Regioselectivity in the Ring Opening of Epoxides: A Metal-Free Cascade C–S/C–O Bond Formation Approach to 1,3-Oxathiolan-2-ylidenes through Heteroannulation of α-Enolic Dithioesters at Room Temperature

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Abstract: An operationally simple and efficient approach to hitherto unreported and synthetically demanding 1,3-oxathiolan-2-ylidenes has been developed. The approach involves a cascade [2+3] heteroannulation of α-enolic dithioesters with epoxides promoted by non-nucleophilic moderate base Cs_2CO_3 at room temperature. Typical features of this strategy include metal-free mild reaction conditions, atom-economy, high yields, and efficacy of forming two consecutive C–S and C–O bonds, and one ring in a single stroke. MeSH is the only by-product, and the stereochemistry of the exocyclic α-oxoketene moiety of 1,3-oxathiolane was assigned to have *Z*-configuration.

Key words: epoxides, oxathiolanes, heteroannulation, metal-free conditions, regioselective, cascade reaction

The design, development and implementation of domino/cascade protocols that provide maximum structural diversity with economies of step, atom, labor, and cost for the rapid generation of function-oriented molecules is a key goal in modern organic synthesis.[1] A pressing challenge for synthetic chemists is to develop new synthetic strategies by improving resource efficiency, avoiding the use of toxic reagents, and reducing the amount of waste and hazardous by-products. The synthesis of heterocycles has become essential in chemical synthesis because they are a vital part of new drug discovery, a major component of the bulk chemical industry, and are indispensable materials in many areas of society.[2] In this context, 1,3-oxathiolanes, an important class of heterocyclic compounds, have a wide range of applications in many industrial fields such as organic semiconductors, photosensitive materials, and light-emitting devices.[3] They have also been utilized in the construction of analogues of biological products such as apricitabine (**I**), lamivudine (**II**), and emtricitabine (**III**), which act as reverse transcriptase inhibitors (RTI) against the HIV virus[4] (Figure 1).

1,3-Oxathiolanes and their derivatives are not only important privileged structural motifs, they are also utilized as synthetic building blocks for the construction of a diverse range of biologically active compounds.[5] For these reasons, the development of new methodologies for the regioselective synthesis of functionalized 1,3-oxathiolanes and their structural analogues continues to be an active area of research in fine chemistry. Among the limited number of approaches used for the construction of 1,3-oxathiolan-2-ylidenes,[6,7] the major route typically involves reaction of 2-mercaptoethanol with α-oxoketene dithioacetals in the presence of strong base.[6] However, most of these transformations involve the use of harsh reaction conditions such as high-boiling solvents, expensive starting material, step-wise synthesis, and they can also suffer from low functional group tolerance.[7] Although the opening of epoxides with carbon, nitrogen, and oxygen nucleophiles is well known,[8a–e] ring opening of epoxides with sulfur nucleophiles is rare,[8f,g] despite the clear synthetic utility. In this context, we report herein a new one-pot method for the regioselective synthesis of 1,3-oxathiolan-2-ylidenes by the coupling of α-enolic dithioesters with epoxides at room temperature.

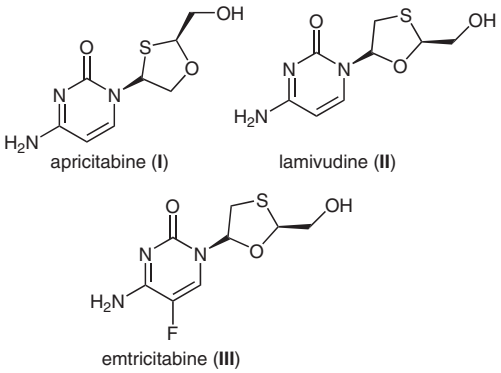

Figure 1 Selected examples of bioactive 1,3-oxathiolanes

Chemical species containing both electrophilic and nucleophilic sites have great potential for the development of novel protocols and diverse molecular entities. Importantly, the suitable selection of synthons is crucial for the success of a protocol. Two such simple polyfunctional chemical species are α-enolic dithioesters **1** and epoxides **2**, both of which can be exploited synthetically (Figure 2).

The continuing interest in the chemistry of these frameworks is mainly due to their nucleophilic and electrophilic centers coupled with their versatile reactivity, making them very useful building blocks in modern organic syn-

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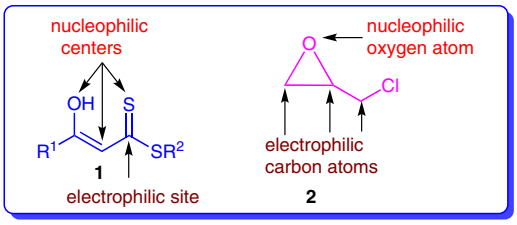
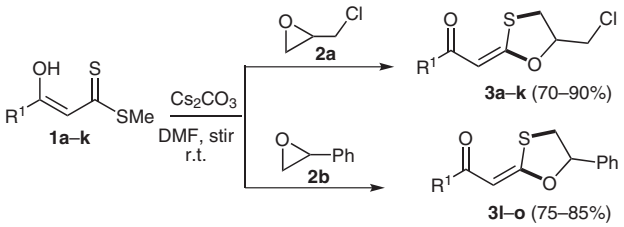


Figure 2 Reactive sites in α-enolic dithioester **1** and epoxide **2**

thesis. Epoxides (oxiranes) constitute a well-known, versatile three-atom synthon with high synthetic potential,[9] and such compounds are highly prone to ring opening and/or nucleophilic substitution reactions with various nucleophiles.[10] Moreover, unsymmetrical substitution of the epoxide allows the introduction of chirality, making these molecules valuable substrates in enantioselective synthesis.

The utility of α-enolic dithioesters as versatile intermediates in organic synthesis has been well-recognized.[11] In a continuation of our ongoing research on the synthetic utility of α-enolic dithioesters for the synthesis of heterocyclic systems,[12,13] we report herein a simple, straightforward, and efficient synthesis of 1,3-oxathiolan-2-ylidenes through [2+3] heteroannulation of α-enolic dithioesters with epoxides. Thus, when α-enolic dithioesters **1** were treated with epoxides **2** in *N*,*N*-dimethylformamide (DMF) in the presence of Cs_2CO_3 at room temperature, the corresponding 1,3-oxathiolan-2-ylidenes **3** were obtained in good to excellent yields (Scheme 1). As an interesting alternative, this two-component cascade process led to the concomitant creation of two new (C–S and C–O) bonds and one ring. To our knowledge, this is the first report on the use of α-enolic dithioesters and epoxides for the synthesis of 1,3-oxathiolan-2-ylidenes.

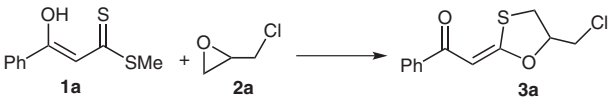


1a: R^1 = Ph, **1b**: R^1 = 4-MeC_6H_4, **1c**: R^1 = 4-$MeOC_6H_4$,
1d: R^1 = 4-BrC_6H_4, **1e**: R^1 = 4-ClC_6H_4, **1f**: R^1 = 2-ClC_6H_4,
1g: R^1 = 2-naphthyl, **1h**: R^1 = 4-$F_3CC_6H_4$,
1i: R^1 = 3,4-$OCH_2OC_6H_3$, **1j**: R^1 = 2-thienyl, **1k**: R^1 = 2-furyl

Scheme 1 Synthesis of 1,3-oxathiolan-2-ylidenes **3a–o**

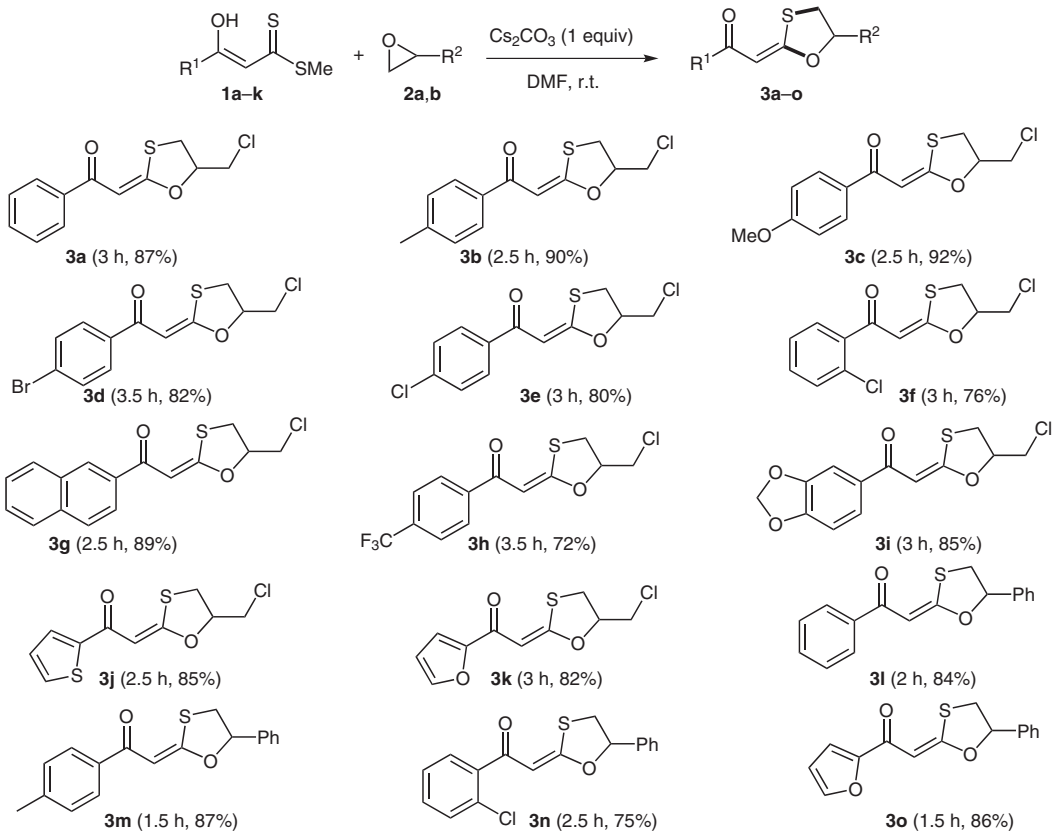
At the outset of our research, we envisioned that 1,3-oxathiolan-2-ylidenes might be formed by the coupling of α-enolic dithioesters with epoxides. Initially, to optimize the reaction conditions for the synthesis of 1,3-oxathiolan-2-ylidenes, methyl 3-hydroxy-3-phenylprop-2-enedithioate (**1a**) and epichlorohydrin (**2a**) were taken as model substrates. Thus, equimolar amounts of test substrates **1a** and **2a** were examined under an array of conditions; the results are listed in Table 1. Generally, the base plays a crucial role in enabling the thiocarbonyl sulfur to act as a strong nucleophile by abstracting the enolic proton of **1**.[13d] A test reaction was performed without any base in ethanol at room temperature to establish the real effectiveness of the base, and it was found that, under these conditions, only a trace amount of the desired product was obtained after 24 hours stirring, with the starting materials remaining entirely unconsumed (Table 1, entry 1). With this result, we then performed the above model reaction in the presence of $NaHCO_3$ in ethanol. Work up of the reaction provided the desired compound **3a** in 30% yield (Table 1, entry 2). To improve the reaction efficiency and yield of **3a**, a range of solvents (MeOH, H_2O, MeCN, THF, and DMF) were evaluated (Table 1, entries 3–7). The use of polar protic solvent MeOH resulted in the formation of product **3a** in 40% yield (Table 1, entry 3), whereas the use of water as the solvent shut down the reaction because of the low solubility of the substrates in this medium (Table 1, entry 4). Further screening of solvents revealed that the reaction proceeded better in polar aprotic solvents, and DMF turned out to be the most suitable solvent for the present cascade annulation (Table 1, entry 7). Other inorganic bases such as Na_2CO_3, K_2CO_3 and Cs_2CO_3 (1 equiv) were screened to check their competence in the reaction (Table 1, entries 8–10) and it was found that all the bases tested afforded the desired product **3a** in good yield; Cs_2CO_3 promoted this transformation more efficiently than other bases, resulting the desired product **3a** in 87% yield within three hours (Table 1, entry 10). Reducing the

Table 1 Optimization of Reaction Conditions[a]



Entry	Base	Solvent	Time (h)	Yield (%)[b]
1	none	EtOH	24	trace
2	$NaHCO_3$	EtOH	24	30
3	$NaHCO_3$	MeOH	24	40
4	$NaHCO_3$	H_2O	24	–[c]
5	$NaHCO_3$	MeCN	12	60
6	$NaHCO_3$	THF	12	55
7	$NaHCO_3$	DMF	10	65
8	Na_2CO_3	DMF	8	70
9	K_2CO_3	DMF	5	75
10	Cs_2CO_3	DMF	3	87
11	Cs_2CO_3[d]	DMF	7	78

[a] Reaction conditions: **1a** (1 mmol), **2a** (1 mmol), base (1 equiv), solvent (5 mL), r.t., stirring.
[b] Isolated pure yield.
[c] No reaction.
[d] Cs_2CO_3 (0.5 equiv).

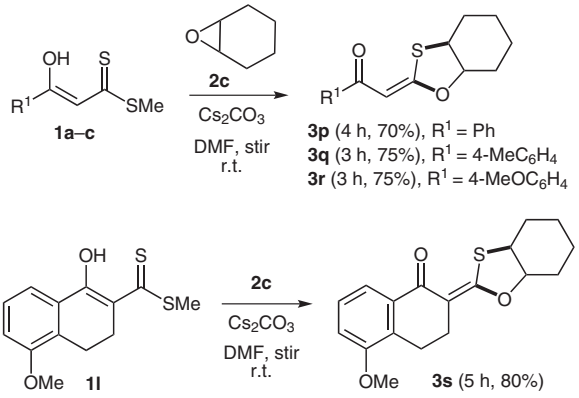


Scheme 2 Substrate scope for the synthesis of **3**

amount of Cs_2CO_3 (0.5 equiv) increased the required reaction time and decreased the yield to 78% (Table 1, entry 11). Thus, the best reaction conditions for the synthesis of **3a** was found to be equimolar amounts of **1a** and **2a** in the presence of 1.0 equivalent Cs_2CO_3 in DMF (5 mL) at room temperature (Table 1, entry 10).

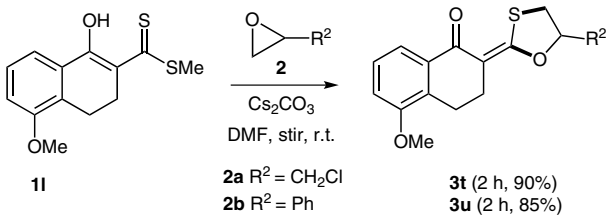
The scope and generality of this process with respect to substrate under the optimized conditions is summarized in Scheme 2. A broad spectrum of α-enolic dithioesters **1**, bearing R^1 as aryl (containing either electron-donating or electron-withdrawing groups), hetaryl, and extended aromatics, and R^2 as chloromethyl and phenyl groups, could be employed to afford 1,3-oxathiolanes **3** in good to excellent yields. All the reactions proceeded smoothly and resulted in the formation of the corresponding products **3** in high yields. The steric and electronic nature of the substituents had no noticeable impact on either the yield or the rate of the reaction. To further investigate the scope of the current method, styrene oxide (**2b**) was employed instead of epichlorohydrin (**2a**), which was tolerated well under the optimized reaction conditions and furnished the desired products in 75–87% yields (**3l**–**o**; Scheme 2).

To illustrate the broad synthetic utility and generality of the developed methodology, we then undertook the formal synthesis of annulated 1,3-oxathiolane. Thus, when α-enolic dithioesters **1a**–**c** and **1l** were separately treated with epoxycyclohexane (**2c**) under the previously described one-pot conditions, annulated 1,3-oxathiolanes **3p**–**s** were obtained in 70–80% yield (Scheme 3).



Scheme 3 Synthesis of annulated 1,3-oxathiolanes **3p**–**s**

We then extended our study by using cyclic α-enolic dithioester **1l** derived from 5-methoxy-α-tetralone as one of the reaction partners with a view to adding a further point of diversity at the 2-position of the 1,3-oxathiolane ring. Thus, when α-enolic dithioester **1l** was treated with either epoxide **2a** or **2b**, under the optimized conditions, the desired oxathiolanes **3t** and **3u** were obtained in 90 and 85% yield, respectively (Scheme 4).



Scheme 4 Synthesis of 1,3-oxathiolanes **3t** and **3u**

The structures of 1,3-oxathiolan-2-ylidenes **3a**–**u** were deduced from their satisfactory spectral (IR, ^{1}H, ^{13}C NMR and HRMS) analysis and unequivocally established by the X-ray single crystal diffraction analysis of **3e** and **3r** as two representative compounds (Figure 3).[14] It is noteworthy that the stereochemistry of the exocyclic double bond of the α-oxoketene moiety was assigned as having *Z*-configuration. The mass spectra of these compounds displayed molecular ion peaks at the expected *m*/*z* values. The introduction of a chloromethyl functional group at the 5-position of the newly formed 1,3-dithiolane is of particular interest because it can act as an effective chemical handle for further functionalization and diversification through metal-catalyzed cross-coupling reactions.

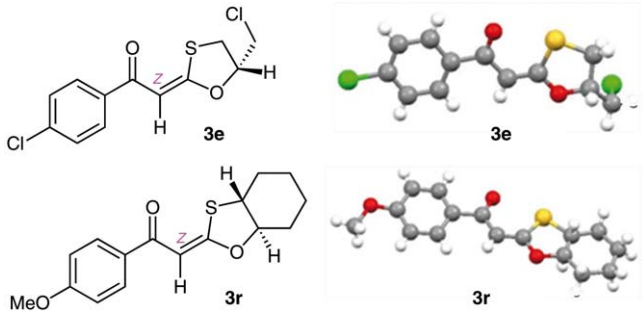
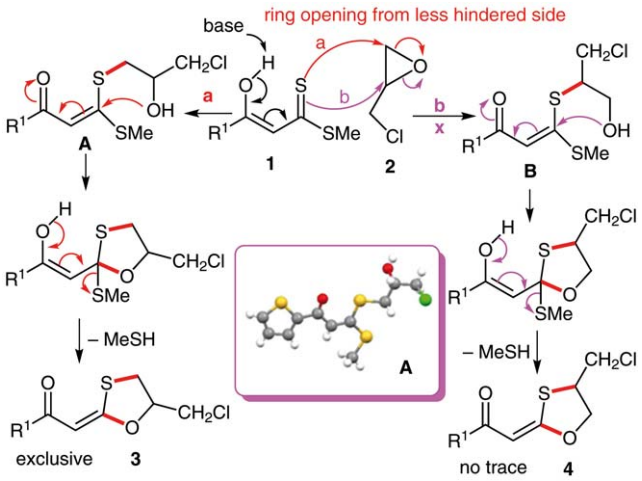


Figure 3 ORTEP diagrams of **3e** and **3r**

On the basis of the above experimental results together with related reports, a plausible reaction scenario for a domino [2+3] heteroannulation is outlined in Scheme 5. We speculate that the reaction occurs as a tandem oxirane-opening/1,3-oxathiolane-closure process. The first step in the mechanism is believed to be the abstraction of an acidic enolic proton of α-enolic dithioester **1** by base followed by regioselective nucleophilic attack of the thiocarbonyl sulfur to the less hindered side of epoxide **2** to generate the open-chain adduct intermediate α-oxoketene dithioacetal **A**. Intermediate **A** then undergoes intramolecular O-cyclization with the extrusion of MeSH to give 1,3-oxathiolan-2-ylidene **3**. The intermediacy of α-oxoketene dithioacetal **A** has been confirmed by its isolation and characterization through spectroscopic (^{1}H and ^{13}C NMR) and X-ray crystallographic analyses.[14] We did not detect the alternative regioisomer **4** even in trace amounts, making this protocol highly regioselective. It was not possible to distinguish between structures **3** or **4** on the basis of NMR and IR spectra alone. The ultimate proof of structure of compound **3** was made by X-ray analysis of two representative compounds **3e** and **3r** (Figure 3).[14]



Scheme 5 Plausible mechanism for the synthesis of 1,3-oxathiolanes **3**

In summary, we have developed an experimentally convenient, straightforward, and regioselective protocol for the synthesis of functionalized 1,3-oxathiolan-2-ylidenes through [2+3] heteroannulation of α-enolic dithioesters with epoxides in the presence of Cs_2CO_3 at room temperature. This transformation avoids the use of metal catalyst and constructs two new bonds (C–S and C–O) and one ring with both reactants being utilized efficiently. Importantly, the presence of the α-oxoketene moiety and the chloromethyl group at the 2- and 5-positions of the 1,3-oxathiolane ring makes these compounds excellent precursors for further derivatization. We expect that this facile and efficient protocol should be of value for both synthetic and medicinal chemists for academic research and practical applications.

Commercially available materials were purchased from Merck, Aldrich, or Fluka and were used as received. THF was distilled over sodium, and other solvents were dried over 4 Å molecular sieves prior to use. α-Enolic dithioesters were prepared by a reported procedure.[7c] IR spectra were recorded with a Varian 3100 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL AL 300 FT NMR spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane. Coupling constants (*J*) are given in hertz (Hz). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets), and m (multiplets). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m). High-resolution mass spectrometry (HRMS) was performed with a Water-Q-Tof premier HAB 213 instrument using the electrospray ionization (ESI) technique. X-ray crystallographic analysis was performed with an X-calibur Oxford CCD diffractometer. All the reactions were monitored by thin-layer chromatography (TLC) using pre-coated sheets of silica gel G/UV-254 of 0.25 mm thickness (Merck 60 F_{254}) using UV light for visualization. Melting points were determined with a Büchi B-540 melting point apparatus and are uncorrected.

(*Z*)-2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-phenylethanone (3a); Typical Procedure

A dry 25 mL round-bottomed flask equipped with a magnetic stir bar was charged with a solution of α-enolic dithioester **1a** (0.210 g, 1 mmol) in DMF (5 mL), and Cs_2CO_3 (0.325 g, 1 mmol) was added. The solution was stirred at r.t. for 10 min, then epichlorohydrin (**2a**; 0.079 mL, 1 mmol) was added slowly to the reaction mixture by using a syringe. The resulting mixture was then stirred at r.t. until the reaction was complete (monitored by TLC; time indicated in Scheme 2), then H_2O (20 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extract was dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude residue thus obtained was purified by column chromatography over silica gel (EtOAc–*n*-hexane) to afford the pure product **3a**.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-phenylethanone (3a)

Yield: 0.220 g (87%); yellow solid; mp 150–152 °C.

IR (KBr): 2924, 1623, 1575, 1519, 765, 680 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.27 (dd, *J* = 11.1, 6.9 Hz, 1 H), 3.38 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.76 (d, *J* = 6.0 Hz, 2 H), 4.96–4.88 (m, 1 H), 6.84 (s, 1 H), 7.53–7.41 (m, 3 H), 7.92 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 42.7, 82.9, 94.9, 128.7, 128.9, 136.5, 138.3, 176.5, 187.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{12}ClO_2S^+$: 255.0241; found: 255.0242.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(*p*-tolyl)ethanone (3b)

Yield: 0.241 g (90%); yellow solid; mp 142–144 °C.

IR (KBr): 3095, 1611, 1598, 1516, 762, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 3.25 (dd, *J* = 10.8, 6.6 Hz, 1 H), 3.36 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.75 (d, *J* = 5.7 Hz, 2 H), 4.94–4.86 (m, 1 H), 6.82 (s, 1 H), 7.82 (d, *J* = 8.1 Hz, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 32.6, 42.8, 82.6, 95.0, 127.4, 129.0, 135.5, 142.6, 175.4, 188.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}ClO_2S^+$: 269.0398; found: 269.0406.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(4-methoxyphenyl)ethanone (3c)

Yield: 0.261 g (92%); yellow solid; mp 155–157 °C.

IR (KBr): 2995, 1620, 1590, 1520, 770, 680 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.24 (dd, *J* = 11.4, 6.9 Hz, 1 H), 3.36 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.75 (d, *J* = 5.7 Hz, 2 H), 3.86 (s, 3 H), 4.94–4.85 (m, 1 H), 6.81 (s, 1 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 7.91 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 42.8, 55.4, 82.6, 95.0, 113.6, 114.0, 129.6, 130.8, 162.7, 175.0, 187.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}ClO_3S^+$: 285.0347; found: 285.0355.

1-(4-Bromophenyl)-2-[5-(chloromethyl)-1,3-oxathiolan-2-ylidene]ethanone (3d)

Yield: 0.272 g (82%); yellow solid; mp 160–162 °C.

IR (KBr): 2925, 1624, 1540, 1456, 790, 694 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.27 (dd, *J* = 11.4, 6.9 Hz, 1 H), 3.38 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.76 (d, *J* = 5.7 Hz, 2 H), 4.97–4.88 (m, 1 H), 6.77 (s, 1 H), 7.57 (d, *J* = 8.4 Hz, 2 H), 7.78 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.8, 42.8, 82.9, 94.9, 129.0, 131.7, 137.0, 176.4, 189.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{11}BrClO_2S^+$: 332.9346; found: 332.9359.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(4-chlorophenyl)ethanone (3e)

Yield: 0.230 g (80%); yellow solid; mp 148–150 °C.

IR (KBr): 2920, 1735, 1675, 1580, 792, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.27 (dd, *J* = 11.4, 6.9 Hz, 1 H), 3.38 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.76 (d, *J* = 5.7 Hz, 2 H), 4.97–4.89 (m, 1 H), 6.78 (s, 1 H), 7.41 (d, *J* = 8.4 Hz, 2 H), 7.85 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.8, 42.7, 83.0, 95.1, 125.5, 127.8, 177.3, 187.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{11}Cl_2O_2S^+$: 288.9851; found: 288.9850.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(2-chlorophenyl)ethanone (3f)

Yield: 0.218 g (76%); yellow solid; mp 140–142 °C.

IR (KBr): 2922, 1732, 1632, 1570, 793, 695 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.29 (dd, *J* = 11.1, 7.2 Hz, 1 H), 3.40 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.76 (d, *J* = 5.4 Hz, 2 H), 4.97–4.88 (m, 1 H), 6.57 (s, 1 H), 7.40–7.39 (m, 3 H), 7.52 (d, *J* = 7.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 42.7, 83.0, 99.2, 126.7, 129.4, 130.2, 131.1, 132.8, 139.5, 175.7, 189.7.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(naphthalen-2-yl)ethanone (3g)

Yield: 0.270 g (89%); yellow solid; mp 152–154 °C.

IR (KBr): 2926, 1625, 1525, 1434, 790, 697 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.29 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.40 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.78 (d, *J* = 5.7 Hz, 2 H), 4.99–4.90 (m, 1 H), 7.01 (s, 1 H), 7.59–7.50 (m, 2 H), 7.95–7.85 (m, 3 H), 8.03 (d, *J* = 8.7 Hz, 1 H), 8.42 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.8, 42.8, 82.8, 95.4, 123.9, 126.5, 127.7, 127.8, 128.2, 128.5, 129.1, 129.4, 130.5, 132.7, 135.1, 175.8, 188.6.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-[4-(trifluoromethyl)phenyl]ethanone (3h)

Yield: 0.231 g (72%); yellow solid; mp 160–162 °C.

IR (KBr): 2920, 1615, 1590, 1480, 790, 660 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.29 (dd, *J* = 11.1, 6.9 Hz, 1 H), 3.40 (dd, *J* = 11.1, 6.9 Hz, 1 H), 3.77 (d, *J* = 5.7 Hz, 2 H), 5.00–4.91 (m, 1 H), 7.70 (d, *J* = 8.1 Hz, 2 H), 8.00 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 42.7, 82.9, 94.9, 128.7, 128.9, 129.2, 136.5, 138.3, 176.5, 187.3.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{11}ClF_3O_2S^+$: 323.0115; found: 323.0121.

1-(Benzo[*d*][1,3]dioxol-5-yl)-2-[5-(chloromethyl)-1,3-oxathiolan-2-ylidene]ethanone (3i)

Yield: 0.253 g (85%); yellow solid; mp 165–167 °C.

IR (KBr): 2918, 1624, 1598, 1489, 791, 655 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.24 (dd, *J* = 11.4, 6.9 Hz, 1 H), 3.36 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.75 (d, *J* = 6.0 Hz, 2 H), 4.94–4.85 (m, 1 H), 6.02 (s, 2 H), 6.75 (s, 1 H), 6.83 (d, *J* = 8.4 Hz, 1 H), 7.50–7.43 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.7, 42.8, 82.6, 95.0, 101.6, 107.7, 107.8, 123.1, 148.0, 150.9, 162.1, 173.6, 182.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}Cl_4O_4S^+$: 299.0139; found: 299.0144.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(thiophen-2-yl)ethanone (3j)
Yield: 0.220 g (85%); yellow solid; mp 155–157 °C.

IR (KBr): 2940, 1690, 1540, 1458, 792, 690 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.26 (dd, *J* = 10.8, 6.9 Hz, 1 H), 3.35 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.75 (d, *J* = 6.0 Hz, 2 H), 4.95–4.86 (m, 1 H), 6.67 (s, 1 H), 7.11–7.08 (m, 1 H), 7.55 (d, *J* = 4.8 Hz, 1 H), 7.63 (d, *J* = 3.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.9, 42.8, 82.9, 95.4, 127.9, 129.6, 132.1, 145.6, 175.2, 181.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{10}H_{10}ClO_2S_2^+$: 260.9805; found: 260.9810.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-1-(furan-2-yl)ethanone (3k)
Yield: 0.200 g (82%); yellow liquid.

IR (KBr): 2924, 1623, 1575, 1469, 781, 680 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.24 (dd, *J* = 10.8, 6.9 Hz, 1 H), 3.37 (dd, *J* = 11.1, 6.6 Hz, 1 H), 3.74 (d, *J* = 5.7 Hz, 2 H), 4.94–4.86 (m, 1 H), 6.50 (s, 1 H), 6.70 (s, 1 H), 7.12 (d, *J* = 3.0 Hz, 1 H), 7.52 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.8, 42.7, 82.6, 95.1, 112.2, 114.8, 145.1, 153.5, 175.1, 177.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{10}H_{10}ClO_3S^+$: 245.0034; found: 245.0030.

1-Phenyl-2-(5-phenyl-1,3-oxathiolan-2-ylidene)ethanone (3l)
Yield: 0.236 g (84%); yellow solid; mp 155–157 °C.

IR (KBr): 2925, 1687, 1577, 1516, 770, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.28 (dd, *J* = 11.1, 9.6 Hz, 1 H); 3.55 (dd, *J* = 11.1, 6.3 Hz, 1 H), 5.61 (dd, *J* = 9.6, 6.3 Hz, 1 H), 6.90 (s, 1 H), 7.50–7.42 (m, 8 H), 7.94 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.3, 85.9, 94.9, 123.6, 126.1, 127.5, 128.4, 128.9, 129.2, 131.9, 136.8, 138.4, 172.7, 188.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{15}O_2S^+$: 283.0787; found: 283.0798.

2-(5-Phenyl-1,3-oxathiolan-2-ylidene)-1-(*p*-tolyl)ethanone (3m)
Yield: 0.257 g (87%); yellow liquid.

IR (KBr): 2926, 1682, 1607, 1495, 758, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.27 (dd, *J* = 9.9, 9.6 Hz, 1 H), 3.54 (dd, *J* = 9.6, 6.6 Hz, 1 H), 5.59 (dd, *J* = 9.6, 7.2 Hz, 1 H), 6.89 (s, 1 H), 7.23 (s, 3 H), 7.40 (s, 4 H), 7.85 (d, *J* = 7.2 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 37.3, 85.7, 94.9, 126.0, 127.6, 128.9, 129.1, 135.9, 136.9, 142.5, 176.3, 188.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{17}O_2S^+$: 297.0944; found: 297.0941.

1-(2-Chlorophenyl)-2-(5-phenyl-1,3-oxathiolan-2-ylidene)ethanone (3n)
Yield: 0.237 g (75%); yellow liquid.

IR (KBr): 2940, 1680, 1565, 1215, 787, 690 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.30 (dd, *J* = 15.9, 9.9 Hz, 1 H), 3.57 (dd, *J* = 11.1, 6.3 Hz, 1 H), 5.62 (dd, *J* = 9.9, 6.3 Hz, 1 H), 6.63 (s, 1 H), 7.34–7.29 (m, 2 H), 7.42 (s, 6 H), 7.55 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.3, 86.2, 99.0, 126.1, 126.7, 128.5, 128.9, 129.2, 129.6, 130.1, 130.3, 131.0, 136.6, 176.5, 191.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{14}ClO_2S^+$: 317.0398; found: 317.0392.

1-(Furan-2-yl)-2-(5-phenyl-1,3-oxathiolan-2-ylidene)ethanone (3o)
Yield: 0.233 g (86%); yellow solid; mp 138–140 °C.

IR (KBr): 2923, 1680, 1523, 1516, 777, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.27 (dd, *J* = 11.1, 9.9 Hz, 1 H), 3.55 (dd, *J* = 11.4, 6.3 Hz, 1 H), 5.60 (dd, *J* = 9.3, 6.3 Hz, 1 H), 6.51 (s, 1 H), 6.77 (s, 1 H), 7.13 (d, *J* = 3.3 Hz, 1 H), 7.41 (s, 5 H), 7.52 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.4, 85.9, 94.7, 112.1, 114.6, 126.0, 128.8, 129.1, 136.7, 145.0, 153.7, 176.1, 178.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{13}O_3S^+$: 273.0580; found: 273.0588.

2-(Hexahydrobenzo[*d*][1,3]oxathiol-2-ylidene)-1-phenylethanone (3p)
Yield: 0.182 g (70%); yellow solid; mp 180–182 °C.

IR (KBr): 2920, 1625, 1519, 1230, 780, 620 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.66–1.37 (m, 4 H), 2.01–1.89 (m, 2 H), 2.40–2.27 (m, 2 H), 3.11 (dd, *J* = 11.7, 8.4 Hz, 1 H), 3.81 (dd, *J* = 11.4, 8.1 Hz, 1 H), 6.81 (s, 1 H), 7.51–7.40 (m, 3 H), 7.91 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.7, 25.1, 28.0, 29.6, 50.5, 88.9, 95.7, 127.4, 128.3, 128.9, 131.8, 138.7, 174.8, 191.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{17}O_2S^+$: 261.0944; found: 261.0944.

2-(Hexahydrobenzo[*d*][1,3]oxathiol-2-ylidene)-1-(*p*-tolyl)ethanone (3q)
Yield: 0.205 g (75%); yellow solid; mp 185–187 °C.

IR (KBr): 2921, 1620, 1518, 1236, 784, 623 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.65–1.49 (m, 4 H), 1.95–1.87 (m, 2 H), 2.55–2.26 (m, 5 H), 3.07 (dd, *J* = 20.4, 11.7 Hz, 1 H), 3.77 (dd, *J* = 19.2, 11.1 Hz, 1 H), 6.79 (s, 1 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 7.81 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5, 23.7, 25.1, 28.0, 29.6, 50.4, 88.8, 95.6, 127.5, 129.0, 136.1, 142.3, 165.5, 176.0, 188.5.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{19}O_2S^+$: 275.1100; found: 275.1102.

2-(Hexahydrobenzo[*d*][1,3]oxathiol-2-ylidene)-1-(4-methoxyphenyl)ethanone (3r)
Yield: 0.217 g (75%); yellow solid; mp 182–184 °C.

IR (KBr): 2922, 1628, 1515, 1485, 790, 620 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.54–1.25 (m, 4 H), 2.00–1.88 (m, 2 H), 2.55–2.26 (m, 2 H), 3.08 (dd, *J* = 11.7, 8.4 Hz, 1 H), 3.77 (dd, *J* = 11.1, 3.6 Hz, 1 H), 3.85 (s, 3 H), 6.78 (s, 1 H), 6.92 (d, *J* = 8.7 Hz, 2 H), 7.90 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.7, 25.1, 28.1, 29.6, 50.5, 55.4, 88.6, 95.5, 113.5, 129.5, 129.8, 131.7, 162.5, 175.6, 187.6.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{19}O_3S^+$: 291.1049; found: 291.1056.

2-(Hexahydrobenzo[*d*][1,3]oxathiol-2-ylidene)-5-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (3s)
Yield: 0.252 g (80%); yellow liquid.

IR (KBr): 2912, 1656, 1540, 1490, 780, 635 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.41–1.25 (m, 4 H), 2.00–1.87 (m, 2 H), 2.41–2.25 (m, 2 H), 2.93–2.78 (m, 4 H), 3.13–3.04 (m, 1 H), 3.85–3.74 (m, 4 H), 6.97 (d, *J* = 8.1 Hz, 1 H), 7.69 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4; 23.2, 23.7, 25.1, 28.1, 29.7, 50.7, 55.6, 88.6, 106.9, 113.3, 119.0, 126.6, 131.2, 135.3, 155.9, 168.0, 186.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{21}O_3S^+$: 317.1206; found: 317.1213.

2-[5-(Chloromethyl)-1,3-oxathiolan-2-ylidene]-5-methoxy-3,4-dihydronaphthalen-1(2*H*)-one (3t)
Yield: 0.279 g (90%); yellow liquid.

IR (KBr): 2944, 1674, 1575, 1474, 792, 697 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.87 (s, 4 H), 3.24 (dd, *J* = 11.4, 6.9 Hz, 1 H), 3.37 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.77 (dd, *J* = 5.4, 1.5 Hz, 2 H), 3.86 (s, 3 H), 4.94–4.85 (m, 1 H), 6.99 (d, *J* = 8.1 Hz, 1 H), 7.29 (d, *J* = 7.8 Hz, 1 H), 7.69 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 23.2, 33.4, 43.0, 55.7, 82.6, 106.8, 113.6, 119.0, 126.8, 131.3, 134.9, 156.1, 167.3, 186.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{16}ClO_3S^+$: 311.0503; found: 311.0505.

5-Methoxy-2-(5-phenyl-1,3-oxathiolan-2-ylidene)-3,4-dihydronaphthalen-1(2*H*)-one (3u)
Yield: 0.287 g (85%); yellow liquid.

IR (KBr): 2930, 1686, 1573, 1469, 798, 698 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.89 (s, 4 H), 3.26 (dd, *J* = 11.1, 10.2 Hz, 1 H), 3.53 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.85 (s, 3 H), 5.58 (dd, *J* = 9.9, 6.0 Hz, 1 H), 6.98 (d, *J* = 8.1 Hz, 2 H), 7.41–7.27 (m, 4 H), 7.70 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 23.3, 38.1, 55.6, 85.9, 106.4, 113.4, 126.1, 126.8, 128.8, 131.3, 135.1, 137.2, 156.0, 171.5, 190.8.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{19}O_3S^+$: 339.1049; found: 339.1059.

Intermediate A
Yellow solid; mp 110–112 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3 H), 2.85 (s, 1 H, D_2O exchangeable), 3.32–3.25 (m, 2 H), 3.73–3.70 (m, 2 H), 4.18–4.06 (m, 1 H), 6.69 (s, 1 H), 7.11 (s, 1 H), 7.58 (d, *J* = 4.8 Hz, 1 H), 7.67 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.4, 35.7, 48.1, 70.1, 112.1, 128.0, 130.2, 132.7, 145.7, 168.6, 178.6.

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References

(1) (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115. (c) Tietze, L. F.; Brasche, G.; Gericke, K. M. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, **2006**. (d) Pellissier, H. *Tetrahedron* **2006**, *62*, 2143. (e) Coquerel, Y.; Boddaert, T.; Presset, M.; Mailhol, D.; Rodriguez, J. In *Ideas in Chemistry and Molecular Sciences: Advances in Synthetic Chemistry*; Vol. I; Pignataro, B., Ed.; Wiley-VCH: Weinheim, **2010**, 187. (f) Pellissier, H. *Adv. Synth. Catal.* **2012**, *354*, 237. (g) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442.

(2) (a) Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. *Heterocycles in life and society: An introduction to heterocyclic chemistry, biochemistry and applications*, 2nd ed.; John Wiley & Sons: Chichester, **2011**. (b) Li, J. J. *Heterocyclic Chemistry in Drug Discovery*; John Wiley & Sons: Hoboken, **2013**. (c) Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed.; John Wiley & Sons: Chichester, **2010**. (d) For a special issue, see: *Chem. Rev.* **2004**, *104*, issue 5.

(3) (a) Tokitoh, N.; Suzuki, T.; Itami, A.; Goto, M.; Ando, W. *Tetrahedron Lett.* **1989**, *30*, 1249. (b) Bryce, M. R.; Finn, T.; Batsanov, A. S.; Kataky, R.; Howard, J. A. K.; Lyubchik, S. B. *Eur. J. Org. Chem.* **2000**, 1199. (c) Bryce, M. R.; Coffin, M. A.; Moore, A. J.; Batsanov, A. S.; Howard, J. A. K. *Tetrahedron* **1999**, *55*, 9915. (d) Martin, N.; Orti, E.; Sanchez, L.; Viruela, P. M.; Viruela, R. *Eur. J. Org. Chem.* **1999**, 1239. (e) Clausen, R. P.; Becher, J. *Tetrahedron* **1996**, *52*, 3171. (f) Hansen, T. K.; Bryce, M. R.; Howard, J. A. K.; Yufit, D. S. *J. Org. Chem.* **1994**, *59*, 5324.

(4) (a) Cahn, P.; Cassetti, I.; Wood, R.; Phanuphak, P.; Shiveley, L.; Bethell, R. C.; Sawyer, J. *AIDS* **2006**, *20*, 1261. (b) Fox, Z.; Dragsted, U. B.; Gerstoft, J. *Antiviral Therapy* **2006**, *11*, 761. (c) Khan, N.; Bastola, S. R.; Witter, K. G.; Scheiner, P. *Tetrahedron Lett.* **1999**, *44*, 8989. (d) Ingate, S. T.; Perez-Perez, M.-J.; De Clercq, E.; Balzarini, J.; Camarasa, M.-J. *Antiviral Res.* **1995**, *27*, 281. (e) Ingate, S. T.; Marco, J.; Witvrouw, M.; Pannecouque, C.; De Clercq, E. *Tetrahedron* **1997**, *53*, 17795.

(5) (a) Junjappa, H. *Tetrahedron* **1990**, *46*, 5423. (b) Bhat, L.; Ila, H.; Junjappa, H. *Synthesis* **1993**, 959. (c) Bhat, L.; Ila, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1749. (d) Guidot, J. P.; Gall, T. L. *J. Org. Chem.* **1993**, *58*, 5271. (e) Condreay, L. D.; Condreay, J. P.; Jansen, R. W.; Paff, M. T.; Averett, D. R. *Antimicrob. Agents Chemother.* **1996**, *40*, 520. (f) Bollinger, F. G. Eur. Pat. Appl EP, 11473, **1980**; *Chem. Abstr.* **1981**, *94*, 175100a.

(6) Zhang, S.-J.; Liu, Q.; Chen, Y.-Z. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2000**, *39*, 147.

(7) (a) Purkayastha, M. L.; Chandrasekharan, M.; Vishwakarma, J. N.; Illa, H.; Junjappa, H. *Synthesis* **1993**, 245. (b) Liu, Q.; Xu, B. L.; Zhao, H. W. *Chemical Research in Chinese University* **1994**, *10*, 369. (c) Samuel, R.; Asokan, C. V.; Suma, S.; Chandran, P.; Retnamma, S.; Anabha, E. R. *Tetrahedron Lett.* **2007**, *48*, 8376.

(8) (a) Alam, M.; Wise, C.; Baxter, C. A.; Cleator, E.; Walkinshaw, A. *Org. Process Res. Dev.* **2012**, *16*, 435. (b) Smith, J. G. *Synthesis* **1984**, 629. (c) Pineschi, M. *Eur. J. Org. Chem.* **2006**, 4979. (d) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437. (e) Schneider, C.; Brauner, J. *Eur. J. Org. Chem.* **2001**, 4445. (f) Ozaki, S.; Matsui, E.; Yoshinaga, H.; Kitagawa, S. *Tetrahedron Lett.* **2000**, *41*, 2621. (g) Li, Z.; Zhou, Z.; Li, K.; Wang, L.; Zhou, Q.; Tang, C. *Tetrahedron Lett.* **2002**, *43*, 7609.

(9) (a) Williams, D. R.; Plummer, S. V.; Patnaik, S. *Tetrahedron* **2011**, *67*, 5083. (b) Singh, G. S.; Mollet, K.; D'hooghe, M.; De Kimpe, N. *Chem. Rev.* **2013**, *113*, 1441. (c) Huerou, Y. L.; Doyon, J.; Gree, R. L. *J. Org. Chem.* **1999**, *64*, 6782. (d) Gu, X.-P.; Ikeda, I.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 667. (e) Chen, Y.-L.; Lu, C.-M.; Lee, S.-J.; Kuo, D.-H.; Chen, I.-L.; Wang, T.-C.; Tzeng, C.-C. *Bioorg. Med. Chem.* **2005**, *13*, 5710. (f) Toda, T.; Karikomi, M.; Ohshima, M.; Yoshida, M. *Heterocycles* **1992**, *33*, 511.

(10) (a) Bellur, E.; Bottcher, D.; Bornscheuer, U. T.; Langer, P. *Tetrahedron: Asymmetry* **2006**, *17*, 892. (b) Maslak, V.; Matovic, R.; Saicic, R. N. *Tetrahedron* **2004**, *60*, 8957. (c) Madhusudhan, G.; Reddy, G. O.; Rajesh, T.; Ramanatham, J.; Dubey, P. K. *Tetrahedron Lett.* **2008**, *49*, 3060. (d) Zhang, X.; Chen, W.; Zhao, C.; Li, C.; Wu, X.; Chen, Z. *Synth. Commun.* **2010**, *40*, 3654. (e) Osa, Y.; Hikima, Y.; Sato, Y.; Takino, K.; Ida, Y.; Hirono, S.;

Nagase, H. *J. Org. Chem.* **2005**, *70*, 5737. (f) Martin, B. P.; Cooper, M. E.; Donald, D. K.; Guile, S. D. *Tetrahedron Lett.* **2006**, *47*, 7635. (g) Suzdalev, K. F.; Denkina, S. F.; Borodkin, G. S.; Tkachev, V. V.; Kiskin, M. A.; Kletsky, M. E.; Burov, O. N. *Tetrahedron* **2011**, *67*, 8775. (h) Zhang, Y.; Wang, M.; Li, P.; Wang, L. *Org. Lett.* **2012**, *14*, 2206.

(11) (a) Singh, O. M.; Devi, N. S.; Thokchom, D. S.; Sharma, G. J. *Eur. J. Med. Chem.* **2010**, *45*, 2250. (b) Samuel, R.; Chandran, P.; Retnamma, S.; Sasikala, K. A.; Sridevi, N. K.; Anabha, E. R.; Asokan, C. V. *Tetrahedron* **2008**, *64*, 5944. (c) Peruncheralathan, S.; Khan, T. A.; Illa, H.; Junjappa, H. *J. Org. Chem.* **2005**, *70*, 10030. (d) Singh, M. S.; Nandi, G. C.; Chanda, T. *RSC Adv.* **2013**, *3*, 14183.

(12) (a) Nandi, G. C.; Samai, S.; Singh, M. S. *J. Org. Chem.* **2010**, *75*, 7785. (b) Nandi, G. C.; Samai, S.; Singh, M. S. *J. Org. Chem.* **2011**, *76*, 8009. (c) Chowdhury, S.; Nandi, G. C.; Samai, S.; Singh, M. S. *Org. Lett.* **2011**, *13*, 3762. (d) Verma, R. K.; Verma, G. K.; Raghuvanshi, K.; Singh, M. S. *Tetrahedron* **2011**, *67*, 584.

(13) Recent papers: (a) Verma, R. K.; Verma, G. K.; Shukla, G.; Nagaraju, A.; Singh, M. S. *ACS Comb. Sci.* **2012**, *14*, 224. (b) Nandi, G. C.; Ila, H.; Junjappa, H.; Singh, M. S. *Eur. J. Org. Chem.* **2012**, 967. (c) Nagaraju, A.; Verma, G. K.; Shukla, G.; Verma, R. K.; Srivastava, A.; Raghuvanshi, K.; Singh, M. S. *Green Chem.* **2013**, *15*, 954. (d) Shukla, G.; Verma, G. K.; Nagaraju, A.; Verma, R. K.; Raghuvanshi, K.; Singh, M. S. *RSC Adv.* **2013**, *3*, 13811. (e) Chowdhury, S.; Chanda, T.; Koley, S.; Ramulu, B. J.; Jones, R. C. F.; Singh, M. S. *Org. Lett.* **2013**, *15*, 5386. (f) Koley, S.; Chowdhury, S.; Chanda, T.; Ramulu, B. J.; Singh, M. S. *Tetrahedron* **2013**, *69*, 8013. (g) Samai, S.; Chanda, T.; Ila, H.; Singh, M. S. *Eur. J. Org. Chem.* **2013**, 4026. (h) Chowdhury, S.; Chanda, T.; Koley, S.; Ramulu, B. J.; Raghuvanshi, K.; Singh, M. S. *Tetrahedron* **2014**, *70*, 914.

(14) CCDC 981652 (**3e**), CCDC 981650 (**3r**) and CCDC 981651 (**A**). Crystallographic data for these compounds can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk.

