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Synthesis of Alkenyl Sulfides Through the Iron-Catalyzed Cross-Coupling Reaction of Vinyl Halides with Thiols

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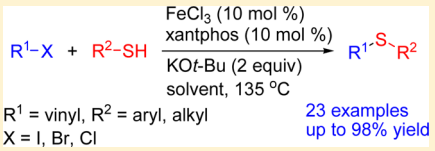
Supporting Information

ABSTRACT: We report here the iron-catalyzed cross-coupling reaction of alkyl vinyl halides with thiols. While many works are devoted to the coupling of thiols with alkyl vinyl iodides, interestingly, the known S-vinylation of vinyl bromides and chlorides is limited to 1-(2-bromovinyl)benzene and 1-(2-chlorovinyl)benzene. Investigation on the coupling reaction of challenging alkyl vinyl bromides and chlorides with thiols is rare. Since the coupling of 1-(2-bromovinyl)benzene and 1-(2-chlorovinyl)benzene with thiols can be performed in the absence of any catalyst, here we focus on the coupling of thiols with alkyl vinyl halides. This system is generally reactive for alkyl vinyl iodides and bromides to provide the products in good yields. 1-(Chloromethylidene)-4-*tert*-butyl-cyclohexane was also coupled with thiols, giving the targets in moderate yields.



INTRODUCTION

The transition-metal-catalyzed cross-coupling reaction of aryl or vinyl halides with thiols[1] is a growing area because aryl thioethers[2] and alkenyl sulfides[3] are important building blocks in organic synthesis and nature.[1−3] In 1980, Migita et al. reported the first palladium-catalyzed coupling reaction of thiols with aryl halides.[4] Since this pioneering work, many systems consisting of palladium with the appropriate ligands have been reported for the same purpose.[5] Other transition metals including copper,[6] nickel,[7a,b] cobalt,[8] gold,[9] indium,[10] and iron[11] are also known to couple aryl halides with thiols. Surprisingly, the coupling reaction between vinyl halides with thiols has been less studied.[12−19] 1-(2-iodovinyl)benzene, 1-(2-bromovinyl)benzene, and 1-(2-chlorovinyl)benzene are the most commonly used in the transition-metal-catalyzed S-vinylation with thiols to give the corresponding styryl thioethers.[12]

Other protocols to access alkenyl sulfides from alkyl vinyl halides using transition metals include the palladium-catalyzed coupling of thiols with alkyl vinyl iodides,[13] bromides,[14,12j,k] and chlorides;[15] copper-catalyzed coupling of thiols with alkyl vinyl iodides,[12c−g,16] bromides,[12e,16,17] and chlorides;[17] cobalt-catalyzed coupling of thiols with alkyl vinyl iodide;[8] nickel-catalyzed coupling of thiols with alkyl vinyl bromides;[12i] and ruthenium-catalyzed coupling of thiols with alkyl vinyl iodides.[18] Additionally there are numerous reports of the coupling of thiols with alkyl vinyl iodides.[8,12c−g,13a,b,16,18]

The reaction of alkyl vinyl bromides is more demanding than using alkyl vinyl iodides for S-vinylation; however, this transformation is known when using palladium,[12j,k,14] copper,[17,12e,16] and nickel[12i] catalysts. Moreover, although the intramolecular copper-catalyzed formation of thiols with alkyl chlorides is known,[17] the general procedure for preparing alkenyl sulfides from alkyl vinyl chlorides relies on palladium catalysis.[15a,b] Recently, we described that 1-(2-bromovinyl)-benzene and 1-(2-chlorovinyl)benzene can be coupled with thiols *in the absence of any catalyst*; an addition−elimination pathway was proposed.[12e] Although the alkyl vinyl bromides can be coupled with thiols in the presence of copper salt with 1,10-phenanthroline as a ligand, this system could not applied to the challenging alkyl vinyl chlorides.[12e] Iron is cheap and nontoxic, and the iron salts have been applied in many useful chemical transformations.[19,20]

Herein we report the iron-catalyzed coupling reaction of thiols with vinyl halides by using xantphos, **L1**, as a ligand (see Figure 1). To the best of our knowledge, this is the first iron-catalyzed coupling of alkyl vinyl chloride with thiols.

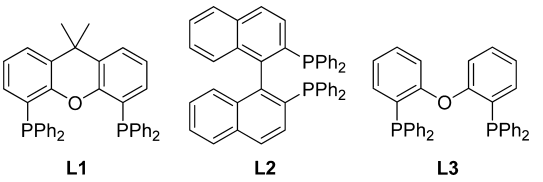


Figure 1. Structures of the ligands **L1**−**L3**.

RESULTS AND DISCUSSION

Initially, 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane, and 1-dodecanethiol were selected as the substrates to screen the optimized conditions. The results are summarized in Table 1; it is interesting to note that **L1**, **L2**, and **L3** have been used as ligands for metal-catalyzed coupling reaction of thiols with aryl halides, but we found that **L1** is superior to **L2** and **L3** for this reaction (Table 1, entries 1−3), providing the target in a 98% isolated yield. In order to exclude the possibility of metal impurity (especially copper),[21] we have carried out the reaction by using high purity of $FeCl_3$ (>99.99%) as the iron source.

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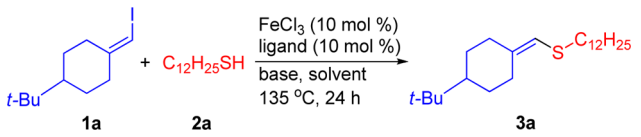
Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

entry	[Fe]	ligand	base	solvent	yield (%)
1	$FeCl_3$	**L1**	KO*t*-Bu	dioxane	98
2	$FeCl_3$	**L2**	KO*t*-Bu	dioxane	84
3	$FeCl_3$	**L3**	KO*t*-Bu	dioxane	43
4	$FeCl_3$	**L1**	KO*t*-Bu	dioxane	92[b]
5	$FeCl_3$	**L1**	KO*t*-Bu	DMSO	9
6	$FeCl_3$	**L1**	KO*t*-Bu	NMP	20
7	$FeCl_3$	**L1**	KO*t*-Bu	DME	57
8	$FeCl_3$	**L1**	KO*t*-Bu	DMF	70
9	$FeCl_3$	**L1**	KO*t*-Bu	toluene	83
10	$FeCl_3$	**L1**	NaO*t*-Bu	dioxane	71
11	$FeCl_3$	**L1**	Cs_2CO_3	dioxane	58
12	$FeCl_3$	**L1**	K_3PO_4	dioxane	40
13	$FeCl_3$	**L1**	K_2CO_3	dioxane	37
14	$FeCl_3$	**L1**	KO*t*-Bu	dioxane	74[c]
15	$FeCl_2$	**L1**	KO*t*-Bu	dioxane	51
16	$FeBr_2$	**L1**	KO*t*-Bu	dioxane	37
17	FeF_2	**L1**	KO*t*-Bu	dioxane	50
18	Cu_2O	**L1**	KO*t*-Bu	dioxane	22
19	$FeCl_3$		KO*t*-Bu	dioxane	68
20			KO*t*-Bu	dioxane	29
21	$FeCl_3$	**L1**	KO*t*-Bu	dioxane	39[d]

[a]Reaction conditions: iron source (0.05 mmol, 10 mol %), ligand (0.05 mmol, 10 mol %), 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (0.55 mmol), 1-dodecanethiol (0.5 mmol), base (1.0 mmol) in 0.5 mL of solvent. [b]99.99% $FeCl_3$. [c]120 °C. [d]1 equiv of TEMPO was added.

The product was obtained in 92% yield (Table 1, entry 4); this result indicates that the $FeCl_3$/**L1** is a very reactive system in this catalytic reaction. Solvents such as DMSO, NMP, DME, DMF, and toluene could not provide satisfactory results (Table 1, entries 5–9). We also studied the effect of bases (Table 1, entries 10–13), and the results showed that KO*t*-Bu is the best for this transformation. Lower temperature will decrease the yield of the product (Table 1, entry 14). When the reaction was carried out using other iron sources such as $FeCl_2$, $FeBr_2$, or FeF_2 to replace $FeCl_3$ (Table 1, entries 15–17), the lower yields were obtained. A further study using Cu_2O as a catalyst, however, gave the target in only 22% isolated yield. This result will rule out the participation of copper in this reaction (Table 1, entry 18). Lower yields of **3a** were observed when the reaction was carried out without ligand (Table 1, entry 19) or without catalyst (Table 1, entry 20). A 39% yield of the product was obtained when the reaction was carried out in the presence of TEMPO (Table 1, comparing entry 21 with entry 1). This result implies the radical mechanism in this reaction; however, the oxidative addition/reductive elimination steps is also possible in this transformation.[22]

In order to extend the scope of this catalytic system, we explored alkenyl iodides with many thiols. The results are summarized in Table 2, The alkyl and aryl thiols are all coupled with alkenyl iodides, giving the alkenyl sulfides in moderate to good yields. Compound **3m** was formed when the reaction was carried out by reacting iodomethylene cyclopentane with 4-chlorobenzenethiol; interestingly, the regioisomer **3m′** was detected in this reaction (Table 2, entry 12). Remarkably, the nitrogen-containing heterocyclo- and chloro-groups can be tolerated by the reaction conditions employed.

We then turned our attention to alkyl alkenyl bromides and chlorides. As shown in Table 3, both alkyl thiols and aryl thiols are suitable to couple with alkyl vinyl bromides, giving the alkenyl sulfides in 50–74% isolated yields (Table 3, entries 1–6). Furthermore, the challenging alkyl chlorides also react with alkyl and aryl thiols, giving the corresponding alkenyl sulfides in 32–71% combined yields. The alkyl thiol is less reactive in this reaction, providing the product in 32% yield. The regioisomers were also detected when (1) bromomethylene cyclopentane was reacted with 4-chlorobenzenethiol (Table 3, entry 6) and (2) 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane was reacted with aryl thiols including thiophenol (Table 3, entry 8 as the sole product), 4-methoxybenzenethiol (Table 3, entry 9), and chlorobenzenethiol (Table 3, entry 10). The regioisomers are formed in most cases when alkyl vinyl chloride is used; for instance, the initially formed exocyclic double bond in product **3m** could isomerize to the thermodynamically more stable endocyclic double bond in **3m′** (Table 3, entry 6). The moderate yields were obtained in the products **3d**, **5a**, **5b**, and **3a** (Table 3, entries 2–4 and 7), and the corresponding disulfides were formed in such cases. It seems that the *t*-Bu is an important group in alkyl vinyl chloride. Many alkyl vinyl chlorides have been studied; however, 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane, **4c**, is the only successful example for this transformation. The reason is not clear yet.

CONCLUSION

In conclusion, we have demonstrated that the catalytic system comprised of $FeCl_3$ and xantphos is a reactive catalyst toward the coupling reaction of alkyl vinyl halides with thiols. Both alkyl vinyl iodides and bromides were shown to be suitable as the coupling partners, giving the corresponding alkenyl sulfides in moderate to good yields. So far, 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane is the only successful alkyl vinyl chloride to work with thiols, giving the corresponding alkenyl sulfides. To the best of our knowledge, this is the first iron-catalyzed S-vinylation of alkyl vinyl halides.

EXPERIMENTAL SECTION

General Information. All chemicals were purchased from commercial suppliers and used without further purification. Toluene was dried over sodium; dioxane, DME, DMSO, and DMF were dried over CaH_2 and stored in the presence of activated molecular sieves. All reactions were carried out under an inert atmosphere. Flash chromatography was performed on silica gel 60 (230–400 mesh).

Analysis. NMR spectra were recorded using $CDCl_3$ as solvent. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent resonance. Coupling constants (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, q = quartet, m = multiplet, b = broad. Melting points (mp) were determined using an apparatus and are reported uncorrected. High-resolution mass spectra were performed on an electron ionization mass spectrometer.

General Procedure for the Synthesis of Vinyl Halides. Anhydrous $CrCl_2$ (5.92 g, 48.0 mmol) was suspended in THF (60 mL) under an argon atmosphere. A solution of ketone (12.0 mmol) and haloform (24.0 mmol) in THF (30 mL) was added dropwise to the suspension at 25 °C. After stirring at this temperature for 24 h, the reaction mixture was poured into water (25 mL) and extracted with ether. The combined extracts are dried over $MgSO_4$ and concentrated to give the crude material, which was then purified by column chromatography (SiO_2, hexane) to provide vinyl halide.

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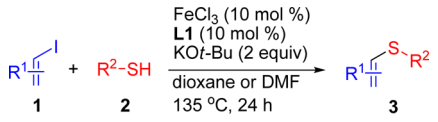
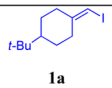
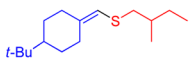
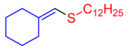
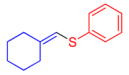
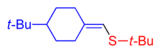
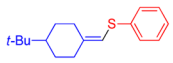
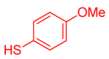
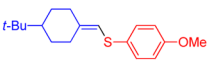
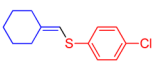
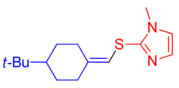
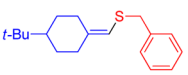
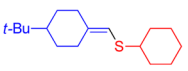
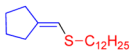
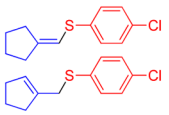
Table 2. Iron-Catalyzed Coupling Reaction of Vinyl Iodides with Thiols[a]



Entry	1	2	3		Yield (%)
1	 **1a**			**3b**	73[a]
2	 **1b**			**3c**	90[a]
3	**1b**			**3d**	65[a]
4	**1a**			**3e**	67[a]
5	**1a**			**3f**	70[b]
6	**1a**			**3g**	63[b]
7	**1b**			**3h**	90[b]
8	**1a**			**3i**	53[b]
9	**1a**			**3j**	37[b]
10	**1a**			**3k**	57[b]
11	 **1c**			**3l**	74[b]
12	**1c**			**3m** **3m'**	45[b] 50[b]

[a]Reaction conditions: $FeCl_3$ (0.05 mmol, 10 mol %), **L1** (0.05 mmol, 10 mol %), vinyl iodide (0.55 mmol), thiol (0.5 mmol), KO*t*-Bu (1.0 mmol) in dioxane (0.5 mL). [b]DMF as solvent.

1-(Iodomethylidene)-4-*tert*-butyl-cyclohexane 1a.[23] Following the general procedure for the synthesis of vinyl halide, using 4-*tert*-butylcyclohexanone (1.84 g, 12.0 mmol) and iodoform (9.48 g, 24.0 mmol), and then purification by column chromatography (SiO_2, hexane) provided **1a** as a colorless oil (2.33 g, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.86 (s, 9 H), 1.01−1.22 (m, 3 H), 1.77−1.90 (m, 3 H), 2.04−2.11(m, 1 H), 2.12−2.58(m, 1 H), 2.78−2.83 (m, 1 H), 5.76(s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.6, 27.7, 28.7, 32.3, 35.8, 37.0, 70.7, 151.3.

(Iodomethylene)cyclohexane 1b.[23] Following the general procedure for the synthesis of vinyl halide, using cyclohexanone (1.24 mL, 12.0 mmol) and iodoform (9.48 g, 24.0 mmol), and then purification by column chromatography (SiO_2, hexane) provided **1b** as a colorless oil (1.66 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ =1.51−1.59 (m, 6 H), 2.26−2.30 (m, 4 H), 5.77 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.1, 17.0, 18.0, 35.9, 37.3, 71.0, 151.3.

(Iodomethylene)cyclopentane 1c.[24] Following the general procedure for the synthesis of vinyl halide, using cyclopentanone (1.06 mL, 12.0 mmol) and iodoform (9.48 g, 24.0 mmol), and then purification by column chromatography (SiO_2, hexane) provided **1c** as a colorless oil (2.33 g, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.72−1.82(m, 4 H), 2.22−2.26(m, 2 H), 2.31−2.35(m, 2 H), 5.88(m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.7, 28.2, 35.1, 37.2, 68.1., 156.6.

1-(Iodomethylidene)-4-*tert*-butyl-cyclohexane 4c.[25] Following the general procedure for the synthesis of vinyl halide, using 4-*tert*-butylcyclohexanone (1.84 g, 12.0 mmol) and chloroform (1.92 mL, 24.0 mmol), and then purification by column chromatography (SiO_2, hexane) to give **4c** as a colorless oil (1.76 g, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.87 (s, 9 H), 1.02−1.08 (m, 2 H), 1.14−1.20 (m, 1 H), 1.71−1.72(m, 1 H), 1.75−1.99(m, 3 H), 2.29−2.35 (m, 1 H), 2.94−2.99 (m, 2 H), 5.73−5.74 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.4, 27.6, 28.4, 28.6, 32.4, 34.0, 48.0, 108.1, 142.0.

General Procedure for Table 1. A 4 mL vial, sealed and equipped with a magnetic stirrer bar, was charged with base (1.0 mmol), $FeCl_3$ (0.008 g, 0.05 mmol), and ligand (0.05 mmol) under a nitrogen atmosphere. The vial was covered with a rubber septum, and 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol), 1-dodecanethiol (**2a**, 0.120 mL, 0.5 mmol), and solvent (0.5

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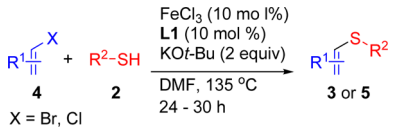
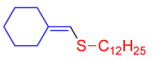
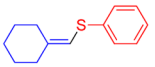
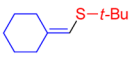
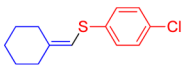
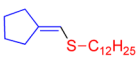
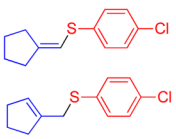
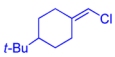
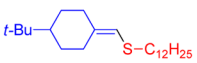
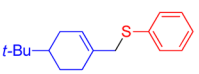
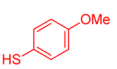
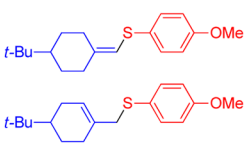
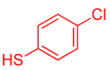
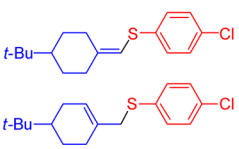
Table 3. Iron-Catalyzed Coupling Reaction of Alkyl Vinyl Bromides and Chlorides with Thiols[a]



Entry	4	2	Product		Yield (%)
1	 **4a**			**3c**	74
2	**4a**			**3d**	58
3	**4a**			**5a**	57
4	**4a**			**5b**	50
5	 **4b**			**3l**	66
6	**4b**			**3m** **3m'**	33 39
7	 **4c**			**3a**	32[b]
8	**4c**			**3f'**	62[b]
9	**4c**			**3g** **3g'**	16[b] 49[b]
10	**4c**			**3h** **3h'**	37[b] 34[b]

[a]Reaction conditions: $FeCl_3$ (0.05 mmol, 10 mol %), **L1** (0.05 mmol, 10 mol %), alkyl vinyl bromide or chloride (0.55 mmol), thiol (0.5 mmol), KO*t*-Bu (1.0 mmol) in 0.5 mL of DMF for 24 h. [b]30 h.

mL) were added by syringe under a nitrogen atmosphere. The septum was then replaced by a screw cap containing a Teflon-coated septum, and the reaction vessel was heated at 135 °C. After stirring at this temperature for 24 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material, which was then purified by column chromatography (SiO_2, hexane) to give **3a**.

Representative Example Of Table 1. ((4-*tert*-Butylcyclohexylidene)methyl)(dodecyl)sulfane 3a (Entry 1).[12e] Following the general procedure for Table 1, using KO*t*-Bu (0.112 g, 1.0 mmol) and **L1** (0.029 g, 0.05 mmol) in 1,4-dioxane (0.5 mL), and then purification by column chromatography (SiO_2, hexane) provided **3a** as a colorless oil (0.172 g, 98% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.81−0.89 (m, 12 H), 0.95−1.18 (m, 3 H), 1.25−1.38 (m, 18 H), 1.57−1.63 (m, 2 H), 1.70−1.78 (m, 1 H), 1.80−1.87 (m, 2 H), 1.99−2.06 (m, 1 H), 2.28−2.33 (m, 1 H), 2.62 (t, J = 7.6 Hz, 2 H), 2.76−2.82 (m, 1 H), 5.56 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.2, 22.7, 27.6, 27.8, 28.7, 28.9, 29.3, 29.4, 29.6, 29.6, 29.7, 29.7, 30.2, 30.2, 31.9, 32.5, 34.1, 36.3, 48.0, 114.6, 141.8.

General Procedure for Table 2. A 4 mL vial, sealed and equipped with a magnetic stirrer bar, was charged with KO*t*-Bu (112 mg, 1.0 mmol), $FeCl_3$ (0.008 g, 0.05 mmol), and **L1** (0.029 g, 0.05 mmol) under a nitrogen atmosphere. The vial was covered with a rubber septum, and vinyl iodide (**1**, 0.55 mmol), alkyl or aryl thiol (**2**, 0.5 mmol), and 1,4-dioxane (0.5 mL) were added by syringe under a nitrogen atmosphere. The septum was then replaced by a screw cap containing a Teflon-coated septum, and the reaction vessel was heated at 135 °C. After stirring at this temperature for 24 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material, which was then purified by column chromatography on silica gel to yield **3**.

((4-*tert*-Butylcyclohexylidene)methyl)(2-methylbutyl)-sulfane 3b (Table 2, Entry 1).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**,

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0.153 g, 0.55 mmol) and 2-methylbutane-1-thiol (0.0625 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3b** as a colorless oil (0.093 g, 73% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.83−0.91 (m, 12 H), 0.95−1.25 (m, 7 H), 1.46−1.61 (m, 2 H), 1.70−1.88 (m, 3 H), 1.98−2.05 (m, 1 H), 2.27−2.33 (m, 1 H), 2.43−2.49 (m, 1 H), 2.59−2.65 (m, 1 H), 2.79−2.83 (m, 1 H), 5.54 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 11.3, 18.7, 27.6, 27.7, 28.5, 28.9, 30.1, 32.4, 35.2, 36.3, 41.4, 48.0, 115.3, 141.3.

(Cyclohexylidenemethyl)(dodecyl)sulfane 3c (Table 2, Entry 2).[12e] Following the general procedure for Table 2, using iodomethylenecyclohexane (0.122 g, 0.55 mmol) and 1-dodecanethiol (0.120 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3c** as a colorless oil (0.133 g, 90% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.26−1.51 (m, 24 H), 1.53−1.62 (m, 2 H), 2.13−2.14 (m, 2 H), 2.24−2.26 (m, 2 H), 2.60 (t, J = 7.6 Hz, 2 H), 5.57 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.1, 22.7, 26.4, 27.0, 28.2, 28.6, 29.2, 29.3, 29.5, 29.61, 29.63, 30.1, 30.3, 31.9, 34.0, 36.4, 115.0, 141.9.

Phenylthiomethylenecyclohexane 3d (Table 2, Entry 2).[7b] Following the general procedure for Table 2, using iodomethylenecyclohexane (0.122 g, 0.55 mmol) and thiophenol (0.05 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3d** as a yellow oil (0.076 g, 58% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.58 (s, 6 H), 2.25−2.28 (m, 2 H), 2.36−2.39 (m, 2 H), 5.88 (s, 1 H), 7.13−7.17 (m, 1 H), 7.26−7.32 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.4, 27.3, 28.3, 30.3, 36.6, 111.8, 125.4, 127.6, 128.8, 137.6, 148.2.

***tert*-Butyl((4-*tert*-butylcyclohexylidene)methyl)sulfane 3e (Table 2, Entry 4).**[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and 2-methylpropane-2-thiol (0.0587 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3e** as a colorless oil (0.080 g, 67% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.85 (s, 9 H), 0.97−1.18 (m, 3 H), 1.33 (s, 9 H), 1.68−1.88 (m, 3 H), 2.05−2.13 (m, 1 H), 2.34−2.39 (m, 1 H), 2.93−2.99 (m, 1 H), 5.77 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.6, 28.0, 29.1, 30.2, 30.8, 32.4, 36.8, 43.6, 48.1, 110.7, 146.3.

((4-*tert*-Butylcyclohexylidene)methyl)(phenyl)sulfane 3f (Table 2, Entry 5).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and thiophenol (0.051 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3f** white solid (0.091 g, 70% yield): mp 54−55 °C (lit.[12e] 54−55 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.87 (s, 9 H), 1.02−1.24 (m, 3 H), 1.79−1.92 (m, 3 H), 2.12−2.18 (m, 1 H), 2.42−2.47 (m, 1 H), 2.97−3.02 (m, 1 H), 5.87 (s, 1 H), 7.12−7.17 (m, 1 H), 7.25−7.32 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.6, 28.0, 29.0, 30.2, 32.4, 36.5, 48.0, 111.5, 125.4, 127.7, 128.8, 137.6, 147.9.

((4-*tert*-Butylcyclohexylidene)methyl)(4-methoxyphenyl)-sulfane 3g (Table 2, Entry 6).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and 4-methoxybenzenethiol (0.062 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane/EA = 15:1) provided **3g** as a white solid (0.091 g, 63% yield): mp 39−40 °C (lit.[12e] 39−40 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.86 (s, 9 H), 1.01−1.26 (m, 3 H), 1.76−1.91 (m, 3 H), 2.05−2.12 (m, 1 H), 2.34−2.39 (m, 1 H), 2.93−2.98 (m, 1 H), 3.75 (s, 3 H), 5.78 (s, 1 H), 6.82 (d, J = 9.2 Hz, 2 H), 7.26 (d, J = 9.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.5, 27.9, 28.9, 30.1, 32.4, 36.3, 48.0, 55.2, 113.9, 114.5, 127.7, 130.7, 144.8, 158.3.

((4-*tert*-Butylcyclohexylidene)methyl)(4-chlorophenyl)-sulfane 3h (Table 2, Entry 7).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3h** as a colorless oil (0.132 g, 90% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.86 (s, 9 H), 1.01−1.21 (m, 3 H), 1.81−1.92 (m, 3 H), 2.10−2.17 (m, 1 H), 2.41−2.47 (m, 1 H), 2.95−2.99 (m, 1 H), 5.81 (s, 1 H), 7.18−7.24 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.6, 28.1, 29.0, 30.2, 32.4, 36.5, 48.0, 110.9, 128.75, 128.84, 131.2, 136.3, 149.1.

2-((4-*tert*-Butylcyclohexylidene)methylthio)-1-methyl-1*H*-imidazole 3i (Table 2, Entry 8). Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and 1-methyl-1H-imidazole-2-thiol (0.057 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane/EA = 9:1) provided **3i** as a yellow oil (0.070 g, 53% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.78 (s, 9 H), 0.97−1.12 (m, 3 H), 1.75−1.85 (m, 3 H), 1.99−2.00 (m, 1 H), 2.31−2.35 (m, 1 H), 2.80−2.83 (m, 1 H), 3.55 (s, 3 H), 5.86 (s, 1H), 6.868−6.871(d, J = 1.2 Hz, 1H), 6.98−6.99(d, J = 1.2 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.4, 27.6, 28.5, 30.2, 32.3, 33.2, 35.9, 47.7, 109.7, 122.3, 129.0, 140.8, 144.9; HRMS (EI) (m/z) calcd. for $C_{15}H_{24}N_2S$ 264.1660, found 264.1662. Elemental analysis calcd for $C_{15}H_{24}N_2S$: C 68.13; H 9.15; N 10.59; S 12.13. Found: C 68.13; H 9.15; N 10.59; S 12.13.

Benzyl((4-*tert*-butylcyclohexylidene)methyl)sulfane 3j (Table 2, Entry 9).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and phenylmethanethiol (0.059 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3j** as a pink oil (0.051 g, 37% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.80−1.27 (m, 12 H), 1.62−1.81 (m, 3 H), 1.98−2.03 (m, 1 H), 2.23−2.27 (m, 1 H), 2.74−2.76 (m, 1 H), 3.78 (s, 2 H) 5.57 (s, 1 H), 7.20−7.30 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.5, 27.7, 28.8, 30.2, 32.4, 36.3, 38.4, 47.9, 113.0, 126.8, 128.3, 128.8, 138.5, 144.4.

((4-*tert*-Butylcyclohexylidene)methyl)(cyclohexyl)sulfane 3k (Table 2, Entry 10).[12e] Following the general procedure for Table 2, using 1-(iodomethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.153 g, 0.55 mmol) and cyclohexanethiol (0.062 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3k** as a white solid (0.076 g, 57% yield): mp 44−45 °C (lit.[12e] 44−45 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.83−0.90 (s, 9 H), 0.98−1.18 (m, 3 H), 1.23−1.41 (m, 5 H), 1.60−1.87 (m, 6 H), 1.97−2.07 (m, 3 H), 2.30−2.34 (m, 1 H), 2.68−2.74 (m, 1 H), 2.81−2.85 (m, 1 H), 5.64 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 25.7, 26.1, 27.6, 27.8, 28.9, 30.2, 32.4, 33.7, 36.4, 45.6, 48.0, 112.7, 142.7.

(Cyclopentylidenemethyl)(dodecyl)sulfane 3l (Table 2, Entry 11). Following the general procedure for Table 2, using (iodomethylene)cyclopentane (0.114 g, 0.55 mmol) and 1-dodecanethiol (0.12 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3k** as a colorless oil (0.104 g, 74% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.25−1.39 (m, 24 H), 2.19−2.21 (m, 2 H), 2.23−2.31 (m, 2 H), 2.61−2.64 (m, 2 H), 5.72 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.1, 22.7, 26.3, 26.8, 28.7, 29.2, 29.3, 29.5, 29.58, 29.61, 29.64, 30.4, 30.7, 31.9, 34.05, 34.07, 113.3, 144.5; HRMS (EI) (m/z) calcd. for $C_{12}H_{13}ClS$ 282.2381, found 282.2377.

(Cyclopentylidenemethyl)(dodecyl)sulfane 3m (Table 2, Entry 12). Following the general procedure for Table 2, using (iodomethylene)cyclopentane (0.114 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3m** as a colorless oil (0.050 g, 45% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.56−1.76 (m, 4 H), 2.35−2.36 (m, 2 H), 2.41−2.42 (m, 2 H), 5.97 (s, 1 H), 7.19−7.26 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.1, 26.7, 31.1, 34.3, 109.7, 128.8, 128.9, 131.3, 136.1, 152.3; HRMS (EI) (m/z) calcd. for $C_{12}H_{13}ClS$ 224.0427, found 224.0424.

(4-Chlorophenyl)(cyclopentenylmethyl)sulfane 3m′ (Table 2, Entry 12). Following the general procedure for Table 2, using (iodomethylene)cyclopentane (0.114 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3m′** as a colorless oil (0.056 g, 50% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.86−1.91 (m, 2 H), 2.27−2.30 (m, 2 H), 2.34−2.38 (m, 2 H), 3.59(s, 2 H), 5.97 (t, J = 2.0 Hz, 1 H), 7.23−7.25 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 23.5, 32.5, 34.0, 35.3, 128.7, 128.8, 130.9, 131.9, 135.3, 139.2; HRMS (EI) (m/z) calcd. for $C_{12}H_{13}ClS$ 224.0427, found 224.0420.

General Procedure for Table 3, Entries 1−6 (Method A). A 4 mL vial, sealed and equipped with a magnetic stirrer bar, was charged

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with KO*t*-Bu (0.112 g, 1.0 mmol), $FeCl_3$ (0.008 g, 0.05 mmol), and **L1** (0.029 g, 0.05 mmol) under a nitrogen atmosphere. The vial was covered with a rubber septum, and alkenyl bromide (0.55 mmol), alkyl or aryl thiol (**2**, 0.5 mmol), and DMF (0.5 mL) were added by syringe under a nitrogen atmosphere. The septum was then replaced by a screw cap containing a Teflon-coated septum, and the reaction vessel was heated at 135 °C. After stirring at this temperature for 24 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material, which was then purified by column chromatography on silica gel to yield product **5**.

(Cyclohexylidenemethyl)(dodecyl)sulfane 3c (Table 3, Entry 1).[14] Following the method A, using bromomethylenecyclohexane (0.073 mL, 0.55 mmol) and 1-dodecanethiol (0.120 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3c** as a colorless oil (0.109 g, 74% yield).

Phenylthiomethylenecyclohexane 3d (Table 3, Entry 2).[7b] Following the method A, using bromomethylenecyclohexane (0.073 mL, 0.55 mmol) and thiophenol (0.05 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3d** as a yellow oil (59 mg, 58% yield).

***tert*-Butyl(cyclohexylidenemethyl)sulfane 5a (Table 3, Entry 3).**[14] Following the method A, using bromomethylenecyclohexane (0.073 mL, 0.55 mmol) and 2-methylpropane-2-thiol (0.059 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **5a** as a colorless oil (0.052 g, 57% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.32 (s, 9 H), 1.48−1.54 (m, 6 H), 2.19−2.33 (m, 4 H), 5.78 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.5, 27.3, 28.4, 30.3, 30.8, 37.0, 43.6, 110.9, 146.7.

4-Chlorophenylthiomethylenecyclohexane 5b (Table 3, Entry 4).[14] Following the method A, using bromomethylenecyclohexane (0.073 mL, 0.55 mmol) and 4-chlorothiophenol (0.087 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **5b** as a yellow oil (0.060 g, 50% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.59 (br s, 6 H), 2.25−2.28 (m, 2 H), 2.36−2.39 (m, 2 H), 5.82 (s, 1 H), 7.19−7.25 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.3, 27.3, 28.3, 30.4, 36.6, 111.2, 128.7, 128.8, 131.2, 136.3, 149.4.

(Cyclopentylidenemethyl)(dodecyl)sulfane 3l (Table 3, Entry 5). Following the method A, using (bromomethylene)cyclopentane (0.044 g, 0.55 mmol) and 1-dodecanethiol (0.120 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3l** as a colorless oil (0.093 g, 66% yield).

(Cyclopentylidenemethyl)(dodecyl)sulfane 3m (Table 3, Entry 6). Following the method A, using (bromomethylene)-cyclopentane (0.044 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3m** as a colorless oil (0.037 g, 33% yield).

(4-Chlorophenyl)(cyclopentenylmethyl)sulfane 3m′ (Table 3, Entry 6). Following the method A, using (iodomethylene)-cyclopentane (0.114 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3m′** as a colorless oil (0.044 g, 39% yield).

General Procedure for Table 3, Entries 7−10 (Method B). A 4 mL vial, sealed and equipped with a magnetic stirrer bar, was charged with KO*t*-Bu (0.112 g, 1.0 mmol), $FeCl_3$ (0.008 g, 0.05 mmol), and **L1** (0.029 g, 0.05 mmol) under a nitrogen atmosphere. The vial was covered with a rubber septum, and alkenyl chloride (0.55 mmol), alkyl or aryl thiol (**2**, 0.5 mmol), and DMF (0.5 mL) were added by syringe under a nitrogen atmosphere. The septum was then replaced by a screw cap containing a Teflon-coated septum, and the reaction vessel was heated at 135 °C. After stirring at this temperature for 30 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was filtered through a pad of silica gel and then washed with ethyl acetate (20 mL) and concentrated to give the crude material, which was then purified by column chromatography on silica gel to yield product **5**.

((4-*tert*-Butylcyclohexylidene)methyl)(dodecyl)sulfane 3a (Table 3, Entry 7).[14] Following the method B, using 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane (0.103 g, 0.55 mmol) and 1-dodecanethiol (0.120 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3a** as a colorless oil (0.056 g, 32% yield).

((4-*tert*-Butylcyclohex-1-enyl)methyl)(phenyl)sulfane 3f′ (Table 3, Entry 8).[7c] Following the method B, using 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane (0.103 g, 0.55 mmol) and thiophenol (0.05 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **5d** as a colorless oil (0.081 g, 62% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.87 (s, 9 H), 1.11−1.28 (m, 2 H), 1.71−1.88 (m, 2 H), 1.98−2.09 (m, 1 H), 2.13−2.26 (m, 2 H), 3.50 (s, 2 H), 5.59 (s, 1 H), 7.27−7.35(m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 24.0, 26.9, 27.2, 28.7, 32.1, 41.7, 43.8, 125.8, 125.9, 128.6, 129.8, 132.8, 137.0.

((4-*tert*-Butylcyclohexylidene)methyl)(4-methoxyphenyl)-sulfane 3g and 3g′ (Table 3, Entry 9).[14] Following the method B, using 1-(chloromethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.103 g, 0.55 mmol) and 4-methoxybenzenethiol (0.062 mL, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane/EA = 15:1) provided **3g** and **3g′** isomer as a white solid (0.093 g, 64% combined yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.86 (s, 18 H, **3g** and **3g′** isomer), 1.01−1.25 (m, 6 H, **3g** and **3g′** isomer), 1.58−2.44 (m, 10 H, **3g** and **3g′** isomer), 2.92−2.98 (m, 1 H, **3g**), 3.31−3.39 (m, 2 H, **3g′**), 3.80 (s, 6 H, **3g** and **3g′** isomer), 5.34 (m, 1 H, **3g′**), 5.78 (s, 1 H, **3g**), 6.80−6.87 (m, 4 H, **3g** and **3g′** isomer), 7.26−7.33 (m, 4 H, **3g** and **3g′** isomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 24.1, 26.7, 27.1, 27.6, 27.9, 28.5, 28.9, 30.1, 32.1, 32.5, 36.3, 43.8, 43.9, 48.0, 113.8, 114.1, 114.5, 125.7, 130.8, 133.1, 134.0, 145.0, 158.9; HRMS (EI) (*m*/*z*) calcd. for $C_{18}H_{26}OS$ 290.1704, found 290.1707. Elemental analysis calcd for $C_{18}H_{26}OS$: C 74.43; H 9.02; O 5.51; S 11.04. Found: C 74.33; H 8.89; O 5.39; S 10.74.

((4-*tert*-Butylcyclohexylidene)methyl)(4-chlorophenyl)-sulfane 3h (Table 3, Entry 10).[14] Following the method B, using 1-(cholormethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.103 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3h** as a colorless oil (0.054 g, 37% yield).

((4-*tert*-Butylcyclohex-1-enyl)methyl)(4-chlorophenyl)-sulfane 3h′ (Table 3, Entry 10). Following the method B, using 1-(cholormethylidene)-4-*tert*-butyl-cyclohexane (**1a**, 0.103 g, 0.55 mmol) and 4-chlorobenzenethiol (0.072 g, 0.5 mmol), and then purification by column chromatography (SiO_2, hexane) provided **3h′** as a colorless oil (0.049 g, 34% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ =0.85 (s, 9 H), 1.12−1.24 (m, 2 H), 1.57−1.86 (m, 2 H), 1.97−2.23 (m, 3 H), 3.46 (s, 2 H), 5.53 (s, 1 H), 7.13−7.33 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 24.0, 26.9, 27.2, 28.6, 32.1, 42.0, 43.8, 126.2, 128.7, 131.4, 132.0, 132.6, 135.4; HRMS (EI) (*m*/*z*) calcd. for $C_{17}H_{23}ClS$ 294.1209, found 294.1203. Elemental analysis calcd for $C_{17}H_{23}ClS$: C 69.24; H 7.86; S 10.87. Found: C 68.90; H 8.00; S 10.58.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra for **1a**−**1c**, **4c**, and products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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