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Sequential One-Pot Synthesis of Tri- and Tetrasubstituted Thiophenes and Fluorescent Push–Pull Thiophene Acrylates Involving (Het)aryl Dithioesters as Thiocarbonyl Precursors

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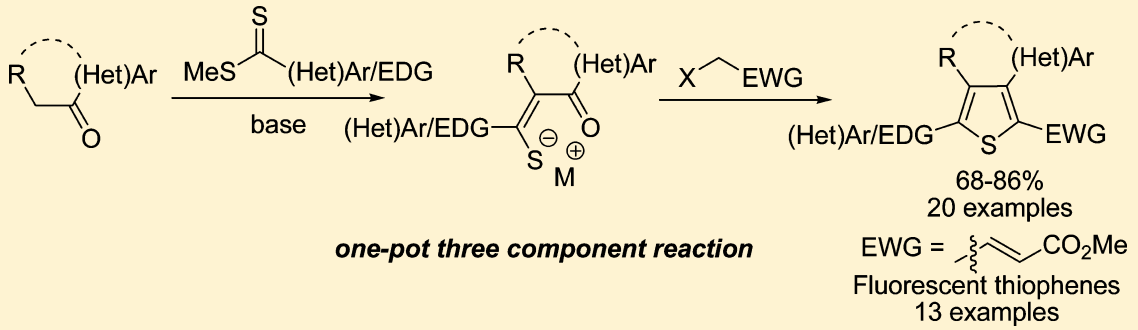
Supporting Information



ABSTRACT: An efficient, one-pot three component synthesis of highly functionalized tri- and tetrasubstituted thiophenes has been reported involving (het)aryl dithioesters as thiocarbonyl precursors. Thus, sequential base mediated condensation of readily available (het)aryl active methylene ketones with (het)aryl dithioesters followed by *S*-alkylation of the resulting enethiolate salts with activated halomethylene compounds and concurrent intramolecular aldol-type condensation of *S*-alkylated compounds affords substituted thiophenes in excellent yields. The methodology has also been extended for the synthesis of highly fluorescent push–pull substituted thiophene-5-acrylates by using bromocrotonate as the activated methylene alkylating agent.

INTRODUCTION

The thiophene structural motif constitutes an important class of five-membered heterocycles that is prevalent in several bioactive natural products, pharmaceuticals,[1,2] and some of the top-selling marketed drugs such as plavix, spiriva, raloxifene, zileuton, and clopidogrel.[3] Moreover, because of their structural rigidity and specific electronic properties, thiophene derivatives also find applications in design and synthesis of novel organic materials[2a,b,4] such as organic solar cells, liquid crystals, field effect transistors, molecular wires, organic semiconductors, and organic light-emitting diodes. Also, biosteric replacement of annulated benzene ring by thiophene in some biologically active compounds is known to alter their biological profile and selectivity.[5] Thiophene derivatives also serve as versatile intermediates in organic synthesis.[6] In view of their applications in various fields, development of new efficient methods for highly functionalized polysubstituted thiophenes has received considerable attention in recent years.[7] Synthetic approaches to multisubstituted thiophenes involve either direct functionalization of preconstructed thiophene ring via α- (or directed) metalation[3c]/halogenation or via ring closure of appropriately substituted precursors.[1,7−14] The latter approach is apparently more versatile in terms of efficiency and flexibility of substitution pattern. Among these, Gewald[8a] or Paal–Knorr reactions[8b,c] represent classical methods for thiophene synthesis in which a sulfur atom is introduced using elemental sulfur, H_2S, Lawesson's reagent, phosphorus pentasulfide, or bis(trimethylsilyl)sulfide.[8d] Recently, efficient synthesis of substituted thiophenes have been reported through copper (or Pd)-catalyzed cross-coupling of sulfides with halogen-substituted dienes, enynes,[2c,9a] or 1,3-diynes.[9b,c] Other recent thiophene syntheses include Pd-catalyzed (or iodine-mediated) heterocyclodehydration of 1-mercapto-3-yn-2-ols[9d−f] and thiannulation of Morita–Baylis–Hillman adducts.[9g,h] Although these methods are efficient, they do not represent general approaches for thiophene synthesis and require prior synthesis of the desired precursors.

One of the useful alternative approaches for the synthesis of substituted thiophenes and thienothiophene utilizes functionalized polarized ketene dithioacetals as precursors.[10] The overall protocol involves deprotonation of active methylene compounds and nucleophilic addition of the resulting carbanion to carbon disulfide furnishing dimetaloketenedithiolate salts, which on alkylation with activated methylene halides bearing electron-withdrawing groups (EWG) affording either substituted 2-(alkylthio)thiophenes or symmetrically substituted thienothiophenes via double-intramolecular aldol/Thorpe–Ziegler/Dieckmann- type cyclization (Scheme 1, eq 1).[10a−c] On the other hand, stepwise sequential alkylation of dithiolate salt with

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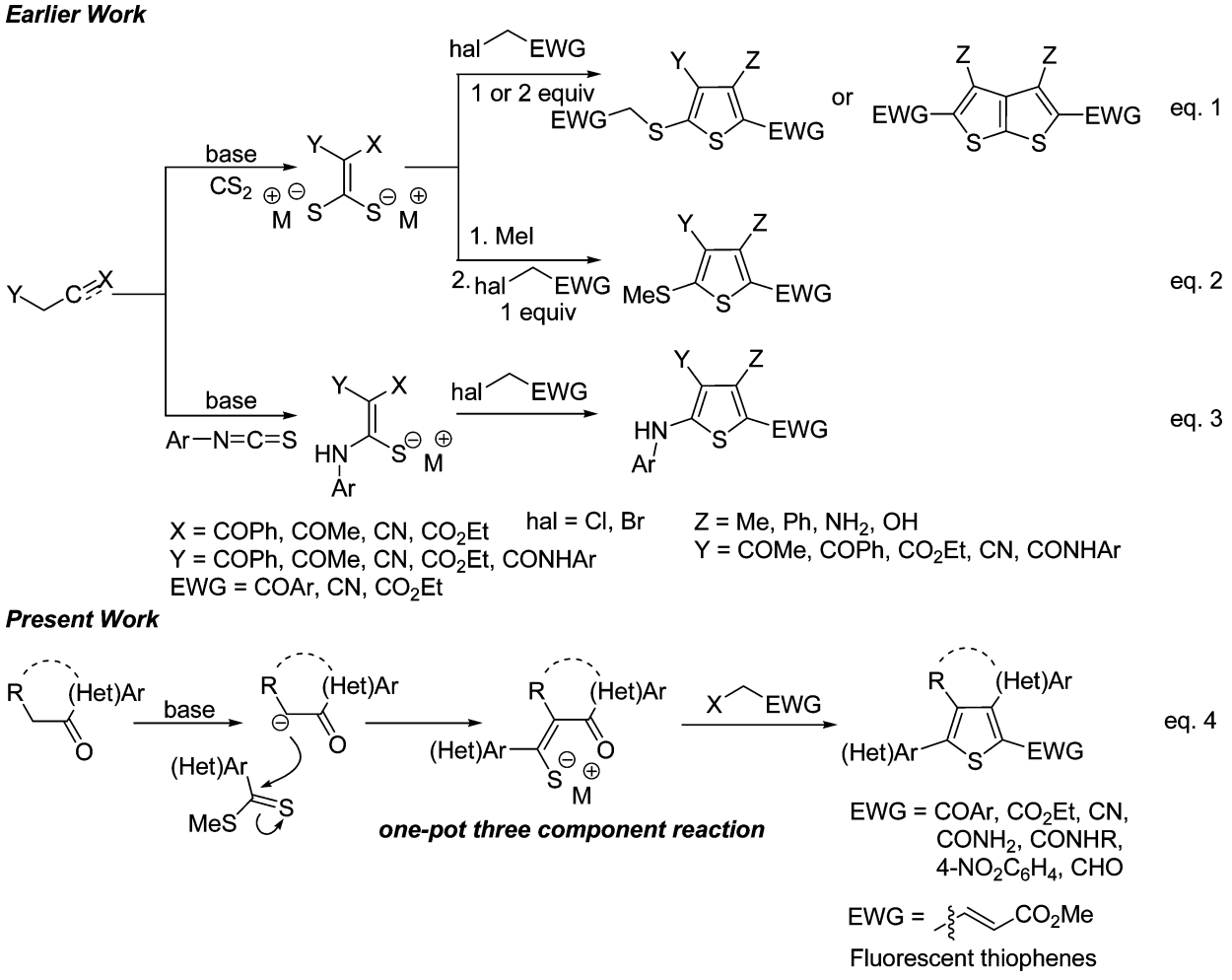
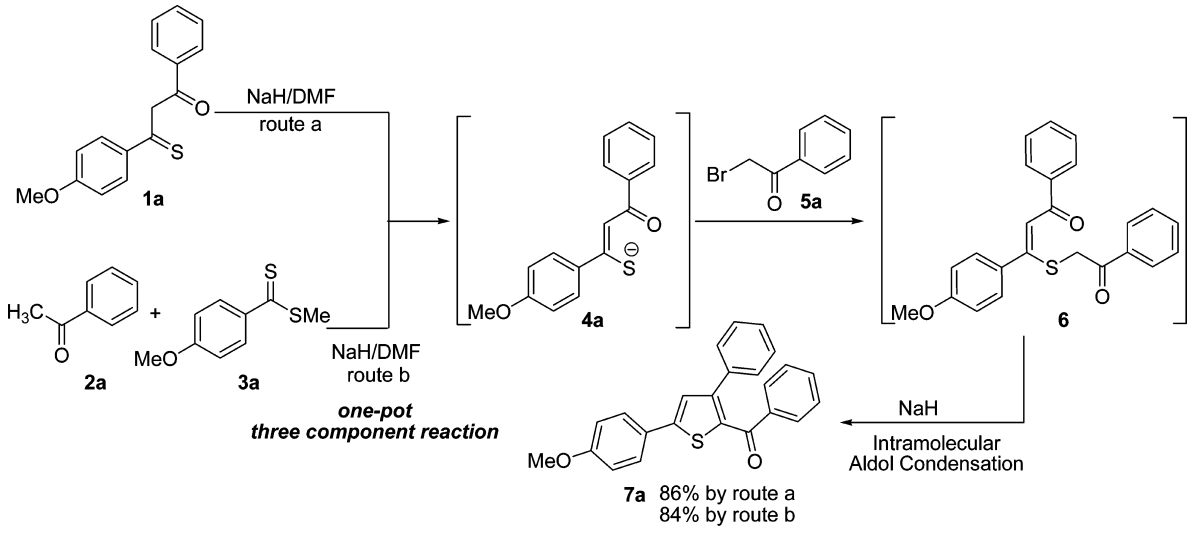
Scheme 1. Synthesis of Substituted Thiophenes



Scheme 2. Designed Strategy for the Synthesis of Thiophenes 7



alkyl halide (usually MeI or EtI) and an EWG group containing halomethylene compounds provides 2-(alkylthio)-3,4,5-substituted thiophenes in moderate to good yields (Scheme 1, eq 2).[10d,e] The active methylene compounds employed in these reactions usually comprise β-diketones, β-ketoesters, malononitrile, α-cyanoacetate, or α-acylacetonitriles, yielding 4-alkyl/aryl/hydroxy or aminothiophenes depending on the nature of the electrophilic partner in the final intramolecular cyclization step.[10] However, this method suffers from significant limitations such as modest yields of thiophenes and formation of mixed alkylation products during one-pot sequential alkylation with different alkyl halides.[10] Asokan and co-workers

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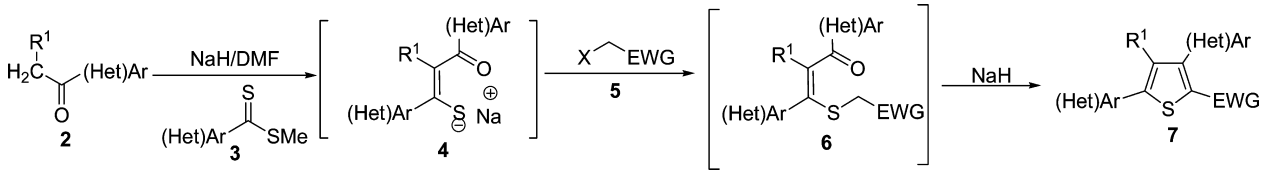
Table 1. One-Pot, Three-Component Synthesis of Multisubstituted Thiophenes 7



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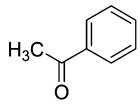
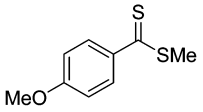
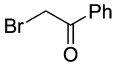
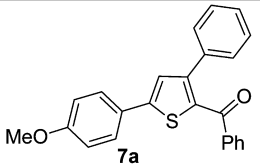
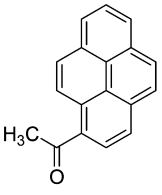
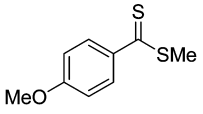
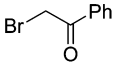
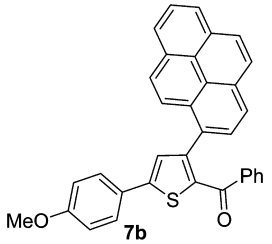
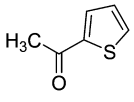
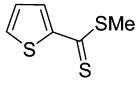
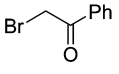
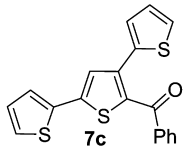
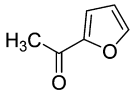
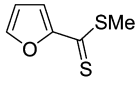
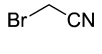
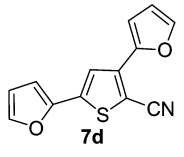
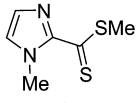
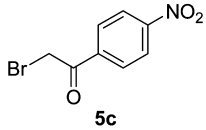
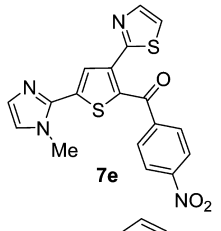
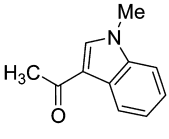
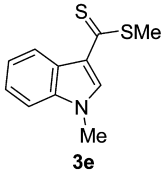
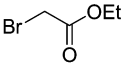
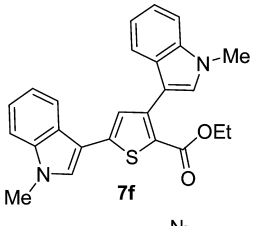
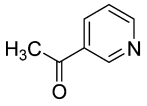
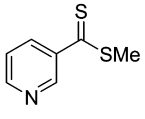
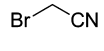
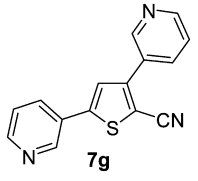
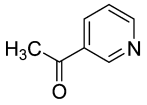
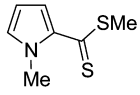
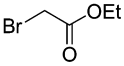
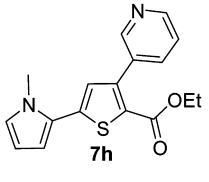
1	 **2a**	 **3a**	 **5a**	 **7a**	84
2	 **2b**	 **3a**	 **5a**	 **7b**	77
3	 **2c**	 **3b**	 **5a**	 **7c**	68
4	 **2d**	 **3c**	 **5b**	 **7d**	80
5	 **2e**	 **3d**	 **5c**	 **7e**	76
6	 **2f**	 **3e**	 **5d**	 **7f**	75
7	 **2g**	 **3f**	 **5b**	 **7g**	79
8	 **2g**	 **3g**	 **5d**	 **7h**	72

dx.doi.org/10.1021/jo502429c | J. Org. Chem. 2015, 80, 414−427

Table 1. continued

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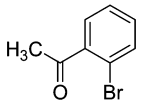
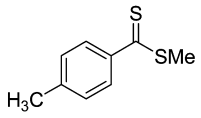
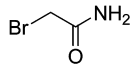
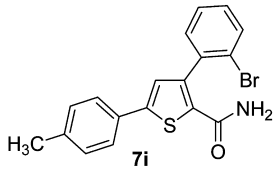
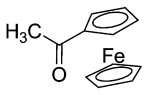
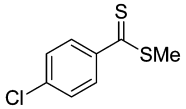
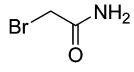
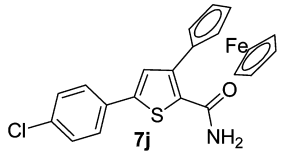
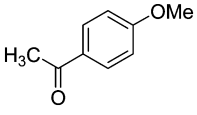
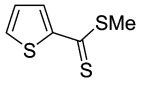
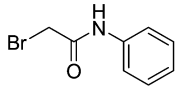
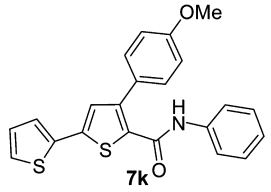
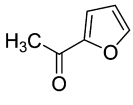
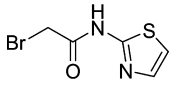
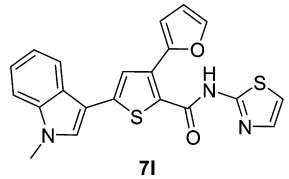
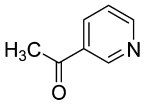
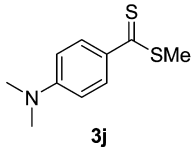
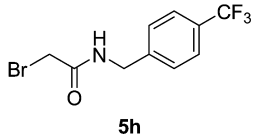
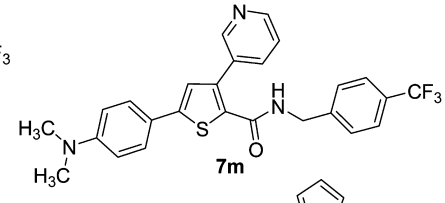
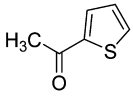
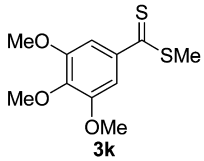
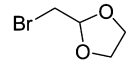
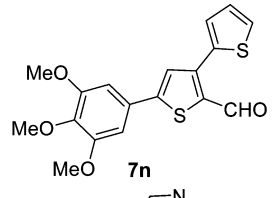
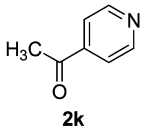
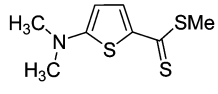
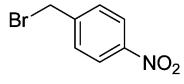
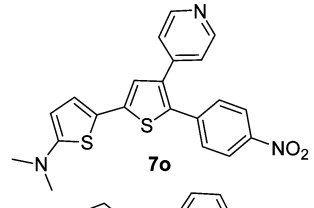
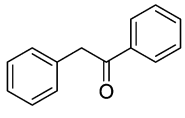
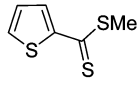
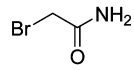
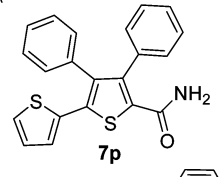
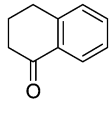
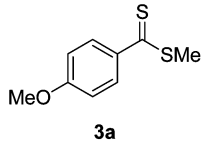
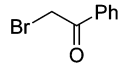
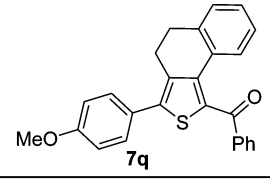
9	 **2h**	 **3h**	 **5e**	 **7i**	69
10	 **2i**	 **3i**	 **5e**	 **7j**	69
11	 **2j**	 **3b**	 **5f**	 **7k**	76
12	 **2d**	 **3e**	 **5g**	 **7l**	82
13	 **2g**	 **3j**	 **5h**	 **7m**	70
14[b]	 **2c**	 **3k**	 **5i**	 **7n**	80
15	 **2k**	 **3l**	 **5j**	 **7o**	86
16	 **2l**	 **3b**	 **5e**	 **7p**	74
17	 **2m**	 **3a**	 **5a**	 **7q**	85

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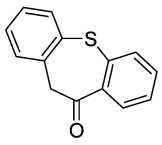
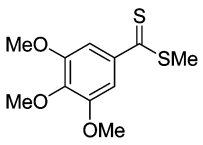
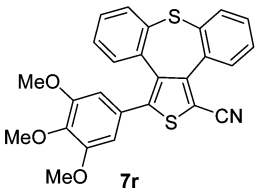
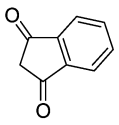
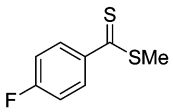
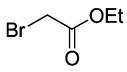
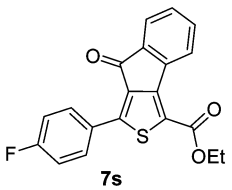
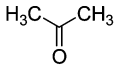
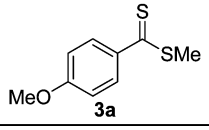
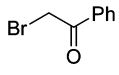
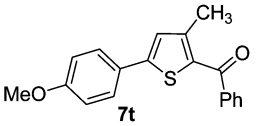
Table 1. continued

entry	2	3	5	product	yield (%)
18	 **2n**	 **3k**	 **5b**	 **7r**	72
19	 **2o**	 **3m**	 **5d**	 **7s**	70
20[c]	 **2p**	 **3a**	 **5a**	 **7t**	68

[a]Isolated yields. Reaction conditions: **2** (1.0 mmol), **3** (1.0 mmol) and (NaH 3.0 mmol) in DMF (6 mL), stirred for 1 h; **5** (1.0 mmol) in DMF (2 mL) added and stirred for 6−7 h. [b]After the reaction crude product refluxed in 50% aqueous AcOH for 2 h. [c]NaO-*t*-Bu was used as base.

have previously demonstrated the use of β-ketodithioesters with built-in dithioester functionality, which circumvents the problem in selective sequential alkylation.[2a,11] However, these methods are limited by the choice of thiocarbonyl compound introducing only alkylthio groups in the 2-position of thiophene derivatives. Recently, in a few examples, thioamides or β-ketothioamides have also been employed as a source of sulfur in the synthesis of 2-cycloamino-substituted thiophenes.[11a,12,13] Kirsch and co-workers have recently reported, in a series of papers,[14] the synthesis of 2-arylaminothiophenes by employing aryl isothiocyanates as thiocarbonyl precursors in these reactions (Scheme 1, eq 3).[14a−c] In an alternative procedure, they have elaborated the synthesis of 2-arylaminothiophenes by displacement reaction on keteneamino-*S*-methylacetal with ethyl thioglycolate and subsequent intramolecular cyclization.[14d,e] However, this method suffers from limitations such as modest to good yields (only in very few cases) of 2-anilinothiophenes and limited availability of isothiocyanates or mercapto-substituted active methylene compounds.[14]

We have been involved for several years in developing new efficient routes for substituted and fused five- and six-membered heterocycles employing organosulfur synthons such as α-oxoketenedithioacetals and β-ketodithioesters.[15] Recently, we further designed and elaborated synthetic application of new class of organosulfur building blocks, such as 2,3-(het)aryl-3-(methylthio)acrylonitriles, 1,3-monothiodiketones, and 1,3-(het)aryl-3-(methylthio)propenones, which are synthesized via base-mediated condensation of active methylene compounds with (het)aryl dithioesters and subsequent alkylation of the resulting thiolate salt.[15a−d] Such (het)aryldithioesters are readily available from the corresponding organometallic reagents and CS_2 in high yields.[16] In continuation of these studies, we further conceived of developing an efficient high-yield synthesis of multisubstituted thiophenes involving base-mediated condensation of active methylene ketones with (het)aryl dithioesters as thiocarbonyl partners and subsequent alkylation of the resulting enethiolate salts with a range of activated methylene halides followed by in situ intramolecular cyclocondensation (Scheme 1, eq 4). We have successfully achieved this goal and report in this paper a diversity-oriented, sequential one-pot, three-component synthesis of tri- and tetrasubstituted thiophenes along with the synthesis of highly fluorescent thiophenes employing bromocrotonate as halomethylene alkylating agent.

RESULTS AND DISCUSSION

In a preliminary experiment, we first reacted 1,3-monothioketone **1a** with sodium hydride followed by treatment of the resulting enethiolate salt **4a** with α-bromoacetophenone to generate intermediate β-alkylthioenone **6**, which underwent in situ intramolecular aldol condensation to afford 5-benzoyl-2-(4-methoxyphenyl)-4-phenylthiophene **7a** in 86% yield (Scheme 1). Alternatively, the enethiolate salt **4a** was generated in situ by reacting acetophenone **2a** with 4-methoxyphenyl dithioate **3a** in the presence of sodium hydride, with a view to develop a one-pot, three-component version of the reaction (route b). Subsequent alkylation of intermediate **4a** with α-bromoacetophenone followed by concurrent intramolecular aldol condensation of **6** furnished the thiophene **7a** in a comparable yield of 84% (Scheme 2). We therefore pursued this sequential one-pot, three-component procedure to develop a general diversity-oriented synthesis of highly functionalized polysubstituted thiophenes, and these results are depicted in Table 1.

A variety of (het)aryl acyclic and cyclic active methylene ketones were selected as coupling partners in this study (Table 1). It should be noted that most of the active methylene compounds employed in the previous thiophene synthesis (by annulation with either CS_2 or aryl isothiocyanate) comprise β-diketones, β-ketoesters, malononitrile, and cyano esters, whereas the simple α-methyl/methylene ketones have not been used as active methylene partners in these studies. Similarly, the (het)aryl dithioesters have not been employed as thiocarbonyl precursors in the previous thiophene syntheses. Therefore, in order to enhance substituent scope at the 2-position of product thiophenes, a number of either known or newly synthesized structurally diverse (het)aryl dithioesters

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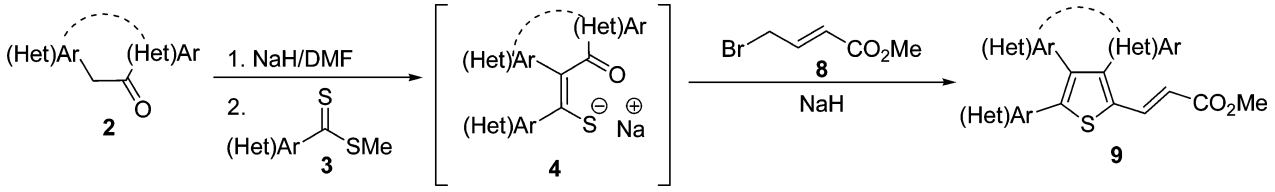
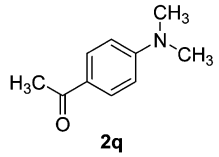
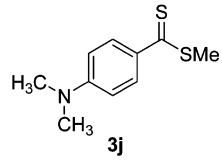
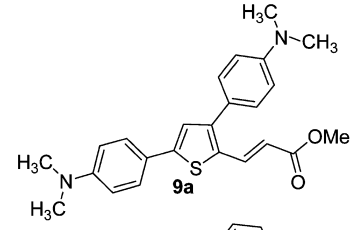
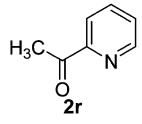
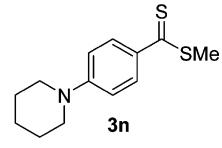
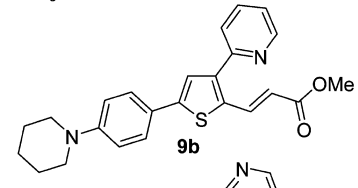
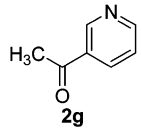
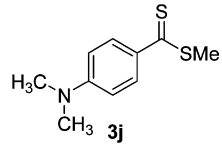
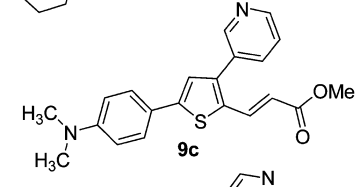
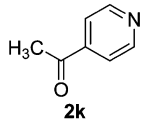
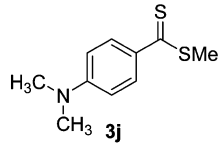
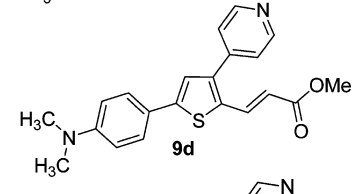
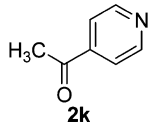
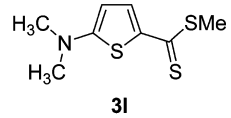
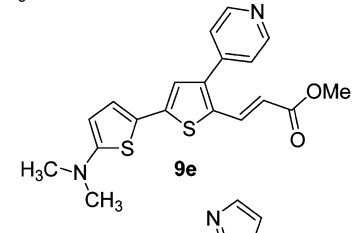
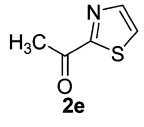
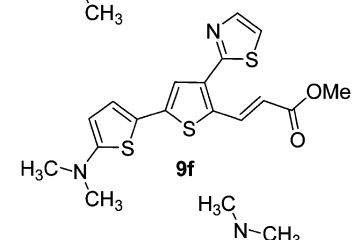
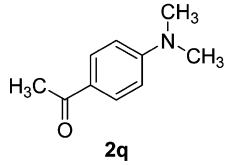
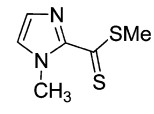
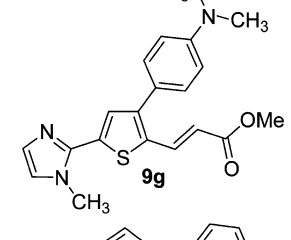
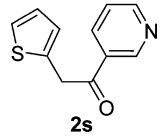
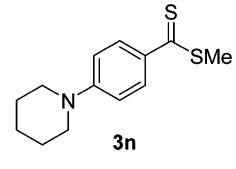
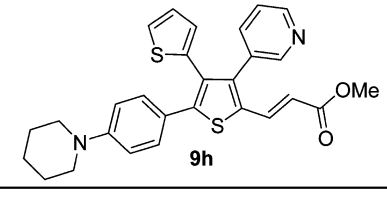
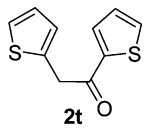
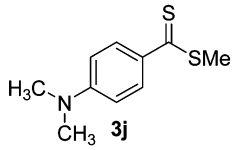
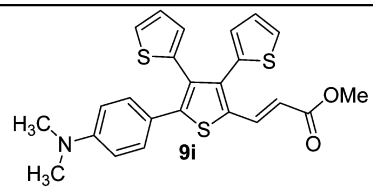
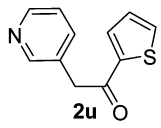
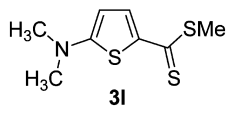
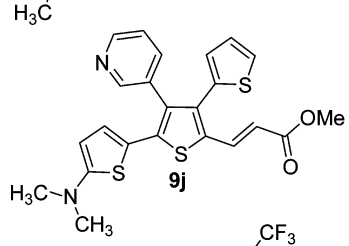
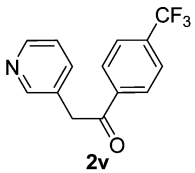
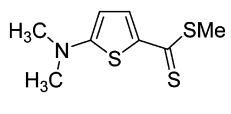
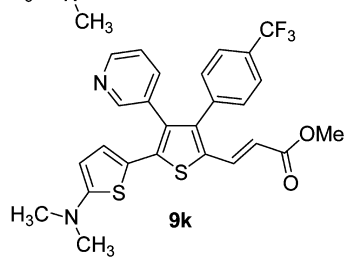
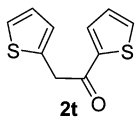
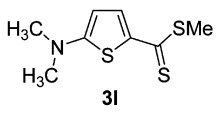
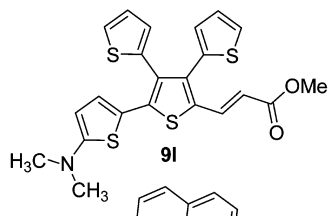
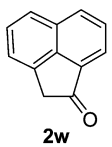
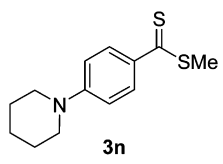
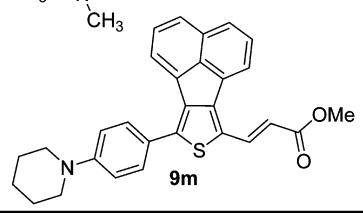
Table 2. Synthesis of Fluorescent 2,4-Di- and 2,3,4-Trisubstituted Thiophene-5-acrylates



entry	2	3	product	yield (%)
1	 2q	 3j	 9a	74
2	 2r	 3n	 9b	84
3	 2g	 3j	 9c	81
4	 2k	 3j	 9d	75
5	 2k	 3l	 9e	7
6	 2e	 3l	 9f	7
7	 2q	 3g	 9g	7
8	 2s	 3n	 9h	7

dx.doi.org/10.1021/jo502429c | J. Org. Chem. 2015, 80, 414−427

Table 2. continued

entry	2	3	product	yield (%)
9	 **2t**	 **3j**	 **9i**	79
10	 **2u**	 **3l**	 **9j**	77
11	 **2v**	 **3l**	 **9k**	79
12	 **2t**	 **3l**	 **9l**	85
13	 **2w**	 **3n**	 **9m**	78

[a]Isolated yields. Reaction conditions: **2** (1.0 mmol), **3** (1.0 mmol) and NaH (3.0 mmol) in DMF (3 mL), stirred for 1 h; **8** (1.0 mmol) added and stirred for 6−7 h.

3 were chosen as thiocarbonyl partners for this synthetic study (Table 1). To further add functional group diversity at 5-position of newly synthesized thiophenes, a diverse range of α-halomethylene alkylating agents bearing a variety of electron-withdrawing groups (EWG) are employed as shown in Table 1.

The broad scope and generality of the present thiophene synthesis are depicted in Table 1. Thus, thiophene **7b** with a 4-(1-pyrenyl) group could be obtained in high yield by utilizing 1-acetylpyrene **2b**, as active methylene partner (entry 2). Similarly, it was possible to install a variety of five- or six-membered (het)aryl groups at 2- and 4-positions of product thiophenes, along with a range of electron-withdrawing groups at the 5-position, depending on choice of (het)aryl ketones, (het)aryl dithioesters, and α-halomethylene alkylating agents, thus allowing access to a broad range of diversely substituted thiophenes (entries 3−8). Entries 9−13 and 16 represent the synthesis of substituted thiophenes bearing a primary or secondary amide functionality in the 5-position by using relevant α-halomethylene amides as alkylating agents.[10b] The reaction could also be extended for the introduction of the aldehyde functionality in the 5-position by employing bromoacetaldehyde acetal **5i** as the alkylating partner (entry 14), whereas the use of 4-nitrobenzyl bromide (**5j**) afforded the corresponding 2,4,5-tri(het)arylthiophene **7o** in excellent yield (entry 15). Similarly, the methodology could also be extended for the synthesis of a tetrasubstituted thiophene **7p** from deoxybenzoin as active methylene component (entry 16). Further scope and versatility of the reaction was demonstrated by high-yield synthesis of functionalized polycyclic condensed thiophenes such as **7q−s** by annulation with cyclic active methylene ketones **2m−o**, respectively (entries 17−19). Finally, in one example, thiophene **7t**, bearing a 4-methyl group, could be obtained in 68% yield by extending the reaction to an aliphatic ketone, such as acetone (Table 1, entry 20).

In view of the continued search of tailor-made functional π-electronic systems by diversity-oriented strategies for photonic applications,[4,17] we planned to extend our newly developed methodology for the synthesis of thiophenes with extended π-conjugation (Table 2). Thienyl-based push−pull chromophores are known to display excellent NLO properties[18] and also serve as useful fluorophores in optoelectronic devices.[18] A few of the (het)aryl dithioesters bearing electron-donating groups such as 4-(*N*,*N*-dimethylamino)phenyl (**3j**), 5-(*N*,*N*-dimethylamino)thienyl (**3l**), and 4-(*N*-piperidino)-phenyl (**3n**) substituents and the bromocrotonate **8** as activated

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Table 3. UV−vis Absorption and Emission Data of Thiophene-5-acrylates 9

compd	absorption $\lambda_{max,abs}$(nm) (ε L mol^{-1}cm^{-1})[a]	emission $\lambda_{max,em}$ (nm)[b]	Stokes shift Δ (cm^{-1})
9a	310 (12000), 410 (17500)	575	6999
9b	300 (26600), 410 (23700)	610	7997
9c	295 (22400), 415 (26600)	590	7147
9d	290 (27100), 420 (28300)	610	7416
9e	288 (24900), 460 (19900)	645	6235
9f	335 (18200), 470 (16900)	666	6261
9g	270 (27400), 360 (22800)	605	11248
9h	260 (20200), 395 (20000)	600	8650
9i	270 (11300), 405 (7500)	596	7913
9j	315 (10200), 450 (29300)	612	5882
9k	300 (18700), 460 (20300)	625	5739
9l	320 (16500), 465 (21000)	627	5556

[a]Recorded in MeCN, T = 293 K, c(**9**) = 12.5 × 10^{-6} M. [b]Recorded in MeCN, T = 293 K, c(**9**) = 12.5 × 10^{-6} M.

methylene alkylating partner[19] were selected for introducing extended π-conjugation in the newly constructed thiophenes as depicted in Table 2. Thus, the sequential treatment of active methylene ketones such as 4-(dimethylamino)acetophenone **2q**, 2-, 3-, and 4-acetylpyridines (**2r**, **2g**, and **2k**), and 2-acetylthiazole **2e** with various dithioesters and bromocrotonates under previously described one-pot reaction conditions afforded the corresponding 2,4-(het)arylthiophene-5-acrylates **9a−g** in overall high yields (Table 2, entries 1−7). Further elaboration of reaction to α-(het)arylmethylene ketones such as **2s−v** allowed facile access to 2,3,4-trisubstituted thiophene-5-acrylates **9h−l** in excellent yields (entries 8−12). Finally, with a view to enhance further π-conjugation in the product thiophene, acenaphthenone (**2w**) was subjected to annulation reaction with dithioester **3n** and bromocrotonate **8** under identical conditions furnishing the 2-aryl-3,4-anulated thiophene acrylate **9m** in 78% yield (entry 13).

Because of the extended π-conjugation between the electron-donating 2-substituent and electron-withdrawing 5-thiophene acrylate moiety, all of the newly synthesized thiophenes (**9a−l** except **9m**) are found to display pronounced yellow−green, yellow to red fluorescence, which was visible even on TLC during reaction monitoring. We therefore studied absorption and emission spectra of these thiophene acrylates, which are depicted in Table 3 and Figure 1.

The electronic absorption spectra of tri- (**9a−g**) and tetrasubstituted (**9h−l**) thiophene acrylates display longest wavelength absorption band between 360−470 nm with molar extinction coefficient varying between 7500−29,300 L mol^{-1}cm^{-1} (Table 3, Figure 1). All these thiophenes exhibit yellow−green to yellow and in two cases (**9e−f**), red fluorescence (Figure 1A−D) in solution with emission maxima between 575−666 nm along with pronounced Stokes shift ranging from 5556−8650 cm^{-1} (11,248 cm^{-1} for **9g**) (Figure 1A, 1E). A study of substituent effects in a consanguineous series of 2,4-substituted thiophene-5-acrylates (**9a−f**) bearing an electron-donating [4-(*N*,*N*-dimethylamino)phenyl] (**9a**,**c**,**d**), [4-(*N*-piperidino)phenyl] (**9b**), or [5-(*N*,*N*-dimethylamino)-thiophene-2-yl] (**9e**,**f**) groups at 2-position reveals that the presence of an electron-donating [4-(*N*,*N*-dimethylamino)phenyl] (**9a**) or electron-deficient 2-, 3-, 4-pyridyl groups (**9b−d**) at the 4-position has only a minor effect on the absorption band (λ_{max}) and varies from 410 (**9a−b**), 415 (**9c**) to 420 nm for **9d** (Figure 1A). The bathochromic shift of this absorption band in the UV−vis spectra of **9e** and **9f** to 460 and 470 nm, respectively, can be ascribed to the $\pi^6$5 system of 5-(*N*,*N*-dimethylamino)thienyl ring, which is more electron donating than the contemporary $\pi^6$6 system of phenyl ring (**9a−d** vs **9e−f**). A similar trend is also observed for the emission band in this series (**9a−f**) ranging from 575 (**9a**), 590 (**9c**), 610 (**9b**, **9d**) to 645 and 666 nm for the thiophenes **9e−f**, respectively (Figure 1B, 1D). The increase of both emission wavelength and Stokes shift in these trisubstituted thiophene acrylates (**9a−f**) might be attributed to enhanced "push−pull" effect of π-electrons due to presence of electron-donating and electron-withdrawing groups (pyridyl/thiazolyl) groups at the 2- and 4-positions, respectively, thus influencing the stabilization of the S_1 state.[20]

Among the tetrasubstituted thiophene series **9h−l**, the longer wavelength absorption band is spread over from 395 nm for 2-(4-*N*-piperidinophenyl) (**9h**), 405 nm for 2-(4-dimethylaminophenyl)thiophene (**9i**), which shows bathochromic shift in 2-(5-dimethylamino)thienyl-substituted thiophenes **9j−l** ranging from 450 to 465 nm (Figures 1C, 1E). A similar bathochromic shift is also observed in the emission spectra of **9h−l** varying from 596 (**9i**) to 600, 612, 625, 627 nm for **9h**,**j−l**, respectively. The blue shift observed in the absorption band of **9h** (395 nm) in comparison to **9c** (415 nm) on introduction of (2-thienyl) moiety at 4-position (**9h** vs **9c**), may be explained due to steric crowding in tetrasubstituted thiophene (**9h**), which reduces the planarity of various substituents, thus resulting in decreased conjugation. On the other hand 55−60 nm bathochromic shift of the absorption band in **9j−l** in comparison to thiophenes **9h−i** (**9h** vs **9j**, **9i** vs **9l**) (Figure 1C) could be rationalized due to greater electron releasing effect of 5-(*N*,*N*-dimethylamino)thienyl group than 4-(*N*-piperidino/*N*,*N*-dimethylamino)phenyl moieties, thus increasing the conjugation in these thiophenes. Similarly, the bathochromic shift of absorption band in tetrasubstituted thiophene **9k** is probably due to greater push−pull effect of π-electrons due to the presence of electron-withdrawing 4-(4-trifluoromethyl)phenyl group (Figures 1E,F).

CONCLUSION

In conclusion, we have developed an efficient, high yield sequential one-pot three component route to a broad range of tri- and tetrasubstituted/annulated thiophenes. The protocol employs a variety of acyclic and cyclic active methylene ketones, (het)aryl dithioesters as thiocarbonyl precursors and halomethylene alkylating agents with a range of electron withdrawing groups in this heterocyclization reaction, thus displaying high level of diversity at various positions of thiophene scaffold. Also the methodology could be extended for the synthesis of several push−pull thiophenes with extended π-conjugation, displaying yellow−red fluorescence with large Stokes shift, by using bromocrotonate as active methylene alkylating agent. The reaction employs readily available starting materials and is operationally simple to perform, thus nicely complementing existing methods for thiophene synthesis and would be potentially useful for finding lead compounds for development of thiophene based functional molecules. Our efforts in this direction are in progress.

EXPERIMENTAL SECTION

General Information. All reagents were purchased from commercial suppliers and used without further purification. Solvents were dried according to the standard procedures. All of the reactions were monitored by thin-layer chromatography using standard TLC

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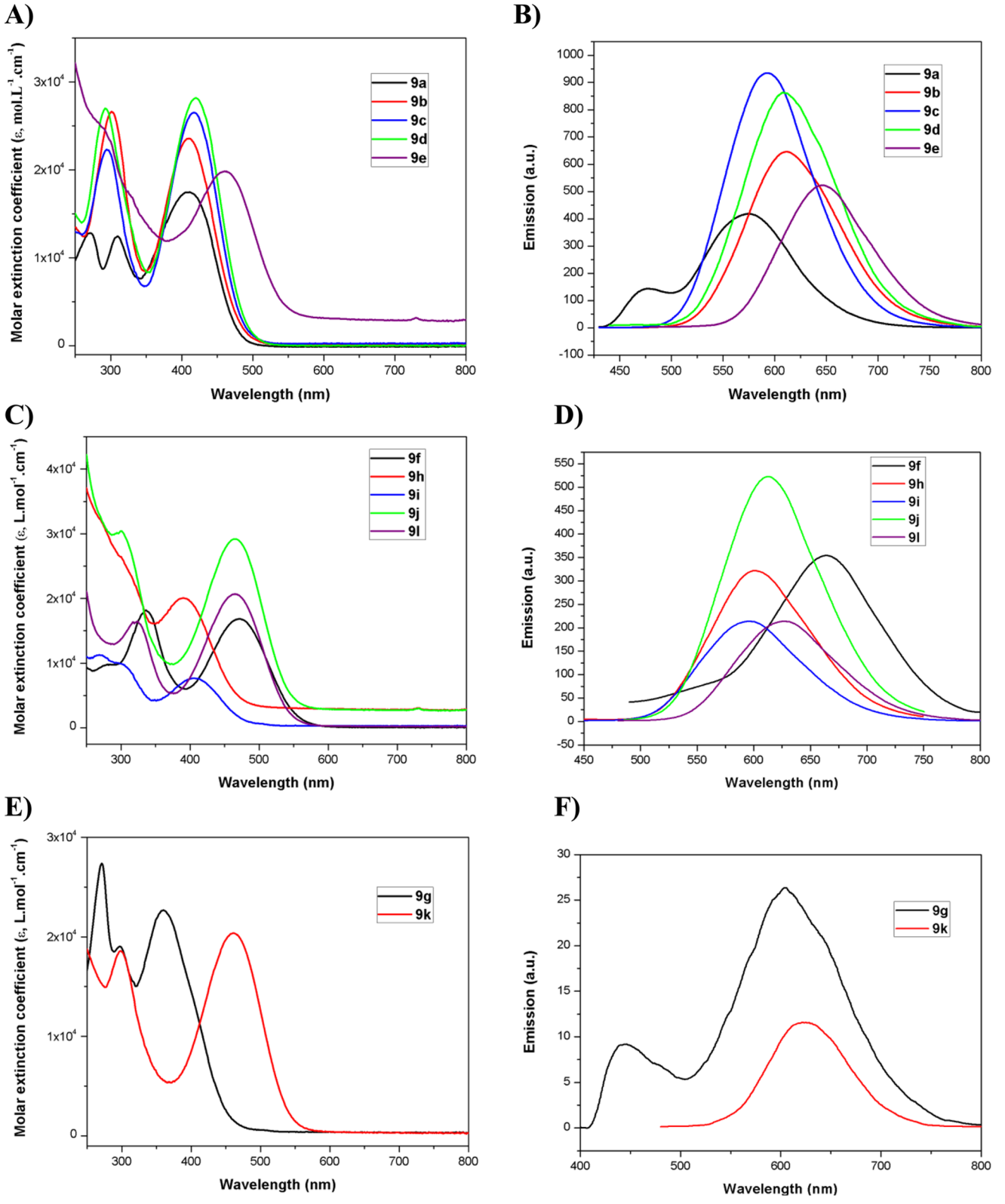

Figure 1. UV−vis absorption and emission spectra of compounds **9a−l**: (A) UV−vis absorption spectra of **9a−e**; (B) emission spectra of **9a−e**; (C) UV−vis absorption spectra of **9f,h−j,l**; (D) emission spectra of **9f,h−j,l**; (E) UV−vis absorption spectra of **9g,k**; (F) emission spectra of **9g,k**; recorded in MeCN, T = 293 K, c(**9**) = 12.5 × 10^{-6} M; excitation at longest absorption wavelength of all compounds.

silica gel plates and visualized with UV light. Column chromatography was performed using silica gel (100−200 mesh). Nuclear magnetic resonance spectra were recorded on (400 MHz) FT-NMR spectrometer with $CDCl_3$ (or) DMSO-d_6 as solvent. Chemical shifts were reported in δ ppm using residual solvent protons as internal standard (δ 7.26 for $CDCl_3$ and δ 2.50 for DMSO-d_6 in ^{1}H NMR, δ 77.16 for $CDCl_3$ and δ 39.52 for DMSO-d_6 in ^{13}C NMR). Coupling constants were reported as J values in hertz (Hz). Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), dd (double doublet), dt (doublet of triplet), td (triplet of doublet), ddd

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(doublet of doublet of doublet), m (multiplet), and br (broad). Infrared spectra of neat samples were recorded in ATR (attenuated total reflectance) mode using FT-IR instrument and HRMS on Q-TOF spectrometer. Melting points were recorded using an electrothermal capillary melting point apparatus and are uncorrected. Electronic absorption spectra were recorded on a UV−Vis−NIR spectrometer. Emission spectra were recorded on a luminescence spectrometer.

All active methylene ketones **2a−m,o−r** and halomethylene compounds **5a−g** were purchased commercially. The ketones **2n,t** and the previously unreported ketones **2s,u−v** were prepared according to the methods reported in the literature.[21a,b] All the known dithioesters **3a−i,k,m** and the unknown **3j,l,n** were also prepared according to the literature procedure.[16] The spectral and analytical data of new ketones **2s,u,v** and the dithioesters **3j,l,n** is given below.

*1-(Pyridin-3-yl)-2-(thiophene-2-yl)ethanone (**2s**):* brown liquid (870 mg, 69%): R_f 0.24 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1685, 1583, 1417, 1223, 696; ^1H NMR (400 MHz, $CDCl_3$) δ 9.23 (dd, J = 2.2 Hz, 0.8 Hz, 1H), 8.78 (dd, J = 4.8 Hz, 1.6 HZ, 1H), 8.27 (dt, J = 8.0 Hz, 1.6 Hz, 1H), 7.42 (ddd, J = 8.0 Hz, 4.8 Hz, 1.6 Hz, 1H), 7.23 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 6.98−6.94 (m, 2H), 4.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 153.7, 150.0, 136.1, 134.6, 131.6, 127.3, 127.2, 125.6, 123.9, 39.9; HRMS (ESI) m/z calcd for $C_{11}H_{10}NOS$ $[M + H]^+$ 204.0483, found 204.0467.

*2-(Pyridin-3-yl)-1-(thiophene-2-yl)ethanone (**2u**):* yellow−brown semisolid (880 mg, 72%); R_f 0.21 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1651, 1469, 1241, 1021, 746; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (br s, 1H), 8.53 (br s, 1H), 7.80 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 7.68 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.65 (t, J = 1.6 Hz, 1H)), 7.28 (dd, J = 8.4 Hz, 4.8 Hz, 1H), 7.15 (dd, J = 4.8 Hz, 4.0 Hz, 1H), 4.21 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3, 150.4, 148.4, 143.6, 137.4, 134.6, 132.8, 128.5, 123.7, 43.2; HRMS (ESI) m/z calcd for $C_{11}H_{10}NOS$ $[M + H]^+$ 204.0483, found 204.0472.

*1-(4-(Trifluoromethyl)phenyl)-2-(pyridin-3-yl)ethanone (**2v**):* pale yellow semisolid (906 mg, 78%); R_f 0.86 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1683, 1409, 1320, 1064, 828; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (br s, 2H), 8.12 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.31 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 4.34 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 150.4, 148.5, 139.0, 137.6, 135.2, 134.9, 130.3, 128.9, 126.12, 126.09, 126.06, 126.0, 123.8, 42.7; HRMS (ESI) m/z calcd for $C_{14}H_{11}F_3NO$ $[M + H]^+$ 266.0793, found 266.0783.

*Methyl 4-(dimethylamino)benzodithioate (**3j**):* orange solid (908 mg, 86%): mp 151−153 °C; R_f 0.92 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 1413, 1375, 1227, 1309, 1022, 879; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 9.2 Hz, 2H), 6.58 (d, J = 9.2 Hz, 2H), 3.04 (s, 6H), 2.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 224.4, 153.8, 133.5, 129.3, 110.5, 40.1, 19.8; HRMS (ESI) m/z calcd for $C_{10}H_{14}NS_2$ $[M + H]^+$ 212.0568, found 212.0563.

*Methyl 5-(dimethylamino)thiophene-2-carbodithioate (**3l**):* red solid (910 mg, 65%): mp 142−144 °C; R_f 0.87 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 1560, 1474, 1311, 1360, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 4.8 Hz, 1H), 5.96 (d, J = 4.8 Hz, 1H), 3.06 (s, 6H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5, 170.4, 135.7, 131.2, 105.4, 42.0, 18.3; HRMS (ESI) m/z calcd for $C_8H_{12}NS_3$ $[M + H]^+$ 218.0132, found 218.0115.

*Methyl 4-(piperidin-1-yl)benzodithioate (**3n**):* orange solid (944 mg, 71%); mp 149−151 °C; R_f 0.91 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2934, 1594, 1384, 1224, 1029, 811; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 9.2 Hz, 2H), 6.78 (d, J = 9.2 Hz, 2H), 3.36 (d, J = 5.6 Hz, 4H), 2.76 (s, 3H), 1.66 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 224.7, 154.6, 134.6, 129.2, 112.9, 48.6, 25.5, 24.5, 19.9; HRMS (ESI) m/z calcd for $C_{13}H_{18}NS_2$ $[M + H]^+$ 252.0881, found 252.0874.

General Procedure for the Synthesis of 2,4,5-Tri- and 2,3,4,5-Tetrasubstituted/Annulated Thiophenes 7a−t and 9a−m. To a stirring suspension of NaH (60% suspension in mineral oil) (120 mg, 3.0 mmol) in DMF (2 mL) at 0 °C was added dropwise ketone **2** (1.0 mmol) in DMF (2 mL). After further stirring for 10 min, a solution of dithioester **3** (1.0 mmol) in DMF (2 mL) was added to the reaction mixture at 0 °C, followed by further stirring for 1 h at ambient temperature. The reaction mixture was cooled to 0 °C and a solution of halomethylene alkylating agent (**5a−i** or **8**) (1.0 mmol) in DMF (2 mL) was added to the reaction mixture followed by further stirring for 5−6 h at room temperature (monitored by TLC). It was then diluted with satd NH_4Cl solution (25 mL) and extracted with EtOAc (3 × 25 mL), and the combined organic layer was washed with water (3 × 25 mL) and brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/hexane as eluent.

*(5-(4-Methoxyphenyl)-3-phenylthiophene-2-yl)(phenyl)-methanone (**7a**).* Obtained from ketone **2a**, dithioester **3a** and bromo compound **5a**, yellow solid (259 mg, 84%): mp 131−133 °C; R_f 0.3 (1:9 EtOAc/hexane); IR (KBr, cm^{-1}) 3058, 2932, 1610, 1451, 1255, 1186, 827; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.8 Hz, 2H), 7.68 (s, 1H), 7.56−7.53 (m, 2H), 7.40 (tt, J = 7.2 Hz, 1.2 Hz, 1H), 7.29−7.21 (m, 4H), 7.18−7.16 (m, 3H), 7.04 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.8, 160.1, 148.5, 147.9, 137.5, 135.2, 133.8, 132.2, 129.14, 129.07, 127.9, 127.7, 127.5, 126.3, 125.0, 114.7, 55.3; HRMS (ESI) m/z calcd for $C_{24}H_{19}O_2S$ $[M + H]^+$ 371.1106, found 371.1098.

*(5-(4-Methoxyphenyl)-3-(pyren-1-ylthiophene-2-yl)(phenyl)-methanone (**7b**).* Obtained from ketone **2b**, dithioester **3a**, and bromo compound **5a**, yellow solid (156 mg, 77%): mp 189−191 °C; R_f 0.56 (2:8 EtOAc/hexane); IR (neat, cm^{-1}) 1606, 1254, 1174, 847, 749; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19−8.16 (m, 3H), 8.07−7.99 (m, 3H), 7.95 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 6.4 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.8 Hz, 2H), 7.49 (s, 1H), 7.41−7.39 (m, 2H), 7.99 (d, J = 8.8 Hz, 2H), 6.81 (tt, J = 7.2 Hz, 1.2 Hz, 1H), 6.66 (t, J = 8.0 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0, 160.7, 150.0, 147.2, 138.1, 131.6, 131.4, 131.3, 131.0, 129.3, 128.8, 128.2, 127.8, 127.72, 127.65, 127.4, 127.1, 126.2, 125.5, 125.3, 124.9, 124.7, 124.6, 124.3, 114.8, 55.6; HRMS (ESI) m/z calcd for $C_{34}H_{23}O_2S$ $[M + H]^+$ 495.1419, found 495.1406.

*Phenyl(3,5-di(thiophene-2-yl)thiophene-2-yl)methanone (**7c**).* Obtained from ketone **2c**, dithioester **3b**, and bromo compound **5a**, yellow semisolid (190 mg, 68%): R_f 0.6 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 1720, 1622, 1404, 1267, 867; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75−7.72 (m, 2H), 7.43 (tt, J = 7.2 Hz, 1.6 Hz, 1H), 7.35−7.33 (m, 2H), 7.328 (s, 1H), 7.31−7.27 (m, 2H), 7.20 (dd, J = 5.0 Hz, 1.2 Hz, 1H), 7.07 (dd, J = 5.0 Hz, 3.6 Hz, 1H), 7.00 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 6.81 (dd, J = 5.2 Hz, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 142.2, 139.5, 138.1, 136.7, 135.9, 134.6, 132.6, 129.7, 129.0, 128.4, 128.2, 127.4, 127.0, 126.8, 126.6, 125.8; HRMS (ESI) m/z calcd for $C_{19}H_{13}OS_3$ $[M + H]^+$ 353.0129, found 353.0118.

*3,5-Di(furan-2-yl)thiophene-2-carbonitrile (**7d**).* Obtained from ketone **2d**, dithioester **3c**, and bromo compound **5d**, gray solid (175 mg, 80%): mp 181−183 °C; R_f 0.68 (1:9 EtOAc/hexane); IR (KBr, cm^{-1}) 2200, 1532, 1491, 1015, 739; ^1H NMR (400 MHz, DMSO-d_6) δ 7.93 (dd, J = 2.2 Hz, 0.8 Hz, 1H), 7.87−7.86 (m, 2H), 7.86 (dd, J = 3.6 Hz, 0.8 Hz, 1H), 7.16 (dd, J = 4.8 Hz, 0.8 Hz, 1H), 6.73 (dd, J = 3.2 Hz, 2.0 Hz, 1H), 6.71 (dd, J = 3.2 Hz, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.2, 146.5, 144.7, 144.6, 140.3, 139.1, 120.1, 114.4, 112.8, 112.5, 110.9, 109.8, 96.8; HRMS (ESI) m/z calcd for $C_{13}H_8NO_2S$ $[M + H]^+$ 242.0276, found 242.0264.

*(5-(1-Methyl-1H-imidazol-2-yl)-3-(thiazol-2-yl)thiophene-2-yl)(4-nitrophenyl)methanone (**7e**).* Obtained from ketone **2e**, dithioester **3d**, and bromo compound **5c**, yellow solid (235 mg, 80%): mp 152−154 °C; R_f 0.3 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1628, 1516, 1267, 935, 853; ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 9.2 Hz, 2H), 7.94−7.92 (m, 3H), 7.69 (d, J = 3.2 Hz, 1H), 7.35 (d, J = 3.2 Hz, 1H), 7.14 (d, J = 0.8 Hz, 1H), 7.03 (d, J = 0.8 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 187.6, 159.4, 149.3, 143.2, 142.8, 139.4, 138.8, 138.2, 135.5, 130.0, 128.6, 125.8, 125.4, 123.4, 122.6, 34.7; HRMS (ESI) m/z calcd for $C_{18}H_{13}N_4O_3S_2$ $[M + H]^+$ 397.0429, found 397.0425.

*Ethyl 3,5-Bis(1-methyl-1H-indol-3-yl)thiophene-2-carboxylate (**7f**).* Obtained from ketone **2f**, dithioester **3e**, and bromo compound **5d**, off−white solid (180 mg, 75%): mp 193−195 °C;

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R_f 0.38 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 2899, 1698, 1558, 1232, 1088, 738; ^1H NMR (400 MHz, DMSO-d_6) δ 8.07 (s, 1H), 7.95 (d, J = 7.6 Hz,, 1H), 7.84 (s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.58 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.31−7.21 (m, 3H), 7.14 (t, J = 7.6 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.7, 142.8, 142.0, 137.1, 136.3, 131.3, 129.3, 126.5, 124.9, 124.7, 122.2, 121.4, 120.8, 119.7, 119.6, 119.2, 119.1, 110.7, 110.1, 108.8, 108.0, 60.2, 32.8, 32.6, 14.1; HRMS (ESI) m/z calcd for $C_{25}H_{23}N_2O_2S$ $[M + H]^+$ 415.1475, found 415.1473.

*3,5-Di(pyridin-3-yl)thiophene-2-carbonitrile (**7g**).* Obtained from ketone **2g**, dithioester **3f**, and bromo compound **5b**, gray solid (172 mg, 79%): mp 186−188 °C; R_f 0.2 (8:2 EtOAc/hexane); IR (KBr, cm^{-1}) 2205, 1565, 1432, 1032, 797, 697; ^1H NMR (400 MHz, DMSO-d_6) δ 9.08 (dd, J = 2.4 Hz, 0.4 Hz, 1H), 9.04 (dd, J = 2.0 Hz, 0.4 Hz, 1H), 8.71 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.66 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 8.25−8.22 (m, 3H), 7.63 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 1H), 7.56 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.5, 150.3, 148.7, 148.3, 135.1, 133.6, 128.6, 127.6, 126.2, 124.2, 124.0, 114.2, 103.4; HRMS (ESI) m/z calcd for $C_{15}H_{10}N_3S$ $[M + H]^+$ 264.0595, found 264.0584.

*Ethyl 5-(1-Methyl-1H-pyrrol-2-yl)-3-(pyridin-3-yl)thiophene-2-carboxylate (**7h**).* Obtained from ketone **2g**, dithioester **3g**, and bromo compound **5d**, yellow−brown oil (185 mg, 72%): R_f 0.4 (4:6 EtOAc/hexane); IR (neat, cm^{-1}) 1704, 1254, 1073, 708, 616; ^1H NMR (400 MHz, DMSO-d_6) δ 8.71 (d, J = 1.6 Hz, 1H), 8.58 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.94 (dt, J = 8.0 Hz, 1.6 Hz, 1H), 7.45 (ddd, J = 8.0 Hz, 1.0 Hz, 0.4 Hz, 1H), 7.34 (s, 1H), 6.98 (t, J = 2.0 Hz, 1H), 6.54 (dd, J = 3.6 Hz, 2.0 Hz, 1H), 6.10 (dd, J = 3.6 Hz, 2.0 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 149.5, 148.7, 145.0, 139.9, 136.7, 131.1, 127.0, 126.8, 125.2, 123.8, 122.8, 111.3, 108.2, 60.7, 35.5, 13.9; HRMS (ESI) m/z calcd for $C_{17}H_{17}N_2O_2S$ $[M + H]^+$ 313.1011, found 313.0996.

*3-(2-Bromophenyl)-5-p-tolylthiophene-2-carboxamide (**7i**).* Obtained from ketone **2h**, dithioester **3h** and bromo compound **5e**, pale brown solid (129 mg, 69%): mp 189−191 °C; R_f 0.38 (4:6 EtOAc/hexane); IR (neat, cm^{-1}) 3460, 1654, 1597, 1441, 764; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.45−7.42 (m, 2H), 7.35−7.31 (m, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.13 (s, 1H), 5.76 (br s, 1H), 5.32 (br s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 148.3, 142.3, 139.0, 136.8, 133.7, 133.4, 131.2, 130.62, 130.57, 129.9, 128.1, 126.2, 126.1, 123.7, 21.4; HRMS (ESI) m/z calcd for $C_{18}H_{15}BrNOS$ $[M + H]^+$ 372.0058 and 374.0037, found 372.0039 and 374.0029.

*5-(p-Chlorophenyl)-3-(1-ferrocenyl)thiophene-2-carboxamide (**7j**).* Obtained from ketone **2i**, dithioester **3i**, and bromo compound **5e**, brown solid (127 mg, 69%): mp 213-215 °C; R_f 0.4 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3453, 1659, 1600, 1275, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.4 Hz, 2H), 7.45 (s, 1H), 7.41 (d, J = 8.4 Hz, 2H), 5.93 (br s, 2H), 4.59 (t, J = 1.6 Hz, 2H), 4.39 (t, J = 1.6 Hz, 2H), 4.22 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 145.2, 140.9, 134.7, 132.6, 132.1, 129.5, 128.6, 127.4, 81.0, 70.0, 69.9, 69.3; HRMS (ESI) m/z calcd for $C_{21}H_{17}ClFeNOS$ $[M + H]^+$ 422.0069 and 424.0039, found 422.0047 and 424.0024.

*3-(4-Methoxyphenyl)-N-phenyl-5-(thiophene-2-yl)thiophene-2-carboxamide (**7k**).* Obtained from ketone **2j**, dithioester **3b**, and bromo compound **5f**, gray solid (198 mg, 76%): mp 177−179 °C; R_f 0.49 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 3261, 1632, 1519, 1253, 1027, 803; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (br s, 1H), 7.94−7.92 (m, 2H), 7.88−7.85 (m, 2H), 7.53 (dd, J = 8.4 Hz, 7.6 Hz, 2H), 7.48 (dd, J = 8.4 Hz, 7.6 Hz, 1H), 7.38 (tt, J = 7.2 Hz, 1.2 Hz, 1H), 7.31 (tt, J = 7.6 Hz, 1.2 Hz, 1H), 6.86 (dd, J = 2.8 Hz, 1.6 Hz, 1H), 6.56 (dd, J = 3.6 Hz, 1.6 Hz, 1H), 6.27 (dd, J = 3.6 Hz, 2.8 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 159.8, 147.7, 137.7, 136.1, 134.6, 134.2, 129.1, 128.6, 128.1, 127.9, 127.5, 126.4, 125.8, 124.3, 119.6, 114.6, 55.5; HRMS (ESI) m/z calcd for $C_{22}H_{18}NO_2S_2$ $[M + H]^+$ 392.0779, found 392.0770.

*3-(Furan-2-yl)-5-(1-methyl-1H-indol-3-yl)-N-(thiazol-2-yl)-thiophene-2-carboxamide (**7l**).* Obtained from ketone **2d**, dithioester **3e**, and bromo compound **5g**, brown solid (300 mg, 82%): mp 183−185 °C; R_f 0.4 (2:8 EtOAc/hexane); IR (KBr, cm^{-1}) 3335, 2930, 1645, 1549, 1325, 1282, 730; ^1H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H) 8.0 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 1.2 Hz, 1H), 7.45 (d, J = 3.6 Hz, 1H), 7.44 (d, J = 3.6 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.33 (td, J = 7.2 Hz, 1.2 Hz, 1H), 7.27 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 6.99 (d, J = 3.6 Hz, 1H), 6.93 (dd, J = 3.6 Hz, 0.4 Hz, 1H), 6.62 (dd, J = 3.2 Hz, 2.0 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 158.6, 149.0, 144.2, 143.2, 137.8, 137.6, 132.2, 127.9, 126.4, 125.5, 123.6, 123.0, 121.2, 120.1, 113.9, 112.5, 111.5, 110.1, 109.2, 33.3; HRMS (ESI) m/z calcd for $C_{21}H_{16}N_3O_2S_2$ $[M + H]^+$ 406.0684, found 406.0687.

*N-(4-(Trifluoromethyl)benzyl)-5-(4-(dimethylamino)phenyl)-3-(pyridin-3-yl)thiophene-2-carboxamide (**7m**).* Obtained from ketone **2g**, dithioester **3j**, and bromo compound **5h**, off-white solid (278 mg, 70%): mp 170−172 °C; R_f 0.3 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3266, 1630, 1609, 1324, 1107, 751; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (br s, 1H), 8.61 (br s, 1H), 7.77 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.28−7.26 (m, 3H), 7.07 (s, 1H), 6.71 (d, J = 8.8 Hz, 2H), 5.82 (br s, 1H), 4.50 (d, J = 6.0 Hz, 2H), 3.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 151.0, 149.6, 149.5, 148.9, 142.0, 140.4, 136.8, 130.4, 130.1, 128.0, 127.2, 125.81, 121.77, 125.73, 125.70, 125.53, 124.1, 122.8, 120.9, 112.4, 43.6, 40.4 ; HRMS (ESI) m/z calcd for $C_{26}H_{23}F_3N_3OS$ $[M + H]^+$ 482.1514, found 482.1501.

*5-(3,4,5-Trimethoxyphenyl)-3-(thiophene-2-yl)thiophene-2-carbaldehyde (**7n**).* Obtained from ketone **2c**, dithioester **3k**, and bromo compound **5i**, yellow−brown oil (228 mg, 80%): R_f 0.6 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 3100, 2933, 1632, 1579, 1500, 1121, 709; ^1H NMR (400 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.93 (s, 1H), 7.81 (d, J = 4.4 Hz, 1H), 7.67 (d, J = 2.4 Hz,), 7.25 (dd, J = 4.8 Hz, 3.6 Hz, 1H), 7.11 (s, 2H), 3.88 (s, 6H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.9, 153.4, 151.8, 143.0, 139.0, 135.3, 134.5, 129.7, 128.9, 128.3, 127.6, 126.8, 103.9, 60.1, 56.2; HRMS (ESI) m/z calcd for $C_{18}H_{17}O_4S_2$ $[M + H]^+$ 361.0568, found 361.0563.

*N,N-Dimethyl-5-(5-(4-nitrophenyl)-4-(pyridin-4-yl)thiophene-2-yl)thiophene-2-amine (**7o**).* Obtained from ketone **2k**, dithioester **3l**, and bromo compound **5j**, reddish-brown solid (289 mg, 86%): mp 153−155 °C; R_f 0.38 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1586, 1503, 1419, 1328, 850, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.10 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H), 7.19 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 6.98 (d, J = 4.0 Hz, 1H), 6.96 (s, 1H), 5.80 (d, J = 4.0 Hz, 1H), 2.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 150.4, 146.7, 143.9, 140.9, 140.3, 138.1, 133.1, 129.3, 125.5 124.1 123.7, 123.5, 119.5, 102.7, 42.7; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O_2S_2$ $[M + H]^+$ 408.0840, found 408.0834.

*3,4-Diphenyl-5-(thiophene-2-yl)thiophene-2-carboxamide (**7p**).* Obtained from ketone **2l**, dithioester **3b**, and bromo compound **5e**, pale brown solid (136 mg, 74%): mp 132−134 °C; R_f 0.37 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 3458, 1648, 1399, 757, 693; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30−7.28 (m, 3H), 7.20−7.18 (m, 5H), 7.15 (dd, J = 4.0 Hz, 0.8 Hz, 1H), 7.05−7.03 (m, 3H), 6.90 (dd, J = 4.8 Hz, 0.4 Hz, 1H), 5.34 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 143.1, 139.6, 134.9, 134.72, 134.70, 134.4, 132.8, 130.5, 129.7, 128.2, 128.1, 127.9, 127.8, 127.6, 127.3, 126.8; HRMS (ESI) m/z calcd for $C_{21}H_{16}NOS_2$ $[M + H]^+$ 362.0673, found 362.0659.

*(4,5-Dihydro-3-(4-methoxyphenyl)naphtho[2,1-c]thiophene-1-yl)(phenyl)methanone (**7q**).* Obtained from ketone **2m**, dithioester **3a** ,and bromo compound **5a**, yellow solid (230 mg, 85%): mp 129−131 °C; R_f 0.48 (2:8 EtOAc/hexane); IR (neat, cm^{-1}) 1603, 1413, 1286, 1031, 833, 747; ^1H NMR (400 MHz, DMSO-d_6) δ 7.76 (dd, J = 8.0 Hz, 1.6 Hz, 2H), 7.57−7.53 (m, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.40 (t, J = 8.0 Hz, 2H), 7.31 (d, J = 6.8 Hz, 1H), 7.15 (td, J = 5.4 Hz, 1.2 Hz, 1H), 7.13 (dd, J = 8.0 Hz, 0.8 Hz, 1H), 7.08 (d, J = 8.8 Hz, 2H), 6.90 (td, J = 7.6 Hz, 1.2 Hz, 1H), 3.82 (s, 3H), 2.85 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1, 159.6, 141.2, 140.8, 137.8, 137.5, 136.4, 133.1, 130.9, 130.0, 129.5, 128.7, 128.5, 128.1, 127.9, 125.8, 124.7, 114.5, 55.3, 29.7, 24.5; HRMS (ESI) m/z calcd for $C_{26}H_{21}O_2S$ $[M + H]^+$ 397.1262, found 397.1255.

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*[2,3-a,6,7-a′]Dibenzo-(5-(3,4,5-trimethoxyphenyl)-3-cyano)-thieno[3,4-d]thiepane (**7r**).* Obtained from ketone **2n**, dithioester **3k**, and bromo compound **5b**, yellow semisolid (145 mg, 72%): R_f 0.36 (2:8 EtOAc/hexane); IR (neat, cm^{-1}) 2854, 2209, 1662, 1457, 1274, 1104, 749; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.2 Hz, 1.6 Hz, 1H), 7.71 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 7.68 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.55 (td, J = 7.2 Hz, 1.6 Hz, 1H), 7.44 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.37 (td, J = 7.6 Hz, 1.6 Hz, 1H), 7.22 (td, J = 7.2 Hz, 1.6 Hz, 1H), 7.06 (td, J = 7.2 Hz, 1.6 Hz, 1H), 6.42 (s, 2H), 3.86 (s, 3H), 3.65 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 151.3, 146.8, 139.0, 137.8, 137.3, 137.2, 136.9, 136.0, 133.5, 133.3, 132.5, 130.9, 130.1, 129.3, 128.8, 128.5, 127.8, 126.0, 125.3, 107.2, 61.1, 56.2; HRMS (ESI) m/z calcd for $C_{26}H_{20}NO_3S_2$ $[M + H]^+$ 458.0885, found 458.0864.

*Ethyl 1-(4-Fluorophenyl)-8-oxo-8H-indeno[2,1-c]thiophene-3-carboxylate (**7s**).* Obtained from ketone **2o**, dithioester **3m**, and bromo compound **5d**, yellow–brown oil (169 mg, 70%): R_f 0.72 (2:8 EtOAc/hexane); IR (neat, cm^{-1}) 1698, 1667, 1448, 1353, 1077, 1005, 729; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.0 Hz, 1H), 7.75 (dd, J = 8.0 Hz, 2.8 Hz, 1H), 7.37–7.34 (m, 2H), 7.29–7.27 (m, 1H), 7.18–7.14 (m, 2H), 4.17 (q, J = 7.2 Hz, 2H), 1.16 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 177.6, 167.4, 145.2, 142.6, 137.3, 133.4, 132.4, 129.0, 128.9, 128.7, 128.5, 128.0, 127.8, 127.3, 126.9, 125.4, 124.8, 122.5, 109.8, 62.4, 14.1; HRMS (ESI) m/z calcd for $C_{20}H_{14}FO_3S$ $[M + H]^+$ 353.0648, found 353.0643.

*(5-(4-Methoxyphenyl)-3-methylthiophene-2-yl)(phenyl)-methanone (**7t**).* Obtained from ketone **2p**, dithioester **3a**, and bromo compound **5a** with NaO^{t}Bu (288 mg, 3.0 mmol) as base, off-white solid (106 mg, 68%): mp 118–120 °C; R_f 0.86 (1:9 EtOAc/hexane); IR (neat, cm^{-1}) 2923, 1734, 1622, 1414, 1251, 1036, 717; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85–7.82 (m, 2H), 7.58–7.54 (m, 3H), 7.49–7.45 (m, 2H), 7.13 (s, 1H), 6.91 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 160.5, 149.9, 147.5, 140.5, 133.2, 132.0, 129.0, 128.4, 127.6, 127.5, 126.1, 114.6, 55.5, 17.2; HRMS (ESI) m/z calcd for $C_{19}H_{17}O_2S$ $[M + H]^+$ 309.0949, found 309.0945.

*(E)-Methyl 3-(3,5-Bis(4-(dimethylamino)phenyl)thiophene-2-yl)-acrylate (**9a**).* Obtained from ketone **2q**, dithioester **3j**, and bromocrotonate **8**, yellow solid (184 mg, 74%): mp 172–174 °C; R_f 0.49 (2:8 EtOAc/hexane); IR (neat, cm^{-1}) 1708, 1600, 1508, 1261, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 15.6 Hz, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.16 (s, 1H), 6.80 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.8 Hz, 2H), 6.17 (d, J = 15.6 Hz, 1H), 3.76 (s, 3H), 3.02 (s, 6H), 3.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 150.7, 150.3, 148.1, 146.6, 137.9, 130.2, 130.0, 127.1, 123.9, 123.8, 121.9, 114.3, 112.5, 112.4, 51.6, 40.6, 40.4; HRMS (ESI) m/z calcd for $C_{24}H_{27}N_2O_2S$ $[M + H]^+$ 407.1793, found 407.1795.

*(E)-Methyl 3-(5-(4-(Piperidin-1-yl)phenyl)-3-(pyridin-2-yl)-thiophene-2-yl)acrylate (**9b**).* Obtained from ketone **2r**, dithioester **3j**, and bromocrotonate **8**, yellow solid (280 mg, 84%): mp 180–182 °C; R_f 0.2 (8:2 EtOAc/hexane); IR (neat, cm^{-1}) 2989, 1703, 1601, 1275, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (ddd, J = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 8.22 (d, J = 15.6 Hz, 1H), 7.78 (td, J = 8.0 Hz, 2.0 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.50 (dt, J = 8.0 Hz, 0.8 Hz, 1H), 7.43 (s, 1H), 7.28 (td, J = 2.8 Hz, 1.2 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.28 (d, J = 15.6 Hz, 1H), 3.77 (s, 3H), 3.25 (t, J = 5.6 Hz, 4H), 1.74–1.69 (m, 4H), 1.64–1.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 154.0, 152.1, 150.0, 146.5, 144.9, 137.4, 136.8, 134.0, 127.1, 123.9, 123.8, 123.6, 122.5, 116.6, 1115.9, 51.7, 49.9, 25.7, 24.4; HRMS (ESI) m/z calcd for $C_{24}H_{25}N_2O_2S$ $[M + H]^+$ 405.1637, found 405.1630.

*(E)-Methyl 3-(5-(4-(Dimethylamino)phenyl)-3-(pyridin-3-yl)-thiophene-2-yl)acrylate (**9c**).* Obtained from ketone **2g**, dithioester **3j**, and bromocrotonate **8**, orange solid (240 mg, 81%): mp 184–186 °C; R_f 0.51 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1711, 1605, 1430, 1276, 1167, 800; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 1.6 Hz, 1H), 8.64 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.74–7.72 (m, 1H), 7.69 (d, J = 15.6 Hz, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.40 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 7.16 (s, 1H), 6.72 (d, J = 8.8 Hz, 2H), 6.24 (d, J = 15.6 Hz, 1H), 3.75 (s, 3H), 3.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 150.8, 149.7, 149.0, 147.7, 143.1, 136.4, 135.9, 132.2, 131.5, 127.1, 123.5, 123.2, 121.0, 116.3, 112.3, 51.7, 40.3; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_2O_2S$ $[M + H]^+$ 365.1324, found 365.1327.

*(E)-Methyl 3-(5-(4-(Dimethylamino)phenyl)-3-(pyridin-4-yl)-thiophene-2-yl)acrylate (**9d**).* Obtained from ketone **2g**, dithioester **3j**, and bromocrotonate **8**, orange solid (225 mg, 75%): mp 182–184 °C; R_f 0.46 (6:4 EtOAc/hexane); IR (neat, cm^{-1}) 1702, 1603, 1276, 1165, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 5.2 Hz, 2H), 7.74 (d, J = 15.2 Hz, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 6.0 Hz, 2H), 7.16 (s, 1H), 6.71 (d, J = 8.8 Hz, 2H), 6.25 (d, J = 15.2 Hz, 1H), 3.76 (s, 3H), 3.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 150.9, 150.3, 147.9, 143.9, 143.3, 135.8, 132.7, 127.2, 123.9, 122.9, 121.0, 116.7, 112.4, 51.8, 40.4; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_2O_2S$ $[M + H]^+$ 365.1324, found 365.1309.

*(E)-Methyl 3-(5-(4-(Dimethylamino)phenyl)-3-(pyridin-4-yl)-thiophene-2-yl)acrylate (**9e**).* Obtained from ketone **2k**, dithioester **3l** and bromocrotonate **8**, maroon red solid (230 mg, 76%): mp 189–191 °C; R_f 0.38 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1707, 1606, 1352, 1034, 794; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 15.2 Hz, 1H), 7.31 (dd, J = 4.8 Hz, 1.2 Hz, 2H), 7.02 (d, J = 4.0 Hz, 1H), 6.89 (s, 1H), 7.16 (d, J = 15.2 Hz, 1H), 5.80 (d, J = 4.0 Hz, 1H), 3.75 (s, 3H), 2.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 160.4, 150.2, 143.7, 143.2, 141.6, 135.6, 131.4, 126.5, 123.9, 122.1, 119.7, 116.3, 102.8, 51.8, 42.6; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_2O_2S_2$ $[M + H]^+$ 371.0888, found 371.0884.

*(E)-Methyl 3-(5-(5-(Dimethylamino)thiophene-2-yl)-3-(thiazol-2-yl)thiophene-2-yl)acrylate (**9f**).* Obtained from ketone **2e**, dithioester **3l** and bromocrotonate **8**, brown solid (230 mg, 79%): mp 175–177 °C; R_f 0.25 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1708, 1603, 1510, 1409, 1161, 729; ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 15.6 Hz, 1H), 7.91 (d, J = 3.6 Hz, 1H), 7.38 (d, J = 3.2 Hz, 1H), 7.16 (s, 1H), 7.01 (d, J = 4.0 Hz, 1H), 6.21 (d, J = 15.6 Hz, 1H), 5.80 (d, J = 4.0 Hz, 1H), 3.79 (s, 3H), 2.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 162.0, 160.4, 144.1, 141.0, 136.9, 136.4, 132.6, 126.5, 121.7, 119.6, 119.3, 117.1, 102.8, 51.8, 42.7; HRMS (ESI) m/z calcd for $C_{17}H_{17}N_2O_2S_3$ $[M + H]^+$ 377.0452, found 377.0444.

*(E)-Methyl 3-(3-(4-(Dimethylamino)phenyl)-5-(1-methyl-1H-imidazol-2-yl)thiophene-2-yl)acrylate (**9g**).* Obtained from ketone **2q**, dithioester **3g** ,and bromocrotonate **8**, yellow solid (173 mg, 77%): mp 167–169 °C; R_f 0.34 (6:4 EtOAc/hexane); IR (neat, cm^{-1}) 2987, 1719, 1598, 1274, 1168, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 15.6 Hz, 1H), 7.31–7.28 (m, 3H), 7.10 (s, 1H), 6.94 (s, 1H), 6.78 (d, J = 7.2 Hz, 2H), 6.25 (d, J = 15.6 Hz, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 150.4, 147.0, 141.7, 137.1, 133.7, 132.9, 130.2, 129.2, 128.0, 123.4, 122.9, 116.6, 112.5, 51.7, 40.5, 35.0; HRMS (ESI) m/z calcd for $C_{20}H_{22}N_3O_2S$ $[M + H]^+$ 368.1433, found 368.1420.

*(E)-Methyl 3-(5-(4-(Piperidin-1-yl)phenyl)-3-(pyridin-4-yl)-4-(thiophene-2-yl)thiophene-2-yl)acrylate (**9h**).* Obtained from ketone **2s**, dithioester **3n**, and bromocrotonate **8**, yellow solid (177 mg, 74%): mp 174–176 °C; R_f 0.52 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1698, 1601, 1358, 1076, 1022, 814; ^1H NMR (400 MHz, DMSO-d_6) δ 8.44 (br d, J = 4.0 Hz, 1H), 8.22 (br s, 1H), 7.60 (d, J = 15.6 Hz, 1H), 7.60 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.47 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.28 (ddd, J = 8.0 Hz, 5.0 Hz, 0.8 Hz, 1H), 7.07 (dd, J = 5.2 Hz, 3.2 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.96 (dd, J = 3.2 Hz, 1.2 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 6.33 (d, J = 15.6 Hz, 1H), 3.68 (s, 3H), 3.17 (d, J = 5.2 Hz, 4H), 1.53 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.2, 151.0, 150.4, 148.4, 143.4, 139.1, 137.8, 135.3, 134.6, 134.0, 133.5, 131.3, 129.8, 129.6, 128.4, 127.2, 123.2, 120.9, 116.5, 114.6, 51.5, 48.2, 24.9, 23.8; HRMS (ESI) m/z calcd for $C_{28}H_{27}N_2O_2S_2$ $[M + H]^+$ 487.1514, found 487.1512.

*(E)-Methyl 3-(5-(4-(Dimethylamino)phenyl)-3,4-di(thiophene-2-yl)thiophene-2-yl)acrylate (**9i**).* Obtained from ketone **2t**, dithioester **3j**, and bromocrotonate **8**, orange solid (171 mg, 79%): mp 186–188 °C; R_f 0.28 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1699, 1603, 1410, 1261, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 15.6 Hz, 1H), 7.32 (dd, J = 5.2 Hz, 1.6 Hz, 1H), 7.24 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.19 (d, J = 8.8 Hz, 2H), 7.01 (dd, J = 5.2 Hz, 3.6 Hz, 1H),

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6.92−6.90 (m, 2H), 6.75 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 6.58 (d, J = 8.8 Hz, 2H), 6.27 (d, J = 15.6 Hz, 1H), 3.76 (s, 3H), 2.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 150.4, 144.9, 140.0, 136.9, 136.7, 135.4, 133.9, 130.4, 129.9, 129.5, 129.0, 127.4, 126.94, 126.86, 126.7, 120.9, 116.4, 111.9, 51.8, 40.3; HRMS (ESI) m/z calcd for $C_{24}H_{22}NO_2S_3$ $[M + H]^+$ 452.0813, found 452.0794.

*(E)-Methyl 3-(5-(5-(Dimethylamino)thiophene-2-yl)-4-(pyridin-3-yl)-3-(thiophene-2-yl)thiophene-2-yl)acrylate (**9j**).* Obtained from ketone **2u**, dithioester **3l**, and bromocrotonate **8**, dark red solid (171 mg, 77%): mp 177−179 °C; R_f 0.42 (4:6 EtOAc/hexane); IR (neat, cm^{-1}) 1697, 1347, 1022, 795; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.51 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.38 (dd, J = 2.0 HZ, 0.4 Hz, 1H), 7.62 (dt, J = 8.0 Hz, 2.0 Hz, 1H), 7.57 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 7.37 (ddd, J = 8.0 Hz, 4.8 Hz, 0.8 Hz, 1H), 7.26 (d, J = 15.6 Hz, 1H), 7.05−7.03 (m, 2H), 6.91 (d, J = 4.0 Hz, 1H), 6.17 (d, J = 15.6 Hz, 1H), 5.84 (d, J = 4.0 Hz, 1H), 3.64 (s, 3H), 2.83 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.2, 161.2, 149.7, 149.0, 144.4, 139.7, 137.2, 134.9, 134.3, 130.5, 129.9, 129.5, 128.8, 128.5, 127.4, 127.1, 123.1, 116.8, 115.4, 102.2, 51.4, 41.8; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_2O_2S_3$ $[M + H]^+$ 453.0765, found 453.0760.

*(E)-Methyl 3-(5-(5-(Dimethylamino)thiophene-2-yl)-3-(4-(trifluoromethyl)phenyl)-4-(pyridin-3-yl)thiophene-2-yl)acrylate (**9k**).* Obtained from ketone **2v**, dithioester **3l**, and bromocrotonate **8**, brick red solid (153 mg, 79%): mp 192−194 °C; R_f 0.26 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1700, 1509, 1412, 1128, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, J = 4.8 Hz, 1.6 Hz, 1H), 8.38 (d, J = 1.6 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 15.6 Hz, 1H), 7.37 (dt, J = 8.0 Hz, 1.6 Hz, 1H), 7.19 (dd, J = 8.0 Hz, 4.8 Hz, 1H), 7.14 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 4.0 Hz, 1H), 6.21 (d, J = 15.6 Hz, 1H), 5.67 (d, J = 4.0 Hz, 1H), 3.74 (s, 3H), 2.85 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 161.2, 151.5, 148.8, 145.6, 138.8, 138.7, 138.1, 135.9, 132.1, 132.0, 131.7, 130.8, 130.3, 129.9, 128.7, 125.5, 125.41, 125.37, 125.3, 123.5, 118.2, 116.5, 102.2, 51.8, 42.5; HRMS (ESI) m/z calcd for $C_{26}H_{22}F_3N_2O_2S_2$ $[M + H]^+$ 515.1075, found 515.1074.

*(E)-Methyl 3-(5-(5-(Dimethylamino)thiophene-2-yl)-3,4-di(thiophene-2-yl)thiophene-2-yl)acrylate (**9l**).* Obtained from ketone **2t**, dithioester **3l**, and bromocrotonate **8**, red solid (187 mg, 85%): mp 180−182 °C; R_f 0.42 (1:1 EtOAc/hexane); IR (neat, cm^{-1}) 1695, 1494, 1408, 1263, 1034, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 15.6 Hz, 1H), 7.36 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.28 (dd, J = 5.2 Hz, 1.2 Hz, 1H), 7.01 (dd, J = 4.8 Hz, 3.2 Hz, 1H), 6.97 (dd, J = 5.2 Hz, 1.6 Hz, 1H), 6.95 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 6.90 (dd, J = 3.6 Hz, 1.2 Hz, 1H), 6.85 (d, J = 4.4 Hz, 1H), 6.19 (d, J = 15.6 Hz, 1H), 5.70 (d, J = 4.0 Hz, 1H), 3.75 (s, 3H), 2.87 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 161.3, 140.5, 139.8, 136.7, 135.8, 135.2, 131.3, 130.3, 129.4, 128.3, 127.9, 127.7, 127.4, 127.2, 126.8, 119.0, 115.7, 102.1, 51.7, 42.4; HRMS (ESI) m/z calcd for $C_{22}H_{20}NO_2S_4$ $[M + H]^+$ 458.0377, found 458.0353.

*(E)-Methyl 3-(7-(4-(Piperidin-1-yl)phenyl)acenaphtho[1,2-c]thiophene-9-yl)acrylate (**9m**).* Obtained from ketone **2w**, dithioester **3n**, and bromocrotonate **8**, orange solid (210 mg, 78%): mp 169−171 °C; R_f 0.75 (3:7 EtOAc/hexane); IR (neat, cm^{-1}) 1706, 1351, 1077, 818, 773; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 15.6 Hz, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.88 (d, J = 6.8 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.73−7.69 (m, 3H), 7.60 (dd, J = 8.0 Hz, 7.2 Hz, 1H), 7.47 (dd, J = 8.0 Hz, 7.8 Hz, 1H), 7.03 (d, J = 8.8 Hz, 2H), 6.27 (d, J = 15.6 Hz, 1H), 3.85 (s, 3H), 3.32 (t, J = 5.6 Hz, 4H), 1.77−1.72 (m, 4H), 1.67−1.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 152.3, 147.8, 140.1, 138.8, 135.6, 132.9, 132.6, 131.3, 129.3, 129.0, 128.3, 127.9, 127.8, 126.7, 125.8, 123.2, 121.2, 119.7, 116.6, 115.7, 51.9, 49.8, 25.8, 24.5; HRMS (ESI) m/z calcd for $C_{29}H_{26}NO_2S$ $[M + H]^+$ 452.1684, found 452.1664.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra for compounds **2s,u−v**, **3j,l,m**, **7a−t**, and **9a−m**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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