), 2.91 (t, J = 7.3 Hz, 2H), 3.99 (s, 2H), 7.15 (d, J = 8.1 Hz, 2H), 7.20 - 7.28 (m, 3H), 7.29 - 7.36 (m, 4H). 13C NMR (CDCl3, 125 MHz) δ 13.7 (CH3), 22.8 (CH2), 36.3 (CH2), 41.7 (CH2), 126.4 (CH), 128.7 (CH), 129.2 (CH), 129.7 (CH), 129.8 (CH), 134.5 (C), 139.2 (C), 141.2 (C). GC-MS (EI) 242 ([M]+, 100%), 213 (16%), 200 (17%), 179 (8%), 167 (7%), 152 (16%), 91 (48%). FT-IR (cm⁻¹, neat, ATR) 3061 (vw), 3032 (vw), 2961 (w), 2929 (w), 1492 (m), 1453(w), 1092, 788 (m) 745 (s), 696 (vs).

4-(Propylthio)benzonitrile, 2c (68 mg, 77%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.5 mmol). The desired thioether was obtained as a clear, pale yellow oil.

1H NMR (CDCl3, 500 MHz) δ 1.06 (t, J = 7.3 Hz, 3H), 1.69 - 1.77 (m, 2H), 2.96 (t, J = 7.3 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 8.5 Hz, 2H). 13C NMR (CDCl3, 125 MHz) δ 13.7 (CH3), 22.3 (CH2), 34.1 (CH2), 108.1 (C), 119.2 (C), 127.0 (CH), 132.4 (CH), 145.5 (C). GC-MS (EI) 179 ([M]+, 79%), 148 (43%), 135 (100%), 108 (6%), 104 (7%), 91 (7%), 76 (4%), 63 (5%). FT-IR (cm⁻¹, neat, ATR) 2964 (w), 2225 (m), 1593 (s), 1485 (m), 1088 (vs), 818 (vs), 542 (vs). HRMS (ES+) calcd for C10H12NS [M+H]+: 178.0690, found: 178.0692.

1-(4-(Propylthio)phenyl)ethanone, 2d (74 mg, 76%) was prepared according to the general procedure for thioetherification from 4-bromoacetophenone (95 mg, 0.5 mmol). The desired thioether was obtained as a clear, pale yellow oil which solidified upon standing to a white, waxy solid (mp = 36 °C).

1H NMR (CDCl3, 500 MHz) δ 1.06 (t, J = 7.3 Hz, 3H), 1.69 - 1.77 (m, 2H), 2.55 - 2.56 (m, 3H), 2.97 (t, J = 7.3 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H). 13C NMR (CDCl3, 125 MHz) δ 13.8 (CH3), 22.5 (CH2), 26.7 (CH3), 34.3 (CH2), 126.6 (CH), 129.0 (CH), 134.1 (C), 145.2 (C), 197.4 (C). GC-MS (EI) 194 ([M]+, 88%), 179 (100%).

20 Blackaby, W. P. et al. WO 2006134341, 2006.
21 Cutler, R. A.; Stenger, R. J.; Suter, C. M. J. Am. Chem. Soc., 1952, 74, 5475.
137 (71%), 123 (13%), 109 (20%), 69 (6%). **FT-IR** (cm⁻¹, neat, ATR) 2967 (w), 1673 (vs), 1587 (s) 1356 (s), 1264 (s), 1180 (s), 1096 (s), 956 (s), 813 (vs), 745 (m), 586 (s). **HRMS** (Cl+) calcd for C₁₁H₁₄O₅S [M⁺]: 194.0765, found: 194.0762.

**Methyl 3-(Propylthio)benzoate, 2f** (89 mg, 85%) was prepared according to the general procedure for thioetherification from methyl 3-bromobenzoate (108 mg, 0.5 mmol). The desired thioether was obtained as a light yellow oil.

**¹H NMR** (CDCl₃, 500 MHz) δ 1.04 (t, J = 7.3 Hz, 3H), 1.64 - 1.73 (m, 2H), 2.94 (t, J = 7.6 Hz, 2H), 3.92 (s, 3H), 7.34 (t, J = 7.6 Hz, 1H), 7.49 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 7.82 (dt, J = 7.8, 1.2 Hz, 1H), 7.98 (t, J = 1.7 Hz, 1H). **¹³C NMR** (CDCl₃, 125 MHz) δ 13.7 (CH₃), 22.7 (CH₂), 35.7 (CH₂), 52.5 (CH₃), 127.0 (CH), 129.0 (CH), 129.7 (CH), 131.1 (C), 133.3 (CH), 138.2 (C), 167.0 (C). **GC-MS** (EI) 210 ([M⁺], 100%), 181 (31%), 168 (70%), 151 (10%), 149 (11%), 137 (54%), 121 (9%), 109 (21%), 91 (9%), 69 (7%), 59 (8%). **FT-IR** (cm⁻¹, neat, ATR) 2961 (w), 2930 (w), 1722 (vs), 1569 (s), 1516 (s), 1436 (m), 1336 (m), 1281 (s), 1260 (vs), 1124 (m), 745 (s). **HRMS** (Cl+) calcd for C₁₁H₁₄O₂S [M⁺]: 210.0715, found: 210.0719.

**2-(Propylthio)benzonitrile, 2g** (74 mg, 84%) was prepared according to the general procedure for thioetherification from 2-bromobenzonitrile (91 mg, 0.5 mmol). The desired thioether was obtained as a clear, yellow oil.

**¹H NMR** (CDCl₃, 500 MHz) δ 1.05 (t, J = 7.3 Hz, 3H), 1.67 - 1.75 (m, 2H), 2.99 (t, J = 7.2 Hz, 2H), 7.24 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.9 Hz, 1H), 7.49 (t, J = 7.3 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H). **¹³C NMR** (CDCl₃, 125 MHz) δ 13.6 (CH₃), 22.5 (CH₂), 35.8 (CH₂), 113.8 (C), 117.5 (C), 126.0 (CH), 129.1 (CH), 133.0 (CH), 133.9 (CH), 142.4 (C). **GC-MS** (EI) 177 ([M⁺], 37%), 148 (13%), 135 (100%), 108 (8%), 91 (6%), 76 (3%) 69 (3%). **FT-IR** (cm⁻¹, neat, ATR) 2964 (w), 2222 (w), 1585 (w), 1463 (m), 1433 (m), 753 (vs). **HRMS** (ES+) calcd for C₁₀H₁₂NS [M+H⁺]: 178.0690, found: 178.0695.

**4-(Propylthio)benzoic acid, 2h** (75 mg, 87%) was prepared according to the general procedure for thioetherification from 4-bromobenzoic acid (101 mg, 0.5 mmol) with the following modified workup: The reaction mixture was quenched with saturated aqueous NH₄Cl. The quenched reaction mixture was extracted with EtOAc (3 × 20 mL). The solvent was removed in vacuo by rotary evaporation, giving a brown oil. The brown oil was taken up in ~40 mL of Et₂O and extracted with saturated aqueous NaHCO₃ (3 × 20 mL). The combined aqueous layers were mixed with ~40 mL of EtOAc and acidified by dropwise addition of concentrated HCl to pH 1 (~10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with deionized H₂O (~60 mL) and dried (MgSO₄). The solvent was removed in vacuo by rotary evaporation. The desired thioether was obtained as a fluffy off-white powder (mp = 119 °C).

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22 Murata, T. et al. EP 2842946, 2015.
**1H NMR** (CDCl₃, 500 MHz) δ 1.07 (t, J = 7.3 Hz, 3H), 1.68 - 1.81 (m, 2H), 2.98 (t, J = 7.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.99 (d, J = 8.1 Hz, 2H). **13C NMR** (CDCl₃, 125 MHz) δ 13.77 (CH₃), 22.43 (CH₂), 34.18 (CH₂), 125.82 (C), 126.45 (CH), 130.77 (CH₂), 146.17 (C), 172.29 (C). **FT-IR** (cm⁻¹, neat, ATR) 3132 - 2745 (cm, very br), 2654 (w), 2528 (m), 1667 (vs), 1591 (s), 1418 (s), 1181 (m), 1091 (s), 954 (s), 847 (m), 761 (s), 549 (m). **HRMS** (ES-) calcd for C₁₀H₁₁O₂S [M-H]⁻: 195.0480, found: 195.0486.

**1-(5-(Propylthio)thiophen-2-yl)ethane, 2i** (62 mg, 62%) was prepared according to the general procedure for thioetherification from 2-acetyl-5-bromothiophene (102.5 mg, 0.5 mmol). The desired thioether was obtained as a clear, pale yellow oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.03 (t, J = 7.3 Hz, 3H), 1.68 - 1.76 (m, 2H), 2.50 (s, 3H), 2.94 (t, J = 7.3 Hz, 2H), 6.97 (d, J = 4.0 Hz, 1H), 7.52 (d, J = 3.7 Hz, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 13.3 (CH₃), 22.8 (CH₂), 26.5 (CH₃), 39.5 (CH₂), 129.6 (CH), 133.0 (CH), 144.5 (C), 148.2 (C), 189.7 (C). **GC-MS** (EI) 200 ([M]+, 100%), 185 (22%), 158 (49%), 143 (96%), 114 (11%), 71 (11%). **FT-IR** (cm⁻¹, neat, ATR) 3078 (vw), 2963 (w), 1652 (vs), 1407 (vs), 1313 (s), 1269 (vs), 996 (m), 799 (m), 603 (s). **HRMS** (ES+) calcd for C₉H₁₀O₂S [M+H]+: 201.0408, found: 201.0412.

**2-Fluoro-4-(propylthio)pyridine, 2j** (62 mg, 72%) was prepared according to the general procedure for thioetherification from 4-bromo-2-fluoropyridine (88 mg, 0.5 mmol). The desired thioether was obtained as a clear, colorless oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.08 (t, J = 7.3 Hz, 3H), 1.72 - 1.80 (m, 2H), 2.96 (t, J = 7.3 Hz, 2H), 6.70 (t, J = 1.2 Hz, 1H), 6.97 (dt, J = 5.5, 1.7 Hz, 1H), 7.99 (d, J = 5.5 Hz, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 13.7 (CH₃), 22.1 (CH₂), 33.1 (CH₂), 105.5 (d, J_{C-CF} = 40.9 Hz, CH), 118.8 (d, J_{C-C-C-C-F} = 3.6 Hz, CH), 147.1 (d, J_{C-N-C-C} = 16.3 Hz, CH), 155.5 (d, J_{C-C-C-C} = 9.1 Hz, C), 164.3 (d, J_{C-F} = 238.9 Hz, CF). **19F NMR** (CDCl₃, 282 MHz) δ -71.08 (s, 1F). **GC-MS** (EI) 171 ([M]+, 90%), 142 (44%), 129 (100%), 122 (8%), 101 (7%), 85 (10%), 69 (22%), 57 (8%). **FT-IR** (cm⁻¹, neat, ATR) 2966 (w), 1588 (vs), 1540 (s), 1396 (vs), 1088 (w), 900 (vs), 819 (s), 703 (w). **HRMS** (Cl+) calcd for C₈H₁₁FNS [M+H]⁺: 172.0591, found: 172.0593.

**3-Chloro-5-(propylthio)pyridine, 2k** (68 mg, 72%) was prepared according to the general procedure for thioetherification from 3-bromo-5-chloropyridine (96 mg, 0.5 mmol). The desired thioether was obtained as a clear, colorless oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.05 (t, J = 7.3 Hz, 3H), 1.66 - 1.74 (m, 2H), 2.93 (t, J = 7.2 Hz, 2H), 7.59 (t, J = 2.0 Hz, 1H), 8.35 (d, J = 1.8 Hz, 1H), 8.41 (d, J = 1.5 Hz, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 13.6 (CH₃), 22.6 (CH₂), 35.5 (CH₂), 132.2 (C), 135.5 (CH), 136.0 (C), 145.7 (CH), 147.4 (CH). **GC-MS** (EI) 189 ([M]+, 37Cl, 38%), 187 ([M]+, 37Cl, 100%), 160 (37Cl 13%), 158 (35Cl 36%), 147 (37Cl 34%), 145 (35Cl 96%), 118 (12%), 114 (8%), 112 (9%), 101 (12%), 82 (13%), 76(8%), 73 (16%). **FT-IR** (cm⁻¹, neat, ATR) 3040 (vw), 2963 (w), 2822 (w), 1660 (vs), 1591 (s), 1472 (m), 1364 (m), 1241 (w), 1186 (s), 1156 (s), 742 (s), 717 (m). **HRMS** (ES+) calcd for C₈H₁₀Cl₂N₃S [M+H]+: 238.0626, found: 238.0621.

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23 Josey, A. D. et al. US 4683091, 1987.
3-Methoxy-5-(propythio)pyridine, 2l (67 mg, 73%) was prepared according to the general procedure for thioetherification from 3-bromo-5-methoxypyridine (94 mg, 0.5 mmol). The desired thioether was obtained as a clear, yellow oil.

\[ \text{H NMR (CDCl}_3, 500 MHz) \delta 1.02 \text{ (t, } J = 7.3 \text{ Hz, 3H)}, 1.63 - 1.71 \text{ (m, 2H), 2.90 (t, } J = 7.2 \text{ Hz, 2H), 3.83 (s, 3H), 7.13 (t, } J = 2.2 \text{ Hz, 1H), 8.09 (d, } J = 2.7 \text{ Hz, 1H), 8.15 (d, } J = 2.0 \text{ Hz, 1H).} \]

\[ \text{C NMR (CDCl}_3, 125 MHz) \delta 13.5 \text{ (CH}_3\text{), 22.7 (CH}_2\text{), 55.8 (CH}_2\text{), 121.3 (CH), 134.7 (C), 134.9 (CH), 142.2 (CH), 155.7 (C).} \]

\[ \text{GC-MS (EI) 183 ([M]^+), 154 (29%), 141 (100%), 126 (19%), 110 (9%), 98 (12%), 70 (7%).} \]

5-Methyl-2-(propythio)pyridine, 24 2m (68 mg, 81%) was prepared according to the general procedure for thioetherification from 2-bromo-5-methylpyridine (86 mg, 0.5 mmol). The desired thioether was obtained as a clear, colorless oil.

\[ \text{H NMR (CDCl}_3, 500 MHz) \delta 1.04 \text{ (t, } J = 7.3 \text{ Hz, 3H)}, 1.68 - 1.76 \text{ (m, 2H), 2.26 (s, 3H), 3.12 (t, } J = 7.3 \text{ Hz, 2H), 7.08 (d, } J = 8.2 \text{ Hz, 1H), 7.29 (dd, } J = 8.2, 1.8 \text{ Hz, 1H), 8.26 (s, 1H).} \]

\[ \text{C NMR (CDCl}_3, 125 MHz) \delta 13.8 \text{ (CH}_3\text{), 18.1 (CH}_2\text{), 23.1 (CH}_3\text{), 32.6 (CH}_2\text{), 122.1 (CH), 128.9 (C), 137.1 (CH), 150.0 (CH), 156.3 (C).} \]

\[ \text{GC-MS (EI) 167 ([M]^+), 152 (94%), 138 (100%), 134 (66%), 125 (99%), 118 (10%), 97 (16%), 92 (41%), 81 (47%), 53 (11%).} \]

4-(Propythio)quinoline, 2n (72 mg, 71%) was prepared according to the general procedure for thioetherification from 4-bromoquinoline (104 mg, 0.5 mmol). The desired thioether was obtained as a clear, yellow oil.

\[ \text{H NMR (CDCl}_3, 500 MHz) \delta 1.12 \text{ (t, } J = 7.3 \text{ Hz, 3H)}, 1.80 - 1.88 \text{ (m, 2H), 3.07 (t, } J = 7.3 \text{ Hz, 2H), 7.16 (d, } J = 4.6 \text{ Hz, 1H), 7.54 (t, } J = 7.6 \text{ Hz, 1H), 7.70 (t, } J = 7.6 \text{ Hz, 1H), 8.06 (d, } J = 8.5 \text{ Hz, 1H), 8.13 (d, } J = 8.5 \text{ Hz, 1H), 8.70 (d, } J = 4.6 \text{ Hz, 1H).} \]

\[ \text{C NMR (CDCl}_3, 125 MHz) \delta 13.9 \text{ (CH}_3\text{), 22.0 (CH}_2\text{), 33.3 (CH}_3\text{), 116.0 (CH), 123.9 (CH), 126.5 (CH), 126.9 (C), 129.9 (CH), 130.2 (CH), 147.7 (C), 148.2 (C), 149.5 (CH).} \]

\[ \text{GC-MS (EI) 203 ([M]^+), 173 (18%), 161 (100%), 133 (5%), 117 (15%), 101 (10%), 89 (13%), 75 (7%), 63 (3%).} \]

\[ \text{FT-IR (cm}^{-1}\text{, neat, ATR) 3061 (vw), 2963 (w), 2933 (w), 1569 (s), 1469 (m), 1419 (s), 1340 (vs), 1251 (s), 1182 (s), 1087 (w), 972 (s), 810 (vs).} \]

4. Bauer, L.; Hirsch, A. L. J. Org. Chem. 1966, 31, 1210.
4-(Propylthio)isoquinoline, 2o (78 mg, 76%) was prepared according to the general procedure for thioetherification from 4-bromoisoquinoline (104 mg, 0.5 mmol). The desired thioether was obtained as a clear, light brown oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 1.04 (t, J = 7.3 Hz, 3H), 1.64 - 1.72 (m, 2H), 2.96 (t, J = 7.2 Hz, 2H), 7.64 (tt, J = 7.9, 1.0 Hz, 1H), 7.77 (tt, J = 8.0, 1.5 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.57 (s, 1H), 9.12 (s, 1H).

$^{13}$C NMR (CDCl$_3$, 125 MHz) δ 13.6 (CH$_3$), 22.9 (CH$_2$), 36.6 (CH$_2$), 124.4 (CH), 127.8 (CH), 128.3 (CH), 128.7 (C), 128.9 (CH), 130.9 (CH), 136.1 (C), 144.6 (CH), 151.6 (CH). GC-MS (EI) 203 ([M$^+$], 97%), 174 (15%), 161 (100%), 134 (38%), 117 (21%), 101 (6%), 89 (27%), 75 (5%), 63 (5%). FT-IR (cm$^{-1}$, neat, ATR) 3051 (vw), 2961 (w), 1563 (w), 1376 (m), 1227 (m), 777 (vs), 748 (vs), 547 (m). HRMS (ES+) calcd for C$_{12}$H$_{14}$NS [M+H$^+$]: 204.0847, found: 204.0854.

8-(Propylthio)isoquinoline, 2p (73 mg, 72%) was prepared according to the general procedure for thioetherification from 8-bromoisoquinoline (104 mg, 0.5 mmol). The desired thioether was obtained as a clear, yellow oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 1.06 (t, J = 7.3 Hz, 3H), 1.68 - 1.76 (m, 2H), 3.02 (t, J = 7.3 Hz, 2H), 7.56 - 7.67 (m, 4H), 8.56 (d, J = 5.8 Hz, 1H), 9.78 (s, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 13.7 (CH$_3$), 22.7 (CH$_2$), 36.4 (CH$_2$), 120.9 (CH), 125.1 (CH), 128.0 (C), 128.2 (CH), 130.2 (CH), 136.3 (C), 136.9 (C), 143.7 (CH), 150.2 (CH). GC-MS (EI) 203 ([M$^+$], 83%), 173 (16%), 161 (100%), 134 (17%), 128 (8%), 117 (24%), 89 (12%), 75 (5%), 63 (4%). FT-IR (cm$^{-1}$, neat, ATR) 3049 (vw), 2963 (w), 1756 (m), 1733 (s), 619 (w), 5907 (cm$^{-1}$), neat, ATR) 3051 (vw), 2961 (w), 1563 (w), 1376 (m), 1227 (m), 777 (vs), 748 (vs), 547 (m). HRMS (ES+) calcd for C$_{12}$H$_{14}$NS [M+H$^+$]: 204.0847, found: 204.0842.

**tert-Butyl 5-(Propylthio)-1H-indazole-1-carboxylate, 2q** (130 mg, 89%) was prepared according to the general procedure for thioetherification from tert-butyl 5-bromo-1H-indazole-1-carboxylate (149 mg, 0.5 mmol). The desired thioether was obtained as a clear, light brown oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 1.16 - 1.79 (m, 2H), 1.73 (s, 9H), 3.02 (t, J = 7.3 Hz, 2H), 7.23 (dd, J = 8.3, 0.9 Hz, 1H), 7.58 (d, J = 8.56 Hz, 1H), 8.08 (s, 1H), 8.10 (s, 1H), $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 13.7 (CH$_3$), 22.4 (CH$_2$), 28.4 (CH$_3$), 35.3 (CH$_2$), 85.1 (C), 112.7 (CH), 121.1 (CH), 123.9 (C), 124.4 (CH), 139.5 (CH), 140.1 (C), 140.6 (C), 149.4 (C). FT-IR (cm$^{-1}$, neat, ATR) 2963 (w), 1756 (m), 1733 (s), 1406 (s), 1369 (s), 1292 (s), 1147 (vs), 1027 (s), 919 (s), 846 (m) 619 (w). HRMS (ES+) calcd for C$_{15}$H$_{21}$N$_2$O$_2$S [M+H$^+$]: 293.1324, found: 293.1323.

1,3,7-Trimethyl-8-(propylthio)-1H-purine-2,6(3H,7H)-dione,$^{25}$ 2r (94 mg, 70%) was prepared according to the general procedure for thioetherification from 8-bromocaffeine (136 mg, 0.5 mmol). The desired thioether was obtained as an off white powder (mp = 124 °C).

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$^{25}$ He, Z.; Luo, F.; Li, Y.; Zhu, G. *Tetrahedron Lett.*, 2013, 54, 5907.
\textbf{\textsuperscript{1}H NMR} (CDCl\textsubscript{3}, 500 MHz) δ 1.00 (t, \(J = 7.3\) Hz, 3H), 1.70 - 1.78 (m, 2H), 3.20 (t, \(J = 7.2\) Hz, 2H), 3.32 (s, 3H), 3.50 (s, 3H), 3.79 (s, 3H). \textbf{\textsuperscript{13}C NMR} (CDCl\textsubscript{3}, 125 MHz) δ 13.4 (CH\textsubscript{3}), 23.2 (CH\textsubscript{2}), 28.0 (CH\textsubscript{3}), 29.8 (CH\textsubscript{3}), 32.3 (CH\textsubscript{3}), 34.9 (CH\textsubscript{2}), 108.6 (C), 148.7 (C), 151.5 (C), 151.7 (C), 154.7 (C). \textbf{FT-IR} (cm\textsuperscript{-1}, neat, ATR) 2961 (vw), 1690 (s), 1645 (vs), 1532 (m), 1451 (m), 1364 (m), 1282 (w), 1034 (w), 746 (s), 493 (m). \textbf{HRMS} (ES+) calcd for \(\text{C}_{11}\text{H}_{17}\text{N}_{4}\text{O}_{2}\text{S} [\text{M+H}]^+\): 269.1072, found: 269.1075.
General Procedure for Thioetherification Using Thiols and 1b

\[
\text{RH}_2 + \text{PhNC-Br} \xrightarrow{\text{[Ru(bpy)_3](PF_6)_2} (2 \text{ mol } \%)} \text{PhNC-S-RH}_2
\]

4-(Butylthio)benzonitrile\(^{26}\) (3a)

To an 8 mL reaction vial equipped with an appropriately sized stir bar were added dtbbpy (6.7 mg, 0.025, 0.05 equiv) and [NiCl\(_2\)(dme)] (5.5 mg, 0.025 mmol, 0.05 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and placed under a N\(_2\) atmosphere via an inlet needle. The vial was charged with ~1.5 mL of anhyd THF and the resulting suspension was heated briefly with a heat gun until a homogenous pale green solution was observed. The solution was cooled in an ice water bath, resulting in the immediate precipitation of an evergreen solid. The solution was then evaporated in vacuo to give the ligated nickel complex.\(^{27}\) The cap was removed from the vial and alkylsilicate 1b (303 mg, 0.75 mmol, 1.5 equiv), 4-bromobenzonitrile (91 mg, 0.50 mmol, 1 equiv), and [Ru(bpy)_3](PF\(_6\)) (8.6 mg, 0.01 mmol, 0.02 equiv) were added. The vial was sealed with a cap containing a TFE lined silicone septa and was evacuated three times via an inlet needle then purged with argon. The vial was then charged with a solution of 1-butanethiol (64.6 \(\mu\)L, 54 mg, 0.60 mmol, 1.2 equiv) dissolved in anhyd, degassed DMF (5 mL) via a syringe. The cap was sealed with Parafilm\(^{\text{®}}\), and the now bright red solution was irradiated in the aforementioned LED reactor. The temperature of the reaction was maintained at approximately 27 °C via a fan. The solution was stirred vigorously while being irradiated. Reaction progress was monitored by HPLC and/or GC/MS. Once judged to be complete, the now opaque, milky-brown solution was transferred to a separatory funnel and diluted with saturated aqueous Na\(_2\)CO\(_3\) (20 mL)\(^{29}\) and Et\(_2\)O (20 mL)\(^{30}\). The layers were separated,\(^{31}\) and the aqueous layer was extracted with Et\(_2\)O (3 \(\times\) ~20 mL). The combined organic layers were washed with saturated aqueous Na\(_2\)CO\(_3\) (2 \(\times\) ~30 mL), deionized H\(_2\)O (~30 mL), and brine (~50 mL).\(^{32}\) The combined organic layer were dried (MgSO\(_4\)) and the solvent was removed.

\(^{26}\) Qiao, Z.; Wei, J.; Jiang, X. Org. Lett. 2014, 16, 1212.

\(^{27}\) We have performed the reaction with and without pre-ligation of the ligand. We found that there is no effect on the yield of cross couplings performed here. However, it was necessary for certain systems in our previous report, see ref 3.

\(^{28}\) Liquid bromides were added later as a solution in DMF

\(^{29}\) Alternatively 2 M NaOH may be used

\(^{30}\) EtOAc was used in place of Et\(_2\)O for the extractions when isolating products containing polar functional groups.

\(^{31}\) Note that a precipitate will often form and rest at the interface between the organic and aqueous layers. It can be discarded during the washes without compromising yield.

\(^{32}\) In certain cases, specifically when working with systems that did not contain basic moieties, an optionally four wash can be added. Following the saturated aqueous Na\(_2\)CO\(_3\) (or 2 M NaOH) wash, a 2 M HCl (~30 mL) may be used. This will remove any residual dtbbpy.
in vacuo by rotary evaporation. Further purification was accomplished by SiO₂ column chromatography (gradient hexane/EtOAc) to give the desired thioether, 3a, as a colorless oil (94 mg, 98%).

1H NMR (CDCl₃, 500 MHz) δ 0.94 (t, J = 7.3 Hz, 3H), 1.43 - 1.51 (m, 2H), 1.63-1.71 (m, 2H), 2.97 (t, J = 7.3 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H). 13C NMR (CDCl₃, 125 MHz) δ 13.8 (CH₃), 22.2 (CH₂), 30.9 (CH₂), 31.8 (CH₂), 108.2 (C), 119.2 (C), 126.9 (CH), 132.4 (CH), 145.6 (C). GC-MS (EI) 191 ([M]+, 80%), 148 (33%), 135 (100%), 104 (8%), 90 (10%), 63 (6%), 57 (19%). FT-IR (cm⁻¹, neat, ATR) 2958 (m), 2931 (m), 2225 (s), 1732 (vs), 1592 (m), 1485 (s), 1088 (vs), 818 (vs), 542 (vs). HRMS (CI+) calcd for C₁₁H₁₃NS [M]+: 191.0769, found: 191.0768.

4-(Phenethylthio)benzonitrile, 3b (115 mg, 96%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and 2-phenylethanethiol (79.6 µL, 82 mg, 0.60 mmol). The desired thioether was obtained as a clear, light brown oil.

1H NMR (CDCl₃, 500 MHz) δ 3.00 (t, J = 7.7 Hz, 2H), 3.25 (t, J = 7.7 Hz, 2H), 7.21 - 7.29 (m, 3H), 7.30 - 7.37 (m, 4H), 7.54 (d, J = 8.1 Hz, 2H). 13C NMR (CDCl₃, 125 MHz) δ 33.7 (CH₂), 35.3 (CH₂), 108.5 (C), 119.1 (C), 127.1 (CH), 127.2 (CH), 128.7 (CH), 128.9 (CH), 132.5 (CH), 139.6 (C), 144.8 (C). GC-MS (EI) 239 ([M]+, 100%), 146 (76%), 105 (92%), 91 (74%), 79 (10%), 77 (20%), 65 (9%). FT-IR (cm⁻¹, neat, ATR) 3028 (vw), 2926 (vw), 2224 (s), 1592 (s), 1485 (s), 1087 (vs), 817 (vs), 697 (vs), 542 (vs). HRMS (CI+) calcd for C₁₅H₁₄NS [M+H]+: 240.0847, found: 240.0839.

Methyl 3-((4-Cyanophenyl)thio)propanoate, 3c (95 mg, 86%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and methyl 3-mercapto propanoate (66.6 µL, 72 mg, 0.60 mmol). The desired thio ether was obtained as a white solid (mp = 46 °C).

1H NMR (CDCl₃, 500 MHz) δ 2.69 (t, J = 7.3 Hz, 2H), 3.71 (s, 3H), 7.33 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H). 13C NMR (CDCl₃, 125 MHz) δ 27.4 (CH₂), 33.8 (CH₂), 52.3 (CH₃), 109.1 (C), 118.9 (C), 127.7 (CH), 132.7 (CH), 143.8 (C), 171.9 (C). GC-MS (EI) 221 ([M]+, 100%), 161 (67%), 148 (45%) 134 (27%), 87 (13%), 59 (16%). FT-IR (cm⁻¹, neat, ATR) 2951 (vw), 2226 (m), 1732 (vs), 1593 (m), 1174 (s), 1087 (s), 820 (s), 543 (s). HRMS (CI+) calcd for C₁₁H₁₂NO₂S [M+H]+: 222.0589, found: 222.0591.

4-((2-Hydroxyethyl)thio)benzonitrile, 3d (64 mg, 71%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and 2-mercaptopoethanol (35.8 µL, 31 mg, 0.60 mmol). The desired thioether was obtained as a yellow solid (mp = 52 °C).

1H NMR (CDCl₃, 500 MHz) δ 2.29 (br s, 1H), 3.18 (t, J = 5.9 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H). 13C NMR (CDCl₃, 125 MHz) δ 27.4 (CH₂), 33.8 (CH₂), 52.3 (CH₃), 109.1 (C), 118.9 (C), 127.7 (CH), 132.7 (CH), 143.8 (C), 171.9 (C). GC-MS (EI) 221 ([M]+, 100%), 161 (67%), 148 (45%) 134 (27%), 87 (13%), 59 (16%). FT-IR (cm⁻¹, neat, ATR) 2951 (vw), 2226 (m), 1732 (vs), 1593 (m), 1174 (s), 1087 (s), 820 (s), 543 (s). HRMS (CI+) calcd for C₁₁H₁₂NO₂S [M+H]+: 222.0589, found: 222.0591.

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34 Klenke, B. et al. WO 2013110643, 2013.
2H), 3.83 (t, J = 5.9 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 35.2 (CH$_2$), 60.7 (CH$_2$), 108.8 (C), 118.9 (C), 127.7 (CH), 132.5 (CH), 143.9 (C). GC-MS (EI) 179 ([M]$^+$, 76%), 177 (7%), 162 (12%), 148 (100%), 135 (60%), 121 (26%), 104 (23%), 91 (31%), 75 (31%) 63 (18%). FT-IR (cm$^{-1}$, neat, ATR) 3403 (m, br), 2930 (w), 2878 (w), 2225 (s), 1592 (s), 1486 (s), 1087 (s), 1042 (s), 817 (vs), 543 (vs). HRMS (ES+) calcd for C$_9$H$_9$NOSNa [M+Na]$^+$: 202.0303, found: 202.0304.

4-((2-Aminoethyl)thio)benzonitrile, 3e (81 mg, 91%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and cysteamine hydrochloride (68 mg, 0.60 mmol). The desired thioether was obtained as a clear, yellow oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 1.96 (br s, 2H), 2.96 (t, J = 6.4 Hz, 2H), 3.07 (t, J = 6.4 Hz, 2H), 7.31 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 36.1 (CH$_2$), 40.8 (CH$_2$), 108.6 (C), 119.0 (C), 127.5 (CH), 132.5 (CH), 144.2 (C). GC-MS (EI) 178 ([M]$^+$, 52%), 149 (100%), 134 (17%), 116 (8%), 104 (9%), 90 (8%), 76 (9%) 63 (7%). FT-IR (cm$^{-1}$, neat, ATR) 3364 (vw, br), 2926 (w), 2224 (s), 1591 (vs), 1485 (s), 1087 (vs), 817 (vs), 543 (vs). HRMS (ES+) calcd for C$_9$H$_9$N$_2$S [M+H]$^+$: 179.0643, found: 179.0635.

4-(Cyclohexylthio)benzonitrile, $^{35}$ 3f (104 mg, 96%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and cyclohexanethiol (73.4 μL, 70 mg, 0.60 mmol). The desired thioether was obtained as a light yellow oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 1.24 - 1.50 (m, 5H), 1.61 - 1.71 (m, 1H), 1.76 - 1.86 (m, 2H), 1.98 - 2.12 (m, 2H), 3.30 (tt, J = 10.3, 3.7 Hz, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 25.8 (CH$_2$), 26.1 (CH$_2$), 33.1 (CH$_2$), 45.1 (CH), 108.7 (C), 119.1 (C), 128.8 (CH), 132.4 (CH), 144.2 (CH). GC-MS (EI) 217 ([M]$^+$, 91%), 135 (100%), 90 (10%), 83 (81%), 67 (24%), 55 (79%). FT-IR (cm$^{-1}$, neat, ATR) 2929 (s), 2853 (m), 2225 (s), 1592 (s), 1485 (s), 1087 (vs), 818 (vs), 543 (vs). HRMS (ES+) calcd for C$_{13}$H$_{15}$NS [M]$^+$: 217.0925, found: 217.0927.

4-((1-Hydroxyhexan-3-ylthio)benzonitrile, 3g (114 mg, 97%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and 3-mercaptophexan-1-ol (83.0 μL, 80 mg, 0.60 mmol). The desired thioether was obtained as a clear, pale yellow oil.

$^1$H NMR (CDCl$_3$, 500 MHz) δ 0.91 (t, J = 7.2 Hz, 3H), 1.41 - 1.56 (m, 2H), 1.57 - 1.72 (m, 3H), 1.82 (dtt, J = 14.2, 8.3, 5.7 Hz, 1H), 1.94 (dtt, J = 14.3, 8.3, 5.7 Hz 1H), 3.46-3.52 (m, 1H), 3.80 (qd, J = 11.3, 6.4 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.2 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 14.2 (CH$_3$), 20.2 (CH$_2$), 37.4 (CH$_2$), 37.6 (CH$_2$), 44.4 (CH), 60.3 (CH$_2$), 108.8 (C), 119.1 (C), 129.0 (CH), 132.5 (CH), 144.7 (C). GC-MS

$^{35}$ Fernandez-Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. Chem.–Eur. J. 2006, 12, 7782.
(R)-Methyl 2-((tert-Butoxycarbonyl)amino)-3-((4-cyanophenyl)(thio)propanoate, 3h (140 mg, 83%) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and (R)-methyl 2-((tert-butoxycarbonyl)amino)-3-mercaptopropanoate (141 mg, 0.60 mmol). The desired thioether was obtained as a white solid (mp = 57 °C). \( [\alpha]^{23}_{D} = +28.2 \) (CHCl\(_3\), c = 1.00).

\(^1\)H NMR (CDCl\(_3\), 500 MHz) \( \delta \) 1.41 (s, 9 H), 3.40 (dd, \( J = 13.7, 4.7 \) Hz, 1H), 3.51 (dd, \( J = 13.9, 4.7 \) Hz, 1H), 3.67 (s, 3H), 4.37 - 4.70 (m, 1H), 5.01 - 5.51 (m, 1H), 7.40 (d, \( J = 8.3 \) Hz, 2H), 7.53 (d, \( J = 8.6 \) Hz, 2H).

\(^13\)C NMR (CDCl\(_3\), 125 MHz) \( \delta \) 28.5 (CH), 52.9 (CH\(_3\)), 53.4 (CH\(_2\)), 80.7 (C), 109.5 (C), 118.8 (C), 128.6 (CH), 132.5 (CH), 143.2 (C), 155.1 (C), 170.8 (C).

\(^3\)J H NMR (CDCl\(_3\), 500 MHz) \( \delta \) 1.62 (d, \( J = 12.0 \) Hz, 3H), 1.84 (br s, 6H), 2.05 (br s, 3H), 7.60 (br s, 4H).

\(^13\)C NMR (CDCl\(_3\), 125 MHz) \( \delta \) 30.2 (CH), 36.2 (CH\(_2\)), 44.0 (CH\(_2\)), 49.8 (C), 112.4 (C), 118.8 (C), 131.9 (CH), 137.8 (CH), 138.0 (C), \( \text{GC-MS (EI) 269 ([M]+, 5%), 135 (100%), 107 (8%), } 93 (15%), 79 (15%), 67 (5%), 55 (3%) \).

\(^3\)J FT-IR (cm\(^{-1}\), neat, ATR) 3063 (vw), 2903 (s), 2847 (m), 2227 (w), 1299 (w), 1038 (m), 851 (m), 831 (s), 556 (vs).

**HRMS (Cl+) calcd for C\(_{17}\)H\(_{20}\)NS [M+H]\(^+\): 270.1311, found: 270.1307.**

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36 Ahbala, M.; Hapiot, P.; Houmam, A.; Jouini, M.; Pinson, J.; Saveant, J.-M. *J. Am. Chem. Soc.*, 1995, 117, 11488.
trans and cis 4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile, 3k & 3k’ (124 mg, 86% combined yield of both diastereomers) was prepared according to the general procedure for thioetherification from 4-bromobenzonitrile (91 mg, 0.50 mmol) and a diastereomeric mixture of 8-mercaptomenthone (112 mg, 0.6 mmol). The diasteromeric thioethers were separated by flash column chromatography to give trans (86 mg, 60%) and cis (38 mg, 26%) as clear, pale yellow oils. Ratio: 30:70 cis:trans.

(1S,4S)- & (1R,4R)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile

\[ \text{trans, 3k} \]

1H NMR (CDCl₃, 500 MHz) δ 1.02 (d, J = 6.2 Hz, 3H), 1.39 (s, 3H), 1.43 (s, 3H), 1.62 (qd, J = 13.2, 3.3 Hz, 1H), 1.86 - 2.03 (m, 3H), 2.29 (dd, J = 11.7, 3.7, 2.0 Hz, 1H), 2.35 (dd, J = 13.2, 4.4 Hz, 1H), 2.67 (dq, J = 13.4, 3.6 Hz, 1H), 7.59 (d, J = 8.6 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H).

\[ \text{cis, 3k'} \]

13C NMR (CDCl₃, 125 MHz) δ 22.4 (C₃H₃), 24.8 (CH₂), 28.4 (CH₃), 30.0 (CH₃), 34.8 (CH), 37.0 (CH₂), 52.5 (CH₂), 52.9 (C), 58.1 (CH), 112.8 (C), 118.6 (C), 132.2 (C), 137.8 (CH), 139.2 (C), 210.3 (C).

GC-MS (EI) 287 ([M]+, 9%), 153 (100%), 135 (47%), 109 (74%), 95 (12%), 93 (11%), 91 (11%), 81 (39%), 69 (78%), 67 (21%), 55 (16%).

FT-IR (cm⁻¹, neat, ATR) 2957 (m), 2873 (w), 2229 (m), 1709 (vs), 1455 (m), 1119 (m), 1085 (m), 834 (s), 546 (s). HRMS (ES+) calcd for C₁₇H₂₁NOSNa [M+Na]⁺: 310.1242, found: 310.1243.

(1R,4S)- & (1R,4S)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile

1H NMR (CDCl₃, 500 MHz) δ 0.98 (d, J=7.1 Hz, 3H), 1.42 (s, 3H), 1.43 (s, 3H), 1.67 - 1.75 (m, 1H), 1.85 - 2.00 (m, 2H), 2.10 (dd, J=12.7, 3.9, 1.7 Hz, 1H), 2.40 (dd, J=11.1, 5.0 Hz, 2H), 2.44 - 2.53 (m, 2H), 7.62 (br s, 4H).

13C NMR (CDCl₃, 125 MHz) δ. GC-MS (EI) 287 ([M]+, 10%), 153 (100%), 135 (45%), 109 (71%), 95 (13%), 93 (10%), 91 (12%), 81 (41%), 69 (75%), 67 (19%), 55 (12%).

FT-IR (cm⁻¹, neat, ATR) 2957 (m), 2873 (w), 2229 (m), 1709 (vs), 1456 (m), 1119 (m), 1085 (m), 833 (s), 554 (s). HRMS (ES+) calcd for C₁₇H₂₁NOSNa [M+Na]⁺: 310.1242, found: 310.1245.
(R)-Methyl 2-(((tert-Butyloxycarbonyl)amino)-3-((2-fluoropyridin-4-yl)thio)propanoate, 3l (160 mg, 97%) was prepared according to the general procedure for thioetherification from 4-bromo-2-fluoropyridine (88 mg, 0.50 mmol, 1 equiv) and (R)-methyl 2-(((tert-butyloxycarbonyl)amino)-3-mercaptopropanoate (141 mg, 0.60 mmol, 1.2 equiv). The desired thioether was obtained as a white powder (mp = 58 °C). $[\alpha]^{23}_D = +17.22$ (CHCl$_3$, c = 1.00).

$^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 1.42 (s, 9 H), 3.41 (dd, $J = 13.7, 3.9$ Hz, 1H), 3.57 (dd, $J = 13.9, 4.4$ Hz, 1H), 3.74 (s, 3H), 4.61 - 4.70 (m, 1H), 5.36 - 5.44 (m, 1H), 6.81 (s, 1H), 7.04 (d, $J = 5.4$ Hz, 1H), 8.01 (d, $J = 5.4$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 28.4 (CH$_3$), 33.8 (CH$_2$), 53.1 (CH$_3$), 53.4 (CH), 80.9 (C), 106.4 (d, $J_{C-C-F} = 39.4$ Hz, CH), 119.3 (d, $J_{C-C-C-C-F} = 3.7$ Hz, CH), 147.3 (d, $J_{C-N-C-F} = 16.5$ Hz, CH), 153.4 (C), 155.2 (C), 164.1 (d, $J_{CF} = 239.2$ Hz, CF), 170.6 (C). $^1$F NMR (CDCl$_3$, 282 MHz) $\delta$ -71.08 (s, 1F). FT-IR (cm$^{-1}$, neat, ATR) 3355 (w, br), 2964 (w), 1745 (m), 1705 (s, br), 1590 (s), 1251 (s), 1217 (s), 1159 (vs), 900 (m). HRMS (ES+) caleld for C$_{14}$H$_{20}$FN$_2$O$_4$S [M+H]$^+$: 331.1128, found: 331.1129. $[\alpha]^{23}_D = +17.22$ (CHCl$_3$, c = 1.00).

(R)-Methyl 2-(((tert-Butyloxycarbonyl)amino)-3-((5-methoxypyridin-3-yl)thio)propanoate, 3m (127 mg, 90%) was prepared according to the general procedure for thioetherification from 3-bromo-5-methoxypyridine (77 mg, 0.41 mmol) and (R)-methyl 2-(((tert-butyloxycarbonyl)amino)-3-mercaptopropanoate (115 mg, 0.49 mmol). The desired thioether was obtained as a clear, colorless oil. $[\alpha]^{23}_D = +46.7$ (CHCl$_3$, c = 1.00).

$^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 1.42 (s, 9 H), 3.35 (dd, $J = 13.7, 4.7$ Hz, 1H), 3.42 (dd, $J = 13.7, 4.7$ Hz, 1H), 3.63 (s, 3H), 3.86 (s, 3H), 4.52 - 4.62 (m, 1H), 5.30 - 5.40 (m, 1H), 7.27 (s, 1H), 8.17 (d, $J = 2.7$ Hz, 1H), 8.23 (d, $J = 1.7$ Hz, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 28.3 (CH$_3$), 37.4 (CH$_2$), 52.8 (CH$_3$), 53.6 (CH), 55.9 (CH$_3$), 80.6 (C), 122.9 (CH), 132.6 (C), 136.6 (CH), 143.8 (CH), 155.2 (C), 155.8 (C), 171.1 (C). FT-IR (cm$^{-1}$, neat, ATR) 3365 (vw, br), 2967 (w), 1746 (m), 1705 (s), 1505 (m), 1265 (s), 1220 (s), 1160 (vs), 1013 (m), 859 (w), 701 (w). HRMS (ES+) caleld for C$_{16}$H$_{22}$N$_2$O$_5$S [M+H]$^+$: 343.1328, found: 343.1331.

(R)-Methyl 2-(((tert-Butyloxycarbonyl)amino)-3-((5-methylpyridin-2-yl)thio)propanoate, 3n (158 mg, 97%) was prepared according to the general procedure for thioetherification from 2-bromo-5-methylpyridine (86 mg, 0.50 mmol) and (R)-methyl 2-(((tert-butyloxycarbonyl)amino)-3-mercaptopropanoate (141 mg, 0.60 mmol). The desired thioether was obtained as a white solid (mp = 60 °C). $[\alpha]^{23}_D = +14.0$ (CHCl$_3$, c = 1.00).

$^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ 1.37 (s, 9 H), 2.22 (s, 3H), 3.39 - 3.60 (m, 2H), 3.66 (s, 3H), 4.30 - 4.59 (m, 1H), 6.29 - 6.52 (m, 1H), 7.07 (d, $J = 8.1$ Hz, 1H), 7.27 (d, $J = 8.0$, 2.3 Hz, 1H), 8.20 (s, 1H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ 17.9 (CH$_3$), 28.4 (CH$_3$), 32.5 (CH$_2$), 52.4 (CH$_3$), 54.6 (CH), 79.7 (C), 122.4 (CH), 129.8 (C), 137.4 (CH), 149.6 (CH), 154.3 (C), 155.6 (C), 171.7 (C). FT-IR (cm$^{-1}$, neat, ATR) 3351 (w, br), 2978 (w), 1745 (m), 1712 (s), 1505 (m), 1464 (s), 1365 (s), 1162 (vs), 1111 (m) 820 (w), 490 (w). HRMS (ES+) caleld for C$_{15}$H$_{23}$N$_2$O$_5$S [M+H]$^+$: 327.1379, found: 327.1367.
(R)-Methyl 2-((tert-Butoxycarbonyl)amino)-3-(quinolin-4-ylthio)propanoate, 3o (133 mg, 73%) was prepared according to the general procedure for thioetherification from 4-bromoquinoline (104 mg, 0.50 mmol) and (R)-methyl 2-((tert-butoxycarbonyl)amino)-3-mercaptopropanoate (141 mg, 0.60 mmol). The desired thioether was obtained as a clear, yellow oil. [α]23D = +56.6 (CHCl3, c = 1.00).

1H NMR (CDCl3, 500 MHz) δ 1.41 (s, 9 H), 3.54 (dd, J = 13.7, 4.7 Hz, 1H), 3.67 (dd, J = 13.7, 4.9 Hz, 1H), 3.70 (s, 3H), 4.74 (q, J = 5.9 Hz, 1H), 5.43 (d, J = 6.9 Hz, 1H), 7.34 (d, J = 4.4 Hz, 1H), 7.56 (t, J = 7.7 Hz, 1H), 7.72 (t, J = 7.6 Hz, 1H), 8.08 (d, J = 8.6 Hz, 1H), 8.15 (d, J = 8.3 Hz, 1H), 8.74 (d, J = 4.7 Hz, 1H). 13C NMR (CDCl3, 125 MHz) δ 28.5 (CH3), 34.4 (CH2), 53.0 (CH3), 53.3 (CH), 80.7 (C), 117.8 (CH), 124.1 (CH), 126.8 (s, 3 C), 127.1 (C), 130.1 (CH), 146.1 (C), 149.6 (CH), 155.2 (C), 170.9 (C). FT-IR (cm−1, neat, ATR) 3355 (w, br), 2964 (w), 1745 (m), 1705 (s), 1563 (m), 1497 (s), 1366 (m), 1247 (m), 1160 (vs), 1051 (m), 823 (m), 757 (s), 730 (s), 667 (m).

HRMS (ES+) calcd for C18H23N2O4S [M+H]+: 363.1379, found: 363.1385.

(R)-Methyl 2-((tert-Butoxycarbonyl)amino)-3-(isoquinolin-4-ylthio)propanoate, 3p (111 mg, 83%) was prepared according to the general procedure for thioetherification from 4-bromoisoquinoline (78 mg, 0.37 mmol) and (R)-methyl 2-((tert-butoxycarbonyl)amino)-3-mercaptopropanoate (106 mg, 0.45 mmol). The desired thioether was obtained as an off white powder (mp = 89 °C). [α]23D = +76.5 (CHCl3, c = 1.00).

1H NMR (CDCl3, 500 MHz) δ 1.36 (s, 9 H), 3.37 (dd, J = 13.4, 4.6 Hz, 1H), 3.46 (dd, J = 14.0, 4.0 Hz, 1H), 3.52 (s, 3H), 4.55 (br q, J = 7.0 Hz, 1H), 5.39 (br d, J = 6.7 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.79 (t, J = 7.3 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 8.33 (d, J = 8.5 Hz, 1H), 8.66 (s, 1H), 9.15 (s, 1H). 13C NMR (CDCl3, 125 MHz) δ 28.5 (CH3), 38.0 (CH2), 52.7 (CH3), 53.8 (CH), 80.4 (C), 124.7 (CH), 127.2 (C), 128.1 (CH), 128.5 (CH), 129.0 (C), 131.5 (CH), 136.6 (C), 147.5 (CH), 153.0 (CH), 155.1 (C), 171.1 (C). FT-IR (cm−1, neat, ATR) 3353 (w), 2962 (vw), 1738 (s), 1713 (s), 1521 (s), 1225 (m), 1158 (vs), 1014 (m), 782 (m), 753 (m).

HRMS (ES+) calcd for C18H23N2O4S [M+H]+: 363.1379, found: 363.1386.

3-(Pyrimidin-5-ylthio)hexan-1-ol, 3q (74 mg, 70%) was prepared according to the general procedure for thioetherification from 5-bromopyrimidine (80 mg, 0.50 mmol) and 3-mercaptophexan-1-ol (83.0 μL, 80 mg, 0.60 mmol). The desired thioether was obtained as a clear, yellow oil.

1H NMR (CDCl3, 500 MHz) δ 0.90 (t, J = 7.30 Hz, 3H), 1.42 - 1.66 (m, 4H), 1.75 (ddt, J = 14.3, 8.5, 5.6 Hz, 1H), 1.90 (ddt, J = 14.6, 7.5, 5.5 Hz, 1H), 2.20 (br s, 1H), 3.33 (ddt, J = 8.2, 7.2, 5.5 Hz, 1H), 3.76 - 3.83 (m, 1H), 3.84 - 3.91 (m, 1H), 8.73 (s, 2H), 9.03 (s, 1H). 13C NMR (CDCl3, 125 MHz) δ 14.1 (CH3), 20.2 (CH2), 37.5 (CH2), 37.6 (CH2), 46.3 (CH), 60.0 (CH2), 132.2 (C), 156.6 (CH), 159.4 (CH). GC-MS (EI) 212 ([M]+, 72%), 148 (7%), 125 (10%), 112 (100%), 83 (58%), 68 (9%), 57 (24%), 55 (99%). FT-IR (cm−1, neat,
tert-Butyl 4-((1-hydroxyhexan-3-yl)thio)pyrimidin-2-yl)piperazine-1-carboxylate, 3r (136 mg, 69%) was prepared according to the general procedure for thioetherification from tert-butyl 4-((5-bromopyrimidin-2-yl)piperazine-1-carboxylate (172 mg, 0.50 mmol) and 3-mercaptohexan-1-ol (83.0 μL, 80 mg, 0.60 mmol). The desired thioether was obtained as a white solid (mp = 56 °C).

\[ \text{C}_{10} \text{H}_{17} \text{N}_{2} \text{OS} [\text{M+H}^+]^+ : 213.1062 \text{, found: 213.1068.} \]

**3r**

3-((3-Methylpyridin-2-yl)thio)hexan-1-ol, 3s (60 mg, 53%) was prepared according to the general procedure for thioetherification from 3-bromo-2-methylpyridine (86 mg, 0.50 mmol) and 3-mercaptopropan-1-ol (83.0 μL, 80 mg, 0.60 mmol). The desired thioether was obtained as a colorless oil.

\[ \text{C}_{19} \text{H}_{32} \text{N}_{4} \text{O}_{3} \text{SNa} [\text{M+Na}^+]^+ : 419.2093 \text{, found: 419.2093.} \]

**3s**

N-(4-((1-Hydroxyhexan-3-yl)thio)phenyl)acetamide, 3t (69 mg, 52%) was prepared according to the general procedure for thioetherification from N-(4-bromophenyl)acetamide (107 mg, 0.50 mmol) and 3-mercaptopropan-1-ol (83.0 μL, 80 mg, 0.60 mmol). The desired thioether was obtained as a white solid (mp = 96 °C).

\[ \text{C}_{12} \text{H}_{20} \text{NOS} [\text{M+H}^+]^+ : 226.1266 \text{, found: 226.1257.} \]

**3t**
4-((1-Hydroxyhexan-3-yl)(thio)benzenesulfonamide, 3u (139 mg, 96%) was prepared according to the general procedure for thioetherification from 4-bromobenzenesulfonamide (118 mg, 0.50 mmol) and 3-mercaptophexan-1-ol (83.0 μL, 0.60 mmol). The desired thioether was obtained as a colorless oil.

1H NMR (CDCl3, 500 MHz) δ 0.90 (t, J = 7.34 Hz, 3H), 1.39 - 1.54 (m, 2H), 1.54 - 1.69 (m, 2H), 1.73 - 1.82 (m, 1H), 1.85 - 1.94 (m, 1H), 2.40 (br s, 1H), 3.42 - 3.50 (m, 1H), 3.65 - 3.83 (m, 2H), 5.49 (br s, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 8.3 Hz, 2H), 13C NMR (CDCl3, 125 MHz) δ 14.2 (CH3), 20.3 (CH2), 37.5 (CH2), 37.6 (CH2), 44.7 (CH), 60.4 (CH2), 127.1 (CH), 129.4 (CH), 139.0 (C), 141.4 (C). FT-IR (cm⁻¹, neat, ATR) 3262 (w, br), 2957 (w), 2932 (w), 1579 (w), 1323 (s), 1157 (vs), 1077 (s), 905 (w), 752 (m), 619 (s), 541 (s). HRMS (ES+) calcd for C12H20NO2S2 [M+H]+: 290.0885, found: 290.0890.

4-(tert-butylthio)benzoic acid, 3v (99 mg, 94%) was prepared according to the general procedure for thioetherification from 4-bromobenzoic acid (101 mg, 0.5 mmol) and tert-butylthiol (67.6 μL, 54 mg, 0.60 mmol) with the following modified workup: The reaction mixture was quenched with saturated aqueous NH4Cl. The quenched reaction mixture was extracted with EtOAc (3 × 20 mL). The solvent was removed in vacuo by rotary evaporation, giving a brown oil. The brown oil was taken up in ~40 mL of Et2O and extracted with saturated aqueous NaHCO3 (3 × 20 mL). The combined aqueous layers were mixed with ~40 mL of EtOAc and extracted with HCl to pH 1 (~10 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with deionized H2O (~60 mL) and dried (MgSO4). The solvent was removed in vacuo by rotary evaporation. The resulting off-white solid was further purified by SiO2 column chromatography (gradient CH2Cl2:MeOH, 97:3 to 95:5), giving the desired thioether as a fluffy white powder (mp = 144 °C).

1H NMR (CDCl3, 500 MHz) δ 1.34 (s, 9H), 7.63 (d, J = 7.9 Hz, 2H), 8.06 (d, J = 7.9 Hz, 2H), 12.65 (br s, 1H), 13C NMR (CDCl3, 125 MHz) δ 31.4 (CH3), 47.3 (C), 129.3 (C), 130.3 (CH), 137.0 (CH), 140.7 (CH), 172.4 (C), FT-IR (cm⁻¹, neat, ATR) 3120-2751 (m, very br), 2552 (w), 1682 (vs) 1422 (s) 1277 (s), 1176 (w), 943 (m), 851 (w), 767 (m), 537 (w). HRMS (ES-) calcd for C11H13O2S [M-H]−: 209.0636, found: 209.0639.

(4-Benzylphenyl)(tert-butyl)sulfane, 3w (102 mg, 80%) was prepared according to the general procedure for thioetherification from 1-benzyl-4-bromobenzene (124 mg, 0.50 mmol) and tert-butylthiol (67.6 μL, 54 mg, 0.60 mmol). The desired thioether was obtained as a clear, colorless oil.

1H NMR (CDCl3, 500 MHz) δ 1.28 (s, 9 H), 3.99 (s, 2H), 7.15 (d, J = 8.2 Hz, 2H), 7.17 - 7.24 (m, 3H), 7.30 (t, J = 7.6 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 13C NMR (CDCl3, 125 MHz) δ 31.2 (CH3), 41.9 (CH2), 46.0 (C), 126.5 (CH), 128.8 (CH), 129.2 (CH), 132.1 (CH), 140.7 (CH), 151.4 (C), 163.4 (C), 165.5 (C), 172.4 (C), FT-IR (cm⁻¹, neat, ATR) 3120-2751 (m), 2552 (w), 1682 (vs) 1422 (s) 1277 (s), 1176 (w), 943 (m), 851 (w), 767 (m), 537 (w). HRMS (ES+) calcd for C14H12O2S2 [M+H]+: 268.1370, found: 268.1370.
129.3 (CH), 130.4 (C), 137.8 (CH), 140.9 (C), 142.1 (C). GC-MS (EI) 256 ([M]⁺, 31%), 200 (100%), 167 (87%), 165 (44%), 152 (14%), 115 (6%), 91 (16%), 57 (22%). FT-IR (cm⁻¹, neat, ATR) 3031 (vw), 2960 (w), 1490 (w), 1454 (w), 1167 (w), 794 (w), 746 (m), 724 (m), 697 (vs). HRMS (Cl⁺) calcd for C_{17}H_{20}S [M]⁺: 256.1286, found: 256.1277.

2-(tert-Butylthio)benzonitrile, 3x (71 mg, 74%) was prepared according to the general procedure for thioetherification from aryl halide (91 mg, 0.5 mmol) and tert-butylthiol (67.6 μL, 54 mg, 0.60 mmol). The desired thioether was obtained as a clear, yellow oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.36 (s, 9 H), 7.47 (td, J = 7.7, 1.2 Hz, 1H), 7.55 (td, J = 7.7, 1.5 Hz, 1H), 7.69 (ddd, J = 7.6, 1.3, 0.6 Hz, 1H), 7.73 (ddd, J = 7.6, 1.5, 0.6 Hz, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 31.3 (CH₃), 49.2 (C), 118.5 (C), 121.6 (C), 129.5 (CH), 132.5 (CH), 134.0 (CH), 136.9 (C), 139.2 (CH). GC-MS (EI) 191 ([M]⁺, 20%), 176 (4%), 135 (100%), 108 (6%), 90 (7%), 57 (65%). FT-IR (cm⁻¹, neat, ATR) 3062 (vw), 2963 (w), 2228 (w), 1485 (w), 1365 (w), 1164 (m), 761 (vs), 73 (12%), 57 (100%). HRMS (ES⁺) calcd for C_{11}H_{13}NSNa[MNa⁺]: 214.0666, found: 214.0658.

3-(tert-Butylthio)-5-chloropyridine, 3y (61 mg, 61%) was prepared according to the general procedure for thioetherification from 3-bromo-5-chloropyridine (96 mg, 0.5 mmol) and tert-butylthiol (67.6 μL, 54 mg, 0.60 mmol). The desired thioether was obtained as a clear, colorless oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.31 (s, 9 H), 7.84 (dd, J = 2.4, 1.8 Hz, 1H), 8.56 (d, J = 2.4 Hz, 1H), 8.58 (d, J = 1.8 Hz, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 31.2 (CH₃), 47.3 (C), 131.3 (C), 131.7 (C), 143.9 (CH), 148.8 (CH), 154.7 (CH). GC-MS (EI) 203 ([M]⁺, 8%), 201 ([M]⁺, 35Cl 21%), 147 (35Cl 34%), 145 (35Cl 90%), 117 (7%), 101 (5%), 82(9%), 73 (12%), 57 (100%). FT-IR (cm⁻¹, neat, ATR) 3042 (vw), 2962 (w), 1553 (w), 1398 (m), 1365 (m), 1167 (m), 1102 (m), 1020 (m), 882 (m), 812 (m), 700 (s). HRMS (Cl⁺) calcd for C_{9}H_{12}ClINS [M]⁺: 201.0379, found: 201.0386.

8-(tert-Butylthio)isoquinoline, 3z (80 mg, 73%) was prepared according to the general procedure for thioetherification from aryl halide (104 mg, 0.5 mmol) and tert-butylthiol (67.6 μL, 54 mg, 0.60 mmol). The desired thioether was obtained as a clear, pale yellow oil.

**1H NMR** (CDCl₃, 500 MHz) δ 1.32 (s, 9 H), 7.64 - 7.70 (m, 2H), 7.87 (dd, J = 7.0, 6.1 Hz, 2H), 8.57 (d, J = 5.5 Hz, 1H), 10.08 (s, 1H). **13C NMR** (CDCl₃, 125 MHz) δ 31.5 (CH₃), 48.1 (C), 120.5 (CH), 128.4 (CH), 129.9 (CH), 131.5 (C), 132.1 (C), 136.9 (C), 138.8 (CH), 143.4 (CH), 152.6 (CH). GC-MS (EI) 217 ([M]⁺, 11%), 161 (100%), 134 (6%), 117 (12%), 89 (7%), 57 (11%). FT-IR (cm⁻¹, neat, ATR) 3049 (vw), 2961 (w), 1611 (w), 1363 (w), 1155 (m), 974 (w), 833 (vs), 753 (w), 652 (w). HRMS (ES⁺) calcd for C_{13}H_{16}NS [M+H⁺]: 218.1003, found: 218.0997.
Representative Procedure for Large Scale Thioetherification

Using silicate 1a:

![Chemical structure of the reaction](image)

1-(4-(Propylthio)phenyl)ethanone (2d)

To an oven dried, 100 mL round bottom flask equipped with an appropriately sized stir bar were added alkylthiolsilicate 1a (2.53 g, 6 mmol, 1.2 equiv), [NiCl2(dme)] (55 mg, 0.250 mmol, 0.025 equiv), dtbbpy (67.1 mg, 0.250 mmol, 0.025 equiv), and [Ru(bpy)3]2(PF6)3 (86.0 mg, 0.100 mmol, 0.02 equiv). The flask was sealed with rubber a septum and was evacuated three times via its inlet valve and purged with argon. The flask was then charged with the 4-bromoacetophenone (0.995 g, 5 mmol, 1 equiv) dissolved in anhyd, degassed DMF (50 mL) via a syringe. The now bright red solution was irradiated in the aforementioned LED reactor. The temperature of the reaction was maintained at approximately 27 °C via a fan. The solution was stirred vigorously while being irradiated. Reaction progress was monitored by GC/MS. Once complete (~8 h), the now opaque, milky-brown solution was transferred to a separatory funnel and diluted with deionized H2O (~150 mL) and Et2O (~100 mL). The layers were separated, and the aqueous layer was extracted with Et2O (3 × ~100 mL). The combined organic layers were washed with 2 M NaOH (2 × ~100 mL), 2 M HCl (~100 mL), deionized H2O (~100 mL), and brine (~100 mL). The organic layer was dried (Na2SO4), and the solvent was removed in vacuo by rotary evaporation. Further purification was accomplished by SiO2 column chromatography (gradient hexane to 9:1 hexane/EtOAc) to give the desired thioether 2d (0.748 g, 77%). as a clear, colorless oil that solidified upon standing to a white, waxy solid (mp = 36 °C).

1H NMR (CDCl3, 500 MHz) δ 1.06 (t, J = 7.3 Hz, 3H), 1.69 - 1.77 (m, 2H), 2.55 - 2.56 (m, 3H), 2.97 (t, J = 7.3 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H). 13C NMR (CDCl3, 125 MHz) δ 13.8 (CH3), 22.5 (CH2), 26.7 (CH3), 34.3 (CH2), 126.6 (CH), 129.0 (CH), 134.1 (C), 145.2 (C), 197.4 (C). GC-MS (EI) 194 ([M]+, 88%), 179 (100%), 137 (71%), 123 (13%), 109 (20%), 69 (6%). FT-IR (cm\(^{-1}\), neat, ATR) 2967 (w), 1673 (vs), 1587 (s) 1356 (s), 1264 (s), 1180 (s), 1096 (s), 956 (s), 813 (vs), 745 (m), 586 (s). HRMS (CI+) calcd for C11H14OS [M]+: 194.0765, found: 194.0762.
II. Using thiols with silicate 1b as a hydride abstractor

To a 100 mL round bottom flask equipped with an appropriately sized stir bar were added added alkylsilicate 1b (3.03 g, 7.5 mmol, 1.5 equiv), [NiCl₂(dme)] (55 mg, 0.250 mmol, 0.025 equiv), dtbbpy (67.1 mg, 0.250 mmol, 0.025 equiv), and [Ru(bpy)₃](PF₆) (86.0 mg, 0.100 mmol, 0.02 equiv). The flask was sealed with rubber septum and was evacuated three times via its inlet valve and purged with argon. The flask was then charged with the 4-bromo benzonitrile (0.910 g, 5 mmol, 1 equiv) and 3-mercaptohexan-1-ol (0.805 g, 6 mmol, 1.2 equiv) dissolved in anhyd, degassed DMF (50 mL) via a syringe. The now bright red solution was irradiated in the aforementioned LED reactor. The temperature of the reaction was maintained at approximately 27 °C via a fan. The solution was stirred vigorously while being irradiated. Reaction progress was monitored by GC/MS. Once complete (~12 h), the now opaque milky-brown solution was transferred to a separatory funnel an diluted with deionized H₂O (~150 mL) and Et₂O (~100 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × ~100 mL). The combined organic layers were washed with 2 M NaOH (~100 mL), 2 M HCl (~100 mL), deionized H₂O (~100 mL), and brine (~100 mL). The organic layer was dried (Na₂SO₄), and the solvent was removed in vacuo by rotary evaporation. Further purification was accomplished by SiO₂ column chromatography (gradient hexane to 9:1 hexane:EtOAc). to give the desired thioether 3g (1.01 g, 86%) as a thick yellow oil.

**¹H NMR** (CDCl₃, 500 MHz) δ 0.91 (t, J = 7.2 Hz, 3H), 1.41 - 1.56 (m, 2H), 1.57 - 1.72 (m, 3H), 1.82 (ddt, J = 14.2, 8.3, 5.7 Hz, 1H), 1.94 (ddt, J = 14.3, 8.3, 5.7 Hz 1H), 3.44-3.53 (m, 1H), 3.80 (qd, J = 11.3, 6.4 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.51 (d, J = 8.2 Hz, 2H). **¹³C NMR** (CDCl₃, 125 MHz) δ 12.0 (CH₃), 20.2 (CH₂), 37.4 (CH₂), 37.6 (CH₂), 44.4 (CH), 60.3 (CH₂), 108.8 (C), 119.1 (C), 129.0 (CH), 132.5 (CH), 144.7 (C). **GC-MS** (EI) 235 ([M]+, 4%), 207 (17%), 135 (10%), 125 (100%), 83 (15%), 55 (24%). **FT-IR** (cm⁻¹, neat, ATR) 3434 (m, br), 2957 (m), 2931 (m), 2226 (s), 1591 (vs), 1485 (s), 1086 (vs), 1048 (s), 820 (vs), 543 (vs). **HRMS** (ES+) calcd for C₁₃H₁₈NOS [M+H]⁺: 236.1109, found: 236.1105.
Control and Mechanistic Studies

Procedure for control studies using alkylthiolasilicate 1a

To a 4 mL reaction vial equipped with an appropriately sized stir bar, was added alkylthiolasilicate 1a (44 mg, 0.105 mmol, 1.05 equiv) and 4-bromoacetophenone (20 mg, 0.60 mmol, 1 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and was evacuated three times via an inlet needle then purged with argon. The vial was then charged with NiCl₂•dme (1.1 mg, 0.025 mmol, 0.05 equiv), dtbbpy (1.3 mg, 0.025, 0.05 equiv), and Ru(bpy)₃(PF₆) (1.8 mg, 0.01 mmol, 0.02 equiv) dissolved in anhyd, degassed DMF (1 mL) via a syringe. The cap was sealed with Parafilm® and the now bright red solution was irradiated in the aforementioned LED reactor for 12 h. The temperature of the reaction was maintained at approximately 27 °C via a fan. After 12 h, reaction progress was evaluated by GC/MS.

Table S1: Control Studies using Alkylthiolasilicate 1a

| Entry | Deviation from procedure                  | Conversion to 2d |
|-------|------------------------------------------|-----------------|
| 1     | None                                     | 100%            |
| 2     | No photocatalyst ([Ru(bpy)₃](PF₆)₂)       | 0%              |
| 3     | No light                                 | 0%              |
| 4     | No [NiCl₂(dme)]                          | 0%              |
| 5     | No ligand (dtbbpy)                       | 57%             |

*Percentages determined by area/(total area of 4-bromoacetophenone and 2d) of GC/MS trace of run.

Procedure for evaluating effect of alkysilicate structure on photoredox thioetherification

To a 4 mL reaction vial equipped with an appropriately sized stir bar, was added the appropriate alkysilicate (0.15 mmol, 1.5 equiv) and 4-bromobenzonitrile (18.2 mg, 0.10 mmol, 1 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and was evacuated three times via an inlet needle then purged with argon. The vial was then charged [NiCl₂(dme)] (1.1 mg, 0.005 mmol, 0.05 equiv), dtbbpy (1.3 mg, 0.005, 0.05 equiv), and [Ru(bpy)₃](PF₆) (1.8 mg, 0.002 mmol, 0.02 equiv) all dissolved in anhyd, degassed DMF (1 mL) via a syringe. This was followed by rapid addition of cyclohexanethiol (14.7 µL, 13.9 mg, 0.120 mmol, 1.2 equiv) via a
μL syringe. The cap was sealed with Parafilm® and the now bright red solution was irradiated in the aforementioned LED reactor for 36 h. The temperature of the reaction was maintained at approximately 27 °C via a fan. After 36 h, reaction progress was evaluated by GC/MS.

Table S2: Effect of Alkylsilicate Structure on the Outcome of Photoredox Thioetherification

| Entry | Alkylsilicate | I   | II  | III | IV  | V   |
|-------|---------------|-----|-----|-----|-----|-----|
| 1     | ![Chemical Structure](attachment:structure1d.png) | 6%  | 69% | 22% | 0%  | 3%  |
| 2     | ![Chemical Structure](attachment:structure1e.png) | trace | 48% | 46% | 0%  | 6%  |
| 3     | ![Chemical Structure](attachment:structure1f.png) | trace | 3%  | 12% | 85% | trace |
| 4     | ![Chemical Structure](attachment:structure1g.png) | trace | 0%  | 99% | 0%  | 1%  |
| 5     | ![Chemical Structure](attachment:structure1h.png) | 0%  | 0%  | 98% | 0%  | 2%  |
| 6     | ![Chemical Structure](attachment:structure1a.png) | 0%  | 0%  | 99% | 0%  | 1%  |
| 7     | ![Chemical Structure](attachment:structure1a.png) | None | 34% | 62% | 0%  | 4%  |

"Percentages determined by area/(total area of mixture components) of GC/MS trace of run."
Procedure for evaluating effect of alkylsilicate structure on photoredox thioetherification

To a 4 mL reaction vial equipped with an appropriately sized stir bar, was added the appropriate alkylsilicate 1b (61 mg, 0.15 mmol, 1.5 equiv) and 4-bromoacetophenone (20 mg, 0.10 mmol, 1 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and was evacuated three times via an inlet needle then purged with argon. The vial was then charged [NiCl_2(dme)] (1.1 mg, 0.005 mmol, 0.05 equiv), dtbbpy (1.3 mg, 0.005, 0.05 equiv), and [Ru(bpy)_3](PF_6) (1.8 mg, 0.002 mmol, 0.02 equiv) all dissolved in anhyd, degassed DMF (1 mL) via a syringe. This was followed by rapid addition of cyclohexanethiol (14.7 µL, 13.9 mg, 0.120 mmol, 1.2 equiv) via a µL syringe. The cap was sealed with Parafilm® and the now bright red solution was irradiated in the aforementioned LED reactor for 24 h. The temperature of the reaction was maintained at approximately 27 °C via a fan. After 24 h, reaction progress was evaluated by GC/MS and tabulated.

Table S3: Control Studies using Thiols and Alkylthiolsilicate 1b

| Entry | Deviation from procedure | I (%) | II (%) | III (%) | IV (%) | V (%) |
|-------|--------------------------|-------|-------|---------|--------|-------|
| 1     | None                     | 6%    | 0%    | 92%     | 0%     | 2%    |
| 2     | No photocatalyst ([Ru(bpy)_3](PF_6)_2) | 33%   | 64%   | 0%      | 0%     | 3%    |
| 3     | No [NiCl_2(dme)]         | 28%   | 66%   | 0%      | 0%     | 6%    |
| 4     | No ligand (dtbbpy)       | 14%   | 60%   | 0%      | 0%     | 26%   |
| 5     | No light                 | 34%   | 63%   | 0%      | 0%     | 3%    |
| 6     | No alkylsilicate         | 34%   | 62%   | 0%      | 0%     | 4%    |
| 7     | No cyclohexanethiol      | 0%    | 0%    | 0%      | 100%   | 0%    |

*Percentages determined by area/(total area of mixture components) of GC/MS trace of run.*
**Determination of fate of alkyl component using hexadecylsilicate 1c**

To a 4 mL reaction vial equipped with an appropriately sized stir bar, was added the appropriate alkylsilicate 1g (60 mg, 0.105 mmol, 1.05 equiv) and 4-bromoacetophenone (20 mg, 0.10 mmol, 1 equiv). The vial was sealed with a cap containing a TFE lined silicone septa and was evacuated three times via an inlet needle then purged with argon. The vial was then charged with cyclohexanethiol (14.7 µL, 13.9 mg, 0.120 mmol, 1.2 equiv) followed by [NiCl₂(dme)] (1.1 mg, 0.005 mmol, 0.05 equiv), dtbbpy (1.3 mg, 0.005, 0.05 equiv), and [Ru(bpy)₃](PF₆)₂ (1.8 mg, 0.002 mmol, 0.02 equiv) all dissolved in anhyd, degassed DMF (1 mL) via a syringe. The cap was sealed with Parafilm and the now bright red solution was irradiated in the aforementioned LED reactor for 24 h. The temperature of the reaction was maintained at approximately 27 °C via a fan. Reaction progress was monitored by GC/MS and hexadecane was found to form in approximately equal quantity to the expected thioether over time.
$^1$H NMR Spectra of Synthesized Compounds

diisopropylammonium bis(catecholato)(3-mercaptopropyl)silicate
500 MHz, MeCN-d3
diisopropylammonium bis(catecholato)isobutylsilicate
500 MHz, DMSO–d6
diisopropylammonium Bis(catecholato)hexadecylsilicate
500 MHz, DMSO–d6
[1,1’-biphenyl]-4-yl(propyl)sulfane
500 MHz, CDCl3
(4-benzylphenyl)(propyl)sulfane
500 MHz, CDCl3
4-(propythio)benzonitrile

500 MHz, CDCl3
1-(4-(propylthio)phenyl)ethanone
500 MHz, CDCl3
methyl 3-((propylthio)benzoate
500 MHz, CDCl₃
2-(propythio)benzonitrile
500 MHz, CDCl3

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S39
4-(propylthio)benzoic acid
500 MHz, CDCl₃
1-(5-(propylthiothiophen-2-yl)ethanone
500 MHz, CDCl3
2-fluoro-4-(propylthio)pyridine
500 MHz, CDCl3
3-chloro-5-(propylthio)pyridine
500 MHz, CDCl3

8.4 ppm
7.60 ppm
3.0  2.9 ppm
1.8  1.7 ppm
1.1  1.0 ppm

ppm
3-methoxy-5-(propylthio)pyridine
500 MHz, CDCl₃
5-methyl-2-(propylthio)pyridine
500 MHz, CDCl3
4-\textit{\{(propylthio\}quinoline
500 MHz, CDCl$_3$
4-(propylthio)isoquinoline
500 MHz, CDCl3
8-(propylthio)isoquinoline
500 MHz, CDCl3
tert-butyl 5-(propylthio)-1H-indazole-1-carboxylate
500 MHz, CDCl3
1,3,7-trimethyl-8-(propylthio)-1H-purine-2,6(3H,7H)-dione
500 MHz, CDCl3
4-(butylthio)benzonitrile
500 MHz, CDCl3
4-(phenethylthio)benzonitrile
500 MHz, CDCl3
methyl 3-((4-cyanophenyl)thio)propanoate
500 MHz, CDCl3
4-((2-hydroxyethyl)thio)benzonitrile
500 MHz, CDCl3
4-((2-aminoethyl)thio)benzonitrile
500 MHz, CDCl₃
4-(cyclohexylthio)benzonitrile
500 MHz, CDCl3
4-((1-hydroxyhexan-3-yl)thio)benzonitrile
500 MHz, CDCl3
R)-methyl 2-(((tert-butoxycarbonyl)amino)-3-((4-cyanophenyl)thio)propanoate
500 MHz, CDCl₃
(4-tert-butylthio)benzonitrile
500 MHz, CDCl3
4-\{adamantan-1-ythio\}benzonitrile

500 MHz, CDCl₃
(1S,4S)- & (1R,4R)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile
500 MHz, CDCl₃

trans, 3k
(1R,4S)- & (1R,4S)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thiobenzonitrile
500 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((2-fluoropyridin-4-yl)thio)propanoate
500 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((5-methoxypyridin-3-yl)thio)propanoate
500 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((5-methylpyridin-2-yl)thio)propanoate
500 MHz, CDCl3

![NMR Spectra](Image)
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-(quinolin-4-ylthio)propanoate
500 MHz, CDCl3
(R)-methyl 2-(((tert-butoxycarbonyl)amino)-3-(isoquinolin-4-ylthio)propanoate
500 MHz, CDCl3

![NMR spectrum](image_url)
3-(pyrimidin-5-ylthio)hexan-1-ol
500 MHz, CDCl3
tert-butyl 4-((1-hydroxyhexan-3-yl)thio)pyrimidin-2-yl)piperazine-1-carboxylate
500 MHz, CDCl3
3-((3-methylpyridin-2-yl)(thio)hexan-1-ol
500 MHz, CDCl3
N-(4-((1-hydroxyhex-3-yl)thio)phenyl)acetamide
500 MHz, CDCl3
4-((1-hydroxyhexan-3-yl)thio)benzenesulfonamide
500 MHz, CDCl3
4-(tert-butylthio)benzoic acid
500 MHz, CDCl3
(4-benzylphenyl)((tert-butyl)sulfane
500 MHz, CDCl3
2-(tert-butylthio)benzonitrile
500 MHz, CDCl₃
3-(tert-butylthio)-5-chloropyridine
500 MHz, CDCl3
8-(tert-butylthio)isoquinoline
500 MHz, CDCl3

S77
$^{13}$C NMR Spectra of Synthesized Compounds

diisopropylammonium bis(catecholato)(3-mercaptopropyl)silicate

125 MHz, MeCN-d3

![NMR Spectra Image]
diisopropylammonium bis(catecholato)isobutylsilicate

125 MHz, DMSO–d6
diisopropylammonium bis(catecholato)hexadecysilicate
125 MHz, DMSO–d6
[1,1’-biphenyl]-4-yl(propyl)sulfane
125 MHz, CDCl₃
(4-benzylphenyl)(propyl)sulfane
125 MHz, CDCl3
4-(propylthio)benzonitrile
125 MHz, CDCl₃
1-(4-(propylthio)phenyl)ethanone
125 MHz, CDCl₃
2-(propylthio)benzonitrile
125 MHz, CDCl3
2-(propylthio)benzonitrile
125 MHz, CDCl3
4-(propylthio)benzoic acid
125 MHz, CDCl₃
1-\{(5-\text{propylthio})\text{thiophen-2-yl}\}\text{ethanone} \\
125 MHz, CDCl3

\begin{align*}
189.74 & \quad 148.23 & \quad 133.63 & \quad 296.83 & \quad 39.45 & \quad 26.49 & \quad 22.78 & \quad 13.33 \\
144.50 & \quad 123.63 & \quad 139.83 & \quad 219.63 & \quad 39.45 & \quad 26.49 & \quad 22.78 & \quad 13.33 \\
\end{align*}
2-fluoro-4-(propylthio)pyridine
125 MHz, CDCl₃
3-chloro-5-(propylthio)pyridine
125 MHz, CDCl₃
3-methoxy-5-(propylthio)pyridine
125 MHz, CDCl₃
5-methyl-2-(propylthio)pyridine
125 MHz, CDCl₃
4-(propythio)quinoline
125 MHz, CDCl3
4-(propylthio)isoquinoline
125 MHz, CDCl3
8-(propylthio)isoquinoline
125 MHz, CDCl3
tert-butyl 5-(propylthio)-1H-indazole-1-carboxylate
125 MHz, CDCl₃
1,3,7-trimethyl-8-((propylthio)-1H-purine-2,6(3H,7H)-dione
125 MHz, CDCl3
4-(butylthio)benzonitrile
125 MHz, CDCl3
4-(phenethylthio)benzonitrile
125 MHz, CDCl3
methyl 3-((4-cyanophenyl)thio)propanoate
125 MHz, CDCl3
4-((2-hydroxyethyl)thio)benzonitrile
125 MHz, CDCl3
4-((2-aminoethyl)thio)benzonitrile
125 MHz, CDCl3
4-(cyclohexylthio)benzonitrile
125 MHz, CDCl₃
4-((1-hydroxyhexan-3-yl)thio)benzonitrile
125 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((4-cyanophenylthio)propanoate
125 MHz, CDCl3
(4-(tert-butylthio)benzonitrile
125 MHz, CDCl3
4-(adamantan-1-ylthio)benzonitrile
125 MHz, CDCl3
(1S,4S)- & (1R,4R)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile
125 MHz, CDCl3
(1R,4S)- & (1R,4S)-4-((2-(4-Methyl-2-oxocyclohexyl)propan-2-yl)thio)benzonitrile
125 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((2-fluoropyridin-4-yl)thio)propanoate

125 MHz, CDCl3

![Chemical Structure](image)

S110
(R)-methyl 2-\(((\text{tert-butoxycarbonyl})\text{amino})\)-3-\(((5\text{-methoxy}\text{pyridin}-3\text{-yl})\text{thio})\text{propanoate}
125 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((5-methylpyridin-2-yl)thio)propanoate
125 MHz, CDCl3

\[
\begin{align*}
\text{MeO} & \quad \text{NHBOc} \\
\end{align*}
\]
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-((quinolin-4-ylthio)propanoate
125 MHz, CDCl3
(R)-methyl 2-((tert-butoxycarbonyl)amino)-3-(isoquinolin-4-ylthio)propanoate
125 MHz, CDCl₃
3-((pyrimidin-5-ylthio)hexan-1-ol
125 MHz, CDCl₃
tert-butyl 4-((1-hydroxyhexan-3-yl)thio)pyrimidin-2-yl)piperazine-1-carboxylate

125 MHz, CDCl3
3-[(3-methylpyridin-2-yl)thio]hexan-1-ol
125 MHz, CDCl3
N-(4-((1-hydroxyhexan-3-yl)thio)phenyl)acetamide
125 MHz, CDCl3
4-[(1-hydroxyhexan-3-yl)thio]benzenesulfonamide
125 MHz, CDCl3
1-(3-((tert-butylthio)phenyl)ethanone
125 MHz, CDCl3

[Chemical structure image]
(4-benzylphenyl)((tert-butyl)sulfane
125 MHz, CDCl3

S121
2-(tert-butylthio)benzonitrile
125 MHz, CDCl3
3-(tert-butylthio)-5-chloropyridine
125 MHz, CDCl3
8-[(tert-butylthio)isoquinoline
125 MHz, CDCl3

δ: 152.61, 143.38, 138.67, 136.00, 132.14, 131.51
129.00, 128.51, 48.06, 31.49

ppm
\textbf{19F NMR Spectra of Synthesized Compounds}

2-fluoro-4-(propythio)pyridine
282 MHz, CDCl$_3$
(R)-methyl 2-[(tert-butoxycarbonyl)amino]-3-[(2-fluoropyridin-4-ylthio)propanoate
282 MHz, CDCl3