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Metal-Free Difunctionalization of Alkynes with 2-Chlorodithiane for Synthesis of β-Ketodithianes

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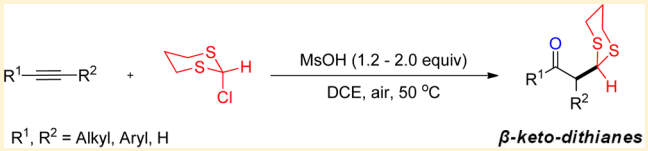
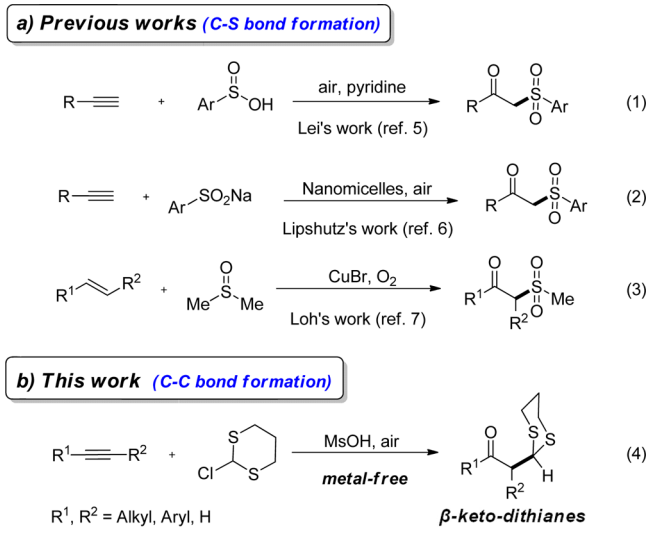
Supporting Information

ABSTRACT: Dithianes are versatile umpolung intermediates in organic synthesis but have rarely been employed in radical cross-coupling reactions. Here we describe the oxidative coupling method for alkyne difunctionalization under metal-catalyst-free conditions. The efficient protocol directly affords a variety of β-ketodithianes in good to excellent yields with high regioselectivities. It provides a general pathway for accessing valuable dithianes with controlled formation of a new C−C bond and a C−O bond via a radical coupling pathway.



Radical addition of unactivated alkynes is believed to be the most convenient procedure to generate reactive vinyl radicals, which could be trapped via subsequent transformation and thus appear in many diverse applications in organic chemistry.[1] Among various strategies for alkyne difunctionalization, radical oxidative coupling (ROC)[2] reactions have played important roles in synthetic organic chemistry for bond formations, and those processes can offer many complementary methods to efficiently increase molecular complexity (Scheme 1). Recently, several remarkable advances of ROC catalyzed by nonprecious metals (Fe, Cu, Ni) and metal-catalyst-free mild conditions for bond construction in the presence of a green oxidant such as oxygen have been developed.[3−7] In particular, Lei and co-workers elegantly reported a pioneering metal-catalyst-free aerobic oxysulfonylation of terminal alkynes (eq 1).[5] More recently, Lipshutz[6] and Loh[7] independently developed this ROC of aryl alkynes using a hydrocarbon nanomicelle (eq 2) and DMSO (eq 3) in a number of C−S bond-forming transformations. Despite the remarkable extensions and developments of alkyne difunctionalization, the discovery of new atom-economical protocols toward advanced intermediates is still highly worthwhile.

Scheme 1. Novel Strategies for Alkyne Difunctionalization



Dithiane compounds serve as valuable synthetic intermediates (umpolung synthons) in the field of natural product synthesis and can participate in a range of useful transformations.[8] However, dithiane anion chemistry applied in various synthetic sequences requires either lithiation or the use of anhydrous and anaerobic technology.[8a,b] Access to β-ketodithianes by radical cross-coupling would have advantages over traditional dithiane anion strategies, and the ability to form dithiane derivatives directly would improve the efficiency of synthetic routes. In this regard, our group has a long-standing interest in the novel and versatile protocols to construct dithiane derivatives.[9] Recently, our group introduced the first protocol for the direct cross-coupling of alkene involving a novel dithianyl radical coupling mechanism.[9a,c] On this basis, we postulated that an oxidative dithiane radical strategy[10] could serve as a platform for the difunctionalization of unactivated alkynes (Scheme 1, eq 4). Mechanistically, we expected that radical addition of alkyne with the dithianyl radical should give the dithiane vinyl radical intermediate, where subsequent interaction with molecular oxygen would be highly favored and ultimately lead to β-ketodithiane, which is known to be a key intermediate for useful transformations.[11] To the best of our knowledge, the alkyne difunctionalization with a dithianyl radical for tandem C−C and C−O bond formations has not yet been reported. In this paper, we report our recent progress on the first metal-free oxidative coupling protocol for alkyne

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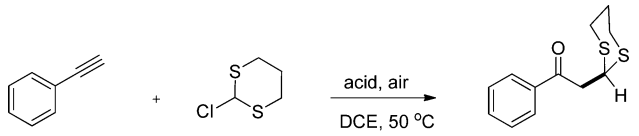
difunctionalization to give β-ketodithianes, which affords a marked improvement over functionalization with anion-initiated dithiane chemistry developed previously.[8,12]

We began our study via a model reaction to investigate the coupling reaction of phenylacetylene **1a** with easily accessible 2-chlorodithiane **2** (Table 1). To identify conditions for the coupling reaction, we hypothesized that the factors that influence the reactivity of the reaction would exhibit a dependence on various parameters, such as metal sources, acids, solvents, and reaction temperature. Initially, the coupling of **1a** with **2** employing Lewis acid sources such as $FeCl_3$, $FeCl_2$, $FeCl_3{\cdot}6H_2O$, and $BF_3{\cdot}Et_2O$ gave **3a**, albeit in low yields. However, these results indicated that the process involving the C−C coupling and the subsequent transformation was indeed possible (Table 1, entries 1−6). A number of commercially available protic acids was examined. To our delight, further optimization showed that the combination of a stoichiometric amount of methanesulfonic acid (MsOH) at 50 °C under an atmosphere of air[5−7,13] served as the best condition, providing a good yield of β-ketodithiane product **3a** (Table 1, entry 7). It is important to note that when the reactions were employed by Lei and Loh's reaction systems,[5,7] the reactions were unsuccessful and trace amounts of product **3a** were obtained.

Table 1. Reaction Conditions for the Coupling of Phenylacetylene[a]



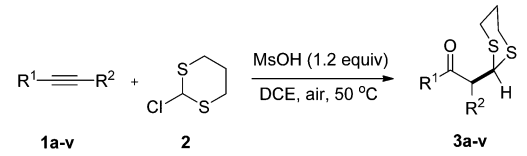
1a **2** **3a**

entry	acid (equiv)	time (h)	**3a** (%)[b]
1		48	trace
2	$FeCl_3$ (0.15)	48	trace
3	$FeCl_3$ (1.2)	24	12
4	$BF_3{\cdot}Et_2O$ (0.15)	24	12
5[b]	$FeCl_3{\cdot}6H_2O$ (0.15)	24	18
6[b]	$FeCl_2{\cdot}4H_2O$ (0.15)	24	32
7	**MsOH (1.2)**	**6**	**79**
8	TsOH (1.2)	12	65
9	H_2SO_4 (1.2)	24	trace
10	HCl (1.2)[c]	24	trace
11	MsOH (0.15)	24	trace

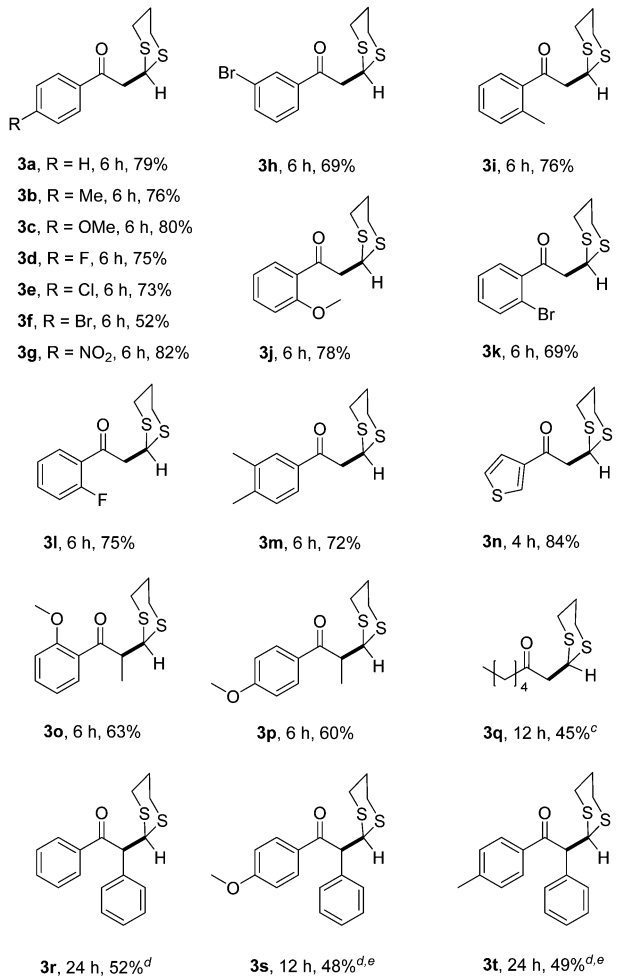
[a]Reaction conditions: phenylacetylene (**1a**, 0.225 mmol), 2-chloro-1,3-dithiane (**2**, 0.25 mmol), acid (*x* equiv), DCE (2 mL), 50 °C, air, 6−48 h. [b]Isolated yields. [c]12 mol/L.

With optimized reaction conditions established (Table 1, entry 7), we next turned our attention to a variety of aryl and aliphatic alkynes that can participate in this novel process. As shown in Table 2, the standard reaction system using 1.2 equiv of MsOH in the presence of air was highly effective with terminal aryl alkynes, affording the desired β-ketodithiane products **3a**−**3n** in moderate to good yields and excellent chemoselectivities. Substrates with ortho (**1j**−**1l**), meta (**1h**), and para (**1b**−**1g**) substituents provided good yields of coupled products regardless of the electronic nature of the substituents. Furthermore, the internal alkynes ranging from aryl to aliphatic substituents (**1o**, **1p**, **1r**−**1t**) could also be effectively coupled in 12 h, although the steric crowding of alkynes lowered the yield slightly. For example, using 2 equiv of MsOH in DCE for 12−24 h at 50 °C, the hindered 1,2-diarylalkynes **1r**−**1t** afforded the desired products **3r**−**3t** and high regioselectivities (>95:5) for **3s** and **3t**, as determined by ^1H NMR analysis. Importantly, 1-heptyne also proved to be a suitable substrate and gave the corresponding dithiane **3q** in satisfactory yield based on the recovered starting material.

Table 2. Substrate Scope of Alkyne Difunctionalization[a,b]



1a-v **2** **3a-v**



[a]Reaction conditions: alkynes (**1a**−**1t**, 0.225 mmol), 2-chloro-1,3-dithiane (**2**, 0.25 mmol), MsOH (1.2 equiv), DCE (2 mL), 50 °C, air, 4−48 h. [b]Isolated yield after column chromatography. [c]17% **1q** recovery. [d]2 equiv of MsOH was used. [e]Regioselectivities by ^1H NMR (>95:5).

In order to aid our interpretation of the mechanism, radical-trapping experiments were conducted. The addition of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO)[14] and butylated hydroxytoluene (BHT)[15] as radical scavenger under the standard reaction conditions completely quenched the coupling reaction and provided trace cross-coupled product, demonstrating that a radical process might take place (Scheme 2). Meanwhile, we also performed oxygen-labeling experiments to understand the origin of the new C−O bond in the target molecule. In the presence of $H_2{}^{18}O$/air, product **3a** was obtained in 72% yield

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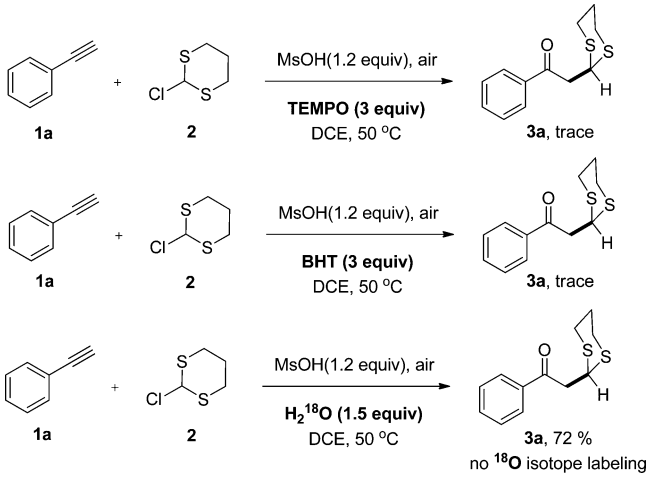
Scheme 2. Radical-Trapping Experiments and $H_2{}^{18}O$ Isotope Labeling Experiment



and no isotope-labeled product was formed. The ^{18}O-labeling result suggested that water was not involved in the reaction process,[16] and the oxygen molecule was the possible source of the carbonyl oxygen atom of the β-ketodithiane.[5,6,13]

On the basis of previous works in our group,[9] we anticipated that the dithianyl radical was generated via the homolysis of 2-chlorodithiane under air and heating. The generated dithianyl radical would be highly nucleophilic and thereby readily facilitate conjugate addition with alkyne to forge a new C−C bond with concomitant formation of the vinyl radical intermediate (**II**). Subsequently, the generated vinyl radical species are further oxidized by air to give a peroxyl radical (**III**), which may stabilize to a hydroperoxide intermediate (**IV**) by hydrogen abstraction from DCE.[17] The hydroperoxide could undergo heterolysis to generate enol intermediate (**V**), thus completing the ROC reaction to form the desired β-ketodithiane. It was worthy to note that one possible difficulty may be the issue of C−O versus C−Cl bond formation; however, the appropriate choice of acid can block the C−Cl bond formation toward the desired β-keto product (Scheme 3).

In summary, we have described the direct alkyne difunctionalization for the efficient construction of β-ketodithianes. We have demonstrated that the versatile method tolerates broad substrate scope and good functional group compatibility. More importantly, this novel process provides an alternative to generate highly substituted dithiane derivatives without the requirement of organolithium reagents or metal catalysts.

EXPERIMENTAL SECTION

General Information. Flash chromatography columns were generally performed on silica gel (200−300 mesh) in petroleum (bp 60−90 °C), and reactions were monitored by thin layer chromatography (TLC) using silica gel GF254 plates with UV light to visualize the course of the reaction. All new compounds were characterized by ^1H NMR, ^{13}C NMR, IR, MS, and HRMS. ^1H and ^{13}C NMR spectra were run with tetramethylsilane as an internal standard at 300 and 75 MHz, respectively. All chemical shifts (δ) are reported in parts per million and coupling constants (J) in hertz. IR spectra were obtained with neat thin films on a sodium chloride disk and were recorded on an Fourier transform infrared spectrometer.

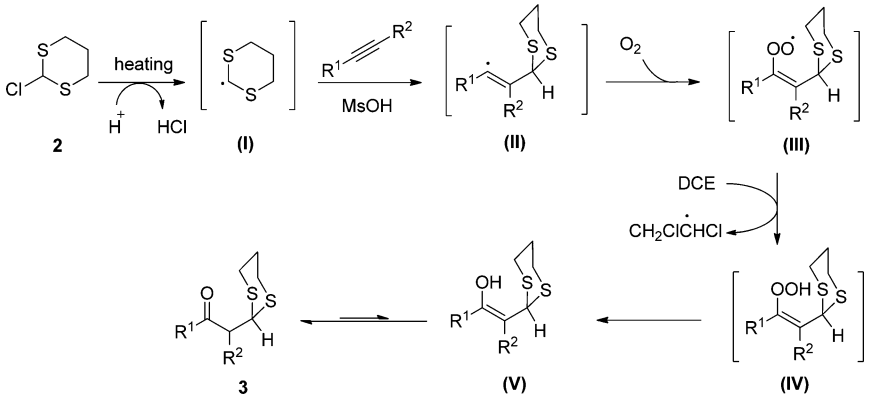
Materials. Analytical grade solvents and commercially available reagents were used as received. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Alkynes **1a−e**, **1n**, and **1q−1t** were purchased and used as received. 2-Chloro-1,3-dithiane **2** and alkynes **1f−1m**, **1o**, and **1p** were prepared according to the reported procedure.[18,19]

General Procedure for the Alkyne Difunctionalization. To a flame-dried 10 mL flask were added 2-chloro-1,3-dithiane **2** (34 mg, 0.25 mmol), **1a−1t** (0.225 mmol), and methanesulfonic acid (1.2−2.0 equiv) in 2 mL of DCE. The reaction mixture was stirred at 50 °C for 4−24 h and then cooled to rt. The reaction solution was diluted with ethyl acetate (5 mL) and saturated aqueous $NaHCO_3$ (5 mL). The organic layer was separated, and the aqueous phase was re-extracted with ethyl acetate (3 × 3 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure and purified by column chromatography on silica gel with petroleum/ethyl acetate (EA/PE = 1:50) to yield products **3a−3t**.

Radical-Trapping Experiments. To a flame-dried 10 mL flask were added 2-chloro-1,3-dithiane **2** (34 mg, 0.25 mmol), **1a** (25 mg, 0.25 mmol), methanesulfonic acid (25 mg, 0.25 mmol), and TEMPO (150 mg, 0.75 mmol) or BHT (165 mg, 0.75 mmol) in 2 mL of DCE. The reaction mixture was stirred at 50 °C for 24 h. The reaction mixture was diluted with ethyl acetate (10 mL) and H_2O (5 mL). The organic layer was separated, and the aqueous phase was re-extracted with ethyl acetate (3 × 3 mL). The combined organic extracts were washed with H_2O (10 mL) and dried over anhydrous Na_2SO_4.

$H_2{}^{18}O$-Labeling Experiment. To a flame-dried 10 mL flask were added methanesulfonic acid (25 mg, 0.25 mmol) and $H_2{}^{18}O$ (7 mg, 0.38 mmol) in 2 mL of DCE and stirred for a while (methanesulfonic acid and DCE in this experiment had been dried), then 2-chloro-1,3-dithiane **2** (34 mg, 0.25 mmol) and **1a** (25 mg, 0.25 mmol) were added. The reaction mixture was stirred at 50 °C for 6 h. The reaction solution was diluted with ethyl acetate (5 mL) and saturated aqueous $NaHCO_3$ (5 mL). The organic layer was separated, and the aqueous

Scheme 3. Proposed Mechanism



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phase was re-extracted with ethyl acetate (3 × 3 mL). The combined organic extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. The solvent was concentrated under reduced pressure and purified by column chromatography on silica gel with petroleum/ethyl acetate (EA/PE = 1:50) to yield the product **3a**.

*2-(1,3-Dithian-2-yl)-1-phenylethanone (**3a**):* White solid; R_f = 0.47 (EA/PE = 1:10); mp (°C) 58−59; isolated yield 79% (42 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04−7.87 (m, 2H), 7.62−7.55 (m, 1H), 7.55−7.40 (m, 2H), 4.70 (t, J = 6.7 Hz, 1H), 3.36 (d, J = 6.8 Hz, 2H), 3.03−2.94 (m, 2H), 2.94−2.82 (m, 2H), 2.17−2.08 (m, 1H), 1.97−1.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.0, 136.1, 133.1, 128.3, 127.8, 43.5, 41.1, 29.8, 24.9; MS (EI, 70 eV) m/z = 238 (M+). This known compound had been characterized previously.[20]

*2-(1,3-Dithian-2-yl)-1-(p-tolyl)ethanone (**3b**):* White solid; R_f = 0.49 (EA/PE = 1:10); mp (°C) 105−106; isolated yield 76% (43 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 9 Hz, 2H), 7.27 (d, J = 9 Hz, 2H), 4.69 (t, J = 6.9 Hz, 1H), 3.33 (d, J = 6.9 Hz, 2H), 2.97 (t, J = 14.2, 2H), 2.85 (t, J = 14.2 Hz, 2H), 2.41 (s, 3H), 2.21−2.05 (m, 1H), 1.94−1.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.4, 143.7, 133.5, 128.8, 128.4, 127.8, 43.2, 41.2, 29.7, 24.8, 21.2; IR (neat, cm^{-1}) 2920 (w), 2890 (w), 1688 (s), 1606 (m), 1412 (m), 1344 (m), 1227 (m), 1180 (m), 1043 (m), 978 (m), 818 (m), 724 (w), 679 (w), 589 (m), 559 (m); MS (EI, 70 eV) m/z = 252 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{13}H_{16}OS_2Na$) calcd 275.0540, found 275.0542.

*2-(1,3-Dithian-2-yl)-1-(4-methoxyphenyl)ethanone (**3c**):* Yellow solid; R_f = 0.42 (EA/PE = 1:10); mp (°C) 75−76; isolated yield 80% (48 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 4.67 (t, J = 6.9 Hz, 1H), 3.83 (s, 3H), 3.29 (d, J = 6.9 Hz, 2H), 2.94 (t, J = 12.5 Hz, 2H), 2.88−2.74 (m, 2H), 2.15−2.03 (m, 1H), 1.91−1.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.5, 163.4, 130.1, 129.2, 113.5, 55.2, 43.1, 41.5, 29.9, 25.0; MS (EI, 70 eV) m/z = 268 (M+). This known compound had been characterized previously.[21]

*2-(1,3-Dithian-2-yl)-1-(4-fluorophenyl)ethanone (**3d**):* White solid; R_f = 0.45 (EA/PE = 1:10); mp (°C) 88−89; isolated yield 75% (43 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16−7.88 (m, 2H), 7.27−6.97 (m, 2H), 4.68 (t, J = 6.8 Hz, 1H), 3.33 (d, J = 6.9 Hz, 2H), 3.03−2.92 (m, 2H), 2.90−2.82 (m, 2H), 2.18−2.08 (m, 1H), 1.95−1.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 167.4, 164.0, 130.8, 130.6, 115.8, 115.5, 43.6, 41.4, 30.1, 25.1; IR (neat, cm^{-1}) 3072 (w), 2977 (w), 2903 (w), 1688 (m), 1599 (m), 1506 (m), 1402 (m), 1352 (m), 1220 (m), 1093 (m), 1050 (m), 980 (m), 841 (m), 584 (m), 562 (m); MS (EI, 70 eV) m/z = 256 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}FOS_2Na$) calcd 279.0290, found 279.0293.

*1-(4-Chlorophenyl)-2-(1,3-dithian-2-yl)ethanone (**3e**):* White solid; R_f = 0.45 (EA/PE = 1:10); mp (°C) 97−98; isolated yield 73% (45 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.9 Hz, 2H), 7.43 (d, J = 8.9 Hz, 2H), 4.65 (t, J = 6.9 Hz, 1H), 3.33 (d, J = 6.9 Hz, 2H), 2.95 (dt, J = 11.2, 7.0 Hz, 2H), 2.89−2.77 (m, 2H), 2.18−2.04 (m, 1H), 1.95−1.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.4, 140.0, 134.9, 129.7, 129.1, 43.9, 41.6, 30.3, 25.3; IR (neat, cm^{-1}) 2970 (w), 2900 (w), 1683 (m), 1589 (m), 1404 (m), 1347 (m), 1277 (m), 1170 (m), 1085 (m), 1050 (m), 1005 (m), 826(m), 754 (w), 562 (m), 527 (m); MS (EI, 70 eV) m/z = 272 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}ClOS_2Na$) calcd 294.9994, found 294.9998.

*1-(4-Bromophenyl)-2-(1,3-dithian-2-yl)ethanone (**3f**):* White solid; R_f = 0.45 (EA/PE = 1:10); mp (°C) 119−120; isolated yield 52% (37 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 8.6 Hz, 2H), 7.55 (d, J = 8.6 Hz, 2H), 4.61 (t, J = 6.9 Hz, 1H), 3.27 (d, J = 6.9 Hz, 2H), 2.98−2.86 (m, 2H), 2.85−2.73 (m, 2H), 2.14−1.98 (m, 1H), 1.94−1.77 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3, 135.0, 131.8, 129.5, 128.5, 43.6, 41.3, 30.0, 25.0; IR (neat, cm^{-1}) 3080 (w), 2908 (w), 1681 (m), 1576 (m), 1417 (m),1277 (m), 1176 (m), 1068 (m), 985 (m), 818 (m), 746 (m), 664 (m), 564 (m), 452 (m); MS (EI, 70 eV) m/z = 318 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}BrOS_2Na$) calcd 338.9489, found 338.9492.

*2-(1,3-Dithian-2-yl)-1-(4-nitrophenyl)ethanone (**3g**):* White solid; R_f = 0.36 (EA/PE = 1:10); mp (°C) 129−130; isolated yield 82% (52 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 8.5 Hz, 2H), 8.18−7.97 (m, 2H), 4.60 (t, J = 6.9 Hz, 1H), 3.34 (d, J = 6.9 Hz, 2H), 3.00−2.86 (m, 2H), 2.85−2.75 (m, 2H), 2.14−2.00 (m, 1H), 1.91−1.77 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.2, 150.4, 140.8, 129.2, 123.9, 44.4, 41.2, 30.2, 29.6, 25.1; IR (neat, cm^{-1}) 3109 (w), 2975 (m), 2905 (m), 1694 (s), 1599 (w), 1519 (s), 1339 (s), 1215 (m), 1053 (m), 980 (w), 854 (m), 751 (m), 671 (w), 554 (w), 504 (w); MS (EI, 70 eV) m/z = 283 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}NO_3S_2Na$) calcd 306.0235, found 306.0239.

*1-(3-Bromophenyl)-2-(1,3-dithian-2-yl)ethanone (**3h**):* White solid; R_f = 0.37 (EA/PE = 1:10); mp (°C) 116−117; isolated yield 69% (49 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.9 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 4.69 (t, J = 6.8 Hz, 1H), 3.37 (d, J = 6.9 Hz, 2H), 3.03−2.93 (m, 2H), 2.91−2.76 (m, 2H), 2.19−2.07 (m, 1H), 1.98−1.81 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 137.9, 136.0, 130.9, 130.0, 126.5, 122.8, 43.7, 41.1, 29.9, 25.0; IR (neat, cm^{-1}) 3077 (w), 2935 (w), 2890 (w), 1686 (s), 1561 (m), 1419 (s), 1344 (m), 1275 (m), 1215 (s), 1065 (w), 898 (m), 798 (s), 706 (m), 684 (m), 619 (m), 447 (m); MS (EI, 70 eV) m/z = 318 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}BrOS_2Na$) calcd 338.9489, found 338.9493.

*2-(1,3-Dithian-2-yl)-1-(o-tolyl)ethanone (**3i**):* White solid; R_f = 0.45 (EA/PE = 1:10); mp (°C) 84−85; isolated yield 76% (43 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, J = 7.7 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 15.3 Hz, 2H), 4.63 (t, J = 7.0 Hz, 1H), 3.30 (d, J = 7.0 Hz, 2H), 2.95−2.85 (m, 4H), 2.51 (s, 3H), 2.14−2.03 (m, 1H), 1.93−1.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 138.4, 137.0, 131.9, 131.5, 128.3, 125.6, 46.5, 41.6, 29.9, 25.1, 21.2; IR (neat, cm^{-1}) 3062 (w), 2977 (w), 2895 (w), 1683 (m), 1459 (m), 1409 (m), 1272 (m), 1220 (m), 1170 (m), 1048 (s), 973 (m), 881 (m), 766 (m), 724 (m), 629 (m), 462 (m); MS (EI, 70 eV) m/z = 252 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{13}H_{16}OS_2Na$) calcd 275.0540, found 275.0542.

*2-(1,3-Dithian-2-yl)-1-(2-methoxyphenyl)ethanone (**3j**):* Yellow oil; R_f = 0.40 (EA/PE = 1:10); isolated yield 78% (47 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.7, 1.8 Hz, 1H), 7.58−7.42 (m, 1H), 7.08−6.85 (m, 2H), 4.69 (t, J = 6.9 Hz, 1H), 3.91 (s, 3H), 3.41 (d, J = 6.9 Hz, 2H), 3.00−2.90 (m, 2H), 2.89−2.78 (m, 2H), 2.16−2.04 (m, 1H), 1.92−1.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 158.6, 133.9, 130.6, 127.3, 120.6, 111.4, 55.4, 48.9, 41.7, 30.1, 25.3; IR (neat, cm^{-1}) 3072 (w), 2942 (w), 2908 (w), 2828 (w), 1671 (s), 1596 (s), 1481 (s), 1457 (m), 1432 (m), 1282 (s), 1247 (s), 1160 (m), 1028 (m), 980 (w), 936 (w), 911 (w), 763 (s), 621 (m); MS (EI, 70 eV) m/z = 268 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{13}H_{16}O_2S_2Na$) calcd 291.0489, found 291.0493.

*1-(2-Bromophenyl)-2-(1,3-dithian-2-yl)ethanone (**3k**):* White solid; R_f = 0.45 (EA/PE = 1:10); mp (°C) 71−72; isolated yield 69% (49 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.56 (m, 1H), 7.49−7.27 (m, 3H), 4.62 (t, J = 7.1 Hz, 1H), 3.39 (d, J = 7.1 Hz, 2H), 2.96−2.86 (m, 4H), 2.17−2.07 (m, 1H), 1.94−1.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.3, 140.9, 133.6, 131.9, 128.9, 127.5, 118.7, 47.8, 41.4, 29.9, 25.2; IR (neat, cm^{-1}) 2948 (w), 2885 (w), 1700 (s), 1584 (m), 1429 (m), 1344 (m), 1275 (m), 1212 (m), 1028 (m), 978 (m), 943 (w), 766 (s), 671 (w), 624 (w), 459 (m); MS (EI, 70 eV) m/z = 318 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}BrOS_2Na$) calcd 338.9489, found 338.9490.

*2-(1,3-Dithian-2-yl)-1-(2-fluorophenyl)ethanone (**3l**):* White solid; R_f = 0.44 (EA/PE = 1:10); mp (°C) 31−32; isolated yield 75% (43 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (dd, J = 10.6, 4.6 Hz, 1H), 7.52 (ddd, J = 7.1, 6.2, 4.1 Hz, 1H), 7.19 (ddd, J = 19.6, 15.0, 9.8 Hz, 2H), 4.67 (t, J = 6.8 Hz, 1H), 3.40 (dd, J = 6.8, 2.7 Hz, 2H), 2.99−2.80 (m, 4H), 2.17−2.03 (m, 1H), 1.96−1.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.6, 163.4, 160.0, 134.9, 130.7, 124.5, 116.7, 116.4, 48.6, 40.8, 29.8, 25.2; IR (neat, cm^{-1}) 3084 (w), 2967 (w), 2890 (w), 1634 (m), 1543 (m), 1472 (m), 1390 (m), 1332 (m), 1201 (m), 1068 (m), 1023 (m), 943 (m), 770 (m), 598 (m), 469 (m); MS (EI, 70 eV) m/z = 256 (M+); HRMS (ESI) m/z [M + Na]$^+$ ($C_{12}H_{13}FOS_2Na$) calcd 279.0290, found 279.0294.

*1-(3,4-Dimethylphenyl)-2-(1,3-dithian-2-yl)ethanone (**3m**):* White solid; R_f = 0.47 (EA/PE = 1:10); mp (°C) 83−84; isolated yield 72% (43 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.69 (d, J = 7.8 1H), 7.22 (d, J = 7.6 Hz, 1H), 4.69 (t, J = 6.9 Hz, 1H), 3.32 (d, J = 6.9

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Hz, 2H), 3.02−2.91 (m, 2H), 2.89−2.80 (m, 2H), 2.31 (s, 6H), 2.18−2.07 (m, 1H), 1.98−1.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.3, 143.0, 136.9, 134.4, 129.8, 129.2, 125.9, 43.5, 41.8, 30.2, 25.2, 20.0, 19.7; IR (neat, cm^{-1}) 3047 (w), 2982 (w), 2942 (w), 2888 (w), 1686 (s), 1606 (m), 1449 (m), 1402 (m), 1339 (m), 1247 (m), 1125 (m), 1053 (m), 988 (m), 901 (m), 826 (m), 726 (m), 606 (m), 534 (w), 432 (m); MS (EI, 70 eV) m/z = 266 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{14}H_{18}OS_2Na$) calcd 289.0697, found 289.0700.

*2-(1,3-Dithian-2-yl)-1-(thiophen-3-yl)ethanone (**3n**):* White solid; R_f = 0.40 (EA/PE = 1:10); mp (°C) 56−57; isolated yield 84% (46 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 2.9 Hz, 1H), 7.56 (d, J = 5.1 Hz, 1H), 7.39−7.25 (m, 1H), 4.67 (t, J = 6.9 Hz, 1H), 3.25 (d, J = 6.9 Hz, 2H), 3.00−2.90 (m, 2H), 2.88−2.81 (m, 2H), 2.16−2.08 (m, 1H), 1.91−1.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 141.9, 132.6, 126.9, 126.6, 45.0, 41.7, 30.4, 25.3; IR (neat, cm^{-1}) 3077 (w), 2928 (w), 2890 (w), 1678 (s), 1507 (m), 1412 (m), 1392 (m), 1337 (w), 1232(m), 1185 (m), 1155 (m), 1078 (w), 874 (w), 808 (s), 709 (m), 619 (m); MS (EI, 70 eV) m/z = 244 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{10}H_{12}OS_3Na$) calcd 266.9948, found 266.9952.

*2-(1,3-Dithian-2-yl)-1-(2-methoxyphenyl)propan-1-one (**3o**):* Colorless oil; R_f = 0.38 (EA/PE = 1:10); isolated yield 63% (40 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.7, 1.8 Hz, 1H), 7.52−7.40 (m, 1H), 7.06−6.92 (m, 2H), 4.44 (d, J = 8.1 Hz, 1H), 3.90 (s, 3H), 3.89−3.87 (m, 1H), 2.90−2.75 (m, 4H), 2.11−2.04 (m, 1H), 1.89−1.78 (m, 1H), 1.33 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.7, 157.9, 133.3, 130.8, 120.8, 111.3, 55.5, 50.2, 49.3, 30.4, 29.9, 25.8, 14.5; IR (neat, cm^{-1}) 3077 (w), 2978 (w), 2932 (w), 2912 (w), 2851 (w), 1683 (m), 1624 (s), 1523 (m), 1455 (w), 1350 (m), 1247 (s), 1145 (s), 1053 (m), 973 (m), 886 (m), 765 (m), 624 (m); MS (EI, 70 eV) m/z = 282 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{14}H_{18}O_2S_2Na$), calcd 305.0646, found 305.0650.

*2-(1,3-Dithian-2-yl)-1-(4-methoxyphenyl)propan-1-one (**3p**):* Colorless oil; R_f = 0.37 (EA/PE = 1:10); isolated yield 65% (41 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 9.0 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 4.44 (d, J = 9.1 Hz, 1H), 3.88 (s, 3H), 3.87−3.85 (m, 1H), 2.92−2.80 (m, 4H), 2.16−2.05 (m, 1H), 1.99−1.81 (m, 1H), 1.35 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.4, 163.7, 130.6, 129.4, 113.8, 55.4, 49.8, 44.0, 30.2, 29.8, 25.7, 15.7; IR (neat, cm^{-1}) 3067 (w), 2972 (w), 2927 (w), 2903 (w), 2840 (w), 1673 (m), 1604 (s), 1514 (m), 1454 (w), 1422 (m), 1237 (s), 1170 (s), 1033 (m), 975 (m), 846 (m), 796 (m), 601 (m); MS (EI, 70 eV) m/z = 282 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{14}H_{18}O_2S_2Na$), calcd 305.0646, found 305.0651.

*1-(1,3-Dithian-2-yl)heptan-2-one (**3q**):* Colorless oil; R_f = 0.52 (EA/PE = 1:10); isolated yield 45% (23 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51 (t, J = 7.0 Hz, 1H), 2.96−2.82 (m, 4H), 2.79 (d, J = 7.0 Hz, 2H), 2.44 (t, J = 7.4 Hz, 2H), 2.15−2.07 (m, 1H), 1.86 (dt, J = 12.6, 2.4 Hz, 1H), 1.59 (dt, J = 14.5, 7.3 Hz, 2H), 1.33−1.24 (m, 4H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.1, 47.6, 43.5, 41.1, 41.1, 31.1, 30.1, 25.2, 23.1, 22.3, 13.8; IR (neat, cm^{-1}) 2962 (m), 2930 (m), 2900 (m), 2865 (m), 2853 (w), 1719 (s), 1676 (w), 1472 (w), 1427 (m), 1364 (m), 1277(m), 1080 (m), 1038 (m), 911 (m), 873 (w), 776 (w), 726 (w), 661 (w), 619 (w); MS (EI, 70 eV) m/z = 232 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{11}H_{20}OS_2Na$), calcd 255.0853, found 255.0857.

*2-(1,3-Dithian-2-yl)-1,2-diphenylethanone (**3r**):* White solid; R_f = 0.38 (EA/PE = 1:10); mp (°C) 136−137; isolated yield 52% (37 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (dd, J = 8.4, 1.2 Hz, 2H), 7.49 (d, J = 7.2 Hz, 1H), 7.40 (dd, J = 8.1, 7.0 Hz, 4H), 7.30 (td, J = 8.5, 4.1 Hz, 3H), 5.05−4.90 (m, 2H), 2.98−2.76 (m, 4H), 2.13−2.01 (m, 1H), 1.91−1.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 136.5, 134.7, 133.2, 128.7, 128.6, 128.5, 128.4, 128.0, 57.0, 48.6, 29.7, 25.4; IR (neat, cm^{-1}) 3087 (w), 3062 (w), 3027 (w), 2950 (w), 2937 (w), 2843 (w), 1663 (s), 1581(m), 1452 (m), 1429 (m), 1329 (m), 1260 (m), 1212 (m), 1182 (m), 973 (m), 756 (m), 691 (m), 636 (m), 537 (m); MS (EI, 70 eV) m/z = 314 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{18}H_{18}OS_2Na$), calcd 337.0697, found 337.0701.

*2-(1,3-Dithian-2-yl)-1-(4-methoxyphenyl)-2-phenylethanone (**3s**):* White solid; R_f = 0.35 (EA/PE = 1:10); mp (°C) 93−94; isolated yield 48% (37 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 6.8 Hz, 2H), 7.28−7.09 (m, 3H), 6.79 (d, J = 8.8 Hz, 2H), 4.88 (d, J = 11.1 Hz, 1H), 4.79 (d, J = 11.1 Hz, 1H), 3.70 (s, 3H), 2.88−2.64 (m, 4H), 1.97 (d, J = 13.6 Hz, 1H), 1.83−1.69 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.2, 163.6, 135.1, 130.9, 129.5, 128.7, 128.6, 127.9, 113.7, 56.7, 55.3, 48.8, 30.0, 29.9, 25.5; IR (neat, cm^{-1}) 3092 (w), 3055 (w), 3040 (w), 2960 (w), 2939 (w), 2853 (w), 1660 (s), 1595(m), 1472 (m), 1440 (m), 1350 (m), 1290 (m), 1233 (m), 1200 (m), 1104 (m), 983 (m), 767 (m), 690 (m), 630 (m), 570 (m), 534 (m); MS (EI, 70 eV) m/z = 344 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{19}H_{20}O_2S_2Na$), calcd 367.0802, found 367.0805.

*2-(1,3-Dithian-2-yl)-2-phenyl-1-(p-tolyl)ethanone (**3t**):* White solid; R_f = 0.37 (EA/PE = 1:10); mp (°C) 122−123; isolated yield 49% (36 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 2H), 7.41 (dd, J = 8.0, 1.4 Hz, 2H), 7.36−7.21 (m, 3H), 7.18 (t, J = 7.7 Hz, 2H), 5.02−4.86 (m, 2H), 2.94−2.72 (m, 4H), 2.30 (s, 3H), 2.08−1.97 (m, 1H), 1.86−1.76 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 143.8, 134.8, 133.7, 128.9, 128.5, 128.3, 127.6, 56.5, 48.4, 29.5, 25.2, 21.2; IR (neat, cm^{-1}) 3060 (w), 3035 (w), 2977 (w), 2932 (w), 2898 (w), 2838 (w), 1666(s), 1604 (m), 1457 (m), 1427 (m), 1327 (m), 1267 (m), 1177 (m), 1048 (m), 975 (m), 811 (m), 701 (s), 599 (m), 529 (m); MS (EI, 70 eV) m/z = 328 (M+); HRMS (ESI) m/z $[M + Na]^+$ ($C_{19}H_{20}OS_2Na$), calcd 351.0853, found 351.0856.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00187.

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Notes

The authors declare no competing financial interest.

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