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PREPARATION OF BENZOTHIOPYRANO[2,3-*b*]INDOLES BY THE REACTION OF 1,3-DIHYDROINDOLE-2-THIONES WITH CERTAIN DIENOPHILES

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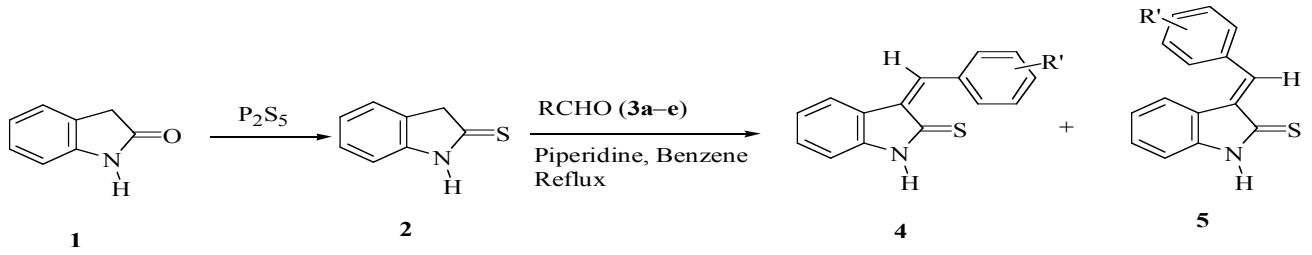
Abstract – Benzothiopyrano[2,3-*b*]indoles were prepared by the cyclization of 1,3-dihydroindole-2-thiones with various dienophiles. The 1,3-dihydroindole-2-thiones were readily synthesized by the reaction of oxindole with P_2S_5 followed by a piperidine-mediated condensation of the resulting thioindole with a suitable aromatic aldehyde.

INTRODUCTION

3-Substituted 1-alkylidine-3*H*-benzo[*b*]indolin-2-ones have been shown to exhibit inhibitory properties against various receptor tyrosine kinases (RTKs).[1,2] We[3] recently expanded the chemical diversity of this structural type by developing a new strategy towards the synthesis of 3-1-alkylidine-3*H*-benzo[*b*]thiophene-2-ones in which the nitrogen atom has been replaced by a sulfur atom. We were also interested in exploring the possibility of these benzo[*b*]thiophene-2-ones serving as dienes in Diels–Alder cyclization reactions since we[4] had shown that selonoazadienes react with benzynes to give 4*H*-1,3-benzoselenazines. However, our attempts to carrying out Diels–Alder reactions with benzo[*b*]thiophene-2-ones failed. We subsequently prepared the pyrrole analogs, benzo[*b*]pyrrole-2-thiones (in which the carbonyl oxygen atom of the indolin-2-one ring was placed by a sulfur atom) and found that 2-thiones did reaction with benzynes and dimethyl acetylenedicarboxylate to give new benzothiopyrano[2,3-*b*]indoles. The results are reported herein.

RESULTS AND DISCUSSION

As shown in Scheme 1, the starting benzo[*b*]-2-thiones (4 and 5) were prepared[5] by the conversion of 2*H*-indol-2-one (**1**), commonly called oxindole, to the thioindole (**2**) with P_2S_5 followed by a piperidine-mediated condensation of **2** with aldehydes (**3a–e**) in refluxing benzene. The results are listed in Table 1.



Scheme 1

As shown, *(Z)*-1,3-dihydro-3-(pyrrol-2-ylmethylene)indole-2-thione **(4b)** (Entry 2), (*Z*)-3-(furan-2-ylmethylene)-1,3-dihydroindole-2-thione **(4e)** (Entry 5), and (*E*)-1,3-dihydro-3-(thien-2-ylmethylene)indole-2-thione **(5d)** (Entry 4) were obtained essentially as single products. However, a mixture of (*Z*)-(**4a**)- and (*E*)-1,3-dihydro-3-(4-isopropylbenzylidine)indole-2-thione (**5a**), were obtained in a ratio of 72:15, respectively (Entry 1) and a mixture of (*Z*)- (**4c**)- and *E*-1,3-dihydro-3-(4-*N,N*-dimethylaminobenzylidine)indole-2-thione (**5c**) was obtained in a ratio of 78:18, respectively (Entry 3). Since analytical samples of **4a**,**c** and **5a,c** were obtained by subjecting a small portion of each mixture to column chromatography. Diasteromeric assignments of the indole-2-thiones (**4** and **5**) were made on the basis of their olefinic proton chemical shifts with the *Z* isomers occurring around δ 7.8 ppm and the *E* isomers appearing around 7.5 ppm. These chemical shifts were similar to those previously reported for similarly structured indol-2-ones.[4] In addition, the structure of compound (**4b**) was confirmed by X-Ray crystallography; the ORTEP drawing of **4b** is shown in Figure 1.

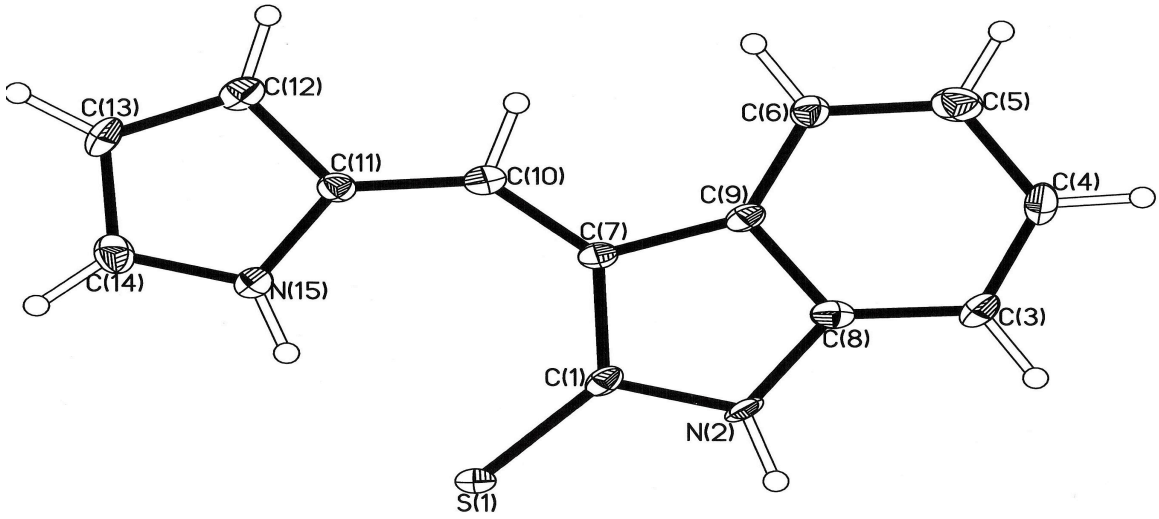
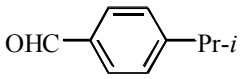
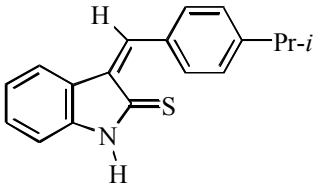
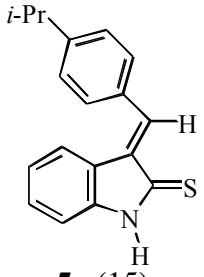
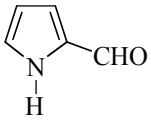
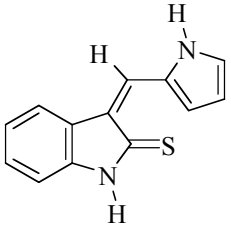
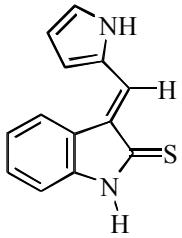
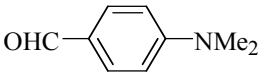
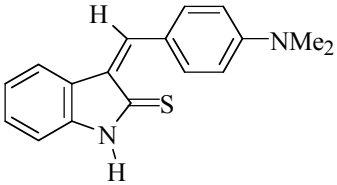
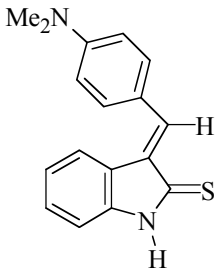
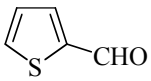
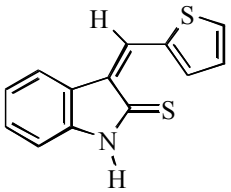
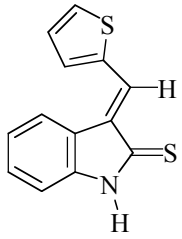
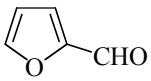
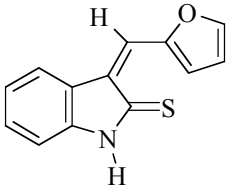
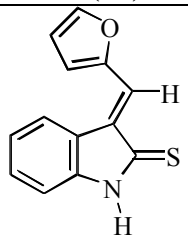


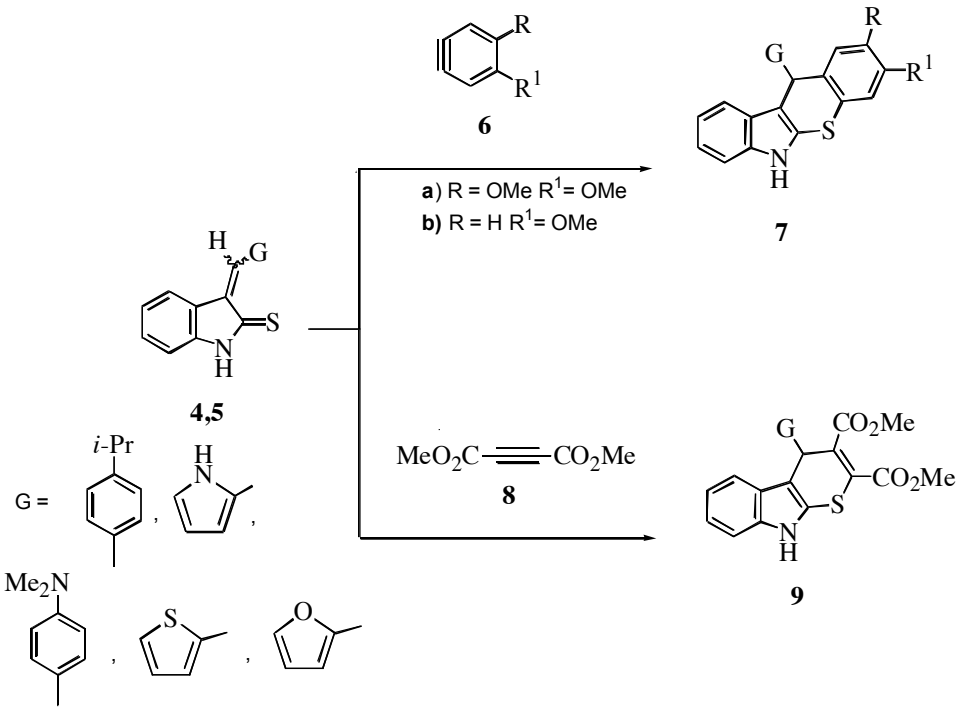
Figure 1. ORTEP of Compound (**4b**)

Table 1. Preparation of *Z*- (**4**) and *E*-Pyrrol-2-thiones (**5**)

Entry	**3**	**4** (yield, %)	**5** (yield, %)
1	 **3a**	 **4a** (72)	 **5a** (15)
2	 **3b**	 **4b** (83)	 **5b** (trace)
3	 **3c**	 **4c** (78)	 **5c** (18)
4	 **3d**	 **4d** (trace)	 **5d** (82)
5	 **3e**	 **4e** (79)	 **5e** trace

With the indole-2-thiones on hand, their reactions with 4,5-dimethoxybenzyne (**6a**), 3-methoxybenzyne (**6b**), and dimethyl acetylenedicarboxylate (**8**) were carried out. Since dienophiles (**6a** and **8**) would

yield a single adduct, the mixtures (**4a**/**5a** and **4c**/**5c**) were used as is. The overall reactions schemes are shown in Scheme 1. We first studied the reaction of indole-2-thiones with **6a** since the identification of the structure of Diels–Alder adducts by ^{1}H NMR and ^{13}C NMR spectroscopy would be simplified, and the

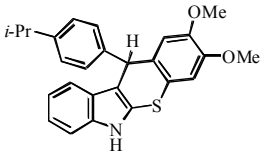
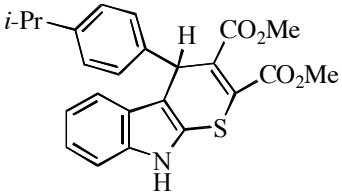
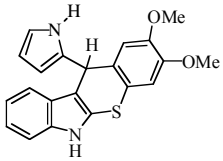
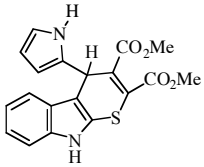
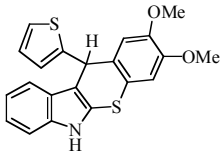
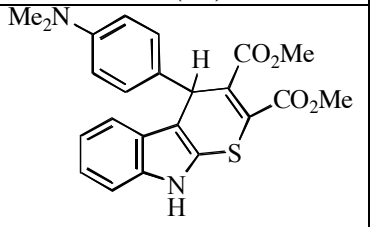
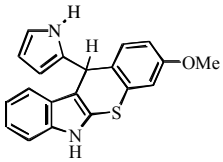
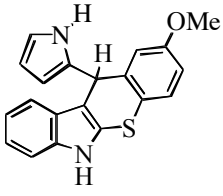
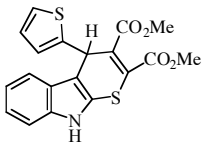
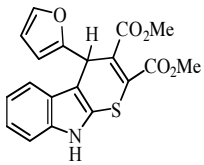


Scheme 2

introduction of the dimethoxy groups might induce some biological activity in the resulting adducts. As shown in Scheme 1, compounds (**4a**/**5a**,**4b, 4c**/**5c**) indeed reacted with **6a** to yield single adducts, *i.e.,* 2,3-dimethoxy[1]benzothiopyrano[2,3-*b*]indoles (**7a–c**) in 52–65% yields. The results listed in Table 2 (Entries 1–3)) were obtained by generating 4,5-dimethoxybenzyne (**6a**) *in situ* from a mixture of 2-diazonio 4,5-dimethoxybenzenecarboxylate hydrochloride in refluxing benzene.[6] The yields of **7a–c** were lower when **6** was generated by the addition of isoamyl nitrite to a refluxing benzene solution (~80 °C) containing 4,5-dimethoxyanthranilic acid.[7] Interestingly, these indole-2-thiones, unlike selonoazadienes,[1] failed to react when **6** was generated by the reaction of (phenyl)[*o*-(trimethylsilyl)phenyl]iodonium triflate and Me_4NF at room temperature,[7] or by the reaction of anthranilic acid and isoamyl nitrite in THF 0 °C.[8] Subsequently, the reaction of 3-methoxybenzyne (**6b**) with *(Z)*-1,3-dihydro-3-(pyrrol-2-ylmethylene)indole-2-thione **(4b**) afforded a 1:1 mixture of 3-methoxy- and 4-methoxyindoles (**7d**) (Entry 4). This indicates that **4b** adds non-regioselectively and in a concerted manner to 3-methoxybenzyne which is consistent with other reports of Diels-Alder cycloadditions to unsymmetric arynes.[9]

Lastly, the reaction of **4** and **5** with dimethyl acetylenedicarboxylate (**8**) gave the indole-2,3-dicarboxylic acid dimethyl esters (**9a–e**) in yields of 68–78% (Entries 5–9). These reactions also required refluxing MeCN for 6 h. The structures of **7** and **9** were confirmed by ^{1}H NMR and ^{13}C NMR spectral analysis. For example, in the ^{1}H NMR spectra of compounds (**7a–c**) the benzylic hydrogen (H-11) exhibited a singlet in the vicinity of δ 3.8–4.0 ppm whereas the allylic hydrogen (H-1) in **9a–e** exhibited a singlet in the

Table 2. Yields of Diels-Alder Adducts (**7** and **9)**

Entry	Diene	Dieno-Phile	Adduct, Yield (%)	Entry	Diene	Dieno-phile	Adduct, Yield (%)
1	**4a/5a**	**6a**	 **7a** (56)	6	**4a/5a**	**8**	 **9a** (21)
2	**4b**	**6a**	 **7b** (45)	7	**4b**	**8**	 **9b**(78)
3	**4c/5c**	**6a**	 **7c** (56)	8	**4c/5c**	**8**	 **9c** (72)
4	**4b**	**6b**	 **7d** (21) **+**  **7e** (22)	9	**8**	**5d**	 **9d** (73)
				10	**8**	**4e**	 **9e** (68)

range of 3.9–4.3ppm. Additionally, the structure of **9d** was confirmed by X-Ray spectroscopy; an ORTEP drawing of **9d** is shown in Figure 2.

In conclusion, we have shown that 1,3-dihydroindole-2-thiones undergo reaction with 4,5-dimethoxybenzyne and dimethyl acetylendicarboxylate to give benzothiopyrano[2,3-*b*]indoles in modest yields. We are not aware of other synthetic methodology that would allow the facile synthesis of these multi-substituted heterocycles.

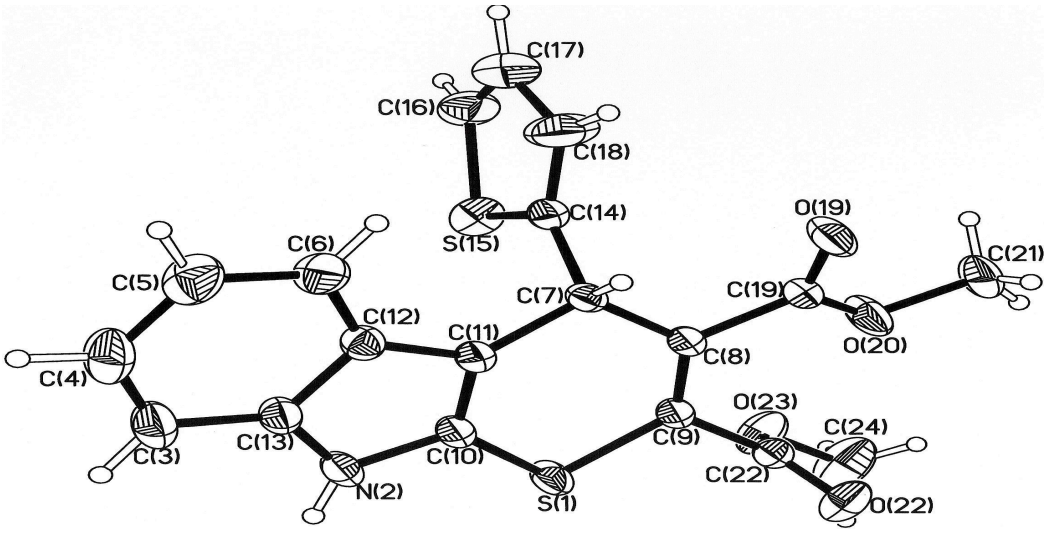


Figure 2. ORTEP of Compound (**9d**)

EXPERIMENTAL

General Data: Melting points were taken on a Mel-Temp capillary apparatus and are uncorrected with respect to stem correction. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AVANCE DRX-400 Multinuclear NMR spectrometer. Chemical shifts are reported in reference to TMS as internal standard.

1,3-Dihydroindole-2-thione (2)

To a solution of oxiindole (5 g, 37 mmol) in 30 mL of dry THF was added P_2S_5 (16.6 g, 37 mmol). The resulting mixture was stirred at rt for 45 min then $NaHCO_3$ (10.41 g, 123 mmol) was added in three portions and the resulting mixture stirred at rt for an additional 3 h. The solid material, which precipitated during stirring, was separated by vacuum filtration and the mother liquor was concentrated to dryness. The residue was treated with 100 mL of ice water, extracted with $CHCl_3$ (3X 60 mL) and purified by column chromatography on SiO_2 to give **2** (4.5 g, 82%) as a light yellow solid (EtOAc-hexane), mp 79–82 °C. ^{1}H NMR ($CDCl_3$) δ 4.10 (s, 2H, -CH_2-), 7.10 (m, 2H, Ar-H-5, H-6), 7.27 (m, 2H, Ar-H-4, H-7), 10.80 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 36.7, 110.3, 122.6, 124.9, 125.7, 128.3, 143.1, 178.9. *Anal.* Calcd for C_8H_7NS: C, 64.39; H, 4.73; N, 9.39. Found: C, 64.47; H, 4.80; N, 9.45.

General Procedure for the Preparation of 1,3-Dihydroindole-2-thiones (4 ,5)

A reaction mixture of **2** (0.5 g, 3.3 mmol), the appropriate aldehyde (**3**) (4.0 mmol) and piperidine (0.09 g, 1 mL, 0.3 mmol) in dry benzene (6 mL) was stirred at 90 °C for 4 h. The reaction mixture was then cooled to rt, during which time a precipitate was obtained. The precipitate was filtered, washed (benzene), and dried. The dried solid was subjected to column chromatography on SiO_2 with EtOAc-hexane (1:4, v/v) to give **4** and **5**.

(*Z*)- 1,3-Dihydro-4-isopropylbenzylidineindole-2-thione (4a)

This compound was isolated as a light yellow solid (EtOAc-hexane), mp 213–215 °C. ^{1}H NMR ($CDCl_3$) δ 1.13 (d, *J*=8.0 Hz, 6H), 2.80 (m, 1H), 6.35 (d, *J*=8.0 Hz, 1H), 6.75 (d, *J*=8.0 Hz, 2H), 7.10 (d, *J*=8.1 Hz, 2H), 7.23 (dd, *J*=7.5, 7.8 Hz, 1H), 7.35 (dd, *J*=7.5, 7.8 Hz, 1H), 7.80 (s, 1H, vinylic H), 7.91 (d, *J*=7.8 Hz, 1H), 8.02 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 24.1, 24.3, 33.9, 110.2, 119.8, 121.5, 122.5, 125.5, 126.2, 129.3, 130.4, 131.9, 132.2, 132.4, 134.7, 147.7, 149.4, 186.5. *Anal.* Calcd for $C_{18}H_{17}NS$: C, 77.38; H, 6.13; N, 5.01. Found: C, 77.29; H, 6.09; N, 4.99.

***(E)*-1,3-Dihydro-3-(4-isopropylbenzylidine)indole-2-thione (5a)**

This compound was isolated as a light red solid (EtOAc-hexane), mp 214–216 °C. ^{1}H NMR ($CDCl_3$) δ 1.17 (d, *J*=8.0 Hz, 6H), 2.74 (m, 1H), 6.30 (d, *J*=8.0 Hz, 1H), 6.76 (d, *J*=8.0 Hz, 2H), 6.90 (d, *J*=8.0 Hz, 2H), 7.13 (dd, *J*=7.5, 7.8 Hz, 1H), 7.23 (dd, *J*=7.5 Hz, 7.8 Hz, 1H), 7.50 (s, 1H, vinylic-H), 7.88, (d, *J*=7.8 Hz, 1H), 8.01 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 24.1, 24.2, 33.9, 110.2, 119.8, 121.5, 123.2, 125.5, 126.2, 129.2, 130.4, 131.9, 132.2, 132.3, 134.6, 147.7, 149.4, 183.5. *Anal.* Calcd for $C_{18}H_{17}NS$: C, 77.38; H, 6.13; N, 5.01. Found: C, 77.39; H, 6.07; N, 4.97.

***(Z)*-1,3-Dihydro-3-pyrrol-2-ylmethyleneindole-2-thione (4b)**

This compound was isolated as light red needles (EtOAc-hexane), mp 193–195 °C. ^{1}H NMR ($CDCl_3$) δ 6.53 (s, 1H), 7.00 (d, *J*=7.5 Hz, 1H), 7.05 (d, *J*=8.0 Hz, 1H), 7.18 (dd, *J*=7.5, 8.0 Hz, 1H), 7.23 (d, *J*=7.5 Hz, 1H), 7.32 (dd, *J*=2.5, 7.5 Hz, 1H), 7.60 (dd, *J*=2.1, 8.0 Hz, 1H), 7.73 (s, 1H, vinylic-H), 8.40 (s, 1H, NH), 8.50 (s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 109.7, 113.6, 118.4, 123.1, 125.2, 125.3, 126.9, 127.0, 129.8, 130.0, 130.9, 139.6, 184.2. *Anal.* Calcd for $C_{13}H_{10}N_2S$: C, 69.00; H, 4.45; N, 12.38. Found: C, 69.10; H, 4.42; N, 12.33.

(*Z*)-1,3-Dihydro-3-(4-*N,N*-dimethylaminobenzylidine)indole-2-thione (4c)

This compound was isolated as a light red solid (EtOAc-hexane), mp 210–213 °C. ^{1}H NMR ($CDCl_3$) δ 2.85 (s, 6H), 6.22 (d, *J*=8.0 Hz, 1H), 7.02 (dd, *J*=7.8, 8.0 Hz, 2H), 7.22 (d, *J*=8.0 Hz, 2H), 7.77 (d, *J*=8.0 Hz, 2H), 7.98 (s, 1H, vinyl-H), 8.0 (d, *J*=8.0 Hz, 1H), 8.37 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 40.4, 110.4, 121.4, 123.2, 125.5, 125.7, 127.6, 128.9, 131.9, 132.9, 135.5, 136.0, 141.0, 141.1, 152.2, 153.1, 195.4. *Anal.* Calcd for $C_{17}H_{16}N_2S$: C, 72.82; H, 5.75; N, 9.99. Found: C, 72.83; H, 5.77; N, 10.02.

(*E*)-1,3-Dihydro-3-(4-*N,N*-dimethylaminobenzylidine)indole-2-thione (5c)

This compound was isolated as a purple solid (EtOAc-hexane), mp 209–210 °C. ^{1}H NMR ($CDCl_3$) δ 2.85 (s, 6H), 6.18 (d, *J*=8.0 Hz, 1H), 6.36 (d, *J*=8.0 Hz, 2H), 6.50 (dd, *J*=7.8, 8.0 Hz, 2H), 6.68 (d, *J*=8.0 Hz, 2H), 7.45 (s, 1H, vinylic-H), 7.98 (d, *J*=8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 42.1, 111.5, 121.4, 123.3, 125.1, 125.5, 127.6, 127.9, 131.9, 133.1, 135.5, 136.1, 141.1, 142.3, 152.3, 153.1, 194.4. *Anal.* Calcd for $C_{17}H_{16}N_2S$: C, 72.82; H, 5.75; N, 9.99. Found: C, 72.80; H, 5.78; N, 9.98.

(*E*)-1,3-Dihydro-3-thien-2-ylmethyleneindole-2-thione (5d)

This compound was isolated as a light brown solid (EtOAc-hexane), mp 217–218 °C. ^{1}H NMR ($CDCl_3$) δ 6.18 (d, *J*=8.0 Hz, 1H), 6.70 (d, *J*=7.5 Hz, 2H), 6.90 (s, 1H), 7.01–7.14 (m, 3H), 7.45 (s, 1H, vinylic-H), 8.02 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 109.3, 110.2, 110.5, 119.0, 119.6, 121.5, 123.7, 126.2, 127.9, 128.5, 129.6, 194.4. *Anal.* Calcd for $C_{13}H_9NS_2$: C, 64.16; H, 3.73; N, 5.78. Found: 64.18; H, 3.78; N, 5.80.

(*Z*)-3-Furan-2-ylmethylene-1,3-dihydroindole-2-thione (4e)

This compound was obtained as a light red solid (EtOAc-hexane), mp 180–183 °C. ^{1}H NMR ($CDCl_3$) δ 6.60 (d, *J*=7.8 Hz, 1H), 7.03 (d, *J*=5.5 Hz, 1H), 7.10–7.14 (m, 2H), 7.29 (dd, *J* =2.3, 7.5 Hz, 1H), 7.81 (s, 1H, vinylic-H), 8.05 (dd, *J*=2.1, 7.8 Hz, 1H), 8.57 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 110.2, 114.3, 123.6, 123.8, 124.7, 125.7, 126.3, 129.7, 130.6, 143.1, 147.1, 152.2, 193.6. *Anal.* Calcd for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.73; H, 3.97; N, 6.19.

General Procedure for the Preparation of 2,3-Dimethoxy[1]benzothiopyrano[2,3-*b*]indoles (7a–c) A well stirred solution containing **4a/5a** (0.52 g, 0.18mmol) and a catalytic amount of trichloroacetic acid in dry benzene (10 mL) was heated under reflux in a three-necked flask fitted with a reflux condenser and two addition funnels under argon atmosphere. At this point the dropwise addition of solutions of 4,5-dimethoxyanthranilic acid (1.4 g, 6.9 mmol) and isoamyl nitrite (0.96 g, 6.9 mmol) in dry benzene (5 mL) from the addition funnels was started. The addition was stopped when the starting materials were no longer detected in the reaction mixture by TLC (~1.5 h). ßThe resulting solution was cooled to rt and evaporated to dryness. The residue was dissolved in CH_2Cl_2, washed with 5% HCl solution, 5% NaOH and water and finally dried over Na_2SO_4. Evaporation of the solvent under reduced pressure afforded the crude compound which was purified by column chromatography using SiO_2 with EtOAc-hexane (1:4, v/v) as eluent. The physical and spectral data are given below for compounds (**7a–c**).

6,11-Dihydro-11-(4-isopropylphenyl)-2,3-dimethoxy[1]benzothiopyrano[2,3-*b*]indole (7a)

This compound was obtained as a light yellow viscous oil. ^{1}H NMR ($CDCl_3$) δ 1.01 (d, *J*=8.0 Hz, 6H), 2.81 (m, 6H), 3.86 (s, 3H), 3.89 (s, 3H), 3.94 (s, 1H), 6.59 (s, 1H), 6.80 (s, 1H), 7.25 (d, *J*=7.8 Hz, 2H), 7.40 (d, *J*=7.8 Hz, 2H), 7.41–7.45 (m, 4H), 8.03 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 24.2, 32.1, 38.0, 55.9, 56.1, 111.1, 112.2, 115.1, 120.1, 121.0, 122.2, 123.3, 125.7, 127.0, 128.3, 133.5, 138.1, 155.4, 155.9. *Anal.* Calcd for $C_{26}H_{25}NO_2S$: C, 75.15; H, 8.06; N, 3.37. Found: C, 75.26; H, 6.05; N, 3.40.

6,11-Dihydro-2,3-dimethoxy-11-(pyrrol-2-yl)[1]benzothiopyrano[2,3-*b*]indole (7b)

This compound was obtained as a light red viscous liquid. ^{1}H NMR ($CDCl_3$) δ 3.92 (s, 3H), 3.95 (s, 1H, H-11), 3.98 (s, 3H), 6.38 (d, *J*=1.1 Hz, 1H), 6.80 (s, 1H), 6.90 (dd, *J*=7.5, 8.0 Hz, 1H), 7.12 (d, *J*=1.1 Hz, 1H), 7.28–7.35 (m, 3H), 7.39 (s, 1H), 7.69 (dd, *J*=2.1, 8.0 Hz, 1H), 8.01 (br s, 1H NH), 8.16 (br s, 1H, NH).^{13}C NMR ($CDCl_3$) δ 41.5, 55.9, 56.0, 107.3, 108.5, 110.9, 111.8, 114.9, 117.5, 118.3, 120.5, 121.2, 123.5, 126.8, 130.1, 131.9, 138.1, 152.1, 153.1. *Anal.* Calcd for $C_{21}H_{18}N_2O_2S$: C, 69.59; H, 5,01; N, 7.73. Found: C, 69.56; H, 4.96; N, 7.78.

6,11-Dihydro-2,3-dimethoxy-11-(thien-2-yl)[1]benzothiopyrano[2,3-*b*]indole (7c)

This compound was obtained as a yellow viscous oil. ^{1}H NMR ($CDCl_3$) δ 3.98 (s), 4.01 (s, 1H, H-11), 4.02 (s, 3H), 6.18 (s, 1H), 6.90 (s, 1H), 7.03 (s, 1H), 7.08 (d, *J*=7.5 Hz, 1H), 7.16 (dd, *J*=7.8, 8.0 Hz, 1H), 7.27–7.30 (m, 2H), 7.49 (s, 1H), 7.80 (dd, *J*=2.5, 8.0 Hz, 1H), 8.06 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 38.9, 54.5, 56.3, 107.5, 109.1, 110.9, 111.3, 115.0, 117.3, 118.9, 120.8, 121.1, 123.2, 126.3, 130.1, 131.3, 139.3, 154.1, 155.0. *Anal.* Calcd for $C_{21}H_{17}NOS_2$: C, 66.46; H, 4.52; N, 3.69. Found: C, 66.42; H, 4.58; N, 3.81.

General Procedure for the Preparation of Thiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Esters (9)

To a well stirred solution of a diasteromeric mixture of **4** and **5** (0.35 mmol) in dry MeCN (5 mL) contained in a round bottom flask fitted with a reflux condenser under argon atmosphere, a solution of dimethyl acetylenedicarboxylate (0.25 g, 1.7 mmol) in MeCN (1 mL) was added through a needle syringe system. The mixture was heated to reflux for 6 h then cooled to rt. The solvent was removed under reduced pressure to afford he crude product (**9**) which was purified by column chromatography using SiO_2 with EtOAc-hexane (1:4, v/v).

1,5-Dihydro[1](4-isopropylphenyl)thiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Ester (9a)

This compound was obtained as a light red viscous oil. ^{1}H NMR ($CDCl_3$) δ 1.19 (d, *J*=8.0 Hz, 6H), 2.82 (m, 1H), 3.69 (s, 3H), 3.87 (s, 3H), 4.16 (s, 1H, vinylic-H, H-9), 7.03 (dd, *J*=7.8, 8.0 Hz, 1H), 7.11 (d, *J*=8.0 Hz, 2H), 7.24 (d, *J*=8.0 Hz, 2H), 7.20–7.28 (m, 3H), 8.01 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 24.3, 34.1, 43.5, 52.9, 53.7, 109.9, 110.8, 118.3, 120.7, 122.7, 123.3, 127.2, 128.0, 128.3, 129.2, 134.2, 137.6, 148.7, 164.2. *Anal.* Calcd for $C_{24}H_{23}NO_4S$: C, 68.39; H, 5.50; N, 3.32. Found: C, 68.45; H, 5.53; N, 3.29.

1,5-Dihydro-9-pyrrol-2-ylthiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Ester (9b)

This compound was obtained as a light red viscous oil. ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 3H), 3.8 (s, 3H), 4.71 (s, 1H, vinylic-H, H-9), 6.61 (s, 1H), 6.98 (d, *J*=1.1 Hz, 1H), 7.07 (dd, *J*=7.8, 8.0 Hz, 1H), 7.08 (dd, *J*=7.8, 8.0 Hz, 1H), 7.19 (d, *J*=1.1 Hz, 1H), 7.31-7.39 (m, 2H), 8.02 (br s, 1H, NH), 8.12 (br s, 1H, NH).
^{13}C NMR ($CDCl_3$) δ 36.6, 53.2, 53.7, 107.2, 108.6, 110.9, 118.2, 118.5, 121.0, 123.0, 165.0, 165.1. *Anal.* Calcd for $C_{19}H_{16}N_2O_4S$: C, 61.94; H, 4.38; N, 7.60. Found: C, 61.98; H, 4.37; N, 7.69.

1,5-Dihydro[1](4-*N*,*N*-dimethylaminophenyl)thiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Ester (9c)

This compound was obtained as colorless oil. ^{1}H NMR ($CDCl_3$) δ 2.86 (s, 6H), 3.71 (s, 3H), 3.82 (s, 3H), 4.26 (s, 1H, vinylic-H, H-9), 7.02 (d, *J*=8.0 Hz, 1H), 7.12 (d, *J*=8.0 Hz, 2H), 7.34 (d, *J*=8.0 Hz, 2H), 7.30–7.38 (m, 3H), 8.16 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 24.3, 43.2, 52.8, 53.6, 109.8, 110.8, 119.3, 121.6, 122.6, 123.3, 126.9, 127.9, 128.3, 129.2, 134.2, 137.6, 147.9, 165.1. *Anal.* Calcd for $C_{23}H_{22}N_2O_4S$: C, 65.38; H, 5.25; N, 6.63. Found: C, 65.42; H, 5.27; N, 6.60.

1,5-Dihydro-9-thien-2-ylthiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Ester (9d)

This compound was obtained as a light orange solid (CH_2Cl_2-hexane), mp 150–153 °C. ^{1}H NMR ($CDCl_3$) δ 3.78 (s, 3H), 3.86 (s, 3H), 4.16 (s, 1H, H-9), 7.04–7.18 (m, 3H), 7.28 (dd, *J*=7.8 Hz, 8.0 Hz, 1H), 7.37 (dd, *J*=2.1, 7.8 Hz, 1H), 7.56 (d, *J*=7.5 Hz, 1H), 7.58 (d, *J*=7.5 Hz, 1H), 8.05 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 37.9, 53.2, 53.8, 109.5, 110.1, 118.0, 120.8, 121.9, 122.9, 125.3, 125.6, 126.0, 127.1, 130.4, 131.5, 137.7, 145.8, 165.4, 167.1. *Anal.* Calcd for $C_{19}H_{15}NO_5S$: C, 61.78; H, 4.09; N, 3.79. Found: C, 61.89; H, 4.18; N, 3.85.

9-Furan-2-yl-1,5-Dihydrothiopyrano[2,3-*b*]indole-2,3-dicarboxylic Acid Dimethyl Ester (9e)

This compound was obtained as a tan viscous oil. ^{1}H NMR ($CDCl_3$) δ 3.77 (s, 3H), 3.87 (s, 3H), 3.89 (s, 1H, H-9), 6.99 (d, *J*=5.6 Hz, 1H), 7.24 (d, *J*=5.6 Hz, 1H), 7.32 (dd, *J*=7.8, 8.0 Hz, 1H), 7.36 (dd, *J* =7.8, 8.0 Hz, 1H), 7.48 (m, 2H), 7.54 (dd, *J*=1.5, 7.8 Hz, 1H), 8.17 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ 37.0, 53.2, 53.8, 106.9, 107.1, 110.7, 111.0, 118.2, 120.8, 122.2, 122.8, 126.3, 129.8, 131.0, 137.6, 142.6, 153.7, 165.2, 167.2. *Anal.* Calcd for $C_{21}H_{17}NO_3S$: C, 61.78; H, 4.09; N, 3.79. Found: C, 61.78; H, 4.08; N, 3.80.

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