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Synthesis of 1,3,4-Thiadiazoles and 1,4,2-Oxathiazoles from α-Enolic Dithioesters and Active 1,3-Dipoles

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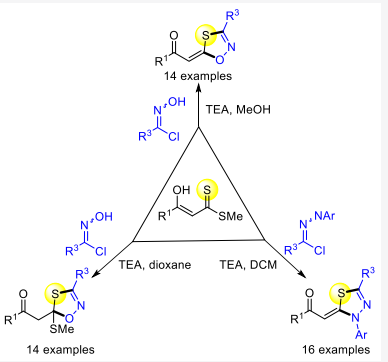
ABSTRACT: The synthesis of two kinds of five-membered organosulfur heterocycles (i.e., 1,4,2-oxathiazoles and 1,3,4-thiadiazoles) from α-enolic dithioesters with active 1,3-dipoles (nitrile oxides and nitrilimines) generated in situ was achieved under mild reaction conditions. This transformation further expands the synthetic application of α-enolic dithioesters as the sulfur-containing building blocks.



INTRODUCTION

Sulfur is one of the essential elements in life and exists in most biomolecules (e.g., protein), which play a crucially important role in life. In addition, organosulfur compounds constitute a large family of natural products, pharmaceutical molecules, perfumes, and others. Moreover, some organosulfur molecules, such as sulfones, sulfoxides, and trialkylsulfoniums, are often used as useful synthetic reagents or intermediates in organic synthesis. As a consequence, considerable effort has been devoted to the development of practical and efficient approaches to access these functional molecules.[1] Traditionally, in addition to elemental sulfur, the incorporation of sulfur atoms into organic frameworks is accomplished by using inorganic sulfur compounds (e.g., sulfites and sulfides) or organosulfur small molecules (e.g., thiols and sulfoxides).[2] Among the latter, α-enolic dithioesters **A** have been proven to be a class of useful and versatile synthons, and their synthetic applications have been extensively studied to access various sulfur-containing heterocyclic compounds (e.g., thiopyrans,[3b] isothiazoles,[3c] and thiazoles[3d]) in the past decades.[3]

Continuing our ongoing interest in sulfur-containing building block,[3g,4] we were also attracted to α-enolic dithioesters, because α-enolic dithioesters, structurally, possess two electrophilic and three nucleophilic reactive sites and could react with suitable reaction partners in a regioselective manner (Scheme 1). For example, Junjappa reported a cyclocondensation reaction of arylhydrazines with α-enolic dithioesters to afford substituted pyrazoles using two electrophilic sites (C═O and C═S, eq a).[3e] Singh disclosed an acid-controlled chemodivergent synthesis of differently substituted quinolines via site-selective coupling of *o*-aminoaryl ketones (i.e., C and C═S vs C and C═O, eqs b and c) with α-enolic dithioesters.[3f] Recently, the two nucleophilic reactive sites (i.e., C and S, eq c) were applied in the formal (3+3) annulation reaction with 1,3,5-triazinanes to access 3,4-dihydro-2*H*-1,3-thiazines by us.[3g] Despite these great advances, the development and application of this kind of versatile synthon with multiple reactive sites are still highly desired.

An extensive literature search of α-enolic dithioesters revealed that only two documents referred to dipole equivalents generated in situ from epoxides or donor−acceptor cyclopropanes.[3h,i] Therefore, we were motivated to further explore whether nitrile oxides and nitrilimines, two different active dipoles, could react with α-enolic dithioesters and which reactive sites of α-enolic dithioesters will be involved. Nitrile oxides and nitrilimines are commonly generated in situ from hydroximoyl halides and hydrazonoyl halides and inclined to be dimerized, which made the designed plan very challenging. Herein, we will present our preliminary results on this subject.

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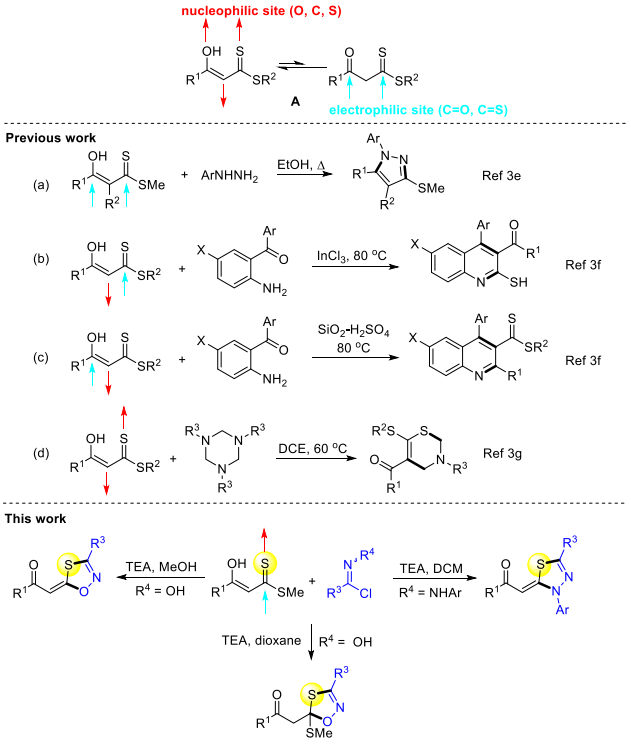
Scheme 1. Previous Applications of the α-Enolic Dithioester and This Work

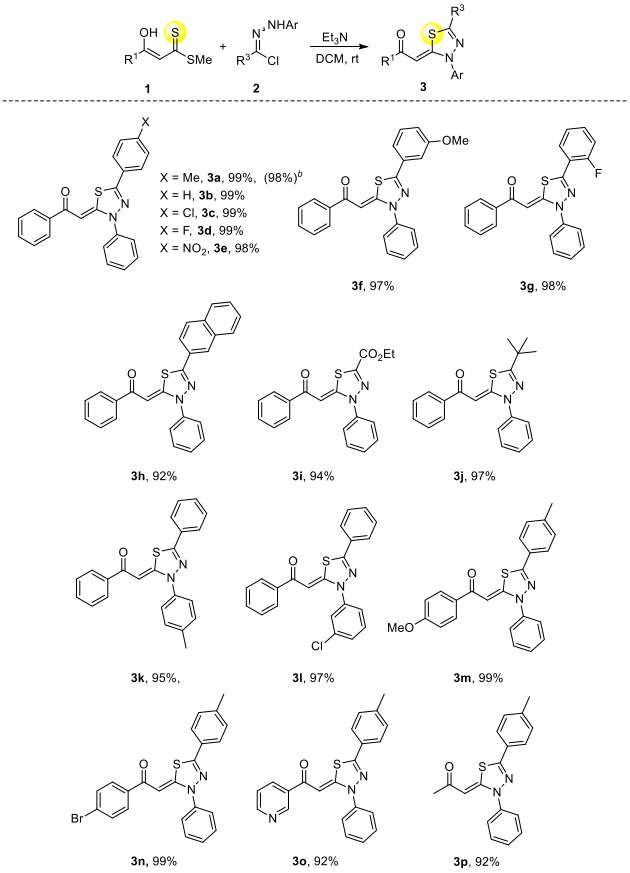


RESULTS AND DISCUSSION

To be economic, equimolar α-enolic dithioester **1a** and benzohydrazonoyl chloride **2a** were chosen and mixed in dichloromethane at room temperature, using Et_3N (1.5 equiv) as the base. Delightfully, 1,3,4-thiadiazole derivative **3a** was obtained as a single *Z* geometrical isomer in almost quantitative yield (99%).[5] The exact structure of **3a** was confirmed by X-ray diffraction.[6] In addition, a smaller amount of Et_3N resulted in a long reaction time. In view of the high efficiency of this annulation reaction, we decided to directly explore the substrate scope of this transformation without further optimization, and the results are summarized in Scheme 2. Generally, various hydrazonoyl chlorides tested in this reaction were well-tolerated and gave excellent yields. The substituents on the phenyl ring of R^3 could be electron-donating or electron-withdrawing groups, and the position of the substituents made no difference to the yields (**3a**−**3h**). The ethoxycarbonyl and *tert*-butyl group-substituted hydrazonoyl chlorides were also investigated, and their annulation reactions proceeded smoothly (**3i** and **3j**). The substituents of the phenyl group in the Ar and R^1 moiety had no influence on the yields (**3k**−**3n**). α-Enolic dithioester with a heteroaryl group (e.g., 3-pyridyl) or a methyl group in R^1 also performed well, delivering high yields (**3o** and **3p**). The scale-up experiment for **3a** was conducted, and no corrosion in the yield was observed. It is worth noting that all of the substrates exhibited exclusive *Z* selectivity, and the geometrical configuration of the products was determined by analogy with **3a**.

Encouraged by the initial success with nitrilimine, we hoped to extend this strategy to access 1,4,2-oxathiazoles, another important class of five-membered organosulfur heterocycles, which are structural analogues of 1,3,4-thiadiazoles. Thus, α-enolic dithioester **1a** and tolyl hydroximoyl chloride **4a** were

Scheme 2. Substrate Scope of 1,3,4-Thiadiazole[a]



[a]Reaction conditions: **1** (0.3 mmol), **2** (1 equiv), and Et_3N (1.5 equiv) in DCM (3 mL) at rt. [b]The reaction was conducted on a gram scale.

exposed to the standard conditions for accessing 1,3,4-thiadiazole. Unexpectedly, two 1,4,2-oxathiazole derivatives of **5a** and **6a** were obtained. Possibly, the 5-(methylthio)-1,4,2-oxathiazole **6a** was the precursor for the formation of **5a** via the elimination of the methylthio moiety. To gain a better selectivity between two 1,4,2-oxathiazole products, the optimization of reaction conditions was elaborately conducted, and the detailed results are listed in Table 1. In general, the solvent and the equivalent of the base seemed to be the key parameters for product selectivity. For example, testing of a series of common solvents (e.g., DCM, $CHCl_3$, DMF, etc., entries 1−8) indicated that methanol gave the highest yield of **5a** (entry 8), while variant of the equivalent of Et_3N from 2 to 1.5 made no difference in the formation of this product (entry 9). It is worth noting that ether solvents, such as THF and dioxane, could significantly suppress the formation of **5a** (entries 5 and 6, respectively), and prolonging the reaction time was detrimental for the formation of **6a** (entries 10 and 11 vs entries 5 and 6). Finally, it was found that decreasing the amount of Et_3N was effective (entries 12 and 13), and dioxane gave the highest yield of **6a** (entry 13).

With the optimal conditions (Table 1, entries 9 and 13) in hand, a survey of the generality and scope of this divergent synthesis was then conducted. As demonstrated in Scheme 3, methanol was used as the solvent to access 1,4,2-oxathiazole **5**. Like the annulation reaction of nitrilimine, the electronic property and position of the substituent on the phenyl ring of

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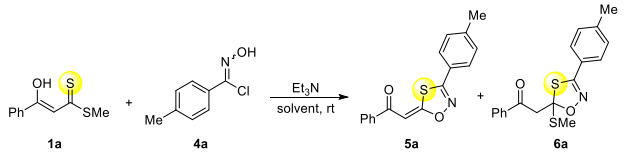
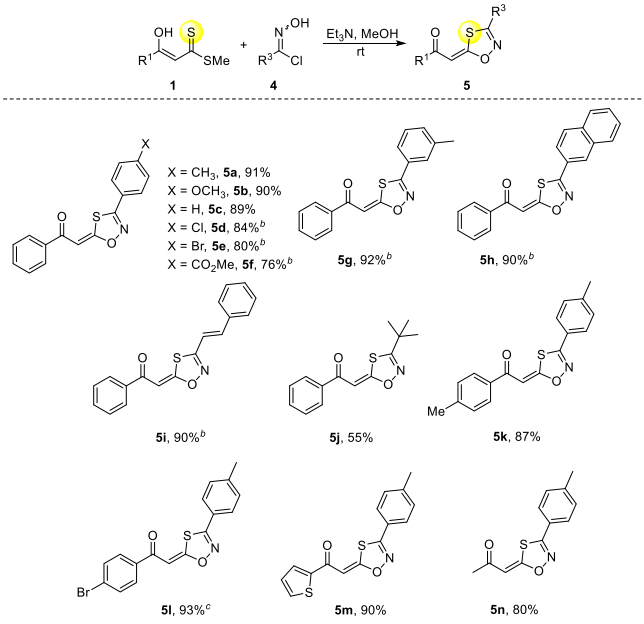
Table 1. Optimization of the Product Selectivity between 1,4,2-Oxathiazole Derivatives of 5a and 6a[a]



				yield (%)[b]	
entry	1a/4a/Et_3N	solvent	time (min)	5a	6a
1	1:1:2	DCM	10	60	43
2	1:1:2	$CHCl_3$	10	54	50
3	1:1:2	DMF	40	83	14
4	1:1:2	CH_3CN	50	83	10
5	1:1:2	THF	50	22	63
6	1:1:2	dioxane	50	30	68
7	1:1:2	$PhCH_3$	50	39	55
8	1:1:2	MeOH	10	95	trace
9	1:1:1.5	MeOH	10	95	trace
10	1:1:2	THF	90	61	30
11	1:1:2	dioxane	90	60	30
12	1:1:1	THF	50	6	83
13	1:1:1	dioxane	50	trace	90

[a]Reaction conditions: **1a** (0.1 mmol), **4a**, and Et_3N in solvent (1 mL) at rt. [b]The yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as the internal standard.

Scheme 3. Substrate Scope of 1,4,2-Oxathiazole 5[a]

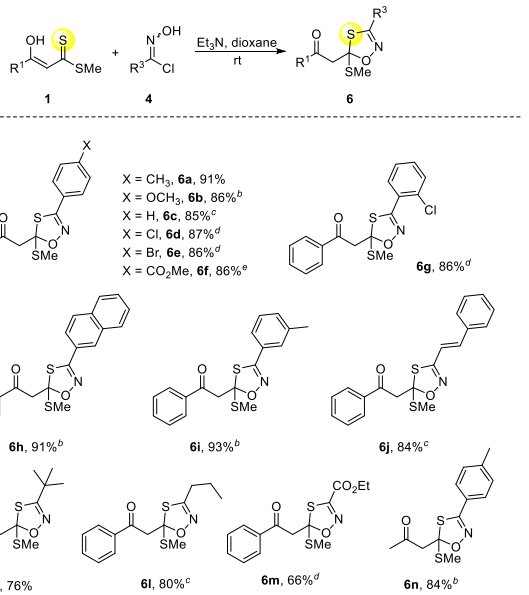


[a]Reaction conditions: **1** (0.3 mmol), **4** (1 equiv), and Et_3N (1.5 equiv) in MeOH (3 mL) at rt, unless otherwise noted. [b]**4** (1.2 equiv) was used instead. [c]**4** (1.5 equiv) was used instead.

the R^3 group were tested, and all of the substrates worked well, giving high yields of 1,4,2-oxathiazoles (**5a**−**5h**). Hydroximoyl chlorides with an alkenyl or alkyl substituent were also viable (see **5i** and **5j**), albeit 1,4,2-oxathiazole **5j** was obtained in a moderate yield of only 55%. α-Enolic dithioester with a methyl group or bromo group at position 4 of the phenyl ring afforded high yields of 87% or 93%, respectively (**5k** and **5l**). Heteroaryl (e.g., 2-thienyl) group-substituted α-enolic dithioester was also investigated, delivering the desired 1,4,2-oxathiazole in 90% yield (**5m**). Finally, the reaction of methyl (*Z*)-3-hydroxybut-2-enedithioate was investigated, which proceeded smoothly to afford **5n** in 80% yield. It should be mentioned that hydroximoyl chloride was consumed within 30 min normally, much faster than the reaction of hydrazonoyl chloride, which resulted in the remnant of dithioester in some cases. Thus, additional hydroximoyl chloride needed to be replenished to improve the yield. The *Z*/*E* selectivity was also perfect,[7] as no any *E* isomers were detected.

To selectively access 5-(methylthio)-1,4,2-oxathiazole **6**, dioxane was selected as the solvent (Scheme 4). The substrate

Scheme 4. Substrate Scope of 1,4,2-Oxathiazole 6[a]



[a]Reaction conditions: **1** (0.3 mmol), **4** (1 equiv), and Et_3N (1 equiv) in dioxane (3 mL) at rt, unless otherwise noted. [b]**4** (1.2 equiv) and Et_3N (1.2 equiv) were used instead. [c]**4** (1.5 equiv) and Et_3N (1.5 equiv) were used instead. [d]**4** (2 equiv) and Et_3N (2 equiv) were used instead. [e]**4** (2.2 equiv) and Et_3N (2.2 equiv) were used instead.

compatibility also proved to be satisfactory. The substituents of R^3 in hydroximoyl chlorides could be an aryl (**6a**−**6i**), an alkenyl (**6j**), an alkyl (**6k** and **6l**), or an ethoxylcarbonyl (**6m**) group. Among them, the yields of alkyl and ethoxylcarbonyl group-substituted substrates were relatively lower. In addition, the R^1 group in α-enolic dithioester could be phenyl (**6a**−**6m**) and methyl (**6n**) groups. Likewise, additional hydroximoyl chloride needed to be replenished for improving the yield in some cases.

On the basis of previous works,[3] a possible mechanism was proposed as shown in Scheme 5. Nucleophilic attack of the sulfur of the thiocarbonyl moiety in α-enolic dithioester **1** on the active 1,3-dipole derived from hydrazonoyl chloride **2** or hydroximoyl chloride **4** in situ provides β-dithioenone **B**, which undergoes intramolecular 1,4-addition of oxygen or nitrogen anion to deliver enolate **C**. At this junction, enolate **C** can be quenched by a proton in the case of nitrile oxide (Y = O) to give 5-(methylthio)-1,4,2-oxathiazole **6**, while elimination (i.e., retro-*S*-Michael addition) of the methylthio moiety affords **3** and **5**. Alternative pathways, for example, synergetic 1,3-dipolar cycloaddition of nitrile oxide and the C═S bond of α-enolic dithioester **1** to afford 5-(methylthio)-1,4,2-oxathia-

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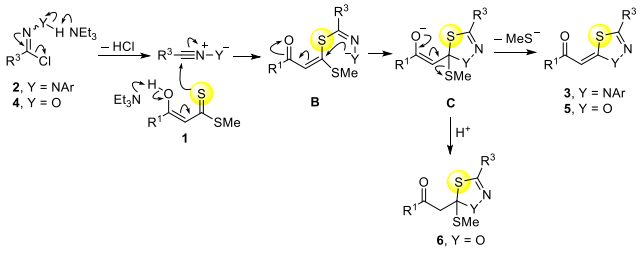
Scheme 5. Proposed Mechanism



zole **6**, could not be excluded. Possibly, the intramolecular noncovalent S···O interaction determine the stereoselectivity of elimination products **3** and **5**, because the single-crystal X-ray structure of **5i** revealed a S···O distance of ∼2.597 Å, which is shorter than the sum of the van der Waals radii of the respective atoms (3.32 Å).[7]

CONCLUSIONS

In summary, a cyclocondensation of α-enolic dithioesters with two types of active 1,3-dipoles generated in situ to access various 1,3,4-thiadiazoles and 1,4,2-oxathiazoles was achieved under mild reaction conditions. This approach facilitates diversity-oriented synthesis of sulfur-containing heterocycles and expands the new synthetic applications of α-enolic dithioester. The other intriguing explorations of an α-enolic dithioester in our laboratory are in progress and will be reported in due course.

EXPERIMENTAL SECTION

General Information. All isolated compounds were characterized on Bruker 400 spectrometers in $CDCl_3$ or $(CD_3)_2CO$. Chemical shifts are reported as δ values relative to internal $CHCl_3$ (δ 7.26 for ^1H NMR and δ 77.16 for ^{13}C NMR) and $(CH_3)_2CO$ (δ 2.05 for ^1H NMR and δ 29.84 for ^{13}C NMR). ^{19}F NMR chemical shifts were determined as δ values relative to external standard $PhCF_3$ at δ −63.50. High-resolution mass spectra (HRMS) were recorded on a 4G mass spectrometer using electrospray ionization (ESI) analyzed by a quadrupole time-of-flight (QTof) instrument. All melting points were measured with the samples after column chromatography and uncorrected. Column chromatography was performed on silica gel. Solvents (analytical reagent) were used as obtained from commercial sources without further purification and drying. α-Enolic dithioesters,[8] hydrazonoyl chlorides,[9] and hydroximoyl chlorides[10] were all known and prepared according to the literature.

General Procedure for the Preparation of 1,3,4-Thiadiazoles 3a−3p. To a solution of α-enolic dithioester **1** (0.3 mmol, 1.0 equiv) in DCM (3 mL) was added hydrazonoyl chloride **2** (0.3 mmol, 1.0 equiv), and then the mixture was stirred at rt. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (10:1 to 3:1 PE/EtOAc) to afford the corresponding 1,3,4-thiadiazole.

Scale-up Experiment for 3a. To a solution of α-enolic dithioester **1a** (4.75 mmol, 1.0 equiv) in DCM (48 mL) was added 4-methyl-*N*-phenylbenzohydrazonoyl chloride **2a** (4.75 mmol, 1.0 equiv), and then the mixture was stirred at rt. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (10:1 to 3:1 PE/EtOAc) to afford 1,3,4-thiadiazole **3a** as a yellow solid (1.72 g, 98%).

General Procedure for the Preparation of 1,4,2-Oxathiazoles 5a−5n. To a solution of α-enolic dithioester **1** (0.3 mmol, 1.0 equiv) in MeOH (3 mL) were added hydroximoyl chloride **4** (0.3 mmol, 1.0 equiv) and NEt_3 (0.45 mmol, 1.5 equiv), and then the mixture was stirred at rt. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (50:1 to 20:1 PE/EtOAc) to afford the corresponding 1,4,2-oxathiazole. Additional hydroximoyl chloride (0.2 equiv) needed to be replenished after 30 min to improve the yield of 1,4,2-oxathiazoles **5d−5i**. Additional hydroximoyl chloride (0.5 equiv) was needed for 1,4,2-oxathiazole **5l**.

General Procedure for the Preparation of 1,4,2-Oxathiazoles 6a−6n. To a solution of α-enolic dithioester (0.3 mmol, 1.0 equiv) in 1,4-dioxane (3 mL) were added hydroximoyl chloride (0.3 mmol, 1.0 equiv) and NEt_3 (0.3 mmol, 1.0 equiv), and then the mixture was stirred at rt. After completion of the reaction as monitored by TLC, the solvent was evaporated and the resulting crude product was directly purified by silica gel column chromatography (50:1 to 20:1 PE/EtOAc) to afford the corresponding 1,4,2-oxathiazole. Additional hydroximoyl chloride (0.2 equiv) and NEt_3 (0.2 equiv) needed to be replenished after 30 min to improve the yield of 1,4,2-oxathiazoles **6b**, **6h**, **6i**, and **6n**. For the preparation of 1,4,2-oxathiazoles **6c**, **6j**, and **6l**, additional hydroximoyl chloride (0.5 equiv) and NEt_3 (0.5 equiv) were divided into two equivalent parts and added with an interval of 30 min. For the preparation of 1,4,2-oxathiazoles **6d**, **6e**, **6g**, and **6m**, additional hydroximoyl chloride (1.0 equiv) and NEt_3 (1.0 equiv) were divided into four equivalent parts and added with an interval of 30 min. For the preparation of 1,4,2-oxathiazole **6f**, additional hydroximoyl chloride (1.2 equiv) and NEt_3 (1.2 equiv) were divided into six equivalent parts and added with an interval of 30 min.

Characterization Data of Products. *(Z)-1-Phenyl-2-[3-phenyl-5-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]ethan-1-one.* Compound **3a** [110 mg, 99% yield, R_f = 0.35 (5:1 PE/EA)] was isolated as a yellow solid: mp 151−152 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 6.4 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.45−7.35 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.71 (s, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.8, 160.2, 155.0, 141.4, 139.6, 139.0, 131.1, 129.9 (2C), 129.1, 128.4, 127.3, 127.0, 126.7, 125.6, 85.7, 21.6; ESI-HRMS *m/z* calcd for $C_{23}H_{19}N_2OS$ $[M + H]^+$ 371.1213, found 371.1216.

(Z)-2-[3,5-Diphenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3b** [106 mg, 99% yield, R_f = 0.36 (5:1 PE/EA)] was isolated as a yellow solid: mp 154−155 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95−7.86 (m, 4H), 7.68−7.64 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 2H), 7.55−7.37 (m, 7H), 6.74 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.9, 160.2, 154.8, 139.6, 139.0, 131.2, 130.9, 129.9, 129.8, 129.2 (2C), 128.4, 127.3, 126.8, 125.6, 85.8; ESI-HRMS *m/z* calcd for $C_{22}H_{17}N_2OS$ $[M + H]^+$ 357.1056, found 357.1058.

(Z)-2-(5-(4-Chlorophenyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-1-phenylethan-1-one. Compound **3c** [116 mg, 99% yield, R_f = 0.44 (5:1 PE/EA)] was isolated as a yellow solid: mp 165−166 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.66−7.54 (m, 4H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.45−7.34 (m, 5H), 6.71 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.7, 159.8, 153.4, 139.4, 138.7, 136.8, 131.1, 129.8, 129.4, 129.1, 128.3, 128.2, 127.8, 127.2, 125.4, 85.9; ESI-HRMS *m/z* calcd for $C_{22}H_{16}ClN_2OS$ $[M + H]^+$ 391.0666, found 391.0669.

(Z)-2-[5-(4-Fluorophenyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3d** [111 mg, 99% yield, R_f = 0.36 (5:1 PE/EA)] was isolated as a yellow solid: mp 142−143 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92−7.84 (m, 4H), 7.66−7.57 (m, 4H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.45−7.36 (m, 3H), 7.16 (t, *J* = 8.8 Hz, 2H), 6.72 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.9, 164.3 (d, *J* = 250.4 Hz), 160.1, 153.7, 139.5, 138.9, 131.2, 129.9, 129.2, 128.8 (d, *J* = 8.6 Hz), 128.4, 127.3, 126.1 (d, *J* = 3.3 Hz), 125.6, 116.4 (d, *J* = 22.0 Hz), 85.9; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −109.2; ESI-HRMS *m/z* calcd for $C_{22}H_{16}FN_2OS$ $[M + H]^+$ 375.0962, found 375.0963.

(Z)-2-[5-(4-Nitrophenyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3e** [118 mg, 98% yield, R_f = 0.41 (3:1 PE/EA)] was isolated as a yellow solid: mp 201−202 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.8 Hz, 2H), 8.00 (d, *J* = 8.4 Hz,

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2H), 7.85 (d, J = 7.2 Hz, 2H), 7.68−7.60 (m, 4H), 7.58−7.51 (m, 1H), 7.47−7.35 (m, 3H), 6.75 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.1, 159.8, 152.0, 148.8, 139.2, 138.4, 135.6, 131.5, 130.0, 129.5, 128.5, 127.4, 127.3, 125.5, 124.4, 86.5; ESI-HRMS m/z calcd for $C_{22}H_{16}N_3O_3S$ $[M + H]^+$ 402.0907, found 402.0909.

(Z)-2-[5-(3-Methoxyphenyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3f** [112 mg, 97% yield, R_f = 0.48 (5:1 PE/EA)] was isolated as a yellow solid: mp 156−157 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 6.8 Hz, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.6 Hz, 2H), 7.53−7.32 (m, 7H), 7.00 (d, J = 5.6 Hz, 1H), 6.72 (s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.7, 160.1, 160.0, 154.6, 139.5, 138.8, 131.0, 130.8, 130.2, 129.8, 129.1, 128.3, 127.2, 125.5, 119.3, 117.3, 111.2, 85.7, 55.4; ESI-HRMS m/z calcd for $C_{23}H_{19}N_2O_2S$ $[M + H]^+$ 387.1162, found 387.1162.

(Z)-2-[5-(2-Fluorophenyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3g** [110 mg, 98% yield, R_f = 0.46 (3:1 PE/EA)] was isolated as a yellow solid: mp 178−179 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (t, J = 7.6 Hz, 1H), 7.88 (d, J = 7.2 Hz, 2H), 7.67−7.55 (m, 4H), 7.50 (t, J = 7.2 Hz, 1H), 7.45−7.32 (m, 4H), 7.24−7.14 (m, 2H), 6.71 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.6, 160.5 (d, J = 7.0 Hz) 160.0 (d, J = 252.9 Hz), 149.8 (d, J = 5.5 Hz), 139.3, 138.8, 132.3 (d, J = 8.4 Hz), 131.0, 129.8, 129.1, 128.6 (d, J = 2.4 Hz), 128.3, 127.2, 125.5, 124.6 (d, J = 3.3 Hz), 117.8 (d, J = 11.7 Hz), 116.6 (d, J = 21.2 Hz), 85.6; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ −111.8; ESI-HRMS m/z calcd for $C_{22}H_{16}FN_2OS$ $[M + H]^+$ 375.0962, found 375.0962.

(Z)-2-[5-(Naphthalen-2-yl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3h** [112 mg, 92% yield, R_f = 0.5 (5:1 PE/EA)] was isolated as a yellow solid: mp 148−149 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.95−7.80 (m, 5H), 7.68 (d, J = 7.8 Hz, 2H), 7.61 (t, J = 7.8 Hz, 2H), 7.57−7.48 (m, 3H), 7.48−7.37 (m, 3H), 6.76 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.7, 160.0, 154.7, 139.5, 138.9, 134.3, 133.0, 131.1, 129.8, 129.0, 128.9, 128.6, 128.3, 127.9, 127.6, 127.2 (2C), 127.1, 127.0, 125.5, 123.1, 85.9; ESI-HRMS m/z calcd for $C_{26}H_{19}N_2OS$ $[M + H]^+$ 407.1213, found 407.1215.

Ethyl (Z)-5-(2-Oxo-2-phenylethylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate. Compound **3i** [99 mg, 94% yield, R_f = 0.41 (5:1 PE/EA)] was isolated as a yellow solid: mp 165−166 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 6.8 Hz, 2H), 7.63−7.51 (m, 5H), 7.47−7.36 (m, 3H), 6.71 (s, 1H), 4.47 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.3, 160.8, 158.9, 146.4, 138.7, 138.2, 131.4, 129.9, 129.8, 128.4, 127.3, 125.7, 87.2, 63.0, 14.2; ESI-HRMS m/z calcd for $C_{19}H_{17}N_2O_3S$ $[M + H]^+$ 353.0954, found 353.0954.

(Z)-2-[5-(tert-Butyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3j** [98 mg, 97% yield, R_f = 0.14 (10:1 PE/EA)] was isolated as a yellow solid: mp 128−129 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 6.0 Hz, 2H), 7.60−7.51 (m, 4H), 7.47−7.33 (m, 4H), 6.66 (s, 1H), 1.45 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.5, 166.7, 160.7, 139.6, 139.2, 130.8, 129.7, 128.7, 128.2, 127.1, 125.4, 85.1, 35.8, 30.0; ESI-HRMS m/z calcd for $C_{20}H_{21}N_2OS$ $[M + H]^+$ 337.1369, found 337.1370.

(Z)-1-Phenyl-2-[5-phenyl-3-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]-ethan-1-one. Compound **3k** [106 mg, 95% yield, R_f = 0.22 (10:1 PE/EA)] was isolated as a yellow solid: mp 149−150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.94−7.86 (m, 4H), 7.51 (d, J = 8.4 Hz, 2H), 7.47−7.35 (m, 8H), 6.70 (s, 1H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 183.6, 160.2, 154.5, 139.2, 138.9, 136.9, 131.0, 130.7, 130.3, 129.7, 129.1, 128.3, 127.2, 126.6, 125.3, 85.7, 21.3; ESI-HRMS m/z calcd for $C_{23}H_{19}N_2OS$ $[M + H]^+$ 371.1213, found 371.1216.

(Z)-2-[3-(3-Chlorophenyl)-5-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-phenylethan-1-one. Compound **3l** [114 mg, 97% yield, R_f = 0.2 (10:1 PE/EA)] was isolated as a yellow solid: mp 165−166 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91−7.84 (m, 4H), 7.68 (t, J = 2.0 Hz, 1H), 7.57 (dt, J = 8.0, 1.6 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.48−7.37 (m, 7H), 6.74 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.0, 159.6, 155.0, 140.5, 138.7, 135.5, 131.2, 131.0, 130.7, 129.4, 129.2, 129.1, 128.4, 127.3, 126.7, 125.8, 123.4, 86.0; ESI-HRMS m/z calcd for $C_{22}H_{16}ClN_2OS$ $[M + H]^+$ 391.0666, found 391.0668.

(Z)-1-(4-Methoxyphenyl)-2-[3-phenyl-5-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]ethan-1-one. Compound **3m** [119 mg, 99% yield, R_f = 0.35 (5:1 PE/EA)] was isolated as a yellow solid: mp 120−121 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.8 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.68−7.57 (m, 4H), 7.54−7.47 (m, 1H), 7.28 (d, J = 7.6 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.68 (s, 1H), 3.83 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.8, 162.0, 159.6, 154.7, 141.2, 139.6, 131.6, 129.8 (2C), 129.1, 128.9, 126.9, 126.6, 125.5, 113.5, 85.2, 55.3, 21.5; ESI-HRMS m/z calcd for $C_{24}H_{21}N_2O_2S$ $[M + H]^+$ 401.1318, found 401.1316.

(Z)-1-(4-Bromophenyl)-2-[3-phenyl-5-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]ethan-1-one. Compound **3n** [133 mg, 99% yield, R_f = 0.26 (20:1 PE/EA)] was isolated as a yellow solid: mp 213−214 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.66−7.56 (m, 4H), 7.54−7.47 (m, 3H), 7.26 (d, J = 8.0 Hz, 2H), 6.62 (s, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 182.3, 160.5, 155.2, 141.5, 139.4, 137.8, 131.5, 129.9, 129.2, 128.8, 126.8, 126.7, 125.7, 125.6, 85.3, 21.6 (1C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{23}H_{18}BrN_2OS$ $[M + H]^+$ 449.0318, found 449.0319.

(Z)-2-[3-Phenyl-5-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]-1-(pyridin-3-yl)ethan-1-one. Compound **3o** [102 mg, 92% yield, R_f = 0.18 (2:1 PE/EA)] was isolated as a yellow solid: mp 134−135 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.64 (d, J = 3.2 Hz, 1H), 8.19 (dt, J = 8.0, 2.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.67−7.58 (m, 4H), 7.56−7.50 (m, 1H), 7.35 (dd, J = 8.0, 4.8 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 6.65 (s, 1H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 181.2, 160.7, 155.3, 151.4, 148.5, 141.6, 139.2, 134.9, 134.3, 129.9 (2C), 129.4, 126.7, 126.6, 125.5, 123.5, 85.5, 21.6; ESI-HRMS m/z calcd for $C_{22}H_{18}N_3OS$ $[M + H]^+$ 372.1165, found 372.1165.

(Z)-1-[3-Phenyl-5-(p-tolyl)-1,3,4-thiadiazol-2(3H)-ylidene]propan-2-one. Compound **3p** [85 mg, 92% yield, R_f = 0.27 (5:1 PE/EA)] was isolated as a yellow solid: mp 179−180 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.59−7.52 (m, 4H), 7.50−7.43 (m, 1H), 7.25 (d, J = 8.0 Hz, 2H), 6.00 (s, 1H), 2.39 (s, 3H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.4, 158.3, 154.3, 141.2, 139.5, 129.8, 129.7, 128.9, 127.0, 126.7, 125.5, 88.7, 28.6, 21.6; ESI-HRMS m/z calcd for $C_{18}H_{17}N_2OS$ $[M + H]^+$ 309.1056, found 309.1056.

(Z)-1-Phenyl-2-[3-(p-tolyl)-1,4,2-oxathiazol-5-ylidene]ethan-1-one. Compound **5a** [81 mg, 91% yield, R_f = 0.33 (10:1 PE/EA)] was isolated as a white solid: mp 117−118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 6.8 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 7.58−7.46 (m, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.17 (s, 1H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.4, 176.2, 160.8, 143.1, 137.5, 132.6, 130.2, 128.8, 127.9, 127.8, 123.2, 90.9, 21.7; ESI-HRMS m/z calcd for $C_{17}H_{14}NO_2S$ $[M + H]^+$ 296.0740, found 296.0745.

(Z)-2-[3-(4-Methoxyphenyl)-1,4,2-oxathiazol-5-ylidene]-1-phenylethan-1-one. Compound **5b** [84 mg, 90% yield, R_f = 0.31 (5:1 PE/EA)] was isolated as a white solid: mp 100−101 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.50 (m, 3H), 7.15 (s, 1H), 6.99 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.4, 176.2, 162.8, 160.3, 137.6, 132.5, 129.6, 128.7, 127.8, 118.3, 114.9, 90.8, 55.6; ESI-HRMS m/z calcd for $C_{17}H_{14}NO_3S$ $[M + H]^+$ 312.0689, found 312.0694.

(Z)-1-Phenyl-2-(3-phenyl-1,4,2-oxathiazol-5-ylidene)ethan-1-one. Compound **5c** [75 mg, 89% yield, R_f = 0.31 (10:1 PE/EA)] was isolated as a white solid: mp 92−93 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.83 (d, J = 7.2 Hz, 2H), 7.59−7.46 (m, 6H), 7.19 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.5, 176.0, 160.9, 137.5, 132.6, 132.4, 129.5, 128.8, 128.0, 127.8, 126.2, 91.0; ESI-HRMS m/z calcd for $C_{16}H_{12}NO_2S$ $[M + H]^+$ 282.0583, found 282.0588.

(Z)-2-[3-(4-Chlorophenyl)-1,4,2-oxathiazol-5-ylidene]-1-phenylethan-1-one. Compound **5d** [80 mg, 84% yield, R_f = 0.44 (10:1 PE/EA)] was isolated as a yellow solid: mp 122−123 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.60−7.45 (m, 5H), 7.20 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ

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186.5, 175.7, 160.0, 138.7, 137.4, 132.7, 129.9, 129.2, 128.8, 127.8, 124.6, 91.2; ESI-HRMS m/z calcd for $C_{16}H_{10}ClNO_2SNa$ $[M + Na]^+$ 338.0013, found 338.0017.

(Z)-2-[3-(4-Bromophenyl)-1,4,2-oxathiazol-5-ylidene]-1-phenylethan-1-one. Compound **5e** [86 mg, 80% yield, R_f = 0.16 (10:1 PE/EA)] was isolated as a white solid: mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 8.6, 1.6 Hz, 2H), 7.72−7.64 (m, 4H), 7.60−7.54 (m, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.20 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.5, 175.7, 160.1, 137.4, 132.8, 132.8, 129.3, 128.8, 127.9, 127.2, 125.1, 91.2; ESI-HRMS m/z calcd for $C_{16}H_{11}BrNO_2S$ $[M + H]^+$ 359.9688, found 359.9697.

Methyl (Z)-4-[5-(2-Oxo-2-phenylethylidene)-1,4,2-oxathiazol-3-yl]-benzoate. Compound **5f** [77 mg, 76% yield, R_f = 0.18 (10:1 PE/EA)] was isolated as a yellow solid: mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz, 2H), 8.01 (d, J = 7.2 Hz, 2H), 7.90 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.21 (s, 1H), 3.96 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.5, 175.6, 166.0, 160.2, 137.4, 133.5, 132.8, 130.6, 130.1, 128.8, 128.0, 127.9, 91.2, 52.7; ESI-HRMS m/z calcd for $C_{18}H_{14}NO_4S$ $[M + H]^+$ 340.0638, found 340.0644.

(Z)-1-Phenyl-2-[3-(m-tolyl)-1,4,2-oxathiazol-5-ylidene]ethan-1-one. Compound **5g** [82 mg, 92% yield, R_f = 0.39 (10:1 PE/EA)] was isolated as a yellow solid: mp 108−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.66−7.58 (m, 2H), 7.54 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.41−7.33 (m, 2H), 7.16 (s, 1H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.4, 176.0, 160.9, 139.4, 137.5, 133.2, 132.5, 129.3, 128.7, 128.5, 127.8, 125.9, 125.1, 90.9, 21.4; ESI-HRMS m/z calcd for $C_{17}H_{14}NO_2S$ $[M + H]^+$ 296.0740, found 296.0746.

(Z)-2-[3-(Naphthalen-2-yl)-1,4,2-oxathiazol-5-ylidene]-1-phenylethan-1-one. Compound **5h** [89 mg, 90% yield, R_f = 0.33 (10:1 PE/EA)] was isolated as a yellow solid: mp 109−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.02 (d, J = 7.2 Hz, 2H), 7.98−7.86 (m, 4H), 7.64−7.53 (m, 3H), 7.50 (t, J = 7.6 Hz, 2H), 7.20 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.4, 176.0, 160.9, 137.5, 135.0, 132.9, 132.6, 129.4 (2C), 128.9, 128.8, 128.5, 128.1, 127.8, 127.5, 123.5 (2C), 91.0; ESI-HRMS m/z calcd for $C_{20}H_{13}NO_2S$ $[M + H]^+$ 332.0740, found 332.0747.

(Z)-1-Phenyl-2-[3-(E)-styryl-1,4,2-oxathiazol-5-ylidene]ethan-1-one. Compound **5i** [83 mg, 90% yield, R_f = 0.30 (10:1 PE/EA)] was isolated as a white solid: mp 107−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 6.8 Hz, 2H), 7.59−7.46 (m, 5H), 7.45−7.38 (m, 3H), 7.19 (s, 1H), 7.19 (s, 1H), 7.15 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.5, 175.2, 160.4, 142.4, 137.5, 134.5, 132.6, 130.5, 129.2, 128.8, 127.8, 127.7, 113.6, 90.9; ESI-HRMS m/z calcd for $C_{18}H_{14}NO_2S$ $[M + H]^+$ 308.0740, found 308.0745.

(Z)-2-[3-(tert-Butyl)-1,4,2-oxathiazol-5-ylidene]-1-phenylethan-1-one. Compound **5j** [43 mg, 55% yield, R_f = 0.20 (10:1 PE/EA)] was isolated as a yellow solid: mp 69−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 8.2, 1.6 Hz, 2H), 7.57−7.51 (m, 1H), 7.50−7.45 (m, 2H), 7.10 (s, 1H), 1.44 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.6, 176.6, 171.3, 137.7, 132.5, 128.8, 127.8, 90.5, 35.5, 29.6; ESI-HRMS m/z calcd for $C_{14}H_{16}NO_2S$ $[M + H]^+$ 262.0896, found 262.0899.

(Z)-1-(p-Tolyl)-2-[3-(p-tolyl)-1,4,2-oxathiazol-5-ylidene]ethan-1-one. Compound **5k** [81 mg, 87% yield, R_f = 0.35 (20:1 PE/EA)] was isolated as a white solid: mp 108−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.15 (s, 1H), 2.42 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 186.2, 175.7, 160.8, 143.3, 143.1, 134.9, 130.1, 129.5, 127.9, 127.8, 123.3, 90.8, 21.7, (the 1C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{18}H_{16}NO_2S$ $[M + H]^+$ 310.0896, found 310.0896.

(Z)-1-(4-Bromophenyl)-2-[3-(p-tolyl)-1,4,2-oxathiazol-5-ylidene]-ethan-1-one. Compound **5l** [104 mg, 93% yield, R_f = 0.41 (20:1 PE/EA)] was isolated as a white solid: mp 122−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.8 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.10 (s, 1H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 185.3, 176.8, 160.9, 143.3, 136.3, 132.0, 130.2, 129.3, 127.9, 127.5, 123.1, 90.6, 21.8; ESI-HRMS m/z calcd for $C_{17}H_{13}BrNO_2S$ $[M + H]^+$ 373.9845, found 373.9850.

(Z)-1-(Thiophen-2-yl)-2-[3-(p-tolyl)-1,4,2-oxathiazol-5-ylidene]-ethan-1-one. Compound **5m** [81 mg, 90% yield, R_f = 0.31 (20:1 PE/EA)] was isolated as a yellow solid: mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 3.6 Hz, 1H), 7.69 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 5.2 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.16 (t, J = 4.4 Hz, 1H), 6.99 (s, 1H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 179.5, 175.4, 160.9, 144.8, 143.2, 132.8, 130.2, 130.1, 128.3, 127.9, 123.1, 91.1, 21.8; ESI-HRMS m/z calcd for $C_{15}H_{12}NO_2S_2$ $[M + H]^+$ 302.0304, found 302.0306.

(Z)-1-[3-(p-Tolyl)-1,4,2-oxathiazol-5-ylidene]propan-2-one. Compound **5n** [56 mg, 80% yield, R_f = 0.15 (10:1 PE/EA)] was isolated as a white solid: mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 6.43 (s, 1H), 2.40 (s, 3H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.6, 173.8, 160.5, 143.0, 130.1, 127.8, 123.2, 94.2, 29.3, 21.7; ESI-HRMS m/z calcd for $C_{12}H_{12}NO_2S$ $[M + H]^+$ 234.0583, found 234.0588.

2-[5-(Methylthio)-3-(p-tolyl)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6a** [94 mg, 91% yield, R_f = 0.17 (10:1 PE/EA)] was isolated as a yellow solid: mp 93−94 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 6.8 Hz, 2H), 7.67−7.58 (m, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 7.6 Hz, 2H), 4.47 (d, J = 17.6 Hz, 1H), 3.97 (d, J = 17.6 Hz, 1H), 2.39 (s, 3H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.1, 157.9, 141.8, 136.0, 134.2, 129.7, 129.0, 128.4, 127.8, 124.9, 109.2, 49.9, 21.6, 13.9; ESI-HRMS m/z calcd for $C_{18}H_{17}NO_2S_2Na$ $[M + Na]^+$ 366.0593, found 366.0599.

2-[3-(4-Methoxyphenyl)-5-(methylthio)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6b** [93 mg, 86% yield, R_f = 0.26 (5:1 PE/EA)] was isolated as a yellow solid: mp 95−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.2 Hz, 2H), 7.71−7.58 (m, 3H), 7.51 (t, J = 7.5 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 4.47 (d, J = 17.6 Hz, 1H), 3.96 (d, J = 17.6 Hz, 1H), 3.84 (s, 3H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.1, 162.0, 157.6, 136.0, 134.2, 129.5, 129.0, 128.4, 120.1, 114.4, 108.9, 55.6, 49.7, 13.9; ESI-HRMS m/z calcd for $C_{18}H_{17}NO_3S_2Na$ $[M + Na]^+$ 382.0542, found 382.0549.

2-[5-(Methylthio)-3-phenyl-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6c** [84 mg, 85% yield, R_f = 0.27 (10:1 PE/EA)] was isolated as a yellow solid: mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 6.8 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.56−7.39 (m, 5H), 4.48 (d, J = 17.6 Hz, 1H), 3.98 (d, J = 17.6 Hz, 1H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 194.0, 157.9, 135.9, 134.2, 131.3, 129.0, 128.4, 127.8, 127.7, 109.4, 49.9, 13.8 (the 1C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{17}H_{15}NO_2S_2Na$ $[M + Na]^+$ 352.0436, found 352.0444.

2-[3-(4-Chlorophenyl)-5-(methylthio)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6d** [95 mg, 87% yield, R_f = 0.19 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.68−7.58 (m, 3H), 7.52 (t, J = 7.6 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 4.48 (d, J = 17.6 Hz, 1H), 3.97 (d, J = 17.6 Hz, 1H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.9, 157.0, 137.4, 135.9, 134.3, 129.3, 129.0 (2C), 128.4, 126.2, 109.8, 49.8, 13.9; ESI-HRMS m/z calcd for $C_{17}H_{14}ClNO_2S_2Na$ $[M + Na]^+$ 386.0047, found 386.0052.

2-[3-(4-Bromophenyl)-5-(methylthio)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6e** [105 mg, 86% yield, R_f = 0.31 (10:1 PE/EA)] was isolated as a yellow solid: mp 98−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 6.8 Hz, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.60−7.54 (m, 4H), 7.52 (t, J = 8.0 Hz, 2H), 4.47 (d, J = 17.6 Hz, 1H), 3.97 (d, J = 17.6 Hz, 1H), 2.28 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.9, 157.1, 135.9, 134.3, 132.3, 129.2, 129.0, 128.4, 126.7, 125.7, 109.9, 49.8, 13.9; ESI-HRMS m/z calcd for $C_{17}H_{14}BrNO_2S_2Na$ $[M + Na]^+$ 429.9542, found 429.9549.

Methyl 4-[5-(Methylthio)-5-(2-oxo-2-phenylethyl)-1,4,2-oxathiazol-3-yl]benzoate. Compound **6f** [100 mg, 86% yield, R_f = 0.15 (10:1 PE/EA)] was isolated as a white solid: mp 119−120 °C; ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.14 (d, J = 7.2 Hz, 2H), 8.12 (d, J = 6.8 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H), 7.71 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 7.6 Hz, 2H), 4.77 (d, J = 17.6 Hz, 1H), 4.09 (d, J = 18.0 Hz, 1H), 3.92 (s, 3H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR [100 MHz, $(CD_3)_2CO$] δ 194.7,

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166.4, 157.8, 137.0, 134.8, 133.3, 132.8, 130.8, 129.7, 129.2, 128.5, 110.6, 52.7, 49.5, 13.7; ESI-HRMS m/z calcd for $C_{19}H_{17}NO_4S_2Na$ [M + Na]$^+$ 410.0491, found 410.0496.

2-[3-(2-Chlorophenyl)-5-(methylthio)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6g** [94 mg, 86% yield, R_f = 0.18 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.14 (d, J = 8.0 Hz, 2H), 7.74−7.68 (m, 2H), 7.64−7.53 (m, 4H), 7.48 (t, J = 7.6 Hz, 1H), 4.74 (d, J = 17.6 Hz, 1H), 4.11 (d, J = 17.6 Hz, 1H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.8, 156.1, 137.0, 134.8, 133.4, 133.1, 132.0, 131.6, 129.7, 129.2, 128.4, 127.9, 110.9, 49.8, 13.8; ESI-HRMS m/z calcd for $C_{17}H_{14}ClNO_2S_2Na$ [M + Na]$^+$ 386.0047, found 386.0054.

2-[5-(Methylthio)-3-(naphthalen-2-yl)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6h** [104 mg, 91% yield, R_f = 0.22 (10:1 PE/EA)] was isolated as a yellow solid: mp 111−112 °C; ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.22 (s, 1H), 8.16 (d, J = 7.2 Hz, 2H), 8.12−8.06 (m, 1H), 8.04−7.90 (m, 3H), 7.71 (t, J = 7.6 Hz, 1H), 7.66−7.55 (m, 4H), 4.78 (d, J = 17.6 Hz, 1H), 4.08 (d, J = 17.6 Hz, 1H), 2.27 (s, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.8, 158.7, 137.1, 135.4, 134.8, 134.0, 129.7, 129.6 (3C), 129.2, 128.7, 128.0, 126.3, 124.2, 109.8, 49.4, 13.7 (the 1C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{21}H_{17}NO_2S_2Na$ [M + Na]$^+$ 402.0593, found 402.0599.

2-[5-(Methylthio)-3-(m-tolyl)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6i** [96 mg, 93% yield, R_f = 0.38 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.14 (d, J = 7.2 Hz, 2H), 7.70 (t, J = 7.2 Hz, 1H), 7.63−7.50 (m, 4H), 7.43−7.34 (m, 2H), 4.73 (d, J = 17.6 Hz, 1H), 4.03 (d, J = 18.0 Hz, 1H), 2.40 (s, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.8, 158.6, 139.8, 137.1, 134.8, 132.8, 129.8, 129.7, 129.2, 128.8, 128.7, 125.5, 109.6, 49.4, 21.2, 13.7; ESI-HRMS m/z calcd for $C_{18}H_{17}NO_2S_2Na$ [M + Na]$^+$ 366.0593, found 366.0598.

(E)-2-[5-(Methylthio)-3-styryl-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6j** [90 mg, 84% yield, R_f = 0.15 (10:1 PE/EA)] was isolated as a white solid: mp 117−118 °C; ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.13 (d, J = 7.2 Hz, 2H), 7.74−7.67 (m, 3H), 7.58 (t, J = 7.6 Hz, 2H), 7.48−7.35 (m, 3H), 7.16 (d, J = 16.4 Hz, 1H), 7.10 (d, J = 16.4 Hz, 1H), 4.71 (d, J = 17.6 Hz, 1H), 3.98 (d, J = 18.0 Hz, 1H), 2.22 (s, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.8, 158.8, 141.0, 137.1, 136.2, 134.7, 130.4, 129.8, 129.7, 129.2, 128.3, 116.4, 109.0, 49.2, 13.7; ESI-HRMS m/z calcd for $C_{19}H_{17}NO_2S_2Na$ [M + Na]$^+$ 378.0593, found 378.0601.

2-[3-(tert-Butyl)-5-(methylthio)-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6k** [70 mg, 76% yield, R_f = 0.28 (10:1 PE/EA)] was isolated as a yellow solid: mp 95−96 °C; ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.10 (d, J = 6.8 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.57 (t, J = 7.6 Hz, 2H), 4.62 (d, J = 17.6 Hz, 1H), 3.88 (d, J = 17.6 Hz, 1H), 2.18 (s, 3H), 1.29 (s, 9H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.8, 168.4, 137.2, 134.6, 129.7, 129.2, 108.8, 49.4, 35.8, 29.4, 13.6; ESI-HRMS m/z calcd for $C_{15}H_{19}NO_2S_2Na$ [M + Na]$^+$ 332.0749, found 332.0754.

2-[5-(Methylthio)-3-propyl-1,4,2-oxathiazol-5-yl]-1-phenylethan-1-one. Compound **6l** [71 mg, 80% yield, R_f = 0.18 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.10 (d, J = 6.8 Hz, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.57 (t, J = 7.6 Hz, 2H), 4.63 (d, J = 17.6 Hz, 1H), 3.89 (d, J = 17.6 Hz, 1H), 2.61−2.47 (m, 2H), 2.19 (s, 3H), 1.71−1.60 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.7, 159.8, 137.1, 134.6, 129.7, 129.2, 108.6, 49.2, 30.2, 21.8, 13.7, 13.6; ESI-HRMS m/z calcd for $C_{14}H_{17}NO_2S_2Na$ [M + Na]$^+$ 318.0593, found 318.0597.

Ethyl 5-(Methylthio)-5-(2-oxo-2-phenylethyl)-1,4,2-oxathiazole-3-carboxylate. Compound **6m** [64 mg, 66% yield, R_f = 0.14 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 8.11 (d, J = 7.2 Hz, 2H), 7.70 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 2H), 4.69 (d, J = 18.0 Hz, 1H), 4.37 (q, J = 7.2 Hz, 2H), 4.12 (d, J = 18.0 Hz, 1H), 2.24 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 194.5, 158.7, 152.6, 136.8, 134.9, 129.7, 129.2, 112.6, 63.7, 49.9, 14.2, 13.5; ESI-HRMS m/z calcd for $C_{14}H_{15}NO_4S_2Na$ [M + Na]$^+$ 348.0335, found 348.0339.

1-[5-(Methylthio)-3-(p-tolyl)-1,4,2-oxathiazol-5-yl]propan-2-one. Compound **6n** [71 mg, 84% yield, R_f = 0.28 (10:1 PE/EA)] was isolated as a yellow oil: ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ 7.59 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 4.02 (d, J = 18.0 Hz, 1H), 3.56 (d, J = 17.6 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2CO$] δ 202.6, 158.2, 142.6, 130.5, 128.2, 125.8, 108.7, 53.3, 30.6, 21.4, 13.5; ESI-HRMS m/z calcd for $C_{13}H_{15}NO_2S_2Na$ [M + Na]$^+$ 304.0436, found 304.0439.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00156.

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

Accession Codes

CCDC 2041487 and 2041852 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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