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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c01006 • Publication Date (Web): 12 Jun 2020

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

A Domino Synthetic Strategy for Tetrahydrothiopyran Derivatives from Benzaldehydes, 2-Acetylfuran/2-Acetylthiophene and Sodium Sulfide

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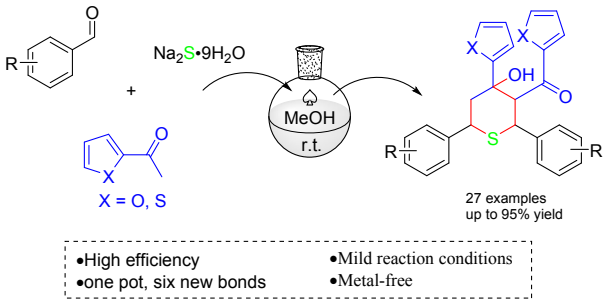


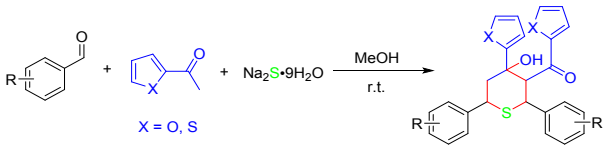
ABSTRACT: A novel domino reaction from benzaldehydes and 2-acetylfuran/2-acetylthiophene with sodium sulfide was developed to synthesize a series of tetrahydrothiopyran (THTP) derivatives. The reaction proceeded well to construct a tetrahydrothioan ring and five new bonds in one step. A mechanism is proposed, involving a stepwise of Aldol/double Michael addition/Aldol (AMMA) reaction cascade. In this transformation, sodium sulfide acts as a nucleophile and base. This method is characterized by transition-metal free, commercially available starting materials and mild reaction conditions.

INTRODUCTION

Sulfur-containing compounds are widely applied as pesticides, medicines and synthons playing its irreplaceable roles in academic and industrial communities.[1-3] THTP derivatives have been testified to exhibit many pharmaceutical properties such as anti-bacterial, anti-cancer, anti-inflammatory and anti-viral activities.[4-7] In the past decades, some convenient methods for the synthesis of THTP derivatives have been developed. However, most of them suffer from a number of drawbacks such as the introduction of expensive or toxic metal catalysts, long synthesis routes, limited substrate

scopes and low yields.[8-11] These problems greatly limited its practical applications. The exploration of a simple and efficient new method for obtaining sulfur-containing heterocyclic compounds caused huge attention in chemical synthesis. In this context, domino reactions exhibited significant potential in the construction of complex molecules from simple precursors[12]. Sodium sulfide, the simplest inorganic compound bearing both a useful base and a sulfur source often, is often employed in organic synthesis.[13]

Recently, we explored a novel and general tandem AMMA reaction from benzaldehydes and 2-acetylfuran/2-acetylthiophene with sodium sulfide (acts as nucleophile and base), which is a convenient and mild method to synthesize THTP derivatives with no catalysts needed. (Scheme 1). To the best of our knowledge, this new class of THTP derivatives have never been reported.

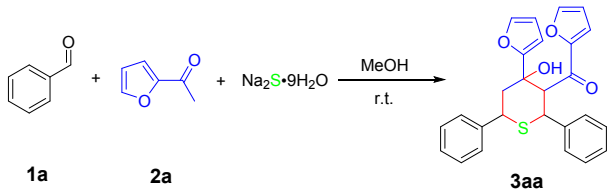


Scheme 1. Synthesis of THTP Derivatives.

RESULTS AND DISCUSSION

To begin with, the investigation into the adaptability of a tandem process from benzaldehyde **1a**, 2-acetylfuran **2a**, and $Na_2S·9H_2O$ was conducted followed by the optimization of reaction conditions (Table 1). As shown in Table 1, we found that it failed to yield the desired product **3aa** in dichloromethane (DCM) or toluene at 25 °C for 48 h (Table 1, entries 1 and 2). we got the target compound **3aa** with low yields when *N*,*N*-dimethylformamide (DMF), acetonitrile (CH_3CN) and ethanol (EtOH) were selected as the solvent (Table 1, entry 3-5). The yield of **3aa** was raised to 72% within 6 h in methanol (MeOH) (Table 1, entry 6), which means MeOH is the most optimal solvent for the reaction (Table 1, entry 1-6). In terms of reaction time, yield is increasing when reaction time is increased from 6 h to 48 h, while the yield decreased when the reaction time was extended to 72 h (Table 1, entry 6-10). Therefore, the treatment to the reaction solution of benzaldehyde **1a** (1 equiv, 1 mmol) plus 2-acetylfuran **2a** (1.1 equiv, 1.1 mmol**)** with $Na_2S·9H_2O$ (1 equiv, 1 mmol) in MeOH (5 mL) at 25 °C for 48 h was selected as the most optimal condition (Table 1, entry 9).

Table 1. Optimization of the Reaction Conditions[a]



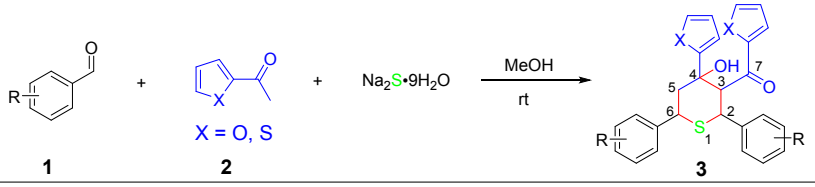
1a **2a** **3aa**

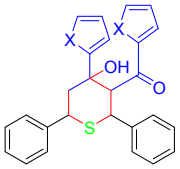
entry	solvent	Time (h)	temp (°C)	Yield (%)[b]
1	DCM	48	25	0
2	toluene	48	25	0
3	DMF	48	25	4[c]
4	CH_3CN	48	25	11
5	EtOH	6	25	14
6	MeOH	6	25	72
7	MeOH	12	25	81
8	MeOH	24	25	85
9	**MeOH**	**48**	**25**	**91**
10	MeOH	72	25	88
11	MeOH	48	50	83
12	MeOH	48	0	82

[a]Reaction conditions: 1a (1 mmol), 2a (1.1 mmol), $Na_2S{\cdot}9H_2O$ (1 mmol), solvent (5 mL). [b]Isolated yield based on **1a**. [c]The reaction generated a complex mixture from which pure product could nevertheless be isolated.

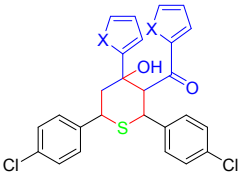
With optimized reaction condition in hand (Table 1, entry 9), it was applied in to a variety of substituted benzaldehydes **1a** and 2-acetylfuran **2a**/2-Acetylthiophene **2b** to yield the corresponding THTP derivatives **3** (Scheme 2). It was found that the domino reaction exhibited a wide tolerance for different substituents in substrates **1**. The yields for the compounds **3a** and **3b** series showed that an oxygen or sulfur atom in the pent-heterocycle exerted little influence on the yield. The selection for substituents in the benzene ring of benzaldehydes **1a** can significantly influence the yields of THTP derivatives **3**. Compared to the yields from non-substituted benzaldehyde substrates (**3aa**, **3ba**), benzaldehydes substituted by an alkyl group at the 4-position [methyl (**3ad**, **3bd**), ethyl (**3ai**, **3bj**), *n*-propyl (**3ak**, **3bk**), isopropyl (**3ah**, **3bh**) and tert-butyl (**3ai**, **3bi**)] exhibited excellent yields. In terms of substitution sites of methyl groups in the benzene ring showed no obvious differences in the yields. The introduction of a weak electron-withdrawing group such as chloro (**3ab**, **3bb**) or bromo (**3ac**, **3bc**) led to a slightly reduction in the yield. The presence of a strong electron-donating group such as methoxy (**3an**) or methylthio (**3al**, **3bl**) led to decreased yields. In the intermediate I (Scheme 3), the electron-rich β position donated by benzyl group resulted in slow formation rate of intermediate Ⅱ. While the fairly non-reactive diphenyl group in aldehyde (**3am** and **3bm**) substantially stabilized intermediate I, which hindered the formation of intermediate Ⅱ.

Scheme 2. Synthesis of THTP Derivatives **3**[a]

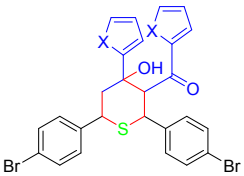




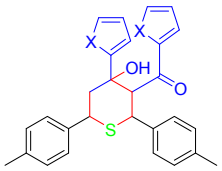
3aa, X = O, 91%
3ba, X = S, 89%



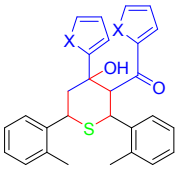
3ab, X = O, 85%
3bb, X = S, 91%



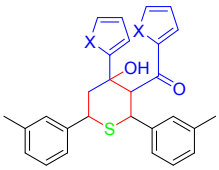
3ac, X = O, 76%
3bc, X = S, 89%



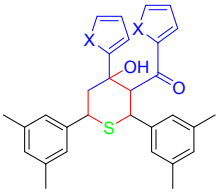
3ad, X = O, 72%
3bd, X = S, 70%



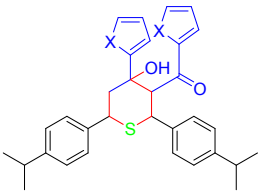
3ae, X = O, 75%
3be, X = S, 80%



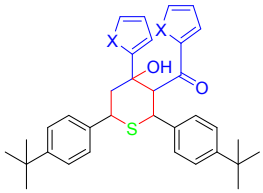
3af, X = O, 74%
3bf, X = S, 82%



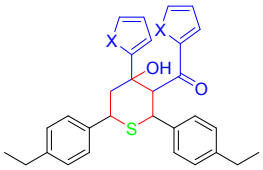
3ag, X = O, 92%
3bg, X = S, 88%



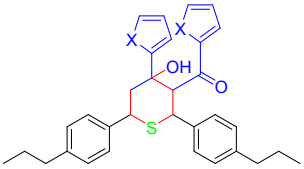
3ah, X = O, 95%
3bh, X = S, 94%



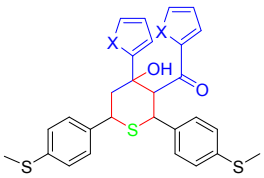
3ai, X = O, 93%
3bi, X = S, 94%



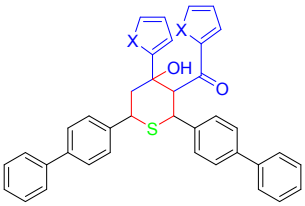
3aj, X = O, 82%
3bj, X = S, 89%



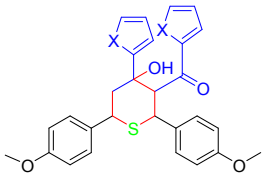
3ak, X = O, 76%
3bk, X = S, 83%



3al, X = O, 43%
3bl, X = S, 42%



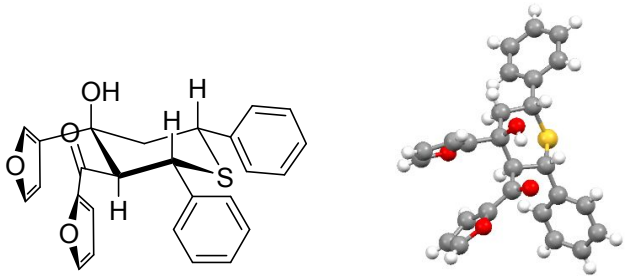
3am, X = O, 33%
3bm, X = S, 34%



3an, X = O, 38%

[a]Reaction conditions: **1a** (1 mmol), **2a** (1.1 mmol) and $Na_2S·9H_2O$ (1 mmol) in MeOH (5 mL) at room temperature. Isolated yield based on **1**.

The relative stereochemistry of compound **3aa** was confirmed by the X-ray single crystal analysis (Figure 1)[14]. The THTP ring exists as the stable chair conformation. Two phenyl groups (2,6-position) and a 2-furyl group (4-position) on the same side in the equatorial positions, while the hydroxyl (4-position) group directed to another side in the axial direction.

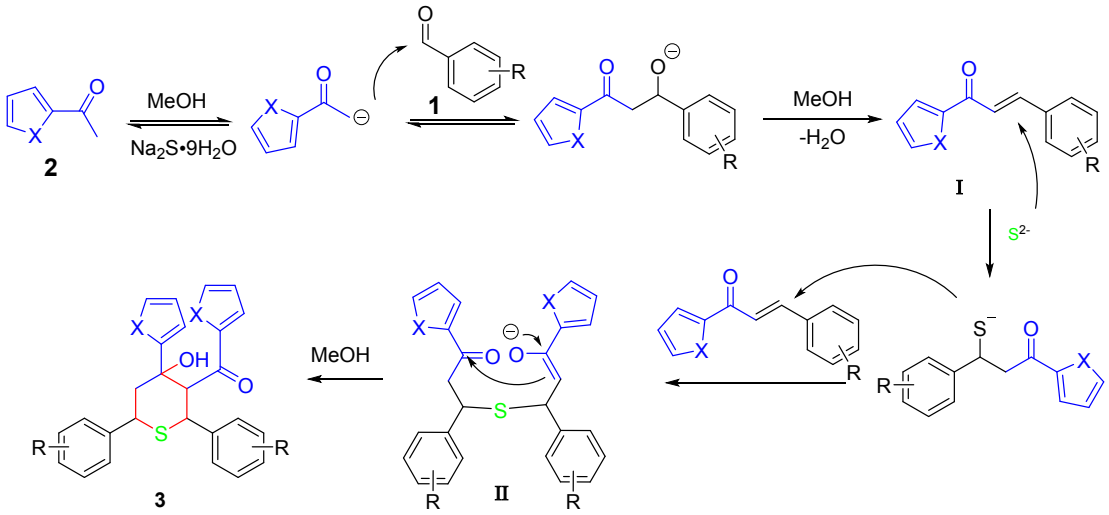


3aa **CCDC 2006752**

Figure 1. The relative stereochemistry and single-crystal X-ray structures of compound **3aa**

A plausible reaction mechanism was proposed as shown in scheme 3. The mechanism involves three steps: (1) A base-promoted intermolecular Aldol reaction of substituted benzaldehyde **1a** and 2-acetylfuran (**2a**)/2-acetylthiophene (**2b**) to yield intermediate I (We have captured intermediate I of compound **3aa**[15]); (2) Michael addition of sulfide anion takes place with two molecular equivalence of intermediate I to generate intermediate Ⅱ (we have not captured intermediate Ⅱ unfortunately); (3) An intramolecular Aldol reaction of II furnishes the THTP derivatives **3**. Thus, the mechanism involvs a stepwise Aldol reaction/double Michael addition/Aldol reaction (AMMA) is a reaction cascade mechanism.

Scheme 3. Plausible Reaction Mechanism



CONCLUSION

In summary, we have explored a novel and strategic one pot reaction through a sequential Aldol reaction/double Michael addition/Aldol, which provides straightforward access to THTP derivatives with high yields from readies available substrates (benzaldehydes, 2-acetylfuran/2-acetylthiophene and $Na_2S·9H_2O$). This domino strategy features transition-metal free, wide substrate scope and mild

reaction conditions. Further investigations and applications of this protocol are under study in our laboratory.

EXPERIMENTAL SECTION

General Information. All starting materials were purchased from commercial suppliers and used without further purification unless otherwise stated. Melting points (mp) were determined on an XT-4 micro-melting point apparatus and uncorrected. Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker AVANCE III operating at 500 or 400 MHz (Bruker, Karlsruhe, Germany) instrument in $CDCl_3$ or DMSO-d_6 and using tetramethyl silane (TMS) as an internal standard. All chemical shifts (δ values) are given in ppm and coupling constants (J values) are given in Hz. High resolution mass spectra (HRMS) were obtained using a Bruker micrOTOF-Q II focus spectrometer (ESI).

General Experimental Procedures for the Synthesis of compounds **3** (with **3aa** as an example). To a solution of benzaldehyde **1a** (1.0 mmol) and 2-acetylfuran **2a** (1.1 mmol) in MeOH (5 mL) was added $Na_2S{\cdot}9H_2O$ (1 mmol) at room temperature. The reaction mixture was stirred at room temperature until the completion of reaction (checked by TLC). To the resulting mixture was added DCM (30 mL) and washed with water (30 mL) three times. The organic layer was dried over anhydrous $MgSO_4$ and evaporated under vacuum. The residue was purified by silica gel column using petroleum ether/ethyl acetate (5:1, v/v) mixture to afford **3aa** (195.8 mg) in 91% yield as a white solid.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-diphenyltetrahydro-2*H*-thiopyran-3-yl)methanone (**3aa**). Obtained as a white solid; isolated yield: 195.8 mg (91%); mp 142–143 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.50 (m, 2H), 7.45–7.36 (m, 5H), 7.32–7.30 (m, 1H), 7.20–7.17 (m, 3H), 7.13–7.10 (m, 1H), 6.93 (d, 1H, J = 3.6 Hz), 6.31 (dd, 1H, J = 3.6, 1.6 Hz), 6.23 (dd, 1H, J = 3.3, 0.9 Hz), 6.16 (dd, 1H, J = 3.3, 1.8 Hz), 4.98–4.95 (m, 2H), 4.88 (dd, 1H, J = 12.2, 2.7 Hz), 4.48 (d, 1H, J = 11.2 Hz), 2.68 (td, 1H, J = 13.0, 2.7 Hz), 2.50 (dd, 1H, J = 14.0, 2.7 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 192.8, 158.3, 152.5, 147.3, 141.5, 140.5, 137.7, 128.7, 128.5, 128.4, 128.0, 127.8, 127.7, 119.2, 112.3, 110.3, 105.5, 73.8, 56.6, 47.2, 44.6, 43.0; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{23}O_4S$ 431.1312; found 431.1311.

(2,6-Bis(4-chlorophenyl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-

yl)methanone (**3ab**). Obtained as a white solid; isolated yield: 210.9 mg (85%); mp 180–181 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71–7.52 (m, 1H), 7.52–7.40 (m, 7H), 7.27–7.25 (m, 3H), 6.46 (d, 1H, J = 3.6 Hz), 6.19 (s, 1H), 6.14 (s, 1H), 5.56 (s, 1H), 4.98 (d, 1H, J = 11.2 Hz), 4.73 (d, 1H, J = 12.1 Hz), 4.33 (d, 1H, J = 11.2 Hz), 2.79 (t, 1H, J = 12.9 Hz), 2.24 (d, 1H, J = 13.4 Hz); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d) δ 187.8, 158.2, 152.7, 148.2, 142.1, 139.9, 138.2, 132.7, 132.6, 130.8, 130.0, 129.2, 128.8, 119.5, 112.7, 110.6, 106.1, 72.9, 56.9, 45.3, 44.9, 41.9; HRMS (ESI) m/z: [M+Cl]$^-$ calcd for $C_{26}H_{20}Cl_3O_4S$ 533.0153; found 533.0147.

(2,6-Bis(4-bromophenyl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-yl)methanone (**3ac**). Obtained as a white solid; isolated yield: 224.0 mg (76%); mp 185–186 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71–7.58 (m, 3H), 7.46–7.26 (m, 8H), 6.46 (d, 1H, J = 3.6 Hz), 6.19-6.14 (m, 2H), 5.56 (s, 1H), 4.97 (d, 1H, J = 11.2), 4.71 (d, 1H, J = 12.1 Hz), 4.32 (d, 1H, J = 11.2 Hz), 2.79 (t, 1H, J = 13.0 Hz), 2.24 (d, 1H, J = 13.5); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d) δ 187.8, 158.2, 152.7, 148.2, 142.1, 140.4, 138.7, 132.2, 131.8, 131.1, 130.3, 121.2, 119.5, 112.7, 110.6, 106.1, 72.9, 56.9, 45.4, 44.8, 42.0; HRMS (ESI) m/z: [M+H]$^+$ calcd for $C_{26}H_{21}Br_2O_4S$ 586.9522; found 586.9521.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-di-p-tolyltetrahydro-2*H*-thiopyran-3-yl)methanone (**3ad**). Obtained as a white solid; isolated yield: 164.7 mg (72%); mp 183–184 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.38 (m, 3H), 7.31–7.30 (m, 2H), 7.19–7.17 (m, 3H), 7.98 (d, 2H, J = 7.7 Hz), 6.94 (d, 1H, J = 3.6 Hz), 6.33–6.32 (m, 1H), 6.21 (d, 1H, J = 3.2 Hz), 6.15-6.14 (m, 1H), 4.92 (d, 1H, J = 11.1 Hz), 4.91 (s, 1H), 4.83 (dd, 1H, J = 12.3, 2.6 Hz), 4.45 (d, 1H, J = 11.2 Hz), 2.66 (td, 1H, J = 13.0, 2.7 Hz), 2.45 (dd, 1H, J = 13.9, 2.6 Hz), 2.37 (s, 3H), 2.21 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 192.9, 158.4, 152.5, 147.3, 141.5, 137.6, 137.3, 134.7, 129.4, 129.1, 128.3, 127.6, 119.2, 112.3, 110.3, 105.4, 73.9, 56.7, 46.8, 44.6, 42.7, 21.1, 21.0; HRMS (ESI) m/z: [M+Na]$^+$ calcd for $C_{28}H_{26}O_4SNa$ 481.1444; found 481.1438.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-di-o-tolyltetrahydro-2*H*-thiopyran-3-yl)methanone (**3ae**). Obtained as a white solid; isolated yield: 172.3 mg (75%); mp 139–140 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, 1H, J = 7.4 Hz), 7.54 (d, 1H, J = 7.6 Hz), 7.44 (d, 1H, J = 1.8 Hz), 7.26–7.19 (m, 4H), 7.05–6.99 (m, 4H), 6.35 (dd, 1H, J = 3.7, 1.6 Hz), 6.22 (d, 1H, J = 3.3 Hz), 6.15 (dd, 1H, J = 3.3, 1.8 Hz), 5.26 (d, 1H, J = 11.1 Hz), 5.08 (dd,

1H, J = 12.1, 2.5 Hz), 4.84 (d, 1H, J = 2.5 Hz), 4.56 (d, 1H, J = 11.2 Hz), 2.75 (td, 1H, J = 13.0, 2.6 Hz), 2.57 (s, 3H), 2.48 (s, 3H), 2.42 (dd, 1H, J = 14.0, 2.6 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 192.8, 158.3, 152.4, 147.4, 141.5, 138.4, 136.3, 135.9, 130.7, 130.6, 127.7, 127.6, 127.4, 126.6, 126.4, 125.9, 119.2, 112.3, 110.3, 105.5, 74.0, 56.3, 43.9, 41.7, 39.0, 19.7, 19.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_4SNa$ 481.1444; found 481.1432.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-di-m-tolyltetrahydro-2*H*-thiopyran-3-yl)methanone (**3af**). Obtained as a white solid; isolated yield: 170.0 mg (74%); mp 125–127 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, 1H, J = 1.7, 0.7 Hz), 7.27–7.25 (m, 1H), 7.24–7.14 (m, 5H), 7.08–6.99 (m, 2H), 6.90–6.85 (m, 2H), 6.28 (dd, 1H, J = 3.6, 1.7 Hz), 6.17 (dd, 1H, J = 3.3, 0.9 Hz), 6.11 (dd, 1H, J = 3.6, 1.7 Hz), 4.90 (s, 1H), 4.85 (d, 1H, J = 11.2 Hz), 4.78 (dd, 1H, J = 12.2, 2.6 Hz), 4.43 (d, 1H, J = 11.2 Hz), 2.61 (t, 1H, J = 13.0 Hz), 2.42 (dd, 1H, J = 13.9, 2.7 Hz), 2.34 (s, 3H), 2.20 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.9, 158.4, 152.6, 147.2, 141.5, 140.4, 138.3, 138.0, 137.5, 129.2, 128.7, 128.6, 128.42, 128.40, 128.2, 125.5, 124.8, 119.0, 112.3, 110.3, 105.4, 73.8, 56.4, 47.1, 44.6, 42.9, 21.4, 21.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_4SNa$ 481.1444; found 481.1440.

(2,6-Bis(3,5-dimethylphenyl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-yl)methanone (**3ag**). Obtained as a white solid; isolated yield: 224.1 mg (92%); mp 200–201 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, 1H, J = 1.7 Hz), 7.20 (d, 1H, J = 1.8 Hz), 7.12 (s, 2H), 7.04 (s, 2H), 6.96 (d, 1H, J = 3.6 Hz), 6.94 (s, 1H), 6.73 (s, 1H), 6.34 (dd, 1H, J = 3.7, 1.7 Hz), 6.23 (d, 1H, J = 3.3 Hz), 6.16 (dd, 1H, J = 3.3, 1.8 Hz), 4.93 (d, 1H, J = 2.6 Hz), 4.87 (d, 1H, J = 11.2 Hz), 4.80 (dd, 1H, J = 12.2, 2.6 Hz), 4.51 (d, 1H, J = 11.2 Hz), 2.64 (td, 1H, J = 13.0, 2.6 Hz), 2.50 (dd, 1H, J = 13.9, 2.7 Hz), 2.35 (s, 6H), 2.20 (s, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.0, 158.5, 152.7, 147.1, 141.5, 140.4, 138.2, 137.8, 137.3, 129.5, 129.3, 126.3, 125.5, 118.9, 112.3, 110.3, 105.4, 73.9, 56.3, 47.0, 44.7, 43.0, 21.3, 21.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{30}H_{30}O_4SNa$ 509.1757; found 509.1756.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-bis(4-isopropylphenyl)tetrahydro-2*H*-thiopyran-3-yl)methanone (**3ah**). Obtained as a white solid; isolated yield: 245.0 mg (95%); mp 169–171 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.43–7.39 (m, 3H), 7.34–7.31 (m, 2H), 7.24–7.19 (m, 3H), 7.01 (d, 2H, J = 8.0 Hz), 6.90 (d, 1H, J = 3.6 Hz), 6.29 (dd, 1H, J = 3.6, 1.7 Hz), 6.22 (d, 1H, J = 3.3 Hz), 6.15 (dd, 1H, J = 3.3, 1.8 Hz), 5.02 (d, 1H, J = 2.6

Hz), 4.92 (d, 1H, *J* = 11.1 Hz), 4.85 (dd, 1H, *J* = 12.2, 2.6 Hz), 4.41 (d, 1H, *J* = 11.2 Hz), 2.97–2.89 (m, 1H), 2.81–2.72 (m, 1H), 2.64 (td, 1H, *J* = 13.0, 2.7 Hz), 2.50 (dd, 1H, *J* = 13.9, 2.7 Hz), 1.28 (d, 6H, *J* = 6.9 Hz), 1.13 (d, 6H, *J* = 6.9 Hz); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 193.1, 158.5, 152.5, 148.5, 148.2, 147.2, 141.5, 137.9, 135.0, 128.3, 127.6, 126.7, 126.4, 119.1, 112.2, 110.3, 105.4, 73.8, 56.8, 47.0, 44.8, 42.6, 33.8, 33.7, 23.82, 23.79; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{32}H_{35}O_4S$ 515.2251; found 515.2232.

(2,6-Bis(4-(tert-butyl)phenyl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-yl)methanone (**3ai**). Obtained as a white solid; isolated yield: 251.6 mg (93%); mp 186–188 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.39 (m, 5H), 7.34–7.31 (m, 2H), 7.19–7.16 (m, 3H), 6.89 (d, 1H, *J* = 3.6 Hz), 6.28 (dd, 1H, *J* = 3.7, 1.7 Hz), 6.23 (d, 1H, *J* = 3.3 Hz), 6.16 (dd, 1H, *J* = 3.3, 1.8 Hz), 5.04 (d, 1H, *J* = 2.6 Hz), 4.93 (d, 1H, *J* = 11.1 Hz), 4.85 (dd, 1H, *J* = 12.2, 2.6 Hz), 4.41 (d, 1H, *J* = 11.1 Hz), 2.63 (td, 1H, *J* = 13.0, 2.7 Hz), 2.48 (dd, 1H, *J* = 14.0, 2.7 Hz), 1.35 (s, 9H), 1.21 (s, 9H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 193.1, 158.5, 152.6, 150.8, 150.5, 147.1, 141.5, 137.6, 134.6, 128.1, 127.4, 125.6, 125.2, 119.1, 112.1, 110.3, 105.4, 73.8, 56.8, 46.9, 44.9, 42.5, 34.5, 34.4, 31.4, 31.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{34}H_{38}O_4SNa$ 565.2383; found 565.2387.

(2,6-Bis(4-ethylphenyl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-yl)methanone (**3aj**). Obtained as a white solid; isolated yield: 200.1 mg (82%); mp 177–178 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.33 (m, 3H), 7.32–7.31 (m, 2H), 7.21–7.19 (m, 3H), 7.00 (d, 2H, *J* = 7.7 Hz), 6.92 (d, 1H, *J* = 3.7 Hz), 6.31 (d, 1H, *J* = 3.7, 1.7 Hz), 6.22 (d, 1H, *J* = 3.3 Hz), 6.15-6.14 (m, 1H), 4.97 (d, 1H, *J* = 2.6 Hz), 4.92 (d, 1H, *J* = 11.1 Hz), 4.84 (dd, 1H, *J* = 12.1, 2.7 Hz), 4.43 (d, 1H, *J* = 11.1 Hz), 2.69–2.62 (m, 3H), 2.53–2.48 (m, 3H), 1.26 (t, 3H, *J* = 7.6 Hz), 1.12 (t, 3H, *J* = 7.6 Hz); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 193.0, 158.4, 152.5, 147.3, 143.9, 143.6, 141.5, 137.8, 134.9, 128.4, 128.2, 127.9, 127.7, 119.2, 112.2, 110.3, 105.4, 73.9, 56.7, 46.9, 44.7, 42.6, 28.5, 28.4, 15.5, 15.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{30}H_{30}O_4SNa$ 509.1757; found 509.1746.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-bis(4-propylphenyl)tetrahydro-2*H*-thiopyran-3-yl)methanone (**3ak**). Obtained as a white solid; Obtained as a white solid; isolated yield: 195.7 mg (76%); mp 153–154 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.31 (m, 5H), 7.19–7.17 (m, 3H), 6.97 (d, 2H, *J* = 7.8 Hz), 6.91 (d, 1H, *J* = 3.6 Hz), 6.30

(dd, 1H, J = 3.7, 1.7 Hz), 6.22 (d, 1H, J = 3.3 Hz), 6.15 (dd, 1H, J = 3.5, 1.8 Hz), 5.00 (d, 1H, J = 2.6 Hz), 4.91 (d, 1H, J = 11.1 Hz), 4.84 (dd, 1H, J = 12.2, 2.6 Hz), 4.42 (d, 1H, J = 11.1 Hz), 2.67–2.59 (m, 3H), 2.48–2.43 (m, 3H), 1.69–1.63 (m, 2H), 1.53–1.48 (m, 2H), 0.97 (t, 3H, J = 7.3 Hz), 0.81 (t, 3H, J = 7.3 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.0, 158.5, 152.5, 147.2, 142.3, 142.1, 141.5, 137.8, 134.9, 128.8, 128.5, 128.3, 127.6, 119.2, 112.2, 110.3, 105.4, 73.9, 56.8, 47.0, 44.7, 42.6, 37.7, 37.5, 24.5, 24.3, 13.9, 13.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{32}H_{34}O_4SNa$ 537.2070; found 537.2073.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-bis(4-(methylthio)phenyl)tetrahydro-2*H*-thiopyran-3-yl)methanone (**3al**). Obtained as a white solid; isolated yield: 111.7 mg (43%); mp 184–185 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.44–7.33 (m, 5H), 7.27–7.19 (m, 3H), 7.07–7.05 (m, 2H), 6.89 (d, 1H, J = 3.6 Hz), 6.35–6.34 (m, 1H), 6.21 (d, 1H, J = 3.4 Hz), 6.15 (dd, 1H, J = 3.4, 1.8 Hz), 4.90 (d, 1H, J = 11.2 Hz), 4.88 (d, 1H, J = 2.5 Hz), 4.81 (dd, 1H, J = 12.2, 2.6 Hz), 4.43 (d, 1H, J = 11.2 Hz), 2.63 (td, 1H, J = 13.0, 2.6 Hz), 2.51 (s, 3H), 2.48 (dd, 1H, J = 13.9, 2.7 Hz), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 192.6, 158.1, 152.4, 147.5, 141.5, 138.2, 137.9, 137.2, 134.4, 128.8, 128.2, 126.9, 126.5, 119.3, 112.4, 110.4, 105.5, 73.8, 56.5, 46.7, 44.4, 42.5, 15.9, 15.7; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_4S_3Na$ 545.0885; found 545.0898.

(2,6-Di([1,1'-biphenyl]-4-yl)-4-(furan-2-yl)-4-hydroxytetrahydro-2*H*-thiopyran-3-yl)(furan-2-yl)methanone (**3am**). Obtained as a white solids; isolated yield: 96.4 mg (33%); mp 171–172 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.64–7.59 (m, 6H), 7.53–7.47 (m, 6H), 7.44–7.39 (m, 6H), 7.38–7.31 (m, 2H), 6.98 (d, 1H, J = 3.6 Hz), 6.32 (d, 1H, J = 3.6), 6.26 (d, 1H, J = 3.3), 6.18 (d, 1H, J = 3.3), 5.04 (d, 1H, J = 11.2), 4.99 (d, 1H, J = 2.4), 4.96 (dd, 1H, J = 12.2, 2.6 Hz), 4.54 (d, 1H, J = 11.2 Hz), 2.74 (td, 1H, J = 13.0, 2.6 Hz), 2.55 (dd, 1H, J = 13.9, 2.6 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 192.8, 158.2, 152.5, 147.4, 141.6, 140.8, 140.6, 140.5, 139.5, 136.7, 128.9, 128.8, 128.7, 128.2, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 119.3, 112.4, 110.4, 105.6, 73.9, 56.6, 46.9, 44.6, 42.7; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{38}H_{30}O_4SNa$ 605.1757; found 605.1767.

Furan-2-yl(4-(furan-2-yl)-4-hydroxy-2,6-bis(4-methoxyphenyl)tetrahydro-2*H*-thiopyran-3-yl)methanone (**3an**). Obtained as a white solid; isolated yield: 92.2 mg (38%); mp 150–151 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.43–7.40 (m, 3H),

7.34 (d, 2H, J = 8.3 Hz), 7.19 (s, 1H), 6.95 (d, 1H, J = 3.6 Hz), 6.90 (d, 2H, J = 8.2 Hz), 6.71 (d, 2H, J = 8.2 Hz), 6.31 (dd, 1H, J = 3.7, 1.7 Hz), 6.21 (d, 1H, J = 3.3 Hz), 6.15 (dd, 1H, J = 3.5, 1.8 Hz), 4.92–4.89 (m, 2H), 4.81 (dd, 1H, J = 12.2, 2.6 Hz), 4.42 (d, 1H, J = 11.2 Hz), 3.83 (s, 3H), 3.71 (s, 3H), 2.63 (td, 1H, J = 13.0, 2.7 Hz), 2.44 (dd, 1H, J = 13.9, 2.7 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 193.0, 159.1, 159.0, 158.4, 152.5, 147.4, 141.5, 132.6, 129.8, 129.5, 128.8, 119.2, 114.1, 113.8, 112.3, 110.3, 105.4, 73.9, 56.8, 55.3, 55.2, 46.5, 44.6, 42.3; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{28}H_{27}O_6S$ 491.1523; found 491.1529.

(4-Hydroxy-2,6-diphenyl-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3ba**). Obtained as a white solid; isolated yield: 206.5 mg (89%); mp 173–175 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, $CDCl_3$) δ 7.52–7.31 (m, 9H), 7.18–6.99 (m, 5H), 6.87–6.79 (m, 2H), 5.72 (s, 1H), 5.50 (d, 1H, J = 10.8 Hz), 4.92 (d, 1H, J = 11.7 Hz), 4.30 (d, 1H, J = 10.9 Hz), 2.67–2.54 (m, 2H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 197.5, 151.9, 144.7, 140.4, 137.8, 135.3, 133.8, 128.8, 128.6, 128.5, 128.1, 127.8, 127.7, 127.7, 126.8, 124.1, 122.9, 75.6, 61.2, 48.7, 48.4, 43.3; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{22}O_2S_3$ 463.0855; found 463.0843.

(2,6-Bis(4-chlorophenyl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bb**). Obtained as a white solid; isolated yield: 240.4 mg (91%); mp 164–165 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, DMSO-d_6) δ 7.82 (d, 1H, J = 3.8), 7.73 (d, 1H, J = 5.0), 7.54–7.46 (m, 6H), 7.24 (d, 3H, J = 7.3), 7.14 (d, 1H, J = 5.0), 6.96 (t, 1H, J = 4.3), 6.79 (t, 1H, J = 4.2), 5.86 (s, 1H), 4.99 (d, 1H, J = 11.0), 4.76 (dd, 1H, J = 12.1, 2.5 Hz), 4.67 (d, 1H, J = 11.1 Hz), 2.81 (t, 1H, J = 12.9 Hz), 2.35 (dd, 1H, J = 13.5, 2.6 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d) δ 194.5, 152.8, 145.8, 139.9, 138.1, 135.9, 135.1, 132.7, 132.6, 130.9, 130.0, 129.3, 128.8, 128.6, 127.4, 124.6, 123.9, 74.9, 59.0, 47.7, 46.7, 42.4; HRMS (ESI) m/z: $[M+Cl]^-$ calcd for $C_{26}H_{20}Cl_3O_2S_3$ 564.9696; found 564.9701.

(2,6-Bis(4-bromophenyl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bc**). Obtained as a white solid; isolated yield: 275.4 mg (89%); mp 189–190 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^1H NMR (500 MHz, DMSO-d_6) δ 7.81 (d, 1H, J = 4.0), 7.73 (d, 1H, J = 4.0), 7.60 (d, 2H, J = 8.3), 7.47–7.36 (m, 6H), 7.23 (d, 1H, J = 3.6), 7.14 (d, 1H, J = 5.0), 6.96 (t, 1H, J = 4.2), 6.79 (t, 1H, J = 4.0), 5.86 (s, 1H), 4.98 (d, 1H, J = 10.9), 4.74 (dd, 1H, J = 11.9, 2.4 Hz), 4.66 (d, 1H, J = 11.1 Hz), 2.81 (t, 1H, J = 12.8 Hz), 2.35

(d, 1H, J = 13.1 Hz); $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-*d*) δ 194.4, 152.7, 145.8, 140.4, 138.5, 135.9, 135.0, 132.2, 131.7, 131.2, 130.4, 128.6, 127.4, 124.6, 123.9, 121.21, 121.19, 74.9, 58.9, 47.7, 46.7, 42.5; HRMS (ESI) m/z: $[M-H]^-$ calcd for $C_{26}H_{19}Br_2O_2S_3$ 616.8919; found 616.8918.

(4-Hydroxy-4-(thiophen-2-yl)-2,6-di-p-tolyltetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bd**). Obtained as a white solid; isolated yield: 171.9 mg (70%); mp 195–196 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.32 (m, 3H), 7.26–7.24 (m, 2H), 7.14–7.12 (m, 3H), 7.93 (d, 2H, J = 7.9 Hz), 6.89 (dd, 1H, J = 3.6, 0.8 Hz), 6.28 (dd, 1H, J = 3.6, 1.7 Hz), 6.16 (dd, 1H, J = 3.3, 0.9 Hz), 6.09 (dd, 1H, J = 3.3, 1.7 Hz), 4.86 (d, 2H, J = 11.2 Hz), 4.77 (dd, 1H, J = 12.3, 2.6 Hz), 4.39 (d, 1H, J = 11.2 Hz), 2.60 (td, 1H, J = 13.0, 2.7 Hz), 2.40 (dd, 1H, J = 13.9, 2.7 Hz), 2.32 (s, 3H), 2.17 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 192.9, 158.4, 152.5, 147.3, 141.4, 137.5, 137.3, 134.6, 129.3, 129.1, 128.3, 127.6, 119.1, 112.2, 112.2, 110.3, 105.4, 73.8, 56.6, 46.8, 44.6, 42.6, 21.1, 21.0; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_2S_3Na$ 513.0987; found 513.0968.

(4-Hydroxy-4-(thiophen-2-yl)-2,6-di-o-tolyltetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3be**). Obtained as a white solid; isolated yield: 195.7 mg (80%); mp 149–151 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, 1H, J = 7.8 Hz), 7.54 (d, 1H, J = 7.6 Hz), 7.46–7.44 (m, 2H), 7.27–7.21 (m, 3H), 7.07–6.95 (m, 5H), 6.90–6.79 (m, 2H), 5.61 (d, 1H, J = 2.4 Hz), 5.31 (d, 1H, J = 10.7 Hz), 5.11 (dd, 1H, J = 11.2, 3.0 Hz), 4.37 (d, 1H, J = 10.8 Hz), 2.67–2.58 (m, 5H), 2.45 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 197.6, 151.8, 144.6, 138.3, 136.4, 136.02, 135.98, 135.1, 133.8, 130.72, 130.70, 128.0, 127.8, 127.7, 127.4, 126.8, 126.5, 126.4, 126.1, 124.0, 123.0, 75.9, 60.8, 47.9, 42.8, 39.5, 19.7, 19.3; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_2S_3Na$ 513.0987; found 513.0968.

(4-Hydroxy-4-(thiophen-2-yl)-2,6-di-m-tolyltetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bf**). Obtained as a white solid; isolated yield: 199.9 mg (82%); mp 142–143 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, 1H, J = 4.9 Hz), 7.40 (d, 1H, J = 3.9 Hz), 7.32–7.21 (m, 5H), 7.13–6.98 (m, 4H), 6.88–6.79 (m, 3H), 5.70 (d, 1H, J = 2.6 Hz), 4.93 (d, 1H, J = 10.8 Hz), 4.87 (dd, 1H, J = 11.2, 3.0 Hz), 4.30 (d, 1H, J = 10.8 Hz), 2.63 (dd, 1H, J = 13.9, 2.8 Hz), 2.54 (td, 1H, J = 13.0, 2.6 Hz), 2.40 (s, 3H), 2.23 (s, 3H); $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 197.6, 152.0, 144.8, 140.3, 138.4, 138.1, 137.6, 135.2, 133.7, 129.2, 128.7, 128.6, 128.5, 128.4, 127.6, 126.8, 125.5, 124.8, 124.0, 122.9, 75.7, 61.1, 48.7, 48.3,

43.3, 21.5, 21.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_2S_3Na$ 513.0987; found 513.0982.

(2,6-Bis(3,5-dimethylphenyl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bg**). Obtained as a white solid; isolated yield: 227.5 mg (88%); mp 181–182 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, 1H, J = 4.9 Hz), 7.41 (d, 1H, J = 3.8 Hz), 7.12 (s, 2H), 7.06 (d, 1H, J = 5.0 Hz), 7.00 (s, 2H), 6.99 (d, 1H, J = 3.6 Hz), 6.94 (s, 1H), 6.89–6.79 (m, 2H), 6.68 (s, 1H), 5.69 (d, 1H, J = 2.6 Hz), 4.88 (d, 1H, J = 10.8 Hz), 4.83 (dd, 1H, J = 11.8, 2.8 Hz), 4.29 (d, 1H, J = 10.7 Hz), 2.61 (dd, 1H, J = 13.9, 2.7 Hz), 2.52 (td, 1H, J = 13.0, 2.6 Hz), 2.35 (s, 6H), 2.18 (s, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.7, 152.2, 144.9, 140.3, 138.2, 137.9, 137.4, 135.0, 133.5, 129.5, 129.3, 127.4, 126.8, 126.3, 125.5, 124.0, 122.8, 75.7, 61.1, 48.8, 48.3, 43.3, 21.3, 21.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{30}H_{30}O_2S_3Na$ 541.1300; found 541.1313.

(4-Hydroxy-2,6-bis(4-isopropylphenyl)-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bh**). Obtained as a white solid; isolated yield: 255.3 mg (94%); mp 187–188 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44–7.40 (m, 3H), 7.34–7.31 (m, 3H), 7.25 (d, 2H, J = 8.0 Hz), 7.06 (dd, 1H, J = 5.0, 1.1 Hz), 6.99–6.97 (m, 3H), 6.84–6.79 (m, 2H), 5.76 (d, 1H, J = 2.5 Hz), 4.96 (d, 1H, J = 10.8 Hz), 4.89 (dd, 1H, J = 11.9, 2.7 Hz), 4.24 (d, 1H, J = 10.7 Hz), 2.96–2.91 (m, 1H), 2.76–2.70 (m, 1H), 2.63 (dd, 1H, J = 14.0, 2.7 Hz), 2.63 (td, 1H, J = 13.0, 2.7 Hz), 1.29 (d, 6H, J = 6.9 Hz), 1.09 (d, 6H, J = 6.9 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.9, 152.2, 148.7, 148.3, 144.8, 137.8, 135.2, 134.9, 133.8, 128.4, 127.6, 127.5, 126.8, 126.5, 124.0, 122.8, 75.7, 61.4, 49.0, 48.2, 43.0, 33.8, 33.7, 24.0, 23.83, 23.77; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{32}H_{35}O_2S_3$ 547.1794; found 547.1775.

(2,6-Bis(4-(tert-butyl)phenyl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bi**). Obtained as a white solid; isolated yield: 268.4 mg (94%); mp 196–197 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.34 (m, 5H), 7.33–7.31 (m, 3H), 7.14–7.12 (m, 2H), 7.06 (dd, 1H, J = 3.6, 1.2 Hz), 6.98 (dd, 1H, J = 3.6, 1.2 Hz), 6.82–6.79 (m, 2H), 5.76 (d, 1H, J = 2.6 Hz), 4.95 (d, 1H, J = 10.8 Hz), 4.89 (dd, 1H, J = 11.8, 2.6 Hz), 4.23 (d, 1H, J = 10.7 Hz), 2.63 (dd, 1H, J = 14.0, 2.7 Hz), 2.50 (td, 1H, J = 13.0, 2.7 Hz), 1.36 (s, 9H), 1.17 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.9, 152.3, 150.9, 150.5, 144.9, 137.5, 134.9, 134.8, 133.7, 128.1, 127.44, 127.36, 126.7, 125.6, 125.3, 124.0, 122.7, 75.7, 61.5, 49.0, 48.1, 42.8, 34.5, 34.4, 31.3, 31.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for

$C_{34}H_{38}O_2S_3Na$ 597.1926; found 597.1943.

(2,6-Bis(4-ethylphenyl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bj**). Obtained as a white solid; isolated yield: 229.3 mg (89%); mp 151–152 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.35 (m, 4H), 7.33–7.31 (m, 2H), 7.22 (d, J = 7.7 Hz, 2H), 7.06–6.97 (m, 4H), 6.86–6.78 (m, 2H), 5.71 (d, 1H, J = 2.5 Hz), 4.95 (d, 1H, J = 10.8 Hz), 4.87 (dd, 1H, J = 11.8, 2.7 Hz), 4.26 (d, 1H, J = 10.8 Hz), 2.70–2.55 (m, 3H), 2.53–2.45 (m, 3H), 1.27 (t, 3H, J = 7.6 Hz), 1.07 (t, 3H, J = 7.6 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.8, 152.1, 144.8, 144.1, 143.7, 137.7, 135.05, 134.99, 133.8, 128.4, 128.2, 128.0, 127.7, 127.6, 126.8, 124.0, 122.8, 75.7, 61.3, 48.8, 48.1, 43.0, 28.5, 28.4, 15.52, 15.49; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{30}H_{30}O_2S_3Na$ 541.1300; found 541.1278.

(4-Hydroxy-2,6-bis(4-propylphenyl)-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bk**). Obtained as a white solid; isolated yield: 225.6 mg (83%); mp 165–167 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.34 (m, 4H), 7.27–7.24 (m, 2H), 7.14 (d, 2H, J = 8.1 Hz), 7.00 (dd, 1H, J = 5.1, 1.2 Hz), 6.92–6.87 (m, 3H), 6.80–6.73 (m, 2H), 5.67 (s, 1H), 4.89 (d, 1H, J = 10.8 Hz), 4.82 (dd, 1H, J = 11.7, 2.8 Hz), 4.20 (d, 1H, J = 10.8 Hz), 2.59–2.53 (m, 3H), 2.46 (t, 1H, J = 13.0 Hz), 2.37 (t, 2H, J = 7.4 Hz), 1.64–1.59 (m, 2H), 1.43–1.38 (m, 2H), 0.92 (t, 3H, J = 7.3 Hz), 0.70 (t, 3H, J = 7.3 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.8, 152.1, 144.7, 142.4, 142.1, 137.7, 135.0, 133.7, 128.8, 128.6, 128.3, 127.5, 126.7, 123.9,122.8, 75.7, 61.4, 48.8, 48.1, 43.0, 37.7, 37.4, 24.5, 24.3, 13.8, 13.4; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{32}H_{35}O_2S_3Na$ 569.1613; found 569.1620.

(4-Hydroxy-2,6-bis(4-(methylthio)phenyl)-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bl**). Obtained as a white solid; isolated yield: 115.3 mg (42%); mp 151–153 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, 1H, J = 4.9 Hz), 7.42–7.38 (m, 3H), 7.34–7.31 (m, 3H), 7.28–7.27 (m, 1H), 7.06–7.03 (m, 3H), 6.97 (dd, 1H, J = 3.6, 1.2 Hz), 6.89–6.87 (m, 1H), 6.80–6.78 (m, 1H), 5.62 (d, 1H, J = 2.5 Hz), 4.93 (d, 1H, J = 10.9 Hz), 4.85 (dd, 1H, J = 11.9, 2.7 Hz), 4.25 (d, 1H, J = 10.8 Hz), 2.61 (dd, 1H, J = 14.0, 2.7 Hz), 2.53–2.48 (m, 4H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.4, 151.7, 144.6, 138.4, 137.9, 137.1, 135.4, 134.5, 133.8, 12.8.9, 128.2, 127.8, 126.9, 126.8, 126.7, 124.1, 123.0, 75.6, 61.1, 48.4, 47.9, 42.9, 15.9, 15.8; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{28}H_{26}O_2S_5Na$ 577.0429; found 577.0435.

(2,6-Di([1,1'-biphenyl]-4-yl)-4-hydroxy-4-(thiophen-2-yl)tetrahydro-2*H*-thiopyran-3-yl)(thiophen-2-yl)methanone (**3bm**). Obtained as a white solid; isolated yield: 104.3 mg (34%); mp 185–186 °C. Eluent: petroleum ether/ethyl acetate = 5/1, v/v. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.53 (m, 6H), 7.47–7.29 (m, 14H), 7.04–6.96 (m, 2H), 6.81–6.75 (m, 2H), 5.68 (s, 1H), 5.01 (d, 1H, J = 10.7 Hz), 4.93 (dd, 1H, J = 11.7, 2.6 Hz), 4.29 (d, 1H, J = 10.7 Hz), 2.65 (dd, 1H, J = 14.0, 2.6 Hz), 2.55 (t, 1H, J = 12.7 Hz); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 197.6, 151.8, 144.7, 140.9, 170.73, 140.66, 140.5, 139.4,136.8, 135.4, 133.8, 128.9, 128.8, 128.7, 128.2, 127.7, 127.5, 127.3, 127.2, 127.1, 127.0, 126.8, 124.1, 122.9, 75.6, 61.2, 48.6, 48.1, 43.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{38}H_{30}O_2S_3Na$ 637.1300; found 637.1315.

(*E*)-1-(furan-2-yl)-3-phenylprop-2-en-1-one (intermediate I of compound **3aa**). mp 85–86 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89 (d, 1H, J = 15.8 Hz), 7.64–7.66 (3H, m), 7.45 (d, 1H, J = 15.8), 7.41–7.43 (m, 3H), 7.33 (dd, 1H, J = 3.5, 0.4 Hz), 6.59 (dd, 1H, J = 3.5, 1.6 Hz). The NMR data were consistent with those in the literature [15].

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. ^{1}H, ^{13}C NMR spectra and HRMS for new compounds (PDF).

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The work is financially supported by Scientific and Technological Innovation Programs of Higher Education Institutions in Shanxi (2019L0941, 2019L0937, 2019L0966).

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data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam. ac.uk/data_request/cif.

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