Regioselective synthesis of thieno[2,3-*b*]indoles by tandem cyclisation involving sequential sigmatropic rearrangements

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Thieno[2,3-*b*]indoles can be synthesised in 70–80 % yield by the sulfoxide rearrangement of 2-(4'-aryloxybut-2'-ynylthio)-1-methylindoles. The substrates are prepared by phase-transfer-catalysed alkylation of 1-methylindoline-2-thione with 1-aryloxy-4-chlorobut-2-ynes.

Keywords: 1-methylindoline-2-thione, sulfoxide rearrangement, phase transfer, fused thiophenes, indoles

The indole ring fused with a five-membered heterocyclic ring at C_2 and C_3 is found in a number of biologically active compounds. Furo[3,2-*b*]indoles[1] show analgesic and anti-inflammatory activity. Cyclic tautomers[2] of tryptophan and serotonin are also important molecules. Thienoindole derivatives[3] are potentially biologically active. The indole nucleus is present in a wide range of natural products.[4] The biological activity displayed by various indole derivatives has made this heterocyclic system one of the most frequent subunits encountered in pharmacologically active compounds.[5] So, there has been a continuous interest in the synthesis of indole derivatives.

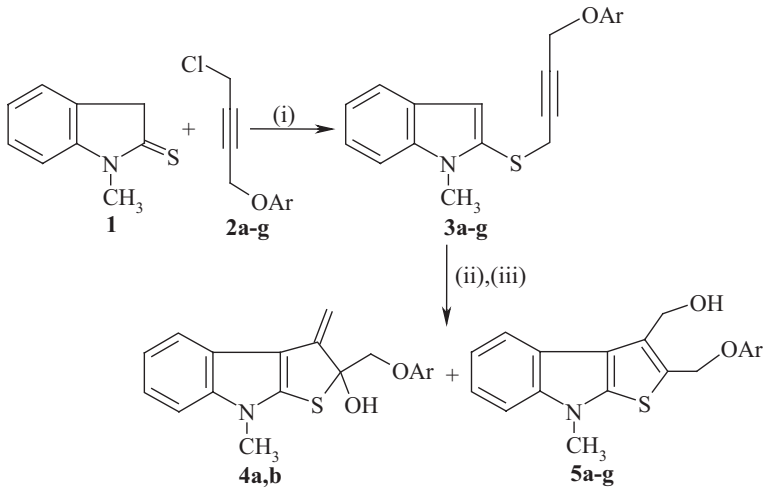
Thieno[2,3-*b*]indole derivatives are the synthetic target molecule in our present study. Indoline-2-thiones are important intermediates in the synthesis of heteroaromatic molecules and have found some use in the synthesis of biologically active compounds.[6] The five-membered heterocyclic ring fused indole derivatives are potentially biologically active compounds and the synthesis of this important system has been a steady topic of interest for many years. The important bioactivities of these compounds prompted us to undertake a study on the synthesis of fused thienoindole derivatives.

There are various methodologies for the synthesis of furoindole,[1] indolopyrrolidine[2] and thienoindole[3] derivatives. Thyagarajan and Majumdar developed a synthetic methodology for the construction of a five-membered heterocyclic ring with an aromatic ring. They reported an unusual sulfoxide rearrangement[7-9] for the synthesis of benzo[*b*]thiophene derivatives, and an amine oxide rearrangement[10] to give indole derivatives. These reactions involve [2,3] and [3,3] sigmatropic rearrangements. The sulfoxide rearrangement has been shown to be an excellent method for C–C bond formation as well as for the construction of thiophene rings in fused heterocycles under mild condition in excellent yield. We adapted this sigmatropic rearrangement protocol for our present study, as the reaction condition is mild and the products are obtained in high yield. The extensive bioactivity of indole derivatives and the exceedingly facile rearrangement reaction for their synthesis motivated us to undertake a study on the synthesis of thieno[2,3-*b*]indole derivatives by the application of the sulfoxide rearrangement of tailored sulfides. Here we report the results of our experimental study.

Results and discussion

The required precursors for our present study, 2-(4'-aryloxybut-2'-ynylthio)-1-methylindoles (**3a**–**g**), were synthesised in 88–94 % yield by the reaction of 1-methylindoline-2-thione (**1**) with 1-aryloxy-4-chlorobut-2-yne (**2a**–**g**) at room temperature under phase-transfer-catalysed conditions using benzyltriethylammonium chloride (BTEAC) as phase transfer catalyst (Scheme 1).

The sulfide **3a** contains a suitably placed alkynyl segment so as to allow the occurrence of a [2,3] sigmatropic rearrangement in the corresponding sulfoxide. The sulfide **3a** was subjected to selective oxidation to the corresponding sulfoxide by the slow addition of one equivalent of *m*-chloroperoxybenzoic acid (*m*-CPBA) at 0–5 °C in dichloromethane solution over 1 h. After the completion of the reaction the resultant sulfoxide was refluxed in dichloromethane. After 30 min the green-coloured reaction mixture became



Scheme 1 Reagents and conditions: (i) 1 % aq. NaOH sol., CH_2Cl_2, BTEAC, Stirring, 15 min, rt. 88–94 %. (ii) *m*-CPBA (1 equiv.), CH_2Cl_2, 0–5 °C, Stirring, 1 h. (iii) CH_2Cl_2, Reflux, 2.5 h, 70–80 %

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red and two new spots appeared on TLC but the conversion was only partial. Complete conversion required 2.5 h. The compounds corresponding to these new spots were isolated and characterised to be **4a** (10 %) and **5a** (70 %) from their elemental analyses and spectral data. The ^{1}H NMR spectrum of compound **4a** displayed two one-proton doublets at δ 5.72 (J = 3 Hz) and 5.96 (J = 3 Hz) indicating the presence of two exocyclic methylene protons, and two one-proton doublets at δ 4.68 (J = 9 Hz) and 5.04 (J = 9 Hz) showing the presence of two aryloxymethylene protons adjacent to chiral carbon C(2). The compound **5a** displayed two two-protons singlets at δ 4.28 and 5.39 indicating the presence of the two OCH_2 groups (Scheme 1).

Encouraged by the initial success, all the remaining substrates (**3b–g**) were similarly treated, to afford **4b** (8 %) and **5b–g** (70–80 %).

The formation of products from **3a–g** may be mechanistically interpreted as depicted in Scheme 2. Initial [2,3] sigmatropic rearrangement of the sulfoxide **6** may generate the intermediate allenyl derivative **7** followed by a [3,3] sigmatropic rearrangment through the S-O bond may give the intermediate **8** which tautomerises to **9**. The thiophenolate anion in intermediate **8** can add to the carbonyl carbon of the enone part, leading to the formation of the intermediate allylic alcohol[7] (monothiohemiacetal) **4** (Pathway a, Scheme 2). The intermediates (**4**) are very much susceptable to S_N2' nucleophilic displacement and therefore may undergo S_N2' nucleophilic displacement by the water molecule[10c] present in the reaction mixture to afford the aromatised products **5a–g**. Only in two cases did we succeed to isolate the monothiohemiacetal intermediate as a stable compound **4** (**a,b**) along with compounds **5** (**a,b**). The isolation of the monothiohemiacetal intermediates **4** established the mechanistic pathway (Pathway a) leading to the formation of compounds **5a–g**.

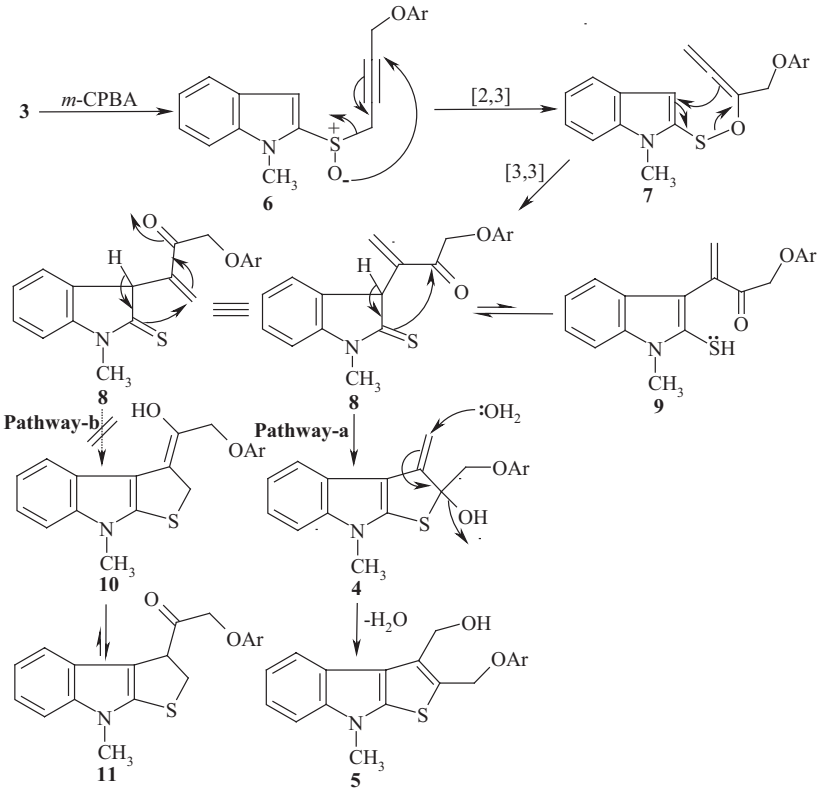
Another mode of cyclisation[9] of the intermediate **8** (Pathway b, Scheme 2) involving an internal Michael type addition to the α,β-enone moiety leading to compound **11** may also be considered. However, compound **11** was not obtained in our present study.

In conclusion, it is interesting to note that the labile monothiohemiacetal intermediate **4** has been isolated. We have been able to synthesise potentially bioactive compounds structurally analogous to annulated furan[1] and pyrrolidine[2] derivatives. This rearrangement methodology displayed appreciable regioselectivity. This is an extremely facile, mild and direct method for synthesising fused thienoindole heterocycles.

Experimental

Melting points were determined in an open capillary. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer (ν_{max} in cm^{-1}) on KBr disks. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer (λ_{max} in nm). ^{1}H NMR (300, 400, 500 and 600 MHz) and ^{13}C NMR (75, 125 and 150 MHz) spectra were recorded on Bruker DPX-300, Varian-400 FT and Bruker DPX-500 and Varian-600 FT spectrometers in $CDCl_3$ (chemical shift in δ) with TMS as internal standard. Mass spectra were recorded on a JEOL JMS-600 (+Q1) instrument and elemental analyses were recorded on a LECO CHNS-932 analyser. ^{1}H and ^{13}C NMR spectra were recorded at the Indian Institute of Chemical Biology, Kolkata and Bose Institute, Kolkata. Silica gel [(230–400 mesh), Spectrochem, India] was used for chromatographic separation. Silica gel G [E-Merck (India)] was used for TLC. Petroleum ether refers to the fraction boiling between 60-80 °C. The 1-aryloxy-4-chlorobut-2-ynes were prepared according to the earlier published procedure.[8]

1-Methyl-2-(4'-aryloxybut-2'-ynylthio)indoles (**3a–g**): To a mixture of 1-methylindoline-2-thione (**1**) (0.49 g, 3 mmol) and 1-aryloxy-4-chlorobut-2-yne (**2a–g**) (3 mmol) in dichloromethane (30 ml) was added a solution of benzyltriethylammonium chloride (BTEAC, 0.5 g, 1.8 mmol) in 1 % aqueous NaOH (30 ml) and the mixture was magnetically stirred at room temperature for 15 minutes. The reaction mixture was then diluted with water (20 ml) and the dichloromethane layer was washed with 2 N HCl (2 × 20 ml), water (2 × 20 ml), brine (20 ml) and dried (Na_2SO_4). Removal of dichloromethane at room temperature left a oily residue, which was subjected to column chromatography over silica gel (230–400 mesh).



Scheme 2

Elution of the column with petroleum ether–ethyl acetate (50 : 1) afforded compounds **3a–g**.

1-Methyl-2-(4'-phenoxybut-2'-ynylthio)indole (**3a**): Viscous liquid (0.81 g, 88 %). IR (neat): ν_{max} 2936 (C–H stretching), 1494 (C–H bending) cm^{-1}. UV (EtOH): λ_{max} 220 (log ε 4.01), 289 (log ε 3.74) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.48 (s, 2H, SCH_2), 3.78 (s, 3H, NCH_3), 4.63 (s, 2H, OCH_2), 6.77 (s, 1H, =CH), 6.86–7.58 (m, 9H, ArH). MS: *m/z* 308 (M^++1, 20 %), 307 (M^+, 12), 306 (22), 215 (57), 213 (52), 162 (58), 137 (100). Anal. Calcd for $C_{19}H_{17}NOS$: C, 74.23; H, 5.57; N, 4.56. Found C, 74.38; H, 5.62; N, 4.41 %.

1-Methyl-2-[4'-(4-methoxyphenyloxy)but-2'-ynylthio]indole (**3b**): viscous liquid (0.91 g, 90 %). IR (neat): ν_{max} 2903 (ν_{C-H}), 1505 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 222 (log ε 4.03), 289 (log ε 3.77) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.49 (s, 2H, $–SCH_2$), 3.74 (s, 3H, $–NCH_3$), 3.81 (s, 3H, OCH_3), 4.58 (s, 2H, OCH_2), 6.71–6.74 (m, 2H, ArH), 6.79 (s, 1H, =CH), 6.81–7.59 (m, 6H, ArH). MS: *m/z* 338 (M^++1, 38 %), 337 (M^+, 14), 336 (28), 226 (47), 213 (100), 162 (50). Anal. Calcd for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N, 4.15. Found C, 71.35; H, 5.71; N, 4.27 %.

1-Methyl-2-[4'-(4-chloro-2-methylphenyloxy)but-2'-ynylthio] indole (**3c**): Viscous liquid (0.97 g, 91 %). IR (neat): ν_{max} 2922 (ν_{C-H}), 1491 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 231 (log ε 4.02), 288 (log ε 3.76) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 3H, $ArCH_3$), 3.43 (s, 2H, SCH_2), 3.74 (s, 3H, NCH_3), 4.58 (s, 2H, OCH_2), 6.62–6.65 (m, 1H, ArH), 6.75 (s, 1H, =CH), 6.89–7.56 (m, 6H, ArH). MS: *m/z* 358 (M^++1, 7 %), 357 (M^+, 10), 356 (M^++1, 37), 355 (M^+, 8), 354 (15), 213 (40), 162 (100). Anal. Calcd for $C_{20}H_{18}ClNOS$: C, 67.50; H, 5.10; N, 3.94. Found C, 67.66; H, 4.95; N, 4.13 %.

1-Methyl-2-[4'-(4-chlorophenyloxy)but-2'-ynylthio]indole (**3d**): Viscous liquid (0.95 g, 93 %). IR (neat): ν_{max} 2930 (ν_{C-H}), 1496 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 220 (log ε 4.02), 288 (log ε 3.72) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.47 (s, 2H, SCH_2), 3.78 (s, 3H, NCH_3), 4.60 (s, 2H, SCH_2), 6.76–6.78 (m, 2H, ArH), 6.79 (s, 1H, =CH), 7.05–7.58 (m, 6H, ArH). MS: *m/z* 344 (M^++1, 15 %), 343 (M^+, 8), 342 (M^++1, 46), 341 (M^+, 11), 214 (16), 162 (100). Anal. Calcd for $C_{19}H_{16}ClNOS$: C, 66.75; H, 4.72; N, 4.10. Found C, 66.55; H, 4.81; N, 4.01 %.

1-Methyl-2-[4'-(2,4-dichlorophenyloxy)but-2'-ynylthio]indole (**3e**): Viscous liquid (1.06 g, 94 %). IR (neat): ν_{max} 2924 (ν_{C-H}), 1495 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 224 (log ε 4.00), 286 (log ε 3.73) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.47 (s, 2H, SCH_2), 3.79 (s, 3H, NCH_3), 4.69 (s, 2H, OCH_2), 6.74 (m, 1H, ArH), 6.77 (s, 1H, =CH), 6.89–7.58 (m, 6H, ArH). MS: *m/z* 380 (M^++1, 4 %), 379 (M^+, 7), 378 (M^++1, 24), 377 (M^+, 10), 376 (M^++1, 38), 375 (M^+, 18), 215 (51), 214 (16), 162 (100). Anal. Calcd for $C_{19}H_{15}Cl_2NOS$: C, 60.64; H, 4.02; N, 3.72. Found C, 60.75; H, 3.91; N, 3.92 %.

1-Methyl-2-[4'-(4-methylphenyloxy)but-2'-ynylthio]indole (**3f**): Viscous liquid (0.85 g, 88 %). IR (neat): ν_{max} 2921 (ν_{C-H}), 1509 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 219 (log ε 4.01), 286 (log ε 3.76) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 3H, $ArCH_3$), 3.46 (s, 2H, SCH_2), 3.76 (s, 3H, NCH_3), 4.58 (s, 2H, OCH_2), 6.75–6.77 (m, 3H, ArH), 6.98 (s, 1H, =CH), 7.01–7.57 (m, 5H, ArH). MS: *m/z* 322 (M^++1, 40 %), 321 (M^+, 12), 214 (80), 213 (41), 162 (100). Anal. Calcd for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36. Found C, 74.55; H, 5.85; N, 4.47 %.

1-Methyl-2-[4'-(3,5-dimethylphenyloxy)but-2'-ynylthio]indole (**3g**): Viscous liquid (0.93 g, 92 %). IR (neat): ν_{max} 2917 (ν_{C-H}), 1459 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 221 (log ε 4.00), 287 (log ε 3.75) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (s, 6H, $ArCH_3$), 3.43 (s, 2H, SCH_2), 3.72 (s, 3H, NCH_3), 4.55 (s, 2H, OCH_2), 6.51 (s, 2H, ArH), 6.58 (s, 1H, ArH), 6.75 (s, 1H, =CH), 7.04–7.54 (m, 4H, ArH). MS: *m/z* 336 (M^++1, 65 %), 335 (M^+, 12), 334 (43), 214 (31), 213 (95), 162 (100). Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18. Found C, 75.38; H, 6.35; N, 3.99 %.

Thieno[2,3-b]indoles (**4a,b**, **5a–g**): 50 % *m*-CPBA (1 equiv. 172.5 mg, 1 mmol) in dry dichloromethane (10 ml) was added slowly to a well-stirred solution of the sulfides **3a–g** (0.5 mmol) in dry dichloromethane (10 ml) at 0-5 °C over a period of 30 minutes. The colourless solution became green in colour. The reaction mixture was stirred for additional 30 minutes and then washed with saturated sodium carbonate solution (3 × 20 ml) to remove the organic acid followed by water (2 × 20 ml), brine solution (20 ml) and dried (Na_2SO_4). The reaction mixture was then refluxed for 2.5 h. On heating the reaction mixture became red in colour. The solvent was distilled off and a viscous liquid was obtained. It was chromatographed over silica gel (230–400 mesh) using petroleum ether-ethyl acetate (50:1) as eluant to give **4a,b** and **5a–g**, both as white solids.

2-Hydroxy-3-methylene-8-methyl-2-phenoxymethyl-2H-thieno [2,3-b]indole (**4a**): White solid (0.02 g, 10 %), m.p. 154–156 °C. IR (KBr): ν_{max} 3405 (ν_{O-H}), 3050, 2917 (ν_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 230 (log ε 4.10), 282 (log ε 4.00) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.70 (s, 3H, NCH_3), 4.68 (1H, d, *J* = 9.0 Hz, OCH), 5.04 (1H, d, *J* = 9.0 Hz, OCH), 5.72 (1H, d, *J* = 3.0 Hz, =CH), 5.96 (1H, d, *J* = 3.0 Hz, =CH), 6.84–7.70 (m, 9H, ArH). MS: *m/z* 324 (M^++1, 7 %), 323 (M^+, 15), 322 (100), 213 (30). Anal. Calcd for $C_{19}H_{17}NO_2S$: C, 70.56; H, 5.30; N, 4.33. Found C, 70.75; H, 5.46; N, 4.25 %.

2-Hydroxy-3-methylene-8-methyl-2-(4'-methoxyphenyloxy-methyl)-2H-thieno[2,3-b]indole (**4b**): White solid (0.01 g, 8 %), m.p. 160–162 °C. IR (KBr): ν_{max} 3388 (ν_{O-H}), 3043, 2928 (ν_{C-H}), 1506 (δ_{C-H}) cm $^{-1}$. UV (EtOH): λ_{max} 231 (log ε 4.11), 282 (log ε 4.01) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.70 (s, 3H, NCH_3), 3.72 (s, 3H, $–OCH_3$), 4.63 (1H, d, *J* = 9.0 Hz, OCH), 5.00 (1H, d, *J* = 9.0 Hz, OCH), 5.73 (1H, d, *J* = 3.0 Hz, =CH), 5.97 (1H, d, *J* = 3.0 Hz, =CH), 6.75–7.69 (m, 8H, ArH). MS: *m/z* 354 (M^++1, 6 %), 353 (M^+, 5), 332 (100), 213 (85). Anal. Calcd for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96. Found C, 67.78; H, 5.55; N, 3.83 %.

2-Phenoxymethyl-3-hydroxymethyl-8-methylthieno[2,3-b]indole (**5a**): White solid (0.11 g, 70 %), m.p. 122–124 °C. IR (KBr): ν_{max} 3430 (O-H), 2922 (C–H stretching), 1492 (C–H bending) cm^{-1}. UV (EtOH): λ_{max} 228 (log ε 4.17), 280 (log ε 4.03) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (s, 3H, NCH_3), 4.28 (s, 2H, OCH_2), 5.39 (s, 2H, OCH_2), 7.01–7.82 (m, 9H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.2, 53.4, 63.5, 99.3, 108.9, 114.7, 119.7, 120.2, 121.3, 122.0, 122.2, 122.3, 129.6, 130.4, 142.1, 143.8, 158.5. MS: *m/z* 324 (M^++1, 100 %), 323 (M^+, 14), 216 (67). Anal. Calcd for $C_{19}H_{17}NO_2S$: C, 70.56; H, 5.30; N 4.33; Found C, 70.74; H, 5.41; N, 4.22 %.

2-(4'-methoxyphenyloxymethyl)-3-hydroxymethyl-8-methyl-thieno[2,3-b]indole (**5b**): White solid (0.12 g, 70 %), m.p. 140–142 °C. IR (KBr): ν_{max} 3444 (O–H), 3058, 2933 (C–H stretching), 1505 (C–H bending) cm^{-1}. UV (EtOH): λ_{max} 231 (log ε 4.20), 280 (4.05) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78 (s, 3H, NCH_3), 3.84 (s, 3H, OCH_3), 4.26 (s, 2H, OCH_2), 5.34 (s, 2H, OCH_2), 6.85-7.84 (m, 8H, ArH). MS: *m/z* 354 (M^++1, 15 %), 353 (M^+, 11), 213 (100). Anal. Calcd for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96. Found C, 68.11; H, 5.27; N, 4.14 %.

2-(4'-Chloro-2'-methylphenyloxymethyl)-3-hydroxymethyl-8-methylthieno[2,3-b]indole (**5c**): White solid (0.14 g, 75 %), m.p. 130–132 °C. IR (KBr): ν_{max} 3452 (ν_{O-H}), 3040, 2925 (ν_{C-H}), 1491 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 232 (log ε 4.28), 280 (log ε 4.08) nm. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.12 (s, 3H, $ArCH_3$), 3.87 (s, 3H, NCH_3), 4.28 (s, 2H, OCH_2), 5.36 (s, 2H, OCH_2), 6.94–7.72 (m, 7H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.7, 32.6, 53.8, 64.3, 99.7, 109.4, 112.4, 120.1, 120.3, 122.4, 122.6, 122.8, 126.0, 126.8, 129.5, 130.7, 131.1, 142.5, 144.1, 155.7. MS: *m/z* 374 (M^++1, 16 %), 373 (M^+, 9), 372 (M^++1, 7), 371 (M^+, 5), 230 (41), 214 (46), 213 (100), 199 (43), 137 (77). Anal. Calcd for $C_{20}H_{18}ClNO_2S$: C, 64.59; H, 4.88; N 3.77. Found C, 64.73; H, 4.93; N, 3.89 %.

2-(4'-Chlorophenyloxymethyl)-3-hydroxymethyl-8-methyl-thieno[2,3-b]indole (**5d**): White solid (0.13 g, 73 %), m.p. 128–130 °C. IR (KBr): ν_{max} 3442 (ν_{O-H}), 2920 (ν_{C-H}), 1490 (δ_{C-H}) cm $^{-1}$. UV (EtOH): λ_{max} 231 (log ε 4.18), 280 (log ε 4.04) nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 3H, -NCH_3), 4.27 (s, 2H, $–OCH_2$), 5.36 (s, 2H, $–OCH_2$), 6.96–7.77 (m, 8H, ArH). ^{13}C NMR (150 MHz, $CDCl_3$): δ 32.2, 53.4, 63.9, 99.2, 109.0, 116.1, 119.8, 120.0, 121.8, 121.9, 122.5, 126.2, 129.5, 130.0, 142.1, 143.8, 157.1. MS: *m/z* 360 (M^++1, 22 %), 359 (M^+, 8), 358 (M^++1, 100), 357 (M^+, 20), 216 (28). Anal. Calcd for $C_{19}H_{16}ClNO_2S$: C, 63.77; H, 4.51; N, 3.91. Found C, 64.88; H, 4.62; N, 3.76 %.

2-(2',4'-Dichlorophenyloxymethyl)-3-hydroxymethyl-8-methyl-thieno[2,3-b]indole (**5e**): White solid (0.15 g, 74 %), m.p. 148–150 °C. IR (KBr): ν_{max} 3450 (ν_{O-H}), 3052, 2926 (ν_{C-H}), 1481 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 232 (log ε 4.22), 283 (log ε 4.08) nm. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.84 (s, 3H, NCH_3), 4.30 (s, 2H, OCH_2), 5.46 (s, 2H, OCH_2), 6.9–7.85 (m, 7H, ArH). MS: *m/z* 396 (M^++1, 14 %), 395 (M^+, 10), 394 (M^++1, 50), 393 (M^+, 16), 392 (M^++1, 60), 391 (M^+, 20), 372 (50), 370 (100), 213 (20). Anal. Calcd for $C_{19}H_{15}Cl_2NO_2S$: C, 58.17; H, 3.85; N, 3.57. Found C, 57.98; H, 4.01; N, 3.48 %.

2-(4'-Methylphenyloxymethyl)-3-hydroxymethyl-8-methyl-thieno[2,3-b]indole (**5f**): White solid (0.13 g, 76 %), m.p. 132–134 °C. IR (KBr): ν_{max} 3450 (ν_{O-H}), 3028, 2922 (ν_{C-H}), 1509 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 230 (log ε 4.27), 279 (log ε 4.09) nm. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H, $ArCH_3$), 3.84 (s, 3H, NCH_3), 4.27 (s, 2H, OCH_2), 5.35 (s, 2H, OCH_2), 6.94–7.82 (m, 8H, ArH). MS: *m/z* 338 (M^++1, 35 %), 337 (M^+, 17), 216 (100), 136 (31). Anal. Calcd for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N 4.15. Found C, 71.28; H, 5.79; N, 4.34 %.

2-(3',5'-Dimethylphenyloxymethyl)-3-hydroxymethyl-8-methyl-thieno[2,3-b]indole (**5g**): White solid (0.14 g, 80 %), m.p. 138–140 °C.

IR (KBr): ν_{max} 3414 (ν_{O-H}), 2914 (ν_{C-H}), 1498 (δ_{C-H}) cm^{-1}. UV (EtOH): λ_{max} 233 (log ε 4.19), 280 (log ε 4.06) nm. ^1H NMR (500 MHz, $CDCl_3$): δ 2.32 (s, 6H, $ArCH_3$), 3.85 (s, 3H, NCH_3), 4.28 (s, 2H, OCH_2), 5.34 (s, 2H, OCH_2), 6.67–7.81 (m, 7H, ArH). ^{13}C NMR (150 MHz, $CDCl_3$): δ 21.4, 32.2, 53.3, 63.2, 99.3, 108.9, 112.4, 119.7, 120.2, 122.0, 122.1, 122.3, 123.0, 130.5, 139.3, 142.1, 143.8, 158.6. MS: *m/z* 352 (M^++1, 12 %), 351 (M^+, 8), 308 (38), 231 (39), 213 (29), 137 (100). Anal. Calcd for $C_{21}H_{21}NO_2S$: C, 71.76; H, 6.02; N, 3.99. Found C, 71.93; H, 6.06; N, 3.84 %.

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