

AN INTERRUPTED PUMMERER REACTION INDUCED BY
HYPERVALENT IODINE(III) REAGENT: A NEW SYNTHESIS OF
PYRROLO[2,1-*b*]BENZOTHAZOLE

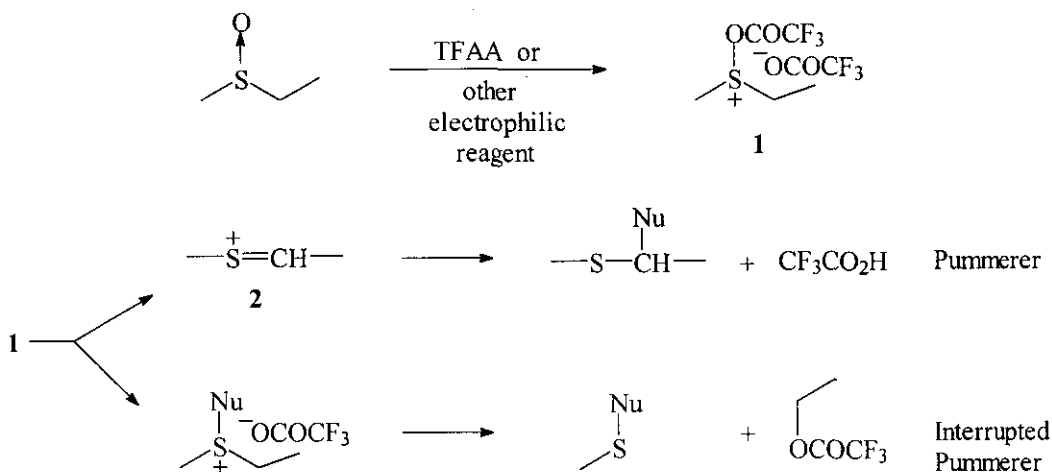
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Abstract—Treatment of 1-(2-alkylthiophenyl)pyrroles with phenyliodine(III) bis(trifluoroacetate) containing trifluoroacetic acid resulted in an interrupted Pummerer reaction to give pyrrolo[2,1-*b*]benzothiazole rather than the normal Pummerer-type products.

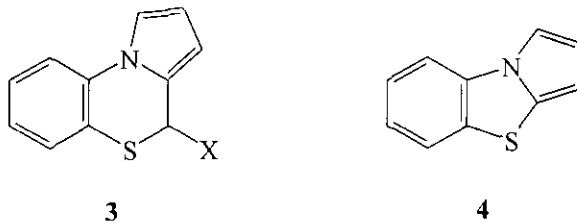
The Pummerer reaction of sulfoxides normally proceeds *via* an activated sulfoxide (1) and then a thionium ion (2) which reacts with a nucleophile at carbon to afford an α -substituted sulfide.¹ In an interrupted Pummerer reaction, the tricoordinate sulfur intermediate (1) undergoes reaction with a nucleophile at sulfur leading to unexpected product.² (Scheme I)



Scheme I

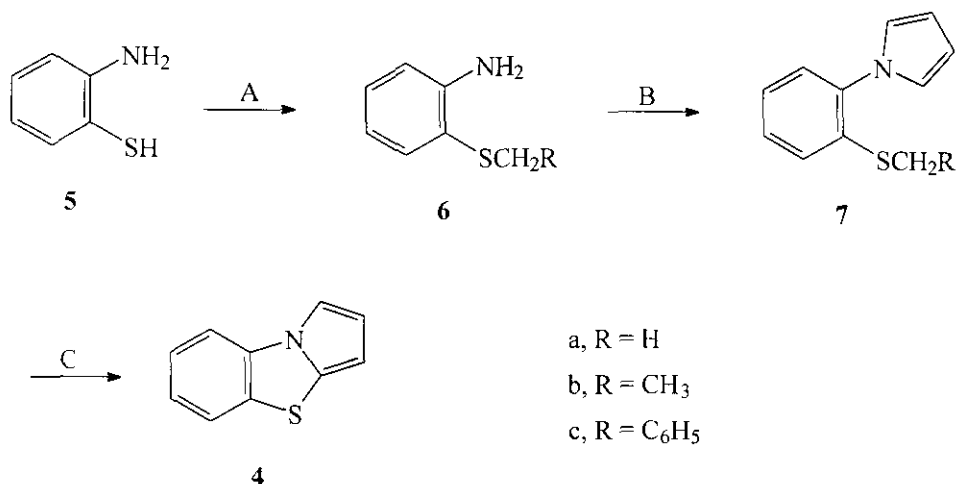
Recently, hypervalent iodine reagents have been extensively used in organic syntheses due to their low toxicity, ready availability and easy handling. As a continuation of our studies concerning hypervalent iodine(III) chemistry,³ we have reported a Pummerer-type reaction that provides a very simple and

convenient procedure for the preparation 4*H*-pyrrolo[2,1-*c*][1,4]benzothiazines (**3**) by treatment of α -acyl sulfides with phenyliodine(III) bis(trifluoroacetate) (PIFA).⁴ In the present work, an interrupted Pummerer-type reaction of sulfides using PIFA has been applied to prepare pyrrolo[2,1-*b*]benzothiazole (**4**) via intramolecular C-S bond formation.^{5,6,7}



- a, X = CO₂C₂H₅
 b, X = COC₆H₅
 c, X = COCH₃

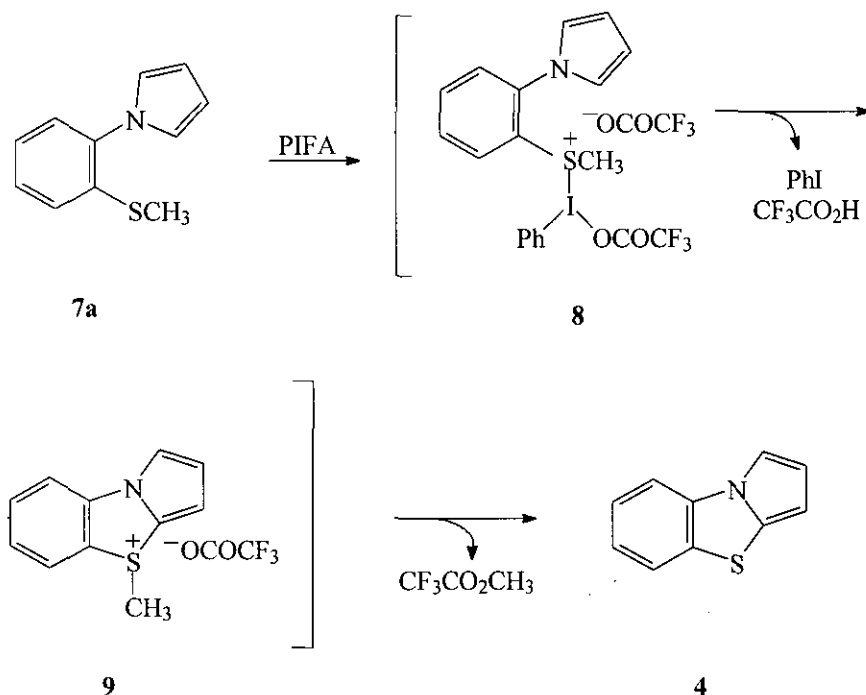
The requisite sulfides (**7**) were readily prepared from 2-aminobenzenethiol (**5**). Preparation of **7a** has been reported.⁴ The anilinosulfides (**6b-c**), prepared from **5**, were converted into sulfides (**7b-c**) by treatment with 2,5-dimethoxytetrahydrofuran in boiling glacial acetic acid.⁸ Treatment of **7a-c** with PIFA containing trifluoroacetic acid (TFA) in CH₂Cl₂ caused cyclization to give pyrrolo[2,1-*b*]benzothiazole (**4**) in 85%, 82%, and 30% yields, respectively. Under these conditions no sulfoxides and Pummerer-type products were obtained (Scheme II).⁹



- Reagents: A) RCH₂Cl / NaOH
 B) 2,5-Dimethoxytetrahydrofuran / CH₃CO₂H
 C) PIFA-TFA / CH₂Cl₂

Scheme II

The proposed mechanism of formation of pyrrolo[2,1-*b*]benzothiazole (**4**) is shown in Scheme III. The cyclization from **7a** to **4** is assumed to proceed through interrupted Pummerer-type reaction intermediate (**9**) which would be formed by attack of PIFA on the sulfur atom of **7a**, followed by simultaneous elimination of the iodobenzene and trifluoroacetic acid from the resultant sulfonium salt (**8**). Apparently without the electron withdrawing group on the carbon alpha to the sulfide group, trifluoroacetate ion is not basic enough to generate the thionium ion. The reaction also exclusively gave the corresponding benzyl sulfonium salt when benzyl sulfide was used as substrate instead of using methyl sulfide. However, the debenzylation has not proceeded in high yield.



Scheme III

In summary, our results here demonstrate that the use of a combined reagent PIFA-TFA in CH₂Cl₂ is a convenient and useful method for interrupted Pummerer-type reaction of sulfides to prepare pyrrolo[2,1-*b*]benzothiazole.

ACKNOWLEDGEMENT

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EXPERIMENTAL

All melting points are uncorrected. The IR absorption spectra were recorded on a Shimadzu IR-27G spectrophotometer, and $^1\text{H-NMR}$ spectra on a Varian Gemini-200 spectrometer. Chemical shifts were measured in ppm (δ) with respect to TMS. MS spectra were obtained on a JEOL JMS D-300 instrument.

2-(Ethylthio)aniline (6b)

A mixture of *o*-aminobenzenethiol (2.5 g, 19.97 mmol), ethyl iodide (3.27 g, 20.97 mmol) and NaOH (1 g, 25 mmol) in ethanol (10 mL) was heated under reflux with stirring for 1 h. A major part of ethanol was removed and the resulting solution was extracted with ether. The organic layer was washed with water and dried over sodium sulfate. Evaporation of the solvent gave an oily residue, which was purified by column chromatography on silica gel with chloroform : hexane (1:1) as an eluting solvent to give **6b** (1.84 g, 60 %) as an oil. IR (neat) ν 750, 1310, 1615 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3): 1.22 (t, $J=7.3$ Hz, 3H, SCH_2CH_3), 2.76 (q, $J=7.3$ Hz, 2H, SCH_2CH_3), 6.65-7.50 (m, 4H, ArH); HRMS m/z Calcd for $\text{C}_8\text{H}_{11}\text{NS}$: 153.0612. Found: 153.0610.

2-(Benzylthio)aniline (6c)

Benzyl chloride (1.21 g, 9.56 mmol) was added dropwise to a stirred ice-cold solution of *o*-aminobenzenethiol (1 g, 7.97 mmol) in 10 % NaOH (15 mL) and stirring was continued for 2.5 h. The reaction mixture was extracted with CHCl_3 , the organic layer was washed with water and dried over sodium sulfate. Evaporation of the solvent gave an oily residue, which was purified by column chromatography on silica gel with chloroform as an eluting solvent to give **6c** (1.24 g, 72 %) as an oil. IR (neat) ν 760, 1305 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3): 3.90 (s, 2H, SCH_2), 6.66 (m, 1H, ArH), 7.06-7.40 (m, 3H, ArH); HRMS m/z Calcd for $\text{C}_{13}\text{H}_{13}\text{NS}$: 215.0768. Found: 215.0770.

1-(2-Ethylthiophenyl)pyrrole (7b)

A mixture of 2,5-dimethoxytetrahydrofuran (2.09 g, 15.79 mmol) and 2-(ethylthio)aniline (2.2 g, 14.36 mmol) in glacial acetic acid (5 mL) was refluxed for 30 min, then poured into crashed ice. The organic solution was washed twice with 5 % sodium bicarbonate, then with water, and dried over sodium sulfate. Evaporation of the solvent gave an oily residue, which was purified by column chromatography on silica gel with chloroform : hexane (1: 4) as an eluting solvent to give **7b** (2.24 g, 78 %) as an oil. IR (neat) ν 725 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3): 1.24 (t, $J=7.3$ Hz, 3H, SCH_2CH_3), 2.76 (q, $J=7.3$ Hz, 2H, SCH_2CH_3), 6.33 (t, $J=2.2$ Hz, pyrrole β -H), 6.87 (t, $J=2.2$ Hz, pyrrole α -H), 7.15-7.45 (m, 4H, ArH); HRMS m/z Calcd for $\text{C}_{12}\text{H}_{13}\text{NS}$: 203.0768. Found: 203.0766.

1-(2-Benzylthiophenyl)pyrrole (7c)

By using a procedure similar to that described for **7b**, **6c** give **7c** (887 mg, 80 %), mp 85-86 $^\circ\text{C}$ (from petroleum ether). IR (neat) ν 720 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3): 3.85 (s, 2H, SCH_2), 6.32 (t, $J=2.2$ Hz, 2H, pyrrole β -H), 6.86 (t, $J=2.2$ Hz, pyrrole α -H), 7.10-7.45 (m, 9H, ArH); MS m/z 256 (M^+). Anal. Calcd for

C₁₇H₁₅NS: C, 76.94; H, 5.70; N, 5.28. Found: C, 76.92; H, 5.60; N, 5.17.

Pyrrolo[2,1-*b*]benzothiazole (4)

A solution of **7a** (372 mg, 2 mmol) in CH₂Cl₂ (5 mL) was added dropwise to a solution of the mixture of PIFA (860 mg, 2 mmol) and TFA (456 mg, 4 mmol) in CH₂Cl₂ (5 mL) at 0°C and the mixture was stirred at the same temperature for 1 h. The resultant mixture was quenched with water and extracted with CH₂Cl₂. The organic layer was washed with water and dried over magnesium sulfate. The solvent was evaporated off and the residue was chromatographed on silica gel with hexane as an eluting solvent to give **4** (294 mg, 85 %), mp 53°C (lit., ⁵mp 57-58.5 °C; lit., ⁶mp 54 °C). IR (neat) ν 3065, 1600, 1500, 1305, 890, 630, cm⁻¹; ¹H-NMR (CDCl₃): 6.23 (dd, 1H, J_{2,3}=3.6 Hz, J_{1,3}=1.2 Hz, H-3), 6.59 (dd, 1H, J_{2,3}=3.6 Hz, J_{2,1}=2.8 Hz, H-2), 7.19-7.65 (m, 4H, ArH), 7.45 (dd, J_{1,2}=2.8 Hz, J_{1,3}=1.2 Hz, H-1); MS m/z 173 (M⁺).

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