Interrupted Pummerer Rearrangement: Capture of Tricoordinate Sulfur Species Generated under Pummerer Rearrangement Conditions[1]

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A new approach to fused N,S-heterocycles is described. Treatment of *N*-(2-(alkylsulfinyl)phenyl)pyrroles (**5**) under conditions which typically promote reaction at the carbon α to the sulfoxide group (i.e., the TFAA-initiated Pummerer Rearrangement) produces selectively either pyrrolo[2,1-*b*]benzothiazole (**9**) or 1-(trifluoroacetyl)-pyrrolo[2,1-*b*]benzothiazole (**7**). It is suggested the process occurs by reaction of the pyrrole nucleus *at sulfur* of the corresponding O-trifluoroacetylated sulfoxide **1** producing an intermediate *S*-alkylpyrrolo[2,1-*b*]benzothiazolium salt **3**. Nucleophilic displacement of the S-alkyl substituent by the trifluoroacetate counterion liberates pyrrolo[2,1-*b*]benzothiazole, which may undergo trifluoroacetylation in the presence of excess TFAA. This approach to sulfur activation for intramolecular cyclizations is superior to other methods (usually involving positive halogen and a sulfide) since polyhalogenation and the instability of derivative halopyrroles are avoided.

Introduction

The traditional Pummerer rearrangement is a reaction in which a sulfoxide, when treated with an acid or an anhydride (typically HCl or acetic anhydride) is converted to an α-substituted sulfide.[2] The generally accepted mechanism for the rearrangement involves activation of the sulfoxide by converting the oxygen atom into a leaving group (such as **1** in Scheme I) either by acylation or protonation, followed by formation of the sulfenium (thionium) ion **2** (path A) and subsequent reaction with a nucleophile.[3] The finding that sulfenium ions may serve as electrophiles in aromatic electrophilic substitution has greatly extended the synthetic range of the Pummerer rearrangement.

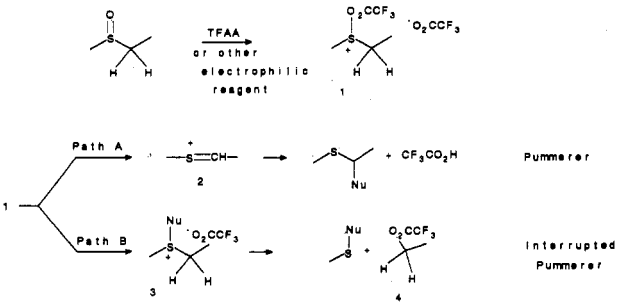
Thus, both intra-[4] and intermolecular[5] versions of the process have been used to prepare a wide range of compounds. We recently used this methodology to prepare 4-substituted pyrrolo[2,1-*c*][1,4]benzothiazines **6** from *N*-(2-(alkylsulfinyl)phenyl)pyrroles **5d-f** using trifluoroacetic acid in refluxing toluene.[6] During the course of this investigation, we discovered that the normal reaction course can be radically altered, providing a general means of C-S bond formation rather than the C-C bond formation typically associated with aromatic electrophilic substitution by Pummerer rearrangement intermediates.

There have been many reports of reactions occurring *at sulfur* under Pummerer reaction conditions.[7] In these cases "anomolous" products resulting from attack at sulfur by a strong nucleophile on tricoordinate intermediate **1** are isolated. This mode of attack is also the critical step in many useful reactions including Swern,[8] Moffatt-Pfitzner,[9] and the Corey-Kim[10] oxidations of primary alcohols to aldehydes. The original Swern reagent (DMSO/trifluoroacetic anhydride[8a]) as well as that of Corey-Kim (succinimidodimethylsulfonium chloride[10a]) have been used as a means of introducing a methylthio group into various heterocyclic and activated aromatic compounds.[11,12]

Mechanistically, all of these reactions are closely related, involving nucleophilic attack at the tricoordinate sulfur with loss of a leaving group (trifluoroacetate from dimethylsulfonium trifluoracetate or chlorine from dimethylsulfonium chloride and dicyclohexylurea from dimethylsulfoniumisourea).

We report here the preparation of an N,S-heterocycle via intramolecular C-S bond formation from sulfoxides under Pummerer rearrangement conditions, but which takes place in a fashion mechanistically similar to those reactions described above. We propose the term inter-

Scheme I



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(1) Part 3 in the series Intramolecular Capture of Pummerer Rearrangement Intermediates, part 1: ref 6. Part 2: ref 14. Parts of this work were presented at the 10th International Congress of Heterocyclic Chemistry, University of Waterloo, Ontario, Canada, Aug 1985, P5-155 and the 189th National Meeting of the American Chemical Society, Miami Beach, FL, April 1985, ORGN-56.

(2) Russell, G. A.; Mikol, G. J. In *Mechanisms of Molecular Migrations*; Thyagarajan, B. S., Ed.; Wiley Interscience: New York, 1968; Vol. 1.

(3) Johnson, C. R.; Phillips, W. G. *J. Am. Chem. Soc.* **1969**, *91*, 682-687.

(4) Cannon, J. G.; Koble, D. L.; Long, J. P.; Verimer, T. *J. Med. Chem.* **1980**, *23*, 750-754. Oikawa, Y.; Yonemitsu, O. *J. Org. Chem.* **1976**, *41*, 1118-1124 and references cited therein.

(5) Bates, D. K. *J. Org. Chem.* **1977**, *42*, 3452-3454.

(6) Bates, D. K.; Winters, R. T.; Sell, B. A. *J. Heterocycl. Chem.* **1986**, *23*, 695-699.

(7) (a) Oxygen nucleophiles: Hiraki, Y.; Kamiya, M.; Tanikaga, R.; Ono, N.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 447-452. Wolfe, S.; Kazmaier, P. M.; Auksi, H. *Can. J. Chem.* **1979**, *57*, 2404-2411; *Ibid.* **1979**, *57*, 2412-2425. Sato, K.; Inoue, S.; Ozawa, K.; Kobayashi, T.; Ota, T.; Tazaki, M. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2715-2719; *Ibid.* **1987**, 1753-1756. (b) Sulfur nucleophiles: Tanikaga, R.; Hiraki, Y.; Ono, N.; Kaji, A. *J. Chem. Soc.* **1980**, 41-42. Senning, A. *Sulfur Lett.* **1985**, *3*(5), 159-162. Wasserman, H. H.; Han, W. T. *J. Am. Chem. Soc.* **1985**, *107*, 1444-1446. Furukawa, N.; Kawada, A.; Kawai, T.; Fujihara, H. *J. Chem. Soc., Chem. Commun.* **1985**, 1266-1267. (c) Nitrogen nucleophiles: Sharma, A. K.; Swern, D. *Tetrahedron Lett.* **1974**, 1503-1506. Oae, S.; Numata, T. *Tetrahedron* **1974**, *30*, 2641-2646. Uchida, Y.; Oae, S. *Gazz. Chim. Ital.* **1987**, *117*, 649-654. Chupp, J. P.; Balthazor, T. M.; Miller, M. J.; Pozzo, M. J. *J. Org. Chem.* **1984**, *49*, 4711-4716.

(8) (a) Omura, K.; Sharma, A. K.; Swern, D. *J. Org. Chem.* **1976**, *41*, 957-962. (b) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480-2482 (DMSO/oxalyl chloride). (c) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148-4150.

(9) Moffatt, J. G.; Pfitzner, K. E. *J. Am. Chem. Soc.* **1965**, *87*, 5666-5667. Moffatt, J. G.; Pfitzner, K. E. *Ibid.* **1965**, *87*, 5670-5678. Moffatt, J. G.; Pfitzner, K. E. *Ibid.* **1966**, *88*, 1762-1765.

(10) (a) Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586-7587 (DMS/Cl_2 or NCS). Corey, E. J.; Kim, C. U. *Tetrahedron Lett.* **1974**, 287-290 (Cl_2/DMSO and Cl_2/thioanisole). (b) Corey, E. J.; Kim, C. U. *Tetrahedron Lett.* **1973**, 919-922 (Cl_2/DMSO).

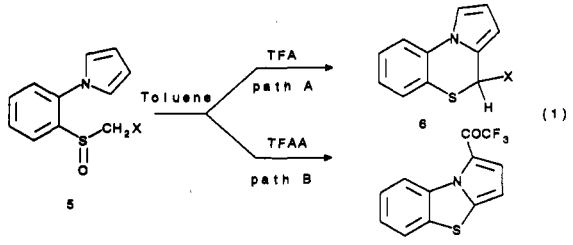
(11) Wendebourg, H. H.; Hartke, K. *Arch. Pharm. (Weinheim)* **1989**, *322*, 473-476. Hartke, K.; Strangemann, D. *Heterocycles* **1986**, *24*, 2399-2402.

0022-3263/92/1957-3094$03.00/0

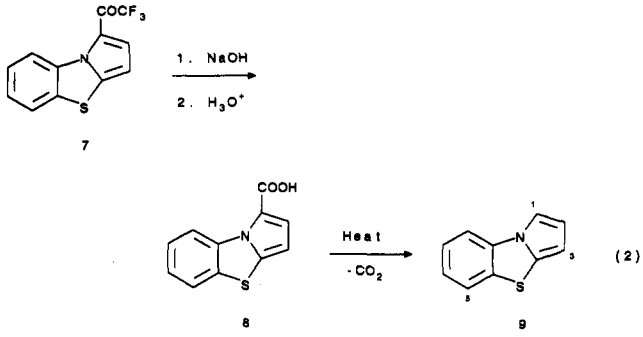
rupted Pummerer reaction to describe this general process (i.e., path B, Scheme I).

Results and Discussion

In contrast to the unreactivity of **5b** in trifluoroacetic acid (TFA), treatment of sulfoxide **5b** with excess trifluoroacetic anhydride (TFAA) in hot toluene (i.e., substituting TFAA for TFA in conditions paralleling those that convert **5d** into **6d**) gave a product that clearly was not a pyrrolobenzothiazine (i.e., **6d**), in 76% yield. The structure of this product was established by spectroscopic means. The infrared spectrum showed a carbonyl stretch at 1670 cm^{-1}; the NMR spectrum indicated absence of the ethyl side chain and the presence of six aromatic hydrogens, one of which was shifted downfield about 1.9 ppm as if adjacent to a carbonyl group. These data, together with combustion analysis and the mass spectrum which showed a molecular ion at m/z 269, indicated that the product was a (trifluoroacetyl)pyrrolo[2,1-*b*]benzothiazole.



The correctness of this skeletal assignment to the product was confirmed chemically. Hydrolysis of **7** was easily accomplished under alkaline conditions giving the corresponding carboxylic acid (**8**) in 72% yield.[13] The carboxylic acid underwent decarboxylation under very mild conditions: heating under vacuum at 80–100 °C in a sublimator gave pyrrolo[2,1-*b*]benzothiazole (**9**) as a crystalline solid in 50% yield (eq 2).



Assignment of the trifluoroacetyl group to the 1-position of the heterocycle was based on NMR spectral data. ^1H NMR of the unsubstituted compound **9** allowed assignment of the three pyrrole protons in the molecule. In **7** the absorption for H-1 is absent; H-8, the hydrogen on the phenyl ring "adjacent" to the trifluoroacetyl group on C-1, is shifted downfield substantially (9.26 ppm) from its position in the aromatic envelope of the parent system (7.23–7.61 ppm); and H-2 is shifted to about 7.4 ppm (from 6.5 ppm in **9**), partially overlapping the signal from one of the aromatic hydrogens. The multiplicity of the peak and the coupling constant for H-3 (to H-2) of 4.78 Hz are in agreement with 1-substitution ($J_{2,3}$ is 3.53 Hz in **9**, 4.35 Hz in the corresponding 1-aldehyde). $J_{1,2}$ is typically smaller than this value, for example, 3.21 Hz in the 3-carbaldehyde derivative of **9**,[14] ruling out placement of the trifluoroacetyl group at C-3.

Table I. Yield of 1-(Trifluoroacetyl)pyrrolo[2,1-*b*]benzothiazole as a Function of Sulfoxide Substituent

compd 5	X	Yield of 7,[a] (%)
a	H	64
b	CH_3	76
c	$CH_2C_6H_5$	39
d	CN	67
e	COC_6H_5	45
f	CO_2Et	61

[a] Conditions: 2 equiv of TFAA in refluxing toluene for 1 h.

Substitution at position 1 is also consistent with reactivity patterns in simple pyrroles[15] and with observations made on the reaction of **9** with other electrophilic reagents. Although formylation of this ring system produces a mixture of 1- and 3-isomers in about a 7:1 ratio,[14] no reactions using TFAA produced any of the 3-substituted isomer.

To explore the generality of the reaction to form this ring system, sulfoxides (**5a,5c–e**) having a range of substituents on the sulfoxide side chain were subjected to the reaction conditions. Although the yields varied, all gave **7** (see Table I).

The reaction also works well with trichloroacetic anhydride in toluene. The corresponding trichloroacetylated derivative **10** is formed from **5b** (60%) or **5d** (31%). The NMR of **10** is very similar to that of **7** except that H-2 is shifted significantly downfield (to 8.0 ppm) and no longer partially overlaps the benzene ring proton envelope.

Activation of the *sulfide* with NCS and to a lesser extent sulfuryl chloride and *N*-bromosuccinimide (NBS) also promote cyclization, but the yield of a mixture of products is low. No conditions have yet been found that do not produce fairly unstable mono- and/or dihalogenated products. In this intramolecular cyclization halogenation is not surprising since the ability of the Swern reagent (prepared from DMSO and oxalyl chloride[8b]) and the Corey–Kim reagent (prepared from dimethyl sulfide and chlorine[10a]) to serve as chlorinating agents,[10b,16] particularly in the presence of reactive heteroaromatic rings such as pyrrole and indole,[17] is well-documented. With DCC in refluxing toluene, no reaction took place.

In order to be synthetically useful, this ring-closure procedure should occur without pyrrole trifluoroacetylation. However, preparation of the unfunctionalized parent system directly was problematic: 1 equiv of TFAA at room temperature gave mixtures of starting material and **7**. Slow addition of TFAA to a cold (0 to −10 °C) solution of **5b** gave **9** free from the 1-trifluoroacetylated compound (i.e., **7**) if the rate of addition and temperature were carefully controlled. This reaction affords yields only

(12) Franco, F.; Greenhouse, R.; Muchowski, J. M. *J. Org. Chem.* **1982**, *47*, 1682–1688. See also: Tomita, K.; Terada, A.; Tachikawa, R. *Heterocycles* **1976**, *4*, 733–737.

(13) Hydrolysis of trifluoroacetyl aromatics is well-known: Anderson, A. G.; Anderson, R. G. *J. Org. Chem.* **1962**, *27*, 3578–3581. Whalley, W. B. *J. Chem. Soc.* **1951**, 665–671.

(14) Bates, D. K.; Sell, B. A.; Picard, J. A. *Tetrahedron Lett.* **1987**, *28*, 3535–3538.

(15) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic Press: London, 1977; p 472.

(16) Smith, A. B.; Leenay, T. L.; Liu, H.-J.; Nelson, L. A. K.; Ball, R. G. *Tetrahedron Lett.* **1988**, *29*, 49–52. Liv, H. J.; Nyangulu, J. M. *Tetrahedron Lett.* **1988**, *29*, 5467–5470. Kende, A. S.; Johnson, J.; Sanfilippo, P.; Hodges, J. C.; Jungheim, L. N. *J. Am. Chem. Soc.* **1986**, *108*, 3513–3515.

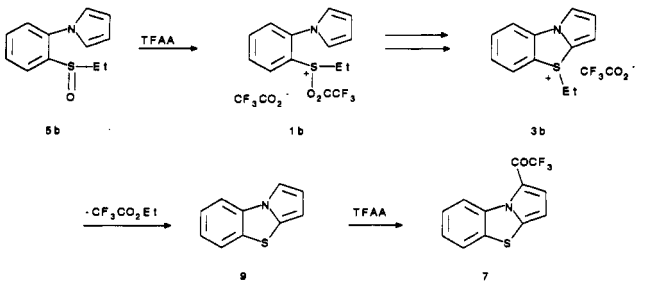
(17) Rubiralta, M.; Diez, A.; Bosch, J.; Solans, X. *J. Org. Chem.* **1989**, *54*, 5591–5597.

Table II. Yield of 9 from 5b/TFAA in Various Solvents

solvent	reaction time (at rt in h)	yield of 9 (%)
TFA	0	87
DMF	3	80
MeCN	overnight	46[a]
HOAc	overnight	33[a]

[a] Based on recovered starting material.

Scheme II



in the 40% range, and on a large scale the extreme care that must be exercised to avoid trifluoroacetylation of the initially formed parent heterocycle makes this approach unattractive.

Several other reaction conditions were examined to optimize yield and ease of workup for preparation of **9**. One alternative involved addition of **5b** to an "aged" solution of 1.5 equiv of TFAA in acetic anhydride at 0 °C followed by neutralization/hydrolysis with 3 M NaOH. Using this procedure **9** could be prepared from **5b** in 70% yield. The sulfoxides **5e–f** gave lower yields of **9**.

Since acetic anhydride is relatively nonvolatile, hydrolyzes slowly, and generally made the workup tedious, several other "solvents" for the conversion of **5b** to **9** were investigated. Under identical reaction conditions, acetonitrile and acetic acid slowly produced product of inferior quality, while DMF and TFA quickly produced pure **9** in high yield (see Table II). Based on our experience, the preferred method for preparation of pure **9** is to add solid **5b** to a solution of TFAA in TFA at 0 °C.

Mechanism

The proposed mechanism of formation of pyrrolobenzothiazoles is shown in Scheme II. The process begins in normal Pummerer rearrangement fashion with activation of the sulfoxide oxygen. Attack by the adjacent electron-rich pyrrole ring on sulfur, displacing trifluoroacetate, forms the pyrrolobenzothiazole nucleus as the sulfonium trifluoroacetate **3**. This process may involve either direct displacement at sulfur or a sulfurane intermediate. Nucleophilic displacement reactions at sulfonium sulfur are well-known,[18a] and a stable sulfurane derived from nucleophilic attack on a sulfoxide sulfur atom has been reported.[18b]

The sulfonium salt (which is readily visualized with van Erk reagent as an intense blue base-line spot by TLC) undergoes displacement of the side chain both during the reaction and during prolonged aqueous workup producing the parent heterocycle **9**. Sulfonium salts are also thermally unstable, undergoing displacement of S-alkyl groups in refluxing dichloroethane.[12] Thus, **9** is formed in reactions in hot toluene by thermal decomposition of the sulfonium salt and subsequently undergoes trifluoroacetylation by excess TFAA present in the reaction mixture to provide the observed product **7**.

After decomposition of the sulfonium salt, the sulfoxide side chain appears in the products as an alkyl trifluoroacetate which is hydrolyzed to the corresponding alcohol (or its decomposition products as in the case of $HOCH_2CN$) during workup. These products are not normally observed; when specifically sought, however, they can be detected. For example, in the reaction of **5c** with 2 equiv of TFAA in refluxing toluene, benzyl trifluoroacetate (but no benzaldehyde or benzyl alcohol) is easily identified by GLC of the reaction mixture before workup.

Compound **9** is highly activated to electrophilic aromatic substitution due to the activating influence of the sulfur atom attached to the pyrrole ring. This is why, in the presence of any excess trifluoroacetic anhydride, the trifluoroacetylated product **7** is readily formed. The activating influence of the sulfur atom is clear when the reactivity of **9** is compared to that of **5**. Stopping the reaction of **5b** with TFAA in refluxing toluene prior to completion produces varying amounts of **7** and **5b**, never any trifluoroacetylated sulfoxide.

It is also clear that sulfonium salt **3** is quite labile. This is expected in hot toluene, but dealkylation must also take place in reactions run at or below room temperature to account for the presence of **7** in the product mixture since formation of **7** is expected to take place only from **9**, not deactivated **3**. In some respects this lability is unfortunate because, if the ring-closure sequence could be stopped at **3**, thermal decomposition in the absence of TFAA should produce **9** cleanly without regard for excess TFAA potentially present during the cyclization process. However, at this time we have been unable to achieve this result.

In summary, we have found that for suitably constructed systems, the limits of which have not yet been determined, intramolecular ring closure with formation of a C–S bond takes place under Pummerer rearrangement conditions. This process, which we term the interrupted Pummerer reaction, is potentially very useful synthetically; this route constitutes the best available synthesis of pyrrolo[2,1-*b*]benzothiazole (**7**).[19] We have also successfully extrapolated this new heterocyclic annelation process to the preparation of a variety of other N,S heterocycles which will be reported in due course.

Experimental Section

Melting points are uncorrected. Elemental analyses were determined by Spang Microanalytical Laboratory, Eagle River, MI. Analytical TLC was performed on silica plates containing a fluorescent indicator using chloroform. Visualization was done with either ultraviolet light or van Erk reagent (*p*-(dimethylamino)benzaldehyde in *n*-butanol/concd HCl). Compounds **5a,c–e** were prepared by alkylation of 1-(2-mercaptophenyl)pyrrole.[6] All other reagents and solvents (reagent grade) were used as purchased.

1-(2-(Ethylthio)phenyl)pyrrole. To a solution of 2-(ethylthio)aniline[20] (61.5 g, 0.4 mol) in glacial acetic acid (340 mL) was added dropwise 2,5-dimethoxytetrahydrofuran (83.4 g, 0.63 mol). A reflux condenser was attached, and the solution was placed on

(18) (a) Tillett, J. G. *Chem. Rev.* **1976**, *76*, 747–772. (b) Adzima, L. J.; Chiang, C. C.; Paul, I. C.; Martin, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 953–959.

(19) (a) Compound **9** obtained as a cyanine dye decomposition product: Schmidt, R. R.; Hensen, H. *Chem. Ber.* **1981**, *114*, 1723–1736. (b) Compound **9** obtained from thermal or photochemical decomposition of 2-azidophenyl thienyl sulfides: Lindley, J. M.; Meth-Cohn, O.; Suschitsky, H. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1198–1204. Two other methods of preparing pyrrolo[2,1-*b*]benzothiazoles, ammenable only to substituted systems, have been reported. (c) Cycloaddition of electron-deficient acetylenes to mesoionic systems: Potts, K. T.; Choudry, D. R. *J. Org. Chem.* **1978**, *43*, 2697–2700. (d) Base-catalyzed condensation of 2-substituted 3-benzothiazolium salts: Ciocoiu, I.; Budeanu, C. H.; Zugravescu, I. *Bul. Inst. Politeh. Iasi, Sect. 2* **1978**, 6109–112 (*Chem. Abstr.* **1978**, *92*, 41819s). Kroehne, F.; Friedrich, W. *Chem. Ber.* **1963**, *96*, 1195–1202.

(20) Nieforth, K. A. *J. Pharm. Sci.* **1963**, *52*, 1136–1139.

a steam bath for 2.25 h while a stream of N_2 was passed through the solution via a fritted glass tube. Volatiles were removed on a rotary evaporator at aspirator vacuum, and the dark residue was vacuum distilled to give 44.2 g (55%) of the pyrrole as a clear pale yellow oil: bp 118 °C (1.1 Torr); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 7.6–7.1 (4 H, m), 6.98 (2 H, t, J = 2.4 Hz), 6.42 (2 H, t, J = 2.4 Hz), 2.70 (2 H, q, J = 7.4 Hz), 1.33 (3 H, t, J = 7.4 Hz); MS m/z (rel int) 203 M^+, 174 (100). Anal. Calcd for $C_{12}H_{13}NS$: C, 70.89; H, 6.45; N, 6.89; Found: C, 70.77; H, 6.42; N, 6.91.

1-(2-(Ethylsulfinyl)phenyl)pyrrole (5b). The corresponding sulfide (10.0 g, 49.3 mmol) in CH_2Cl_2 (145 mL) was cooled to 0 °C in an ice bath. *m*-Chloroperoxybenzoic acid (11.8 g, 80%, 52.3 mmol) in CH_2Cl_2 (200 mL) was then added dropwise over 90 min. After an additional 1 h in ice, the mixture was stored in the freezer (-20 °C) overnight. Precipitated *m*-chlorobenzoic acid was removed by filtration, and the filtrate was washed with 5% K_2CO_3 solution. The organic layer was dried (Na_2SO_4), and the solvent was removed in vacuo to give a brown oil (10.8 g, 100%) that slowly crystallized: mp 76–77.5 °C (from ethanol); ^{1}H NMR ($CDCl_3$, 60 MHz) δ 8.30–7.85 (1 H, m), 7.80–7.20 (3 H, m), 6.83 (2 H, t, J = 2.6 Hz), 6.33 (2 H, t, J = 2.6 Hz), 2.73–1.55 (2 H, AB portion of ABX_3 system, J = 14, 7.6 Hz), 0.88 (3 H, t, J = 7.6 Hz); IR (KBr) 1045 cm^{-1}; MS m/z (rel int) 219 M^+, 162 (100). Anal. Calcd for $C_{12}H_{13}NOS$: C, 65.72; H, 5.97; N, 6.39; Found: C, 65.61; H, 5.83; N, 6.34.

1-(Trifluoroacetyl)pyrrolo[2,1-*b*]benzothiazole (7). To a solution of **5b** (440 mg, 2 mmol) in toluene (25 mL), under dry nitrogen, was added neat TFAA (0.57 mL, 4 mmol) dropwise over 5 min via syringe. The mixture was then refluxed, gradually becoming progressively darker yellow. At the end of 1 h the blood red to dark brown solution was cooled, washed with 5% aqueous K_2CO_3, and dried over Na_2SO_4, and the volatiles were removed in vacuo. The resulting crude solid was recrystallized from hexanes to give 410 mg (76%) of **7**: mp 114–115 °C; IR (KBr) 1675 cm^{-1}; MS m/z (rel int) 269 M^+, 200 (100). Anal. Calcd for $C_{12}H_6F_3NOS$: C, 53.53; H, 2.25; N, 5.20; Found: C, 53.49; H, 2.38; N, 5.11.

Hydrolysis of 7 to 1-Pyrrolo[2,1-*b*]benzothiazolecarboxylic Acid (8). Compound **7** (500 mg, 1.86 mmol) was refluxed with 0.6 M NaOH solution in 50% aqueous ethanol for 24 h. After being cooled to room temperature, the deep red solution was diluted with water (60 mL) and acidified with 3 N HCl. The off-white solid that formed was collected by filtration, slurried with benzene, and rotary evaporated to azeotropically remove residual water to give a beige solid (0.29 g, 72%) which was not purified further: mp 125–130 °C; IR (KBr) 3600–2750, 1660 cm^{-1}; MS m/z (rel int) 217 (100), 200 (58), 173 (88), 172 (55), 145 (20).

Pyrrolo[2,1-*b*]benzothiazole (9) by Decarboxylation of 8. The carboxylic acid **8** (60 mg, 0.276 mmol) was heated under aspirator vacuum in a sublimator to a bath temperature of 120 °C. Sublimation commenced at about 80 °C; after 5–10 min deposition of fine white crystals (24 mg; 50%) of **9** onto the cold finger was complete: mp 52 °C (lit.[19a] mp 54 °C; lit.[19b] mp 57–58.5 °C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.61–7.23 (5 H, m containing a H-1 at δ 7.42 (1 H, dd, $J_{1/2}$ = 2.98 Hz, $J_{1,3}$ = 1.31 Hz), 6.52 (1 H, dd, $J_{2,1}$ = 2.98 Hz, $J_{2,3}$ = 3.57 Hz, H-2), 6.16 (1 H, dd, $J_{2,3}$ = 3.57, $J_{1,3}$ = 1.31 Hz, H-3); IR (neat) 3050, 1600, 1500, 1300, 890, 630 cm^{-1}; MS m/z (rel int) 173 (100).

1-(Trichloroacetyl)pyrrolo[2,1-*b*]benzothiazole (10). Replacing TFAA with an equivalent molar quantitity of trichloroacetic anhydride in the procedure described above for **7** gave **10** as a yellow solid. Recrystallization from hexanes gave analytically pure material (60%) as pale yellow crystals: mp 137–140 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.15–9.10 (1 H, dt, J = 8.2, 1.6 Hz), 8.00 (1 H, d, J = 4.80 Hz), 7.64–7.59 (1 H, dm, J = 7.7 Hz), 7.47–7.28 (2 H, m), 6.47 (1 H, d, J = 4.80 Hz); IR (KBr) 1650 cm^{-1}; MS m/z (rel int) 317 M^+, 200 (100). Anal. Calcd for $C_{12}H_6NOSCl_3$: C, 45.24; H, 1.90; N, 4.40. Found: C, 45.28; H, 1.99; N, 4.35.

General Procedure for Cyclization Using TFA/Ac_2O. Trifluoroacetic anhydride (7.5 mmol) and acetic anhydride (5 mL) were allowed to stand overnight at room temperature. The appropriate sulfoxide (5 mmol) was added in portions to this ice-cooled mixture. After 2.5 h in an ice bath the pH of the dark red solution was adjusted to 7 with 3 N NaOH, and the mixture was stirred for an additional 30 min at room temperature. Extraction with CH_2Cl_2 (2 × 25 mL), drying of the extract over Na_2SO_4, and evaporation of the solvent in vacuo gave a dark oil, which was passed through a short (1- × 5-in) column of alumina eluted with $CHCl_3$. Yields of pure **9** from different sulfoxides were as follows: **5a**, 60%; **5b**, 70%; **5c**, 0%; **5d**, 31%; **5e**, 9%.

Effect of Solvent on Cyclization of 5b. To the appropriate solvent (5 mL, 10 mL for DMF) in ice was added TFAA (1.93 g, 9.2 mmol) dropwise. This mixture was stirred in ice for 20 min before **5b** (1.0 g, 4.9 mmol) in the solvent (15 mL, 30 mL for DMF) was added over 15 min. After being stirred an additional 15 min in ice, the reaction was stirred at room temperature for the times listed in Table II. The mixture was then quenched with water (50 mL), and solid sodium acetate was added until the mixture had a pH of 7. After standing overnight, the mixture was extracted with CH_2Cl_2 (2 × 25 mL). In DMF and TFA most of the product appeared as an off-white precipitate which was collected prior to extraction. Some discoloration occurred in the TFA/sulfoxide mixture during addition; addition of the solid sulfoxide to the TFAA/TFA mixture avoided this problem. In the cases of acetonitrile and acetic acid, the reaction was much slower and the concentrated extract had to be chromatographed to separate product from unreacted starting material. The data are summarized in Table II.

Regiochemistry of Acetylation of Ferrocenylarylethylenes

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We describe the synthesis and Friedel–Crafts acetylation of a series of ferrocenylarylethylenes, $C_5H_5FeC_5H_4CH{=}CH(C_6H_4$-*p*-X), where X = NO_2 (**3a**), Br (**3b**), and NMe_2 (**3c**). Compounds **3a–c** provide a direct comparison of the reactivity of ferrocene, olefin, and aryl functionalities. The regiochemistry of substitution of these compounds depends on the nature of the aryl substituent. Acetylation occurs predominantly at the olefin and the unsubstituted cyclopentadienyl ring; substitution does not occur at the aryl ring or at the substituted cyclopentadienyl ring. Reaction at the olefin is accompanied by olefin isomerization. With the strongly activating dimethylamino substituent (**3c**), substitution at the unsubstituted cyclopentadienyl ring (**5c**) is slightly favored over substitution at the olefin (**4c**). The regiochemistry of olefin substitution suggests that a ferrocenyl substituent is better able to stabilize an adjacent positive charge than a *p*-(dimethylamino)aryl substituent. With the bromine substituent (**3b**), substitution at the olefin (**4b**) is slightly favored over substitution at the unsubstituted cyclopentadienyl ring (**5b**). The nitro group is sufficiently deactivating that **3a** fails to react under our conditions.

In the course of our synthesis of nonlinear optical materials, we investigated the Friedel–Crafts acetylation chemistry of ferrocene derivatives **3a–c** as a potential means of further functionalizing these compounds for ultimate use as electrochemically switchable nonlinear optical materials anchored at the surface of modified

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