

INTRAMOLECULAR SULFENYLATION USING SULFOXIDES.  
PREPARATION OF 5*H*-PYRROLO[1,2-*a*][3,1]BENZOTHAZINES

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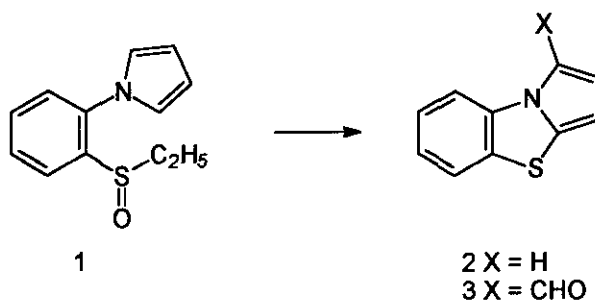
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*Abstract-* *N*-[2-(Phenylsulfinylmethyl)phenyl]pyrrole (**4**) undergoes transfer sulfenylation to *N*-(2-chloromethylphenyl)-2-phenylthiopyrrole (**5'**) presumably via *S*-phenyl 5*H*-pyrrolo[1,2-*a*][3,1]benzothiazonium chloride (**7**). Depending upon the rigor of the reaction conditions, either *N*-(2-hydroxymethylphenyl)-2-phenylthiopyrrole (**5**) or its 5-trifluoroacetyl derivative (**6**) are obtained when **4** is treated with TFAA in trifluoroacetic acid. *N*-[2-(Methylsulfinylmethyl)aryl]pyrroles (**12**), when treated with gaseous hydrogen chloride and the resulting sulfonium salts refluxed in dichloroethane, produce substituted 5*H*-pyrrolo[1,2-*a*][3,1]benzothiazines (**14**). 1-Formyl-5*H*-pyrrolo[1,2-*a*][3,1]benzothiazines (**22**) are formed in one step in good yield when sulfoxides (**12**) are reacted with the Vilsmeier-Haack reagent (DMF/POCl<sub>3</sub>). No Pummerer rearrangement product is isolated from these reactions.

Electrophilic sulfenylation of heteroaromatics may be accomplished in several ways. Historically, sulfonyl halides<sup>1,2</sup> have been used for this purpose. However, chlorosulfonium salts from a sulfide and *N*-chlorosuccinimide (NCS)<sup>3</sup> or *t*-butyl hypochlorite<sup>4</sup> as well as dimethylthiomethylsulfonium tetrafluoroborate<sup>5</sup> are also well suited to this purpose. The electrophilic nature of sulfoxides, especially when activated to a trifluoroacetoxy-sulfonium species, has also proven useful.<sup>6</sup>

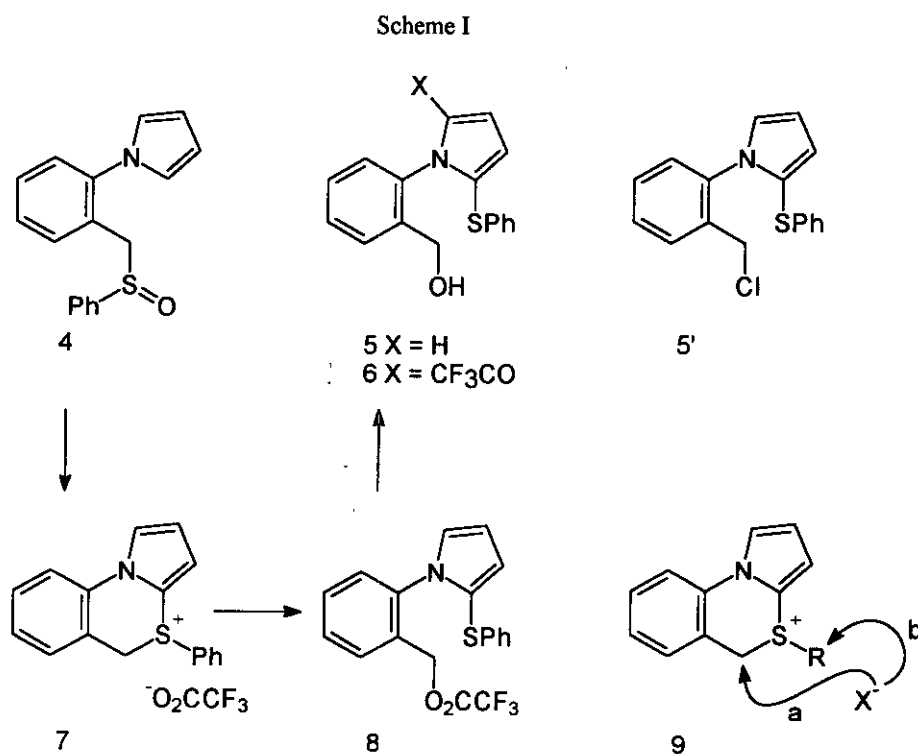
We have exploited the use of sulfoxides as sulfenylating agents for intramolecular cyclizations to form condensed *N,S* heterocyclic systems.<sup>7,8</sup> For example, treatment of sulfoxide (1) with trifluoroacetic anhydride (TFAA) in trifluoroacetic acid (TFA) produces pyrrolo[2,1-*b*]benzothiazole (2) in 87% yield presumably *via* a trifluoroacetoxy-sulfonium species.<sup>7</sup> The alternate method of treating the corresponding sulfide of 1 with more traditional reagents to give electrophilic sulfonium salts results in uncontrollable, competitive halogenation (or thiomethylation in the case of dimethylthiomethylsulfonium BF<sub>4</sub><sup>-</sup>) of the highly reactive pyrrole nucleus *in situ* both before and after forming 2. Sometimes however, this process of incorporating the reagent used to activate the sulfoxide into the heterocycle may be synthetically useful. For example, formation of 3 in one step from sulfoxide (1)<sup>8</sup> in 73% yield introduces the very useful aldehyde functionality directly. In this paper we describe a synthesis of the little studied ring system 5*H*-pyrrolo[1,2-*a*][3,1]benzothiazine employing similar methodologies.



## Results and Discussion

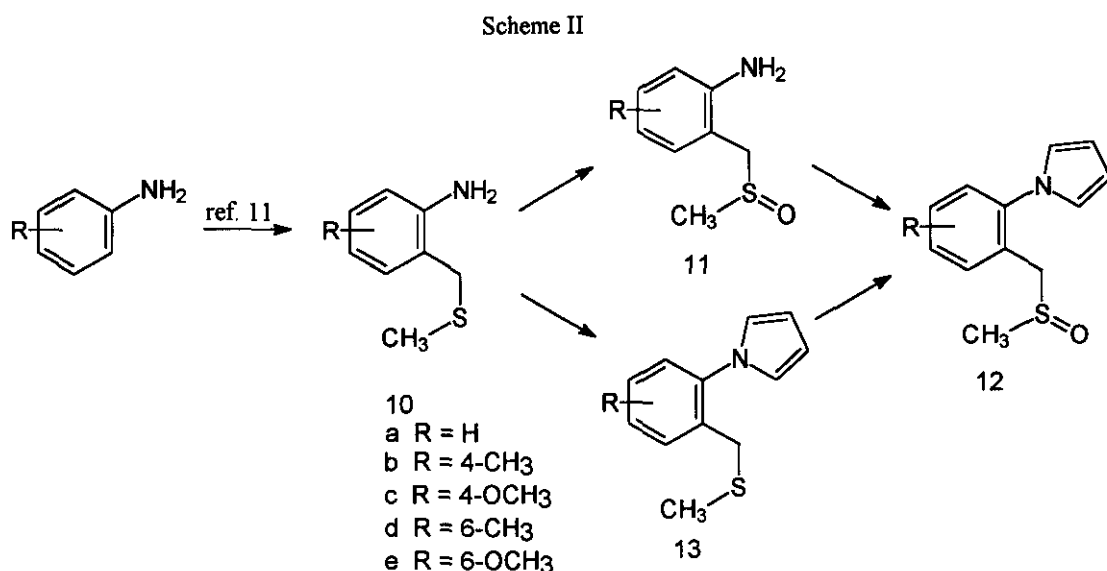
When work directed to the pyrrolobenzothiazine synthesis was begun, the only related cyclization (1 → 2) proceeded by five-membered ring formation. Due to other potentially complicating features, our initial work simply sought to demonstrate that intramolecular sulfenylation *via* a six-membered ring would take place. The requisite sulfoxide (4) was readily synthesized from *N*-(2-bromomethylphenyl)pyrrole<sup>9</sup> by treatment with sodium benzenethiolate in ethanol followed by oxidation with *m*CPBA at 0 °C in methylene chloride. Compound (4) when treated with TFAA in refluxing toluene produced 6 in 28% yield; at 0 °C compound (5) was obtained in similar yield. These were the only products to elute from the chromatography column; none of the normal Pummerer rearrangement product was observed in these experiments.

This intramolecular transfer sulfenylation is thought to proceed *via* the sulfonium salt (7) which undergoes nucleophilic displacement by trifluoroacetate to give 8.<sup>10</sup> Further reaction of 8 with TFAA, followed by hydrolysis of the labile trifluoroacetate ester during workup, produces 6 (Scheme I). Attempting to improve the yield of transfer sulfenylation, we applied conditions similar to those reported<sup>11</sup> by Pummerer in 1909 in his seminal work on the conversion of sulfoxides to  $\alpha$ -chlorosulfides. *Bubbling HCl gas through a cold ether solution of the sulfoxide in ether gave no Pummerer rearrangement product but instead produced only 5' in 51% yield.* These experiments demonstrate that intramolecular cyclization to an intermediate six-membered ring species is a viable process in this system.



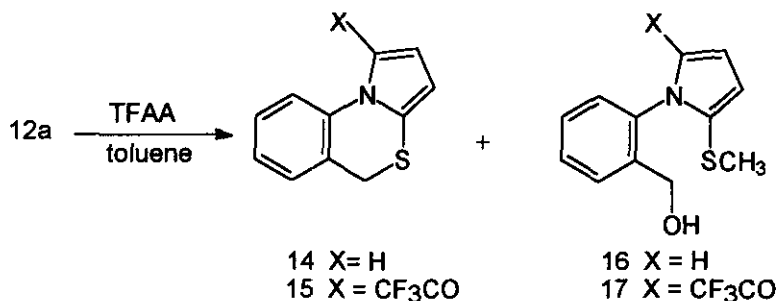
If the *S*-phenyl group was replaced by a displaceable group (i.e. methyl or benzyl), we expected a competition between transfer sulfenylation (path a in 9) and heterocycle formation (path b in 9) to lead to a mixture of products. By judicious choice of conditions we hoped to favor heterocycle formation at the expense of the open chain product.

Compounds (**12**) were readily prepared as shown in Scheme II. The appropriate aniline derivative was treated with dimethyl sulfide (DMS) and NCS according to the procedure of Chupp.<sup>12</sup> The *o*-[(methylthio)methyl]anilines (**10**) were then oxidized to the sulfoxides (**11**) and "capped" to the pyrroles (**12**) using 2,4-dimethoxytetrahydrofuran. These operations could be carried out in reverse order, but the aniline sulfoxides (**11**) were solids and more easily purified than the pyrrole sulfides (**13**), which tended to decompose upon attempted vacuum distillation.

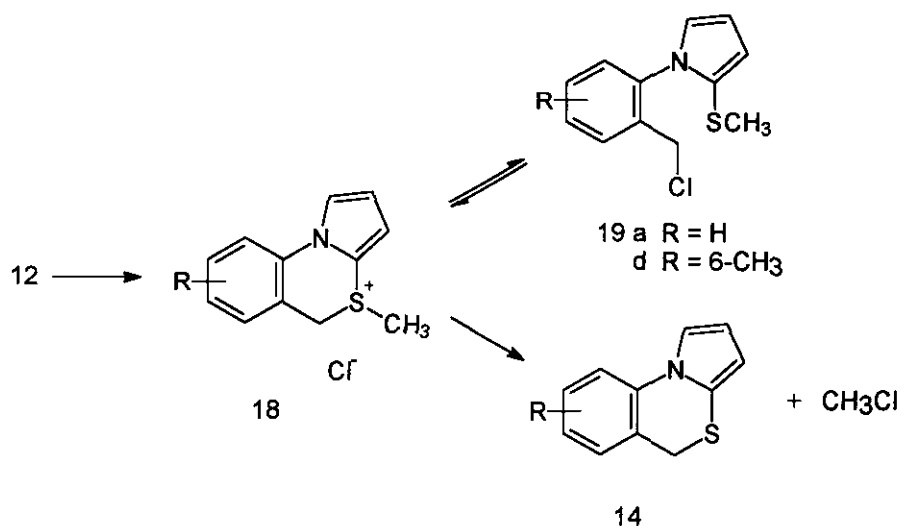


Heating **12a** with TFAA in toluene for 1.5 h gave a disappointing yield (15%) of the trifluoroacetoxy heterocycle (**15**), contaminated presumably with benzyl alcohols (**16**) and (**17**). Conducting the reaction at 0 °C with TFAA/TFA suppressed trifluoroacetylation and gave heterocycle (**14**) and benzyl alcohol (**16**) in nearly equal amounts in about 80% combined yield. Unfortunately, neither result represents a synthetically useful reaction.

We therefore converted **12** into the sulfonium chloride. Bubbling HCl gas through an ether solution of **12a** produced a precipitate of **18a** as white needles in 58% yield. Heating this precipitate in dichloroethane produced **14a** quantitatively. Sulfoxides (**12b-e**) react similarly. Methyl chloride vaporizes from the



reaction mixture as it is formed, accounting for the absence of any open chain product under these conditions. The benzyl chloride (19), which undoubtedly also forms, may revert back to 18 whereas 14 is formed irreversibly due to loss of CH<sub>3</sub>Cl from the reaction mixture. This hypothesis is supported by the tentative finding that the 6-methyl derivative (12d) which forms benzyl chloride derivative (19d) as the major product. This compound is apparently essentially "removed from the reaction" by internal rotation about the pyrrole phenyl bond: reaction of 12d is the only example from which any open chain compound has been isolated. This equilibration may also explain the poor yields associated with use of TFAA. Chloride is a better nucleophile than trifluoroacetate, thereby allowing more facile equilibration of the open chain chloro-compound resulting in enhanced accumulation of the pyrrolobenzothiazine under treatment with HCl.



Comparison of the rotational barriers around the central C-N bond in 19 a,d,e calculated using molecular mechanics (HyperChem 2.0) supports the inability of 19d to recyclize. While 19a has a relatively small

barrier to rotation, the *o*-methyl compound (**19d**) exhibits an "energy well" at torsion angles between about 180-270 degrees (see Figure 1). Ring opening of the sulfonium salt can form two conformations of **19d**. Ring opening in one direction allows the carbon and sulfur atoms to come into close enough proximity (the typical C-S bond distance is 1.82 Å<sup>13a</sup> and the sum of the carbon and sulfur van der Waals radii is 3.5 Å<sup>13b</sup>) to bond, thus initiating a cyclization/ring opening equilibration in competition with attack of chloride at the exocyclic methyl group. However, once the conformation of **19d** falls within the energy well, rotation is restricted, the sulfur atom and the carbon atom of the CH<sub>2</sub>Cl are prevented from getting closer than about 3.8 Å and recyclization can not take place. Each time the sulfonium salt ring opens more of **19d** is locked into the uncyclizable conformation. The calculated relative rotational barrier in **19e**, the 6-OMe compound, is intermediate between **19a** and **19d** and apparently is low enough to allow the molecule to rotate around the C-N bond to the torsion angle where the C and S approach most closely (at about 0° for **19e** and 350° for **19d**). The steric bulk of a methoxy group is greater than that for a methyl group,<sup>14</sup> however the OCH<sub>3</sub> group can achieve a conformation with the methyl group oriented away from the pyrrole ring where it does not interfere with rotation about the central C-N bond. Viewed in this manner, the methyl group is larger (van der Waals volume (V<sub>w</sub>) = 13.67)<sup>13b</sup> than the methoxyl oxygen (V<sub>w</sub> = 5.20)<sup>13b</sup> and, predictably, presents a considerably greater barrier to C-N rotation.

It should be noted that application of these reaction conditions may be limited. For example, treatment of sulfoxide (**1**) in ether solution with hydrogen chloride gas produces no cyclized product, only sulfide (**20**) and chlorosulfide (**21**). Previously, we had successfully cyclized **1** to heterocycle (**2**) in 87% yield using TFAA in TFA,<sup>7</sup> but the reaction conditions must be carefully controlled to avoid trifluoroacetylation of **2** after it is formed. The chlorosulfide (**21**) may form *via* Cl<sup>-</sup> attack on the protonated sulfoxide forming the chlorosulfonium chloride, a well known chlorinating species.<sup>15</sup>

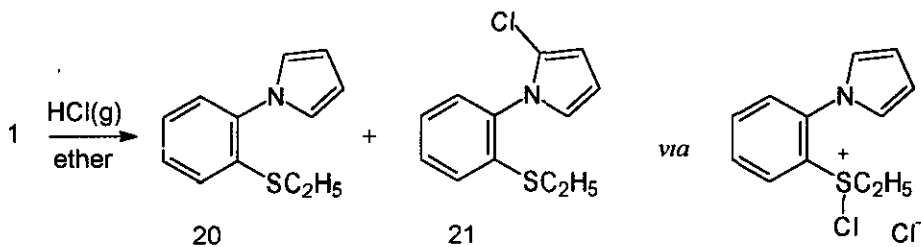
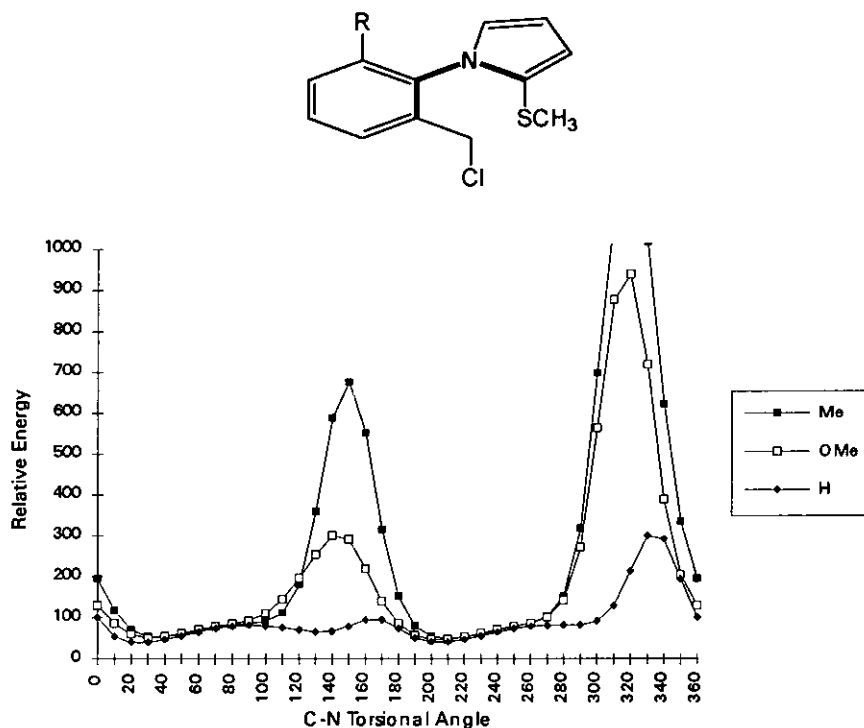
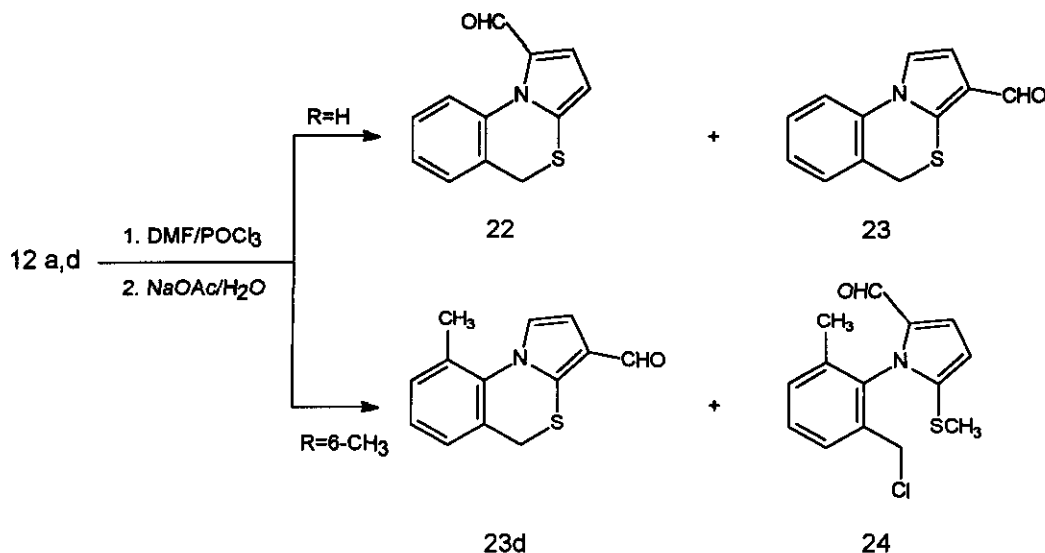


Figure 1. Relative Rotational Barriers about the C-N bond of Compounds (19 a,d,e). (The torsion angle for rotation is highlighted).



Treatment of sulfoxide (12) with DMF/POCl<sub>3</sub> (Vilsmeier-Haack reagent) produces functionalized heterocycles in one step. For example 12a gave a mixture of 1- and 3-carboxaldehydes (22/23) 4.5:1 ratio in 76% yield. *Para*-substituted derivatives (12b,c) gave the 1- and 3-carboxaldehydes in a ratio of about 8/1. The bulky *ortho*-methyl substituted 12d reacted anomalously, producing both the 3-carboxaldehyde (23) and open chain aldehyde derivative (24). The "less bulky" 6-methoxy compound (12e) reacts normally (supporting the discussion above), producing 1-carboxaldehyde and 3-carboxaldehyde in a 6/1 ratio but not ring opened compound. The ratio of isomeric aldehydes formed by Vilsmeier-Haack formylation of *N*-phenylpyrroles may be influenced by reaction conditions<sup>16</sup> therefore no correlation of the aldehyde isomer ratios to *o*- or *p*-substitution should be made without more careful investigation.

It is easy to differentiate the 1-carboxaldehyde from the 3-carboxaldehyde by proton nmr (see Tables II and III): H-3 in the 1-carboxaldehyde appears at *ca*  $\delta$  6.3( $J = 4.2$  Hz) while H-1 in the 3-carboxaldehyde appears at *ca*  $\delta$  6.7( $J = 3.4$  Hz). The formyl proton in the 1-carboxaldehyde also consistently appears upfield of the 3-aldehyde proton ( $\delta$  9.5 vs. 9.9, respectively).



#### ACKNOWLEDGMENT

We wish to thank Ms Tracy Stevenson (Parke-Davis) for providing high resolution mass spectral data.

#### EXPERIMENTAL SECTION

Melting points are uncorrected. Proton nmr spectra were recorded at 60 or 200 MHz with tetramethylsilane as an internal reference. Elemental analyses were determined by Spang Microanalytical Laboratory, Eagle River, MI, Gailbraith Laboratories, Knoxville, TN, or the Parke-Davis Pharmaceutical Research Institute, Ann Arbor, MI. Visualization of tlc plates was accomplished with uv light or, for pyrroles and amines, van Erk reagent (*p*-dimethylaminobenzaldehyde in *n*-butyl alcohol/conc. HCl). All reagents were used as received unless otherwise indicated.

***N*-[2-(Phenylthiomethyl)phenyl]pyrrole.** A solution of KOH (0.98 g, 17.5 mmol in 15 ml ethanol) was added slowly to a solution of thiophenol (1.93 g, 17.5 mmol in 20 ml of ethanol) under a blanket of



nitrogen. To this mixture was added *N*-(2-bromomethylphenyl)pyrrole<sup>9</sup> (3.5 g, 15.6 mmol) in ethanol (20 ml). After stirring overnight at room temperature the mixture was filtered to remove precipitated KBr and the filtrate was concentrated *in vacuo* to brown oil. The oil was partitioned between 5% aqueous K<sub>2</sub>CO<sub>3</sub> and CH<sub>2</sub>Cl<sub>2</sub> (30 ml each). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed to give a pale yellow oil (3.5 g, 84%) which typically was oxidized directly to the sulfoxide (see below). <sup>1</sup>H Nmr (60 MHz, CDCl<sub>3</sub>): δ 7.53-7.03 (9H, m), 6.93 (2H, t, J = 2.1 Hz), 6.33 (2H, t, J = 2.1 Hz), 3.90 (2H, s). HRms (FAB) calcd for C<sub>17</sub>H<sub>15</sub>NS: 266.1003 (M+1). Found: 266.1004.

***N*-[2-(Phenylsulfinylmethyl)phenyl]pyrrole (4).** A solution of *N*-[2-(phenylthiomethyl)phenyl]pyrrole (3.69 g, 13.9 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (25 ml) was cooled to 0 °C in an ice bath. A solution of *m*CPBA (3.60 g, 15.3 mmol, 80% purity) in CH<sub>2</sub>Cl<sub>2</sub> (100 ml) was added dropwise to the cold sulfide solution. The reaction mixture was stirred at 0 °C for 1 h, then stored at -30 °C overnight. The solution was filtered and the filtrate was washed with 5% aqueous K<sub>2</sub>CO<sub>3</sub> (2 x 100 ml) and water (2 x 100 ml). The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed *in vacuo* to give a dark brown oil which crystallized to an off-white solid after filtration of a petroleum ether slurry of the oil through a pad of Florisil (3.3 g, 85%): mp 95-96 °C (hexane). Ir (KBr): 1020 cm<sup>-1</sup>; <sup>1</sup>H nmr (60 MHz, CDCl<sub>3</sub>): δ 7.63-7.27 (9H, m), 6.75 (2H, t, J = 2.1 Hz), 6.38 (2H, t, J = 2.1 Hz), 3.87 (s, 2H). HRms (FAB) calcd for C<sub>17</sub>H<sub>15</sub>NOS: 282.0952(M+1). Found: 282.0950.

**2-Phenylthio-*N*-(2-hydroxymethylphenyl)pyrrole (5).** TFAA (1.50 g, 7.1 mmol) was added dropwise to cold (0-5 °C) TFA (5 ml). After stirring 15 min, sulfoxide (4) (1.00 g, 3.5 mmol) in TFA (10 ml) was slowly added. Over the course of the addition, the color became deep violet and tlc indicated starting material was absent by the end of the addition. The mixture was quenched with water (50 ml) and solid NaOAc was added until the pH was about 8. After prolonged stirring the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 25 ml). The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was evaporated *in vacuo* to give a brown oil. Preparative tlc gave 5 (240 mg, 24%) as a pale yellow oil: Ir (neat): 3420, 1320, 730 cm<sup>-1</sup>; <sup>1</sup>H nmr (60 MHz, CDCl<sub>3</sub>): δ 7.53-6.60 (11 H, m), 6.28 (1H, dd, J = 3.6, 3.0 Hz), 4.08 (2H, s), 2.03 (1H, br s); EIms (m/z, rel int): 281 (M<sup>+</sup>, 16.5), 172 (M-SPh, 37.8), 154 (M-SPh-H<sub>2</sub>O, 66.8), 51 (100). HRms (FAB) calcd for C<sub>17</sub>H<sub>15</sub>NOS (M<sup>+</sup>): 281.0874. Found: 281.0869.

***N*-(2-Hydroxymethylphenyl)-5-phenylthio-2-trifluoroacetylpyrrole (6).** To a stirred solution of sulfoxide (4) (0.50 g, 1.8 mmol) in toluene (10 ml), under N<sub>2</sub>, was added TFAA (0.5 ml, 3.6 mmol) slowly *via* syringe. After the addition was complete, the reaction mixture was refluxed for 2.5 h at which time KOH (10 ml of 1 N solution) was added to the cooled reaction mixture. After stirring for 4 h at room temperature the mixture was extracted with chloroform and the organic phase passed through a short (1 x 3 in) Florisil column to give **6** as a red oil (0.19 g, 28%): Ir (neat): 3420, 1655, 880 cm<sup>-1</sup>; <sup>1</sup>H nmr (60 MHz, CDCl<sub>3</sub>): δ 7.77-6.80 (10 H, m including a singlet at 7.40), 6.39 (1H, d, J = 4.4 Hz), 4.25 (2H, s), 1.93 (1H, br s); EIms (m/z, rel int): 377 (M<sup>+</sup>, 2.3), 360 (M-OH, 0.4), 308 (M-CF<sub>3</sub>, 0.5), 280 (M-CF<sub>3</sub>CO, 0.6), 268 (M-SPh, 5.0), 154 (M-OH-CF<sub>3</sub>CO-SPh, 34.2), 51 (100). HRms (EI<sup>+</sup>) calcd for C<sub>19</sub>H<sub>14</sub>NO<sub>2</sub> F<sub>3</sub>S (M<sup>+</sup>): 377.0697. Found: 377.0688. Anal. Calcd for C<sub>19</sub>H<sub>14</sub>NO<sub>2</sub> F<sub>3</sub>S: C, 60.47; H, 3.74, N, 3.71. Found C, 60.19; H, 3.91; N, 3.64.

**Preparation of *N*-[2-(methylsulfinylmethyl)]pyrroles (12).** The following procedure is illustrative: To a stirred solution of 4-methyl-2-(methylsulfinylmethyl)aniline (**10b**)<sup>12</sup> (26.43 g, 0.144 mol) in glacial acetic acid (350 ml) was added dropwise a solution of 2,5-dimethoxytetrahydrofuran (24.07 g, 0.173 mol) in glacial acetic acid (100 ml). When the addition was complete, the flask was heated over a steam bath for 1.5 h while nitrogen gas was continuously bubbled through the solution. The reaction mixture was concentrated to a small volume under vacuum on the rotary evaporator, then partitioned between CH<sub>2</sub>Cl<sub>2</sub> and water (200 ml of each). The organic layer was washed sequentially with 5% HCl, 5% K<sub>2</sub>CO<sub>3</sub> solution, and water and, after drying over Na<sub>2</sub>SO<sub>4</sub>, the solvent was removed *in vacuo* to give 30.85 g (93%) of a brown oil. Extraction of the oil with boiling hexanes followed by cooling the decanted solution gave pure **12c** as white crystals: mp 62-63 °C (hexane). <sup>1</sup>H Nmr (200 MHz, CDCl<sub>3</sub>): δ 7.33-7.15 (3H, m), 6.79 (2H, apparent t, J = 2.1 Hz), 6.32 (2H, apparent t, J = 2.1 Hz), 3.91 (1H, 1/2 of AB q, J = 12.8 Hz), 3.77 (1H, 1/2 of AB q, J = 12.8 Hz), 2.38 (3H, s), 2.35 (3H, s). Anal. Calcd for C<sub>13</sub>H<sub>15</sub>NOS: C, 66.92; H, 6.48; N, 6.00. Found: C, 67.03; H, 6.49; N, 5.96.

**1-Trifluoroacetyl-5H-pyrrolo[1,2-a][3,1]benzothiazine (15).** To a solution of sulfoxide (**12a**) (0.88 g, 4 mmol) in toluene (50 ml) under a blanket of argon was added over 10 min TFAA (1.13 ml, 8 mmol). The

mixture was refluxed for 1.5 h at which time the solution was cooled, transferred to a separatory funnel and washed successively with 5% aqueous  $K_2CO_3$  and water. The organic layer was dried ( $Na_2SO_4$ ) and the toluene was removed to yield a dark oil which was filtered through a 1 x 6 in column of alumina eluted with petroleum ether to yield **15** (170 mg, 15%) as colorless rectangular crystals: mp 108-109 °C (hexane). Ir (KBr):  $1660\text{ cm}^{-1}$ ;  $^1H$  nmr (60 MHz,  $CDCl_3$ ):  $\delta$  7.73-7.20 (5H, m), 6.47 (1H, d,  $J = 4.4$  Hz), 3.92 (2H, s); Elms ( $m/z$  (rel int)): 282 (48), 214 (100), 186 (36). Anal. Calcd for  $C_{13}H_8NOF_3S$ : C, 55.07; H, 2.85; N, 4.94. Found C, 55.13; H, 2.83; N, 4.87.

**Reaction of Sulfoxides 12 with TFAA/TFA.** TFAA (1.93 g, 9.2 mmol) was stirred with TFA (5 ml) for 15 min at 0 °C before a solution of **12a** (1.0 g, 4.6 mmol) in TFA (10 ml) was added dropwise. Stirring at 0 °C was continued for an additional 30 min at which time the volatiles were evaporated on a rotary evaporator *in vacuo* to afford a brown oil. The oil was dissolved in acetone and allowed to stand over solid  $K_2CO_3$  for a few min to remove any residual acidic material.<sup>17</sup> The brown solid obtained upon evaporation was suspended in toluene (25 ml) and refluxed for 3 h. Evaporation of the solvent *in vacuo* gave a black oil which was chromatographed on alumina (1x7 in). Early fractions contained 5H-pyrrolo[1,2-*a*][3,1]benzothiazine (**14**, 320 mg, 37%). Data for this compound are given at the end of the next description. Subsequent fractions contained *N*-(2-hydroxymethylphenyl)-2-(methylthio)pyrrole (**16**) (410 mg, 41%): mp 72-74 °C (hexane). Ir (melt):  $3425\text{ cm}^{-1}$ ;  $^1H$  nmr (60 MHz,  $CDCl_3$ ):  $\delta$  7.63-7.00 (4H, m), 6.70 (1H, t,  $J = 4.2$  Hz), 6.43-6.10 (2H, m), 4.25 (2H, s), 2.90 (1H, br s), 1.95 (3H, s). Similarly **12d** gave ring closed/ring opened products in 12%/27% yields and **12b** gave 49%/30% yields, respectively. However, the ring opened products from these reactions were characterized by ir and  $^1H$  nmr only.

**Reaction of Sulfoxides 12 with HCl gas.** HCl gas was bubbled for 15 min through a solution of the appropriate sulfoxide (**12**) (4.6 mmol) in ether (50 ml) while the solution was cooled in an ice-bath. After an additional 10 min in ice, the precipitated sulfonium salt was collected by filtration and suspended in dichloroethane (15 ml). After refluxing this mixture for 0.5 h, the solvent was removed *in vacuo* to produce, quantitatively, **14**. If impure sulfoxide is used in this process, the sulfonium salt may form as a gummy precipitate and, consequently, less pure **14** is isolated in lower yield. Attempts to purify **12** by

recrystallization only degraded the samples; heterocycles (**14**) were purified by column chromatography (if needed) and recrystallization from hexane. Treatment of **12b** with HCl gas in ether as above gave **19b** as the major product (80% of the product mixture):  $^1\text{H}$  Nmr (60 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.50-7.05 (3H, m), 6.78-6.17 (3H, m), 4.32 (1H, d,  $J = 12.0$  Hz), 4.09 (1H, d,  $J = 12.0$  Hz), 2.03 (3H, s), 1.98 (3H, s). The nmr spectrum recorded at 200 MHz shows what appears to be overlapping AB quartets of differing intensity in the  $\delta$  4.0-4.5 region, probably from different conformers due to hindered rotation about *N*-phenyl bond. Nmr data for **14** are summarized in Table I. Other data include:

**14a**: (57%); mp 66-67 °C (hexane); EIMS ( $m/z$ , (rel int)): 187 (100), 154(72); HRms ( $\text{EI}^+$ ) calcd for  $\text{C}_{11}\text{H}_9\text{NS}$  ( $\text{M}^+$ ): 187.0456. Found 187.0453. Anal. Calcd for  $\text{C}_{11}\text{H}_9\text{NS}$ : C, 70.55; H, 4.84; N, 7.48. Found: C, 70.63; H, 4.82; N, 7.46.

**14b**: (63%); mp 110-112 °C (hexane); Anal. Calcd for  $\text{C}_{12}\text{H}_{11}\text{NS}$ : C, 71.60; H, 5.55; N, 6.96. Found C, 71.63; H, 5.42; N, 6.88.

**14c**: (48%); mp 84-86 °C (hexane); HRms: ( $\text{EI}^+$ ) calcd for  $\text{C}_{12}\text{H}_{11}\text{NOS}$  ( $\text{M}^+$ ) 217.0561. Found 217.0564. Anal. Calcd for  $\text{C}_{12}\text{H}_{11}\text{NOS}$ : C, 66.33; H, 5.00; N, 6.45. Found C, 66.06; H, 4.88; N, 6.07.

**14d**: (18%); oil, HRms ( $\text{EI}^+$ ) calcd for  $\text{C}_{12}\text{H}_{11}\text{NS}$  ( $\text{M}^+$ ) 201.0612. Found 201.0596.

Table I. Summary of nmr Data<sup>a</sup> for Compounds (**14**).

Compound	R	H-1	H-2	H-3	$\text{CH}_2$	$J_{1,2}$ (Hz)	$J_{1,3}$ (Hz)	$J_{2,3}$ (Hz)
a	$\text{H}^b$	7.28	6.30	6.19	3.84	3.16	1.62	3.49
b	4- $\text{CH}_3^b$	7.24	6.29	6.18	3.80	3.10	1.65	3.50
c	4- $\text{OCH}_3^b$	7.22	6.29	6.18	3.81	3.08	1.63	3.55
d	2- $\text{CH}_3^c$	d	e	e	3.81			

(a)  $\text{CDCl}_3$  solution (b) recorded at 200 MHz (c) recorded at 60 MHz (d) H-1 is buried in the aromatic envelope (e) H-2 and H-3 appear as an apparent d ( $J = 2.4$  Hz) at  $\delta$  6.22.

**Compounds 20 and 21 by Treatment of 1 with HCl gas.** Dry HCl was bubbled through a cold solution of sulfoxide (**1**) (1.0 g, 4.6 mmol) in ether (50 ml) over 15 min, during which time the solution was allowed to reach room temperature. Solid potassium carbonate was added in excess and the mixture stirred overnight. After filtration, the filtrate was concentrated in vacuo to give an orange oil (0.92 g). By

comparison of the nmr spectrum with those of authentic samples,<sup>8</sup> this product was determined to be a mixture of *N*-(2-ethylthiophenyl)pyrrole (**20**, 56%) and 2-chloro-1-(2-ethylthiophenyl)pyrrole (**21**, 44%).

**Compounds 22 and 23 by Reaction of 12 with POCl<sub>3</sub>/DMF.** A mixture of POCl<sub>3</sub> (2.22 g, 14.2 mmol) and DMF (5 ml) was stirred for 20 min in an ice-bath before the appropriate sulfoxide (**12**) (7 mmol) in DMF (20 ml) was added dropwise. The mixture was then stirred in a water bath at 70 °C for 2 h. The solution was poured into water (300 ml) and sodium acetate was added until the pH reached 8. This solution was stirred overnight to complete hydrolysis. The aqueous solution was decanted away from the oily product, which was dissolved in CH<sub>2</sub>Cl<sub>2</sub>, the solution was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent evaporated to give the crude product. Column chromatography on alumina gave the following compounds (nmr data for carboxaldehyde isomers are summarized in Tables II and III):

Table II. Nmr Data<sup>a</sup> for 1-Carboxaldehydes (**22**).

Compound	R <sup>b</sup>	CH <sub>2</sub>	H-2	H-3	J <sub>2,3</sub> (Hz)	CHO
a	H <sup>c</sup>	3.86	7.14	6.35	4.13	9.56
b	4-CH <sub>3</sub> <sup>d</sup>	3.7	e	6.22	4.2	9.42
c	4-OCH <sub>3</sub> <sup>c</sup>	3.72	7.15	6.34	4.14	9.53
e	2-OCH <sub>3</sub> <sup>d</sup>		e	6.32	4.1	9.38

(a) CDCl<sub>3</sub> solution (b) based on the substituent location in the corresponding aniline derivative (c) recorded at 200 MHz (d) recorded at 60 MHz (e) H-2 is not well resolved within the aromatic envelope.

**22a:** (62%); oil; ir (neat): 1660 cm<sup>-1</sup>.

**22b:** (42%); oil; ir (neat): 1660 cm<sup>-1</sup>; HRms (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>11</sub>NOS (M<sup>+</sup>) 229.0561. Found: 229.0560.

**22c:** (59%); mp 100-101 °C (hexane/CHCl<sub>3</sub>); ir (KBr): 1655 cm<sup>-1</sup>. Anal. Calcd for C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub>S: C, 63.65; H, 4.52; N, 5.71. Found: C, 63.21; H, 4.26; N, 5.63.

**22e:** (49%); mp 117-119 °C (hexane/CHCl<sub>3</sub>); ir (KBr): 1635 cm<sup>-1</sup>; HRms (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub>S (M<sup>+</sup>) 245.0510. Found 245.0500.

**23a:** (14%); mp 73-74 °C (hexane); ir (neat/ melt): 1665 cm<sup>-1</sup>.

**23b:** (5%); oil, ir (neat): 1665 cm<sup>-1</sup>.

**23c:** (13%); mp 118-120 °C (hexane/CHCl<sub>3</sub>); ir (KBr): 1670 cm<sup>-1</sup>; HRms (EI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub>S (M<sup>+</sup>) 245.0510. Found 245.0506.

**23d:** (12%); mp 147-149 °C (hexane/ether); ir (KBr): 1650 cm<sup>-1</sup>. Anal. Calcd for C<sub>13</sub>H<sub>11</sub>NOS: C, 68.10; H, 4.83; N, 6.11. Found C, 68.02; H, 4.76; N, 6.09.

**23e:** (8%); oil; ir (neat): 1665 cm<sup>-1</sup>.

Table III. Nmr Data<sup>a</sup> for 3-Carboxaldehydes (23)

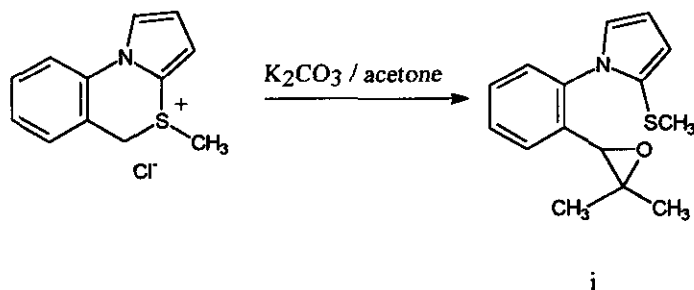
Compound	R <sup>b</sup>	CH <sub>2</sub>	H-2 <sup>c</sup>	J <sub>1,2</sub> (Hz)	CHO
a	H	3.83	6.70	3.4	9.82
b	4-CH <sub>3</sub>	3.82	6.70	3.4	9.78
c	4-OCH <sub>3</sub>	3.83	6.73	3.4	9.93
d	2-CH <sub>3</sub>	3.75	6.71	3.4	9.88
e	2-OCH <sub>3</sub>	3.70	6.80	3.4	9.92

(a) CDCl<sub>3</sub> solution (b) based on the substituent location in the corresponding aniline derivative (c) H-1 not resolved from the aromatic envelope.

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