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A One-Pot Assembly of Fully Substituted Alkyl 5-Aminothiophene-2-carboxylates from Allenes, Isothiocyanates, and Alkyl 2-Bromoacetates

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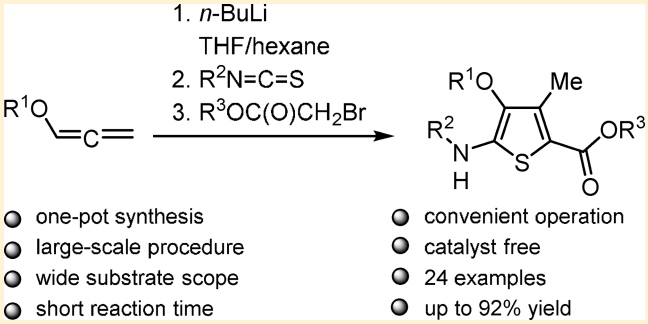
Supporting Information

ABSTRACT: A novel simple approach to highly functionalized multisubstituted thiophenes such as alkyl 4-alkoxy-5-amino-3-methylthiophene-2-carboxylates through the one-pot sequential reaction of α-lithiated alkoxyallenes with isothiocyanates and alkyl 2-bromoacetates has been discovered. The process proceeds quickly (30−45 min) via in situ formation and intramolecular cyclization of alkyl 2-[(2-alkoxybuta-2,3-dienimidoyl)sulfanyl]acetates (1-aza-1,3,4-trienes).



INTRODUCTION

Thiophenes are privileged five-membered sulfa-heterocycles, which have widespread use in pharmacology, agrochemistry, materials science, combinatorial and medicinal chemistry, and many other fields.[1] Among them, aminothiophenes,[2] thiophenecarboxylates,[3] and thiophenes bearing amino and carboxylate functions[4] are one of the most popular structural motifs, especially in recent times. They have a broad spectrum of biological activity,[5] are part of many pharmaceuticals including drugs for treatment of socially significant diseases (HIV, tuberculosis, cancer, flu, etc.),[1,6] a variety of electronic and optoelectronic materials and conductive polymers[7] or serve as important intermediates and building blocks for the synthesis of the above products.[8] Given the synthetic and practical significance of thiophenes and their derivatives, the search for and development of conceptually new rational methodologies for their synthesis, as well as a fundamental extension of their range has acquired particular importance.[9] Until now, the most widely applied synthetic pathway to aminothiophenes, including aminothiophenecarboxylates, is the multicomponent Gewald's methodology (through condensation of a carbonyl compound with a methylene activated acetonitrile followed by heating with elemental sulfur in the presence of base), which has many modifications and variations.[10] However, this approach provides a convenient access only to unsubstituted at the nitrogen atom aminothiophenes. *N*-Mono- and *N*,*N*-disubstituted aminothiophenes are much less available, because known methods for their synthesis are not so common and manifold.[2d,11] Among publications on this topic, no works (except for a few of our preceding reports[12]) on the direct synthesis of *N*-mono- and *N*,*N*-disubstituted thiophen-2-amines from allenic or acetylenic carbanions, isothiocyanates, and alkylating agents are known. We have carried out for the first time one-pot assembly of 2,3- and 2,5-disubstituted thiophene nucleus from available allenes or alkynes and aliphatic or aromatic isothiocyanates via intramolecular cyclization (with formation of new C−S bond) of potassium buta-2,3-dienimidothioates (adducts of allenic or acetylenic carbanions and isothiocyanates) followed by final N-alkylation or N-protolysis of the intermediate potassium 2-thienylamides with alkyl iodides or water, respectively. Numerous earlier unknown and inaccessible *N*-alkyl-, *N*-cycloalkyl-, *N*-aryl-, *N*,*N*-dialkyl-, *N*-alkyl-*N*-cycloalkyl-, and *N*-alkyl-*N*-arylthiophen-2-amines have been synthesized using this procedure. Previously, we have also shown that the reaction of 1-lithio-1-alkoxyallenes[13] with isothiocyanates, followed by S-alkylation of the adducts leads to alkyl 2-alkoxybuta-2,3-dienimidothioates (1-aza-1,3,4-trienes), which further undergo thermally induced structural reorganization into azaheterocycles, e.g., pyrroles, quinolines or 2,3-dihydropyridines depending on the nature and structure of the substituent at the nitrogen atom.[14]

In this work we have pleasingly found that, when methyl 2-bromoacetate is used as an alkylating agent in the reaction of α-lithiated methoxyallene **1a** with methyl isothiocyanate, fully substituted thiophene, namely methyl 4-methoxy-3-methyl-5-(methylamino)thiophene-2-carboxylate (**2a**) is obtained instead of the expected 1-aza-1,3,4-triene **3a** (Scheme 1).

For this reason, we have examined the discovered reaction with a variety of alkoxyallenes **1** and isothiocyanates leading to alkyl 5-aminothiophene-2-carboxylates **2** to clarify its generality

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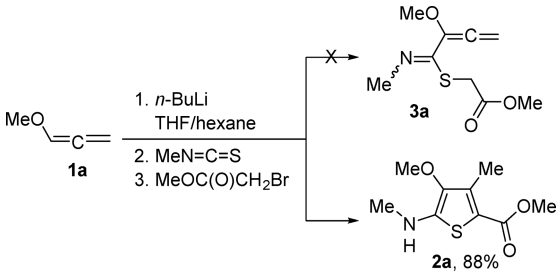
Scheme 1. Unexpected Formation of Methyl 5-Aminothiophene-2-carboxylate 2a from Methoxyallene (1a), Methyl Isothiocyanate, and Methyl 2-Bromoacetate



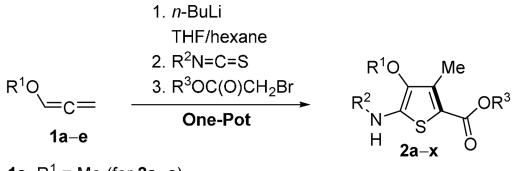
and synthetic potential as well as the tentative reaction mechanism. The results obtained are shown in Table 1.

RESULTS AND DISCUSSION

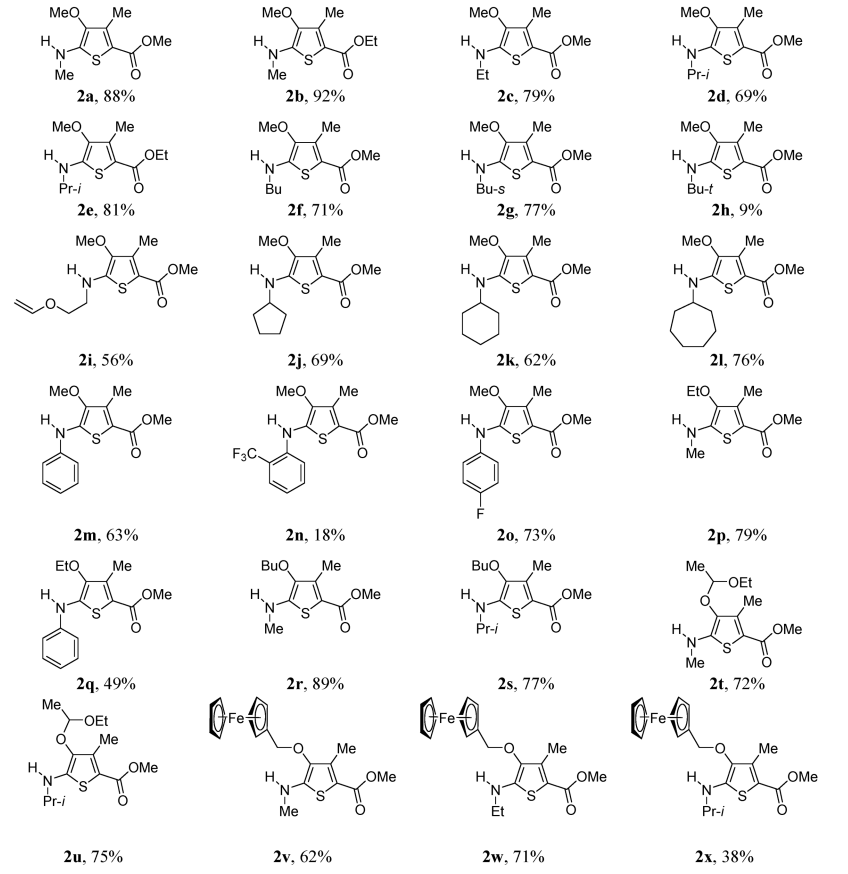
As seen from Table 1, the found protocol of thiophene ring construction was successfully extended to the synthesis of a representative range of tetrasubstituted thiophenes, bearing rare combination of reactive and pharmacophoric substituents, from methoxy-, ethoxy-, butoxy-, 1-(1-ethoxyethoxy)-, and 1-(ferrocenylmethoxy)allenes, methyl, ethyl, isopropyl, *n*-butyl, *sec*-butyl, *tert*-butyl, 2-(vinyloxy)ethyl, cyclopentyl, cyclohexyl, cycloheptyl, phenyl, 2-(trifluoromethyl)phenyl, and 4-fluorophenyl isothiocyanates, and methyl or ethyl 2-bromoacetates predominantly in good to excellent yields, in one preparative step, and for short reaction time (30–45 min).

As depicted in Scheme 2, thiophenes **2** are expected to be formed via unprecedented intramolecular cyclization of 1-aza-1,3,4-trienes **3**, which, in turn, are generated in situ by the reaction of 1-lithio-1-alkoxyallenes **4** with isothiocyanates,[14]

Table 1. One-Pot Synthesis of Alkyl 5-Aminothiophene-2-carboxylates from Alkoxyallenes 1a–e, Isothiocyanates, and Alkyl 2-Bromoacetates (via Formation of New C–C Bond)[a,b]



1a, R^1 = Me (for **2a–o**)
1b, R^1 = Et (for **2p**, **q**)
1c, R^1 = *n*-Bu (for **2r, s**)
1d, R^1 = EtOCH(Me) (for **2t**, **u**)
1e, R^1 = $FcCH_2$ (for **2v–x**)



[a]Reaction conditions: (1) $R^1OCH{=}C{=}CH_2$ (15–57 mmol), *n*-BuLi (16–35 mmol), THF (15–30 mL)/hexane (6.5–14 mL), −100 → −55 to −40 °C, 5–10 min; (2) $R^2N{=}C{=}S$ (15–30 mmol), −90 → −45 to −15 °C, 10–20 min; (3) $R^3OC(O)CH_2Br$ (15–30 mmol), −80 → 15–20 °C, 15 min. [b]Isolated yield.

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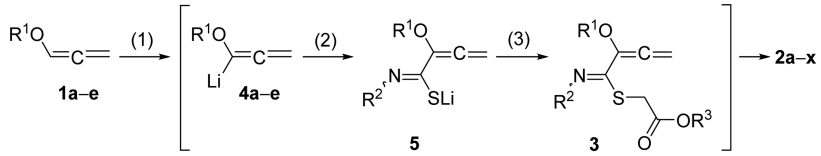
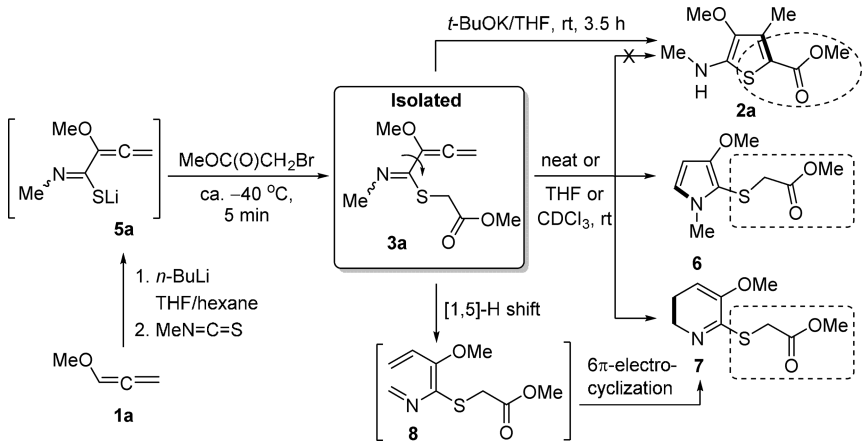
Scheme 2. Sequential Reactions of Alkoxyallenes 1a–e with *n*-BuLi (Step 1), Isothiocyanates (Step 2), and Alkyl 2-Bromoacetates (Step 3) Leading to Alkyl 5-Aminothiophene-2-carboxylates 2a–x



Scheme 3. Synthesis and Structural Transformations of 1-Aza-1,3,4-triene 3a into Thiophene 2a, Pyrrole 6, and 2,3-Dihydropyridine 7



followed by the reaction of lithium 2-alkoxybuta-2,3-dienimidothioates **5** with alkyl 2-bromoacetates.

Lithiation of alkoxyallenes **1** is carried out with *n*-BuLi in THF/hexane at −55 to −40 °C for 5−10 min. Next step is the reaction of 1-lithio-1-alkoxyallene **4** with isothiocyanate, which requires 10 min at −45 to −35 °C (for *n*-alkyl and aryl isothiocyanates) and 15−20 min at −35 to −15 °C (for iso-, *sec*- or *tert*-alkyl and cycloalkyl isothiocyanates). Finally, the reaction of adduct **5** with alkyl 2-bromoacetate, followed by cyclization of intermediary 1-aza-1,3,4-triene **3** into thiophene **2**, occurs at −80 to 15−20 °C for 15 min.

It should be noted that under the above conditions, compounds **3** or their heterocyclic aza-derivatives have not been identified in the reaction mixture even in trace amounts (by ^{1}H NMR). Formation of 2-[(2-alkoxy-2-oxoethyl)sulfanyl]-substituted 3-alkoxy-1-aza-1,3,4-trienes **3** as precursors of thiophenes **2** in the studied reaction was confirmed experimentally on the example of the reaction of the adduct **5a** [derived from 1-lithio-1-methoxyallene (**4a**) and methyl isothiocyanate] with methyl 2-bromoacetate. When carrying out this reaction step at −80 to −40 °C for 5 min (instead of 15 min at −80 to 20 °C), 1-aza-1,3,4-triene **3a** (as a mixture of *E*- and *Z*-isomers) was obtained in 96% yield (Scheme 3). Its structure is fully consistent with the data of NMR (^{1}H, ^{13}C, ^{15}N, ^{1}H−^{13}C-HMBC, ^{1}H−^{13}C-HSQC) and IR spectra. On the contrary, under these conditions, thiophene **2a** was not identified in the reaction mixture even in trace amount (by ^{1}H NMR).

We believed that 1-aza-1,3,4-triene **3a** will be immediately cyclized into thiophene **2a**. But surprisingly, we did not observe any traces of thiophene **2a** either after isolation of compound **3a** or after its storage at room temperature, neat or in solutions of THF or $CDCl_3$. In all cases (with the exception of the freshly isolated compound **3a**), mixtures of 1-aza-1,3,4-triene **3a**, pyrrole **6**, and 2,3-dihydropyridine **7** in different ratios were detected by ^{1}H NMR (Scheme 3). In a solution of $CDCl_3$ (rt, 3 h), almost quantitative transformation of 1-aza-1,3,4-triene **3a** to pyrrole **6** (via intramolecular cyclization with formation of new C−N bond) and 2,3-dihydropyridine **7** (via sequential reactions of isomerization and 6π-electrocyclization of 2-aza-1,3,5-triene **8**) was observed; the ratio of compounds was ∼10:58:32 (by ^{1}H NMR).

In the presence of CuBr (a specific catalyst for the cyclization of 1-aza-1,3,4-trienes to pyrroles[15]) (∼4%, THF, rt, 3.5 h), 1-aza-1,3,4-triene **3a** is quantitatively transformed into the pyrrole **6**. However, the addition of CuBr to the reaction mixture containing the in situ generated 1-aza-1,3,4-triene **3a** has not led to the change of the reaction direction. In this case, instead of the expected pyrrole **6**, thiophene **2a** is obtained. Importantly, in the presence of *t*-BuOK (∼0.08 equiv, THF, rt, 3.5 h), 1-aza-1,3,4-triene **3a**, synthesized according to Scheme 3, is transformed also exclusively to the thiophene **2a** (a qualitative experiment). It should be also noted that the in situ generated 1-aza-1,3,4-triene **3a** cyclizes into thiophene **2a** for ∼10 min at −40 to 15 °C.

On the basis of these data, it seems that the presence of a basic species in the reaction mixture is one of the crucial factors to promote the cyclization of the 1-aza-1,3,4-trienes **3** to thiophene derivatives **2**. The formation of the thiophene ring most likely proceeds through carbanion **A** (Scheme 4), generation of which is additionally facilitated by an activating group such as acyl group, R^{3}OC═O (a strong electron-withdrawing group).

It should be mentioned that until now sulfanyl substituents in the 1-aza-1,3,4-trienes derived from allenic or acetylenic carbanions and isothiocyanates, even with activated methylene fragment at the sulfur atom, such as benzyl-, allyl-, and propargylsulfanyl substituents, did not participate in the construction of heterocyclic rings. And only when 1-aza-1,3,4-trienes, bearing these substituents, were first isomerized into

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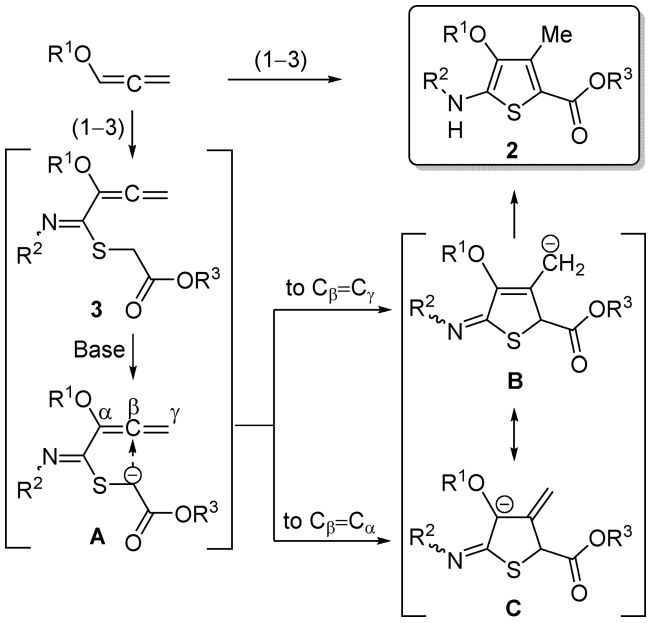
Scheme 4. Plausible Mechanism of the Reaction



conjugated 2-aza-1,3,5-trienes, CH_2=CHC(OR^1)=C(SR^2)-N=CR^{3}R^4 (R^2 = CH_2C≡CH, CH_2CH=CH_2, CH_2Ph) and then treated with *t*-BuOK/DMSO, 4,5-dihydro-1,3-thiazoles containing in the ring structure of a fragment of sulfanyl substituent were obtained (via intramolecular addition of the anion SCH$^-$ to N=C bond).[16]

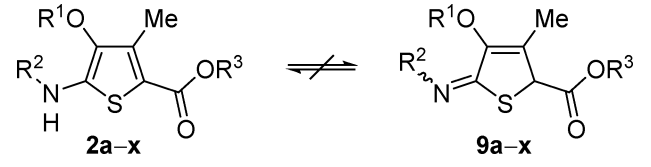
All the synthesized alkyl 4-alkoxy-5-amino-3-methylthiophene-2-carboxylates **2**, 1-aza-1,3,4-triene **3a**, pyrrole **6**, and 2,3-dihydropyridine **7** are novel. Compounds **2** and **6** have been purified by column chromatography and adequately characterized by spectral {NMR [^{1}H, ^{13}C, ^{15}N, ^{19}F (for **2n** and **2o**), HSQC, and HMBC], IR, MS} and elemental analysis data which are in good agreement with the structure of the products. 2,3-Dihydropyridine **7** was identified in NMR spectra of the products mixture with pyrrole **6**.

In contrast to the earlier studied 3-methoxy-*N*-methyl- and 3-methoxy-*N*-phenylthiophen-2-amines that in solutions of CCl_4 and $CDCl_3$ are in equilibrium with imino-tautomers,[12b] their tetrasubstituted analogues **2** in $CDCl_3$ solution exist exclusively in the amino-form, regardless of the structure and the nature of the substituents (Scheme 5). The imino-tautomers **9** were not detected in NMR spectra in any case.

CONCLUSION

In conclusion, a new family of alkyl 4-alkoxy-5-amino-3-methylthiophene-2-carboxylates, synthetically and pharmaceutically valuable, but yet not available representatives of tetrasubstituted thiophenes, have been obtained in one preparative step using fundamental reaction of carbon–carbon bond formation by intramolecular self-cyclization of alkyl 2-[(2-alkoxybuta-2,3-dienimidoyl)sulfanyl]acetates (1-aza-1,3,4-trienes) generated in situ from alkoxyallenic carbanions, isothiocyanates, and alkyl 2-bromoacetates. This conceptually new approach to the thiophene ring construction offers a simple and shortest way to a novel pharmaceutically promising amines and carboxylates of thiophene series that cannot be obtained by any known method. Generality and wide substrate scope of the developed approach have been supported by representative range of the substituents including alkoxy, acetal, alkoxycarbonyl, alkyl(aryl)amino, ferrocenylmethoxy, and other complex functions (e.g., vinyloxyethyl in the amino group), which are successfully introduced into the thiophene ring. Further studies on this topic are currently underway.

Scheme 5. Not Realized Amino-Imino Tautomerism in the Tetrasubstituted Alkyl 5-Aminothiophene-2-carboxylates Series



EXPERIMENTAL SECTION

General Comments. IR spectra were measured neat or as KBr pellets on a Bruker Vertex-70 infrared spectrophotometer. The ^{1}H (400.13 MHz), ^{13}C (100.62 MHz), ^{15}N (40.55 MHz), and ^{19}F (376.50 MHz) NMR spectra were recorded with a Bruker DPX-400 and Bruker AV-400 spectrometers in $CDCl_3$ at an ambient temperature. Chemical shifts (δ) are quoted in ppm, to the nearest 0.01 ppm (for ^{1}H) and 0.1 ppm (for ^{13}C, ^{15}N, and ^{19}F), and are referenced to HMDS (for ^{1}H), $CDCl_3$ (for ^{13}C), $MeNO_2$ (for ^{15}N), and $CFCl_3$ (for ^{19}F) as an internal standards. Coupling constants (J) are reported in Hertz (Hz) to the nearest 0.1 Hz. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), dd (doublet of doublet), dt (doublet of triplet), td (triplet of doublet), tt (triplet of triplet), dq (doublet of quartet), d sept (doublet of septet), dqt (doublet of quartet of triplet), m (multiplet), and br (broad). Assignments of spectra were carried out using 2D experiments. The mass spectra (electron impact, 70 eV) were obtained on a Shimadzu GCMS-QP5050A instrument. The microanalyses were performed on a Flash EA 1112 Series elemental analyzer. Melting points were determined using a SGW X-4 Melting-point apparatus with microscope.

Alkoxyallenes[17] and isothiocyanates[18] (except methyl, ethyl, and phenyl isothiocyanates) were prepared according to the reported procedures. *n*-BuLi (2.5 M solution in hexane), methyl and ethyl 2-bromoacetate, and solvents are commercially available. All solvents were purified according to standard procedures. All reactions were carried out under anhydrous conditions and under argon atmosphere. For all reactions at low temperatures, a cooling bath with liquid N_2 was used. Reaction courses and product mixtures were routinely monitored by thin-layer chromatography using precoated silica gel 60 F_{254} aluminum plates and visualized by exposure to I_2 vapor.

General Experimental Procedure for the Synthesis of Alkyl 4-Alkoxy-3-methyl-5-aminothiophene-2-carboxylates 2a–x. To a vigorously stirred solution of alkoxyallene **1a–e** (15–57 mmol) in dry THF (15–30 mL), *n*-BuLi (16–35 mmol, 6.5–14 mL) was added at −100 to −95 °C under an argon atmosphere. The temperature quickly rose to −40 to −20 °C. After stirring for an additional 5–10 min at ca. −55 to −40 °C, the solution was cooled to −90 °C, and a mixture of isothiocyanate (15–30 mmol) and THF (3–5 mL) was added in one portion. The temperature was allowed to rise to −45 to −15 °C. After being stirred for an additional 10–20 min at this temperature, the mixture was again cooled to ca. −80 °C and alkyl 2-bromoacetate (15–30 mmol) was added in one portion. The temperature quickly (in few minutes) rose to 15–25 °C. After stirring for 15 min at 10–18 °C, the reaction mixture was cooled, and then treated with saturated aqueous solution of NH_4Cl (20–30 mL). The layers were separated, and the aqueous phase was extracted with Et_2O (3 × 40 mL). The organic layers were combined, washed with H_2O (2 × 50 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give a residue consisting of corresponding alkyl 5-aminothiophene-2-carboxylate **2** (by ^{1}H NMR). Pure compounds **2** were isolated by column chromatography on neutral alumina, using hexane/Et_2O (10:1

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and/or 3:1, and/or 1:1) as eluent. Yields (based on isothiocyanate) and characteristic data of thiophenes **2a**–**x** are reported below.

*Methyl 4-methoxy-3-methyl-5-(methylamino)thiophene-2-carboxylate (**2a**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), methyl isothiocyanate (2.19 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2a** was obtained as orange powder (5.66 g, 88%), mp 76–77 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (br s, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 2.91 (d, ^3J = 5.1 Hz, 3H, NCH_3), 2.38 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 149.8 (C^5), 141.1 (C^3), 137.3 (C^4), 104.4 (C^2), 60.6 (OCH_3), 51.1 (CH_3OC=O), 33.3 (NCH_3), 12.6 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −327.7. IR (KBr): 3359, 3015, 2995, 2948, 2926, 2857, 2832, 1656, 1567, 1497, 1471, 1435, 1388, 1330, 1286, 1256, 1200, 1185, 1164, 1134, 1079, 1039, 988, 909, 803, 750, 709, 688, 553, 534 cm^{-1}. MS (EI) *m*/*z* (%) 216 (10) $[M+1]^+$, 215 (58) $[M]^+$, 200 (100), 186 (7), 184 (18), 173 (9), 141 (33), 140 (7), 115 (14), 114 (7), 113 (14), 99 (19), 83 (8), 74 (20), 70 (26), 67 (17), 59 (27), 45 (17), 42 (26), 39 (18). Anal. Calcd (%) for $C_9H_{13}NO_3S$ (215.270): C, 50.21; H, 6.09; N, 6.51; S, 14.90; found: C, 50.30; H, 6.03; N, 6.45; S, 14.78.

*Ethyl 4-methoxy-3-methyl-5-(methylamino)thiophene-2-carboxylate (**2b**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), methyl isothiocyanate (2.19 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Et$ (5.08 g, 30.4 mmol)], **2b** was obtained as orange crystals (6.34 g, 92%), mp 58–59 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (br s, 1H, NH), 4.25 (q, ^3J = 6.9 Hz, 2H, CH_3CH_2OC=O), 3.66 (s, 3H, OCH_3), 2.92 (br s, 3H, NCH_3), 2.38 (s, 3H, CH_3), 1.32 (t, ^3J = 6.9 Hz, 3H, CH_3CH_2OC=O). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (C=O), 149.5 (C^5), 140.7 (C^3), 137.2 (C^4), 104.7 (C^2), 60.5 (OCH_3), 59.8 (CH_3CH_2OC=O), 33.2 (NCH_3), 14.4 (CH_3CH_2OC=O), 12.6 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −329.3. IR (KBr): 3342, 2986, 2933, 2891, 1657, 1567, 1500, 1452, 1389, 1369, 1319, 1280, 1202, 1164, 1137, 1077, 1041, 976, 911, 858, 815, 750, 709, 688, 573, 527 cm^{-1}. MS (EI) *m*/*z* (%) 230 (19) $[M+1]^+$, 229 (66) $[M]^+$, 215 (15), 214 (100), 186 (50), 184 (25), 159 (13), 158 (18), 141 (13), 115 (30), 99 (31), 85 (10), 80 (10), 74 (19), 73 (10), 71 (26), 58 (11), 45 (15), 42 (22), 39 (15). Anal. Calcd (%) for $C_{10}H_{15}NO_3S$ (229.297): C, 52.38; H, 6.59; N, 6.11; S, 13.98; found: C, 52.23; H, 6.43; N, 6.01; S, 13.78.

*Methyl 5-(ethylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2c**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), ethyl isothiocyanate (2.61 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2c** was obtained as cream-colored crystals (5.45 g, 79%), mp 73–74 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (br s, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.67 (s, 3H, OCH_3), 3.19 (quint, $^3J_{NH-CH2}$ = 7.3, $^3J_{CH3-CH2}$ = 7.3 Hz, 2H, NCH_2CH_3), 2.38 (s, 3H, CH_3), 1.28 (t, ^3J = 7.3 Hz, 3H, NCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 148.3 (C^5), 140.9 (C^3), 137.5 (C^4), 104.5 (C^2), 60.5 (OCH_3), 51.0 (CH_3OC=O), 41.9 (NCH_2CH_3), 14.8 (NCH_2CH_3), 12.6 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −311.8. IR (KBr): 3331, 2965, 2942, 2890, 2840, 1667, 1560, 1492, 1457, 1430, 1410, 1386, 1317, 1280, 1269, 1190, 1159, 1125, 1072, 1050, 1000, 943, 912, 884, 820, 801, 754, 712, 651, 564, 533, 496 cm^{-1}. MS (EI) *m*/*z* (%) 230 (13) $[M+1]^+$, 229 (67) $[M]^+$, 215 (11), 214 (100), 198 (20), 186 (8), 173 (8), 155 (13), 154 (9), 141 (35), 140 (12), 127 (16), 126 (24), 115 (21), 114 (7), 113 (13), 101 (8), 99 (41), 85 (6), 83 (9), 72 (13), 71 (23), 70 (13), 69 (13), 67 (23), 66 (15), 60 (14), 59 (32), 45 (22), 42 (31), 39 (22). Anal. Calcd (%) for $C_{10}H_{15}NO_3S$ (229.297): C, 52.38; H, 6.59; N, 6.11; S, 13.98; found: C, 52.50; H, 6.40; N, 6.05; S, 13.88.

*Methyl 5-(isopropylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2d**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), isopropyl isothiocyanate (3.04 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2d** was obtained as amber viscous crystallizing liquid (5.03 g, 69%), mp 70–71 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (br s, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 3.47 [sept, ^3J = 6.4 Hz, 1H, $NCH(CH_3)_2$], 2.38 (s, 3H, CH_3), 1.25 [d, ^3J = 6.4 Hz, 6H, $NCH(CH_3)_2$]. $^{13}C_{jmod}$ NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 147.3 (C^5), 140.9 (C^3), 137.9 (C^4), 104.8 (C^2), 60.6 (OCH_3), 51.0 (CH_3OC=O), 49.1 [$NCH(CH_3)_2$], 23.0 [$NCH(CH_3)_2$], 12.6 (CH_3). The ^{1}H–^{13}C HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −296.2. IR (neat) 3312, 3117, 2995, 2955, 2922, 2878, 2856, 1671, 1634, 1597, 1544, 1521, 1463, 1382, 1338, 1302, 1262, 1229, 1200, 1181, 1145, 1078, 1012, 963, 906, 833, 785, 755, 712, 664, 584, 540 cm^{-1}. MS (EI) *m*/*z* (%) 244 (8) $[M+1]^+$, 243 (43) $[M]^+$, 229 (11), 228 (71), 212 (15), 200 (10), 187 (12), 186 (100), 154 (12), 140 (13), 126 (14), 115 (7), 99 (31), 83 (6), 72 (7), 71 (12), 70 (6), 67 (10), 66 (8), 59 (13), 45 (13), 43 (27), 42 (9), 41 (27), 39 (16). Anal. Calcd (%) for $C_{11}H_{17}NO_3S$ (243.324): C, 54.30; H, 7.04; N, 5.76; S, 13.18; found: C, 54.47; H, 6.93; N, 5.82; S, 13.25.

*Ethyl 5-(isopropylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2e**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), isopropyl isothiocyanate (3.04 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Et$ (5.08 g, 30.4 mmol)], **2e** was obtained as brown viscous liquid (6.26 g, 81%), n_D^{24} 1.558. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (q, ^3J = 7.1 Hz, 2H, CH_3CH_2OC=O), 4.19 (br s, 1H, NH), 3.66 (s, 3H, OCH_3), 3.46 [m, 1H, $NCH(CH_3)_2$], 2.38 (s, 3H, CH_3), 1.31 (t, ^3J = 7.1 Hz, 3H, CH_3CH_2OC=O), 1.25 [d, ^3J = 6.4 Hz, 6H, $NCH(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (C=O), 147.1 (C^5), 140.5 (C^3), 137.5 (C^4), 104.7 (C^2), 60.4 (OCH_3), 59.6 (CH_3CH_2OC=O), 48.8 [$NCH(CH_3)_2$], 22.8 [$NCH(CH_3)_2$], 14.4 (CH_3CH_2OC=O), 12.5 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −297.2. IR (neat) 3323, 2971, 2934, 2875, 1682, 1562, 1497, 1459, 1413, 1373, 1306, 1253, 1170, 1116, 1056, 1007, 961, 914, 871, 837, 756, 708, 578, 538, 511, 453 cm^{-1}. MS (EI) *m*/*z* (%) 258 (14) $[M+1]^+$, 257 (53) $[M]^+$, 243 (13), 242 (100), 212 (19), 201 (10), 200 (93), 173 (8), 172 (64), 170 (6), 154 (6), 145 (6), 144 (6), 140 (8), 126 (8), 115 (13), 114 (6), 99 (45), 83 (6), 72 (7), 71 (13), 70 (6), 67 (8), 66 (8), 60 (6), 45 (14), 43 (32), 42 (8), 41 (30), 39 (19). Anal. Calcd (%) for $C_{12}H_{19}NO_3S$ (257.350): C, 56.00; H, 7.44; N, 5.44; S, 12.46; found: C, 56.09; H, 7.35; N, 5.40; S, 12.39.

*Methyl 5-(n-butylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2f**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), *n*-butyl isothiocyanate (3.46 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2f** was obtained as yellow-brown viscous liquid (5.45 g, 71%), n_D^{23} 1.573. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (br t, ^3J = 6.0 Hz, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 3.14 [dt, ^3J = 6.7, ^3J = 6.0 Hz, 2H, $NCH_2C_3H_7$], 2.37 (s, 3H, CH_3), 1.65–1.57 [m, 2H, $NCH_2CH_2C_2H_5$], 1.43–1.34 [m, 2H, $N(CH_2)_2CH_2CH_3$], 0.92 [t, ^3J = 7.4 Hz, 3H, $N(CH_2)_3CH_3$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 148.6 (C^5), 140.9 (C^3), 137.2 (C^4), 103.9 (C^2), 60.5 (OCH_3), 50.9 (CH_3OC=O), 46.9 ($NCH_2C_3H_7$), 31.4 ($NCH_2CH_2C_2H_5$), 19.9 [$N(CH_2)_2CH_2CH_3$], 13.6 [$N(CH_2)_3CH_3$], 12.5 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −315.2. IR (neat) 3337, 3124, 2956, 2935, 2873, 1695, 1565, 1495, 1464, 1433, 1408, 1372, 1322, 1310, 1266, 1253, 1224, 1187, 1151, 1134, 1110, 1071, 1036, 985, 962, 918, 901, 852, 804, 787, 755, 713, 688, 670, 571, 536 cm^{-1}. MS (EI) *m*/*z* (%) 258 (8) $[M+1]^+$, 257 (46) $[M]^+$, 243 (15), 242 (100), 226 (16), 215 (6), 207 (6), 187 (7), 186 (54), 183 (7), 154 (13), 141 (6), 140 (7), 126 (7), 115 (8), 99 (15), 83 (7), 72 (6), 71 (8), 70 (13), 67 (13), 59 (9), 57 (12), 55 (6), 53 (10), 45 (9), 44 (11), 41 (25), 39 (17). Anal. Calcd (%) for $C_{12}H_{19}NO_3S$ (257.350): C, 56.00; H, 7.44; N, 5.44; S, 12.46; found: C, 56.04; H, 7.55; N, 5.37; S, 12.38.

*Methyl 5-(s-butylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2g**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), *s*-butyl isothiocyanate (3.46 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2g** was obtained as yellow-brown viscous liquid (5.94 g, 77%), n_D^{23} 1.570. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (d, ^3J = 7.6 Hz, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 3.23 [dqt, $^3J_{NH-CH}$ = 7.6, $^3J_{Me-CH}$

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= 6.5, $^3J_{CH2-CH}$ = 6.4 Hz, 1H, NC*H*(CH_3)C_2H_5], 2.38 (s, 3H, CH_3), 1.62, 1.53 [dqd, ^2J = 13.8, ^3J = 7.4, ^3J = 6.4 Hz, 2H, NCH(CH_3)-CH_2CH_3], 1.22 [d, ^3J = 6.5 Hz, 3H, NCH(CH_3)C_2H_5], 0.94 [t, ^3J = 7.4 Hz, 3H, NCH(CH_3)CH_2CH_3]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 147.7 (C^5), 140.9 (C^3), 137.6 (C^4), 104.1 (C^2), 60.4 (OCH_3), 54.8 [NCH(CH_3)C_2H_5], 50.9 (CH_3OC=O), 29.7 [NCH-(CH_3)CH_2CH_3], 20.4 [NCH(CH_3)C_2H_5], 12.5 (CH_3), 10.2 [NCH-(CH_3)CH_2CH_3]. ^{15}N NMR (40 MHz, $CDCl_3$) δ −301.2. IR (neat) 3325, 3113, 2966, 2935, 2876, 1693, 1681, 1564, 1495, 1458, 1433, 1419, 1406, 1374, 1349, 1314, 1267, 1251, 1188, 1121, 1106, 1070, 1038, 1013, 992, 973, 963, 939, 918, 891, 832, 792, 755, 712, 697, 539 cm^{-1}. MS (EI) *m*/*z* (%) 258 (5) $[M+1]^+$, 257 (30) $[M]^+$, 242 (48), 228 (15), 226 (9), 187 (10), 186 (100), 154 (8), 140 (7), 126 (5), 99 (13), 57 (8), 41 (10), 39 (5). Anal. Calcd (%) for $C_{12}H_{19}NO_3S$ (257.350): C, 56.00; H, 7.44; N, 5.44; S, 12.46; found: C, 56.09; H, 7.52; N, 5.42; S, 12.27.

*Methyl 5-(tert-butylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2h**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 3.50 g, 50.0 mmol), *tert*-butyl isothiocyanate (3.46 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2h** was obtained as dark-red viscous liquid (0.70 g, 9%), n_D^{23} 1.555. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (br s, 1H, NH), 3.78 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 1.36 [s, 9H, NC(CH_3)$_3$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (C=O), 144.4 (C^3), 140.1 (C^5), 139.6 (C^4), 106.3 (C^2), 60.6 (OCH_3), 52.7 [NC(CH_3)$_3$], 51.0 (CH_3OC=O), 29.2 [NC(CH_3)$_3$], 12.5 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −292.3. IR (neat) 3334, 2969, 2878, 1736, 1692, 1605, 1553, 1496, 1458, 1409, 1372, 1314, 1262, 1223, 1190, 1126, 1070, 1027, 958, 921, 879, 792, 757, 693, 599 cm^{-1}. MS (EI) *m*/*z* (%) 258 (7) $[M+1]^+$, 257 (32) $[M]^+$, 242 (12), 226 (6), 201 (32), 188 (8), 187 (17), 186 (100), 170 (10), 154 (8), 140 (9), 126 (9), 99 (19), 71 (8), 67 (8), 59 (7), 57 (63), 42 (8), 41 (43), 39 (17). Anal. Calcd (%) for $C_{12}H_{19}NO_3S$ (257.350): C, 56.00; H, 7.44; N, 5.44; S, 12.46; found: C, 55.84; H, 7.51; N, 5.38; S, 12.25.

*Methyl 4-methoxy-3-methyl-5-{[2-(vinyloxy)ethyl]amino}-thiophene-2-carboxylate (**2i**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), 2-(vinyloxy)ethyl isothiocyanate (3.88 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2i** was obtained as orange viscous liquid (4.59 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (dd, $^3J_{trans}$ = 14.4, $^3J_{cis}$ = 6.9 Hz, 1H, OCH=), 4.66 (br s, 1H, NH), 4.21 (dd, $^3J_{trans}$ = 14.4, $^2J_{gem}$ = 2.2 Hz, 1H, CH_2=), 4.04 (dd, $^3J_{cis}$ = 6.9, $^2J_{gem}$ = 2.2 Hz, 1H, CH_2=), 3.87 (t, ^3J = 4.9 Hz, 2H, OCH_2), 3.78 (s, 3H, CH_3OC=O), 3.67 (s, 3H, OCH_3), 3.43 (br q, $^3J_{NH-CH}$ = 4.9, $^3J_{CH-CH}$ = 4.9 Hz, 2H, NCH_2), 2.38 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 151.4 (OCH=), 147.5 (C^5), 141.2 (C^3), 138.6 (C^4), 105.6 (C^2), 87.5 (CH_2=), 66.0 (OCH_2), 60.7 (OCH_3), 51.2 (CH_3OC=O), 46.5 (NCH_2), 12.7 (CH_3). The ^{1}H−^{13}C HSQC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −322.7. IR (neat) 3347, 3117, 2995, 2935, 2876, 1678, 1620, 1568, 1495, 1458, 1433, 1406, 1375, 1351, 1321, 1273, 1257, 1183, 1139, 1073, 1032, 1001, 973, 878, 823, 789, 755, 714, 689, 610, 572, 537 cm^{-1}. MS (EI) *m*/*z* (%) 272 (9) $[M+1]^+$, 271 (59) $[M]^+$, 258 (6), 257 (12), 256 (100), 240 (10), 214 (15), 213 (10), 212 (55), 198 (10), 196 (9), 187 (6), 186 (23), 185 (71), 184 (7), 182 (6), 171 (8), 168 (9), 158 (9), 157 (11), 155 (6), 154 (16), 153 (39), 141 (7), 140 (15), 130 (18), 129 (8), 127 (18), 126 (9), 125 (7), 124 (6), 115 (11), 113 (8), 111 (6), 102 (8), 101 (6), 99 (47), 86 (11), 85 (9), 83 (14), 72 (41), 71 (21), 70 (12), 69 (11), 67 (16), 66 (9), 60 (6), 59 (28), 57 (11), 54 (8), 53 (9), 45 (42), 44 (11), 43 (17), 42 (12), 41 (10), 39 (16). Anal. Calcd (%) for $C_{12}H_{17}NO_4S$ (271.334): C, 53.12; H, 6.32; N, 5.16; S, 11.82; found: C, 53.24; H, 6.20; N, 5.10; S, 11.75.

*Methyl 5-(cyclopentylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2j**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (7 mL, 17.5 mmol), methoxyallene (**1a**, 2.30 g, 32.8 mmol), cyclopentyl isothiocyanate (1.91 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2j** was obtained as amber viscous crystallizing liquid (2.80 g, 69%), mp 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (d, ^3J = 6.1 Hz, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.69 (m, 1H, $H^{1'}$), 3.66 (s, 3H, CH_3O), 2.38 (s, 3H, CH_3), 2.03, 1.53 (m, 4H, $H^{2',5'}$), 1.71, 1.61 (m, 4H, $H^{3',4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 147.8 (C^5), 140.8 (C^3), 137.6 (C^4), 104.5 (C^2), 60.6 (OCH_3), 58.5 ($C^{1'}$), 51.1 (CH_3OC=O), 33.4 ($C^{2',5'}$), 23.9 ($C^{3',4'}$), 12.7 (CH_3). The ^{1}H−^{13}C HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −300.2. IR (neat) 3327, 3098, 2954, 2923, 2870, 1655, 1608, 1560, 1496, 1457, 1385, 1319, 1254, 1195, 1181, 1142, 1076, 990, 953, 916, 851, 823, 789, 755, 718, 564, 537 cm^{-1}. MS (EI) *m*/*z* (%) 270 (7) $[M+1]^+$, 269 (37) $[M]^+$, 255 (10), 254 (68), 238 (9), 188 (6), 187 (13), 186 (100), 154 (10), 126 (9), 99 (20), 72 (6), 71 (12), 69 (16), 67 (15), 59 (10), 45 (14), 41 (46), 39 (13). Anal. Calcd (%) for $C_{13}H_{19}NO_3S$ (269.361): C, 57.97; H, 7.11; N, 5.20; S, 11.90; found: C, 58.10; H, 7.06; N, 5.15; S, 11.78.

*Methyl 5-(cyclohexylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2k**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), cyclohexyl isothiocyanate (4.24 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2k** was obtained as amber very viscous crystallizing liquid (5.28 g, 62%), mp 56−57 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (br s, 1H, NH), 3.75 (s, 3H, CH_3OC=O), 3.64 (s, 3H, OCH_3), 3.07 (m, 1H, $H^{1'}$), 2.36 (s, 3H, CH_3), 2.06, 1.16 (m, 4H, $H^{2',6'}$), 1.73, 1.32 (m, 4H, $H^{3',5'}$), 1.60, 1.20 (m, 2H, $H^{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 147.3 (C^5), 140.9 (C^3), 137.9 (C^4), 104.4 (C^2), 60.5 (OCH_3), 56.3 ($C^{1'}$), 51.0 (CH_3OC=O), 33.4 ($C^{2',6'}$), 25.6 ($C^{4'}$), 24.8 ($C^{3',5'}$), 12.6 (CH_3). The ^{1}H−^{13}C HSQC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −300.2. IR (neat) 3325, 2925, 2854, 1665, 1608, 1562, 1492, 1452, 1430, 1367, 1347, 1322, 1302, 1258, 1183, 1149, 1100, 1075, 1036, 1003, 970, 912, 888, 845, 796, 755, 718, 698, 660, 592, 562, 539 cm^{-1}. MS (EI) *m*/*z* (%) 284 (4) $[M+1]^+$, 283 (26) $[M]^+$, 269 (7), 268 (44), 252 (6), 187 (11), 186 (100), 99 (10), 83 (10), 67 (6), 59 (7), 55 (31), 45 (8), 41 (26), 39 (8). Anal. Calcd (%) for $C_{14}H_{21}NO_3S$ (283.387): C, 59.34; H, 7.47; N, 4.94; S, 11.32; found: C, 59.17; H, 7.40; N, 5.03; S, 11.19.

*Methyl 5-(cycloheptylamino)-4-methoxy-3-methylthiophene-2-carboxylate (**2l**).* Following to the general experimental procedure [using: THF (15 mL), *n*-BuLi (7 mL, 17.5 mmol), methoxyallene (**1a**, 2.30 g, 32.8 mmol), cycloheptyl isothiocyanate (2.33 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2l** was obtained as amber viscous crystallizing liquid (3.38 g, 76%), mp 42−43 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (d, ^3J = 8.0 Hz, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 3.66 (s, 3H, OCH_3), 3.28 (m, 1H, $H^{1'}$), 2.38 (s, 3H, CH_3), 2.04, 1.58 (m, 4H, $H^{2',7'}$), 1.65, 1.52 (m, 8H, $H^{3',4',5',6'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (C=O), 147.5 (C^5), 141.0 (C^3), 137.6 (C^4), 104.3 (C^2), 60.6 (OCH_3), 58.5 ($C^{1'}$), 51.1 (CH_3OC=O), 35.1 ($C^{2',7'}$), 28.1 ($C^{3',6'}$), 24.2 ($C^{4',5'}$), 12.7 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −296.4. IR (neat) 3327, 2989, 2928, 2857, 1693, 1679, 1562, 1493, 1460, 1430, 1420, 1371, 1323, 1304, 1275, 1252, 1187, 1127, 1070, 1036, 993, 963, 919, 895, 836, 787, 755, 716, 697, 651, 561, 538 cm^{-1}. MS (EI) *m*/*z* (%) 298 (5) $[M+1]^+$, 297 (26) $[M]^+$, 282 (44), 266 (6), 187 (9), 186 (100), 99 (11), 97 (8), 71 (7), 67 (9), 59 (6), 55 (38), 45 (8), 41 (19), 39 (9). Anal. Calcd (%) for $C_{15}H_{23}NO_3S$ (297.414): C, 60.58; H, 7.79; N, 4.71; S, 10.78; found: C, 60.44; H, 7.85; N, 4.66; S, 10.60.

*Methyl 5-anilino-4-methoxy-3-methylthiophene-2-carboxylate (**2m**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), phenyl isothiocyanate (4.05 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2m** was obtained as yellow-brown very viscous crystallizing liquid (5.20 g, 63%), n_D^{19} 1.650; mp 61−62 °C (from hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (m, 2H, $H^{3',5'}$, Ph), 7.07 (d, ^3J = 7.6 Hz, 2H, $H^{2',6'}$, Ph), 6.91 (t, ^3J = 7.3 Hz, 1H, $H^{4'}$, Ph), 6.38 (br s, 1H, NH), 3.78 (s, 3H, CH_3OC=O), 3.71 (s, 3H, OCH_3), 2.41 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (C=O), 142.9 (C^4), 142.0 ($C^{1'}$, Ph), 139.6 (C^3), 137.9 (C^5), 129.3 ($C^{3',5'}$, Ph), 121.3 ($C^{4'}$, Ph), 115.9 ($C^{2',6'}$, Ph), 109.4 (C^2), 69.7 (OCH_3), 51.2 (CH_3OC=O), 12.4 (CH_3). The ^{1}H−^{13}C HMBC 2D

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experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −298.5. IR (neat) 3371, 3318, 3187, 3161, 3104, 3053, 2995, 2949, 2899, 2850, 1695, 1683, 1601, 1566, 1515, 1499, 1461, 1443, 1434, 1401, 1375, 1325, 1304, 1275, 1253, 1226, 1188, 1156, 1126, 1071, 1040, 1032, 1000, 961, 923, 883, 844, 829, 786, 753, 710, 693, 658, 618, 580, 550, 538 cm^{-1}. MS (EI) m/z (%) 278 (8) $[M+1]^+$, 277 (40) $[M]^+$, 263 (17), 262 (100), 246 (6), 159 (7), 115 (10), 104 (20), 99 (29), 77 (57), 72 (7), 71 (13), 69 (6), 67 (9), 59 (12), 51 (21), 45 (11), 39 (14). Anal. Calcd (%) for $C_{14}H_{15}NO_3S$ (277.340): C, 60.63; H, 5.45; N, 5.05; S, 11.56; found: C, 60.61; H, 5.54; N, 4.95; S, 11.47.

*Methyl 4-methoxy-3-methyl-5-[2-(trifluoromethyl)anilino]-thiophene-2-carboxylate (**2n**).* Following to the general experimental procedure [using: THF (20 mL), *n*-BuLi (10 mL, 25.0 mmol), methoxyallene (**1a**, 3.00 g, 42.8 mmol), 2-(trifluoromethyl)phenyl isothiocyanate (4.06 g, 20.0 mmol)/THF (5 mL), $BrCH_2CO_2Me$ (3.14 g, 20.5 mmol)], **2n** was obtained as colorless crystals (1.21 g, 18%), mp 102−103 °C (from hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, ^3J = 7.8 Hz, 1H, $H^{3'}$, Ph), 7.43 (dd, ^3J = 8.2, ^3J = 7.6 Hz, 1H, $H^{5'}$, Ph), 7.27 (d, ^3J = 8.2 Hz, 1H, $H^{6'}$, Ph), 6.96 (dd, ^3J = 7.8, ^3J = 7.6 Hz, 1H, $H^{4'}$, Ph), 6.36 (br s, 1H, NH), 3.82 (s, 3H, $CH_3OC{=}O$), 3.75 (s, 3H, OCH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (C=O), 146.5 (C^4), 141.2 ($C^{1'}$, Ph), 139.6 (C^3), 133.4 (C^5), 133.2 ($C^{5'}$, Ph), 126.8 ($C^{3'}$, Ph), 124.6 ($^1J_{CF}$ = 272.4 Hz, CF_3), 120.2 ($C^{4'}$, Ph), 116.2 (q, $^2J_{CF}$ = 29.6 Hz, $C^{2'}$), 116.2 ($C^{6'}$, Ph), 114.2 (C^2), 60.5 (OCH_3), 51.6 ($CH_3OC{=}O$), 12.6 (CH_3). The $^1H-^{13}C$ HSQC and $^1H-^{13}C$ HMBC 2D experiments provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −308.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ −61.2 (s, 3F, CF_3). IR (KBr): 3383, 3097, 3004, 2961, 2937, 2903, 2849, 1705, 1660, 1612, 1587, 1506, 1468, 1446, 1385, 1326, 1292, 1271, 1253, 1223, 1103, 1076, 1058, 1032, 998, 959, 949, 921, 860, 838, 806, 777, 762, 745, 737, 714 cm^{-1}. MS (EI) m/z (%) 346 (11) $[M+1]^+$, 345 (71) $[M]^+$, 332 (6), 331 (16), 330 (88), 314 (8), 311 (6), 310 (38), 282 (19), 262 (19), 251 (6), 250 (18), 222 (7), 184 (10), 172 (10), 162 (14), 153 (11), 152 (100), 145 (22), 126 (13), 125 (12), 115 (14), 102 (9), 100 (6), 99 (30), 95 (10), 83 (13), 75 (14), 72 (11), 71 (20), 70 (10), 69 (14), 67 (12), 63 (10), 59 (26), 51 (5), 50 (6), 45 (19), 39 (17). Anal. Calcd (%) for $C_{15}H_{14}F_3NO_3S$ (345.338): C, 52.17; H, 4.09; N, 4.06; S, 9.29; found: C, 51.98; H, 4.11; N, 3.92; S, 9.34.

*Methyl 5-(4-fluoroanilino)-4-methoxy-3-methylthiophene-2-carboxylate (**2o**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), methoxyallene (**1a**, 4.00 g, 57.1 mmol), 4-fluorophenyl isothiocyanate (4.77 g, 30.0 mmol)/THF (5 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2o** was obtained as amber viscous crystallizing liquid (6.46 g, 73%), mp 55−56 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.06 (m, 2H, $H^{2',6'}$, Ph), 6.97 (m, 2H, $H^{3',5'}$, Ph), 6.40 (br s, 1H, NH), 3.78 (s, 3H, $CH_3OC{=}O$), 3.71 (s, 3H, OCH_3), 2.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (C=O), 157.7 ($^1J_{CF}$ = 240.9 Hz, $C^{4'}$, Ph), 142.5 (C^4), 139.8 (C^3), 138.8 (C^5), 138.2 ($C^{1'}$, Ph), 117.8 ($^3J_{CF}$ = 8.0 Hz, $C^{2',6'}$, Ph), 115.9 ($^2J_{CF}$ = 22.8 Hz, $C^{3',5'}$, Ph), 108.8 (C^2), 60.6 (OCH_3), 51.3 ($CH_3OC{=}O$), 12.4 (CH_3). The $^1H-^{13}C$ HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −300.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ −121.3 (tt, $^3J_{H-F}$ = 8.0, $^4J_{H-F}$ = 4.6 Hz, 1F, F). IR (neat) 3388, 3321, 3174, 3116, 3071, 2996, 2951, 2906, 2843, 1698, 1684, 1611, 1568, 1510, 1466, 1427, 1402, 1375, 1329, 1289, 1276, 1256, 1226, 1189, 1157, 1127, 1099, 1072, 1041, 1007, 999, 962, 923, 856, 827, 799, 767, 757, 734, 719, 705, 658, 620, 554, 544, 504, 482, 429, 404 cm^{-1}. MS (EI) m/z (%) 296 (11) $[M+1]^+$, 295 (55) $[M]^+$, 282 (10), 281 (23), 280 (100), 264 (8), 159 (9), 131 (6), 127 (5), 126 (6), 122 (35), 115 (12), 110 (6), 100 (5), 99 (43), 96 (8), 95 (34), 83 (14), 75 (19), 72 (8), 71 (15), 70 (7), 69 (9), 67 (12), 59 (16), 45 (14), 39 (13). Anal. Calcd (%) for $C_{14}H_{14}FNO_3S$ (295.330): C, 56.94; H, 4.78; N, 4.74; S, 10.86; found: C, 57.09; H, 4.83; N, 4.61; S, 10.77.

*Methyl 4-ethoxy-3-methyl-5-(methylamino)thiophene-2-carboxylate (**2p**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), ethoxyallene (**1b**, 4.80 g, 57.1 mmol), methyl isothiocyanate (2.19 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2p** was obtained as brown viscous crystallizing liquid (5.40 g, 79%), n_D^{24} 1.585, mp 46−47 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 4.35 (br s, 1H, NH), 3.84 (q, ^3J = 6.9 Hz, 2H, OCH_2CH_3), 3.73 (s, 3H, $CH_3OC{=}O$), 2.91 (d, ^3J = 4.9 Hz, 3H, NCH_3), 2.37 (s, 3H, CH_3), 1.31 (t, ^3J = 6.9 Hz, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 150.0 (C^5), 141.4 (C^3), 136.5 (C^4), 104.7 (C^2), 68.9 (OCH_2CH_3), 51.0 ($CH_3OC{=}O$), 33.5 (NCH_3), 15.7 (CH_3), 12.9 (OCH_2CH_3). The $^1H-^{13}C$ HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −329.3. IR (neat) 3357, 3121, 2978, 2952, 2919, 2851, 2812, 1664, 1563, 1498, 1467, 1385, 1319, 1257, 1181, 1144, 1074, 1041, 967, 951, 925, 860, 805, 787, 755, 721, 683, 642, 551 cm^{-1}. MS (EI) m/z (%) 230 (3) $[M+1]^+$, 229 (31) $[M]^+$, 201 (10), 200 (100), 198 (12), 141 (25), 114 (8), 113 (10), 99 (13), 83 (5), 74 (11), 72 (4), 71 (6), 68 (11), 67 (11), 59 (14), 45 (8), 44 (10), 42 (16), 41 (7), 39 (7). Anal. Calcd (%) for $C_{10}H_{15}NO_3S$ (229.297): C, 52.38; H, 6.59; N, 6.11; S, 13.98; found: C, 52.50; H, 6.47; N, 6.17; S, 13.77.

*Methyl 5-anilino-4-ethoxy-3-methylthiophene-2-carboxylate (**2q**).* Following to the general experimental procedure [using: THF (20 mL), *n*-BuLi (8 mL, 20.0 mmol), ethoxyallene (**2b**, 2.58 g, 30.7 mmol), phenyl isothiocyanate (2.03 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2q** was obtained as amber viscous crystallizing liquid (2.16 g, 49%), n_D^{24} 1.637; light-sand colored solid; mp 77−78 °C (from hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 2H, $H^{3',5'}$, Ph), 7.09 (m, 2H, $H^{2',6'}$, Ph), 6.93 (m, 1H, $H^{4'}$, Ph), 6.30 (br s, 1H, NH), 3.93 (q, ^3J = 6.9 Hz, 2H, OCH_2CH_3), 3.79 (s, 3H, $CH_3OC{=}O$), 2.42 (s, 3H, CH_3), 1.31 (t, ^3J = 6.9 Hz, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4 (C=O), 141.9 ($C^{1'}$, Ph), 141.8 (C^4), 140.0 (C^3), 138.4 (C^5), 129.4 ($C^{3',5'}$, Ph), 121.4 ($C^{4'}$, Ph), 116.0 ($C^{2',6'}$, Ph), 109.1 (C^2), 69.2 (OCH_2CH_3), 51.4 ($CH_3OC{=}O$), 15.6 (OCH_2CH_3), 12.8 (CH_3). The $^1H-^{13}C$ HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −297.1. IR (KBr): 3367, 3101, 3054, 3021, 2971, 2927, 2892, 1708, 1598, 1568, 1509, 1463, 1405, 1383, 1311, 1286, 1253, 1219, 1187, 1135, 1067, 973, 942, 870, 833, 788, 754, 692, 640, 614, 578, 537, 499, 442 cm^{-1}. MS (EI) m/z (%) 292 (4) $[M+1]^+$, 291 (18) $[M]^+$, 263 (18), 262 (100), 159 (11), 104 (32), 99 (37), 83 (10), 77 (57), 71 (12), 67 (10), 59 (11), 51 (20), 45 (11), 39 (11). Anal. Calcd (%) for $C_{15}H_{17}NO_3S$ (291.366): C, 61.83; H, 5.88; N, 4.81; S, 11.01; found: C, 61.69; H, 5.80; N, 5.02; S, 11.05.

*Methyl 4-butoxy-3-methyl-5-(methylamino)thiophene-2-carboxylate (**2r**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), butoxyallene (**1c**, 4.00 g, 35.7 mmol), methyl isothiocyanate (2.19 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2r** was obtained as light-brown viscous liquid (6.90 g, 89%), n_D^{23} 1.567. ^1H NMR (400 MHz, $CDCl_3$) δ 4.34 (br s, 1H, NH), 3.77 (s, 3H, $CH_3OC{=}O$), 3.75 (t, ^3J = 6.6 Hz, 2H, $OCH_2C_3H_7$), 2.91 (d, ^3J = 3.9 Hz, 3H, NCH_3), 2.37 (s, 3H, CH_3), 1.68 (m, 2H, $OCH_2CH_2C_2H_5$), 1.45 [m, 2H, $O(CH_2)_2CH_2CH_3$], 0.95 [t, ^3J = 7.3 Hz, 3H, $O(CH_2)_3CH_3$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 149.8 (C^5), 141.3 (C^3), 136.4 (C^4), 104.2 (C^2), 73.1 ($OCH_2C_3H_7$), 51.0 ($CH_3OC{=}O$), 33.3 (NCH_3), 32.2 ($OCH_2CH_2C_2H_5$), 19.2 [$O(CH_2)_2CH_2CH_3$], 13.8 [$O(CH_2)_3CH_3$], 12.8 (CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −329.1. IR (neat) 3354, 2955, 2934, 2872, 1680, 1564, 1496, 1433, 1385, 1319, 1257, 1186, 1123, 1071, 1035, 966, 947, 917, 895, 836, 804, 787, 755, 720, 683, 650, 551, 487 cm^{-1}. MS (EI) m/z (%) 258 (4) $[M+1]^+$, 257 (22) $[M]^+$, 226 (6), 202 (7), 201 (17), 200 (100), 173 (11), 170 (7), 141 (24), 114 (9), 113 (11), 101 (6), 99 (13), 83 (6), 74 (13), 72 (4), 71 (7), 67 (10), 59 (14), 57 (6), 45 (7), 43 (5), 42 (17), 41 (14), 39 (10). Anal. Calcd (%) for $C_{12}H_{19}NO_3S$ (257.350): C, 56.00; H, 7.44; N, 5.44; S, 12.46; found: C, 56.14; H, 7.23; N, 5.35; S, 12.37.

*Methyl 4-butoxy-5-(isopropylamino)-3-methylthiophene-2-carboxylate (**2s**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), butoxyallene (**1c**, 4.00 g, 35.7 mmol), isopropyl isothiocyanate (3.04 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2s** was obtained as amber viscous liquid (6.59 g, 77%), n_D^{18} 1.551. ^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (d, ^3J = 7.8 Hz, 1H, NH), 3.77 (s, 3H, $CH_3OC{=}O$),

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3.75 (t, ^3J = 6.6 Hz, 2H, $OCH_2C_3H_7$), 3.46 [d sept, ^3J = 7.6, ^3J = 6.4 Hz, 1H, $NCH(CH_3)_2$], 2.37 (s, 3H, CH_3), 1.69 (m, 2H, $OCH_2CH_2C_2H_5$), 1.47 [m, 2H, $O(CH_2)_2CH_2CH_3$], 1.25 [d, ^3J = 6.4 Hz, 6H, $NCH(CH_3)_2$], 0.96 [t, ^3J = 7.3 Hz, 3H, $O(CH_2)_3CH_3$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 147.4 (C^5), 141.1 (C^3), 136.9 (C^4), 104.4 (C^2), 73.1 ($OCH_2C_3H_7$), 51.0 (CH_3OC=O), 48.9 [$NCH(CH_3)_2$], 32.2 ($OCH_2CH_2C_2H_5$), 23.0 [$NCH(CH_3)_2$], 19.2 [$O(CH_2)_2CH_2CH_3$], 13.8 [$O(CH_2)_3CH_3$], 12.8 (CH_3). The ^{1}H−^{13}C HMBC and ^{1}H−^{13}C HSQC 2D experiments provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −298.3. IR (neat) 3326, 2960, 2927, 2872, 1687, 1560, 1492, 1461, 1416, 1376, 1307, 1255, 1174, 1118, 1069, 1037, 955, 842, 787, 754, 715, 577, 507, 445 cm^{-1}. MS (EI) m/z (%) 286 (7) $[M+1]^+$, 285 (23) $[M]^+$, 254 (7), 230 (6), 229 (14), 228 (85), 187 (10), 186 (100), 154 (8), 126 (15), 100 (8), 99 (20), 83 (5), 71 (8), 67 (9), 59 (6), 57 (7), 45 (7), 43 (28), 42 (8), 41 (49), 39 (19). Anal. Calcd (%) for $C_{14}H_{23}NO_3S$ (285.403): C, 58.92; H, 8.12; N, 4.91; S, 11.24; found: C, 58.81; H, 7.97; N, 4.95; S, 11.02.

*Methyl 4-(1-ethoxyethoxy)-3-methyl-5-(methylamino)-thiophene-2-carboxylate (**2t**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), 1-(1-ethoxyethoxy)allene (**1d**, 4.50 g, 35.1 mmol), methyl isothiocyanate (2.19 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2t** was obtained as yellow-brown liquid (5.86 g, 72%), n_D^{20} 1.560. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (br s, 1H, NH), 4.92 (q, ^3J = 5.1 Hz, 1H, OCHO), 3.77 (s, 3H, CH_3OC=O), 3.69, 3.54 (dq, ^2J = 8.8, ^3J = 6.9 Hz, 2H, OCH_2CH_3), 2.90 (d, ^3J = 4.9 Hz, 3H, NCH_3), 2.34 (s, 3H, CH_3), 1.37 (d, ^3J = 5.1 Hz, 3H, $OCHCH_3$), 1.16 (t, ^3J = 6.9 Hz, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 151.3 (C^5), 141.5 (C^3), 133.1 (C^4), 104.2 (C^2), 103.8 (OCHO), 64.3 (OCH_2CH_3), 50.9 (CH_3OC=O), 33.2 (NCH_3), 20.6 ($OCHCH_3$), 15.3 (CH_3), 12.8 (OCH_2CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −327.6. IR (neat) 3356, 2981, 2938, 2883, 1688, 1566, 1501, 1441, 1387, 1316, 1257, 1182, 1065, 943, 853, 755, 722, 686, 557 cm^{-1}. MS (EI) m/z (%) 274 (3) $[M+1]^+$, 273 (7) $[M]^+$, 203 (15), 202 (31), 201 (100), 200 (27), 187 (5), 186 (35), 170 (38), 143 (20), 141 (12), 114 (8), 99 (13), 83 (6), 74 (23), 73 (73), 72 (9), 71 (11), 67 (13), 66 (6), 59 (15), 45 (94), 43 (11), 42 (15), 39 (9). Anal. Calcd (%) for $C_{12}H_{19}NO_4S$ (273.350): C, 52.73; H, 7.01; N, 5.12; S, 11.73; found: C, 52.65; H, 6.89; N, 5.02; S, 11.57.

*Methyl 4-(1-ethoxyethoxy)-5-(isopropylamino)-3-methylthiophene-2-carboxylate (**2u**).* Following to the general experimental procedure [using: THF (30 mL), *n*-BuLi (14 mL, 35.0 mmol), 1-(1-ethoxyethoxy)allene (**1d**, 4.50 g, 35.1 mmol), isopropyl isothiocyanate (3.04 g, 30.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (4.65 g, 30.4 mmol)], **2u** was obtained as yellow-brown liquid (6.74 g, 75%), n_D^{20} 1.543. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (d, ^3J = 7.8 Hz, 1H, NH), 4.93 (q, ^3J = 5.1 Hz, 1H, OCHO), 3.76 (s, 3H, CH_3OC=O), 3.76, 3.54 (dq, ^2J = 9.3, ^3J = 7.1 Hz, 2H, OCH_2CH_3), 3.44 [d sept, ^3J = 7.8, ^3J = 6.4 Hz, 1H, $NCH(CH_3)_2$], 2.33 (s, 3H, CH_3), 1.37 (d, ^3J = 5.1 Hz, 3H, $OCHCH_3$), 1.25 [d, ^3J = 6.4 Hz, 6H, $NCH(CH_3)_2$], 1.19 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 148.9 (C^5), 141.3 (C^3), 133.1 (C^4), 103.6 (C^2), 103.5 (OCHO), 64.3 (OCH_2CH_3), 50.8 (CH_3OC=O), 48.8 [$NCH(CH_3)_2$], 22.8 [$NCH(CH_3)_2$], 20.4 ($OCHCH_3$), 15.3 (CH_3), 12.8 (OCH_2CH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −295.4. IR (neat) 3319, 2974, 2932, 2874, 1691, 1563, 1498, 1455, 1424, 1380, 1304, 1254, 1175, 1117, 1090, 1057, 993, 940, 860, 792, 755, 725, 688, 587, 560, 496, 446 cm^{-1}. MS (EI) m/z (%) 302 (2) $[M+1]^+$, 301 (3) $[M]^+$, 231 (5), 230 (13), 229 (77), 228 (9), 214 (15), 198 (11), 187 (16), 186 (62), 126 (8), 99 (15), 73 (43), 72 (4), 71 (6), 67 (7), 59 (6), 45 (100), 43 (21), 42 (4), 41 (15), 39 (8). Anal. Calcd (%) for $C_{14}H_{23}NO_4S$ (301.403): C, 55.79; H, 7.69; N, 4.65; S, 10.64; found: C, 55.71; H, 7.56; N, 4.49; S, 10.47.

*Methyl 4-(ferrocenylmethoxy)-3-methyl-5-(methylamino)-thiophene-2-carboxylate (**2v**).* Following to the general experimental procedure [using: THF (25 mL), *n*-BuLi (6.5 mL, 16.2 mmol), 1-(ferrocenylmethoxy)allene (**1e**, 3.81 g, 15.0 mmol), methyl isothiocyanate (1.09 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2v** was obtained as amber viscous liquid (3.70 g, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (s, 2H, OCH_2Fc), 4.15 (m, 4H, $H^{\alpha,\beta}$, Fc), 4.10 (s, 5H, C_5H_5, Fc), 4.02 (br s, 1H, NH), 3.77 (s, 3H, CH_3OC=O), 2.71 (d, ^3J = 4.0 Hz, 3H, NCH_3), 2.32 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (C=O), 150.8 (C^5), 141.5 (C^3), 135.8 (C^4), 104.2 (C^2), 82.2 (C^i, Fc), 71.7 (OCH_2Fc), 69.6 (C^α, Fc), 69.1 (C^β, Fc), 68.4 (C_5H_5, Fc), 51.0 (CH_3OC=O), 33.3 (NCH_3), 12.9 (CH_3). The ^{1}H−^{13}C HMBC and ^{1}H−^{13}C HSQC 2D experiments provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −324.6. IR (neat) 3378, 3091, 2942, 2871, 1674, 1562, 1498, 1460, 1436, 1384, 1315, 1257, 1182, 1121, 1067, 1032, 953, 925, 884, 822, 756, 692, 641, 561, 488 cm^{-1}. MS (EI) m/z (%) 399 (3) $[M]^+$, 229 (5), 216 (6), 201 (19), 200 (18), 199 (100), 197 (7), 186 (10), 170 (10), 143 (6), 142 (6), 128 (5), 121 (28), 114 (6), 99 (8), 74 (12), 73 (11), 59 (12), 56 (14), 45 (16), 43 (11), 42 (12), 41 (11), 39 (7). Anal. Calcd (%) for $C_{19}H_{21}FeNO_3S$ (399.286): C, 57.15; H, 5.30; N, 3.51; S, 8.03; found: C, 57.33; H, 5.19; N, 3.48; S, 7.95.

*Methyl 5-(ethylamino)-4-(ferrocenylmethoxy)-3-methylthiophene-2-carboxylate (**2w**).* Following to the general experimental procedure [using: THF (25 mL), *n*-BuLi (7 mL, 17.5 mmol), 1-(ferrocenylmethoxy)allene (**1e**, 3.81 g, 15.0 mmol), ethyl isothiocyanate (1.31 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2w** was obtained as amber viscous liquid (4.39 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (s, 2H, OCH_2Fc), 4.14 (s, 4H, $H^{\alpha,\beta}$, Fc), 4.08 (s, 5H, C_5H_5, Fc), 3.94 (t, ^3J = 5.7 Hz, 1H, NH), 3.75 (s, 3H, CH_3OC=O), 2.94 (qd, ^3J = 7.2, $^3J_{NH-CH2}$ = 5.7 Hz, 2H, NCH_2CH_3), 2.33 (s, 3H, CH_3), 1.07 (d, ^3J = 7.2 Hz, 3H, NCH_2CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (C=O), 149.5 (C^5), 141.2 (C^3), 135.5 (C^4), 103.7 (C^2), 82.1 (C^i, Fc), 71.6 (OCH_2Fc), 69.5 (C^α, Fc), 69.0 (C^β, Fc), 68.2 (C_5H_5, Fc), 50.8 (CH_3OC=O), 41.5 (NCH_2CH_3), 14.4 (NCH_2CH_3), 12.8 (CH_3). The ^{1}H−^{13}C HMBC and ^{1}H−^{13}C HSQC 2D experiments provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −309.8. IR (neat) 3367, 3092, 2969, 2940, 2872, 1690, 1680, 1559, 1497, 1454, 1425, 1378, 1343, 1307, 1250, 1186, 1158, 1130, 1067, 1034, 977, 960, 914, 865, 822, 755, 703, 565, 489, 453 cm^{-1}. Anal. Calcd (%) for $C_{20}H_{23}FeNO_3S$ (413.313): C, 58.12; H, 5.61; N, 3.39; S, 7.76; found: C, 58.23; H, 5.78; N, 3.28; S, 7.55.

*Methyl 4-(ferrocenylmethoxy)-5-(isopropylamino)-3-methylthiophene-2-carboxylate (**2x**).* Following to the general experimental procedure [using: THF (25 mL), *n*-BuLi (6.5 mL, 16.2 mmol), 1-(ferrocenylmethoxy)allene (**1e**, 3.81 g, 15.0 mmol), isopropyl isothiocyanate (1.52 g, 15.0 mmol)/THF (3 mL), $BrCH_2CO_2Me$ (2.33 g, 15.2 mmol)], **2x** was obtained as amber viscous liquid (2.45 g, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.58 (s, 2H, OCH_2Fc), 4.16 (s, 2H, H^α, Fc), 4.14 (s, 2H, H^β, Fc), 4.01 (s, 5H, C_5H_5, Fc), 3.88 (br d, ^3J = 7.6 Hz, 1H, NH), 3.76 (s, 3H, CH_3OC=O), 3.28 [m, 1H, $NCH(CH_3)_2$], 2.34 (s, 3H, CH_3), 1.06 [d, ^3J = 6.4 Hz, 6H, $NCH(CH_3)_2$]. ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (C=O), 148.3 (C^5), 141.8 (C^3), 136.1 (C^4), 104.0 (C^2), 82.5 (C^i, Fc), 72.0 (OCH_2Fc), 70.0 (C^α, Fc), 69.5 (C^β, Fc), 68.6 (C_5H_5, Fc), 51.2 (CH_3OC=O), 48.6 [$NCH(CH_3)_2$], 22.9 [$NCH(CH_3)_2$], 13.2 (CH_3). The ^{1}H−^{13}C HMBC 2D experiment provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) δ −296.1. IR (neat) 3375, 3325, 3094, 2967, 2928, 2872, 1738, 1688, 1683, 1558, 1493, 1460, 1433, 1412, 1385, 1373, 1346, 1333, 1302, 1253, 1188, 1173, 1127, 1115, 1106, 1066, 1039, 1027, 1001, 961, 943, 924, 891, 861, 823, 755, 710, 690, 519, 497, 482 cm^{-1}. MS (EI) m/z (%) 427 (0.4) $[M]^+$, 228 (3), 200 (18), 199 (100), 197 (10), 186 (11), 126 (5), 121 (46), 99 (10), 56 (17), 43 (11), 39 (5). Anal. Calcd (%) for $C_{21}H_{25}FeNO_3S$ (427.339): C, 59.02; H, 5.90; N, 3.28; S, 7.50; found: C, 58.89; H, 6.01; N, 3.24; S, 7.43.

*Methyl 2-{[2-methoxy(methyl)buta-2,3-dienimidoyl]sulfanyl}-acetate (**3a**).* To a vigorously stirred solution of methoxyallene (**1a**, 2.00 g, 28.6 mmol) in dry THF (20 mL), *n*-BuLi (7 mL, 17.5 mmol) was added at −100 to −95 °C under argon. The temperature quickly rose to −48 °C. After stirring for an additional 8 min at −47 to −40 °C, the solution was cooled to −90 °C, and a mixture of methyl isothiocyanate (1.10 g, 15.0 mmol) and THF (3 mL) was added in one portion. The temperature was allowed to rise to −45 to −37 °C.

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After being stirred for an additional 10 min at this temperature, the mixture was again cooled to ca. −80 °C and methyl 2-bromoacetate (2.33 g, 15.2 mmol) was added in one portion. The temperature quickly rose to −40 °C. After stirring for 5 min at −43 to −40 °C, the reaction mixture was cooled to −90 °C, and then treated with saturated aqueous solution of NH_4Cl (10 mL). The layers were separated, and the aqueous phase was extracted with Et_2O (2 × 15 mL). The organic layers were combined, washed with H_2O (2 × 20 mL), dried ($MgSO_4$), and concentrated at rt under reduced pressure (on rotary evaporator, then at 1 mmHg) to give a residue (3.10 g, 96%), yellowish-brown transparent liquid, consisting of corresponding 1-aza-1,3,4-triene **3a** as a mixture of *E*- and *Z*-isomers (by NMR). ^{1}H NMR (400 MHz, $CDCl_3$) *(major isomer)* δ 5.73 (s, 2H, CH_2═C═), 3.70 (s, 3H, CH_3OC═O), 3.68 (s, 2H, SCH_2), 3.46 (s, 3H, OCH_3), 3.31 (s, 3H, NCH_3); *(minor isomer)* δ 5.75 (s, 2H, CH_2═C═), 3.73 (s, 3H, CH_3OC═O), 3.71 (s, 2H, SCH_2), 3.49 (s, 3H, OCH_3), 3.41 (s, 3H, NCH_3); the ratio of isomers ∼3:2. ^{13}C NMR (100 MHz, $CDCl_3$) *(major isomer)* δ 199.3 (═C═), 169.9 (C═O), 155.2 (N═C), 127.8 (═C−O), 94.1 (CH_2═C═), 55.9 (OCH_3), 52.2 (CH_3OC═O), 41.2 (NCH_3), 31.8 (SCH_2); *(minor isomer)* δ 200.8 (═C═), 169.1 (C═O), 156.4 (N═C), 132.0 (═C−O), 93.3 (CH_2═C═), 56.3 (OCH_3), 52.5 (CH_3OC═O), 41.2 (NCH_3), 34.0 (SCH_2). The ^{1}H−^{13}C HMBC and ^{1}H−^{13}C HSQC 2D experiments provided additional support for the proposed structure. ^{15}N NMR (40 MHz, $CDCl_3$) *(major isomer)* δ −84.5; *(minor isomer)* δ −58.8. IR (neat) 2953, 2864, 2835, 1944, 1740, 1623, 1545, 1456, 1445, 1436, 1396, 1295, 1268, 1200, 1156, 1091, 1047, 1007, 904, 779, 700, 568 cm^{-1}. Attempts to record mass spectrum of compound **3a** failed because the latter undergo cyclization and decomposition. Elemental analysis data for the 1-aza-1,3,4-triene **3a** were not done because it was impossible to purify the compound by the standard practices [during the vacuum distillation it cyclizes to compounds **6** and **7**, and upon chromatographic separation it decomposes].

*Methyl 2-[(3-methoxy-1-methyl-1H-pyrrol-2-yl)sulfanyl]acetate (**6**).* To a stirred solution of compound **3a** (3.34 g, 15.5 mmol) in dry THF (20 mL), CuBr (0.15 g) was added. The temperature rose to 43 °C. After stirring for an additional 30 min at rt, the reaction mixture was treated with saturated aqueous solution of NH_4Cl (10 mL) contained NaCN (0.2 g). The layers were separated, and the aqueous phase was extracted with Et_2O (2 × 15 mL). The organic layers were combined, washed with H_2O (2 × 20 mL), dried ($MgSO_4$), passed through neutral alumina layer (2 cm), and concentrated under reduced pressure to give a dark-brown mobile liquid (2.86 g, 86%), consisting of pyrrole **6**. Further purification by column chromatography on alumina (hexane/Et_2O, 3:1, 1:1) gave pyrrole **6** (1.81 g, 54%), yellow mobile liquid; n_D^{24} 1.542. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.23 (s, 2H, SCH_2), 3.59 (s, 3H, NCH_3), 3.64 (s, 3H, CH_3OC═O), 3.78 (s, 3H, OCH_3), 5.82 (d, ^3J = 2.8 Hz, 1H, H^4), 6.58 (d, ^3J = 2.8 Hz, 1H, H^5). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (C═O), 152.7 (C^3), 122.4 (C^5), 102.5 (C^2), 94.0 (C^4), 57.9 (OCH_3), 52.1 (CH_3OC═O), 38.6 (SCH_2), 34.0 (NCH_3). ^{15}N NMR (40 MHz, $CDCl_3$) δ −233.6. IR (neat) 3121, 2994, 2948, 2838, 1736, 1543, 1500, 1458, 1439, 1388, 1325, 1276, 1194, 1154, 1126, 1090, 1013, 971, 903, 839, 779, 721, 662, 602, 581, 480 cm^{-1}. Anal. Calcd (%) for $C_9H_{13}NO_3S$ (215.270): C, 50.21; H, 6.09; N, 6.51; S, 14.90; found: C, 50.42; H, 5.98; N, 6.38; S, 14.71.

*Cyclization of 1-Aza-1,3,4-triene **3a** into Methyl 2-[(3-Methoxy-1-methyl-1H-pyrrol-2-yl)sulfanyl]acetate (**6**) and Methyl 2-[(3-Methoxy-5,6-dihydropyridin-2-yl)sulfanyl]acetate (**7**) (A Qualitative Experiment).* A solution of 1-aza-1,3,4-triene **3a** in $CDCl_3$ (after recording the NMR spectra) was maintained for 3 days at ∼20 °C. A mixture of pyrrole **6** and dihydropyridine **7** was obtained in a ratio of about 2:1 (by ^{1}H NMR). Storage of 1-aza-1,3,4-triene **3a** at room temperature and even in the freezer also results in a mixture of compounds **6** and **7**. Product **7** was not isolated as an individual compound. ^{1}H NMR (400 MHz, $CDCl_3$) of pyrrole **6** δ 6.59 (d, ^3J = 2.8 Hz, 1H, H^5), 5.82 (d, ^3J = 2.8 Hz, 1H, H^4), 3.78 (s, 3H, OCH_3), 3.64 (s, 3H, CH_3OC═O), 3.59 (s, 3H, NCH_3), 3.23 (s, 2H, SCH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2 (C═O), 152.7 (C^3), 122.4 (C^5), 102.5 (C^2), 94.0 (C^4), 57.9 (OCH_3), 52.1 (CH_3OC═O), 38.6 (SCH_2), 34.0 (NCH_3). ^{1}H NMR (400 MHz, $CDCl_3$) of dihydropyridine **7** (tentative assignment) δ 5.10 (t, $^3J_{4-5}$ = 4.6 Hz, 1H, H^4), 3.70 (s, 2H, SCH_2), 3.70 (s, 3H, CH_3OC═O), 3.58 (s, 3H, OCH_3), 3.54 (m, 2H, 6-CH_2), 2.18 (td, $^3J_{5-6}$ = 8.0, $^3J_{5-4}$ = 4.6 Hz, 2H, 5-CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0 (C═O), 159.0 (C^2), 147.2 (C^3), 99.2 (C^4), 54.4 (OCH_3), 52.3 (CH_3OC═O), 48.0 (C^6), 30.4 (SCH_2), 21.0 (C^5). The assignment of the signals in the NMR spectra was made with the help of 2D experiments ^{1}H−^{1}H COSY, ^{1}H−^{13}C HMBC, ^{1}H−^{13}C HSQC.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01217.

Copies of NMR spectra of isolated compounds (PDF)

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Notes

The authors declare no competing financial interest.

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