Triflic Anhydride-Promoted Cyclization of Sulfides: A Convenient Synthesis of Fused Sulfur Heterocycles

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Abstract: A new approach to the synthesis of annulated sulfur heterocycles based on triflic anhydride-promoted cyclization of the hetaryl(aryl) containing alkyl sulfides was elaborated. Smooth demethylation of initially formed cyclic sulfonium salts by treatment with triethylamine afforded a number of five-, six- and seven-membered fused sulfur heterocycles. Unexpected ring opening took place in the reaction of diethylamine with 5-membered sulfonium salts.

Key words: cyclizations, electrophilic aromatic substitutions, sulfur heterocycles, bicyclic compounds, sulfonylsulfonium salts

Triflic anhydride (trifluoromethanesulfonic anhydride) is a widely used reagent in organic synthesis due to the unique property of the trifluoromethansulfonate moiety, which belongs to the most activating functional groups for nucleophilic substitution reactions, documented by well-known solvolytic data, as well as many mechanistic and preparative applications.1 However, little is known about the oxidative properties of this reagent. Earlier we have reported that the oxidation of dialkyl sulfides with triflic anhydride leads to the formation of the corresponding dialkyltrifluoromethylsulfonylsulfonium salts.2 In general, it was found that the dialkyltrifluoromethylsulfonylsulfonium salts are active sulfonium electrophiles. The latter can be applied for mild oxidation of alcohols including unsaturated and saturated ones to the corresponding carbonyl compounds, and sulfides to sulfoxides. Moreover, new approaches to S–S dications,3 methyl hetaryl sulfides, and hetaryl sulfonium salts were also studied.4

In this paper we elaborate a novel method for the preparation hetaryl annulated 5-, 6- and 7-membered sulfur heterocycles based on the electrophilic cyclization of hetaryl(aryl) substituted aliphatic sulfides promoted by triflic anhydride. We have proposed that intramolecular cyclization of sulfides promoted by triflic anhydride can lead to cyclic sulfonium salts, and after their demethylation to sulfur heterocycles.

The proposed method includes intermediate formation of sulfonylsulfonium salts followed by electrophilic attack on the aromatic ring (Scheme 1).

We have taken into account the possibility of a competition between inter- and intramolecular reactions, and therefore we started our investigation on the cyclization of model sulfides having rather active MeSCH2CH2- and MeSCH2CH2CH2-substituents for electrophilic attack adjacent to heteroaromatics to avoid the formation of linear oligomers or polymers. In such case the formation of five and six-membered sulfonium salts could take place.

To study the scope and limitation of this new approach we have prepared a number of model sulfides having aromatic or heterocyclic fragment. Reaction of lithiated heterocycles 1 with ethylene oxide followed by transformation to tosylates 2 and treatment with MeSNa allowed us the simple preparation of model hetarylethyl sulfides 3 (Scheme 2).
In the synthesis of MeSCH$_2$CH$_2$CH$_2$-substituted derivatives 5, the key step was the alkylation of organolithiums 1 with excess of 1-bromo-3-chloropropane (Scheme 3). Treatment of the prepared chlorides 4 with sodium methylthiolate gave the target sulfides 5 in high yield.

Having in our hands the precursors for cyclization, we started the preparation of five- and six-membered sulfonium salts. We found that the reaction proceeds readily under low temperature to give condensed sulfur heterocycles up to 92% yield in the case of thiophene, benzo[b]thiophene and indole derivatives.

The method was found to be very sensitive to electronic factors – adjacent position to sulfide moiety should be very active for electrophilic substitution to form cyclic sulfonium salts. Our attempt at cyclization of 2-(2-methylsulfonyl)thiophene was unsuccessful due to formation of linear oligomers formed by intermolecular attack of sulfonysulfonylum salt at the 5-position of the heterocycle.

Table 1  Cyclization of MeS(CH$_2$)$_n$- and MeS(CH$_3$)$_n$-Substituted Heteroaromatics

<table>
<thead>
<tr>
<th>Sulfide</th>
<th>Sulfonium Salt</th>
<th>Yield (%)</th>
<th>Heterocycle</th>
<th>Yield (%)</th>
<th>Ring-Opened Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>6a</td>
<td>92</td>
<td>8a</td>
<td>69</td>
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</tr>
<tr>
<td>3b</td>
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<td>8b</td>
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<tr>
<td>3c</td>
<td>6c</td>
<td>75</td>
<td>8c</td>
<td>65</td>
<td>10c</td>
<td>87</td>
</tr>
<tr>
<td>3d</td>
<td>6d</td>
<td>51</td>
<td>8d</td>
<td>54</td>
<td>10d</td>
<td>64</td>
</tr>
<tr>
<td>5a</td>
<td>7a</td>
<td>–</td>
<td>–</td>
<td>75$^a$</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5b</td>
<td>–</td>
<td>–</td>
<td>9b</td>
<td>64$^a$</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5c</td>
<td></td>
<td>–</td>
<td>9c</td>
<td></td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*One-pot preparation.
thiophene ring, because the α-position of thiophene is significantly more reactive for electrophilic substitution than the β-position. However, cyclization of isomeric sulfide 3b proceeded quite smoothly. Polymerization can be prevented by introduction of a methyl group in 5-position. In such case, the formation of sulfonium salt proceeds almost quantitatively.

Unfortunately, only tars were formed in the reaction of triflic anhydride with furan-substituted sulfide 3e, probably due to the extremely high lability of furan to acids (Scheme 4).

Previsouly we have found that the demethylation of some sulfonium salts can be carried out very easily using diethylamine. Unexpected and very interesting results were obtained when we studied the demethylation of sulfonium salts with this reagent. The reaction of five-membered sulfonium salts with diethylamine led to ring-opened products instead of demethylation (Scheme 5). These products with aminoethyl fragment connected to a heterocyclic ring are attractive for medicinal chemistry (Table 1).

The reaction of diethylamine with six-membered sulfonium salts gave only the corresponding heterocyclic sulfides, no formation of ring-opened products was observed. For example, using diethylamine and triethylamine for demethylation of benzo[b]thiophene sulfonium salt 7a was found to work equally well leading to thiopyrane 9a in good yield.

Demethylation of six-membered cyclic sulfonium salts are in good agreement with literature data concerning dealkylation of sulfonium salts. The rate of nucleophilic substitution is much higher for benzyl and methyl substituted sulfonium salts (Bn > Me > Alk). We believe that high angular strain is the reason for ring opening in the case of 5-membered sulfonium salts; such a strain is important for condensed five-membered heterocycles. However, we succeeded in demethylation of sulfonium salts using the more bulky triethylamine. The use of this nucleophile permits selective preparation of heterocyclic sulfides up to 87% yield. We elaborated also a more convenient one-pot procedure without isolation of sulfonium salts, by treating the reaction mixture with triethylamine to afford the target heterocycles in reasonably high yield.

Very simple and straightforward alkylation of NH-heterocycles permits one-pot preparation of pyrrole and carbazole sulfide models for the reaction with triflic anhydride (Scheme 6).

Cyclization of these sulfides permits us to elaborate the new approach to thiazole, thiazine, and thiazepine derivatives. In the case of cyclization of carbazolyl sulfide 12d it was difficult to isolate the corresponding sulfonium salts, because the formation of 7-membered ring was accompanied with intermolecular polymerization. After demethylation with triethylamine, the target sulfide 14d was obtained in a very low yield of 11%. Nevertheless, all other cyclization leading to formation of 5- and 6-membered sulfonium salts took place quite smoothly. One-pot technique was also found acceptable for these nitrogen heterocycles (Table 2).

We also studied the cyclization of the easily available methythiomethyl-, methylthioethyl- and methylthiopropyl phenyl ethers. Unfortunately, the cyclizations of methythiomethyl- and methylthiopropyl phenyl ethers 15 were unsuccessful – complex mixture of sulfonium salts was formed (Scheme 7). Nevertheless, the formation of six-membered sulfonium salts took place almost quantitatively. The cyclization of naphthalene derivatives proceeded regioselectively giving isomeric sulfonium salts 17b and 17c (Scheme 7). Subsequent demethylation opened the way to benzannulated oxathiine derivatives 18b and 18c (Table 3).

In summary, we have elaborated a new approach to sulfur heterocycles based on electrophilic cyclization of sulfides promoted by triflic anhydride. Demethylation of the prepared sulfonium salts can be carried out using triethylamine to give annulated derivatives of thiophene, thiopyrane, thiazole, thiazine, and oxathiine. In the case of the reaction of 5-membered sulfonium salts
with diethylamine, formation of unusual ring-opened products were noted.

Melting points were determined in sealed capillaries and are uncorrected. Analytical TLC was performed on silica gel (Merck 60 F254) coated on aluminum plates visualizing by UV and by aqueous KMnO4. IR spectra were recorded with a UR-20 spectrometer. NMR spectra were recorded with Varian VXR-400 and Bruker AMX 400 spectrometers using TMS as an internal standard. Column chromatography was performed on silica gel (63–200 mesh, Merck). All solvents used were dried and distilled before use according to standard procedures. Organolithium compounds were prepared according to the literature techniques. Starting 2-bromoethyl aryl ethers were obtained from phenol or naphthols using literature procedure. Triflic anhydride was prepared as described in the literature from trifluoromethanesulfonic acid.

2-(Hetaryl)ethyl p-Toluenesulfonates 2; General Procedure
To a solution of organolithium compound (10 mmol) in THF was added an ethereal solution of ethylene oxide (2 M, 10 mL, 20 mmol) while maintaining the temperature between –70 °C and –60 °C. The mixture was then allowed to warm slowly (over ca. 1 h) to r.t. After quenching the reaction with sat. aq NH4Cl (100 mL), the mixture was extracted with Et2O (3 × 30 mL), the combined organic layers were dried (Na2SO4) and concentrated in vacuo. The crude product was dissolved in anhyd CH2Cl2 (50 mL) and cooled in an ice-bath, whereupon pyridine (1 mL, 12 mmol) was added with stirring, followed by TsCl (1.1 g, 6 mmol) in one portion. The mixture was stirred for 1 h and allowed to stand at 0 °C for 12 h. Then the reaction was quenched with H2O (100 mL) containing AcOH (1 mL), the organic layer was separated, and the aqueous layer was extracted with CH2Cl2 (2 × 30 mL). The combined extracts were dried (Na2SO4) and carefully concentrated in vacuo at r.t. The residue was washed with hexane (2 × 30 mL) and dried in vacuo.

2-(5-Methyl-2-thienyl)ethyl 4-Methylbenzenesulfonate (2a)
Yield: 64%; colorless crystals; mp 32–34 °C (Lit. mp 35.5–36.5 °C).

2-(3-Thienyl)ethyl 4-Methylbenzenesulfonate (2b)
Yield: 73%; colorless crystals; mp 38–40 °C (Lit. mp 47.2–47.8 °C).

2-(1-Benzothien-2-yl)ethyl 4-Methylbenzenesulfonate (2c)
Yield: 81%; colorless crystals; mp 74–76 °C (Lit. mp 78.0–78.8 °C).

2-(1-Methyl-1H-indol-2-yl)ethyl 4-Methylbenzenesulfonate (2d)
Yield: 72%; colorless crystals; mp 132–133 °C (Lit. mp 134–135 °C).

3-Chloropropylhetarenes 4; General Procedure
A solution of organolithium compound (10 mmol) in THF containing HMPTA (5 mL) was cooled to –90 °C. Then 1-bromo-3-chloropropene (1.3 mL, 18 mmol) was added in one portion. The mixture was stirred for 1 h and allowed to warm to r.t. After quenching with...
H₂O (200 mL), the mixture was extracted with CH₂Cl₂ (3 × 30 mL), the combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: hexane) to yield the 3-chloropropylheteroarenes.

2-(3-Chloropropyl)-1-benzothiophene (3a)

Yield: 71%; colorless viscous oil.

1H NMR (CDCl₃): δ = 7.75 (d, 1 H, J = 7.7 Hz, ArH), 7.66 (d, 1 H, J = 7.3 Hz, ArH), 7.50 (dd, 1 H, J = 8.3, 7.3 Hz, ArH), 7.24 (dd, 1 H, J = 8.3, 7.7 Hz, ArH), 7.02 (s, 1 H, ArH), 3.56 (t, 2 H, J = 6.4 Hz, CH₂Cl), 3.06 (t, 2 H, J = 7.2 Hz, ArCH₂), 2.20–2.13 (m, 2 H, CH₂CH₂Cl).

13C NMR (CDCl₃): δ = 144.10 (Ar), 130.42, 127.69, 123.93, 122.75, 121.91 (5C, Ar), 43.76 (CH₂Cl), 33.50 (ArCH₂), 27.65 (CH₃CH₂Cl).


1-Methyl-2-[2-(methylsulfanyl)ethyl]-1H-indole (4c)

Yield: 86%; colorless oil.

1H NMR (CDCl₃): δ = 7.80 (d, 1 H, J = 8.0 Hz, ArH), 7.71 (d, 1 H, J = 8.1 Hz, ArH), 7.34 (d, 1 H, J = 7.3 Hz, ArH), 7.25 (t, 2 H, J = 7.5 Hz, ArCH₂), 2.90 (t, 2 H, J = 7.2 Hz, ArCH₂), 2.82 (s, 3 H, SCH₃).

13C NMR (CDCl₃): δ = 148.10 (C₆Ar), 127.98, 125.47, 120.81 (3 C, Ar), 34.95 (SCH₃), 30.27 (ArCH₂), 15.62 (SCH₃).

Anal. Calcd for C₁₁H₁₀S₂: C, 52.98; H, 6.32.

2-[2-(Methylsulfanyl)ethyl]-1-benzothiophene (3b)

Yield: 85%; colorless oil.

1H NMR (CDCl₃): δ = 7.06 (d, 1 H, J = 5.2, 2.9 Hz, ArH), 7.03 (br s, 1 H, ArH), 6.98 (d, 1 H, J = 5.2 Hz, ArH), 2.95 (t, 2 H, J = 7.7 Hz, ArCH₂), 2.78 (t, 2 H, J = 7.7 Hz, SCH₂), 2.14 (s, 3 H, SCH₃).

13C NMR (CDCl₃): δ = 141.92, 137.36 (2 C₆Ar), 124.55, 124.03 (2 C, Ar), 33.20 (SCH₃), 30.73 (ArCH₂), 28.78 (ArCH₂CH₂S), 15.31, 15.19 (2 C, ArCH₂ and SCH₃).
The reaction was carried out under the similar manner to that described in literature as described above from pyrrole (1.3 g, 20 mmol) and 1-chloro-3-(methylthio)propane (2 g, 20 mmol); yield: 4.3 g (84%); white crystals; mp 64–66 °C.

13 NMR (CDCl3): δ = 8.18 (d, 2 H, CH2S), 7.65 (d, 2 H, Ar), 4.42 (t, 2 H, J = 7.2, 7.2 Hz, CH2S), 2.88 (t, 2 H, J = 6.7 Hz, OCH2), 2.17 (s, 3 H, SCH3).

Yield: 92%; colorless crystals; mp 110–112 °C (dec.).

1H NMR (CDCl3): δ = 5.50 (s, 1 H, ArH), 5.47 (s, 1 H, ArH), 3.75 (t, 2 H, J = 6.7 Hz, OCH2), 1.13 (t, 3 H, SCH3).

Anal. Calcd for C8H14NS: C, 61.89; H, 8.44 (2 C, Ar), 119.13 (2 C, Ar), 108.40 (2C, Ar), 42.87 (NCH3), 32.52 (SCH2), 15.79 (SCH3).

13 C NMR (CDCl3): δ = 139.68 (2 C, Ar), 123.81 (2 C, Ar), 120.19 (2 C, Ar), 119.13 (2 C, Ar), 108.40 (2C, Ar), 42.87 (NCH3), 32.52 (SCH2), 28.17 (NCH3CH2CH2S), 16.62 (SCH2).

Anal. Calcd for C10H17NS: C, 75.25; H, 6.47. Found: C, 75.00; H, 6.32.

9-[3-(Methylsulfanyl)propyl]-9H-carbazole (12d)

This compound was prepared in an analogous manner to that of 12c as described above from carbazole (3.3 g, 20 mmol) and 1-chloro-3-(methylthio)propene (2.5 g, 20 mmol); yield: 4.3 g (84%); white crystals; mp 64–66 °C.

1H NMR (CDCl3): δ = 8.15 (d, 2 H, J = 7.7 Hz, ArH), 7.54 (d, 2 H, J = 7.2, 8.1 Hz, ArH), 7.48 (d, 2 H, J = 8.1 Hz, ArH), 7.34 (d, 2 H, J = 7.7, 7.7 Hz, ArH). 4.42 (t, 2 H, J = 7.2, 7.2 Hz, NCH2), 2.88 (t, 2 H, J = 6.7 Hz, NCH2), 2.17 (s, 3 H, SCH3).

Anal. Calcd for C10H17NS: C, 75.25; H, 6.47. Found: C, 75.00; H, 6.32.

**Cyclization of Sulfides 3a–d, 5a, 12a–c; General Procedure**

To a stirred solution of triflic anhydride (0.9 mL, 5.5 mmol) in anhyd CH2Cl2 (50 mL) was added dropwise a solution of the corresponding sulfide (5 mmol) in anhyd CH2Cl2 (10 mL) while maintaining the temperature between –50 and –60 °C. The mixture was then allowed to stand overnight at –20 °C. Then anhyd Et2O (70 mL) was added slowly, the precipitate formed was collected, washed with Et2O (2 × 20 mL), and dried in vacuo. If the product was obtained as an oil, it was recrystallized from MeCN–Et2O (1:1, 30 mL).

1,5-Dimethyl-2,3-dihydrothieno[3,2-b]thiophen-1-ium Trifluoromethanesulfonate (6a)

Yield: 92%; colorless crystals; mp 110–112 °C (dec.).

IR (Nujol): 3000–2800, 1750–1200, 1100–900 cm⁻¹.

1H NMR (CDCl3): δ = 7.00 (s, 1 H, ArH), 4.41 (ddd, 1 H, J = 8.0, 8.4, 13.6 Hz, S′CH3), 4.14 (ddd, 1 H, J = 2.0, 7.2, 13.6 Hz, S′CH3), 2.73 (s, 3 H, SCH3).

13 C NMR (CDCl3): δ = 140.06 (2 C q , Ar), 125.58 (2 C, Ar), 122.98 (2 C q , Ar), 120.19 (2 C, Ar), 119.13 (2 C, Ar), 108.40 (2C, Ar), 42.87 (NCH3), 32.52 (SCH2), 15.79 (SCH3).

Anal. Calcd for C10H17NS: C, 75.25; H, 6.47. Found: C, 75.00; H, 6.32.
1-Methyl-2,3-dihydrothieno[2,3-b]thiophen-1-ium Trifluoromethanesulfonate (6b)  
Yield: 63%; colorless crystals; mp 93–95 °C (dec.).

IR (Nujol): 1300–1100, 1040 cm⁻¹.

13C NMR (CD₃CN): δ = 157.67, 121.90 (q, 2 C, Ar), 121.17 (q, 2 C, Ar), 121.17 (q, J = 318.6 Hz, CF₃), 52.15 (S + CH₂), 30.96 (ArCH₂), 29.80 (S + CH₂).


1-Methyl-2,3-dihydrothieno[3,2-b][1]benzothiophen-1-ium Trifluoromethanesulfonate (6c)  
Yield: 75%; colorless crystals; mp 112–113 °C (dec.).

IR (Nujol): 1300–1100, 1040 cm⁻¹.

13C NMR (CD₃CN): δ = 156.95, 145.20, 131.63 (3 C q, Ar), 127.16, 126.85, 125.02, 122.40 (4 C, Ar), 122.12 (q, J = 320.0 Hz, CF₃), 121.24 (C q, Ar), 51.33 (S + CH₂), 30.12 (ArCH₂), 29.35 (S + CH₂).

Anal. Calcd for C₁₉H₁₉F₃O₃S₃: C, 45.07 (S + CH₂), 30.26 (S + CH₂).

1,4-Dimethyl-3,4-dihydro-2H-thiopyran[3,2-b][1]indol-1-ium Trifluoromethanesulfonate (6d)  
Yield: 51%; colorless crystals; mp 121–123 °C (dec.).

IR (Nujol): 1300–1100, 1040 cm⁻¹.

13C NMR (CD₃CN): δ = 125.74 (C q, Ar), 124.57 (Ar), 123.22 (C q, Ar), 122.52, 120.94, 119.42, 111.07 (2 C, Ar), 107.26 (C q, Ar), 45.11 (NCH₂), 35.51 (S + CH₂), 18.29 (NCH₂).


1-Methyl-1,2-dihydro[1,4]thiazin-2,3-[4]benzazol-3-iium Trifluoromethanesulfonate (13a)  
Yield: 78%; colorless crystals; mp 112–113 °C (dec.).

IR (Nujol): 1300–1100, 1040 cm⁻¹.

13C NMR (CD₃CN): δ = 147.82, 146.52 (2 H, Ar), 127.21 (Ar), 125.74 (C q, Ar), 124.57 (C q, Ar), 123.22 (C q, Ar), 122.52, 120.94, 119.11, 118.47 (4 C, Ar), 117.15 (C q, Ar), 110.83 (Ar), 43.13 (NCH₂), 39.87 (S + CH₂), 32.91 (S + CH₂).


1-Methyl-3,4-dihydro-2H-thiopyran[3,2-b][1]benzothiophen-1-ium Trifluoromethanesulfonate (7a)  
Yield: 75%; colorless crystals; mp 111–113 °C (dec.).

IR (Nujol): 1300–1100, 1040 cm⁻¹.

13C NMR (CD₃CN): δ = 125.74 (C q, Ar), 124.57 (Ar), 123.22 (C q, Ar), 122.52, 120.94, 119.11, 118.47 (4 C, Ar), 117.15 (C q, Ar), 110.83 (Ar), 43.13 (NCH₂), 39.87 (S + CH₂), 32.91 (S + CH₂).

OCH$_2$), 4.75 (ddd, 1 H, $J = 2.4$, 11.6, 13.6 Hz, OCH$_3$), 4.24–4.16 (m, 1 H, S'CH$_2$), 4.11–4.05 (m, 1 H, S'CH$_3$), 3.46 (s, 3 H, S'CH$_3$).

13C NMR (CD$_2$CN): $\delta$ = 166.02, 136.33 (2 C, Ar), 135.80, 132.48, 132.83 (3 C, Ar), 121.75 (q, $J = 319.4$ Hz, CF$_3$), 121.18 (Ar), 59.16 (OCH$_3$), 33.53 (S'CH$_2$), 30.76 (S'CH$_3$).


4-Methyl-2,3-dihydrothieno[1,2-b][1,4]oxathiin-4-ium Tri-fluoromethanesulfonate (17b)

Yield: 90%; colorless crystals; mp 105–106 °C.

IR (Nujol): 1300–1100, 1040 cm$^{-1}$.

$^1$H NMR (CD$_2$CN): $\delta$ = 8.36 (d, 1 H, $J = 8.8$ Hz, ArH), 8.03 (d, 1 H, $J = 7.6$ Hz, ArH), 7.85–7.74 (m, 3 H, ArH), 7.62 (d, 1 H, $J = 8.8$ Hz, ArH), 5.15 (ddd, 1 H, $J = 2.8$, 3.2, 13.6 Hz, OCH$_2$), 4.76 (ddd, 1 H, $J = 2.0$, 11.6, 13.6 Hz, OCH$_3$), 4.08 (ddd, 1 H, $J = 3.2$, 11.6, 15.0 Hz, S'CH$_3$), 3.96 (ddd, 1 H, $J = 2.0$, 2.8, 15.0 Hz, S'CH$_3$), 3.34 (s, 3 H, S'CH$_3$).

$^{13}$C NMR (CD$_2$CN): $\delta$ = 153.13 (C$_q$, Ar), 137.03, 131.04, 129.07 (3 C, Ar), 128.62, 126.43 (2 C, Ar), 125.70, 123.94, 123.12 (3 C, Ar), 122.10 (q, $J = 319.0$ Hz, CF$_3$), 98.87 (C$_q$, Ar), 59.91 (OCH$_3$), 33.34 (S'CH$_2$), 31.14 (S'CH$_3$).

Anal. Calcd for C$_9$H$_7$F$_2$O$_5$S: C, 50.66; H, 4.25. Found: C, 50.56; H, 4.23.

2,3-Dihydrothieno[2,3-b][1]benzothiophene (8d)

Yield: 65%; colorless crystals; mp 117–118 °C.

$^1$H NMR (CD$_2$CN): $\delta$ = 7.72 (d, 1 H, $J = 8.0$ Hz, ArH), 7.47 (d, 1 H, $J = 7.7$ Hz, ArH), 7.32 (ddd, 1 H, $J = 7.8$, 7.7 Hz, ArH), 7.25 (ddd, 1 H, $J = 7.8$, 8.0 Hz, ArH), 3.83 (t, 2 H, $J = 8.1$ Hz, ArCH$_2$), 3.27 (t, 2 H, $J = 8.1$ Hz, SCH$_2$).

$^{13}$C NMR (CD$_2$CN): $\delta$ = 133.11, 127.87, 125.67, 125.27 (4 C, Ar), 124.41, 123.83, 123.27, 121.93 (4 C, Ar), 38.06 (ArCH$_2$), 32.19 (SCH$_2$).


2-Methyl-3,4-dihydro-2H-thieno-[3,2-b]indole (8d)

Yield: 54%; colorless crystals; mp 90–92 °C.

$^1$H NMR (CD$_2$CN): $\delta$ = 7.65 (d, 1 H, $J = 7.6$ Hz, ArH), 7.36–7.26 (m, 2 H, ArH), 7.23–7.15 (m, 1 H, ArH), 3.58 (s, 3 H, NCH$_3$), 3.16 (t, 2 H, $J = 8.0$ Hz, ArCH$_2$), 2.98 (t, 2 H, $J = 8.0$ Hz, SCH$_2$).

$^{13}$C NMR (CD$_2$CN): $\delta$ = 135.21, 129.23, 124.78 (3 C, Ar), 122.27, 117.63, 115.82, 107.43 (4 H, Ar), 99.86 (C$_q$, Ar), 28.21 (NCH$_3$), 28.92 (ArCH$_2$), 27.46 (SCH$_2$).

Anal. Calcd for C$_{16}$H$_{11}$NS: C, 69.80; H, 5.86. Found: C, 69.67; H, 5.90.

3,4-Dihydro-2H-thiopyran[3,2-b][1]benzothiophene (9a)

Yield: 87%; colorless crystals; mp 117–118 °C.

$^1$H NMR (CD$_2$CN): $\delta$ = 7.73 (d, 1 H, $J = 6.9$ Hz, ArH), 7.55 (d, 1 H, $J = 7.3$ Hz, ArH), 7.37–7.26 (m, 2 H, ArH), 3.12 (t, 2 H, $J = 5.6$ Hz, ArCH$_2$), 2.96 (t, 2 H, $J = 6.3$ Hz, SCH$_2$), 2.35–2.26 (m, 2 H, SCH$_2$CH$_2$CH$_2$Ar).

$^{13}$C NMR (CD$_2$CN): $\delta$ = 137.95, 137.20, 128.66 (3 C, Ar), 124.30, 124.05, 122.08, 120.67 (4 C, Ar), 119.80 (C$_q$, Ar), 26.22 (SCH$_2$), 24.96 (ArCH$_2$), 23.85 (SCH$_2$CH$_2$CH$_2$Ar).

Anal. Calcd for C$_{16}$H$_{11}$S$_2$: C, 64.03; H, 4.89. Found: C, 63.71; H, 4.85.

2-Methyl-6,7-dihydro-5H-thieno-[3,2-b][1]thiophuran (9b)

Yield: 75%; colorless crystals; mp 46–48 °C.

$^1$H NMR (CD$_2$CN): $\delta$ = 6.32 (s, 1 H, ArH), 2.97 (t, 2 H, $J = 5.6$ Hz, ArCH$_2$), 2.77 (t, 2 H, $J = 6.3$ Hz, SCH$_2$), 2.37 (s, 3 H, ArCH$_3$), 2.18–2.11 (m, 2 H, SCH$_2$CH$_2$CH$_2$Ar).

$^{13}$C NMR (CD$_2$CN): $\delta$ = 136.54, 125.58 (2 C, Ar), 124.00 (Ar), 123.58 (C$_q$, Ar), 27.01 (SCH$_2$), 24.27 (ArCH$_2$), 24.01 (SCH$_2$CH$_2$CH$_2$Ar), 15.23 (ArCH$_3$).

Anal. Calcd for C$_{16}$H$_{11}$S$_2$: C, 56.42; H, 5.92. Found: C, 56.31; H, 5.96.

5-Methyl-2,3,4,5-tetrahydrothiopyran[3,2-b]indole (9c)

Yield: 64%; colorless crystals; mp 116–118 °C.

$^1$H NMR (CD$_2$CN): $\delta$ = 7.54 (d, 1 H, $J = 7.8$ Hz, ArH), 7.34–7.26 (m, 2 H, ArH), 7.21–7.16 (m, 1 H, ArH), 3.63 (s, 3 H, NCH$_3$), 3.08 (t, 2 H, $J = 8.0$ Hz, ArCH$_2$), 2.77 (t, 2 H, $J = 5.6$ Hz, SCH$_2$).
H, J = 5.2 Hz, ArCH₂), 2.86 (t, 2 H, J = 5.8 Hz, SCH₂), 2.43–2.37 (m, 2 H, SCH₂CH₂CH₂Ar).

13C NMR (CDCl₃): δ = 136.31, 130.31, 125.67 (3 Cᵦ, Ar), 121.17, 118.73, 117.78, 108.50 (4 C, Ar), 100.00 (Cᵦ, Ar), 28.93 (NCH₂), 26.59 (SCH₂), 24.46 (ArCH₂), 21.63 (SCH₂CH₂CH₂Ar).

Anal. Calcld for C₁₂H₁₁NS: C, 70.89; H, 6.45. Found: C, 71.10; H, 6.46.

2,3-Dihydropyrrolo[2,1-b][1,3]thiazole (14a)

Yield: 76%; colorless crystals; mp 57–59 °C.

1H NMR (CDCl₃): δ = 6.73 (dd, 1 H, J = 1.4, 3.0 Hz, ArH), 6.25 (dd, 1 H, J = 3.0, 3.4 Hz, ArH), 5.86 (dd, 2 H, J = 1.4, 3.4 Hz, ArH), 4.15 (t, 2 H, J = 6.9 Hz, NCH₂), 3.73 (t, 2 H, J = 6.9 Hz, SCH₂).

13C NMR (CDCl₃): δ = 116.02, 113.12 (2 C, Ar), 110.78 (Cᵦ, Ar), 99.89 (Ar), 48.07 (ArCH₂), 35.84 (SCH₂). Anal. Calcld for C₇H₉NS: C, 57.56; H, 5.64. Found: C, 57.45; H, 5.61.

3,4-Dihydro-2H-pyrrolo[2,1-b][1,3]thiazine (14b)

Yield: 81%; colorless crystals; mp 51–53 °C.

1H NMR (CDCl₃): δ = 6.55 (dd, 1 H, J = 1.7, 2.9 Hz, ArH), 6.06 (dd, 1 H, J = 2.9, 3.6 Hz, ArH), 5.83 (dd, 2 H, J = 1.7, 3.6 Hz, ArH), 3.92 (t, 2 H, J = 5.9 Hz, NCH₂), 2.91 (t, 2 H, J = 5.9 Hz, SCH₂), 2.20 (tt, 2 H, J = 5.9, 5.9 Hz, SCH₂CH₂N). Anal. Calcld for C₁₄H₁₁NS: C, 74.63; H, 4.92. Found: C, 74.52; H, 4.93.

Ring-Opening Reaction of Sulfonium Salts to the Amines 10; General Procedure

To a stirred solution of the corresponding five-membered cyclic sulfonium salt (2 mmol) in anhyd MeCN (10 mL) was added dropwise Et₂NH (1.1 mL, 10 mmol) while maintaining the temperature below 0 °C. The mixture was warmed to r.t., stirred for 1 h, and then solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (eluent: CH₂Cl₂–MeOH, 10:1) to yield the corresponding amine.

N,N-Diethyl-2-[5-methyl-3-(methylsulfonyl)-2-thienyl]-1-ethanamine (10a)

Yield: 68%; colorless viscous oil.

1H NMR (CDCl₃): δ = 6.52 (s, 1 H, ArH), 2.92 (t, 2 H, J = 7.9 Hz, ArCH₂CH₃), 2.64 (t, 2 H, J = 7.9 Hz, ArCH₂), 2.57 (q, 4 H, J = 7.1 Hz, NCH₂CH₃), 2.36 (s, 3 H, SCH₂), 2.30 (s, 3 H, ArCH₂), 1.05 (t, 6 H, J = 7.1 Hz, NCH₂CH₃).

13C NMR (CDCl₃): δ = 125.74 (2 C, Ar), 125.72 (2 C, Ar), 123.51 (Cᵦ, Ar), 122.47 (Ar), 121.64 (Cᵦ, Ar), 120.85, 119.47, 119.40, 117.14 (4 C, Ar), 115.21 (Cᵦ, Ar), 108.18 (Ar), 42.33 (NCH₂), 25.74 (SCH₂). Anal. Calcld for C₁₂H₁₅NS₃: C, 74.63; H, 9.42. Found: C, 74.52; H, 4.83.

13C NMR (CDCl₃): δ = 7.89 (d, 1 H, J = 7.8 Hz, ArH), 7.72 (d, 1 H, J = 7.7 Hz, ArH), 7.41 (dd, 1 H, J = 8.1, 7.2 Hz, ArH), 7.27 (d, 1 H, J = 8.1 Hz, ArH), 7.23–7.07 (m, 3 H, ArH), 4.39 (t, 2 H, J = 5.2 Hz, NCH₂), 3.22 (t, 2 H, J = 5.2 Hz, SCH₂). Anal. Calcld for C₁₂H₁₀NS: C, 74.63; H, 6.52. Found: C, 74.60; H, 6.51.

6,7-Dihydro-SH-[1,4]thiazepino[2,3,4-β]carbazole (14d)

Yield: 11%; colorless crystals; mp 108–110 °C.

1H NMR (CDCl₃): δ = 7.89 (d, 1 H, J = 7.8 Hz, ArH), 7.72 (d, 1 H, J = 7.7 Hz, ArH), 7.36–7.06 (m, 4 H, J = 7.7, 7.5 Hz, ArH), 4.64 (t, 2 H, J = 6.0 Hz, NCH₂), 3.26 (t, 2 H, J = 6.8 Hz, SCH₂), 2.30–2.21 (m, 2 H, SCH₂CH₂CH₂N).

13C NMR (CDCl₃): δ = 141.25, 140.76 (2 C, Ar), 127.27, 125.84 (2 C, Ar), 124.06, 122.76, 121.06 (3 C, Ar), 120.30, 119.56, 119.03, 118.51, 108.55 (5 C, Ar), 42.56 (NCH₂), 34.25 (SCH₂), 29.18 (SCH₂CH₂CH₂N). Anal. Calcld for C₁₄H₁₄N₃S: C, 75.27; H, 5.47. Found: C, 75.66; H, 5.40.

2,3-Dihydro-1,4-benzothiophin (18a)

Yield: 86%; colorless oil.

1H NMR (CDCl₃): δ = 6.91 (dd, 1 H, J = 1.9, 8.3, ArH), 6.84 (dd, 1 H, J = 1.6, 7.7, 8.3 Hz, ArH), 6.74–6.68 (m, 2 H, ArH), 4.21 (t, 1 H, J = 4.7 Hz, OCH₂), 2.92 (t, 1 H, J = 4.7 Hz, SCH₂). Anal. Calcld for C₁₂H₁₃NS: C, 63.13; H, 5.30. Found: C, 63.15; H, 5.12.

2,3-Dihydropyrazino[1,2-b][1,4]oxathione (18b)

Yield: 91%; colorless crystals; mp 71–73 °C (dec).

1H NMR (CDCl₃): δ = 8.36 (d, 1 H, ArH), 7.67 (d, 1 H, J = 7.8 Hz, ArH), 7.46–7.33 (m, 2 H, ArH), 7.30 (d, 1 H, J = 8.6 Hz, ArH), 7.06 (d, 1 H, J = 8.6 Hz, ArH), 4.53 (t, 2 H, J = 4.6 Hz, OCH₂), 3.16 (t, 2 H, J = 4.6 Hz, SCH₂).

13C NMR (CDCl₃): δ = 146.18, 132.00 (2 C, Ar), 127.49 (Ar), 125.92 (Ar), 125.78, 125.53, 125.27, 120.80, 120.39 (5 C, Ar), 111.43 (Cᵦ, Ar), 65.37 (OCH₂), 25.70 (SCH₂). Anal. Calcld for C₁₂H₁₂O₂S: C, 71.25; H, 4.98. Found: C, 71.21; H, 4.93.
Anal. Calcd for C_{11}H_{19}NS_{2}: C, 57.59; H, 8.35. Found: C, 57.73; H, 8.31.

**N,N-Diethyl-2-[3-(methylsulfanyl)-1-benzo[phen-2-y]-1-ethanamine (10c)**

Yield: 87%; colorless viscous oil.

^1^H NMR (CDCl₃): δ = 8.01 (d, 1 H, J = 8.0 Hz, ArH), 7.84 (d, 1 H, J = 8.0 Hz, ArH), 7.47 (dd, 1 H, J = 8.0, 7.2 Hz, ArH), 7.37 (t, 1 H, J = 8.0 Hz, NCH₂CH₂Ar), 3.34 (t, 2 H, J = 7.4 Hz, NCΗ₂CH₂Ar), 2.84 (t, 2 H, J = 7.4 Hz, NCH₂CH₂Ar), 2.37 (s, 3 H, SCH₃), 1.14 (t, 6 H, J = 7.2 Hz, NCH₂CH₃).

^1^C NMR (CDCl₃): δ = 149.05, 140.79, 138.76 (3 C q , Ar), 124.81, 124.58 (2 C q , Ar), 124.27 (C q , Ar), 122.72, 120.63, 118.83, 109.89 (4 C, Ar), 109.83, 104.94 (2 C,q, Ar), 54.38 (NCH₂CH₂Ar), 47.25 (2 C, NCH₂CH₃), 27.80 (NCH₂CH₂Ar), 19.43 (SCH₃), 12.33 (2 C, NCH₂CH₃).

Anal. Calcd for C_{15}H_{21}NS_{2}: C, 64.47; H, 7.57. Found: C, 64.59; H, 7.50.

**N,N-Diethyl-2-[1-methyl-3-(methylsulfanyl)-1H-indol-2-yl]-1-ethanamine (10d)**

Yield: 64%; colorless viscous oil.

^1^H NMR (CDCl₃): δ = 7.73 (d, 1 H, J = 7.6 Hz, ArH), 7.36 (d, 1 H, J = 8.1 Hz, ArH), 7.32–7.20 (m, 2 H, ArH), 3.81 (s, 3 H, CH₃N), 3.52–3.47 (m, 2 H, NCH₂CH₂Ar), 2.30 (s, 3 H, SCH₃), 1.45 (t, 6 H, J = 7.3 Hz, NCH₂CH₃).

^1^C NMR (CDCl₃): δ = 137.35, 128.79 (2 C q , Ar), 122.72, 120.63, 118.83, 109.89 (4 C, Ar), 109.83, 104.94 (2 C, q, Ar), 51.20 (NCH₂CH₂Ar), 47.25 (2 C, NCH₂CH₃), 30.42 (NCH₃), 20.34 (NCH₂CHAr), 20.15 (SCH₃), 9.56 (2 C, NCH₂CH₃).

Anal. Calcd for C_{16}H_{24}N₂S: C, 69.52; H, 8.75. Found: C, 70.05; H, 8.72.

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