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p-TSA/Base-Promoted Propargylation/Cyclization of *β*-Ketothioamides for the Regioselective Synthesis of Highly Substituted (Hydro)thiophenes

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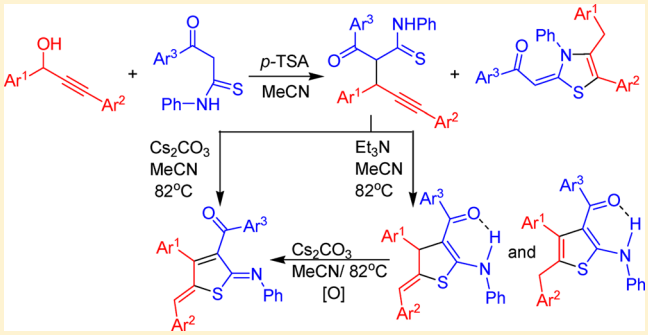
Supporting Information

ABSTRACT: Metal-free, *p*-toluenesulfonic acid (*p*-TSA)-mediated, straightforward propargylation of *β*-ketothioamides with aryl propargyl alcohol has been achieved at room temperature. In addition, the reaction also provided thiazole rings as byproducts. Furthermore, the propargylated thioamides undergo intramolecular 1,5-cyclization to afford fully substituted (hydro)thiophenes in the presence of base. Notably, the approach is pot, atom, and step economical (PASE).



INTRODUCTION

The thiophene structural motif has emerged as an important class of heterocycles because of its presence in numerous bioactive natural products and pharmacophores.[1,2] Thiophenes have been found as central cores in some of the top-selling drugs such as Plavix (potent antiplatelet agent), articaine (dental anasthetic), raloxifene (for osteoporosis), and PaTrin-2 (inhibitor of DNA inhibitor enzyme) (Figure 1).[3] Moreover, a few recent articles have shown that the thiophene moiety could be used as a potent PI3K inhibitor,[4] checkpoint kinase inhibitor,[5] allosteric agonist, and modulator of the adenosine A1 receptor 2A3BTs.[6] In addition, their structural rigidity and specific electronic properties make thiophene derivatives extremely applicable in electrically conducting organic materials, semiconductors, organic solar cells, organic light emitting diodes (OLEDs), lasers, dyes, liquid crystals, and molecular wires.[7]

Regarding the synthesis of thiophene derivatives, different approaches have been reported,[8] performing variations and improvements of classical Gewald and Paal–Knorr reactions.[9] The common approaches to polysubstituted thiophenes involve either direct functionalization of preconstructed thiophene rings via *α*-halogenation/metalation[10] or ring closure of the appropriately substituted open-chain precursors which include Morita–Baylis–Hillman adducts, *α*-enolic dithioesters, and *α*-oxoketene-*S*,*S*-acetals.[11,12]

β-Ketothioamides have been widely used as important building blocks for the construction of nitrogen and sulfur heterocycles.[13] Recently, Li et al.[14a] and Deng and co-workers[14b] independently synthesized thiophenes from *β*-ketothioamides via one-pot multicomponent reactions (MCRs) and ene-yne thiocarbinyl cyclization approaches, respectively. However, the propargylation/cyclization of *β*-ketothioamides to form thiophene has not been disclosed to date. In this regard, a new strategy for the synthesis of thiophene derivatives has been developed via propargylation/cyclization of *β*-ketothioamides (Scheme 1).

RESULTS AND DISCUSSION

Initially, the reaction of 3-oxo-*N*-phenyl-3-*p*-tolylpropanethioamide (**1a**) and 3-phenyl-1-*p*-tolylprop-2-yn-1-ol (**2a**) was carried out in dry dichloromethane (DCM) using 20 mol % of *p*-toluenesulfonic acid (*p*-TSA) at room temperature. Only 15% of propargylated thioamide **3a** was obtained, and most of the starting materials remained unreacted even after 24 h of stirring at room temperature (Table 1, entry 1). When the amount of *p*-TSA was increased to 40 mol %, all of the reactants were consumed within 1 h, affording the propargylated thioamide **3a** in 51% yield (Table 1, entry 2). Additionally, the thiazole ring byproduct **4a** was formed in this case, albeit in low yield (9%). A higher loading of *p*-TSA (60 mol %) led to quick consumption of the alcohol, furnishing the products **3a** (47% yield) and **4a** (8% yield) along with some unreacted thioamide **1a** (Table 1, entry 3). The above observation was encouraging enough to broaden the optimization studies. Consequently, a variety of solvents such as dichloroethane (DCE), toluene, and acetonitrile were

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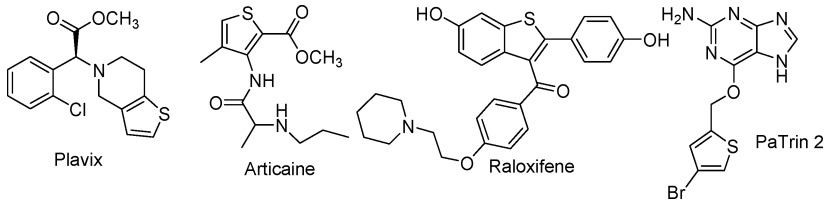
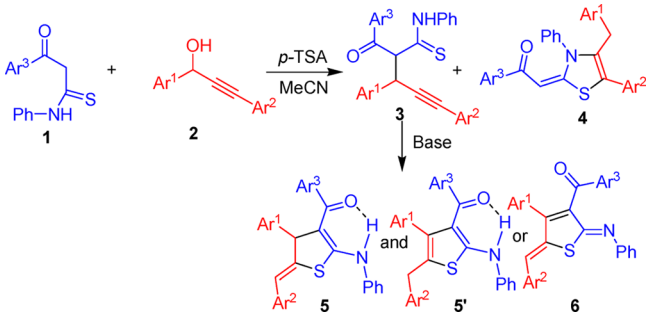


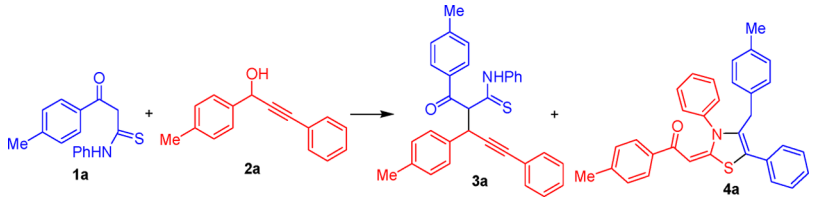
Figure 1. Thiophene-containing drugs.

Scheme 1. Propargylation/Cyclization of β-Ketothioamides



screened in the presence of 40 mol % of *p*-TSA in order to identify a solvent of choice (Table 1, entries 4, 5, and 7). It was found that acetonitrile provided the best result, furnishing 64% of the desired propargylated product **3a** along with 10% of thiazole ring **4a** within 1 h (Table 1, entry 7). A lesser amount of *p*-TSA loading (20 mol %) was found to be insufficient to drive the reaction forward (Table 1, entry 6). On the other hand, the formation of propargylated thioamide **3a** was consistently decreased with increments in *p*-TSA loading (60, 100, 200, and 500 mol %) (Table 1, entries 8−11). This may be due to the fact that a higher loading of *p*-TSA makes the propargylic cation formation process so fast that the thioamide could not compete with the cation, which was thought to transform to some other byproducts immediately. The formation of **4a** was not improved by raising the temperature (82 °C) but slightly lowered the formation of **3a** (Table 1, entry 12). The efficiency of some other catalysts toward the formation of **3a** and/or **4a** was also examined. Camphorsulfonic acid (CSA), indium chloride ($InCl_3$), and ferric chloride showed efficiency almost comparable to that of *p*-TSA toward the formation of **3a** (Table 1, entries 13, 15, 17, and 19). Attempts to examine triflic acid, hexafluorosilver antimonate

Table 1. Optimization Studies for the Reaction of β-Ketothioamide and Propargyl Alcohol[a]



entry	catalyst (amt (mol %))	solvent	yield[b] (%) 3a	4a
1	*p*-TSA (20)	DCM	15	
2	*p*-TSA (40)	DCM	51	9
3	*p*-TSA (60)	DCM	47	8
4	*p*-TSA (40)	DCE	49	8
5	*p*-TSA (40)	toluene	45	5
6	*p*-TSA (20)	MeCN	35	5
7	*p*-TSA (40)	MeCN	64	10
8	*p*-TSA (60)	MeCN	58	9
9	*p*-TSA (100)	MeCN	49	9
10	*p*-TSA (200)	MeCN	36	9
11	*p*-TSA (500)	MeCN	27	trace
12	*p*-TSA (40)	MeCN (82 °C)	59	10
13	CSA (40)	MeCN	61	8
14	triflic acid[c]	MeCN	*d*	*d*
15	$InCl_3$ (10)	MeCN	55	7
16	$AgSbF_6$(10)	MeCN	*d*	*d*
17	$FeCl_3$ (10)	MeCN	38	trace
18	$Cu(OTf)_2$ (10)	Toluene (90 °C)	*d*	*d*
19	$InCl_3$ (10)	DCM	39	7
20	$AgSbF_6$ (10)	Toluene (60 °C)	*d*	*d*
21	$SnCl_2$(10)	CH_3NO_2	trace	trace
22	$BF_3.OEt_2$[c]	DCM	*d*	*d*

[a]All reactions were performed at room temperature unless otherwise stated. [b]Isolated yield. [c]Catalytic amount. [d]Complex reaction mixture.

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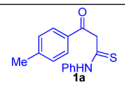
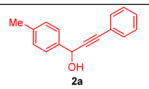
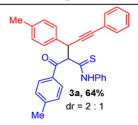
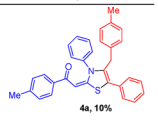
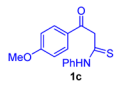
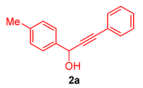
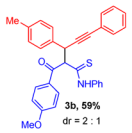
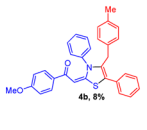
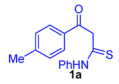
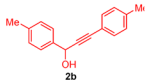
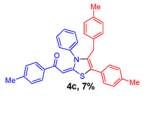
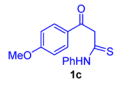
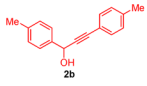
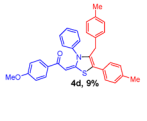
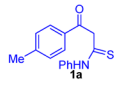
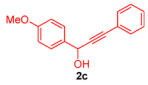
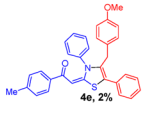
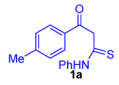
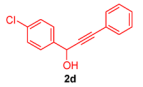
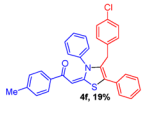
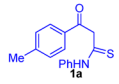
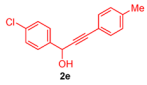
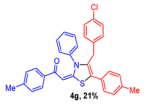
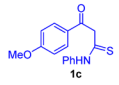
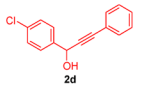
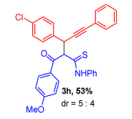
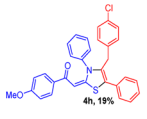
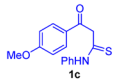
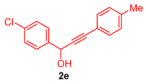
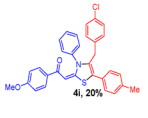
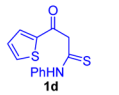
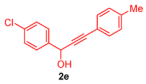
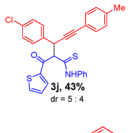
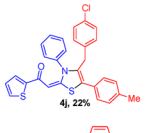
Table 2. Substrate Scope for the Synthesis of 3 and 4

Entry	Thioamide **1**	Propargyl alcohol **2**	Products **3**	Products **4**
1			 **3a, 64%** dr = 2 : 1	 **4a, 10%**
2			 **3b, 59%** dr = 2 : 1	 **4b, 8%**
3			 **3c, 57%** dr = 2 : 1	 **4c, 7%**
4			 **3d, 62%** dr = 2 : 1	 **4d, 9%**
5			 **3e, 66%** dr = 5 : 4	 **4e, 2%**
6			 **3f, 50%** dr =4 : 3	 **4f, 19%**
7			 **3g, 47%** dr = 4 : 3	 **4g, 21%**
8			 **3h, 53%** dr = 5 : 4	 **4h, 19%**
9			 **3i, 57%** dr = 3 : 2	 **4i, 20%**
10			 **3j, 43%** dr = 5 : 4	 **4j, 22%**
11			**3k, 48%** dr = 5 : 2	**4k, 23%**
12			**3l, 50%** dr = 2 : 1	**4l, 22%**
13			trace	**4m, 23%**
14			trace	**4n, 19%**
15			**3o, 58%** dr = 1 : 1	**4o, 8%**
16			**3p, 59%** dr = 1 : 1	**4p, 9%**
17			**3q, 45%** dr = 2.5 : 1	**4q, 19%**

Scheme 2. Reaction of N,N-Disubstituted β-Ketothioamides and Propargyl Alcohols

3*	7
3r; R^1 = Me, R^2 = H	**7a**; R^1 = Me, R^2 = H , 14%
3s; R^1 = Me, R^2 = Me	**7b**; R^1 = Me, R^2 = Me, trace
3t; R^1 = Cl, R^2 = H	**7c**; R^1 = Cl, R^2 = H, trace

*Compounds **3** could not be purified properly

($AgSbF_6$), $BF_3{\cdot}OEt_2$, $Cu(OTf)_2$, and stannous chloride ($SnCl_2$) were unsuccessful, as these offered only complex reaction mixtures (Table 1, entries 14, 16, 18, and 20–22). Thus, it has been found that the use of 40 mol % of *p*-TSA in acetonitrile at room temperature is the optimum condition for the propargylation/thiazole formation from thioamide (Table 1, entry 7). It should be noted that compound **3** was obtained as a diastereoeric mixture and the ratio has been mentioned in Table 2. To check whether **3a** was acting as an intermediate toward **4**, pure **3a** was refluxed with *p*-TSA in MeCN; however, the treatment did not render **4**.

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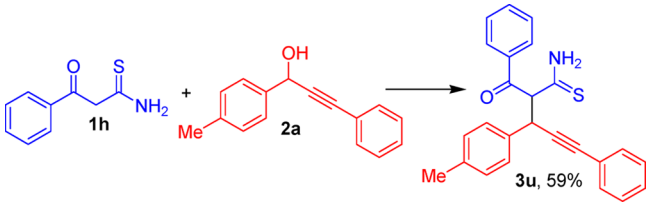
To establish the viability of this method, the substrate scope for the reaction was investigated under the optimized reaction conditions (Table 1, entry 7) by varying the structures of β-ketothioamide and propargylic alcohol, and the results are depicted in Table 2. β-Ketothioamides, irrespective of the electron-withdrawing/-releasing nature of the substituents of the aryl moiety, show moderate to good reactivity toward the total product formation of **3** and **4**. The propargylic alcohol was found to be the deciding factor in the ratios of the formation of **3** and **4**. Electron-rich aryl groups (p-$CH_3C_6H_4$, p-$OCH_3C_6H_4$) linked with the carbinol carbon of propargylic alcohol furnished **3** in good yields (**3a−e**, 57−66%), while **4** was obtained in very low quantity (**4a−e**, 2−10%). In contrast, a chloro-substituted aryl group provided **3** in slightly lower yield (**3f−i**) and **4** in somewhat better amount (**4f−i**) in comparison to the electron-rich counterparts. In an interesting observation, the o-dichloro-substituted and nitro-substituted propargylic alcohols furnished **3** in trace amounts and provided only **4** (**4m,n**). Both of the above reactions required 100 mol % of p-TSA and a longer time (48 h) for completion. β-Ketothioamides bearing an alkyl chain (n-C_4H_{10}) in the thioamide part also work well for the transformation (Table 2, entries 15−17). A modification of the aryl group of the alkyne end did not cause any notable change in the outcome of the reaction (**3c,d,g,i,j,o−q** and **4c,d,g,i,j,o−q**). In addition to the full spectroscopic characterization, the structures of **4** were confirmed by X-ray single-crystal diffraction (i.e. **4i**).[15]

The N,N-disubstituted β-ketothioamide **1g** did not provide any thiazole ring **4** but afforded propargylated thioamide **3**, which underwent in situ cyclization (partially) to the corresponding thiophene **7** in an acidic medium (Scheme 2). Unfortunately, compound **3** could not be isolated in its pure form. On the other hand, only **7a** was isolated in 14% yield and other thiophenes **7b,c** were obtained in trace amounts. The effort to cyclize **3** in the presence of Et_3N (1.0 equiv) in MeCN at 82 °C afforded only a trace amount of **7**. In a similar observation, the N,N-unsubstituted β-ketothioamide **1h** yielded only 59% of propargylated thioamide **3u** without any trace of thiazole **4** (Scheme 3).

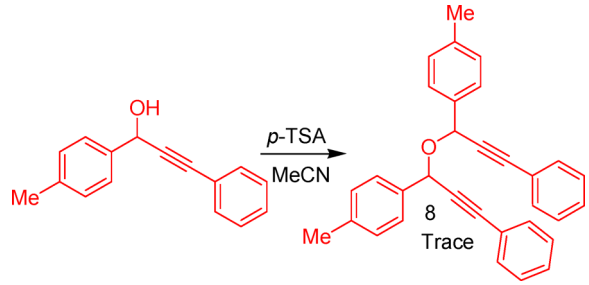
Scheme 3. Reaction of N,N-Unsubstituted β-Ketothioamide and Propargyl Alcohol



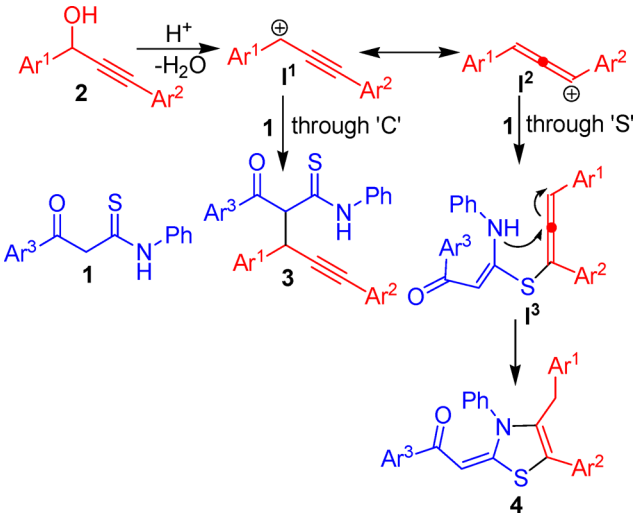
In a control experiment, propargylic alcohol was treated with p-TSA (40 mol %) at room temperature but the reaction provided only a trace of **8**, which was confirmed by mass data (Scheme 4).[16i]

Although the mechanism has not been established, a probable mechanistic pathway is portrayed in Scheme 5 explaining the formation of **3** and **4**. The propargylic alcohol **2** undergoes dehydration in the presence of acid to generate propargylic cation $\mathbf{I^1}$, which could also coexist in its allenic form $\mathbf{I^2}$. $\mathbf{I^1}$ reacts through the α-carbon nucleophilic center of the β-ketothioamide via a common pathway[16a−h] to provide **3**. The β-ketothioamide, through its "S" center, reacts with $\mathbf{I^2}$, generating

Scheme 4. Acid Treatment of Propargylic Alcohol



Scheme 5. Probable Mechanistic Route for 3 and 4



the intermediate $\mathbf{I^3}$. $\mathbf{I^3}$ undergoes intramolecular cyclization through "N" to furnish thiazole ring **4**. The presence of an electron-withdrawing group in Ar^1 decreases the cationic stability of $\mathbf{I^1}$, thereby increasing the generation of $\mathbf{I^2}$ and providing **4** in better yield (Table 2, **4f−n**). A propargylic alcohol with strongly electron -deficient aryl groups ($-NO_2$ and $-Cl_2$ substituted phenyl; **2h,i**) afforded **3** in a trace amount, as the generated cation $\mathbf{I^1}$ may be destabilized by the strongly electron withdrawing group, affording only **4**.

Having successfully developed an efficient route to α-propargylation of β-ketothioamides, we turned our attention to cyclize the propargylated thioamide **3**. A brief literature survey revealed that there are a number of reports available where 1,3-dicarbonyl compounds have been propargylated and further transformed to highly substituted furan rings in the presence of a suitable base or Lewis acid.[16a−h] α-Propargylated β-ketothioamide is a relevant organic intermediate, having polyfunctional groups with multiple reactive sites, which could be further cyclized into various classes of heterocycles with interesting properties (Figure 2). To this end, herein we disclose the transformation of α-propargylated β-ketothioamides **3** into fully substituted dihydrothiophenes **5**/**6** in the presence of base.

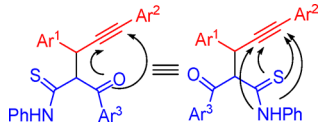


Figure 2. Reactive centers of propargylated thioamide **3**.

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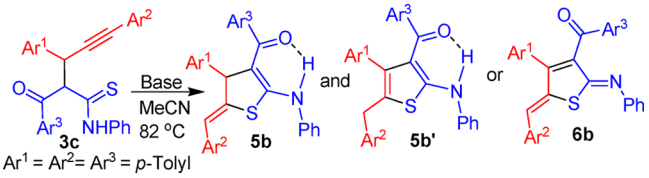
Consequently, the isolated propargylated thioamide **3c** was treated with a number of organic and inorganic bases such as Et_3N, DABCO, DMAP, K_2CO_3, and Cs_2CO_3 (1 equiv each) in separate experiments in acetonitrile and heated at 82 °C (Table 3, entries 1−5). Interestingly, in all cases the propargylated

Table 3. Optimization for Intramolecular Cyclization of 3



$Ar^1 = Ar^2 = Ar^3 = p$-Tolyl

		yield (%)[a]		
entry	base (amt (equiv))	5b	5b′	6b
1[b]	Et_3N (1.0)	89	trace	
2[b]	Cs_2CO_3 (1.0)			96
3[b]	K_2CO_3 (1.0)	85	trace	
4[b]	DABCO (1.0)	81	trace	
5[b]	DMAP (1.0)	82	trace	
6	Et_3N (1.0)[c]	52	34	
7	Et_3N (2.0)[d]	36	45	
8	Et_3N (3.0)[d]	35	44	

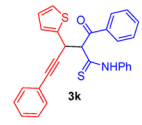
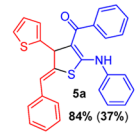
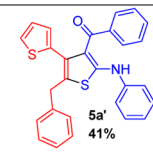
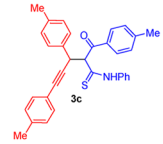
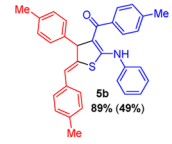
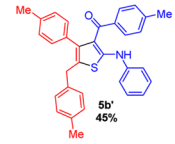
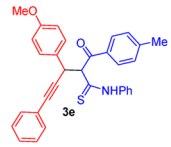
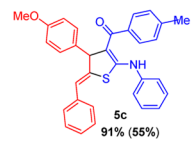
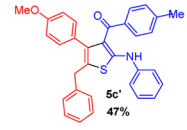
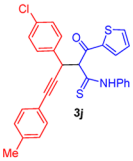
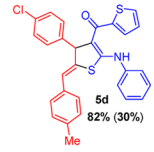
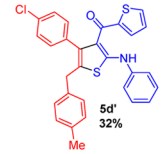
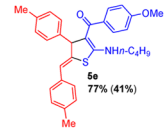
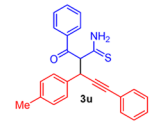
[a]Isolated yield. [b]Reaction mixtures were heated for 30−40 min at 82 °C. [c]The reaction was performed for 12 h at 82 °C. [d]The reaction was performed for 6 h at 82 °C.

thioamide was consumed within 30−40 min. The results in Table 3 displayed that Et_3N, K_2CO_3, DABCO, and DMAP promoted the reaction toward exclusive formation of dihydroaminothiophene **5b** along with a trace amount of **5b′** (Table 3, entries 1 and 3−5). However, Cs_2CO_3 provided only oxidized dihydroiminothiophene **6b** exclusively (Table 3, entry 2). Increasing the amount of base and prolonging the reaction time did not improve the complete conversion of **3c** into **5b′**, although the yield of **5b′** was improved to some extent (Table 3, entries 7 and 8). The π-electron conjugation between the Ar^2 and exocyclic double bond may stabilize **5b** with respect to its aromatic counterpart **5b′**.

As Et_3N and Cs_2CO_3 furnished **5** and **6**, respectively, in maximum yield (Table 3, entries 1 and 2), so the generality of the reaction was also established by treating a variety of propargylated thioamides **3** with Et_3N and Cs_2CO_3 separately to provide the desired compounds **5** and **6**. The results in Table 4 demonstrate that N-monosubstituted propargylated thioamides **3c,e,j,k,p** afforded the corresponding dihydrothiophenes **5a−e** in good to excellent yields in the presence of Et_3N (Table 4, entries 1−5). We observed that all of the N-aryl group containing propargylated thioamides (**3c,e,j,k**) provided **5′** on prolonging the reaction time and using 2.0 equiv of Et_3N. However, the N-alkyl containing propargylated thioamide **3p** did not provide the corresponding **5′** even after 18 h of heating in the presence of Et_3N (Table 4, entry 5). Interestingly, the N,N-unsubstituted propargylated thioamide **3u** transformed to thiophene **5f′** (Table 4, entry 6) and we could not isolate any intermediate (dihydrothiophene **5**).

The substrate scope for the formation of oxidized dihydroiminothiophene **6** using Cs_2CO_3 is described in Table 5. Though N-aryl propargylated thioamides worked well for this transformation under the optimized conditions, N-alkyl propargylated thioamides **3p,q** decomposed on treatment with

Table 4. Substrate Scope for the Synthesis of 5 from 3 using Et_3N[a]

entry	propargylated thioamide **3**	dihydrothiophene **5**[b]	thiophene **5′**[c]
1			
2			
3			
4			
5[d]			Not formed
6[e]			

[a]All reactions were performed in acetonitrile at 82 °C. [b]Reaction mixtures were heated for 30−40 min at 82 °C, and 1.0 equiv of Et_3N was used. [c]The reaction mixtures were heated for 6−7 h at 82 °C, and 2.0 equiv of Et_3N was used. [d]The reaction mixture was heated for 8 h at 82 °C. [e]The reaction mixture was heated for 9 h at 82 °C.

Cs_2CO_3. The N,N-unsubstituted propargylated thioamide **3u** showed reactivity similar to that with Et_3N and afforded only thiophene **5f′** (65%) within 40 min at room temperature. To check whether the oxidative cyclization is proceeding through a radical mechanism or not, we treated **3a** with Cs_2CO_3 (1.0 equiv)/TEMPO (2.0 equiv) and heated the reaction mixture at 82 °C in MeCN for 40 min, but we could not find any drop in the formation of **6**. The skeleton of **6** was confirmed by X-ray single-crystal diffraction analysis of **6a**.[17]

Furthermore, in order to validate the possibility of a one-pot transformation toward the thiophene ring, we added Et_3N and Cs_2CO_3 independently to the in situ generated propargylated thioamide **3** (by the reaction of the respective β-ketothioamide and propargyl alcohol), and the reaction mixture was heated at 82 °C for 30−40 min. As expected, the reaction also provided the corresponding desired compounds **5** and **6** (yields are given in parentheses in Tables 4 and 5). Another experiment exhibited that **5b** could be easily oxidized to **6b** by treating with Cs_2CO_3 at 82 °C in acetonitrile.

CONCLUSION

In conclusion, the first synthesis of α-propargylated β-ketothioamides has been presented in the presence of *p*-TSA.

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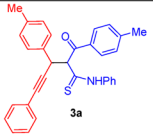
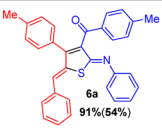
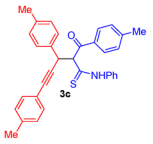
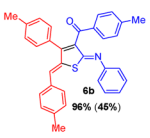
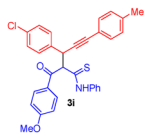
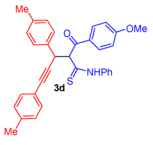
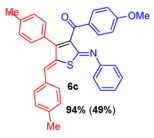
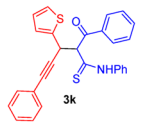
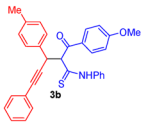
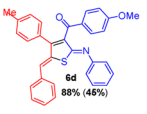
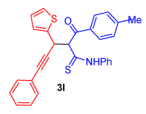
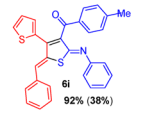
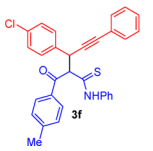
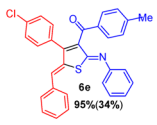
Table 5. Substrate Scope for the Synthesis of Iminothiophenes 6 from 3 using Cs_2CO_3[a]

Entry	Propargylated thioamide 3	Dihydroiminothiophene 6	Entry	Propargylated thioamide 3	Dihydroiminothiophene 6
1			6		
2			7		
3			8		
4			9		
5					

[a]All reactions were performed using 1.0 equiv of Cs_2CO_3 at 82 °C in MeCN; the yields in parentheses refer to the formation of **6** from in situ generated propargylated thioamide.

The process also provides a thiazoline ring as a byproduct. Moreover, the α-propargylated β-ketothioamides were further cyclized to highly substituted thiophenes via a base-promoted intramolecular cycloisomerization. The advantages of this method are atom and pot economy, mild reaction conditions, moderate to good yields, and economic viability of the promoter. In addition, a slight tuning of the base leads to various kinds of thiophenes. Further applications of α-propargylated β-ketothioamides on the extensions of this protocol are underway in the laboratory.

EXPERIMENTAL SECTION

General Considerations. The starting material β-ketothioamides[13a,f,18b] and propargylic alcohols[18a] were synthesized in the laboratory following the reported methods. The catalysts and bases were purchased from various suppliers and used as received. ^{1}H and ^{13}C NMR spectra were recorded on an NMR spectrophotometer operating at 500 and 126 MHz, respectively. Chemical shifts for ^{1}H and ^{13}C NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0). IR spectra were measured in NaCl, and wavelengths are reported in cm^{-1}. Mass spectra were recorded under ESI/HRMS at a resolution of 60000 using an ion trap mass analyzer. Melting points are uncorrected.

General Procedure for the Reaction of β-Ketothioamide 1a and Propargyl Alcohol (2a) for the Synthesis of Propargylated β-Ketothioamide (3a) and Thiazole (4a). To a 1.5 mL acetonitrilic solution of β-ketothioamide **1a** (100 mg, 0.371 mmol) and propargyl alcohol **2a** (82.5 mg, 0.371 mmol) was added *p*-TSA (28 mg, 40 mol %), and the whole reaction mixture was stirred for 1 h at room temperature. After completion of the reaction (checked by TLC), sodium bicarbonate solution was added to it and extracted with dichloromethane (2 × 10 mL). The organic layer was then washed with water followed by brine solution. Then the DCM layer was dried (Na_2SO_4), evaporated, and purified by silica gel column chromatography. Compound **3a** was eluted using 7% of ethyl acetate in hexane as eluent (112 mg; 64%), and **4a** was eluted using 17% of ethyl acetate in hexane as eluent (17 mg, 10%). All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

General Procedure for the Et_3N-Promoted Cycloisomerization of Propargylated β-Ketothioamide 3k for the Synthesis of Dihydroaminothiophene 5a. Triethylamine (9.2 μL, 0.0665 mmol) was added to a 0.5 mL acetonitrilic solution of propargylated β-ketothioamide **3k** (30 mg, 0.0665 mmol) in a Schlenk tube covered with a $CaCl_2$ guard tube, and the whole reaction mixture was heated at 82 °C for 35 min. After completion of the reaction (checked by TLC), the solvent was evaporated and compound **5a** was purified by silica gel column chromatography using 8% of ethyl acetate in hexane as eluent (25 mg, 84%). All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

General Procedure for the Et_3N-Promoted Cycloisomerization of Propargylated β-Ketothioamide 3k for the Synthesis of Aminothiophene 5a′. Triethylamine (18 μL, 0.133 mmol) was added to a 0.5 mL acetonitrilic solution of propargylated β-ketothioamide **3k** (30 mg, 0.0665 mmol) in a Schlenk tube covered with a $CaCl_2$ guard tube, and the whole reaction mixture was heated at 82 °C for 6 h. After completion of the reaction (checked by TLC), the solvent was evaporated and the compound **5a′** was purified by silica gel column chromatography using 5% of ethyl acetate in hexane as eluent (12 mg, 41%). All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

General Procedure for the Cs_2CO_3-Promoted Oxidative Cyclization of Propargylated β-Ketothioamide 3a for the Synthesis of Dihydroiminothiophene 6a. Cs_2CO_3 (20.7 mg, 0.0637 mmol.) was added to a 0.5 mL acetonitrilic solution of propargylated β-ketothioamide **3a** (30 mg, 0.0637 mmol), and the whole reaction mixture was heated at 82 °C for 40 min. After completion of the reaction (checked by TLC), the solvent was

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evaporated and the compound **6a** was purified by silica gel column chromatography using 7% of ethyl acetate in hexane as eluent (27 mg, 91%). All compounds were characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

Characterization Data of the Isolated Compounds. *N-Phenyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-5-phenylpent-4-yne-1-thioamide (**3a**).* Mixture of diastereomers (2:1). Yield: 112 mg, 64% (from 0.371 mmol of thioamide). Pale yellow solid, mp 143−145 °C. IR (NaCl, cm^{-1}): 3301, 3054, 3027, 2921, 2852, 2199, 1715, 1649, 1609, 1452.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.64 (s, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.35−7.27 (m, 5H), 7.24−7.14 (m, 7H), 7.06 (d, J = 8.0 Hz, 2H), 5.53 (d, J = 8.0 Hz, 1H), 4.70 (d, J = 8.0 Hz, 1H), 2.38 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.2, 193.5, 145.2, 138.9, 137.6, 134.9, 134.3, 131.7, 129.5, 129.4, 129.4, 129.3, 128.9, 128.3, 128.2, 126.7, 123.4, 123.1, 87.8, 86.7, 69.6, 44.5, 21.9, 21.3. HRMS (ESI): calcd for $C_{32}H_{27}NOS$ [M + Na]$^+$ 496.1706; found, 496.1711.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.10 (s, 1H), 7.87 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.35−7.27 (m, 5H), 7.24−7.14 (m, 7H), 7.02 (d, J = 7.5 Hz, 2H), 5.60 (d, J = 9.0 Hz, 1H), 4.77 (d, J = 9.0 Hz, 1H), 2.36 (s, 3H),, 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.7, 194.0, 145.4, 138.9, 137.5, 134.6, 134.6, 131.9, 129.6, 129.6, 129.4, 129.3, 128.9, 128.4, 128.3, 126.7, 122.9, 122.5, 87.8, 86.9, 69.4, 43.1, 21.8, 21.2.

*N-Phenyl-2-(4-methoxybenzoyl)-3-(4-methylphenyl)-5-phenylpent-4-yne-1-thioamide (**3b**).* Mixture of diastereomers (2:1). Yield: 101 mg, 59% (from 0.350 mmol of thioamide). Pale yellow solid, mp 125−127 °C. IR (NaCl, cm^{-1}): 3290, 3055, 3025, 2922, 2197, 1654, 1598, 1512.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.72 (s, 1H), 7.95 (d, J = 9.0 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.35−7.32 (m, 4H) 7.24−7.18 (m, 4H), 7.08 (d, J = 7.5 Hz, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.94 (bs, 1H), 6.87−6.84 (m, 2H), 5.50 (d, J = 8.5 Hz, 1H), 4.70 (d, J = 8.5 Hz, 1H), 3.84 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.8, 193.6, 164.6, 138.9, 137.5, 134.4, 131.8, 131.7, 130.4, 129.4, 128.9, 128.6, 128.4, 128.2, 127.2, 126.7, 123.1, 114.0, 87.9, 86.8, 69.1, 55.6, 44.5, 21.3. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ [M + Na]$^+$, 512.1655; found, 512.1640.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.96 (d, J = 9.5 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.35−7.32 (m, 4H) 7.24−7.18 (m, 4H), 7.08 (d, J = 7.5 Hz, 2H), 7.02 (d, J = 8.0 Hz, 1H), 6.87−6.84 (m, 2H), 6.74 (d, J = 8.5 Hz, 1H), 5.55 (d, J = 9.0 Hz, 1H), 4.77 (d, J = 9.0 Hz, 1H), 3.82 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 164.7, 138.9, 137.5, 134.8, 131.9, 131.9, 130.0, 129.3, 128.9, 128.5, 128.3, 128.1, 126.8, 126.7, 123.4, 113.3, 87.1, 86.6, 69.5, 55.6, 43.1, 21.2.

*N-Phenyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3c**).* Mixture of diastereomers (2:1). Yield: 103 mg, 57% (from 0.371 mmol of thioamide). Pale yellow solid, mp 114−116 °C. IR (NaCl, cm^{-1}): 3289, 3026, 2921, 2852, 2195, 1652, 1602, 1512.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.66 (s, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 7.5 Hz, 2H), 7.35−7.26 (m, 4H), 7.23−7.17 (m, 4H), 7.06−6.98 (m, 5H), 5.52 (d, J = 8.5 Hz, 2H), 4.68 (d, J = 8.5 Hz, 1H), 2.39 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.2, 193.5, 145.1, 138.9, 138.2, 137.5, 135.0, 134.4, 131.6, 129.5, 129.4, 129.4, 129.0, 128.9, 128.3, 127.8, 123.1, 119.9, 87.0, 86.8, 69.4, 44.6, 21.9, 21.6, 21.3. HRMS (ESI): calcd for $C_{33}H_{29}NOS$ [M + Na]$^+$, 510.1862; found, 510.1883.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.88 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 6.5 Hz, 2H), 7.35−7.26 (m, 4H), 7.23−7.17 (m, 4H), 7.06−6.98 (m, 5H), 5.59 (d, J = 9.0 Hz, 1H), 4.75 (d, J = 9.0 Hz, 1H), 2.36 (s, 3H), 2.35 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.7, 194.0, 145.3, 138.9, 138.4, 137.5, 134.7, 134.6, 131.8, 129.8, 129.6, 129.3, 129.3, 128.9, 128.3, 126.7, 123.4, 120.1, 87.0, 87.0, 69.6, 43.2, 21.6, 21.4, 21.2.

*N-Phenyl-2-(4-methoxybenzoyl)-3-(4-methylphenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3d**).* Mixture of diastereomers (approx 1:1). Yield: 109 mg, 62% (from 0.350 mmol of thioamide). Pale yellow solid, mp 138−140 °C. IR (NaCl, cm^{-1}): 3299, 3019, 2921, 2854, 2201, 1655, 1603, 1513.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.73 (s, 1H), 7.94 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 7.0 Hz, 2H), 7.38−7.31 (m, 3H), 7.27 (d, J = 8.0 Hz, 1H), 7.22−7.20 (m, 2H), 7.08−6.99 (m, 5H), 6.86 (d, J = 9.0 Hz, 2H), 5.48 (d, J = 8.5 Hz, 1H), 4.68 (d, J = 8.5 Hz, 1H), 3.86 (s, 3H), 2.30 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.8, 193.7, 164.5, 138.9, 138.2, 137.5, 134.5, 131.8, 131.6, 130.4, 129.3, 129.0, 128.9, 128.3, 126.6, 123.1, 119.9, 114.0, 87.1, 86.8, 69.2, 55.6, 44.6, 21.6, 21.3. HRMS (ESI): calcd for $C_{33}H_{29}NO_2S$ [M + Na]$^+$, 526.1811; found, 526.1794.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.97 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 7.5 Hz, 2H), 7.36−7.31 (m, 3H), 7.27 (d, J = 8.0 Hz, 1H), 7.22−7.20 (m, 2H), 7.08−6.99 (m, 5H), 6.86 (d, J = 9.0 Hz, 2H), 5.54 (d, J = 9.0 Hz, 1H), 4.75 (d, J = 9.0 Hz, 1H), 3.83 (s, 3H), 2.33 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.2, 194.3, 164.6, 139.0, 138.1, 137.4, 134.9, 131.9, 131.8, 130.0, 129.3, 129.0, 128.9, 128.4, 126.7, 123.4, 120.1, 114.1, 87.1, 86.9, 69.5, 55.6, 43.1, 21.6, 21.2.

*N-Phenyl-2-(4-methylbenzoyl)-3-(4-methoxyphenyl)-5-phenylpent-4-yne-1-thioamide (**3e**).* Mixture of diastereomers (5:4). Yield: 120 mg, 66% (from 0.371 mmol of thioamide). Pale yellow solid, mp 147−148 °C. IR (NaCl, cm^{-1}): 3305, 3023, 2925, 2199, 1653, 1598.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.66 (s, 1H), 7.88 (d, J = 8.0 Hz, 2H), 7.64 (t, J = 7.0 Hz, 2H), 7.36−7.30 (m, 6H), 7.21−7.17 (m, 6H), 6.78 (d, J = 8.5 Hz, 2H), 5.52 (d, J = 8.0 Hz, 1H), 4.69 (d, J = 8.5 Hz, 1H), 3.75 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.3, 193.5, 159.3, 145.2, 138.9, 134.9, 131.7, 129.5, 129.5, 129.5, 129.4, 128.9, 128.3, 128.3, 126.7, 123.4, 123.1, 114.1, 87.8, 86.8, 69.5, 55.3, 44.2, 21.9. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ [M + Na]$^+$, 512.1655; found, 512.1670.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.64 (t, J = 7.0 Hz, 2H), 7.36−7.30 (m, 6H), 7.21−7.17 (m, 6H), 6.75 (d, J = 8.5 Hz, 2H), 5.59 (d, J = 9.0 Hz, 1H), 4.76 (d, J = 8.5 Hz, 1H), 3.72 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.9, 194.0, 159.3, 145.4, 138.9, 134.6, 131.9, 129.7, 129.6, 129.6, 129.3, 128.9, 128.3, 128.3, 126.8, 123.1, 122.9, 114.0, 87.8, 87.0, 69.6, 55.3, 42.9, 21.9.

*N-Phenyl-2-(4-methylbenzoyl)-3-(4-chlorophenyl)-5-phenylpent-4-yne-1-thioamide (**3f**).* Mixture of diastereomers (4:3). Yield: 92 mg, 50% (from 0.371 mmol of thioamide). Pale yellow solid, mp 159−161 °C. IR (NaCl, cm^{-1}): 3294, 3027, 2960, 2922, 2851, 2198, 1670, 1602, 1569.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.59 (s, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 7.5 Hz, 2H), 7.31−7.26 (m, 4H), 7.21−7.06 (m, 10H), 5.44 (d, J = 7.5 Hz, 1H), 4.73 (d, J = 9.0 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.5, 193.5, 145.6, 138.7, 135.8, 134.7, 133.9, 131.7, 129.8, 129.6, 129.4, 129.0, 128.8, 128.5, 128.3, 126.8, 123.0, 122.5, 87.1, 87.0, 69.1, 44.1, 21.9. HRMS (ESI): calcd for $C_{31}H_{24}ClNOS$ [M + Na]$^+$, 516.1159; found, 516.1138.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.02 (s, 1H), 7.81 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 7.5 Hz, 2H), 7.31−7.26 (m, 4H), 7.21−7.06 (m, 10H), 5.50 (d, J = 9.0 Hz, 1H), 4.66 (d, J = 8.5 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.0, 192.9, 145.8, 138.7, 136.2, 134.3, 133.9, 131.9, 129.9, 129.7, 129.4, 128.9, 128.8, 128.4, 128.3, 126.9, 123.3, 122.7, 87.4, 87.0, 69.3, 42.7, 21.9.

*N-Phenyl-2-(4-methylbenzoyl)-3-(4-chlorophenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3g**).* Mixture of diastereomers (4:3). Yield: 89 mg, 47% (from 0.371 mmol of thioamide). Pale yellow solid, mp 136−138 °C. IR (NaCl, cm^{-1}): 3298, 3021, 2923, 2851, 2197, 1649, 1599, 1508.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.67 (s, 1H), 7.85 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.38−7.32 (m, 4H) 7.24−7.17 (m, 6H), 7.04 (d, J = 7.5 Hz, 2H),

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7.00 (d, J = 8.0 Hz, 1H), 5.50 (d, J = 8.5 Hz, 1H), 4.71 (d, J = 8.0 Hz, 1H), 2.40 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.0, 193.0, 145.5, 138.8, 138.5, 136.0, 134.8, 133.9, 131.6, 129.8, 129.6, 129.4, 129.1, 129.0, 128.8, 126.8, 123.0, 119.5, 87.3, 86.2, 69.1, 44.2, 21.9, 21.6. HRMS (ESI): calcd for $C_{32}H_{26}ClNOS$ [M + Na]$^+$, 530.1316; found, 530.1331.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.08 (s, 1H), 7.88 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.38−7.32 (m, 4H) 7.24−7.17 (m, 6H), 7.04 (d, J = 7.5 Hz, 2H), 7.00 (d, J = 8.0 Hz, 1H), 5.56 (d, J = 9.0 Hz, 1H), 4.78 (d, J = 9.0 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.6, 193.5, 145.7, 138.8, 138.5, 136.3, 134.4, 133.9, 131.8, 130.0, 129.7, 129.5, 129.1, 128.9, 128.8, 126.8, 123.4, 119.7, 87.6, 86.2, 69.3, 42.8, 21.9, 21.6.

*N-Phenyl-2-(4-methoxybenzoyl)-3-(4-chlorophenyl)-5-phenylpent-4-yne-1-thioamide (**3h**).* Mixture of diastereomers (approx 5:4). Yield: 105 mg, 57% (from 0.350 mmol of thioamide). Pale yellow solid, mp 117−119 °C. IR (NaCl, cm^{-1}): 3288, 3027, 2920, 2856, 2195, 1710, 1648, 1604, 1454.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.73 (s, 1H), 7.95 (d, J = 9.0 Hz, 2H), 7.64 (d, J = 7.5 Hz, 2H), 7.39−7.31 (m, 5H), 7.26−7.16 (m, 7H), 6.88 (d, J = 9.0 Hz, 2H), 5.47 (d, J = 8.0 Hz, 1H), 4.72 (d, J = 8.5 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.5, 193.1, 164.8, 138.8, 136.0, 133.9, 131.9, 131.7, 129.9, 129.8, 129.0, 128.9, 128.5, 128.3, 126.8, 123.3, 123.0, 114.1, 87.1, 87.0, 68.9, 55.7, 44.2. HRMS (ESI): calcd for $C_{31}H_{24}ClNO_2S$ [M + Na]$^+$, 532.1109; found, 532.1126.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.97 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 7.5 Hz, 2H), 7.39−7.31 (m, 5H), 7.26−7.16 (m, 7H), 6.87 (d, J = 9.0 Hz, 2H), 5.52 (d, J = 9.0 Hz, 1H), 4.80 (d, J = 9.5 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.0, 193.7, 164.9, 138.8, 136.3, 133.9, 131.9, 131.8, 130.2, 129.8, 128.9, 128.8, 128.4, 128.3, 126.8, 122.8, 122.6, 114.2, 87.3, 87.1, 69.3, 55.6, 42.7.

*N-Phenyl-2-(4-methoxybenzoyl)-3-(4-chlorophenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3i**).* Mixture of diastereomers (3:2). Yield: 105 mg, 57% (from 0.350 mmol of thioamide), Pale yellow solid, mp 128−130 °C. IR (NaCl, cm^{-1}): 3285, 3053, 2921, 2854, 2199, 1645, 1600.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.74 (s, 1H), 7.98−7.93 (m, 2H), 7.65−7.64 (m, 2H), 7.39−7.34 (m, 4H), 7.24−7.20 (m, 4H), 7.05−7.00 (m, 3H), 6.88−6.86 (m, 2H), 5.46 (d, J = 7.5 Hz, 1H), 4.71 (d, J = 8.0 Hz, 1H), 3.85 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.5, 193.2, 164.7, 138.8, 138.5, 136.1, 133.8, 131.8, 131.6, 129.8, 129.8, 129.1, 129.0, 128.8, 126.7, 123.0, 119.6, 114.1, 87.2, 86.3, 68.9, 55.7, 44.2, 21.6. HRMS (ESI): calcd for $C_{32}H_{26}ClNO_2S$ [M + Na]$^+$, 546.1265; found, 546.1282.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.12 (s, 1H),), 7.98−7.93 (m, 2H), 7.65−7.64 (m, 2H), 7.39−7.34 (m, 4H), 7.24−7.20 (m, 5H), 7.05−7.00 (m, 3H), 6.88−6.86 (m, 2H), 5.51 (d, J = 9.0 Hz, 1H), 4.78 (d, J = 8.5 Hz, 1H), 3.83 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.0, 193.8, 164.9, 138.8, 138.4, 136.5, 135.3, 131.9, 131.8, 130.2, 129.9, 129.1, 128.9, 128.8, 126.8, 123.4, 119.8, 114.2, 87.5, 86.3, 69.2, 55.6, 42.7, 21.6.

*N-Phenyl-2-(2-thienoyl)-3-(4-chlorophenyl)-5-(4-methylphenyl)-pent-4-yne-1-thioamide (**3j**).* Mixture of diastereomers (5:4). Yield: 82 mg, 43% (from 0.383 mmol of thioamide). Pale yellow solid, mp 147 °C. IR (NaCl, cm^{-1}): 3299, 3050, 2931, 2851, 2199, 1641, 1612, 1509.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.82 (s, 1H), 7.71−7.70 (m, 1H), 7.67 (d, J = 7.5 Hz, 1H), 7.63−7.59 (m, 2H), 7.41−7.32 (m, 4H), 7.24−7.17 (m, 3H), 7.13−7.08 (m, 2H), 7.06−7.02 (m, 3H), 5.24 (d, J = 7.5 Hz, 1H), 4.76 (d, J = 7.5 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 191.1, 144.3, 138.8, 138.7, 136.7, 136.0, 135.0, 134.0, 131.7, 129.7, 129.1, 129.0, 128.9, 128.8, 126.9, 123.0, 119.6, 87.9, 85.7, 70.6, 44.4, 21.6. HRMS (ESI): calcd for $C_{29}H_{22}ClNOS_2$ [M + Na]$^+$, 522.0724; found, 522.0751.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.10 (s, 1H), 7.87 (d, J = 3.5 Hz, 1H), 7.71−7.70 (m, 1H), 7.67 (d, J = 7.5 Hz, 1H), 7.63−7.59 (m, 1H), 7.41−7.32 (m, 4H), 7.24−7.17 (m, 3H), 7.13−7.08 (m, 2H), 7.06−7.02 (m, 3H), 5.33 (d, J = 8.5 Hz, 1H), 4.80 (d, J = 8.5 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.0, 190.9, 143.9, 138.7, 138.5, 137.0, 136.0, 135.5, 134.0, 131.8, 130.0, 129.1, 128.9, 128.9, 128.8, 126.8, 123.3, 119.5, 87.7, 86.0, 70.7, 42.9, 21.7.

*N-Phenyl-2-benzoyl-3-(2-thienyl)-5-phenylpent-4-yne-1-thioamide (**3k**).* Mixture of diastereomers (approx 5:2). Yield: 85 mg, 48% (from 0.392 mmol of thioamide). Pale yellow solid, mp 123−124 °C. IR (NaCl, cm^{-1}): 3283, 3060, 3028, 2962, 2922, 2853, 2201, 1675, 1590, 1563, 1491.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.47 (s, 1H), 8.04−8.03 (m, 2H), 7.65 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.45−7.42 (m, 2H), 7.36−7.28 (m, 4H), 7.21−7.20 (m, 2H), 7.17−7.15 (m, 3H), 7.07 (d, J = 3.0 Hz, 1H), 6.87 (dd, J = 5.0, 3.6 Hz, 1H), 5.61 (d, J = 7.5 Hz, 1H), 5.06 (d, J = 8.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.0, 192.7, 140.1, 138.7, 137.2, 134.2, 131.7, 129.6, 129.2, 129.0, 128.9, 128.7, 128.5, 128.3, 126.9, 126.8, 125.4, 123.2, 86.9, 86.5, 70.1, 38.4. HRMS (ESI): calcd for $C_{28}H_{21}NOS_2$ [M + Na]$^+$, 474.0957; found, 474.0974.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.04 (s, 1H), 8.04−8.03 (m, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.45−7.42 (m, 2H), 7.36−7.28 (m, 4H), 7.21−7.20 (m, 2H), 7.17−7.15 (m, 3H), 7.03 (d, J = 5.0 Hz, 1H), 6.82 (dd, J = 5.0, 3.6 Hz, 1H), 5.67 (d, J = 9.0 Hz, 1H), 5.15 (d, J = 9.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.8, 193.1, 140.4, 138.8, 137.5, 134.4, 131.9, 129.4, 129.4, 129.3, 128.9, 128.5, 128.1, 128.1, 126.9, 126.4, 126.1, 122.7, 87.0, 86.7, 70.1, 39.5.

*N-Phenyl-2-(4-methylbenzoyl)-3-(2-thienyl)-5-phenylpent-4-yne-1-thioamide (**3l**).* Mixture of diastereomers (approx 2:1). Yield: 86 mg, 50% (from 0.371 mmol of thioamide). Pale yellow solid, mp 115−117 °C. IR (NaCl, cm^{-1}): 3290, 3051, 3030, 2925, 2851, 2198, 1653, 1600, 1451.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.50 (s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 7.36−7.32 (m, 3H), 7.26−7.16 (m, 8H), 7.07 (d, J = 3.0 Hz, 1H), 6.88 (dd, J = 5.1, 3.5 Hz, 1H), 5.57 (d, J = 8.0 Hz, 1H), 5.04 (d, J = 8.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.6, 192.9, 145.4, 140.2, 138.8, 134.8, 131.8, 129.6, 129.4, 129.0, 128.3, 126.9, 126.8, 126.8, 125.4, 123.1, 122.6, 115.2, 87.1, 86.5, 69.9, 39.5, 21.9. HRMS (ESI): calcd for $C_{29}H_{23}NOS_2$ [M + Na]$^+$, 488.1113; found, 488.1142

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.04 (s, 1H), 7.94 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H), 7.36−7.32 (m, 3H), 7.26−7.16 (m, 7H), 7.11 (d, J = 6.5 Hz, 1H), 6.99 (d, J = 3.5 Hz, 1H), 6.82 (dd, J = 5.1, 3.6 Hz, 1H), 5.63 (d, J = 9.5 Hz, 1H), 5.13 (d, J = 9.0 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.4, 193.3, 145.6, 140.5, 138.9, 134.5, 132.0, 129.7, 129.6, 128.5, 128.3, 126.9, 126.8, 126.8, 125.4, 123.4, 122.8, 115.2, 86.9, 86.8, 70.1, 38.4, 21.9.

*N-Butyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3o**).* Mixture of diastereomers (1:1). Yield: 29 mg, 58% (from 0.108 mmol of thioamide **1f**). Yellowish sticky liquid. IR (NaCl, cm^{-1}): 3283, 3021, 2923, 2852, 2194, 1709, 1647, 1610, 1451.

Data for the first isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (t, J = 4.7 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 7.18−7.11 (m, 4H), 7.04−7.01 (m, 4H), 5.50 (d, J = 9.0 Hz, 1H), 4.66 (d, J = 9.0 Hz, 1H), 3.66−3.62 (m, 2H), 2.36 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 1.57−1.54 (m, 2H), 1.36−1.30 (m, 2H), 0.88 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.3, 195.0, 144.8, 138.1, 137.3, 134.8, 134.6, 131.6, 129.3, 129.2, 129.0, 128.9, 128.4, 120.0, 87.1, 86.5, 67.7, 46.5, 42.5, 30.0, 21.8, 21.6, 21.2, 20.3, 13.9. HRMS (ESI): calcd for $C_{31}H_{33}NOS$ [M + Na]$^+$, 490.2175; found, 490.2176.

Data for the second isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.99 (t, J = 4.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.18−7.11 (m, 4H), 7.04−7.01 (m, 4H), 5.44 (d, J =

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7.5 Hz, 1H), 4.60 (d, J = 7.5 Hz, 1H), 3.50−3.42 (m, 2H), 2.36 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 1.57−1.54 (m, 2H), 1.36−1.30 (m, 2H), 0.86 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.7, 195.2, 145.1, 138.2, 135.0, 134.6, 131.7, 129.8, 129.5, 129.4, 129.3, 129.2, 128.2, 120.1, 87.1, 86.7, 67.4, 46.4, 44.0, 29.9, 21.8, 21.6, 21.2, 20.4, 13.9.

N-Butyl-2-(4-methoxylbenzoyl)-3-(4-methylphenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3p**). Mixture of diastereomers (1:1). Yield: 35.5 mg, 59% (from 0.124 mmol of thioamide **1g**). Yellowish sticky liquid.

Data for the first isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.07 (t, J = 4.5 Hz, 1H), 7.95 (d, J = 9.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.04−7.00 (m, 4H), 6.81 (d, J = 9.0 Hz, 2H), 5.40 (d, J = 7.5 Hz, 1H), 4.60 (d, J = 7.5 Hz, 1H), 3.82 (s, 3H), 3.49−3.46 (m, 2H), 2.31 (s, 3H), 2.26 (s, 3H), 1.58−1.55 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.3, 195.2, 164.3, 138.2, 137.3, 134.7, 131.8, 131.6, 130.1, 129.2, 129.0, 128.4, 120.1, 114.0, 87.3, 86.6, 67.7, 55.6, 46.5, 44.0, 30.1, 21.6, 21.2, 20.4, 13.9. HRMS (ESI): calcd for $C_{31}H_{33}NO_2S$ $[M + Na]^+$, 506.2124; found, 506.2126.

Data for the second isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (t, J = 5.0 Hz, 1H), 7.84 (d, J = 9.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.04−7.00 (m, 4H), 6.84 (d, J = 9.0 Hz, 2H), 5.46 (d, J = 9.0 Hz, 1H), 4.66 (d, J = 9.0 Hz, 1H), 3.81 (s, 3H), 3.67−362 (m, 2H), 2.31 (s, 3H), 2.24 (s, 3H), 1.36−1.32 (m, 4H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.9, 195.4, 164.5, 138.1, 137.3, 135.0, 131.8, 131.5, 130.4, 129.2, 128.9, 128.2, 120.0, 113.8, 87.1, 86.4, 67.2, 55.5, 46.4, 42.5, 29.9, 21.6, 21.2, 20.3, 13.9. HRMS (ESI): calcd for $C_{31}H_{33}NO_2S$ $[M + Na]^+$, 506.2124; found, 506.2126.

N-Butyl-2-(4-methoxylbenzoyl)-3-(4-chlorophenyl)-5-(4-methylphenyl)pent-4-yne-1-thioamide (**3q**). Mixture of diastereomers (2.5:1). Yield: 26 mg, 45% (from 0.113 mmol of thioamide **1g**). Pale yellow sticky liquid.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.08 (br, 1H), 7.83 (d, J = 9.0 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 5.36 (d, J = 7.4 Hz, 1H), 4.63 (d, J = 7.5 Hz, 1H), 3.84 (s, 3H), 3.64−3.60 (m, 1H), 3.49−3.45 (m, 1H), 2.32 (s, 3H), 1.59−1.55 (m, 2H), 1.38−1.33 (m, 2H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.0, 194.8, 164.5, 138.5, 136.3, 133.7, 131.8, 131.6, 131.5, 129.7, 129.1, 128.7, 119.7, 114.0, 87.1, 86.3, 66.8, 55.6, 46.5, 43.7, 30.1, 21.6, 20.4, 13.9. HRMS (ESI): calcd for $C_{30}H_{30}ClNO_2S$ $[M + Na]^+$, 526.1578; found, 526.1585.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (br, 1H), 7.95 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 5.42 (d, J = 9.0 Hz, 1H), 4.68 (d, J = 9.0 Hz, 1H), 3.83 (s, 3H), 3.64−3.60 (m, 1H), 3.49−3.45 (m, 1H), 2.33 (s, 3H), 1.59−1.55 (m, 2H), 1.38−1.33 (m, 2H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.7, 196.0, 164.7, 131.8, 130.3, 129.9, 129.0, 128.7, 128.3, 128.2, 119.8, 114.1, 87.0, 86.5, 67.4, 56.6, 46.4, 42.2, 29.9, 21.4, 20.3, 13.9 (some peaks are merged).

2-Benzoyl-3-(4-methylphenyl)-5-(4-phenyl)pent-4-yne-1-thioamide (**3u**). Mixture of diastereomers (5:4). Yield: 50 mg, 59% (from 0.22 mmol of thioamide **1h**). Yellow solid, mp 171−172 °C.

Data for the major isomer are as follows. ^{1}H NMR (500 MHz, DMSO): δ 10.0 (s, 1H), 9.97 (s, 1H), 7.92 (d, J = 7.0 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.8 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.37−7.35 (m, 3H), 7.17−7.09 (m, 3H), 5.46 (d, J = 10.5 Hz, 1H), 4.78 (d, J = 10.5 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (126 MHz, DMSO): δ 198.1, 192.5, 136.3, 135.9, 133.6, 131.3, 129.3, 129.0, 128.8, 128.8, 128.6, 128.5, 128.3, 122.4, 90.6, 83.6, 66.7, 20.7 (one aliphatic carbon has been merged with the solvent peak). HRMS (ESI): calcd for $C_{25}H_{21}NOS$ $[M + Na]^+$, 406.1236; found, 406.1240.

Data for the minor isomer are as follows. ^{1}H NMR (500 MHz, DMSO): δ 9.51 (s, 1H), 9.39 (s, 1H), 8.13 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 8.0 Hz, 2H), 7.37−7.35 (m, 3H), 7.27−7.26 (m, 4H), 7.17−7.09 (m, 3H), 5.39 (d, J = 10.5 Hz, 1H), 4.71 (d, J = 11 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, DMSO): δ 200.1, 191.0, 136.7, 136.5, 134.9, 133.5, 131.0, 129.3, 128.8, 128.7, 128.6, 128.3, 128.1, 122.9, 91.2, 82.6, 66.1, 20.6 (one aliphatic carbon has been merged with the solvent peak).

(2E)-2-(4-(4-Methylbenzyl)-3,5-diphenyl-2(3H)-ylidene)-1-(4-methylphenyl)ethanone (**4a**). Yield: 17 mg, 10% (from 0.371 mmol of thioamide). Yellow solid, mp 182−183 °C. IR (NaCl, cm^{-1}): 3049, 2928, 2851, 1672, 1601. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 7.0 Hz, 2H), 7.42−7.33 (m, 6H), 7.09 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 7.5 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 8.0 Hz, 2H), 5.89 (s, 1H), 3.77 (s, 2H), 2.32 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 183.0, 164.1, 140.4, 137.6, 137.3, 136.3, 133.9, 133.4, 132.1, 129.8, 129.6, 129.3, 129.2, 128.9, 128.8, 128.8, 128.2, 127.8, 127.1, 121.4, 88.3, 31.8, 21.6, 21.2. HRMS (ESI): calcd for $C_{32}H_{27}NOS$ $[M + H]^+$, 474.1886; found, 474.1867.

(2E)-2-(4-(4-Methylbenzyl)-3,5-diphenyl-2(3H)-ylidene)-1-(4-methoxylphenyl)ethanone (**4b**). Yield: 14 mg, 8% (from 0.350 mmol of thioamide). Yellow solid, mp 195−196 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 8.9 Hz, 2H), 7.53 (d, J = 7.1 Hz, 2H), 7.42−7.33 (m, 6H), 7.00 (d, J = 8.5 Hz, 2H), 6.93 (d, J = 7.8 Hz, 2H), 6.80 (d, J = 8.9 Hz, 2H), 6.64 (d, J = 8.0 Hz, 2H), 5.87 (s, 1H), 3.78 (s, 3H), 3.77 (s, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.3, 164.0, 161.5, 137.6, 136.3, 133.9, 133.3, 132.7, 132.1, 129.8, 129.6, 129.3, 129.2, 128.8, 128.8, 128.8, 128.2, 127.8, 121.4, 113.4, 88.0, 55.3, 31.7, 21.2. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ $[M + H]^+$, 490.1835; found, 490.1855.

(2E)-2-(4-(4-Methylbenzyl)-3-phenyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methylphenyl)ethanone (**4c**). Yield: 13 mg, 7% (from 0.371 mmol of thioamide), Yellow solid, mp 160−162 °C. IR (NaCl, cm^{-1}): 3051, 2929, 2854, 1670, 1599. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (d, J = 7.5 Hz, 2H), 7.42−7.33 (m, 5H), 7.20 (d, J = 7.0 Hz, 2H), 7.08 (d, J = 7.5 Hz, 2H), 6.99 (d, J = 7.5 Hz, 2H), 6.92 (d, J = 7.0 Hz, 2H), 6.62 (d, J = 7.0 Hz, 2H), 5.88 (s, 1H), 3.76 (s, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.8, 164.0, 140.3, 138.1, 137.7, 137.4, 136.2, 134.0, 133.0, 129.9, 129.8, 129.5, 129.3, 129.1, 128.9, 128.8, 128.7, 127.9, 127.1, 121.5, 88.2, 31.8, 21.6, 21.4, 21.2. HRMS (ESI): calcd for $C_{33}H_{29}NOS$ $[M + H]^+$, 488.2043; found, 488.2059.

(2E)-2-(4-(4-Methylbenzyl)-3-phenyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4d**). Yield: 16 mg, 9% (from 0.350 mmol of thioamide). Yellow solid, mp 191−192 °C. IR (NaCl, cm^{-1}): 3049, 3025, 2923, 2855, 1668, 1600, 1556, 1510. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 9.0 Hz, 2H), 7.42−7.40 (m, 3H), 7.33 (t, J = 7.5 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.5 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 9.0 Hz, 2H), 6.63 (d, J = 8.0 Hz, 2H), 5.85 (s, 1H), 3.78 (s, 3H), 3.75 (s, 2H), 2.37 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.2, 163.9, 161.4, 138.0, 137.7, 136.2, 134.0, 132.9, 132.8, 129.9, 129.8, 129.5, 129.3, 129.2, 128.8, 128.7, 127.9, 125.3, 121.4, 113.4, 87.8, 55.3, 21.4, 21.2. HRMS (ESI): calcd for $C_{33}H_{29}NO_2S$ $[M + H]^+$, 504.1992; found, 504.1999.

(2E)-2-(4-(4-Methoxybenzyl)-3,5-diphenylthiazol-2(3H)-ylidene)-1-p-tolylethanone (**4e**). Yield: 4 mg, 2% (from 0.371 mmol of thioamide). Yellow solid, mp 205−206 °C. IR (NaCl, cm^{-1}): 3057, 2934, 2850, 1662, 1604, 1487. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 7.5 Hz, 2H), 7.43−7.34 (m, 6H), 7.08 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 7.5 Hz, 2H), 6.65−6.64 (m, 4H), 5.89 (s, 1H), 3.75 (brs, 5H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.0, 164.0, 140.4, 137.7, 137.3, 134.5, 133.5, 132.1, 131.7, 130.0, 130.0, 129.8, 129.2, 129.0, 128.9, 128.9, 128.8, 128.3, 127.1, 123.8, 114.1, 88.3, 55.3, 29.9, 21.6. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ $[M + H]^+$, 490.1835; found, 490.1805.

(2E)-2-(4-(4-Chlorobenzyl)-3,5-diphenylthiazol-2(3H)-ylidene)-1-p-tolylethanone (**4f**). Yield: 35 mg, 19% (from 0.371 mmol of thioamide). Yellow solid, mp 199−200 °C. IR (NaCl, cm^{-1}): 3059, 2958, 2924, 2855, 1657, 1601, 1489, 1265. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 7.0 Hz, 2H), 7.44−7.35 (m, 6H), 7.09 (m, 4H), 7.00 (d, J = 8.0 Hz, 2H), 6.67 (d, J = 8.0 Hz, 2H), 5.91 (s, 1H), 3.78 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 183.1, 163.9, 140.5, 137.5, 137.2, 135.5, 132.8, 132.5, 131.9, 130.0, 129.8, 129.3, 129.3, 128.9, 128.9, 128.8, 128.7, 128.4,

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127.1, 121.8, 88.3, 31.6, 21.6. HRMS (ESI): calcd for $C_{31}H_{24}ClNOS$ $[M + H]^+$, 494.1340; found, 494.1349.

*(2E)-2-(4-(4-Chlorobenzyl)-3-phenyl-5-p-tolylthiazol-2(3H)-ylidene)-1-p-tolylethanone (**4g**).* Yield: 40 mg, 21% (from 0.371 mmol of thioamide). Yellow solid, mp 220−222 °C. IR (NaCl, cm^{-1}): 2923, 2854, 1654, 1604, 1491, 1450. ^1H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 8.0 Hz, 2H), 7.40−7.37 (m, 5H), 7.21 (d, J = 8.0 Hz, 2H), 7.09−7.08 (m, 4H), 7.00 (d, J = 7.5 Hz, 2H), 6.65 (d, J = 8.5 Hz, 2H), 5.90 (s, 1H), 3.77 (s, 2H), 2.38 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 183.0, 163.8, 140.5, 138.3, 137.5, 137.2, 135.6, 132.7, 132.2, 130.0, 129.9, 129.7, 129.2, 128.9, 128.8, 128.7, 128.7, 128.7, 127.1, 121.9, 88.2, 31.6, 21.6, 21.4. HRMS (ESI): calcd for $C_{32}H_{26}ClNOS$ $[M + H]^+$, 508.1496; found, 508.1507.

*(2E)-2-(4-(4-Chlorobenzyl)-3,5-diphenylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4h**).* Yield: 34 mg, 19% (from 0.350 mmol of thioamide). Yellow solid, mp 188−189 °C. IR (NaCl, cm^{-1}): 3029, 2929, 2855, 1676, 1598, 1492. ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, J = 9.0 Hz, 2H), 7.51 (d, J = 7.5 Hz, 2H), 7.47−7.35 (m, 6H), 7.10 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 7.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 6.67 (d, J = 8.5 Hz, 2H), 5.88 (s, 1H), 3.78 (bs, 5H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.4, 163.8, 161.6, 137.5, 135.5, 132.8, 132.5, 131.9, 130.0, 129.8, 129.3, 129.3, 128.9, 128.8, 128.8, 128.8, 128.5, 128.4, 121.8, 113.4, 88.0, 55.3, 31.6. HRMS (ESI): calcd for $C_{31}H_{24}ClNO_2S$ $[M + H]^+$, 510.1289; found, 510.1302.

*(2E)-2-(4-(4-Chlorobenzyl)-3-phenyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4i**).* Yield: 37 mg, 20% (from 0.350 mmol of thioamide). Yellow solid, mp 195−196 °C. IR (NaCl, cm^{-1}): 3058, 3029, 2925, 2853, 1681, 1600, 1465. ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, J = 9.0 Hz, 2H), 7.43−7.36 (m, 5H), 7.21(d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 8.8 Hz, 2H), 6.66 (d, J = 8.3 Hz, 2H), 5.88 (s, 1H), 3.78 (s, 3H), 3.76 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.4, 163.7, 161.5, 138.3, 137.6, 135.6, 132.7, 132.6, 132.1, 130.0, 129.9, 129.7, 129.3, 128.9, 128.8, 128.7, 128.7, 121.8, 113.4, 87.9, 55.3, 31.6, 21.4. HRMS (ESI): calcd for $C_{32}H_{26}ClNO_2S$ $[M + H]^+$, 524.1446; found, 524.1453.

*(2E)-2-(4-(4-Chlorobenzyl)-3-phenyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(thiophen-2-yl)ethanone (**4j**).* Yield: 42 mg, 22% (from 0.383 mmol of thioamide). Yellow solid, mp 204−206 °C. IR (NaCl, cm^{-1}): 3050, 2928, 1683, 1638, 1490. ^1H NMR (500 MHz, $CDCl_3$): δ 7.44 (t, J = 7.5 Hz, 1H), 7.39−7.36 (m, 4H), 7.31 (dd, J = 5.0 Hz, 1.0 Hz, 1H), 7.26−7.25 (m, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H), 6.99 (d, J = 7.5 Hz, 2H), 6.92 (dd, J = 4.5, 4.0 Hz, 1H), 6.65 (d, J = 8.5 Hz, 2H), 5.75 (s, 1H), 3.76 (s, 2H), 2.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.4, 163.5, 147.0, 138.4, 137.3, 135.5, 132.7, 132.2, 130.0, 129.9, 129.8, 129.2, 128.7, 128.7, 128.7, 127.4, 126.8, 122.2, 88.0, 31.6, 21.4. HRMS (ESI): calcd for $C_{29}H_{22}ClNOS_2$ $[M + H]^+$, 500.0904; found, 500.0918.

*(2E)-1-Phenyl-2-(3,5-diphenyl-4-((thiophen-2-yl)methyl)thiazol-2(3H)-ylidene)ethanone (**4k**).* Yield: 41 mg, 23% (from 0.392 mmol of thioamide). Yellow solid, mp 171−173 °C. IR (NaCl, cm^{-1}): 3050, 3026, 2922, 2855, 1679, 1604, 1467. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 7.0 Hz, 2H), 7.57 (d, J = 7.0 Hz, 2H), 7.47−7.41 (m, 5H), 7.37−7.28 (m, 4H), 7.09−7.06 (m, 3H), 6.77 (t, J = 3.0 Hz, 1H), 6.38 (d, J = 2.0 Hz, 1H), 5.94 (s, 1H), 3.93 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 183.1, 164.1, 139.8, 137.4, 132.9, 131.6, 130.3, 130.0, 129.8, 129.2, 128.9, 128.5, 128.4, 128.2, 127.0, 126.9, 125.6, 124.5, 121.6, 88.4, 27.0. HRMS (ESI): calcd for $C_{28}H_{21}NOS_2$ $[M + H]^+$, 452.1137; found, 452.1145.

*(2E)-2-(3,5-Diphenyl-4-((thiophen-2-yl)methyl)thiazol-2(3H)-ylidene)-1-p-tolylethanone (**4l**).* Yield: 38 mg, 22% (from 0.371 mmol of thioamide). Yellow solid, mp 149−151 °C. IR (NaCl, cm^{-1}): 3058, 3031, 2921, 2852, 1681, 1594, 1552, 1464. ^1H NMR (500 MHz, $CDCl_3$): δ 7.61−7.56 (m, 4H), 7.47−7.44 (m, 5H), 7.42 (t, J = 7.5 Hz, 1H), 7.10−7.05 (m, 5H), 6.77 (dd, J = 5.1, 3.5 Hz, 1H), 6.38 (d, J = 4.0 Hz, 1H), 5.91 (s, 1H), 3.92 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 183.1, 164.0, 140.5, 139.9, 137.5, 137.2, 132.7, 131.8, 130.0, 129.7, 129.2, 129.0, 128.9, 128.6, 128.4, 127.1, 126.9, 125.6, 124.5, 121.5, 88.3, 27.1, 21.6. HRMS (ESI): calcd for $C_{29}H_{23}NOS_2$ $[M + H]^+$, 466.1294; found, 466.1286.

*(2E)-2-(4-(2,6-Dichlorobenzyl)-3,5-diphenylthiazol-2(3H)-ylidene)-1-phenylethanone (**4m**).* Yield: 23 mg, 23% (from 0.196 mmol of thioamide). Yellow solid, mp 223−225 °C. IR (NaCl, cm^{-1}): 3036, 2925, 2849, 1676, 1601, 1556. ^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 6.5 Hz, 2H), 7.51−7.50 (m, 3H), 7.34−7.29 (m, 7H), 7.22−7.17 (m, 3H), 6.90 (d, J = 8.0 Hz, 2H), 6.82−6.79 (m, 1H), 5.91 (s, 1H), 4.01 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.9, 164.1, 140.0, 137.8, 136.0, 132.2, 131.3, 130.5, 130.3, 130.2, 129.9, 129.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 127.1, 121.3, 88.1, 30.1. HRMS (ESI): calcd for $C_{30}H_{21}Cl_2NOS$ $[M + H]^+$, 514.0794; found, 514.0804.

*(2E)-2-(4-(4-Nitrobenzyl)-3,5-diphenylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4n**).* Yield: 17 mg, 19% (from 0.175 mmol of thioamide). Yellow solid, mp 215−217 °C. IR (NaCl, cm^{-1}): 3054, 3033, 2921, 2848, 1669, 1604, 1456. ^1H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 7.0 Hz, 2H), 7.46−7.38 (m, 6H), 7.02 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 5.91 (s, 1H), 3.92 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.7, 163.5, 161.7, 147.0, 144.7, 137.5, 132.4, 131.7, 131.3, 130.2, 130.0, 129.4, 128.9, 128.9, 128.8, 128.7, 128.7, 123.8, 122.4, 113.5, 88.2, 55.3, 32.2. HRMS (ESI): calcd for $C_{31}H_{24}N_2O_4S$ $[M + H]^+$, 521.1530; found, 521.1537.

*(2E)-2-(4-(4-Methylbenzyl)-3-butyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methylphenyl)ethanone (**4o**).* Yield: 4 mg, 8% (from 0.108 mmol of thioamide **1f**). Yellowish sticky liquid. IR (NaCl, cm^{-1}): 3029, 2923, 2853, 1675, 1600. ^1H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.15−7.13 (m, 4H), 7.02 (d, J = 8.0 Hz, 2H), 6.35 (s, 1H), 4.02 (s, 2H), 3.74−3.71 (m, 2H), 2.38 (s, 3H), 2.35 (s, 3H), 2.34 (s, 3H) 1.58−1.55 (m, 2H), 1.30−1.26 (m, 2H), 0.89 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.4, 162.3, 140.3, 138.0, 137.8, 136.9, 134.1, 132.3, 130.0, 129.8, 129.2, 129.0, 128.8, 127.7, 127.1, 122.1, 85.9, 47.1, 31.6, 29.5, 21.6, 21.4, 21.2, 20.3, 13.8. HRMS (ESI): calcd for $C_{31}H_{33}NOS$ $[M + H]^+$, 468.2356; found, 468.2374.

*(2E)-2-(4-(4-Methylbenzyl)-3-butyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4p**).* Yield: 5 mg, 9% (from 0.124 mmol of thioamide **1g**). Yellowish sticky liquid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, J = 9.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 6.91 (d, J = 9.1 Hz, 2H), 6.32 (brs, 1H), 4.02 (s, 2H), 3.84 (s, 3H), 3.74−3.70 (m, 2H), 2.35 (s, 3H), 2.34 (s, 3H), 1.58−1.54 (m, 2H), 1.32−1.28 (m, 2H), 0.89 (t, J = 7.5 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$): δ 181.4, 163.0, 162.2, 141.0, 138.0, 136.9, 134.1, 133.2, 130.0, 129.8, 129.2, 128.8, 128.8, 127.7, 121.8, 113.6, 85.8, 55.4, 47.1, 31.6, 29.2, 21.4, 21.2, 20.4, 13.8. HRMS (ESI): calcd for $C_{31}H_{33}NO_2S$ $[M + H]^+$, 484.2305; found, 484.2314.

*(2E)-2-(4-(4-Chlorobenzyl)-3-butyl-5-p-tolylthiazol-2(3H)-ylidene)-1-(4-methoxyphenyl)ethanone (**4q**).* Yield: 11 mg, 19% (from 0.113 mmol of thioamide **1g**). Yellowish sticky liquid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, J = 9.0 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 9.5 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.5 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 6.33 (s, 1H), 4.02 (s, 2H), 3.84 (s, 3H), 3.71−3.68 (m, 2H), 2.36 (s, 3H), 1.60−1.57 (m, 2H), 1.34−1.29 (m, 2H), 0.91 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 182.0, 162.1, 161.5, 138.2, 135.7, 133.3, 133.1, 131.3, 129.9, 129.5, 129.1, 129.0, 128.8, 128.7, 122.4, 113.6, 85.7, 55.4, 47.1, 31.4, 29.5, 25.9, 21.4, 20.3, 13.8. HRMS (ESI): calcd for $C_{30}H_{30}ClNO_2S$ $[M + H]^+$, 504.1759; found, 504.1757.

*((5Z)-5-Benzylidene-4,5-dihydro-4-(2-thienyl)-2-(phenylamino)-thiophen-3-yl)(phenyl)methanone (**5a**).* Yield: 25 mg, 84% (from 0.0665 mmol of corresponding **3**). Yellow solid, mp 172−174 °C. IR (NaCl, cm^{-1}): 3387, 3054, 2922, 2853, 1621, 1563, 1397. ^1H NMR (500 MHz, $CDCl_3$): δ 13.05 (s, 1H), 7.43−7.36 (m, 5H), 7.31−7.28 (m, 7H), 7.23−7.21 (m, 3H), 7.04 (dd, J = 5.5, 0.8 Hz, 1H), 6.72 (dd, J = 5.0, 3.5 Hz, 1H), 6.64 (s, 1H), 6.56 (d, J = 3.5 Hz, 1H), 5.55 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.6, 165.6, 149.0, 142.0, 139.9, 137.6, 135.9, 129.7, 129.4, 128.7, 128.2, 128.1, 127.5, 126.6, 126.5, 126.1, 125.0, 124.3, 123.9, 122.7, 107.2, 54.1. HRMS (ESI): calcd for $C_{28}H_{21}NOS_2$ $[M + H]^+$, 452.1137; found, 452.1154.

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*((5Z)-5-(4-Methylbenzylidene)-4,5-dihydro-4-(4-methylphenyl)-2-(phenylamino)thiophen-3-yl)(4-methylphenyl)methanone (**5b**).* Yield: 27 mg, 87% (from 0.0616 mmol of corresponding **3**). Yellow solid, mp 190−191 °C. IR (NaCl, cm^{-1}): 3435, 2921, 2853, 1637, 1512. ^1H NMR (500 MHz, $CDCl_3$): δ 13.12 (s, 1H), 7.42−7.37 (m, 3H), 7.22 (d, J = 7.0 Hz, 2H), 7.12−7.03 (m, 8H), 6.94−6.89 (m, 4H), 6.48 (s, 1H), 5.20 (s, 1H), 2.34 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.7, 165.7, 142.0, 140.2, 139.4, 139.2, 137.9, 136.9, 136.2, 133.4, 129.6, 129.3, 129.3, 128.6, 128.0, 126.8, 126.7, 125.7, 124.0, 122.5, 107.6, 58.5, 21.6, 21.4, 21.2. HRMS (ESI): calcd for $C_{33}H_{29}NOS$ $[M + H]^+$, 488.2043; found, 488.2057

*((5Z)-5-Benzylidene-4,5-dihydro-4-(4-methoxyphenyl)-2-(phenylamino)thiophen-3-yl)(4-methylphenyl)methanone (**5c**).* Yield: 27 mg, 91% (from 0.613 mmol of corresponding **3**). Yellow solid, mp 201−202 °C. IR (NaCl, cm^{-1}): 3380, 3040, 2918, 2850, 1613, 1557, 1399. ^1H NMR (500 MHz, $CDCl_3$): δ 13.09 (s, 1H), 7.42−7.36 (m, 4H), 7.29−7.26 (m, 3H), 7.19−7.15 (m, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 6.48 (s, 1H), 5.20 (s, 1H), 3.73 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.9, 165.3, 158.5, 140.1, 139.4, 139.3, 139.1, 137.2, 136.2, 129.6, 128.6, 128.6, 128.1, 128.0, 127.2, 126.6, 125.8, 124.0, 122.5, 114.0, 107.7, 58.3, 55.2, 21.6. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ $[M + H]^+$, 490.1835; found, 490.1844.

*((5Z)-5-(4-Methylbenzylidene)-4,5-dihydro-4-(4-chlorophenyl)-2-(phenylamino)thiophen-3-yl)(2-thienyl)methanone (**5d**).* Yield: 25 mg, 82% (from 0.06 mmol of corresponding **3**). Yellow solid, mp 179−181 °C. IR (NaCl, cm^{-1}): 3383, 3054, 2923, 1618, 1562, 1401. ^1H NMR (500 MHz, $CDCl_3$) δ 13.64 (s, 1H), 7.42−7.38 (m, 3H), 7.36−7.34 (m, 4H), 7.28−7.25 (m, 3H), 7.23 (t, J = 7.0 Hz, 1H), 7.11−7.07 (m, 4H), 6.94 (dd, J = 5.0, 3.5 Hz, 1H), 6.75 (s, 1H), 5.54 (s, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 177.4, 168.4, 145.7, 142.2, 139.8, 137.4, 137.2, 133.2, 132.9, 130.5, 129.7, 129.4, 129.3, 129.0, 128.2, 128.2, 127.5, 126.1, 124.5, 122.7, 104.4, 57.7, 21.4. HRMS (ESI): calcd for $C_{29}H_{22}ClNOS_2$ $[M + H]^+$, 500.0904; found, 500.0919.

*((5Z)-5-(4-Methylbenzylidene)-4,5-dihydro-4-(4-methylphenyl)-2-(butylamino)thiophen-3-yl)(4-methoxylphenyl)methanone (**5e**).* Yield: 23 mg, 77% (from 0.062 mmol of **3q**). Yellowish solid, mp 132−133 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 11.03 (t, J = 5.5 Hz, 1H), 7.16 (d, J = 9.0 Hz, 2H), 7.10 (s, 4H), 6.92 (d, J = 8.0 Hz, 2H), 6.88 (d, J = 8.0 Hz, 2H), 6.71 (d, J = 8.5 Hz, 2H), 6.49 (d, J = 1.5 Hz, 1H), 5.19 (d, J = 1.5 Hz, 1H), 3.78 (s, 3H), 3.45−3.42 (m, 2H), 2.32 (s, 3H), 2.24 (s, 3H), 1.73−1.71 (m, 2H), 1.51−1.49 (m, 2H), 0.99 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 187.6, 169.7, 160.2, 142.4, 138.0, 136.9, 136.0, 135.5, 133.6, 129.2, 129.2, 128.3, 128.0, 126.8, 123.8, 113.1, 104.2, 59.2, 55.3, 47.7, 32.3, 21.4, 21.2, 20.2, 13.9. HRMS (ESI): calcd for $C_{31}H_{33}NO_2S$ $[M + H]^+$, 484.2305; found, 484.2306.

*5-Benzyl-3-benzoyl-2-phenylamino-4-(2-thiophenyl)thiophene (**5a′**).* Yield: 12 mg, 41% (from 0.0665 mmol of corresponding **3**). Yellow solid, mp 172−173 °C. IR (NaCl, cm^{-1}): 3401, 3052, 2930, 1615, 1559, 1399, 1252. ^1H NMR (500 MHz, $CDCl_3$): δ 11.30 (s, 1H), 7.36−7.31 (m, 6H), 7.27 (t, J = 7.5 Hz, 2H), 7.20−7.13 (m, 4H), 7.08−7.05 (m, 3H), 6.96 (d, J = 5.0 Hz, 1H), 6.60−6.57 (m, 2H), 4.02 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.0, 160.2, 140.4, 139.3, 136.8, 132.3, 129.7, 129.5, 129.2, 128.8, 128.5, 128.4, 128.3, 128.2, 127.4, 126.7, 126.7, 125.9, 123.9, 120.9, 119.6, 34.2. HRMS (ESI): calcd for $C_{28}H_{21}NOS_2$ $[M + H]^+$, 452.1137; found, 452.1157.

*3-(4-Methylbenzoyl)-5-(4-methylbenzyl)-4-(4-methylphenyl)-2-phenylaminothiophene (**5b′**).* Yield: 13 mg, 45% (from 0.0616 mmol of corresponding **3**). Yellow solid, mp 165−167 °C. IR (NaCl, cm^{-1}): 3395, 3051, 2954, 2852, 1616, 1552, 1401. ^1H NMR (500 MHz, $CDCl_3$): δ 11.38 (s, 1H), 7.33−7.32 (m, 4H), 7.11 (d, J = 8.0 Hz, 2H), 7.07−7.06 (m, 3H), 7.01 (d, J = 7.5 Hz, 2H), 6.82 (d, J = 8.0 Hz, 2H), 6.77−6.73 (m, 4H), 3.88 (s, 2H), 2.31 (s, 3H), 2.19 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.1, 159.9, 140.9, 140.1, 137.6, 137.5, 136.0, 133.3, 130.4, 129.6, 129.4, 128.9, 128.6, 128.4, 128.4, 128.0, 127.8, 123.4, 122.5, 122.1, 119.3, 33.6, 21.5, 21.3, 21.2. HRMS (ESI): calcd for $C_{33}H_{29}NOS$ $[M + H]^+$, 488.2043; found, 488.2057.

*5-Benzyl-3-(4-Methylbenzoyl)-4-(4-methoxyphenyl)-2-phenylaminothiophene (**5c′**).* Yield: 14 mg, 47% (from 0.0613 mmol of corresponding **3**). Yellow solid, mp 189−191 °C. IR (NaCl, cm^{-1}): 3405, 3055, 2926, 2830, 1621, 1545, 1396. ^1H NMR (500 MHz, $CDCl_3$): δ 11.39 (s, 1H), 7.34−7.33 (m, 4H), 7.27−7.24 (m, 2H), 7.19 (t, J = 7.5 Hz, 1H), 7.13−7.11 (m, 4H), 7.04 (d, J = 9.0 Hz, 1H), 6.85 (d, J = 8.5 Hz, 2H), 6.77 (d, J = 7.5 Hz, 2H), 6.50 (d, J = 9.0 Hz, 2H), 3.92 (s, 2H), 3.67 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.2, 160.0, 158.4, 142.2, 140.8, 140.5, 140.1, 137.6, 136.8, 131.5, 129.6, 128.9, 128.7, 128.6, 128.5, 127.9, 126.6, 121.5, 119.3, 117.6, 113.3, 55.3, 34.0, 21.5. HRMS (ESI): calcd for $C_{32}H_{27}NO_2S$ $[M + H]^+$, 490.1835; found, 490.1815.

*4-(4-Chlorophenyl)-5-(4-methylbenzyl)-3-(2-thienoyl)-2-phenylaminothiophene (**5d′**).* Yield: 10 mg, 32% (from 0.06 mmol of corresponding **3**). Yellow solid, mp 175−177 °C. IR (NaCl, cm^{-1}): 3401, 3029, 2928, 2851, 1622, 1539. ^1H NMR (500 MHz, $CDCl_3$): δ 10.73 (s, 1H), 7.34−7.28 (m, 5H), 7.09−7.01 (m, 9H), 6.81 (dd, J = 4.0, 1.0 Hz, 1H), 6.59 (dd, J = 5.0, 3.5 Hz, 1H), 3.92 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 184.1, 159.3, 150.3, 147.1, 140.6, 137.6, 137.0, 136.3, 135.1, 135.0, 132.8, 131.2, 131.1, 129.7, 129.6, 128.3, 128.2, 126.8, 123.3, 119.2, 117.7, 33.5, 21.2. HRMS (ESI): calcd for $C_{29}H_{22}ClNOS_2$ $[M + H]^+$, 500.0904; found, 500.0914.

*(2-Amino-5-benzyl-4-p-tolylthiophen-3-yl)(phenyl)methanone (**5f′**).* Yield: 30 mg, 73% (from 0.104 mmol of **3u**). Yellowish sticky liquid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.28 (t, J = 7,5 Hz, 2H), 7.22−7.20 (m, 3H) 7.13 (d, J = 7.0 Hz, 2H), 7.07 (t, J = 7.5 Hz, 1H), 6.94 (t, J = 7.5 Hz, 2H), 6.82 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.0 Hz, 2H), 6.57 (brs, 2H), 3.88 (s, 2H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.5, 164.2, 140.6, 140.4, 137.1, 136.1, 133.2, 131.8, 130.1, 129.8, 128.6, 128.5, 128.5, 128.3, 127.2, 126.6, 121.3, 33.9, 21.0. HRMS (ESI): calcd for $C_{25}H_{21}NOS$ $[M + H]^+$, 384.1417; found, 384.1418.

*((2Z,5Z)-5-Benzylidene-2,5-dihydro-4-(4-methylphenyl)-2-phenyliminothiophen-3-yl)(4-methylphenyl)methanone (**6a**).* Yield: 27 mg, 91% (from 0.0637 mmol of corresponding **3**). Yellow solid, mp 223−225 °C. IR (NaCl, cm^{-1}): 3059, 3025, 2928, 2850, 1656, 1598, 1322. ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 7.5 Hz, 2H), 7.35−7.32 (m, 4H), 7.26 (d, J = 11.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 7.0 Hz, 2H) 7.02 (d, J = 8.4, 1.1 Hz, 2H), 6.77 (s, 1H), 2.38 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.0, 164.2, 154.4, 151.5, 144.6, 140.8, 139.1, 137.8, 135.7, 134.4, 130.0, 129.8, 129.5, 129.4, 129.4, 129.3, 129.2, 129.2, 128.9, 128.7, 125.2, 120.5, 22.0, 21.5. HRMS (ESI): calcd for $C_{32}H_{25}NOS$ $[M + H]^+$, 472.1730; found, 472.1743.

*((2Z,5Z)-5-(4-Methylbenzylidene)-2,5-dihydro-4-(4-methylphenyl)-2-phenyliminothiophen-3-yl)(4-methylphenyl)methanone (**6b**).* Yield: 28 mg, 96% (from 0.0618 mmol of corresponding **3**). Orange solid, mp 210−212 °C. IR (NaCl, cm^{-1}): 3078, 3029, 2920, 2855, 1668, 1606, 1449, 1323. ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 8.5 Hz, 2H), 7.35−7.31 (m, 4H), 7.22 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.15−7.12 (m, 5H), 7.02 (d, J = 7.5 Hz, 2H), 6.74 (s, 1H), 2.37 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 193.1, 164.3, 154.5, 151.6, 150.5, 150.5, 144.5, 140.4, 139.1, 139.0, 136.7, 134.5, 132.9, 130.0, 129.8, 129.6, 129.4, 129.3, 129.3, 129.2, 125.1, 120.6, 21.9, 21.6, 21.5. HRMS (ESI): calcd for $C_{33}H_{27}NOS$ $[M + H]^+$, 486.1886; found, 486.1897.

*((2Z,5Z)-5-(4-Methylbenzylidene)-2,5-dihydro-4-(4-methylphenyl)-2-phenyliminothiophen-3-yl)(4-methoxyphenyl)methanone (**6c**).* Yield: 27 mg, 94% (from 0.0598 mmol of corresponding **3**). Yellow solid, mp 197−198 °C. IR (NaCl, cm^{-1}): 3058, 2923, 2851, 1653, 1599, 1441. ^1H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, J = 8.5 Hz, 2H), 7.35−7.31 (m, 4H), 7.22 (d, J = 7.5 Hz, 2H), 7.14−7.12 (m, 5H), 7.02 (d, J = 7.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 6.73 (s, 1H), 3.83 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.9, 164.4, 164.0, 154.3, 151.6, 140.5, 139.1, 139.0, 136.7, 132.9, 132.2, 130.1, 129.8, 129.6, 129.5, 129.4, 129.4, 129.3, 129.2,

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125.1, 120.6, 113.8, 55.5, 21.6, 21.5. HRMS (ESI): calcd for $C_{33}H_{27}NO_2S$ [M + H]$^+$, 502.1835; found, 502.1848.

*((2Z,5Z)-(5-Benzylidene-2,5-dihydro-4-(4-methylphenyl)-2-phenyliminothiophen-3-yl)(4-methoxyphenyl)methanone (**6d**).* Yield: 26 mg, 88% (from 0.0616 mmol of corresponding **3**). Yellow solid, mp 160−162 °C. IR (NaCl, cm^{-1}): 3082, 3059, 2920, 2851, 1647, 1451, 1418. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, J = 9.0 Hz, 2H), 7.42 (d, J = 7.5 Hz, 2H), 7.34 (td, J = 8.0, 2.0 Hz, 4H), 7.26 (d, J = 10.5 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.0 Hz, 2H), 7.03 (d, J = 7.5 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 6.76 (s, 1H), 3.84 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.9, 164.2, 164.1, 154.2, 151.6, 140.8, 139.1, 137.8, 135.7, 132.2, 130.1, 129.8, 129.4, 129.4, 129.4, 129.3, 129.2, 128.9, 128.7, 125.2, 120.1, 113.2, 55.3, 21.5. HRMS (ESI): calcd for $C_{32}H_{25}NO_2S$ [M + H]$^+$, 488.1679; found, 488.1683.

*((2Z,5Z)-5-Benzylidene-2,5-dihydro-4-(4-chlorophenyl)-2-phenyliminothiophen-3-yl)(4-methylphenyl)methanone (**6e**).* Yield: 28 mg, 95% (from 0.0609 mmol of corresponding **3**). Yellow solid, mp 175−176 °C. IR (NaCl, cm^{-1}): 2921, 2852, 1649, 1589, 1484, 1343. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 7.5 Hz, 2H), 7.35−7.32 (m, 6H), 7.29−7.27 (m, 3H), 7.20 (d, J = 8.0 Hz, 2H), 7.14 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 7.5 Hz, 2H), 6.69 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.6, 163.7, 152.8, 151.3, 144.9, 141.5, 141.5, 137.5, 135.6, 135.4, 134.3, 130.8, 130.6, 130.0, 129.8, 129.5, 129.4, 129.3, 129.0, 129.0, 125.4, 120.5, 22.0. HRMS (ESI): calcd for $C_{31}H_{22}ClNOS$ [M + H]$^+$, 492.1183; found, 492.1194.

*((2Z,5Z)-5-(4-Methylbenzylidene)-2,5-dihydro-4-(4-chlorophenyl)-2-phenyliminothiophen-3-yl)(4-methylphenyl)methanone (**6f**).* Yield: 28 mg, 93% (from 0.0592 mmol of corresponding **3**). Yellow solid, mp 245−247 °C. IR (NaCl, cm^{-1}): 3028, 2923, 2853, 1663, 1604, 1454, 1324. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 8.0 Hz, 2H), 7.36−7.27 (m, 8H), 7.20 (d, J = 8.0 Hz, 2H), 7.16−7.14 (m, 3H) 7.02 (d, J = 7.5 Hz, 2H), 6.67 (s, 1H), 2.38 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.7, 163.9, 152.9, 151.4, 144.8, 141.1, 139.3, 136.5, 135.5, 134.3, 132.7, 130.8, 130.7, 129.9, 129.8, 129.7, 129.6, 129.4, 129.2, 129.0, 125.3, 120.5, 22.0, 21.6. HRMS (ESI): calcd for $C_{32}H_{24}ClNOS$ [M + H]$^+$, 506.1340; found, 506.1354.

*((2Z,5Z)-5-(4-Methylbenzylidene)-2,5-dihydro-4-(4-chlorophenyl)-2-phenyliminothiophen-3-yl)(4-methoxyphenyl)methanone (**6g**).* Yield: 27 mg, 89% (from 0.0574 mmol of corresponding **3**). Yellow solid, mp 146−148 °C. IR (NaCl, cm^{-1}): 3064, 2921, 2852, 1650, 1596, 1263. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, J = 8.5 Hz, 2H), 7.35−7.29 (m, 8H), 7.16−7.14 (m, 3H) 7.03 (d, J = 7.5 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 6.66 (s, 1H), 3.83 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 164.2, 164.0, 152.8, 151.4, 141.1, 139.3, 136.5, 135.4, 132.7, 132.2, 130.8, 130.7, 129.9, 129.8, 129.7, 129.5, 129.2, 129.0, 125.3, 120.6, 114.0, 55.5, 21.6. HRMS (ESI): calcd for $C_{32}H_{24}ClNO_2S$ [M + H]$^+$, 522.1289; found, 522.1302.

*((2Z,5Z)-5-Benzylidene-2,5-dihydro-4-(2-thienyl)-2-phenyliminothiophen-3-yl)(4-phenyl)methanone (**6h**).* Yield: 27 mg, 90% (from 0.0668 mmol of corresponding **3**). Yellow solid, mp 222−224 °C. IR (NaCl, cm^{-1}): 2921, 2851, 1644, 1594, 1556. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.0 Hz, 2H), 7.53 (t, J = 7.0 Hz, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.43−7.29 (m, 7H), 7.16−7.14 (m, 3H), 7.02−7.01 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 163.0, 151.1, 146.4, 141.2, 137.0, 136.4, 135.3, 133.6, 131.4, 130.1, 129.7, 129.5, 129.4, 129.1, 128.8, 128.5, 127.4, 125.2, 120.4 (two carbon peak is merged with other peaks). HRMS (ESI): calcd for $C_{28}H_{19}NOS_2$ [M + H]$^+$, 450.0981; found, 450.0988.

*((2Z,5Z)-5-Benzylidene-2,5-dihydro-4-(2-thienyl)-2-phenyliminothiophen-3-yl)(4-methylphenyl)methanone (**6i**).* Yield: 28 mg, 92% (from 0.0647 mmol of corresponding **3**). Yellow solid, mp 160−162 °C. IR (NaCl, cm^{-1}): 3058, 3028, 2921, 2853, 1666, 1602, 1448, 1322. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 7.5 Hz, 2H), 7.39−7.32 (m, 6H), 7.20 (d, J = 8.0 Hz, 2H), 7.16−7.13 (m, 3H), 7.02−7.00 (m, 3H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.8, 163.4, 151.4, 146.5, 144.8, 141.6, 137.2, 135.6, 134.3, 131.7, 130.3, 130.0, 129.9, 129.5, 129.5, 129.3, 129.0, 129.0, 128.6, 127.7, 125.4, 120.6, 22.0. HRMS (ESI): calcd for $C_{29}H_{21}NOS_2$ [M + H]$^+$, 464.1137; found, 464.1148.

*((5Z)-5-Benzylidene-4,5-dihydro-4-(4-methylphenyl)-2-(diethylamino)thiophen-3-yl)(4-methylphenyl)methanone (**7a**).* Yield: 13 mg, 14%. Pale yellow sticky liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, J = 8.0 Hz, 2H), 7.31−7.28 (m, 2H), 7.23 (d, J = 7.5 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.16 (t, J = 7.0 Hz, 1H), 7.06−7.04 (m, 4H), 6.48 (d, J = 1.0 Hz, 1H), 5.19 (d, J = 1.5 Hz, 1H), 3.34−3.30 (m, 2H), 3.23−3.18 (m, 2H), 2.34 (s, 3H), 2.29 (s, 3H), 1.14 (t, J = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 188.4, 163.7, 141.8, 140.9, 139.0, 138.8, 136.6, 136.2, 129.4, 128.6, 128.6, 128.4, 128.2, 127.2, 126.8, 123.0, 108.7, 63.0, 49.2, 21.7, 21.3, 13.4. HRMS (ESI): calcd for $C_{30}H_{31}NOS$ [M + H]$^+$, 454.2199; found, 454.2196.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00342.

^{1}H and ^{13}C NMR spectra, X-ray structures, and crystallographic data (PDF)

Crystallographic data (CIF)

Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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