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Synthesis of Oxidized Thienopyrroles using HOF·CH_3CN

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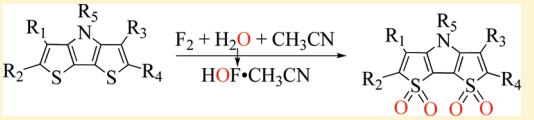
Supporting Information

ABSTRACT: An efficient transformation of the sulfur atoms to the sulfonyl group in a range of thienopyrroles was achieved by using the HOF·CH_3CN complex. Mild conditions, high yields, and easy purification are the main features of this novel route. Most new materials exhibit considerable red-shift absorptions in the UV/visible range relative to the parent compounds.



INTRODUCTION

The optical and electronic properties of conjugated organic materials are of considerable interest to many. Applications for these materials could be found in batteries, sensors, electrochromic devices, light-emitting diodes, and field effect transistors to mention a few.[1] In recent years, combining pyrrole and thiophene units into thienopyrroles is a topic of significant interest, as native polypyrrole and polythiophene materials are already well established in molecular electronics owing to their favorable optoelectronic properties.[2]

The ability to tune the electronic properties at the molecular level is of importance for efficient application of these materials. Tuning is typically accomplished through laborious synthetic modification, such as constructing certain side-chain functionalities.[1] However, in thienopyrroles such tuning may also be achieved by functionalization of the two heteroatoms, each in a different way. We describe here such a successful differentiation hoping to get the best out of each. The nitrogen atom could be attached to alkyl groups in order to achieve good solubility,[3] while the sulfur could, for example, be transformed into a sulfonyl moiety. The latter considerably reduce the HOMO−LUMO band gaps, usually a very desirable feature when various electronic applications are concerned. Specific oxidation of the thiophene ring is not easy since the harsh conditions, usually required to overcome the aromatic stabilization, could lead to Diels−Alder-type reactions, SO_2 eliminations, and the like. What is more, it was not clear whether it would be possible to transfer oxygens atoms specifically to the sulfur without affecting the neighboring basic nitrogen since we have already seen that both atoms are capable of being acceptors of electrophilic oxygen species.[4]

The complex of the hypofluorous acid with acetonitrile, readily prepared by passing dilute fluorine through aqueous CH_3CN, is considered today to be one of the best oxygen-transfer agents organic chemistry has to offer.[5] Unlike all other oxygen-transfer agents, HOF·CH_3CN is a unique source of a permanent electrophilic oxygen species since it is weakly bonded to the most electronegative element—fluorine. This complex is able to serve as an oxygen transfer agent even to very weak nucleophiles[6] under mild conditions. Some of the work with it was described in two reviews,[7] and later it was used for the preparation of episulfones,[8] poly- and fused oligothiophene *S,S*-dioxides,[9] various *N,N*-diazafluorenes,[10] tetrazole-3*N*-oxide derivatives which were believed to be inaccessible,[11] and many other firsts or difficult transformations. Exploring the possibilities offered by this reagent in transforming thienopyrroles directly into the corresponding *S,S*-dioxide derivatives was therefore quite attractive, and the results were rewarding.

RESULTS AND DISCUSSION

The first set of experiments concentrated on a two-ring system of thienopyrroles. Treating ethyl 2-methyl-4*H*-thieno[3,2-*b*]-pyrrole-5-carboxylate (**1a**),[12,13] with 2 molar equiv of HOF·CH_3CN for a few seconds at room temperature resulted in the formation of the previously unknown *S,S*-dioxide (**2a**) in 90% yield where none of the double bonds and the nitrogen atom were affected. Interestingly, the reaction produced neither the potentially possible *N,S,S*-trioxide nor sulfoxide, an issue we encountered previously.[8,14] When only 1 molar equiv of HOF·CH_3CN was applied to **1a**, 50% was converted to the sulfone **2a**, the balance being the starting material. Any attempt to fully oxidize **1a** to its *N,S,S*-trioxide derivative by adding an excess of HOF·CH_3CN was unsuccessful and resulted in the destruction of the starting material.

Groups with electron-withdrawing abilities did not have much impact on the reaction, and replacing the methyl group at the C-2 position with a bromine atom (compound **1b**[12,13]) did not change the outcome. The new ethyl 2-bromo-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate 1,1-dioxide (**2b**) was formed in 85% yield. Attaching the bromine to C-3 as in **1c**[12,13] also did not have much effect, and ethyl 3-bromo-4*H*-thieno[3,2-*b*]pyrrole-5-carboxylate 1,1-dioxide (**2c**) was formed practically instantaneously in quantitative yield. Obviously, the bromine atoms at these positions create many synthetic possibilities for the preparation of other *S,S*-dioxide derivatives.

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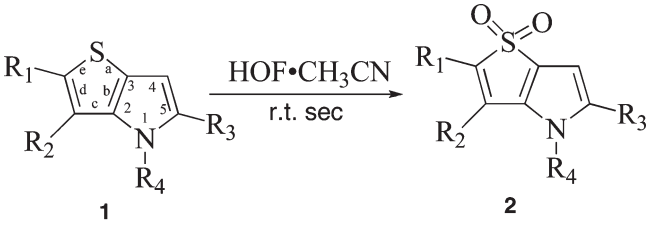
Scheme 1. Oxygenation of Thieno[3,2-*b*]pyrrole



a R_1 = Me; R_2 = R_4 = H; R_3 = COOEt 90%

b R_1 = Br; R_2 = R_4 = H; R_3 = COOEt 85%

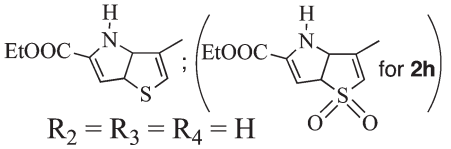
c R_1 = R_4 = H; R_2 = Br; R_3 = COOEt 95%

d R_1 = R_4 = Me; R_2 = H; R_3=COOEt 95%

e R_1 = Br; R_2 = H; R_3 = COOEt; R_4=Me 90%

f R_1, R_2 =  ; R_3 = COOEt; R_4 = H 90%

g R_1, R_2 =  ; R_3 = H; R_4 = H 75%

h R_1 =  for **2h** 85%

R_2 = R_3 = R_4 = H

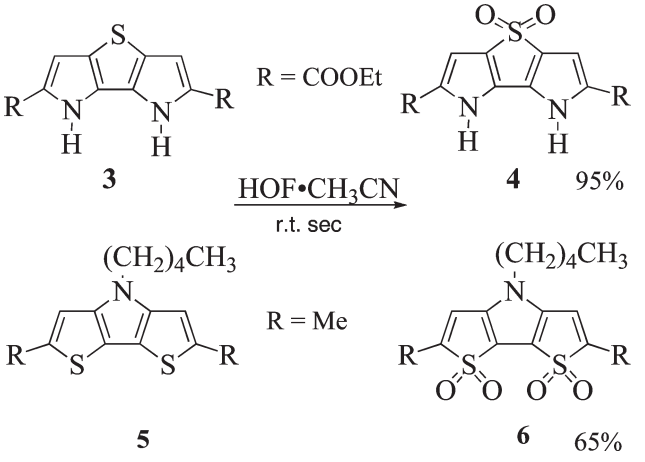
It was of interest to find out whether an *N*-functionalized thieno[3,2-*b*]pyrrole could be transferred to the corresponding *S,S*-dioxide as well. Ethyl 2,4-dimethylthieno[3,2-*b*]pyrrole-5-carboxylate (**1d**) and ethyl 2-bromo-4-methylthieno[3,2-*b*]-pyrrole-5-carboxylate (**1e**) proved that *N*-alkyl groups are compatible with the reaction as both were converted in excellent yields to their respective *S,S*-dioxides **2d** and **2e**.

Potential complications could have been expected with the annulation of an aromatic ring to the 1*H*-thieno[3,2-*b*]pyrrole system, since HOF·CH_3CN is even capable of epoxidizing benzene.[15] However, the initial attack of the reagent on the sulfur atom is much faster than on the aromatic ring as evident from the reactions of ethyl 1*H*-[1]benzothieno[3,2-*b*]pyrrole-2-carboxylate (**1f**)[13] and the unsubstituted 1*H*-[1]benzothieno-[3,2-*b*]pyrrole (**1g**) with HOF·CH_3CN producing the unknown ethyl 1*H*-[1]benzothieno[3,2-*b*]pyrrole-2-carboxylate 4,4-dioxide (**2f**) and 1*H*-[1]benzothieno[3,2-*b*]pyrrole 4,4-dioxide (**2g**) in seconds. A similar pattern was also observed with 4*H*,4*H*′-2,2′-bithieno[3,2-*b*]pyrroles such as **1h**. HOF·CH_3CN (4 molar equiv) was reacted with it to produce one regioisomer which proved to be diethyl 4*H*,4*H*′-2,2′-bithieno[3,2-*b*]pyrrole-5,5′-dicarboxylate 1,1,1′,1′-tetraoxide (**2h**) in 85% yield (Scheme 1).

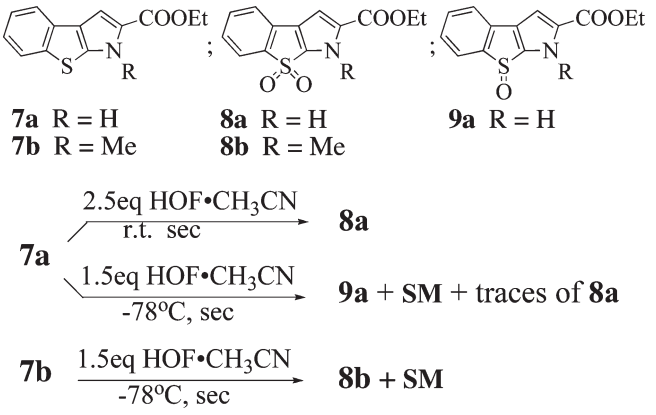
The reaction of thienopyrroles with HOF·CH_3CN was extended to some three-ring systems as well. One family constituted two pyrrole rings fused at each side of a central thiophene. Diethyl 4*H*,5*H*-thieno[3,2-*b*:4,5-*b*′]dipyrrole-3,6-dicarboxylate (**3**)[16] furnished, after a short treatment with HOF·CH_3CN complex, the new *S,S*-dioxide product **4** in high yield.

With two thiophene rings engulfing one pyrrole moiety as in *N*-pentyl 2,6-dimethylditheino[3,2-*b*;2′,3′-*d*]pyrrole (**5**), the

Scheme 2. Oxygenation of Three-Ring Systems



Scheme 3. Oxygenation of Thienopyrroles with Heteroatom Facing the Same Direction



reaction with the HOF·CH_3CN complex formed *N*-pentyl 2,6-dimethyldithieno[3,2-b;2′,3′-d]pyrrole 1,1,7,7-tetraoxide (**6**) instantaneously in 65% yield. Unlike other *S,S*-dioxides mentioned in this work, **6** was not very stable and decomposed with time. It is remarkable, however, that the selectivity toward the sulfur atoms was kept despite the fact that the degree of the aromaticity is higher on the outer rings compared to the inner one.[17] It seems that formation of tertiary *N*-oxides[18] is considerably slower then the attack on sulfur atoms even in cases when the latter is part of an aromatic system (Scheme 2).

Somewhat different results were observed with a system where the sulfur and nitrogen atoms are facing the same direction. When ethyl 1*H*-[1]benzothieno[2,3-*b*]pyrrole-2-carboxylate (**7a**) was reacted with 2.5 molar equiv of the reagent at room temperature only the sulfone **8a** was obtained in quantitative yield. However, when 1.5 molar equiv of the reagent was applied to **7a** at room temperature, 70% was converted to the sulfone **8a** but the balance of 30% proved to be the sulfoxide **9a** (Scheme 3). The amount of this sulfoxide could be further increased to 65% yield by lowering the reaction temperature to −78 °C, achieved by diluting the acetonitrile solution of the hypofluorous acid with propionitrile.[14] It is important to emphasize that under the same

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Scheme 4. Formation of Sulfone vs Sulfoxide in the Opposite Thienopyrrole Isomers

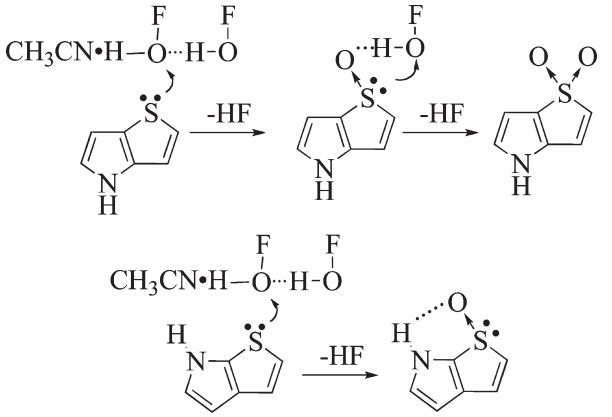
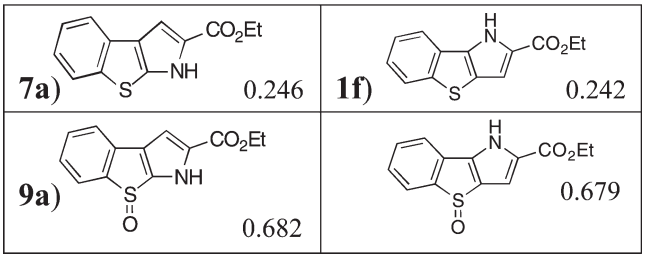


Table 1. Mulliken Charge on Sulfur Atom in Atomic Units



conditions (1.5 molar equiv at −78 °C) the isomeric **1f** was partly converted to the sulfone **2f** with only traces of the sulfoxide (less than 5%).

These conflicting observations could be explained by the fact that HOF·CH_3CN possesses both an acidic hydrogen and a fluoride, enabling formation of the reagent's clusters through hydrogen bonds. Thus, following the sulfoxide formation a second molecule of the agent is already in a close proximity to the sulfur atom ready to deliver the second oxygen atom.[14] When the pyrrole's acidic hydrogen in **7a** is facing the same direction of the thiophene's sulfur atom it provides a competing center for hydrogen bonding with the sulfoxide's oxygen, reducing the chances of two molecules of the reagent to approach the sulfur atom at two fast consecutive steps. When the oxidation was repeated with the *N*-functionalized ethyl 1-methylbenzothieno[2,3-*b*]-pyrrole-2-carboxylate (**7b**)[19] (1.5 molar equiv at −78 °C) almost no sulfoxide was formed, and the sulfone **8b** was the main product despite the steric hindrance from the methyl. A general graphic explanation for this phenomenon is presented in Scheme 4.

It was of interest to find out which thienopyrrole system, the one having the heteroatoms in *anti* configuration represented by **1f**, or the *syn* derivative **7a**, will be more reactive. We reacted an equimolar mixture of these two isomers with a solution of 2 molar equiv of HOF·CH_3CN. More than 70% of sulfone **2f** was formed, with the rest being the sulfone and the sulfoxide **8a** and **9a**. It seems that the closer proximity of the sulfur to the electronegative nitrogen in **7a** reduces this atom nucleophilicity, and consequently its affinity for the electrophilic oxygen of the HOF·CH_3CN, compared to **1f**. Support for this assumption is

Table 2. Absorption λ_{max} (in nm) and HOMO−LUMO Energy Gap (ΔE_g,[a] in eV) in Solution[b]

compd	λ_{max}[d] (ΔE_g)	$\Delta\Delta E_g$[c]
1a	295 (4.20)	
2a	*279*, 318 (3.90)	(0.3)
1b	296 (4.19)	
2b	*281*, 343 (3.61)	(0.58)
1c	286 (4.34)	
2c	*277*, 335 (3.70)	(0.64)
1d	296 (4.19)	
2d	*284*, 332 (3.73)	(0.46)
1e	298 (4.16)	
2e	*286*, 351 (3.53)	(0.43)
1f	270, *307* (4.04)	
2f	307 (4.04)	(0)
1g	285(4.35)	
2g	299 (4.15)	(0.2)
1h	334 (3.71)	
2h	340 (3.65)	(0.06)
3	385 (3.22)	
4	420, *441*, 465 (2.67)	(0.55)
5	302 (4.11)	
6	343 (3.62)	(0.49)
7a	309 (4.01)	
8a	307 (4.04)	(−0.03)
9a	309 (4.01)	(0)
7b	300 (4.14)	(−0.04)
8b	297 (4.18)	

[a] $\Delta E_g = hc/\lambda$. [b] CH_2Cl_2 solution. [c] $\Delta\Delta E_g = \Delta E_g$(SM) − ΔE_g(product). [d] These spectra consist of an italic maximum and corresponding vibronic splitting.

provided also by DFT calculations (B3LYP/6-311G(d,p)) carried out for **1f**, **7a**, and their sulfoxides. These focused on the Mulliken charge distribution on the sulfur atom (Table 1) and showed that its electron density is indeed higher for **1f** in both starting material and sulfoxide intermediate.

Some of the electronic properties of the products could be deduced from their UV−vis spectra. Table 2 lists the maximum wavelength absorption (λ_{max}), the HOMO−LUMO energy gap (ΔE_g), and the lowering of the HOMO−LUMO energy gap following the oxygen-transfer reaction ($\Delta\Delta E_g$). The table reveals that the oxidation of the sulfur atoms causes up to 50 nm red shift of the maximum absorption (λ_{max}). This indicates that a very desirable lowering of the HOMO−LUMO energy gap ($\Delta\Delta E_g$) has taken place. It had been reported in the past[1] that the presence of a benzenoidic ring could be responsible for a band gap reduction. Now it seems that an oxidation of the sulfur atom in compounds containing the aromatic moiety, as in **1f**−**h**, **7a**, and **7b**, does not induce further reduction in the HOMO−LUMO energy gap. While the use of an aromatic ring can be an excellent approach to low band gap polymers, the synthesis of such precursors can be laborious. The incorporation of oxygen atoms attached to the sulfur on the other hand, presents a simple and efficient alternative.

In conclusion, it has been shown that HOF·CH_3CN complex can oxidize, under very mild conditions, a wide range of fused thienopyrrole to the corresponding *S*,*S*-dioxide in excellent yields. The addition of oxygen atoms to thienopyrrole presents

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a unique type of functional organic materials which exhibit reduced band gap. In addition, considering the commercial availability of premixed fluorine/nitrogen mixtures which could be used by an occasional user and the technical ease of the reaction (no special equipment is required), indicates that this oxygen transfer reaction may become the method of choice in many cases were the alternatives are not potent enough.

EXPERIMENTAL SECTION

General Experimental Procedures. ^{1}H NMR spectra were recorded using a 400 MHz spectrometer with $CDCl_3$ as a solvent. The proton broadband decoupled ^{13}C NMR spectra were recorded at 100.5 MHz. Here too, $CDCl_3$ served as a solvent. IR spectra were recorded in KBr with an FTIR spectrometer. Usually the two strong peaks, between 1130 and 1310 cm^{-1}, are indicative to the SO_2 group. MS spectra were measured under ESI, CI, EI, or APPI conditions. UV spectra were recorded in CH_2Cl_2.

General Procedure for Working with Fluorine. Fluorine is a strong oxidant and a corrosive material. It should be used with an appropriate vacuum line. For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, making the process even simpler. Unreacted fluorine should be captured by a trap containing a base such as soda lime located at the outlet of the glass reactor. We have already described a proposed setup.[20] If elementary precautions are taken, the work with fluorine is simple and we have never experienced difficulties working with it.

General Procedure for Producing HOF·CH$_3$CN. A mixture of 10−20% F_2 in nitrogen was used throughout this work. The gas mixture was passed at a rate of about 400 mL/min through a cold (−15 °C) mixture of 100 mL CH_3CN and 10 mL H_2O in a regular glass reactor. The development of the oxidizing power was monitored by reacting aliquots with an acidic aqueous solution of KI. The liberated iodine was then titrated with thiosulfate. Typical concentrations of the oxidizing reagent were around 0.4−0.6 mol/L. The oxidizing reagent shelf life is 2−3 h at room temperature.

General Procedure for Transferring Oxygen Atoms to Thienopyrroles. A thienopyrrole derivative was dissolved in CH_2Cl_2 at room temperature. The oxidizing agent was than added in one portion to the reaction vessel. The reaction was stopped after a few seconds and the mixture was then poured into water, extracted with CH_2Cl_2, the organic layer dried over $MgSO_4$ and the solvent evaporated. The crude product was usually purified either by recrystallization or by vacuum flash chromatography using silica gel 60-H (Merck) with increasing portions of EtOAc in PE as an eluent.

Analytical Data. *Ethyl 2-Methyl-4H-thieno[3,2-b]pyrrole-5-carboxylate-1,1-dioxide (**2a**).* Compound **2a** was prepared from **1a**[12,13] (0.2 g, 0.96 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline pale yellow solid (0.21 g, 90% yield) was obtained: mp 216−217 °C (from hexane); λ_{max} 279, 318 nm; IR 3341, 1699, 1292, 1140 cm^{-1}; ^{1}H NMR 10.176 (bs, 1H), 6.999 (d, ^4J = 1.2 Hz, 1H), 6.563 (q, ^4J = 1.6 Hz, 1H), 4.350 (q, ^3J = 7.2 Hz, 2H), 2.178 (d, ^4J = 1.6 Hz, 3H), 1.373 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 161.2, 149.6, 137.3, 127.2, 121.4, 116.3, 110.0, 61.6, 14.4, 10.2 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{10}H_{11}NO_4S$ 264.0306 (M + Na)$^+$, found 264.0304. Anal. Calcd for $C_{10}H_{11}NO_4S$: N, 5.81; S, 13.29. Found: N, 5.64; S, 12.99 (unfortunately, at the time of the microanalysis the CH part of the machine was found to be out of order, but only after all of the **2a** was consumed).

*Ethyl 2-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylate 1,1-Dioxide (**2b**).* Compound **2b** was prepared from **1b**[12,13] (0.2 g, 0.73 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline pale orange solid (0.19 g, 85% yield) was obtained: mp 212−213 °C (from DCM); λ_{max} 281, 343 nm; IR 3198, 1691, 1294, 1148 cm^{-1}; ^{1}H NMR 10.041 (bs, 1H), 7.047−7.040 (m, 2H), 4.364 (q, ^3J = 7.2 Hz, 2H), 1.384 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.8, 135.7, 128.6, 127.9, 121.5, 120.7, 110.5, 61.9, 14.4 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_9H_8BrNO_4S$ 327.9255 (M + Na)$^+$, found 327.9247. Anal. Calcd for $C_9H_8BrNO_4S$: C, 35.31; H, 2.63; Br, 26.10; N, 4.58; S, 10.47. Found: C, 35.42; H, 2.59; Br, 25.96; N, 4.54; S, 10.40.

*Ethyl 3-Bromo-4H-thieno[3,2-b]pyrrole-5-carboxylate 1,1-Dioxide (**2c**).* Compound **2c** was prepared from **1c**[12,13] (0.2 g, 0.73 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline pale yellow solid (0.21 g, 95% yield) was obtained: mp 173−173.7 °C (from DCM); λ_{max} 271, 335 nm; IR 3117, 1685, 1298, 1139 cm^{-1}; ^{1}H NMR 10.092 (bs, 1H), 7.037 (d, ^4J = 2 Hz, 1H), 6.771 (s, 1H), 4.388 (q, ^3J = 7.2 Hz, 2H), 1.380 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.3, 135.7, 135.1, 129.3, 124.5, 117.0, 109.9, 62.1, 14.4 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_9H_8BrNO_4S$ 327.9255 (M + Na)$^+$, found 327.9253. Anal. Calcd for $C_9H_8BrNO_4S \cdot 0.5H_2O$: C, 34.30; H, 2.88; N, 4.44. Found: C, 34.68; H, 2.79; N, 4.21.

*Ethyl 2,4-Dimethylthieno[3,2-b]pyrrole-5-carboxylate (**1d**).* Compound **1d** was prepared from a solution of **1a** (0.42 g, 2 mmol) in anhydrous DMF (15 mL), and NaH (2 mmol) was added. After 1 h of stirring at room temperature, MeI (2 mmol) was added and the mixture stirred for a further 2 h at room temperature. The reaction mixture was then poured onto crushed ice and the solid filtered off and dried. A crystalline yellow solid (0.42 g, 95% yield) was obtained: mp 69−70 °C; λ_{max} 296 nm; ^{1}H NMR 7.094 (s, 1H), 6.628 (s, 1H), 4.306 (q, ^3J = 7.2 Hz, 2H), 3.993 (s. 3H), 2.554 (s, 3H), 1.363 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 162.0, 145.5, 144.6, 125.4, 120.4, 109.3, 108.5, 60.0, 34.6, 17.2, 14.6 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{11}H_{13}NO_2S$ 223.0667 (M)$^+$, found 223.0666.

*Ethyl 2,4-Dimethylthieno[3,2-b]pyrrole-5-carboxylate 1,1-Dioxide (**2d**).* Compound **2d** was prepared from **1d** (0.3 g, 1.34 mmol) as described above using 2 equiv of the oxidizing agent. A crystalline pale orange solid (0.33 g, 95% yield) was obtained: mp 157−158 °C (from hexane); λ_{max} 284, 332 nm; IR 1708, 1288, 1132 cm^{-1}; ^{1}H NMR 7.052 (s, 1H), 6.587 (q, ^4J = 2 Hz, 1H), 4.293 (q, ^3J = 7.2 Hz, 2H), 3.868 (s. 3H), 2.185 (d, ^4J = 2 Hz, 3H), 1.343 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.7, 149.1, 139.6, 127.6, 119.4, 114.9, 111.8, 60.8, 33.8, 14.4, 10.3 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{11}H_{13}NO_4S$ 278.0463 (M + Na)$^+$, found 278.0462. Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49; S, 12.56. Found: C, 51.85; H, 5.01; N, 5.34; S, 12.53.

*Ethyl 2-Bromo-4-methylthieno[3,2-b]pyrrole-5-carboxylate (**1e**).* Compound **1e** was prepared from **1b** (0.55 g, 2 mmol) as described for **1d**. A crystalline yellow solid (0.55 g, 95% yield) was obtained: mp 90−92 °C; λ_{max} 298 nm; ^{1}H NMR 7.074 (s, 1H), 6.995 (s, 1H), 4.319 (q, ^3J = 7.2 Hz, 2H), 3.999 (s, 3H), 1.369 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 161.8, 143.5, 126.3, 122.0, 116.0, 113.7, 108.9, 60.4, 34.8, 14.6 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{10}H_{10}BrNO_2S$ 286.9616 (M)$^+$, found 286.9610.

*Ethyl 2-Bromo-4-methylthieno[3,2-b]pyrrole-5-carboxylate 1,1-Dioxide (**2e**).* Compound **2e** was prepared from **1e** (0.3 g, 1.0 mmol) as described above using 2 equiv of the oxidizing agent. A crystalline orange solid (0.29 g, 90% yield) was obtained: mp 166−168 °C (from hexane); λ_{max} 286, 351 nm; IR 1711, 1310, 1149 cm^{-1}; ^{1}H NMR 7.082 (s, 1H), 7.076 (s, 1H), 4.306 (q, ^3J = 7.2 Hz, 2H), 3.891 (s, 3H) 1.350 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.5, 138.3, 128.2, 128.0, 120.6, 118.5, 112.4, 61.1, 34.1, 14.4 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{10}H_{10}BrNO_4S$ 341.9412 (M + Na)$^+$, found 341.9418. Anal. Calcd for $C_{10}H_{10}BrNO_4S$: C, 37.51; H, 3.15; Br, 24.96; N, 4.37; S, 10.02. Found: C, 37.21; H, 3.02; Br, 24.78; N, 4.25; S, 9.80.

*Ethyl 1H-[1]Benzothieno[3,2-b]pyrrole-2-carboxylate (**1f**).* Compound **1f** was prepared from benzo[*b*]thiophene-2-carboxaldehyde (1 g, 6.2 mmol) as described for **1a**−**c**.[13] A crystalline orange solid (0.45 g, 30% yield) was obtained: mp 191−192 °C; λ_{max} 270, 305 nm; ^{1}H NMR 10.126 (bs, 1H), 7.905 (d, J_{ortho} = 7.6 Hz, 1H),

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7.799 (d, J_{ortho} = 7.6 Hz, 1H), 7.404−7.310 (m, 2H), 7.184 (d, ^4J = 2 Hz, 1H), 4.451 (q, ^3J = 7.2 Hz, 2H), 1.451 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 161.9, 144.0, 136.4, 126.9, 126.3, 125.0, 124.5, 124.3, 123.6, 119.9, 108.5, 61.1, 14.7 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{13}H_{11}NO_2S$ 245.0511 $(M)^+$, found 245.0510.

Ethyl 1H-[1]Benzothieno[3,2-b]pyrrole-2-carboxylate 4,4-Dioxide (***2f***). Compound **2f** was prepared from **1f** (0.2 g, 0.82 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline white solid (0.2 g, 90% yield) was obtained: mp 288−289 °C (from DCM); λ_{max} 307 nm; IR 3252, 1700, 1289, 1142 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.867 (dd, J_{ortho} = 7.6, J_{meta} = 0.8 Hz, 1H), 7.811 (dd, J_{ortho} = 7.6, J_{meta} = 0.8 Hz, 1H), 7.690 (td, J_{ortho} = 7.6, J_{meta} = 0.8 Hz, 1H), 7.528 (td, J_{ortho} = 7.6, J_{meta} = 0.8 Hz, 1H), 7.205 (s, 1H), 4.328 (q, ^3J = 7.2 Hz, 2H), 1.317 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR (DMSO-d_6) 159.8, 144.7, 136.8, 133.8, 129.8, 128.5, 125.3, 123.0, 122.0, 121.1, 108.9, 60.8, 14.3 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{13}H_{11}NO_4S$ 300.0306 $(M + Na)^+$, found 300.0303. Anal. Calcd for $C_{13}H_{11}NO_4S$: C, 56.31; H, 4.00; N, 5.05; S, 11.56. Found: C, 56.20; H, 3.94; N, 4.99; S, 11.06.

1H-[1]Benzothieno[3,2-b]pyrrole (***1g***). A mixture of the ester **2f** (5 mmol), sodium hydroxide (0.6 g, 15 mmol), methanol (25 mL), and water (10 mL) was stirred and heated to reflux for 3 h, poured onto a mixture of ice, washed with water, and dried to afford the acid. The acid was dissolved into quinoline (20 mL). Copper powder (0.4 g) was added as catalyst. The mixture was heated to 200−230 °C until no gas bubbles were observed. After the solution was cooled slightly, the mixture was filtered and hexane was added to the filtrate. The organic solution was washed with 10% HCl solution until it turned clear. The organic solution then was washed with water until the washes were neutral. After drying over anhydrous $MgSO_4$, solvent was evaporated. A crystalline brown solid (0.56 g, 65% yield) was obtained: mp 117−118 °C; λ_{max} 285 nm; ^{1}H NMR 8.606 (bs, 1H), 7.811 (dd, J_{ortho} =8, J_{meta}= 0.8 Hz, 1H), 7.664 (dd, J_{ortho} =8, J_{meta}= 0.8 Hz, 1H), 7.353 (td, J_{ortho} =8, J_{meta}= 0.8 Hz, 1H), 7.249 (td, J_{ortho} =8, J_{meta}= 0.8 Hz, 1H), 7.056 (dd, ^3J = 2.8 Hz, 1H); 6.541 ppm (dd, ^3J = 2.8, ^4J = 2 Hz, 1H), ^{13}C NMR 142.3, 132.5, 127.0, 124.3, 124.1, 123.0, 122.9, 118.2, 102.7 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{10}H_7NS$ 173.0299 $(M)^+$, found 173.0302.

1H-[1]Benzothieno[3,2-b]pyrrole-4,4-dioxide (***2g***). Compound **2g** was prepared from **1g** (0.2 g, 1.16 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline brown solid (0.18 g, 75% yield) was obtained: mp 206−208 °C (from ethyl acetate); λ_{max} 299 nm; IR 3309, 1261, 1140 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.698 (dd, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.620−7.549 (m, 2H), 7.388 (td, J_{ortho} = 7.6, J_{meta}= 1.2 Hz, 1H), 7.124 (dd, ^3J = 2.8, ^3J = 2.4 Hz, 1H), 6.480 (dd, ^3J = 2.4, ^4J = 2 Hz, 1H); ^{13}C NMR (DMSO-d_6) 144.5, 133.6, 133.4, 128.1, 126.6, 125.7, 122.2, 121.8, 119.3, 102.9 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{10}H_7NO_2S$ 228.0095 $(M + Na)^+$, found 228.0093.

4H,4H′-2,2′-Bithieno[3,2-b]pyrrole-5,5′-dicarboxylate (***1h***). Compound **1h** was prepared from 5,5′-bis(formyl)-2,2′-bithiophene[21] (1 g, 4.5 mmol) as described for **1a**−**c**.[13] A crystalline orange solid (0.35 g, 20% yield) was obtained: mp 213-215 °C; λ_{max} 334 nm; ^{1}H NMR (DMSO-d_6) 12.140 (bs, 2H), 7.194 (s, 2H), 7.070 (s, 2H), 4.275 (q, ^3J = 7.2 Hz, 4H), 1.296 ppm (t, ^3J = 7.2 Hz, 6H); ^{13}C NMR (DMSO-d_6) 160.5, 141.9, 140.0, 126.7, 122.4, 108.1, 107.4, 60.1, 14.4 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{18}H_{16}N_2O_4S_2$ 411.0449 $(M + Na)^+$, found 411.0447.

4H,4H′-2,2′-Bithieno[3,2-b]pyrrole-5,5′-dicarboxylate 1,1,1′,1′-Tetraoxide (***2h***). Compound **2h** was prepared from **1h** (0.3 g, 0.77 mmol) as described above, using 4 equiv of the oxidizing agent. A crystalline red solid (0.29 g, 85% yield) was obtained: mp >380 °C (from2-propanol); λ_{max} 420, 441, 465 nm; IR 3393, 1717, 1305, 1142 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.321 (s, 2H), 7.176 (s, 2H), 4.322 (q, ^3J = 7.2 Hz, 4H), 1.309 ppm (t, ^3J = 7.2 Hz, 6H); ^{13}C NMR (DMSO-d_6) 159.5, 136.5, 136.1, 129.6, 121.8, 116.7, 110.0, 61.0, 14.3 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{18}H_{16}N_2O_8S_2$ 475.0246 $(M + Na)^+$, found 475.0246.

Diethyl 4H,5H-Thieno[3,2-b:4,5-b′]dipyrrole-3,6-dicarboxylate 1,1-Dioxide (***4***). Compound **4** was prepared from **3**[16] (0.2 g, 0.65 mmol) as described above, using 2 equiv of the oxidizing agent. A crystalline yellow solid (0.21 g, 95% yield) was obtained: mp 314−314.6 °C (from DCM); λ_{max} 340 nm; IR 3443, 1703, 1293, 1156 cm^{-1}; ^{1}H NMR (DMSO-d_6) 11.945 (bs, 2H), 7.137 (s, 2H), 4.298 (q, ^3J = 7.2 Hz, 4H), 1.301 ppm (t, ^3J = 7.2 Hz, 6H); ^{13}C NMR (DMSO-d_6) 159.5, 130.4, 129.0, 126.5, 109.8, 60.8, 14.3 ppm; HRMS (ESI) (*m*/*z*) calcd for $C_{14}H_{14}N_2O_6S$: 361.0470 $(M + Na)^+$, found 361.0474. Anal. Calcd for $C_{14}H_{14}N_2O_6S \cdot 0.5H_2O$: C, 48.41; H, 4.35; N, 8.07. Found: C, 48.74; H, 4.21; N, 7.93.

N-Pentyl 2,6-Dimethyldithieno[3,2-b;2′,3′-d]pyrrole (***5***). A solution of 3,3′-dibromo-5,5′-dimethyl-2,2′-bithiophene[22] (5.39 g, 15.3 mmol), NaO-*t*-Bu (3.54 g, 36.8 mmol), Pd_2dba_3 (0.350 g, 0.382 mmol), and BINAP (0.950 g, 1.53 mmol) in dry toluene (30 mL) was purged with argon for 20 min. Pentylamine (15.3 mmol) was added, and the mixture was stirred for 7 h at 110 °C under an argon atmosphere. After cooling, water (20 mL) was added, and the layers were separated. The water phase was extracted twice with diethyl ether. The combined organic layers were dried over $MgSO_4$, and the solvents were removed via rotary evaporation. Finally, the crude compound was purified by column chromatography (silica gel; eluent: hexane). A colorless oil was obtained (2.12 g, 50% yield): λ_{max} 420, 441, 465 nm; ^{1}H NMR 6.668 (s, 2H), 4.065 (t, ^3J = 7.2 Hz, 2H), 2.571 (s, 6H), 1.821 (qui, ^3J = 7.2 Hz, 2H), 1.367−1.297 (m, 4H), 0.883 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 142.8, 136.8, 112.9, 109.5, 47.4, 30.3, 29.2, 22.5, 16.9, 14.1 ppm; HRMS (CI) (*m*/*z*) calcd for $C_{15}H_{19}NS_2$ 278.1037 $(M + H)^+$, found 278.1026.

N-Pentyl 2,6-Dimethyldithieno[3,2-b;2′,3′-d]pyrrole-1,1,7,7-tetraoxide (***6***). Compound **6** was prepared from **5** (0.3 g, 1.08 mmol) as described above, using 4 equiv of the oxidizing agent. A yellow/brown oil (0.24 g, 65% yield) was obtained: λ_{max} 343 nm; ^{1}H NMR 6.499 (q, ^4J = 2 Hz, 2H), 3.901 (t, ^3J = 7.2 Hz, 2H), 2.140 (d, ^4J = 2 Hz, 6H), 1.663 (qui, ^3J = 7.2 Hz, 2H), 1.331−1.254 (m, 4H), 0.908 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 144.8, 138.9, 120.6, 115.9, 45.9, 31.2, 28.7, 22.3, 13.9, 10.1 ppm; HRMS (CI) (*m*/*z*) calcd for $C_{15}H_{19}NO_4S_2$: 342.0834 $(M+H)^+$, found: 342.0839.

Ethyl 1H-[1]Benzothieno[2,3-b]pyrrole-2-carboxylate (***7a***). Compound **7a** was prepared from benzo[*b*]thiophene-3-carboxaldehyde (1 g, 6.2 mmol) as described for **1a**−**c**.[13] A crystalline pale orange solid (0.96 g, 60% yield) was obtained: mp 160−162 °C; λ_{max} 309 nm; ^{1}H NMR 9.713 (bs, 1H), 7.831 (d, J_{ortho} = 7.6 Hz, 1H), 7.727 (d, J_{ortho} = 7.6 Hz, 1H), 7.406−7.370 (m, 2H), 7.279 (t, J_{ortho} = 7.6 Hz, 1H), 4.406 (q, ^3J = 7.2 Hz, 2H), 1.420 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 161.4, 139.9, 136.6, 131.7, 127.7, 127.3, 125.2, 124.0, 123.8, 121.2, 107.8, 60.9, 14.6 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{13}H_{11}NO_2S$ 245.0511 $(M)^+$, found 245.0509.

Ethyl 1H-[1]Benzothieno[2,3-b]pyrrole-2-carboxylate 8,8-Dioxide (***8a***). Compound **8a** was prepared from **7a** (0.2 g, 0.82 mmol) as described above, using 2.5 equiv of the oxidizing agent and chromatographed on silica gel using PE/EtOAc 50:50 as eluent. A crystalline white solid (0.25 g, 95% yield) was obtained: mp 243−244 °C; λ_{max} 307 nm; IR 3276, 1712, 1289, 1155 cm^{-1}; ^{1}H NMR 10.364 (bs, 1H), 7.644 (d, J_{ortho} = 7.6 Hz, 1H), 7.521 (t, J_{ortho} = 7.6 Hz, 1H), 7.425 (d, J_{ortho} = 7.6 Hz, 1H), 7.370 (t, J_{ortho} = 7.6 Hz, 1H), 6.995 (s, 1H), 4.429 (q, ^3J = 7.2 Hz, 2H), 1.412 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.4, 141.9, 133.8, 132.3, 130.7, 129.1, 128.5, 127.6, 122.3, 121.6, 107.5, 62.0, 14.4 ppm; HRMS (EI) (*m*/*z*) calcd for $C_{13}H_{11}NO_4S$ 277.0409 $(M)^+$, found 277.0407. Anal. Calcd for $C_{13}H_{11}NO_4S$: C, 56.31; H, 4.00; N, 5.05; S, 11.56. Found: C, 56.19; H, 3.92; N, 4.75; S, 11.35.

Ethyl 1H-[1]Benzothieno[2,3-b][1]pyrrole-2-carboxylate 8-Oxide (***9a***). Compound **9a** was prepared from **7a** (0.2 g, 0.82 mmol) as described above, using 1.5 equiv of the oxidizing agent at −78 °C, and chromatographed on silica gel using PE/EtOAc 20:80 as eluent. A crystalline white solid (0.14 g, 65% yield) was obtained: mp 173−174 °C; λ_{max} 309 nm; IR 3056, 1727, 1054 (SO) cm^{-1}; ^{1}H NMR 11.448

(bs, 1H), 7.816 (d, J_{ortho} = 7.6, 1H), 7.486−1.476 (m, 2H), 7.336 (ddd, J_{ortho} = 7.6, J_{ortho} = 6.6 J_{meta} = 4 Hz, 1H), 7.008 (s, 1H), 4.336 (q, ^3J = 7.2 Hz, 2H), 1.339 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.3, 148.6, 139.1, 133.7, 132.6, 131.5, 127.7, 127.5, 121.6, 107.5, 61.4, 14.4 ppm; HRMS (EI) (*m*/*z*) calcd for $C_{13}H_{11}NO_3S$ 261.0460 $(M)^+$, found 261.0458. Anal. Calcd for $C_{13}H_{11}NO_3S$: C, 59.76; H, 4.24; N, 5.36; S, 12.27. Found: C, 59.86; H, 4.50; N, 4.72; S, 12.20.

*Ethyl 1-Methyl[1]benzothieno[2,3-b][1]pyrrole-2-carboxylate (**7b**)*[19]. Compound **7b** was prepared from **7a** (0.49 g, 2 mmol) as described for **1d**. A crystalline yellow solid (0.49 g, 95% yield) was obtained: mp 124−126 °C; λ_{max} 300 nm; ^{1}H NMR 7.893 (dd, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.738 (dd, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.418 (s, 1H), 7.380 (td, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.260 (td, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 4.347 (q, ^3J = 7.2 Hz, 2H), 4.053 (s, 3H), 1.402 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 161.4, 141.5, 139.2, 132.2, 127.0, 125.2, 123.9, 123.7, 121.2, 109.6, 60.2, 36.2, 14.6 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{14}H_{13}NO_2S$ 259.0667 $(M)^+$, found 259.0671.

*Ethyl 1-Methyl[1]benzothieno[2,3-b][1]pyrrole-2-carboxylate 8,8-Dioxide (**8b**).* Compound **8b** was prepared from **7b** (0.2 g, 0.78 mmol) as described above, using 2 equiv of the oxidizing agent, and chromatographed on silica gel using PE/EtOAc 90:10 as eluent. A crystalline yellow solid (0.2 g, 90% yield) was obtained: mp 186.2−187 °C; λ_{max} 297 nm; IR 1708, 1291, 1164 cm^{-1}; ^{1}H NMR 7.618 (dd, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.500 (td, J_{ortho} = 7.6, J_{meta} = 1.2 Hz, 1H), 7.388−7.339 (m, 2H), 7.991 (s, 1H), 4.353 (q, ^3J = 7.2 Hz, 2H), 4.135 (s, 3H), 1.391 ppm (t, ^3J = 7.2 Hz, 3H); ^{13}C NMR 160.5, 142.0, 133.8, 129.1, 128.2, 124.6, 124.4, 124.1, 122.1, 121.4, 109.3, 61.2, 35.9, 14.5 ppm; HRMS (APPI) (*m*/*z*) calcd for $C_{14}H_{13}NO_4S$ 291.0565 $(M)^+$, found 291.0570.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR data of all new compounds and theoretical calculations details (including **z**-matrix). This material is available free of charge via the Internet at http://pubs.acs.org.

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