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# (3+2) Cycloadditions of Thiouronium Ylides: A Room-Temperature, One-Pot Approach to Dihydrothiophenes

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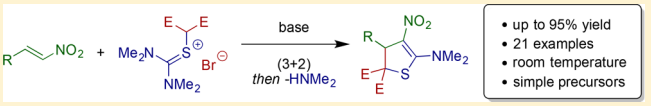
Supporting Information

**ABSTRACT:** A room-temperature (3+2) cycloaddition sequence for the synthesis of highly substituted dihydrothiophene derivatives has been developed. By utilizing structurally unique thiocarbonyl ylides, the reactivity of these traditionally high-energy intermediates can be modulated, enabling a synthetically useful transformation to proceed under mild conditions.

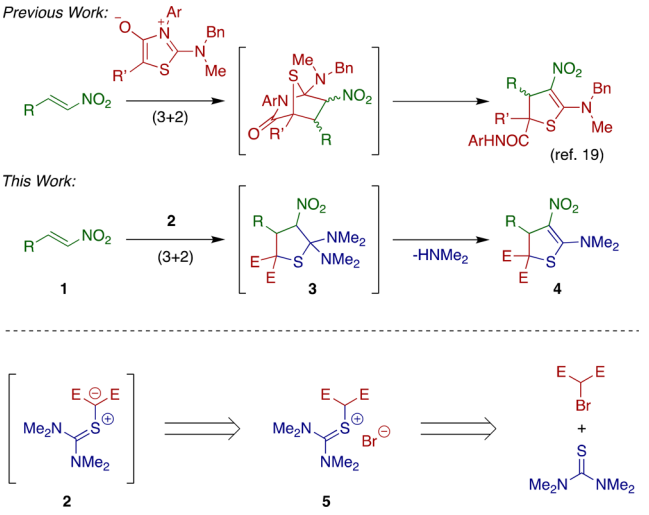



Among the structurally broad family of sufur ylides, doubly stabilized sulfonium ylides have recently attracted considerable attention in synthesis.[1] Given our group's long-standing interest in these compounds following our original report on the concept of ylide transfer,[1c] we were keen to investigate the applications of highly stabilized ylides bearing alternative chemical structures. Thiocarbonyl ylides, formally 1,3-dipoles, represent a conceptually distinct class of sulfonium ylides, with unique reactivity.[2] Reactions involving thiocarbonyl ylides include electrocyclizations,[3] dimerization-type reactions,[4] 1,3 acid−base addition reactions,[5] rearrangements,[6] and cycloadditions.[4a,7] A number of these transformations have been developed to the stage where they have found use as key steps in the syntheses of a number of natural products.[4c,7a,8] However, the high reactivity and instability of these compounds place some limitations on their synthetic utility, and reactions employing thiocarbonyl ylides often have to be very carefully designed.[9] The synthesis of these ylides, almost always undertaken *in situ* for onward reactions, often requires either very high temperatures or cryogenic cooling.[7b,8c,10] One of the most common routes involves the use of alkyl azides, which restricts the scale on which these reactions can safely be undertaken. Although stabilization of the 1,3-dipole by addition of electron-withdrawing and electron-donating groups is possible,[11] the design of thiocarbonyl ylides with enhanced stability and lifetimes would enable the development of novel transformations.

Heterocycles have long been considered privileged templates in the search for biologically active molecules. A number of 4,5-dihydrothiophenes, in particular 2-amino-4,5-dihydrothiophenes, have been investigated for a range of biological effects,[12] including anti-inflammatory,[13] cytotoxic,[12,14] and antimicrobial[15] activity. The presence of a reactive sulfur center, in addition to the double bond, means that these structures can be employed as synthetic intermediates. Examples include desulfurization with Raney nickel to generate acyclic compounds[16] and, in the case of 2-amino-4,5-dihydrothiophenes, further condensation reactions to afford dihydrothiophene-fused nitrogen heterocycles.[16b,17] A number of syntheses of 4,5-dihydrothiophenes have been developed, mostly relying on classical condensation chemistry.[17b,18] Such routes often require high temperatures, and/or reagents that limit functional group compatibility. The application of [3+2] cycloadditions to the synthesis of dihydrothiophenes has hitherto restricted to the use of isothiomünchnones as 1,3-dipoles.[19]

Herein, we report a general and mild synthesis of highly substituted 2-amino-4,5-dihydrothiophenes (**3**) via a formal (3+2) cycloaddition reaction of nitroalkenes (**1**) and "push−pull" stabilized thiocarbonyl ylides (**2**) (Scheme 1). These reactive 1,3-dipoles are formed *in situ* by the deprotonation of thiouronium salts (**5**), which are easily accessed through the combination of tetramethylthiourea and the appropriate alkyl bromide.

**Scheme 1. Synthesis of 2-Amino-4,5-dihydrothiophenes via a Formal (3+2) Reaction between Nitroolefins and *in Situ*-Formed Thiocarbonyl Ylides**

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Investigations began with the combination of malonate-derived thiouronium salt **5a** as the thiocarbonyl ylide precursor, and various dipolarophiles. It soon emerged that Michael acceptors were most effective in enabling a formal cycloaddition. Reactions with acrylonitrile, methyl vinyl ketone, and ethyl propriolate all gave the (3+2) cycloaddition product, albeit in low yields. When 2.0 equiv of nitrostyrene (**1a**) was employed as the coupling partner, it was possible to isolate dihydrothiophene **3a** in 75% yield (Table 1, entry 1). By

**Table 1. Optimization of the Dihydrothiophene Synthesis**[a]


| entry | base | solvent | yield (%)[b] | consumption of **1a** (%)[b] |
|---|---|---|---|---|
| 1 | $Et_3N$ | $CH_2Cl_2$ | (75)[c] | n/a |
| 2 | $Et_3N$ | $CH_2Cl_2$ | 95 (92) | >99 |
| 3 | $Li_2CO_3$ | $CH_2Cl_2$ | <5 | >99 |
| 4 | DBU | $CH_2Cl_2$ | 55 | >99 |
| 5 | *t*-BuOK | $CH_2Cl_2$ | 20 | 43 |
| 6 | pyridine | $CH_2Cl_2$ | 73 | 79 |
| 7 | $Et_3N$ | MeCN | 87 | >99 |
| 8 | $Et_3N$ | DMSO | 60 | >99 |
| 9 | $Et_3N$ | THF | 68 | >99 |
| 10 | $Et_3N$ | MeOH | 92 | >99 |
| 11 | $Et_3N$ | toluene | 88 | >99 |

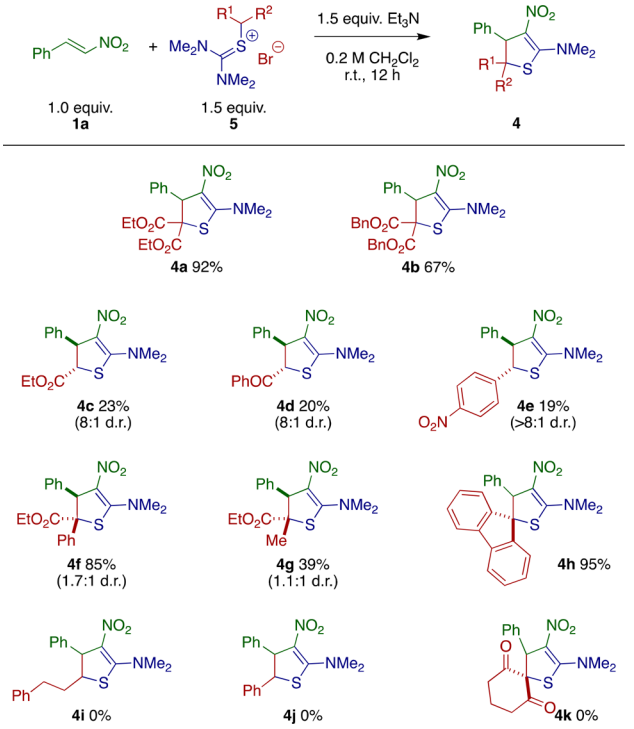
[a]Reaction conditions: **1a** (0.2 mmol), **5a** (0.3 mmol), base (0.3 mmol), solvent (1.0 mL), rt, 12 h. [b]NMR yields using mesitylene as an internal standard, unless inside parentheses. [c]Reaction performed using **5a** (1.0 equiv), $Et_3N$ (1.0 equiv), and **1a** (2.0 equiv).

reversing the stoichiometry, we were able to increase this yield to 92% (entry 2). Beyond this, a screen of both the base (entries 3–6) and the solvent (entries 7–11) offered no improvement on the initial $NEt_3$/dichloromethane combination. This combination also made the purification extremely straightforward, as no workup is required. Compared to those of previously reported (3+2) cycloadditions, it is notable that the conditions are extremely mild, proceeding at room temperature with only the addition of a weak base.

With optimized conditions in hand, we moved on to determine the range of stabilized thiocarbonyl ylides that could be employed in the transformation (Scheme 2). Thiouronium salts (**5**) were prepared via a simple nucleophilic substitution between tetramethylthiourea and the respective alkyl bromide in quantitative yields. Both of the malonate-derived substrates reacted successfully in satisfactory to excellent yields (**4a** and **4b**). When one electron-withdrawing group was removed, the yield dropped dramatically to 23% (**4c**); however, the diastereocontrol was relatively high. Performing the reaction at higher or lower temperatures let to no product formation at all. This reduction in the stability of the thiocarbonyl intermediate has been investigated previously (in the absence of any coupling partner) by the group of Nozaki, and a number of decomposition pathways have been identified.[9]

Exchange of the ester group for either a ketone (**4d**) or a *p*-nitrophenyl group afforded similar results (**4e**). The relative stereochemistry of **4d** (and by analogy those of **4c** and **4e**–**4g**) was assigned using X-ray crystallographic analysis (Figure 1). By further substitution of the ylide with either a phenyl (**4f**) or

**Scheme 2. Substrate Scope of the Ylide Component**[a]




[a]Reaction conditions: **1a** (0.2 mmol), **5** (0.3 mmol), $Et_3N$ (0.3 mmol), dichloromethane (1.0 mL), rt, 12 h.

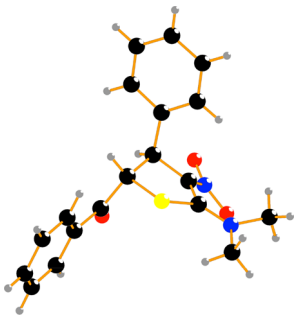


**Figure 1.** X-ray diffraction structure of dihydrothiophene **4d**, showing *trans* relative stereochemistry.

methyl (**4g**) group, the yield could be increased, at the expense of the diastereomeric ratio. Use of a fluorenyl thiocarbonyl ylide afforded product **4h** in an excellent 95% yield. As expected, reducing the level of stabilization even further, with only alkyl or electron-neutral aryl groups, resulted in no product formation, even when stronger bases were employed. An interesting exception to the developing trend was the attempted use of a dimedone-derived ylide (see **4k**). In this instance, the deprotonation was extremely fast and irreversible. However, the ylide is so stabilized that it is completely inert under the reaction conditions, and $^1H$ NMR experiments showed no decomposition of the ylide over multiple days, unlike ylide **2a**, which decomposed slowly over 24 h.

Exploration of the nitroolefin scope showed that a broad range of substrates could be employed (Scheme 3). Both electron-rich (examples **4l**–**4p**) and electron-poor (**4q**–**4u**) aryl groups were well tolerated. Included in this scope were halide moieties that could be used for further functionalization (**4q**–**4t**). Examples **4n** and **4p** showed that steric bulk in the



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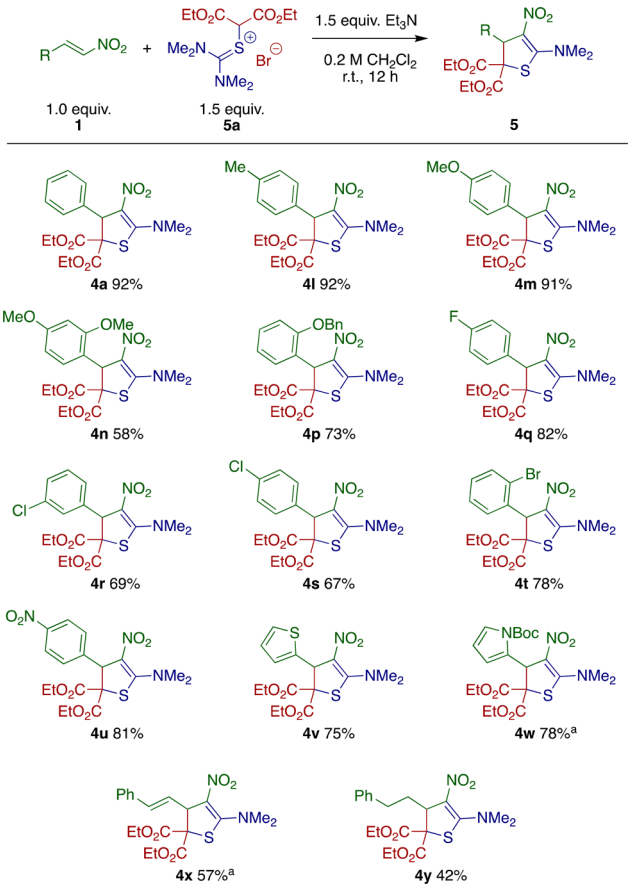
**Scheme 3. Substrate Scope of the Nitroolefin Component**[b]



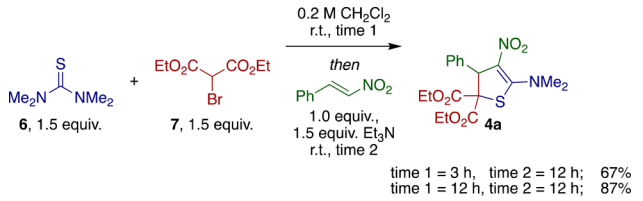

[a]Dropwise addition of the thiouronium salt. [b]Reaction conditions: **1** (0.2 mmol), **5a** (0.3 mmol), $Et_3N$ (0.3 mmol), dichloromethane (1.0 mL), rt, 12 h.

*ortho* position could be tolerated with only a small decrease in the yield. Heterocyclic nitroolefins could also be employed, though in the case of the *N*-Boc-pyrrole substrate, the reaction was found to be improved by a dropwise addition of the thiouronium salt to the reaction mixture. This modified procedure was also found to be useful in boosting the yield of alkenyl example **4x**. When alkyl nitroolefins were employed, the yields were significantly reduced, which $^1$H NMR experiments suggest is due to decomposition/oligomerization of the nitroolefin under the action of triethylamine.[20]

As the *in situ* formation of **5a** from tetramethylthiourea (**6**) and diethyl bromomalonate (**7**) proceeded smoothly at room temperature in dichloromethane, we were interested in probing whether a one-pot, two-step procedure could be developed. In the event, mixing tetramethylthiourea **6** and bromomalonate **7** for 12 h in dichloromethane (Scheme 4) followed by addition of trimethylamine and nitrostyrene afforded an 87% yield of cycloadduct **4a**. Ancillary experiments with shorter reaction times provided less satisfying results (Scheme 4).

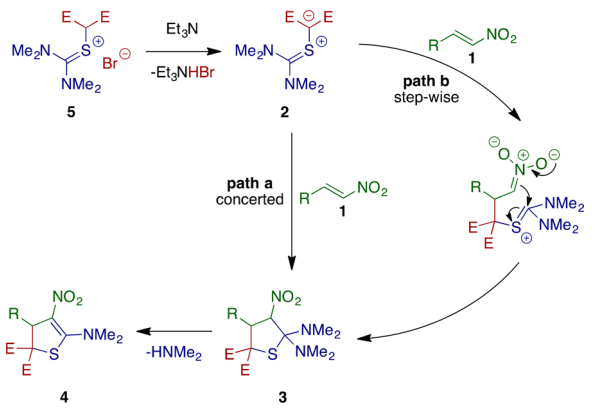
Scheme 5 details our proposed mechanism. $^1$H NMR studies have demonstrated that, for thiouronium salt **5a**, the initial deprotonation step is fast and irreversible, forming thiocarbonyl ylide **2a**, which is reasonably stable in solution for a number of hours.[21] In the presence of a nitroolefin (**1**), this intermediate (**2**) undergoes a (3+2) cycloaddition, either in a concerted, pericyclic manner (path a) or through a two-step process comprising both Michael addition and 5-endotrig cyclization

**Scheme 4. One-Pot, Two-Step Procedure**[a]




[a]Reaction conditions: tetramethylthiourea (0.3 mmol), diethyl bromomalonate (0.3 mmol), dichloromethane (1.0 mL), rt, time 1; then **1a** (0.2 mmol), $Et_3N$ (0.3 mmol), rt, time 2.

**Scheme 5. Proposed mechanism**




steps (path b). The elimination of dimethylamine from intermediate **3** to afford dihydrothiophene **4** is entropically favorable, and we believe that it provides the driving force for the overall process.[22]

In conclusion, we have developed a mild thiocarbonyl-ylide-based (3+2) cycloaddition process for the synthesis of 2-amino-4,5-dihydrothiophenes. A range of nitroolefins can be combined with highly stabilized, push−pull 1,3-dipoles at room temperature in good to excellent yields. The reaction is finely tuned according to the stabilization of the thiocarbonyl ylide, with reduced yields for less stabilized examples and a complete shutdown of reactivity if the ylide is "overstabilized". We hope that the synthetic ease of this process can encourage further investigations into what has been traditionally regarded as a field involving high-energy, sensitive intermediates and harsh reaction conditions.

## EXPERIMENTAL SECTION

All reactions were performed using oven-dried glassware and an anhydrous solvent. Chromatography was performed on silica gel (230−400 mesh, Merck and Co.) with the indicated eluents. Thin-layer chromatography was performed on silica plates. Compounds were visualized by ultraviolet (254 nm) or potassium permanganate staining. Mass spectra were obtained using a Finnigan MAT 8200 (70 eV) or an Agilent 5973 (70 eV) spectrometer, using electrospray ionization (ESI). $^1$H and $^{13}$C NMR spectra were recorded using a Bruker AV-400 (400 MHz) spectrometer, and $^{19}$F NMR spectra were recorded at 101 MHz. Chemical shift values are reported in parts per million with the solvent resonance as the internal standard ($CHCl_3$, 7.26 for $^1$H, 77.0 for $^{13}$C). Data are reported as follows: chemical shifts (parts per million), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; br, broad; m, multiplet), coupling constants (hertz), and integration. All starting materials were purchased from Aldrich or TCI and used without further purification unless otherwise stated.

**General Procedure 1 (GP1) for the Synthesis of Thiouronium Salts.** A solution of *N*,*N*,*N*′,*N*′-tetramethylthiourea (5 mmol)



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and alkyl bromide (5 mmol) in anhydrous $CH_2Cl_2$ (50 mL) or anhydrous acetone (50 mL) was stirred for 12 h at room temperature, after which time the reaction mixture was concentrated *in vacuo* to afford the reaction product. No further purification was necessary.

*2-(1,3-Diethoxy-1,3-dioxopropan-2-yl)-1,1,3,3-tetramethylthiouronium Bromide (**5a**).* Obtained as a colorless oil via GP1 (1.85 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.81 (s, 1H), 4.36−4.26 (m, 4H), 3.51 (s, 12H), 1.32 (t, $J$ = 7.0 Hz, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 172.4, 164.3, 64.0, 53.5, 45.0, 14.0; IR (film) 3387, 2984, 1727, 1609, 1505, 1465, 1396, 1370, 1300, 1256, 1021 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{12}H_{23}N_2O_4S^+$ 291.1373, found 291.1374.

*2-[1,3-Bis(benzyloxy)-1,3-dioxopropan-2-yl]-1,1,3,3-tetramethylthiouronium Bromide (**5b**).* Obtained as a yellow oil via GP1 (2.47 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.35−7.29 (m, 10H), 5.20 (s, 4H), 4.95 (s, 1H), 3.31 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 171.7, 164.0, 134.0, 129.1, 128.9, 128.8, 69.4, 53.5, 44.9; IR (film) 3625, 3399, 1736, 1612, 1501, 1455, 1398, 1276, 1261, 1169, 1113, 1061, 1001 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{22}H_{27}N_2O_4S^+$ 415.1686, found 415.1691.

*2-(2-Ethoxy-2-oxoethyl)-1,1,3,3-tetramethylthiouronium Bromide (**5c**).* Obtained as a white solid via GP1 (1.49 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.23 (q, $J$ = 7.0 Hz, 2H), 3.99 (s, 2H), 3.49 (s, 12H), 1.30 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 174.3, 167.5, 62.97, 44.8, 36.1, 14.1; IR (film) 3491, 3380, 2981, 2938, 1724,1603, 1505, 1463, 1395, 1304, 1261, 1191, 1167, 1112, 1057, 1020 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_9H_{19}N_2O_2S^+$ 219.1162, found 219.1161.

*1,1,3,3-Tetramethyl-2-(2-oxo-2-phenylethyl)thiouronium Bromide (**5d**).* Obtained as a yellow solid via GP1 (1.65 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 (d, $J$ = 7.5 Hz, 2H), 7.63 (t, $J$ = 7.5 Hz, 1H), 7.52 (t, $J$ = 7.5 Hz, 2H), 5.12 (s, 2H), 3.45 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 134.7, 131.2, 129.4, 129.2, 129.0, 125.4, 44.7, 34.6; IR (film) 3400, 3059, 2782, 1669, 1603, 1507, 1467, 1449, 1399, 1345, 1324, 1276, 1261, 1206, 1167, 1112, 1019 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{13}H_{19}N_2OS^+$ 251.1213, found 251.1213.

*1,1,3,3-Tetramethyl-2-(4-nitrobenzyl)thiouronium Bromide (**5e**).* Obtained as a yellow solid via GP1 (1.74 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.21 (d, $J$ = 9.0 Hz, 2H), 7.87 (d, $J$ = 9.0 Hz, 2H), 4.85 (s, 2H), 3.49 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 174.6, 147.7, 141.9, 130.8, 124.2, 45.0, 38.3; IR (film) 3398, 2972, 2936, 1598, 1515, 1463, 1393, 1343, 1252, 1204, 1168, 1108, 1057 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{12}H_{18}N_3O_2S^+$ 268.1114, found 268.1110.

*2-(2-Ethoxy-2-oxo-1-phenylethyl)-1,1,3,3-tetramethylthiouronium Bromide (**5f**).* Obtained as a yellow solid via GP1 (1.87 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (m, 2H), 7.39 (m, 3H), 5.32 (s, 1H), 4.20 (qd, $J$ = 7.0, 1.0 Hz, 2H), 3.47 (s, 12H), 1.20 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 172.9, 168.5, 132.2, 129.9, 129.5, 128.6, 128.6, 63.5, 55.1, 44.9, 14.0; IR (film) 3394, 2971, 2935, 1727, 1604, 1503, 1454, 1393, 1368, 1256, 1208, 1167, 1110, 1057, 1019 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{15}H_{23}N_2O_2S^+$ 295.1475, found 295.1475.

*2-(1-Ethoxy-1-oxopropan-2-yl)-1,1,3,3-tetramethylthiouronium Bromide (**5g**).* Obtained as a white solid via GP1 (1.56 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.21−4.09 (m, 3H), 3.43 (s, 12H), 1.57 (d, $J$ = 7.0 Hz, 3H), 1.24 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 173.6, 170.4, 63.0, 45.4, 44.8, 16.8, 14.2; IR (film) 3387, 2969, 2941, 1716, 1605, 1512, 1434, 1387, 1369, 1270, 1209, 1180, 1113, 1059, 1002 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{10}H_{21}N_2O_2S^+$ 233.1318, found 233.1315.

*2-(9H-Fluoren-9-yl)-1,1,3,3-tetramethylthiouronium Bromide (**5h**).* Obtained as a white solid via GP1 (1.88 g, quantitative yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.74 (dd, $J$ = 6.5, 2.0 Hz, 2H), 7.57−7.50 (m, 2H), 7.49−7.37 (m, 4H), 5.45 (s, 1H), 3.42 (s, 12H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 173.1, 140.9, 140.5, 129.7, 128.8, 125.0, 120.7, 51.6, 45.2; IR (film) 3399, 1602, 1503, 1448, 1392, 1258, 1167, 1109 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M]$^+$) calcd for $C_{18}H_{21}N_2S^+$ 297.1420, found 297.1423.

**General Procedure 2 (GP2) for the (3+2) Cycloaddition.** To an oven-dried flask were added sulfonium salt (0.3 mmol), nitrostyrene (0.2 mmol), and 1.0 mL of anhydrous $CH_2Cl_2$. To this solution was added slowly $Et_3N$ (0.3 mmol), and the reaction mixture was stirred for 12 h, before being concentrated *in vacuo*. The crude mixture was purified by column chromatography (1:1 heptane/EtOAc) to afford the dihydrothiophene product.

**General Procedure 3 (GP3) for the (3+2) Cycloaddition.** To an oven-dried flask were added nitrostyrene (0.2 mmol), $Et_3N$ (0.3 mmol), and 1.0 mL of anhydrous $CH_2Cl_2$. To this mixture was added the solution of sulfonium salt (0.3 mmol) in 0.5 mL of $CH_2Cl_2$ dropwise using a syringe pump over 6 h, and the reaction mixture was stirred for an additional 6 h, before being concentrated *in vacuo*. The crude mixture was purified by column chromatography (1:1 heptane/EtOAc) to afford the dihydrothiophene product.

**General Procedure 4 (GP4) for the Thiouronium Formation/(3+2) Cycloaddition One-Pot Reaction.** A solution of *N,N,N′,N′*-tetramethylthiourea (0.3 mmol) and alkyl bromide (0.3 mmol) in anhydrous $CH_2Cl_2$ (1.0 mL) was stirred for 12 h at room temperature. Then, nitrostyrene (0.2 mmol) was added, followed slowly by $Et_3N$ (0.3 mmol). After being stirred for a further 12 h, the reaction mixture was concentrated *in vacuo*. The crude mixture was purified by column chromatography (1:1 heptane/EtOAc) to afford the dihydrothiophene product.

*Diethyl 5-(Dimethylamino)-4-nitro-3-phenylthiophene-2,2(3H)-dicarboxylate (**4a**).* Obtained as a yellow oil via GP2 (72.1 mg, 92% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47−7.44 (m, 2H), 7.32−7.27 (m, 3H), 5.49 (s, 1H), 4.35 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.27 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.87 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.74 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.26 (s, 6H), 1.29 (t, $J$ = 7.0 Hz, 3H), 0.95 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.6, 164.6, 163.7, 136.9, 128.6, 128.34, 128.25, 118.9, 67.6, 63.2, 62.9, 56.0, 45.8, 13.8, 13.4; IR (film) 2983, 2936, 1736, 1590, 1430, 1372, 1290, 1274, 1245, 1211, 1139, 1094, 1078, 1041, 1021 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{18}H_{22}N_2NaO_6S^+$ 417.1091, found 417.1099.

*Dibenzyl 5-(Dimethylamino)-4-nitro-3-phenylthiophene-2,2(3H)-dicarboxylate (**4b**).* Obtained as a yellow oil via GP2 (69.3 mg, 67% yield): $^1$H NMR (600 MHz, DMSO, 363 K) $\delta$ 7.38−7.28 (m, 13H), 7.08−7.06 (m, 2H), 5.34 (s, 1H), 5.29 (d, $J$ = 12.5 Hz, 1H), 5.25 (d, $J$ = 12.5 Hz, 1H), 4.78 (d, $J$ = 12.5 Hz, 1H), 4.67 (d, $J$ = 12.5 Hz, 1H), 3.22 (s, 6H); $^{13}$C{$^1$H} NMR (150 MHz, DMSO, 363 K) $\delta$ 167.7, 164.4, 163.5, 137.0, 135.4, 134.6, 128.94, 128.91, 12.85, 128.82, 128.81, 128.72, 128.58, 128.50, 128.3, 118.1, 68.8, 68.6, 67.7, 56.3, 46.1; IR (film) 3027, 1737, 1590, 1453, 1430, 1373, 1291, 1261, 1232, 1199, 1139 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{28}H_{26}N_2NaO_6S^+$ 541.1404, found 541.1414.

*Ethyl (2S,3S)-5-(Dimethylamino)-4-nitro-3-phenyl-2,3-dihydrothiophene-2-carboxylate (**4c**).* Obtained as a yellow oil via GP2 (14.8 mg, 23% yield, co-eluted with a minor diastereomer): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.30 (m, 5H), 5.33 (d, $J$ = 1.0 Hz, 1H), 4.30−4.22 (app. qd, $J$ = 7.0, 1.0 Hz, 2H), 3.87 (d, $J$ = 1.5 Hz, 1H), 3.29 (s, 6H), 1.31 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 169.6, 165.9, 140.9, 128.9, 127.7, 126.6, 117.4, 62.6, 53.8, 51.2, 46.0, 14.0; IR (film) 2981, 2930, 1734, 1651, 1587, 1493, 1450, 1428, 1369, 1291, 1271, 1179, 1095, 1028 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{15}H_{18}N_2NaO_4S^+$ 345.0879, found 345.0881.

*[(2S,3S)-5-(Dimethylamino)-4-nitro-3-phenyl-2,3-dihydrothiophen-2-yl](phenyl)methanone (**4d**).* Obtained as a yellow solid via GP2 (14.2 mg, 20% yield, co-eluted with a minor diastereomer). Pure crystals of the major diastereomer were obtained after recrystallization from acetone/heptane: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.89−7.86 (m, 2H), 7.64 (ddt, $J$ = 8.0, 7.0, 1.5 Hz, 1H), 7.53−7.46 (m, 4H), 7.42−7.38 (m, 2H), 7.34 (ddt, $J$ = 8.5, 6.0, 1.5 Hz, 1H), 5.46 (d, $J$ = 1.5 Hz, 1H), 4.71 (d, $J$ = 1.5 Hz, 1H), 3.26 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 191.7, 165.1, 141.4, 133.97, 133.87, 129.05, 129.03, 128.7, 127.8, 126.9, 118.4, 52.51, 52.40, 45.9; IR (film) 3060, 3029, 2931, 1684, 1585, 1448, 1427, 1369, 1269, 1246, 1208, 1150, 1130 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{19}H_{18}N_2NaO_3S^+$ 377.0930, found 377.0929.



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*(4S,5S)-N,N-Dimethyl-3-nitro-5-(4-nitrophenyl)-4-phenyl-4,5-dihydrothiophen-2-amine (**4e**).* Obtained as a yellow solid via GP2 (14.8 mg, 20% yield, co-eluted with a minor diastereomer): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (d, $J$ = 9.0 Hz, 2H), 7.54 (d, $J$ = 8.5 Hz, 2H), 7.43−7.35 (m, 5H), 5.03 (d, $J$ = 1.5 Hz, 1H), 4.46 (d, $J$ = 1.5 Hz, 1H), 3.38 (s, 6H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 166.5, 148.5, 147.7, 141.2, 129.1, 128.0, 127.5, 126.5, 124.6, 116.6, 59.3, 53.7, 46.2; IR (film) 3063, 3029, 2926, 2852, 1706, 1654, 1586, 1517, 1493, 1451, 1427, 1367, 1343, 1275, 1259, 1181, 1130, 1109, 1057 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{18}H_{17}N_3NaO_4S^+$ 394.0832, found 394.0814.

*Ethyl (2S,3S)-5-(Dimethylamino)-4-nitro-2,3-diphenyl-2,3-dihydrothiophene-2-carboxylate (**4f**).* Major diastereomer, obtained as a yellow solid via GP2 (38.3 mg, 48% yield): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.67−7.60 (m, 2H), 7.54−7.30 (m, 8H), 5.54 (s, 1H), 3.80 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.75 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.25 (s, 6H), 0.85 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 168.9, 166.2, 141.3, 138.2, 129.3, 128.9, 128.7, 128.5, 128.2, 127.3, 125.8, 71.2, 62.7, 57.3, 46.0, 13.5; IR (film) 3061, 3031, 2981, 2932, 2242, 1729, 1580, 1445, 1427, 1370, 1286, 1265, 1231, 1186, 1129, 1095, 1053, 1034 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{21}H_{22}N_2NaO_4S^+$ 421.1192, found 421.1193.

*Ethyl (2R,3S)-5-(Dimethylamino)-4-nitro-2,3-diphenyl-2,3-dihydrothiophene-2-carboxylate (**4f′**).* Minor diastereomer, obtained as a yellow solid via GP2 (26.3 mg, 33% yield): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.14−7.00 (m, 10H), 5.70 (s, 1H), 4.33 (dq, $J$ = 11.0, 7.0 Hz, 1H), 4.29 (dq, $J$ = 11.0, 7.0 Hz, 1H), 3.35 (s, 6H), 1.26 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 172.0, 165.0, 137.3, 133.8, 130.1, 128.8, 128.2, 128.0, 127.8, 127.4, 127.3, 68.8, 63.1, 59.0, 46.0, 14.0; IR (film) 3060, 3029, 2977, 2930, 2242, 1726, 1583, 1521, 1447, 1429, 1371, 1287, 1263, 1216, 1188, 1135, 1094, 1078, 1052 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{21}H_{22}N_2NaO_4S^+$ 421.1192, found 421.1189.

*Ethyl (2R,3S)-5-(Dimethylamino)-2-methyl-4-nitro-3-phenyl-2,3-dihydrothiophene-2-carboxylate (**4g**).* First diastereomer obtained as a yellow solid via GP2 (12.8 mg, 19% yield): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.47−7.44 (m, 2H), 7.32−7.26 (m, 3H), 4.70 (s, 1H), 3.83 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.77 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.30 (s, 6H), 2.00 (s, 3H), 0.92 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 170.0, 166.9, 138.5, 128.4, 128.2, 128.1, 118.6, 64.3, 62.4, 61.4, 46.0, 30.4, 13.6; IR (film) 3029, 2978, 2931, 2869, 1717, 1585, 1448, 1425, 1393, 1368, 1289, 1245, 1198, 1175, 1139, 1100, 1064, 1010 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{16}H_{20}N_2NaO_4S^+$ 359.1036, found 359.1036.

*Ethyl (2S,3S)-5-(Dimethylamino)-2-methyl-4-nitro-3-phenyl-2,3-dihydrothiophene-2-carboxylate (**4g′**).* Second diastereomer obtained as a yellow solid via GP2 (12.1 mg, 18% yield): $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.40−7.31 (m, 5H), 5.24 (s, 1H), 4.29 (q, $J$ = 7.0 Hz, 2H), 3.30 (s, 6H), 1.33 (t, $J$ = 7.0 Hz, 3H), 1.22 (s, 3H); $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$) $\delta$ 173.0, 166.5, 137.6, 128.79, 128.75, 128.1, 121.8, 120.1, 62.9, 59.1, 58.0, 45.9, 20.5, 14.1; IR (film) 3028, 2960, 2927, 2870, 1727, 1583, 1450, 1429, 1371, 1289, 1261, 1225, 1136, 1102, 1057, 1015 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{16}H_{20}N_2NaO_4S^+$ 359.1036, found 359.1034.

*N,N-Dimethyl-4′-nitro-3′-phenyl-3′H-spiro[fluorene-9,2′-thiophen]-5′-amine (**4h**).* Obtained as a yellow solid via GP2 (76.1 mg, 95% yield): $^1$H NMR (600 MHz, $CDCl_3$, 363 K) $\delta$ 7.87 (d, $J$ = 7.5 Hz, 1H), 7.81 (d, $J$ = 7.5 Hz, 1H), 7.60 (d, $J$ = 7.5 Hz, 1H), 7.49 (td, $J$ = 7.5, 1.0 Hz, 1H), 7.41 (td, $J$ = 7.5, 1.0 Hz, 1H), 7.34−7.27 (m, 4H), 7.05 (br. s, 2H), 6.88 (td, $J$ = 7.5, 1.0 Hz, 1H), 6.19 (d, $J$ = 7.5 Hz, 1H), 4.79 (s, 1H), 3.39 (s, 6H); $^{13}$C{$^1$H} NMR (150 MHz, $CDCl_3$, 363 K) $\delta$ 168.2, 151.2, 140.7, 140.0, 139.1, 138.0, 129.73, 129.72 129.48, (129.0) (this carbon peak was not observed, even at 363 K, because of peak broadening due to restricted rotation; a rough estimate was obtained via a high-temperature HSQC experiment[23]), 128.5, 128.2, 127.1, 126.9, 121.9, 120.9, 120.7, 117.9, 64.0, 61.8, 46.4; IR (film) 3488, 3059, 2929, 1954, 1579, 1286, 1262, 1191, 1145, 1032 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{24}H_{20}N_2NaO_2S^+$ 423.1138, found 423.1136.

*Diethyl 5-(Dimethylamino)-4-nitro-3-(p-tolyl)thiophene-2,2(3H)-dicarboxylate (**4l**).* Obtained as a yellow oil via GP2 (75.2 mg, 92% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (d, $J$ = 8.0 Hz, 2H), 7.10 (d, $J$ = 8.0 Hz, 2H), 5.45 (s, 1H), 4.34 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.26 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.90 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.76 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.25 (s, 6H), 2.31 (s, 3H), 1.29 (t, $J$ = 7.0 Hz, 3H), 0.98 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.7, 164.7, 163.7, 138.0, 133.7, 129.0, 128.4, 119.0, 67.7, 63.1, 62.9, 55.64, 45.8, 21.1, 13.8, 13.5; IR (film) 2983, 2936, 1735, 1588, 1513, 1429, 1370, 1289, 1242, 1210, 1137, 1094, 1040, 1021 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{19}H_{24}N_2NaO_6S^+$ 431.1247, found 431.1247.

*Diethyl 5-(Dimethylamino)-3-(4-methoxyphenyl)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4m**).* Obtained as a yellow oil via GP2 (77.3 mg, 91% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.36 (d, $J$ = 8.5 Hz, 2H), 6.82 (d, $J$ = 8.5 Hz, 2H), 5.43 (s, 1H), 4.33 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.24 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.90 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.77 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.77 (s, 3H), 3.24 (s, 6H), 1.28 (t, $J$ = 7.0 Hz, 3H), 0.99 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.7, 164.7, 163.6, 159.5, 129.7, 128.8, 119.0, 113.7, 67.8, 63.1, 62.9, 55.30, 55.23, 45.8, 13.8, 13.6; IR (film) 2983, 2936, 1735, 1587, 1511, 1429, 1369, 1290, 1242, 1212, 1178, 1137 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{19}H_{24}N_2NaO_7S^+$ 447.1196, found 447.1192.

*Diethyl 3-(2,4-Dimethoxyphenyl)-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4n**).* Obtained as a yellow oil via GP2 (52.7 mg, 58% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.33 (d, $J$ = 9.0 Hz, 1H), 6.45−6.42 (m, $J$ = 8.5 Hz, 2H), 6.04 (s, 1H), 4.34 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.27 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.90 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.72 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.24 (s, 6H), 1.29 (t, $J$ = 7.0 Hz, 3H), 0.99 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.8, 165.0, 164.0, 160.7, 158.6, 129.2, 119.0, 118.1, 104.5, 98.9, 67.4, 62.9, 62.7, 55.9, 55.3, 48.2, 45.6, 13.8, 13.5; IR (film) 2983, 2937, 1735, 1584, 1506, 1461, 1439, 1372, 1291, 1245, 1208, 1139, 1033 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{20}H_{26}N_2NaO_8S^+$ 477.1302, found 477.1304.

*Diethyl 3-[2-(Benzyloxy)phenyl]-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4p**).* Obtained as a yellow oil via GP2 (73.1 mg, 73% yield): $^1$H NMR (600 MHz, DMSO, 363 K) $\delta$ 7.58 (d, $J$ = 7.5 Hz, 2H), 7.43−7.40 (m, 3H), 7.34 (t, $J$ = 7.5 Hz, 1H), 7.26 (ddd, $J$ = 8.5, 7.5, 1.5 Hz, 1H), 7.08 (d, $J$ = 8.5 Hz, 1H), 6.93 (t, $J$ = 7.5 Hz, 1H), 6.13 (s, 1H), 5.16 (d, $J$ = 12.0 Hz, 1H), 5.13 (d, $J$ = 12.0 Hz, 1H), 4.31 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.24 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.81 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.65 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.15 (s, 6H), 1.22 (t, $J$ = 7.0 Hz, 3H), 0.84 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (150 MHz, DMSO, 363 K) $\delta$ 168.2, 164.8, 164.2, 157.0, 137.8, 129.6, 129.2, 128.6, 128.0, 127.7, 126.6, 121.0, 118.3, 113.3, 70.5, 67.2, 63.3, 62.9, 48.9, 45.9, 14.0, 13.5; IR (film) 3064, 2983, 2936, 1734, 1585, 1492, 1451, 1429, 1373, 1274, 1240, 1139, 1021 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{25}H_{28}N_2NaO_7S^+$ 523.1509, found 523.1509.

*Diethyl 5-(Dimethylamino)-3-(4-fluorophenyl)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4q**).* Obtained as a yellow oil via GP2 (67.6 mg, 82% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 (dd, $J$ = 8.5, 5.5 Hz, 2H), 6.99 (app. t, $J$ = 8.5 Hz, 2H), 5.47 (s, 1H), 4.34 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.26 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.91 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.78 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.26 (s, 6H), 1.29 (t, $J$ = 7.0 Hz, 3H), 0.99 (t, $J$ = 7.0 Hz, 3H); $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$) $\delta$ 167.5, 164.5, 163.5, 162.5 (d, $J_{C-F}$ = 247.0 Hz), 132.9 (d, $J_{C-F}$ = 3.0 Hz), 130.3 (d, $J_{C-F}$ = 8.5 Hz), 118.8, 115.2 (d, $J_{C-F}$ = 21.5 Hz), 67.5 (d, $J_{C-F}$ = 1.0 Hz), 63.3, 63.0, 55.2, 45.8, 13.8, 13.5; $^{19}$F{$^1$H} NMR $\delta$ −113.7; IR (film) 2983, 2937, 1734, 1588, 1508, 1429, 1369, 1288, 1272, 1241, 1160, 1137, 1097, 1039, 1021 cm$^{-1}$; HRMS (ESI-TOF, $m/z$) ([M + Na]$^+$) calcd for $C_{18}H_{21}FN_2NaO_6S^+$ 435.0997, found 435.0994.

*Diethyl 3-(3-Chlorophenyl)-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4r**).* Obtained as a yellow solid via GP2 (59.2 mg, 69% yield): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44−7.42 (m, 1H), 7.35 (dt, $J$ = 7.0, 2.0 Hz, 1H), 7.28−7.22 (m, 2H), 5.45 (s, 1H), 4.34 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.26 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.91 (dq, $J$


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= 10.5, 7.0 Hz, 1H), 3.81 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.26 (s, 6H), 1.29 (t, $J$ = 7.0 Hz, 3H), 1.00 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.3, 164.6, 163.2, 137.0, 133.1, 129.5, 128.4, 127.5, 126.3, 119.1, 67.0, 63.3, 63.1, 53.9, 45.8, 13.9, 13.4; IR (film) 2982, 2927, 2855, 1736, 1590, 1430, 1372, 1286, 1246, 1211, 1168, 1139, 1096, 1040 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{18}H_{21}{}^{35}ClN_2NaO_6S^+$ 451.0701, found 451.0700.

*Diethyl 3-(4-Chlorophenyl)-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4s**).* Obtained as a yellow solid via GP2 (57.5 mg, 67% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.39 (d, $J$ = 8.5 Hz, 2H), 7.26 (d, $J$ = 8.5 Hz, 2H), 5.44 (s, 1H), 4.33 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.25 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.91 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.78 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.24 (s, 6H), 1.28 (t, $J$ = 7.0 Hz, 3H), 0.98 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.4, 164.5, 163.4, 135.7, 134.1, 129.9, 128.5, 118.6, 67.3, 63.3, 63.1, 55.3, 45.8, 13.8, 13.5; IR (film) 2983, 2936, 1734, 1588, 1491, 1429, 1371, 1286, 1241, 1209, 1138, 1089, 1039, 1015 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{18}H_{21}{}^{35}ClN_2NaO_6S^+$ 451.0701, found 451.0698.

*Diethyl 3-(2-Bromophenyl)-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4t**).* Obtained as a yellow solid via GP2 (73.8 mg, 78% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.57−7.51 (m, 2H), 7.23 (td, $J$ = 7.5, 1.0 Hz, 1H), 7.09 (td, $J$ = 7.5, 1.5 Hz, 1H), 6.23 (s, 1H), 4.34 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.28 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.88 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.69 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.22 (s, 6H), 1.28 (t, $J$ = 7.0 Hz, 3H), 0.97 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.3, 164.6, 163.2, 137.0, 133.2, 129.5, 128.4, 127.5, 126.3, 119.0, 67.0, 63.3, 63.1, 53.9, 45.8, 13.9, 13.4; IR (film) 3728, 3703, 3627, 2983, 2924, 2854, 1737, 1589, 1466, 1431, 1376, 1290, 1252, 1211, 1141, 1119, 1095, 1053, 1029 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{18}H_{21}{}^{81}BrN_2NaO_6S^+$ 497.0175, found 497.0177.

*Diethyl 5-(Dimethylamino)-4-nitro-3-(4-nitrophenyl)thiophene-2,2(3H)-dicarboxylate (**4u**).* Obtained as a yellow oil via GP2 (71.2 mg, 81% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.17 (d, $J$ = 9.0 Hz, 2H), 7.68 (d, $J$ = 9.0 Hz, 2H), 5.58 (s, 1H), 4.36 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.28 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.92 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.78 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.28 (s, 6H), 1.30 (t, $J$ = 7.0 Hz, 3H), 0.97 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.1, 164.2, 163.3, 147.7, 144.9, 129.6, 123.5, 117.9, 66.8, 63.6, 63.3, 55.5, 46.0, 13.8, 13.5; IR (film) 2983, 2936, 1735, 1589, 1521, 1430, 1371, 1347, 1274, 1243, 1211, 1139, 1095, 1039, 1020 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{18}H_{21}N_3NaO_8S^+$ 462.0942, found 462.0939.

*Diethyl 5′-(Dimethylamino)-4′-nitro-[2,3′-bithiophene]-2′,2′(3′H)-dicarboxylate (**4v**).* Obtained as a yellow solid via GP2 (60.1 mg, 75% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.18 (dd, $J$ = 5.0, 1.0 Hz, 1H), 7.09 (d, $J$ = 3.0 Hz, 1H), 6.93 (dd, $J$ = 5.0, 3.5 Hz, 1H), 5.79 (s, 1H), 4.33 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.24 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.04 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.94 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.25 (s, 6H), 1.27 (t, $J$ = 7.0 Hz, 3H), 1.08 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.3, 164.3, 163.5, 139.6, 127.3, 126.7, 125.0, 119.4, 68.1, 63.3, 63.2, 51.6, 45.8, 13.8, 13.6; IR (film) 3728, 3704, 3626, 3598, 2923, 2853, 2332, 1736, 1651, 1590, 1430, 1373, 1276, 1374, 1277, 1261, 1140, 1094, 1035 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{16}H_{20}N_2NaO_6S_2{}^+$ 423.0655, found 423.0653.

*Diethyl 3-[1-(tert-Butoxycarbonyl)-1H-pyrrol-2-yl]-5-(dimethylamino)-4-nitrothiophene-2,2(3H)-dicarboxylate (**4w**).* Obtained as a yellow solid via GP3 (60.0 mg, 62% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.28 (dd, $J$ = 3.0, 2.0 Hz, 1H), 6.73 (s, 1H), 6.37 (dd, $J$ = 3.5, 2.0 Hz, 1H), 6.06 (t, $J$ = 3.5 Hz, 1H), 4.32 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.23 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.00 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.91 (dq, $J$ = 10.5, 7.0 Hz, 1H), 3.23 (s, 6H), 1.65 (s, 9H), 1.27 (t, $J$ = 7.0 Hz, 3H), 1.03 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.4, 164.8, 163.2, 149.6, 130.0, 122.9, 119.3, 112.9, 109.8, 84.9, 67.7, 63.2, 63.1, 47.6, 45.7, 28.0, 13.8, 13.7; IR (film): 3728, 3626, 2983, 1736, 1591, 1431, 1370, 1324, 1293, 1274, 1247, 1212, 1160, 1141 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{21}H_{29}N_3NaO_8S^+$ 506.1568, found 506.1565.

*Diethyl (E)-5-(Dimethylamino)-4-nitro-3-styrylthiophene-2,2(3H)-dicarboxylate (**4x**).* Obtained as a yellow solid via GP3 (47.9 mg, 57% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.38−7.35 (m, 2H), 7.32−7.22 (m, 3H), 6.81 (d, $J$ = 15.5 Hz, 1H), 6.19 (dd, $J$ = 15.5, 9.0 Hz, 1H), 5.05 (d, $J$ = 9.0 Hz, 1H), 4.32 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.24 (dq, $J$ = 10.5, 7.0 Hz, 1H), 4.16 (q, $J$ = 7.0 Hz, 2H), 3.22 (s, 6H), 1.28 (s, 3H), 1.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.3, 164.9, 163.3, 136.5, 134.9, 128.5, 127.9, 126.6, 122.2, 116.7, 67.4, 63.3, 63.2, 54.3, 45.8, 14.0, 13.8; IR (film) 3727, 3705, 3626, 2961, 2926, 1735, 1587, 1446, 1428, 1369, 1234, 1136, 1020 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{20}H_{24}N_2NaO_6S^+$ 443.1247, found 443.1256.

*Diethyl 5-(Dimethylamino)-4-nitro-3-phenethylthiophene-2,2(3H)-dicarboxylate (**4y**).* Obtained as a yellow solid via GP2 (35.5 mg, 42% yield): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.29−7.25 (m, 2H), 7.20−7.16 (m, 3H), 4.54 (dd, $J$ = 10.5, 4.5 Hz, 1H), 4.34−4.17 (m, 4H), 3.16 (s, 6H), 2.96 (ddd, $J$ = 14.5, 10.5, 6.0 Hz, 1H), 2.81 (ddd, $J$ = 14.5, 10.5, 6.0 Hz, 1H), 2.09 (dtd, $J$ = 13.0, 10.5, 6.0 Hz, 1H), 1.98 (dddd, $J$ = 13.0, 10.5, 6.0, 4.5 Hz, 1H), 1.30 (t, $J$ = 7.0 Hz, 3H), 1.27 (t, $J$ = 7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) $\delta$ 167.5, 165.3, 164.8, 142.0, 128.35, 128.18, 125.8, 118.2, 68.9, 63.26, 63.09, 50.2, 45.8, 32.6, 31.6, 13.92, 13.77; IR (film) 2983, 2935, 1735, 1589, 1451, 1428, 1370, 1284, 1250, 1211, 1132, 1095, 1030 $cm^{-1}$; HRMS (ESI-TOF, $m/z$) ($[M + Na]^+$) calcd for $C_{20}H_{26}N_2NaO_6S^+$ 445.1404, found 445.1401.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b03255.

NMR spectra for all reported compounds (PDF)
X-ray data for compound **4d** (CIF)

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### Notes

The authors declare no competing financial interest.

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(20) When nitroolefin **1e** was treated with 1.0 equiv of $Et_3N$ in $CDCl_3$, 25% decomposition was observed after just 15 min, with full decomposition achieved after 2 h.
(21) After 18 h at room temperature in $CDCl_3$, 25% decomposition was observed.
(22) In agreement with this postulate, when ylides based on cyclic thioureas were employed, no product was observed.
(23) See the Supporting Information for details.


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