

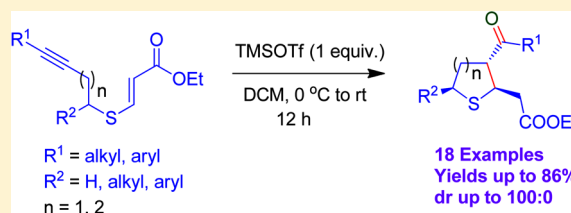
Diastereoselective Synthesis of Substituted Tetrahydrothiophenes and -thiopyrans via Thia-Prins Cyclization Reaction

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S Supporting Information

ABSTRACT: Tetrahydrothiophenes and -thiopyrans have been efficiently synthesized from thioacrylates via thia-Prins cyclization reaction mediated by trimethylsilyltrifluoromethanesulfonate with good diastereoselectivity and in good to high yields.



INTRODUCTION

Tetrahydrothiophenes and -thiopyrans are important structural motifs in many biologically active molecules. The tetrahydrothiophene moiety is found in biologically active compounds such as coenzyme biotin **1**,¹ the cholecystokinin type-B receptor antagonist tetronothiodin **2**,² the nucleoside **3** having potent activity against human cytomegalovirus,³ and glucosidase inhibitor salacinol **4** (Figure 1).⁴ Tetrahydrothiophenes

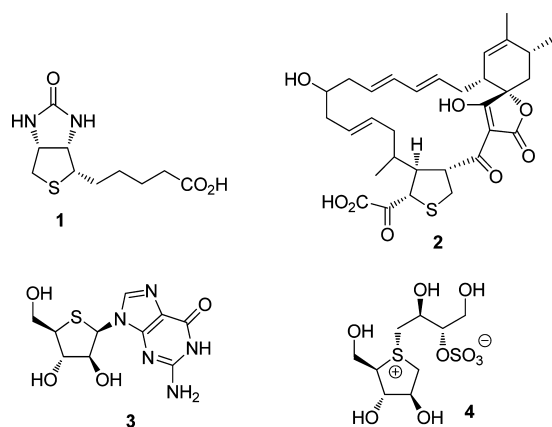


Figure 1. Examples of bioactive tetrahydrothiophenes.

also act as antioxidative agents,⁵ hypercholesterolemic agents,⁶ and plant growth regulators.⁷ Apart from these, they are also used as ligands in catalysis⁸ and substrates for C–C bond forming reactions.⁹ On the other hand, tetrahydrothiopyrans are found in petroleum products.¹⁰ The sulfur analogues of oligosaccharides are known to be potential enzyme inhibitors.¹¹ In addition to these, the tetrahydrothiopyrans can be transformed into a variety of structures.¹² There are numerous methods for the synthesis of sulfur heterocycles, namely, intramolecular ring opening of epoxides by thiolates,¹³ double conjugate addition of sulfide into divinyl ketone,¹⁴ hydrothiolation of nonactivated olefins,¹⁵ Pummerer rearrange-

ment,¹⁶ via (3,5)-thionium-ene cyclization reaction,¹⁷ Michael/Aldol reaction,¹⁸ trapping of thiocarbonyl ylides with suitable dipolarophiles,¹⁹ photolysis of diazo compounds,²⁰ sulfonium ylides,²¹ via oxidative carbon–hydrogen bond functionalization,²² and Baylis–Hillman reaction.²³ Prins cyclization is an important reaction in organic synthesis particularly for the synthesis of cyclic five-²⁴ and six-²⁵ membered oxygen heterocycles. Analogous to Prins cyclization reaction, thia-Prins cyclization leads to five- and six-membered tetrahydrothiophenes and tetrahydrothiopyrans, respectively. Although the Prins cyclization is familiar in organic synthesis, its analogue thia-Prins cyclization is less familiar.²⁶ Recently, we had developed a methodology for the synthesis of a tetrahydrofuran ring system by employing intramolecular Prins cyclization of acrylylenol ethers in which alkyne acts as nucleophiles.^{24d} Herein, we report a general method for the synthesis of tetrahydrothiophenes and -thiopyrans from thioacrylates via intramolecular thia-Prins cyclization reaction.

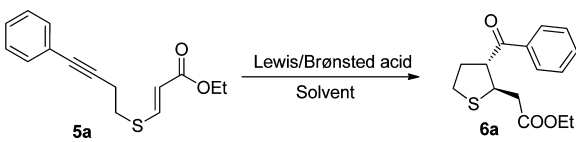
RESULTS AND DISCUSSION

To start with, thioacrylate **5a** was treated with indium(III) triflate in dichloromethane at 0 °C to room temperature, but the reaction gave tetrahydrothiophene **6a** in 25% yield (Table 1, entry 1). The structure of the compound was determined by NMR analysis. The same reaction at room temperature also resulted in the same yield (entry 2). In order to optimize the reaction conditions, the thioacrylate **5a** was subjected to various Lewis and Brønsted acids (Table 1). It was observed from Table 1 that reaction with trimethylsilyltrifluoromethanesulfonate in dichloromethane proceeded well to furnish tetrahydrothiophene **6a** in 77% yield (Table 1, entry 3). Other triflates such as Cu(OTf)₂ gave low yields (Table 1, entry 10), whereas Zn(OTf)₂ yielded only a trace amount of the desired product. Brønsted acids TfOH (entry 6) produced decomposed products, whereas CSA (entry 11) yielded only 10% of the

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Table 1. Optimization of the Reaction



S. No.	Lewis/Brønsted acid (equiv)	time (h)	solvent	temp. (°C)	% yield ^a
1	In(OTf) ₃ (1.0)	24	CH ₂ Cl ₂	0 °C to rt	25
2	In(OTf) ₃ (1.0)	24	CH ₂ Cl ₂	rt	27
3	TMSOTf (1.0)	12	CH ₂ Cl ₂	0 °C to rt	77
4	TMSOTf (1.0)	12	CH ₂ Cl ₂	rt	42
5	BF ₃ ·Et ₂ O (1.0)	12	CH ₂ Cl ₂	0 °C to rt	32
6	TfOH (1.0)	12	CH ₂ Cl ₂	0 °C to rt	d
7	FeCl ₃ (1.0)	24	CH ₂ Cl ₂	0 °C to rt	trace
8	Zn(OTf) ₂ (1.0)	24	CH ₂ Cl ₂	0 °C to rt	trace
9	TMSOTf (1.0)	12	CH ₃ CN	0 °C to rt	52
10	Cu(OTf) ₂ (1.0)	24	CH ₂ Cl ₂	0 °C to rt	22
11	CSA (1.0)	24	CH ₂ Cl ₂	0 °C to rt	10

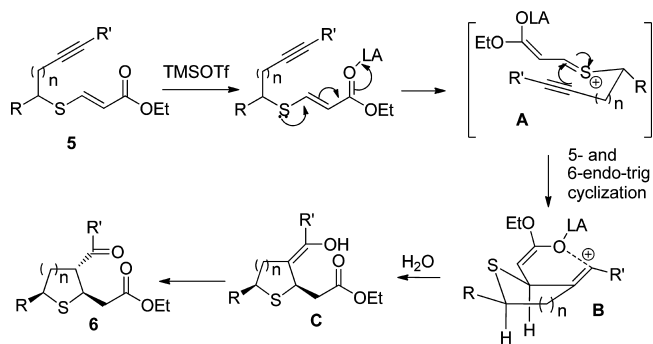
^aYields refer to isolated yield. The compounds were characterized by IR, NMR, and mass spectrometry. d = decomposed product.

desired product. Lewis acid BF₃·Et₂O (entry 5) gave only 32%. On the other hand, metal salt FeCl₃ (entry 7) gave only a trace amount of the product. When the reaction with TMSOTf (entry 5) was carried out at room temperature, it gave only moderate yield, while changing the solvent from dichloromethane to acetonitrile (entry 9) yielded only 52%. Therefore, it has been found that strong Lewis acid TMSOTf in dichloromethane at 0 °C to room temperature stands out the optimum condition for the reaction.

Having obtained the optimized conditions in hand, we further examined the scope of the reaction with a variety of substrates (Table 2). It was observed from Table 2 that the thioacrylates **5a–d** and **5f–l** (entries 1–4 and 6–13) derived from homopropargyl thiol gave tetrahydrothiophenes as single diastereomers in good yields. On the other hand, homologous thioacrylates derived from primary thiols such as **5n–p** yielded mixtures of diastereomers **6n–p** with a ratio ranging from 90:10 to 96:4. The reactions with substrates having electron-withdrawing groups at the ortho position of the aromatic ring present in the alkyne side chain (Table 2, entries 13, 17) decompose under these reaction conditions. On the other hand, the aromatic ring with *p*-substituted electron-withdrawing groups in the alkyne side chain (Table 2, entries 18, 19) gave the desired 2,3 substituted tetrahydrothiopyrans **6r** and **6s** in 81% and 86% yields, respectively, as single diastereomers. The decomposition of **5m** and **5q** might be due the steric factor of the *ortho*-substituted aryl ring of the alkyne side chain. α -Substituted thioacrylates having alkyl and aryl substitutions **5t–u** produced exclusively single diastereomers **6t–u** in good yields. The presence of a strong electron-donating group at the alkyne side chain (Table 2, entry 5) resulted in decomposed products under optimized conditions. The reaction at –78 °C produced neither the desired product nor decomposed product, but starting material was recovered in 96% yield. It was also observed that thioacrylates having an alkyl substituted alkyne side chain (Table 2, entry 4) gave the corresponding tetrahydrothiophene in 61% yield. Unsubstituted alkyne **5v** (entry 22) was found to be unreactive under these reaction conditions. This is attributed to the lower stability of the carbocation **B** (Scheme 1), formed from **5v**.

The reaction is diastereoselective, and the stereochemistry of the trisubstituted tetrahydrothiophenes was determined by 2-D

Scheme 1. Mechanism of the Reaction



nuclear Overhauser effect spectroscopy (NOESY) of **6k** (see the Supporting Information). It showed a clear characteristic NOE correlation between the hydrogens C-2H and C-5H and the absence of NOE between C-3H and C-5H, which clearly indicates that the substituents at 2,5 positions are *cis* to each other and the benzoyl substituent at C-3 is *trans* to the other two substituents. The stereochemistry of the five-membered tetrahydrothiophene products was further confirmed by X-ray crystallographic analysis of **6k** (Figure 2).²⁷

The stereochemistry of 2,3-disubstituted tetrahydrothiopyrans is determined from the vicinal coupling constants of C-2H ($J = 13.6, 11.6, \text{ and } 2.8 \text{ Hz}$) and C-3H ($J = 13.6, 9.6, \text{ and } 4.0 \text{ Hz}$) of compound **6s**. Similarly, the stereochemistry of 2,3,6-trisubstituted tetrahydrothiopyrans was confirmed by NOE spectroscopy of **6t** (see the Supporting Information).

The mechanism of the reaction can be explained as portrayed in Scheme 1. The ester group of thioacrylate **5** is activated by TMSOTf to form thiocarbenium ion **A**, which is then attacked by the alkyne group via a 5-endo-trig and 6-endo-trig cyclization to give carbocation **B**, with five- and six-membered rings ($n = 1$ and 2), respectively. The formation of this five-membered ring is against the Baldwin's rules,²⁸ but in the present situation, the formation of a five-membered ring is possible because of proper alignment of the molecular orbital of the alkyne group with the sp^2 -hybridized thiocarbenium ion.²⁹ The intermediate **B** is stabilized by enolate,^{24d} which is then trapped by water during the workup of the reaction to give enol **C**, which, after tautomerization, gives ketone **6**.

Table 2. TMSOTf-Mediated Intramolecular Thia-Prins Cyclization Reaction

$R^1 = \text{alkyl, aryl}; R^2 = \text{H, alkyl, aryl}; n = 1, 2$

Entry	Thioacrylates 5	Product 6	dr ^a	Yield (%) ^b	Entry	Thioacrylates 5	Product 6	dr ^a	Yield (%) ^b
1			100:0	77	13			---	d
2			100:0	65	14			91:9	69
3			100:0	72	15			90:10	68
4			100:0	61	16			96:4	62
5			---	d ^c	17			---	d
6			100:0	67	18			100:0	81
7			100:0	76	19			100:0	86
8			100:0	82	20			100:0	70
9			100:0	83	21			100:0	65
10			100:0	78	22			---	0
11			100:0	65					
12			100:0	68					

^aThe ratio was determined by ¹H NMR spectroscopy of crude compounds. ^bYield refers to isolated yield. The compounds were characterized by IR, NMR, and mass spectrometry. ^cThe reaction was also performed at -78 °C and recovered starting material in 96% yield. d = Decomposed product.

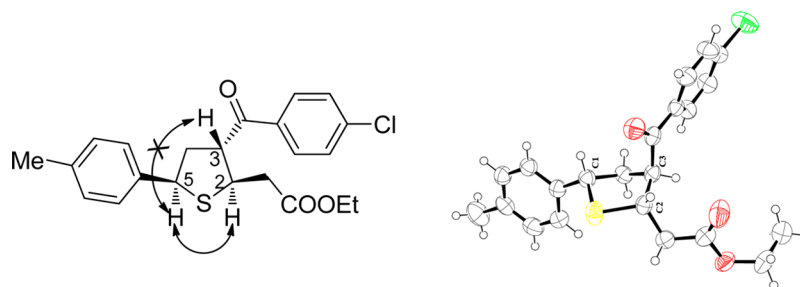


Figure 2. NOE and ORTEP diagrams of 6k.

CONCLUSIONS

In conclusion, we have developed a mild, efficient, and general method for the synthesis of di- and -trisubstituted tetrahydrothiophenes and -thiopyrans via intramolecular thia-Prins cyclization reaction from thioacrylates in good yields. The method is highly diastereoselective.

EXPERIMENTAL SECTION

General Information. All the reagents were of reagent grade (AR grade) and were used as purchased without further purification. Silica gel (60–120 mesh size) was used for column chromatography. Reactions were monitored by TLC on silica gel GF₂₅₄ (0.25 mm). Melting points were recorded in open capillary tubes and are uncorrected. Fourier transform-infrared (FT-IR) spectra were recorded as neat liquid or KBr pellets. NMR spectra were recorded in CDCl₃ with tetramethylsilane as the internal standard for ¹H (600 MHz, 400 MHz) or ¹³C (150 MHz, 100 MHz) NMR. Chemical shifts (δ) are reported in ppm, and spin–spin coupling constants (J) are given in Hz. HRMS spectra were recorded using a Q-TOF mass spectrometer.

General Procedure for Preparation of Thioacrylates. To a solution of thiol (2 mmol) in dichloromethane (3 mL), *N*-methylmorpholine (2 mmol) and ethyl propiolate (2.2 mmol) were added. The reaction mixture was stirred at room temperature, and the progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed on a rotary evaporator and extracted with ethyl acetate (3 \times 10 mL), washed with brine (3 mL), and the combined organic layer was dried over anhydrous Na₂SO₄. The solvent was removed under rotary evaporator, and the crude product was purified on silica gel column chromatography using ethyl acetate and hexane as eluents.

(*E*-Ethyl 3-((4-Phenyl)but-3-yn-1-yl)thio)acrylate (5a). Colorless oil; R_f (hexane/EtOAc 9:1) 0.55; yield 484 mg, 93%; ¹H NMR (400 MHz, CDCl₃) δ 1.19 (t, J = 7.2 Hz, 3 H), 2.72 (t, J = 7.2 Hz, 2 H), 2.97 (t, J = 7.2 Hz, 2 H), 4.09 (q, J = 7.2 Hz, 2 H), 5.75 (d, J = 15.2 Hz, 1 H), 7.20–7.22 (m, 3 H), 7.32–7.44 (m, 2 H), 7.63 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 20.2, 31.3, 60.4, 82.7, 86.9, 114.6, 123.3, 128.2, 128.4, 131.8, 146.1, 165.3. IR (KBr, neat) 2982, 2932, 1712, 1578, 1367, 1170, 1035, 947, 757 cm⁻¹; HRMS (ESI) calcd. for C₁₃H₁₇O₂S (M + H)⁺ 261.0944, found 261.0945.

(*E*-Ethyl 3-((4-(*p*-Tolyl)but-3-yn-1-yl)thio)acrylate (5b). Colorless oil; R_f (hexane/EtOAc 9:1) 0.55; yield 449 mg, 82%; ¹H NMR (400 MHz, CDCl₃) δ 1.26 (t, J = 7.2 Hz, 3 H), 2.32 (s, 3 H), 2.77 (t, J = 7.2 Hz, 2 H), 3.03 (t, J = 7.2 Hz, 2 H), 4.17 (q, J = 7.2 Hz, 2 H), 5.81 (d, J = 15.2 Hz, 1 H), 7.08 (d, J = 7.6 Hz, 2 H), 7.29 (d, J = 8.0 Hz, 2 H), 7.71 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 20.3, 21.6, 31.4, 60.4, 82.7, 86.1, 114.5, 120.2, 129.2, 131.6, 138.2, 146.2, 165.4. IR (KBr, neat) 2980, 2926, 1706, 1581, 1159, 1037, 946, 701 cm⁻¹; HRMS (ESI) calcd. for C₁₆H₁₉O₂S (M + H)⁺ 275.1100, found 275.1102.

(*E*-Ethyl 3-((4-(4-Chlorophenyl)but-3-yn-1-yl)thio)acrylate (5c). Colorless oil; R_f (hexane/EtOAc 9:1) 0.56; yield 506 mg, 86%; ¹H NMR (400 MHz, CDCl₃) δ 1.27 (t, J = 7.2 Hz, 3 H), 2.79 (t, J = 7.2 Hz, 2 H), 3.05 (t, J = 7.2 Hz, 2 H), 4.17 (q, J = 7.2 Hz, 2 H), 5.82 (d, J = 15.2 Hz, 1 H), 7.26 (d, J = 8.8 Hz, 1 H), 7.32 (d, J = 8.8 Hz, 1 H),

7.71 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 20.3, 31.2, 60.5, 81.6, 88.0, 114.6, 121.8, 128.7, 133.0, 134.2, 146.1, 165.3; IR (KBr, neat) 2982, 2927, 1705, 1584, 1484, 1254, 1164, 1039, 828, 702 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₁₆ClO₂S (M + H)⁺ 295.0554, found 295.0553.

(*E*-Ethyl 3-((1-Phenylnon-3-yn-1-yl)thio)acrylate (5d). Colorless oil; R_f (hexane/EtOAc 9:1) 0.71; yield 594 mg, 84%; ¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, J = 7.2 Hz, 3 H), 1.28 (t, J = 7.2 Hz, 3 H), 1.29–1.39 (m, 6 H), 1.43–1.51 (m, 2 H), 2.12–2.17 (m, 2 H), 2.50–2.55 (m, 2 H), 2.94 (t, J = 7.2 Hz, 2 H), 4.18 (q, J = 7.2 Hz, 2 H), 5.78 (d, J = 15.2 Hz, 1 H), 7.69 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.2, 14.5, 18.8, 19.5, 22.7, 28.7, 28.9, 31.5, 31.8, 60.3, 76.9, 82.9, 114.3, 146.4, 165.4; IR (KBr, neat) 2928, 2860, 1709, 1583, 1254, 1164, 1040, 831 cm⁻¹; HRMS (ESI) calcd. for C₁₅H₂₅O₂S (M + H)⁺ 269.1570, found 269.1566.

(*E*-Ethyl 3-((4-(4-Methoxyphenyl)but-3-yn-1-yl)thio)acrylate (5e). Colorless oil; R_f (hexane/EtOAc 9:1) 0.52; yield 412 mg, 71%; ¹H NMR (400 MHz, CDCl₃) δ 1.19 (t, J = 7.6 Hz, 3 H), 2.69 (t, J = 7.2 Hz, 2 H), 2.96 (t, J = 7.2 Hz, 2 H), 3.71 (s, 3 H), 4.09 (q, J = 7.2 Hz, 2 H), 5.74 (d, J = 15.2 Hz, 1 H), 6.73 (d, J = 8.4 Hz, 2 H), 7.26 (d, J = 8.8 Hz, 2 H), 7.64 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.4, 20.2, 31.4, 55.4, 60.4, 82.4, 85.3, 114.0, 114.4, 115.3, 133.1, 146.2, 159.5, 165.3; IR (KBr, neat) 2931, 2837, 1706, 1582, 1509, 1300, 1247, 1169, 1035, 832 cm⁻¹; HRMS (ESI) calcd. for C₁₆H₁₈O₃S (M + H)⁺ 291.1049, found 291.1050.

(*E*-Ethyl 3-((6-Phenylhex-5-yn-3-yl)thio)acrylate (5f). Colorless oil; R_f (hexane/EtOAc 9:1) 0.58; yield 484 mg, 84%; ¹H NMR (400 MHz, CDCl₃) δ 1.07 (t, J = 7.2 Hz, 3 H), 1.26 (t, J = 7.2 Hz, 3 H), 1.72–1.82 (m, 1 H), 1.91–2.01 (m, 1 H), 2.80 (dd, J = 12.0 and 5.6 Hz, 2 H), 3.19 (p, J = 6.0 Hz, 1 H), 4.16 (q, J = 7.2 Hz, 2 H), 5.86 (d, J = 15.2 Hz, 1 H), 7.27–7.29 (m, 3 H), 7.39–7.42 (m, 2 H), 7.76 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 11.6, 14.5, 26.1, 26.9, 48.2, 60.4, 83.2, 86.2, 114.9, 123.4, 128.1, 128.4, 131.8, 146.4, 165.5; IR (KBr, neat) 2978, 2930, 1715, 1576, 1490, 1301, 1157, 1036, 948, 757 cm⁻¹; HRMS (ESI) calcd. for C₁₇H₂₁O₂S (M + H)⁺ 289.1257, found 289.1257.

(*E*-Ethyl 3-((1,4-Diphenyl)but-3-yn-1-yl)thio)acrylate (5g). Colorless oil; R_f (hexane/EtOAc 9:1) 0.57; yield 638 mg, 95%; ¹H NMR (400 MHz, CDCl₃) δ 1.23 (t, J = 7.2 Hz, 3 H), 3.07 (dd, J = 6.4 and 1.6 Hz, 2 H), 4.12 (q, J = 7.2 Hz, 2 H), 4.44 (t, J = 6.8 Hz, 1 H), 5.83 (d, J = 15.6 Hz, 1 H), 7.25–7.27 (m, 3 H), 7.29–7.33 (m, 3 H), 7.38 (t, J = 7.2 Hz, 2 H), 7.42–7.44 (m, 3 H), 7.64 (d, J = 15.2 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 28.2, 50.4, 60.5, 83.9, 85.9, 115.6, 123.3, 127.9, 128.2, 128.3, 128.4, 129.1, 131.8, 139.7, 145.5, 165.4; IR (KBr, neat) 2978, 2923, 1705, 1582, 1449, 1256, 1163, 1035, 754 cm⁻¹; HRMS (ESI) calcd. for C₂₁H₂₁O₂S (M + H)⁺ 337.1257, found 337.1255.

(*E*-Ethyl 3-((1-(3-Bromophenyl)-4-phenyl)but-3-yn-1-yl)thio)acrylate (5h). Colorless oil; R_f (hexane/EtOAc 9:1) 0.58; yield 662 mg, 80%; ¹H NMR (400 MHz, CDCl₃) δ 1.24 (t, J = 7.2 Hz, 3 H), 3.04 (dd, J = 6.4 and 5.6 Hz, 2 H), 4.14 (q, J = 7.2 Hz, 2 H), 4.38 (t, J = 6.8 Hz, 1 H), 5.81 (d, J = 15.2 Hz, 1 H), 7.15–7.28 (m, 3 H), 7.33–7.38 (m, 3 H), 7.45 (d, J = 7.6 Hz, 1 H), 7.60 (d, J = 15.2 Hz, 1 H), 7.62 (s, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 28.1, 49.7, 60.5, 84.3, 85.3, 116.1, 123.0, 123.1, 126.6, 128.3, 128.4, 130.5, 131.0, 131.5, 131.8, 141.9, 144.6, 165.2; IR (KBr, neat) 2983, 2922, 1705, 1581,

1478, 1256, 1164, 1036, 949, 759 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{20}\text{BrO}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 415.0362, found 415.0341.

(*E*)-Ethyl 3-((1-(4-Bromophenyl)-4-phenylbut-3-yn-1-yl)thio)acrylate (**5i**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.58; yield 729 mg, 88%; ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 3.03 (dd, $J = 6.0$ and 5.2 Hz, 2 H), 4.13 (q, $J = 7.2$ Hz, 2 H), 4.39 (t, $J = 7.2$ Hz, 1 H), 5.80 (d, $J = 15.6$ Hz, 1 H), 7.25–7.28 (m, 3 H), 7.31–7.33 (m, 3 H), 7.49 (d, $J = 8.4$ Hz, 2 H), 7.59 (d, $J = 15.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 27.9, 49.6, 60.5, 84.1, 85.4, 116.0, 122.3, 123.1, 128.3, 128.4, 129.6, 131.8, 132.1, 138.7, 144.7, 165.2; IR (KBr, neat) 2982, 1712, 1582, 1484, 1254, 1164, 1038, 830, 757 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{20}\text{BrO}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 415.0362, found 415.0360.

(*E*)-Ethyl 3-((1-(4-Chlorophenyl)-4-phenylbut-3-yn-1-yl)thio)acrylate (**5j**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.59; yield 607 mg, 82%; ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 3.04 (dd, $J = 6.4$ and 5.6 Hz, 2 H), 4.13 (q, $J = 7.2$ Hz, 2 H), 4.40 (t, $J = 7.2$ Hz, 1 H), 5.80 (d, $J = 15.2$ Hz, 1 H), 7.25–7.28 (m, 3 H), 7.31–7.35 (m, 2 H), 7.36–7.39 (m, 4 H), 7.59 (d, $J = 15.2$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.4, 28.0, 49.5, 60.5, 84.1, 85.4, 116.0, 123.1, 128.3, 128.4, 129.1, 129.2, 131.8, 134.1, 138.1, 144.8, 165.2; IR (KBr, neat) 2983, 2925, 1705, 1583, 1490, 1254, 1164, 1031, 830, 758 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{20}\text{ClO}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 371.0867, found 371.0866.

(*E*)-Ethyl 3-((4-(4-Chlorophenyl)-1-(*p*-tolyl)but-3-yn-1-yl)thio)acrylate (**5k**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.61; yield 599 mg, 78%; ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 2.33 (s, 3 H), 3.03 (d, $J = 6.4$ Hz, 2 H), 4.11 (q, $J = 7.2$ Hz, 2 H), 4.40 (t, $J = 7.2$ Hz, 1 H), 5.82 (d, $J = 15.6$ Hz, 1 H), 7.16 (d, $J = 7.2$ Hz, 2 H), 7.23–7.26 (m, 4 H), 7.29 (d, $J = 7.2$ Hz, 2 H), 7.64 (d, $J = 15.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 21.3, 28.1, 50.0, 60.4, 82.6, 87.1, 115.4, 121.8, 127.6, 128.6, 129.7, 133.0, 134.1, 136.4, 138.1, 145.5, 165.3; IR (KBr, neat) 2982, 2926, 1707, 1580, 1483, 1252, 1164, 1039, 827, 710 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{22}\text{ClO}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 385.1024, found 385.1025.

(*E*)-Ethyl 3-((4-Phenyl-1-(*p*-tolyl)but-3-yn-1-yl)thio)acrylate (**5l**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.62; yield 562 mg, 93%; ^1H NMR (600 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 2.34 (s, 3 H), 3.04 (dd, $J = 4.8$ and 2.8 Hz, 2 H), 4.12 (q, $J = 7.2$ Hz, 2 H), 4.40 (t, $J = 7.2$ Hz, 1 H), 5.82 (d, $J = 15.0$ Hz, 1 H), 7.17 (d, $J = 7.8$ Hz, 2 H), 7.24–7.27 (m, 3 H), 7.30–7.34 (m, 4 H), 7.65 (d, $J = 15.0$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 21.3, 28.2, 50.2, 60.4, 83.7, 86.1, 115.5, 123.4, 127.7, 128.2, 128.4, 129.7, 131.8, 136.6, 138.1, 145.7, 165.4; IR (KBr, neat) 2983, 22913, 2358, 1706, 1580, 1449, 1302, 1257, 1166, 1040, 829, 694 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{23}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 351.1413, found 351.1411.

(*E*)-Methyl 2-(4-(3-Ethoxy-3-oxoprop-1-en-1-yl)thio)-4-phenylbut-1-yn-1-ylbenzoate (**5m**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.39; yield 709 mg, 90%; ^1H NMR (400 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 3.15 (d, $J = 7.2$ Hz, 2 H), 3.86 (s, 3 H), 4.12 (q, $J = 7.2$ Hz, 2 H), 4.49 (t, $J = 7.2$ Hz, 1 H), 5.83 (d, $J = 15.2$ Hz, 1 H), 7.28–7.41 (m, 6 H), 7.45 (d, $J = 7.2$ Hz, 2 H), 7.64 (d, $J = 15.2$ Hz, 1 H), 7.88 (d, $J = 8.0$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.4, 28.4, 50.2, 52.3, 60.4, 82.3, 91.3, 115.6, 123.7, 127.9, 128.3 (2C), 129.0, 130.4, 131.7, 132.0, 134.6, 139.6, 145.4, 165.3, 166.8; IR (KBr, neat) 2985, 2899, 2230, 1728, 1580, 1440, 1300, 1164, 1036, 755 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{23}\text{H}_{23}\text{O}_4\text{S}$ ($\text{M} + \text{H}$)⁺ 395.1312, found 395.1312.

(*E*)-Ethyl 3-((5-Phenylpent-4-yn-1-yl)thio)acrylate (**5n**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.60; yield 444 mg, 81%; ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3 H), 1.93–1.99 (m, 2 H), 2.55 (t, $J = 7.2$ Hz, 2 H), 2.97 (t, $J = 7.2$ Hz, 2 H), 4.17 (q, $J = 7.2$ Hz, 2 H), 5.83 (d, $J = 15.2$ Hz, 1 H), 7.26–7.28 (m, 3 H), 7.40–7.43 (m, 2 H), 7.69 (d, $J = 15.2$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.4, 18.6, 27.7, 30.8, 60.3, 82.0, 88.2, 114.1, 123.6, 127.9, 128.3, 131.7, 146.3, 165.3; IR (KBr, neat) 2984, 2842, 2225, 1708, 1582, 1440, 1256, 1164, 1037, 952, 758 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{19}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 275.1100, found 275.1100.

(*E*)-Ethyl 3-((5-(*p*-Tolyl)pent-4-yn-1-yl)thio)acrylate (**5o**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.58; yield 548 mg, 95%; ^1H NMR

(400 MHz, CDCl_3) δ 1.27 (t, $J = 7.2$ Hz, 3 H), 1.93–2.00 (m, 2 H), 2.56 (t, $J = 6.8$ Hz, 2 H), 2.99 (t, $J = 6.8$ Hz, 2 H), 4.17 (q, $J = 7.2$ Hz, 2 H), 5.82 (d, $J = 15.2$ Hz, 1 H), 7.10 (d, $J = 8.0$ Hz, 2 H), 7.30 (d, $J = 8.4$ Hz, 2 H), 7.69 (d, $J = 15.2$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 18.7, 21.6, 27.9, 31.0, 60.4, 82.1, 87.5, 114.3, 120.6, 129.2, 131.7, 138.0, 146.5, 165.5; IR (KBr, neat) 2983, 2923, 2358, 1706, 1580, 1446, 1298, 1165, 1038, 825 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{21}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 289.1257, found 289.1251.

(*E*)-Ethyl 3-((5-(4-Chlorophenyl)pent-4-yn-1-yl)thio)acrylate (**5p**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.60; yield 566 mg, 92%; ^1H NMR (400 MHz, CDCl_3) δ 1.27 (t, $J = 7.2$ Hz, 3 H), 1.94–2.01 (m, 2 H), 2.56 (t, $J = 6.8$ Hz, 2 H), 2.98 (t, $J = 7.2$ Hz, 2 H), 4.18 (q, $J = 7.2$ Hz, 2 H), 5.82 (d, $J = 14.8$ Hz, 1 H), 7.26 (d, $J = 8.4$ Hz, 2 H), 7.33 (d, $J = 8.4$ Hz, 2 H), 7.69 (d, $J = 14.8$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 18.7, 27.7, 30.9, 60.4, 81.0, 89.4, 114.3, 122.1, 128.7, 133.0, 134.0, 146.3, 165.5; IR (KBr, neat) 2925, 2844, 1706, 1581, 1482, 1255, 1164, 1040, 830 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{18}\text{ClO}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 309.0711, found 309.0711.

(*E*)-Ethyl 3-((5-(2-Nitrophenyl)pent-4-yn-1-yl)thio)acrylate (**5q**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.38; yield 484 mg, 76%; ^1H NMR (400 MHz, CDCl_3) δ 1.22 (t, $J = 6.8$ Hz, 3 H), 1.99–2.06 (m, 2 H), 2.66 (t, $J = 6.8$ Hz, 2 H), 3.05 (t, $J = 7.2$ Hz, 2 H), 4.17 (q, $J = 7.2$ Hz, 2 H), 5.83 (d, $J = 15.2$ Hz, 1 H), 7.39–7.45 (m, 1 H), 7.54 (t, $J = 8.4$ Hz, 1 H), 7.61 (d, $J = 8.4$ Hz, 1 H), 7.69 (d, $J = 15.2$ Hz, 1 H), 8.00 (d, $J = 8.0$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 19.0, 27.5, 30.8, 60.4, 77.5, 97.1, 114.3, 119.0, 121.2, 124.7, 128.4, 132.8, 135.0, 146.4, 165.5; IR (KBr, neat) 2921, 2850, 2230, 1703, 1579, 1460, 1260, 1158, 1032, 750 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{18}\text{NO}_4\text{S}$ ($\text{M} + \text{H}$)⁺ 320.0951, found 320.0950.

(*E*)-Ethyl 3-((5-(4-Nitrophenyl)pent-4-yn-1-yl)thio)acrylate (**5r**). Pale yellow semisolid; R_f (hexane/EtOAc 9:1) 0.48; yield 530 mg, 83%; ^1H NMR (400 MHz, CDCl_3) δ 1.28 (t, $J = 6.8$ Hz, 3 H), 1.98–2.05 (m, 2 H), 2.63 (t, $J = 6.4$ Hz, 2 H), 2.99 (t, $J = 6.8$ Hz, 2 H), 4.19 (q, $J = 6.8$ Hz, 2 H), 5.83 (d, $J = 15.2$ Hz, 1 H), 7.55 (d, $J = 8.8$ Hz, 2 H), 7.69 (d, $J = 15.2$ Hz, 1 H), 8.17 (d, $J = 8.8$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 18.8, 27.5, 30.9, 60.5, 80.6, 94.4, 114.4, 123.7, 130.7, 132.5, 146.2, 147.0, 165.4; IR (KBr, neat) 2933, 2853, 2228, 1704, 1585, 1518, 1437, 1344, 1254, 1165, 1039, 848, 750 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{18}\text{NO}_4\text{S}$ ($\text{M} + \text{H}$)⁺ 320.0951, found 320.0955.

(*E*)-Methyl 4-(5-(3-Ethoxy-3-oxoprop-1-en-1-yl)thio)pent-1-yn-1-ylbenzoate (**5s**). Pale yellow oil; R_f (hexane/EtOAc 9:1) 0.46; yield 604 mg, 91%; ^1H NMR (400 MHz, CDCl_3) δ 1.28 (t, $J = 7.2$ Hz, 3 H), 1.96–2.02 (m, 2 H), 2.60 (t, $J = 6.4$ Hz, 2 H), 2.99 (t, $J = 6.8$ Hz, 2 H), 3.91 (s, 3 H), 4.18 (q, $J = 6.8$ Hz, 2 H), 5.83 (d, $J = 15.2$ Hz, 1 H), 7.47 (d, $J = 8.0$ Hz, 2 H), 7.69 (d, $J = 15.2$ Hz, 1 H), 7.97 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 18.7, 27.6, 30.9, 52.4, 60.4, 81.5, 91.7, 114.3, 128.4, 129.3, 129.6, 131.7, 146.3, 165.5, 166.8; IR (KBr, neat) 2944, 2358, 2227, 1931, 1722, 1579, 1440, 1298, 1104, 1035, 954, 762 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{21}\text{O}_4\text{S}$ ($\text{M} + \text{H}$)⁺ 333.1155, found 333.1162.

(*E*)-Ethyl 3-((1,5-Diphenylpent-4-yn-1-yl)thio)acrylate (**5t**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.68; yield 658 mg, 94%; ^1H NMR (400 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 2.15–2.34 (m, 1 H), 2.26–2.37 (m, 2 H), 2.46–2.53 (m, 1 H), 4.13 (q, $J = 7.2$ Hz, 2 H), 4.42 (dd, $J = 9.2$ and 6.0 Hz, 1 H), 5.88 (d, $J = 15.6$ Hz, 1 H), 7.28–7.30 (m, 4 H), 7.34–7.42 (m, 4 H), 7.42–7.46 (m, 2 H), 7.59 (d, $J = 15.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 17.7, 35.4, 49.9, 60.4, 82.3, 88.2, 115.3, 123.7, 128.0, 128.1, 128.2, 128.5, 129.2, 131.8, 140.0, 145.5, 165.5; IR (KBr, neat) 2979, 2932, 2358, 1706, 1582, 1444, 1253, 1162, 1037, 758, 701 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{23}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 351.1413, found 351.1413.

(*E*)-Ethyl 3-((7-Phenylhept-6-yn-3-yl)thio)acrylate (**5u**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.70; yield 562 mg, 93%; ^1H NMR (400 MHz, CDCl_3) δ 1.05 (t, $J = 7.2$ Hz, 3 H), 1.26 (t, $J = 7.2$ Hz, 3 H), 1.63–1.73 (m, 1 H), 1.74–1.84 (m, 1 H), 1.86–2.00 (m, 2 H), 2.59 (t, $J = 6.8$ Hz, 2 H), 3.15–3.23 (m, 1 H), 4.15 (q, $J = 7.2$ Hz, 2 H), 5.92 (d, $J = 15.6$ Hz, 1 H), 7.27–7.30 (m, 3 H), 7.40–7.43 (m, 2 H), 7.73 (d, $J = 15.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 11.4, 14.5, 17.4, 27.8, 33.5, 48.5, 60.4, 81.9, 88.7, 114.9, 123.7, 128.0, 128.4, 131.8, 146.

5, 165.7; IR (KBr, neat) 2970, 2928, 2313, 1707, 1582, 1452, 1252, 1162, 1038, 950, 757 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{23}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 303.1413, found 303.1413.

(*E*)-Ethyl 3-(Pent-4-yn-1-ylthio)acrylate (**5v**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.60; yield 608 mg, 91%; ^1H NMR (400 MHz, CDCl_3) δ 1.29 (t, $J = 7.2$ Hz, 3 H), 1.87–1.94 (m, 2 H), 2.03 (t, $J = 2.8$ Hz, 1 H), 3.05 (dt, $J = 6.4$ and 2.4 Hz, 2 H), 2.94 (t, $J = 6.8$ Hz, 2 H), 4.18 (q, $J = 7.2$ Hz, 2 H), 5.79 (d, $J = 15.2$ Hz, 1 H), 7.67 (d, $J = 15.2$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.5, 17.6, 27.4, 30.7, 60.4, 69.8, 82.7, 114.3, 146.3, 165.4; IR (KBr, neat) 2984, 2927, 1708, 1582, 1446, 1253, 1168, 1038, 640 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{10}\text{H}_{15}\text{O}_2\text{S}$ ($\text{M} + \text{H}$)⁺ 199.0787, found 199.0787.

General Procedure for the Synthesis of Substituted Tetrahydrothiophenes and -thiopyrans (6a–6v). To a suspension of thioenol ether (1 mmol) in dry dichloromethane (4 mL) at 0 °C was added trimethylsilyltriflate (TMSOTf) (1 mmol) dropwise under a nitrogen atmosphere. The reaction mixture was brought to room temperature, and the reaction was stirred for 12 h. After completion of reaction, the reaction mixture was treated with saturated sodium bicarbonate solution (5 mL). The product was extracted with CH_2Cl_2 (2 \times 10 mL), and the combined organic layer was washed with brine. The organic layer was separated and dried over anhydrous Na_2SO_4 and evaporated using a rotary evaporator to obtain the crude product. The crude product was purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford the title compounds **6**.

Ethyl 2-((2*R**,3*R**)-3-Benzoyltetrahydrothiophen-2-yl)acetate (**6a**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.38; Yield 214 mg, 77%; ^1H NMR (400 MHz, CDCl_3) δ 1.20 (t, $J = 7.2$ Hz, 3 H), 2.21–2.27 (m, 1 H), 2.42–2.47 (m, 1 H), 2.61 (dd, $J = 15.6$ and 8.0 Hz, 1 H), 2.73 (dd, $J = 15.6$ and 6.4 Hz, 1 H), 2.95–3.00 (m, 1 H), 3.02–3.07 (m, 1 H), 3.85–3.91 (m, 1 H), 4.08 (q, $J = 7.2$ Hz, 2 H), 4.20 (q, $J = 6.8$ Hz, 1 H), 7.50 (t, $J = 7.6$ Hz, 2 H), 7.60 (t, $J = 7.6$ Hz, 1 H), 7.97 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.2, 31.4, 35.7, 41.3, 45.6, 55.4, 60.9, 128.5, 128.9, 133.6, 136.5, 171.2, 199.5; IR (KBr, neat) 2932, 2858, 1731, 1679, 1447, 1158, 1027, 698 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{19}\text{O}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 279.1049, found 279.1049.

Ethyl 2-((2*R**,3*R**)-3-(4-Methylbenzoyl)tetrahydrothiophen-2-yl)acetate (**6b**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.38; Yield 190 mg, 65%; ^1H NMR (400 MHz, CDCl_3) δ 1.20 (t, $J = 7.2$ Hz, 3 H), 2.18–2.28 (m, 1 H), 2.39–2.47 (m, 4 H), 2.59 (d, $J = 15.6$ and 7.6 Hz, 1 H), 2.73 (dd, $J = 15.6$ and 6.0 Hz, 1 H), 2.94–3.00 (m, 1 H), 3.03–3.08 (m, 1 H), 3.81–3.86 (m, 1 H), 4.06 (q, $J = 7.2$ Hz, 2 H), 4.15–4.23 (m, 1 H), 7.28 (d, $J = 8.0$ Hz, 2 H), 7.87 (t, $J = 7.6$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 21.9, 31.5, 35.9, 41.4, 45.8, 55.3, 60.9, 128.8, 129.7, 134.2, 144.6, 171.3, 199.1; IR (KBr, neat) 2923, 2853, 1733, 1676, 1607, 1447, 1177, 1028, 802, 756 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{21}\text{O}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 293.1206, found 293.1193.

Ethyl 2-((2*R**,3*R**)-3-(4-Chlorobenzoyl)tetrahydrothiophen-2-yl)acetate (**6c**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.47; Yield 225 mg, 72%; ^1H NMR (400 MHz, CDCl_3) δ 1.21 (t, $J = 7.2$ Hz, 3 H), 2.19–2.29 (m, 1 H), 2.36–2.45 (m, 1 H), 2.61 (dd, $J = 15.6$ and 7.6 Hz, 1 H), 2.70 (dd, $J = 15.6$ and 6.8 Hz, 1 H), 2.94–3.00 (m, 1 H), 3.02–3.08 (m, 1 H), 3.84 (q, $J = 6.4$ Hz, 1 H), 4.08 (q, $J = 7.2$ Hz, 2 H), 4.16 (q, $J = 7.2$ Hz, 1 H), 7.46 (d, $J = 8.4$ Hz, 2 H), 7.92 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 31.4, 35.5, 41.3, 45.6, 55.3, 61.0, 129.3, 130.1, 134.9, 140.1, 171.3, 198.4; IR (KBr, neat) 2976, 2860, 1731, 1681, 1584, 1481, 1213, 1166, 1095, 1021, 851, 745 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{18}\text{ClO}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 313.0660, found 313.0646.

Ethyl 2-((2*R**,3*R**)-3-Hexanoyltetrahydrothiophen-2-yl)acetate (**6d**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.52; Yield 206 mg, 61%; ^1H NMR (600 MHz, CDCl_3) δ 0.88 (t, $J = 7.2$ Hz, 3 H), 1.24–1.33 (m, 9 H), 1.54–1.62 (m, 2 H), 2.12–2.21 (m, 1 H), 2.27–2.35 (1 H), 2.51 (t, $J = 7.2$ Hz, 2 H), 2.56 (dd, $J = 16.0$ and 7.6 Hz, 1 H), 2.69 (dd, $J = 16.0$ and 6.4 Hz, 1 H), 2.87–2.98 (m, 3 H), 4.01 (q, $J = 6.8$ Hz, 1 H), 4.14 (q, $J = 7.2$ Hz, 2 H); ^{13}C NMR (150 MHz, CDCl_3) δ 14.5, 14.7, 23.0, 24.1, 29.3, 31.7, 32.1, 34.7, 42.2, 42.3, 45.0, 60.9, 61.3,

171.8, 210.2; IR (KBr, neat) 2964, 2855, 1731, 1708, 1679, 1459, 1165, 1029, 732 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{27}\text{O}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 287.1675, found 287.1672.

Ethyl 2-((2*R**,3*R**,5*S**)-3-Benzoyl-5-ethyltetrahydrothiophen-2-yl)acetate (**6f**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.42; Yield 205 mg, 67%; ^1H NMR (400 MHz, CDCl_3) δ 0.98 (t, $J = 7.2$ Hz, 3 H), 1.20 (t, $J = 7.2$ Hz, 3 H), 1.59–1.67 (m, 1 H), 1.71–1.80 (m, 1 H), 2.09–2.16 (m, 1 H), 2.31–2.39 (m, 1 H), 2.61 (dd, $J = 15.6$ and 8.0 Hz, 1 H), 2.73 (dd, $J = 15.6$ and 6.8 Hz, 1 H), 2.94–3.00 (m, 1 H), 3.34–3.41 (m, 1 H), 3.98 (q, $J = 7.2$ Hz, 1 H), 4.06 (q, $J = 7.2$ Hz, 2 H), 4.17 (q, $J = 7.2$ Hz, 1 H), 7.49 (t, $J = 7.6$ Hz, 2 H), 7.59 (t, $J = 7.6$ Hz, 1 H), 7.96 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 13.2, 14.3, 31.4, 40.4, 41.9, 45.6, 50.0, 54.0, 60.9, 128.6, 129.0, 133.5, 136.5, 171.3, 199.7; IR (KBr, neat) 2965, 2870, 1738, 1678, 1596, 1449, 1373, 1156, 1028, 694 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{23}\text{O}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 307.1362, found 307.1366.

Ethyl 2-((2*R**,3*R**,5*R**)-3-Benzoyl-5-phenyltetrahydrothiophen-2-yl)acetate (**6g**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.40; Yield 269 mg, 76%; ^1H NMR (400 MHz, CDCl_3) δ 1.22 (t, $J = 7.2$ Hz, 3 H), 2.41–2.48 (m, 1 H), 2.62–2.70 (m, 1 H), 2.80 (dd, $J = 15.6$ and 7.6 Hz, 1 H), 2.88 (dd, $J = 15.6$ and 6.8 Hz, 1 H), 4.05–4.15 (m, 3 H), 4.30 (q, $J = 7.2$ Hz, 1 H), 4.69 (t, $J = 7.2$ Hz, 1 H), 7.14–7.28 (m, 1 H), 7.34 (t, $J = 7.2$ Hz, 2 H), 7.44–7.48 (m, 4 H), 7.57 (t, $J = 7.6$ Hz, 1 H), 7.91 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 42.1, 43.1, 46.5, 51.7, 54.2, 61.0, 127.5, 127.8, 128.6, 128.7, 129.0, 133.6, 136.2, 142.0, 171.2, 199.5; IR (KBr, neat) 2976, 2930, 1731, 1681, 1590, 1451, 1165, 1023, 944, 701 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{23}\text{O}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 355.1362, found 355.1358.

Ethyl 2-((2*R**,3*R**,5*R**)-3-Benzoyl-5-(3-bromophenyl)tetrahydrothiophen-2-yl)acetate (**6h**). Colorless solid, mp 87–89 °C; R_f (hexane/EtOAc 9:1) 0.40; Yield 354 mg, 82%; ^1H NMR (400 MHz, CDCl_3) δ 1.24 (t, $J = 7.2$ Hz, 3 H), 2.36–2.44 (m, 1 H), 2.64–2.70 (m, 1 H), 2.80 (dd, $J = 15.6$ and 7.6 Hz, 1 H), 2.88 (dd, $J = 15.6$ and 6.8 Hz, 1 H), 4.08 (q, $J = 5.6$ Hz, 1 H), 4.14 (q, $J = 5.6$ Hz, 2 H), 4.29 (q, $J = 7.2$ Hz, 1 H), 4.65 (t, $J = 6.8$ Hz, 1 H), 7.21 (t, $J = 7.2$ Hz, 1 H), 7.39 (d, $J = 8.0$ Hz, 2 H), 7.48 (t, $J = 8.0$ Hz, 2 H), 7.57–7.62 (m, 2 H), 7.92 (d, $J = 7.2$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 42.0, 42.8, 46.7, 51.1, 54.1, 61.1, 122.8, 126.6, 128.5, 128.7, 129.0, 130.3, 130.6, 130.9, 133.7, 144.5, 171.1, 199.2; IR (KBr, neat) 2924, 2856, 1731, 1681, 1585, 1464, 1155, 1025, 784 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{22}\text{BrO}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 433.0468, found 433.0446.

Ethyl 2-((2*R**,3*R**,5*R**)-3-Benzoyl-5-(4-bromophenyl)tetrahydrothiophen-2-yl)acetate (**6i**). Colorless solid; mp 89–91 °C; R_f (hexane/EtOAc 9:1) 0.45; Yield 359 mg, 83%; ^1H NMR (600 MHz, CDCl_3) δ 1.21 (t, $J = 7.2$ Hz, 3 H), 2.35–2.40 (m, 1 H), 2.59–2.67 (m, 1 H), 2.77 (dd, $J = 15.6$ and 7.8 Hz, 1 H), 2.86 (dd, $J = 15.6$ and 6.6 Hz, 1 H), 4.07 (q, $J = 6.0$ Hz, 1 H), 4.12 (q, $J = 5.6$ Hz, 2 H), 4.27 (q, $J = 7.2$ Hz, 1 H), 4.65 (t, $J = 6.6$ Hz, 1 H), 7.34 (d, $J = 8.4$ Hz, 2 H), 7.43–7.49 (m, 4 H), 7.58 (t, $J = 7.8$ Hz, 1 H), 7.90 (d, $J = 7.8$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 42.0, 43.0, 46.7, 51.1, 54.1, 61.1, 121.3, 128.7, 129.0, 129.6, 131.8, 133.7, 136.1, 141.2, 171.1, 199.3; IR (KBr, neat) 2982, 2926, 1730, 1681, 1587, 1483, 1163, 1015, 699 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{22}\text{BrO}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 433.0468, found 433.0457.

Ethyl 2-((2*R**,3*R**,5*R**)-3-Benzoyl-5-(4-chlorophenyl)tetrahydrothiophen-2-yl)acetate (**6j**). Colorless oil; R_f (hexane/EtOAc 9:1) 0.46; Yield 303 mg, 78%; ^1H NMR (400 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 2.35–2.42 (m, 1 H), 2.62–2.69 (m, 1 H), 2.79 (dd, $J = 15.6$ and 7.2 Hz, 1 H), 2.88 (dd, $J = 15.6$ and 6.8 Hz, 1 H), 4.07 (q, $J = 6.4$ Hz, 1 H), 4.12 (q, $J = 7.2$ Hz, 2 H), 4.27 (q, $J = 5.6$ Hz, 1 H), 4.66 (t, $J = 7.2$ Hz, 1 H), 7.30 (d, $J = 8.8$ Hz, 2 H), 7.40 (d, $J = 8.4$ Hz, 2 H), 7.47 (t, $J = 6.8$ Hz, 1 H), 7.91 (d, $J = 7.2$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 42.1, 43.0, 46.7, 51.1, 54.1, 61.1, 128.7, 128.9, 129.0, 129.2, 133.2, 133.7, 136.1, 140.6, 171.2, 199.3; IR (KBr, neat) 2923, 2857, 1710, 1681, 1488, 1093, 1020, 698 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{21}\text{H}_{22}\text{ClO}_3\text{S}$ ($\text{M} + \text{H}$)⁺ 389.0973, found 389.0968.

Ethyl 2-((2*R**,3*R**,5*R**)-3-(4-Chlorobenzoyl)-5-(*p*-tolyl)tetrahydrothiophen-2-yl)acetate (**6k**). Colorless solid; mp 92–94 °C; R_f (hexane/EtOAc 9:1) 0.50; Yield 261 mg, 65%; ^1H NMR (400 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3 H), 2.33 (s, 3 H), 2.37–2.45 (m, 1 H),

2.57–2.67 (m, 1 H), 2.79 (dd, $J = 16.0$ and 7.2 Hz, 1 H), 2.85 (dd, $J = 16.0$ and 7.6 Hz, 1 H), 4.00–4.07 (m, 1 H), 4.12 (q, $J = 7.1$ Hz, 2 H), 4.23 (q, $J = 4.8$ Hz, 1 H), 4.66 (t, $J = 6.8$ Hz, 1 H), 7.13 (d, $J = 8.0$ Hz, 2 H), 7.33 (d, $J = 8.0$ Hz, 2 H), 7.43 (d, $J = 8.8$ Hz, 2 H), 7.87 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 21.2, 42.0, 43.0, 46.4, 51.4, 54.2, 61.0, 127.7, 129.3, 129.4, 130.1, 134.5, 137.2, 138.8, 140.0, 171.2, 198.4; IR (KBr, neat) 2976, 2930, 1731, 1680, 1587, 1447, 1160, 1095, 1018, 818, 752 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{24}\text{ClO}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 403.1129, found 403.1129.

Ethyl 2-((2*R,3*R**,5*R**)-3-Benzoyl-5-(*p*-tolyl)tetrahydrothiophen-2-yl)acetate (6l).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.46; Yield 250 mg, 68%; ^1H NMR (600 MHz, CDCl_3) δ 1.22 (t, $J = 7.2$ Hz, 3 H), 2.34 (s, 3 H), 2.44 (p, $J = 7.2$ Hz, 1 H), 2.64 (p, $J = 6.6$ Hz, 1 H), 2.80 (dd, $J = 15.6$ and 7.2 Hz, 1 H), 2.87 (dd, $J = 15.6$ and 6.6 Hz, 1 H), 4.07–4.14 (m, 3 H), 4.30 (q, $J = 7.2$ Hz, 1 H), 4.67 (t, $J = 6.0$ Hz, 1 H), 7.14 (d, $J = 7.8$ Hz, 1 H), 7.35 (d, $J = 7.8$ Hz, 2 H), 7.46 (t, $J = 7.2$ Hz, 2 H), 7.57 (t, $J = 7.8$ Hz, 1 H), 7.93 (d, $J = 7.8$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 21.2, 42.0, 43.0, 46.3, 51.3, 54.1, 60.9, 127.6, 128.6, 128.9, 129.3, 133.5, 136.0, 137.1, 138.9, 171.2, 199.4; IR (KBr, neat) 2923, 2858, 1732, 1681, 1588, 1449, 1162, 1026, 701 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{25}\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 369.1519, found 369.1514.

Ethyl 2-((2*R,3*R**)-3-Benzoyltetrahydro-2*H*-thiopyran-2-yl)acetate (6n, Diastereomeric Mixture with a Ratio of 91:9; Data Only for Major Isomer).** Colorless liquid; R_f (hexane/EtOAc 9:1) 0.48; Yield 201 mg, 69%; ^1H NMR (400 MHz, CDCl_3) δ 1.19 (t, $J = 7.2$ Hz, 3 H), 1.48 (q, $J = 10.4$ Hz, 1 H), 1.77 (q, $J = 9.6$ Hz, 1 H), 2.04–2.13 (m, 2 H), 2.37 (dd, $J = 15.2$ and 8.4 Hz, 1 H), 2.56 (dd, $J = 15.2$ and 4.0 Hz, 1 H), 2.59–2.64 (m, 1 H), 2.78–2.85 (m, 1 H), 3.62–3.74 (m, 2 H), 4.09 (q, $J = 7.2$ Hz, 2 H), 7.49 (t, $J = 7.6$ Hz, 1 H), 7.59 (t, $J = 7.2$ Hz, 2 H), 7.97 (d, $J = 7.2$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 27.0, 29.4, 31.1, 38.7, 39.9, 50.2, 60.8, 128.5, 129.0, 133.6, 136.3, 170.9, 202.7; IR (KBr, neat) 2935, 2853, 2275, 1732, 1682, 1587, 1452, 1156, 1033, 781, 701 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{21}\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 293.1206, found 293.1202.

Ethyl 2-((2*R,3*R**)-3-(4-Methylbenzoyl)tetrahydro-2*H*-thiopyran-2-yl)acetate (6o, Diastereomeric Mixture with a Ratio of 90:10; Data Only for Major Isomer).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.52; Yield 208 mg, 68%; ^1H NMR (400 MHz, CDCl_3) δ 1.19 (t, $J = 7.2$ Hz, 3 H), 1.49 (q, $J = 10.4$ Hz, 1 H), 1.78 (q, $J = 10.0$ Hz, 1 H), 2.02–2.16 (m, 2 H), 2.36 (dd, $J = 15.2$ and 8.4 Hz, 1 H), 2.42 (s, 3 H), 2.54 (dd, $J = 15.2$ and 6.4 Hz, 1 H), 2.58–2.64 (m, 1 H), 2.77–2.85 (m, 1 H), 3.61–3.70 (m, 2 H), 4.09 (q, $J = 7.2$ Hz, 2 H), 7.28 (t, $J = 8.0$ Hz, 2 H), 7.88 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (150 MHz, CDCl_3) 14.3, 21.9, 27.1, 29.5, 31.2, 38.8, 40.1, 50.1, 60.8, 128.7, 129.7, 133.9, 144.5, 170.9, 202.3; IR (KBr, neat) 2933, 2853, 1723, 1672, 1605, 1446, 1155, 1028, 825, 740 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{17}\text{H}_{23}\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 307.1362, found 307.1354.

Ethyl 2-((2*R,3*R**)-3-(4-Chlorobenzoyl)tetrahydro-2*H*-thiopyran-2-yl)acetate (6p, Diastereomeric Mixture with a Ratio of 96:4; Data Only for Major Isomer).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.52; Yield 202 mg, 62%; ^1H NMR (400 MHz, CDCl_3) δ 1.20 (t, $J = 7.2$ Hz, 3 H), 1.48 (q, $J = 12.4$ Hz, 1 H), 1.78 (q, $J = 12.8$ Hz, 1 H), 1.98–2.06 (m, 1 H), 2.08–2.20 (m, 1 H), 2.41 (dd, $J = 15.2$ and 8.0 Hz, 1 H), 2.54 (dd, $J = 15.2$ and 3.6 Hz, 1 H), 2.60–2.65 (m, 1 H), 2.77–2.85 (m, 1 H), 3.59–3.71 (m, 2 H), 4.09 (q, $J = 7.2$ Hz, 2 H), 7.46 (d, $J = 7.6$ Hz, 2 H), 7.92 (d, $J = 7.6$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 26.9, 29.3, 31.0, 38.5, 39.8, 50.1, 60.9, 129.3, 129.9, 134.6, 140.1, 170.8, 201.5; IR (KBr, neat) 2925, 2853, 1733, 1677, 1584, 1487, 1180, 1091, 1027, 836, 750 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{20}\text{ClO}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 327.0816, found 327.0820.

Ethyl 2-((2*R,3*R**)-3-(4-Nitrobenzoyl)tetrahydro-2*H*-thiopyran-2-yl)acetate (6r).** White solid, mp $75\text{--}77\text{ }^\circ\text{C}$; R_f (hexane/EtOAc 9:1) 0.42; Yield 273 mg, 81%; ^1H NMR (400 MHz, CDCl_3) δ 1.21 (t, $J = 6.8$ Hz, 3 H), 1.48 (q, $J = 11.6$ Hz, 1 H), 1.78 (q, $J = 13.6$ Hz, 1 H), 1.99–2.05 (m, 1 H), 2.09–2.16 (m, 1 H), 2.46–2.58 (m, 2 H), 2.60–2.67 (m, 1 H), 2.76–2.83 (m, 1 H), 3.58–3.64 (m, 1 H), 3.74–3.81 (m, 1 H), 4.09 (q, $J = 6.8$ Hz, 2 H), 8.13 (d, $J = 8.4$ Hz, 2 H), 8.33 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (150 MHz, CDCl_3) 14.3, 26.7, 29.2, 30.6, 38.3, 39.6, 50.4, 61.0, 124.2, 129.6, 140.9, 150.6, 170.9, 201.4; IR (KBr, neat) 2927, 2855, 1726, 1688, 1525, 1455, 1351, 1136, 1030, 852, 710

cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{20}\text{NO}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 338.1057, found 338.1069.

Methyl 4-((2*R,3*R**)-2-(2-Ethoxy-2-oxoethyl)tetrahydro-2*H*-thiopyran-3-carbonyl)benzoate (6s).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.40; Yield 301 mg, 86%; ^1H NMR (400 MHz, CDCl_3) δ 1.19 (t, $J = 7.6$ Hz, 3 H), 1.43–1.54 (m, 1 H), 1.74–1.85 (m, 1 H), 2.02–2.09 (m, 1 H), 2.12 (dt, $J = 13.6$ and 3.2 Hz, 1 H), 2.44 (dd, $J = 15.2$ and 8.0 Hz, 1 H), 2.56 (dd, $J = 15.2$ and 4.4 Hz, 1 H), 2.60–2.67 (m, 1 H), 2.81 (ddd, $J = 15.2$, 14.0, and 2.4 Hz, 1 H), 3.64 (ddd, $J = 13.6$, 9.6, and 4.0 Hz, 1 H), 3.74 (ddd, $J = 13.6$, 11.6, and 2.8 Hz, 1 H), 3.96 (s, 3 H), 4.09 (q, $J = 6.8$ Hz, 2 H), 8.03 (d, $J = 8.0$ Hz, 2 H), 8.15 (d, $J = 8.0$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 26.8, 29.3, 30.9, 38.5, 39.7, 50.4, 52.7, 60.8, 128.4, 130.2, 134.2, 139.5, 166.3, 170.8, 202.3; IR (KBr, neat) 2925, 2856, 1735, 1682, 1569, 1446, 1283, 1107, 1024, 756 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{23}\text{O}_5\text{S}$ ($\text{M} + \text{H}$) $^+$ 351.1261, found 351.1271.

Ethyl 2-((2*R,3*R**,6*R**)-3-Benzoyl-6-phenyltetrahydro-2*H*-thiopyran-2-yl)acetate (6t).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.53; Yield 257 mg, 70%; ^1H NMR (400 MHz, CDCl_3) δ 1.16 (t, $J = 7.2$ Hz, 3 H), 1.61–1.72 (m, 1 H), 2.04–2.15 (m, 1 H), 2.20–2.29 (m, 2 H), 2.42 (dd, $J = 15.2$ and 4.4 Hz, 1 H), 2.59 (dd, $J = 15.2$ and 4.0 Hz, 1 H), 3.74–3.80 (m, 1 H), 3.85–3.91 (m, 1 H), 4.03–4.06 (m, 1 H), 4.06 (q, $J = 7.2$ Hz, 2 H), 7.26 (t, $J = 8.4$ Hz, 1 H), 7.32 (t, $J = 7.6$ Hz, 2 H), 7.37 (d, $J = 7.6$ Hz, 2 H), 7.37 (t, $J = 7.6$ Hz, 2 H), 7.61 (t, $J = 7.2$ Hz, 1 H), 8.01 (d, $J = 8.4$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 14.3, 32.1, 34.6, 38.4, 42.0, 48.0, 49.7, 60.9, 127.7, 127.8, 128.5, 128.8, 129.1, 133.7, 136.4, 141.3, 170.7, 202.9; IR (KBr, neat) 2926, 2855, 1734, 1675, 1590, 1447, 1148, 1031, 757, 702 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{22}\text{H}_{25}\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 369.1519, found 369.1515.

Ethyl 2-((2*R,3*R**,6*S**)-3-Benzoyl-6-ethyltetrahydro-2*H*-thiopyran-2-yl)acetate (6u).** Colorless oil; R_f (hexane/EtOAc 9:1) 0.55; Yield 208 mg, 65%; ^1H NMR (600 MHz, CDCl_3) δ 1.00 (t, $J = 7.2$ Hz, 3 H), 1.17 (t, $J = 7.2$ Hz, 3 H), 1.47–1.52 (m, 2 H), 1.53–1.58 (m, 2 H), 2.07–2.11 (m, 2 H), 2.39 (dd, $J = 15.0$ and 7.8 Hz, 1 H), 2.54 (dd, $J = 15.0$ and 3.0 Hz, 1 H), 2.79–2.84 (m, 1 H), 3.64–3.67 (m, 2 H), 4.05–4.10 (m, 2 H), 7.48 (t, $J = 7.8$ Hz, 2 H), 7.58 (t, $J = 7.2$ Hz, 1 H), 7.97 (d, $J = 7.8$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) 11.6, 14.3, 28.8, 31.9, 33.8, 38.6, 40.8, 45.5, 50.4, 60.8, 128.5, 129.0, 133.6, 136.5, 170.9, 203.1; IR (KBr, neat) 2926, 2853, 1735, 1676, 1588, 1450, 1293, 1155, 1031, 703 cm^{-1} ; HRMS (ESI) calcd. for $\text{C}_{18}\text{H}_{25}\text{O}_3\text{S}$ ($\text{M} + \text{H}$) $^+$ 321.1519, found 321.1519.

■ ASSOCIATED CONTENT

📄 Supporting Information

NMR spectra, mass spectra, and crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

- (1) (a) De Clercq, P. J. *Chem. Rev.* **1997**, *97*, 1755–1792. (b) Zemleni, J.; Wijeratne, S. S. K.; Hassan, Y. I. *BioFactors* **2009**, *35*, 36–46.

- (2) Ohtsuka, T.; Kotaki, H.; Nakayama, N.; Itezo, Y.; Shimma, N.; Kudoh, T.; Kuwahara, T.; Arisawa, M.; Yokose, K. *J. Antibiot.* **1993**, *46*, 11–17.
- (3) Yoshimura, Y.; Watanabe, M.; Satoh, H.; Ashida, N.; Ijichi, K.; Sakata, S.; Machida, H.; Matsuda, A. *J. Med. Chem.* **1997**, *40*, 2177–2183.
- (4) Yoshikawa, M.; Morikawa, T.; Matsuda, H.; Tanabe, G.; Muraoka, O. *Bioorg. Med. Chem.* **2002**, *10*, 1547–1554.
- (5) Kato, T.; Tsuzuki, K. Patent Application JP 92-147881, CAN 120:106750.
- (6) Smith, A. B., III; Empfield, J. R. *Chem. Pharm. Bull.* **1999**, *47*, 1671–1678.
- (7) Tsygoanko, V. A.; Blume, Y. B. *Biopolim. Kletka* **1997**, *13*, 484–492.
- (8) (a) Hauptman, E.; Shapiro, R.; Marshall, W. *Organometallics* **1998**, *17*, 4976–4982. (b) Zanardi, J.; Lamazure, D.; Minière, S.; Reboul, V.; Metzner, P. *J. Org. Chem.* **2002**, *67*, 9083–9086.
- (9) Li, Z.; Yu, R.; Li, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 7497–7500.
- (10) (a) Gal'pern, G. D. *Int. J. Sulfur Chem., Part B* **1971**, *6*, 115–130. (b) Payzant, J. D.; Cyr, T. D.; Montbomery, D. S.; Strausz, O. P. *Tetrahedron Lett.* **1985**, *26*, 4175–4178.
- (11) Mehta, S.; Andrews, J. S.; Johnston, B. D.; Svensson, B.; Pinto, B. M. *J. Am. Chem. Soc.* **1995**, *117*, 9783–9790.
- (12) (a) Block, E. *Reactions of Organosulfur Compounds*; Academic Press: New York, 1978. (b) Woodward, R. B.; Logusch, E.; Nambiar, K. P.; Sakan, K.; Ward, D. E.; Au-Yeung, B. W.; Balam, P.; Browne, L. J.; Card, P. J.; Chen, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 3210–3213. (c) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1997**, *53*, 5563–5572. (d) Aggarwal, V. K.; Smith, H. W.; Hynd, G.; Jones, R. V. H.; Fieldhouse, R.; Spey, S. E. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3267–3276.
- (13) Ozaki, S.; Matsui, E.; Yoshinaga, H.; Kitagawa, S. *Tetrahedron Lett.* **2000**, *41*, 2621–2624.
- (14) Rosiak, A.; Frey, W.; Christoffers, J. *Eur. J. Org. Chem.* **2006**, 4044–4054.
- (15) (a) Weiwer, M.; Coulombel, L.; Duñach, E. *Chem. Commun.* **2006**, 332–334. (b) Weiwer, M.; Chaminade, X.; Bayón, J. C.; Duñach, E. *Eur. J. Org. Chem.* **2007**, 2464–2469.
- (16) Tamura, Y.; Choi, H.-D.; Shindo, H.; Uenishi, J.; Ishibashi, H. *Tetrahedron Lett.* **1981**, *22*, 81–84.
- (17) Bondalapati, S.; Gogoi, P.; Indukuri, K.; Saikia, A. K. *J. Org. Chem.* **2012**, *77*, 2508–2512.
- (18) (a) Brandau, S.; Maerten, E.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 14986–14991. (b) Li, H.; Zu, L.; Xie, H.; Wang, J.; Jiang, W.; Wang, W. *Org. Lett.* **2007**, *9*, 1833–1835. (c) Ling, J.-B.; Su, Y.; Zhu, H.-L.; Wang, G.-Y.; Xu, P.-F. *Org. Lett.* **2012**, *14*, 1090–1093. (d) Baricordi, N.; Benneti, S.; Bertolasi, V.; Risi, C. D.; Pollini, G. P.; Zamberlan, F.; Zanirato, V. *Tetrahedron* **2012**, *68*, 208–213.
- (19) (a) Achiwa, K.; Terao, Y.; Hyodo, C.; Aono, M. *Tetrahedron Lett.* **1986**, *34*, 4039–4042. (b) Ohno, M.; Ishida, H. *Tetrahedron Lett.* **1999**, *40*, 1543–1546.
- (20) (a) Kondo, K.; Ojima, I. *J. Chem. Soc., Chem. Commun.* **1972**, *1*, 63–64. (b) Kondo, K.; Ojima, I. *J. Chem. Soc., Chem. Commun.* **1972**, *1*, 860–861.
- (21) Nair, V.; Nair, S. M.; Mathai, S.; Liebscher, J.; Ziemer, B.; Narsimulu, K. *Tetrahedron Lett.* **2004**, *45*, 5759–5762.
- (22) Cui, Y.; Floreancig, P. E. *Org. Lett.* **2012**, *14*, 1720–1723.
- (23) Lee, H. S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 6480–6483.
- (24) (a) Arundale, E.; Mikeska, L. A. *Chem. Rev.* **1952**, *51*, 505–555. (b) Adams, D. R.; Bhatnagar, S. P. *Synthesis* **1977**, 661–672. (c) Snider, B. B. In *The Prins Reaction and Carbonyl Ene Reactions*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: New York, 1991; Vol. 2, pp 527–561. (d) Gogoi, P.; Das, V. K.; Saikia, A. K. *J. Org. Chem.* **2014**, *79*, 8592–8598.
- (25) (a) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P. *Tetrahedron* **2010**, *66*, 413–445. (b) Overman, L. E.; Pennington, L. D. *J. Org. Chem.* **2003**, *68*, 7143–7157. (c) Yadav, V. K.; Kumar, N. V. *J. Am. Chem. Soc.* **2004**, *126*, 8652–8653. (d) Yadav, J. S.; Thrimurtulu, N.; Lakshmi, K. A.; Prasad, A. R.; Reddy, B. V. S. *Tetrahedron Lett.* **2010**, *51*, 661–663.
- (26) (a) Yang, X.-F.; Mague, J. T.; Li, C.-J. *J. Org. Chem.* **2001**, *66*, 739–747. (b) Yang, X.-F.; Li, C.-J. *Tetrahedron Lett.* **2000**, *41*, 1321–1325. (c) Reddy, B. V. S.; Venkateswarlu, A.; Borkar, P.; Yadav, J. S.; Sridhar, B.; Grée, R. *J. Org. Chem.* **2014**, *79*, 2716–2722. (d) Reddy, B. V. S.; Venkateswarlu, A.; Borkar, P.; Yadav, J. S.; Sridhar, B.; Grée, R. *J. Org. Chem.* **2011**, *76*, 7677–7690.
- (27) The crystallographic data for the compound **6k** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1038837.
- (28) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 738–741.
- (29) Baldwin, J. E.; Thomas, R. C.; Kruse, L. I.; Silberman, L. *J. Org. Chem.* **1977**, *42*, 3846–3852.