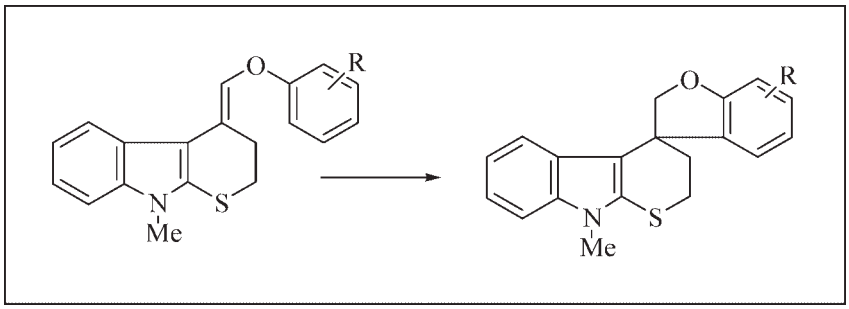
Regioselective Unusual Formation of Spirocyclic 4-{3′-Benzo(2′,3′-Dihydro)furo}-9-Methyl-2,3,9-Trihydrothiopyrano [2,3-*b*]indole by Acid-Catalyzed Reaction of Enol Ethers

K. C. Majumdar,* S. Alam, and B. Chattopadhyay

Department of Chemistry, University of Kalyani, Kalyani 741235, West Bengal, India
*E-mail: kcm_ku@yahoo.co.in
Received February 21, 2008
DOI 10.1002/jhet.31
Published online 11 February 2009 in Wiley InterScience (www.interscience.wiley.com).



Spirocyclic 4-{3′-benzo(2′,3′-dihydro)furo}-9-methyl-2,3,9-trihydrothiopyrano[2,3-*b*]indoles are regioselectively synthesized by treating suitable enol ethers, 4-aryloxymethylene-9-methyl-2,3,9-trihydrothiopyrano[2,3-*b*]indoles with H_2SO_4 in dichloromethane-methanol-water. The substrates for the aforesaid reaction are in turn synthesized by the *thio*-Claisen rearrangement of 2-(4′-aryloxybut-2′-ynylthio)-1-methylindoles.

J. Heterocyclic Chem., **46**, 62 (2009).

INTRODUCTION

Indoline-2-thiones are important starting materials in the synthesis of thiopyranoindole derivatives and have been applied for the synthesis of biologically active compounds [1]. There are many biologically active indole derivatives in the alkaloid family and indole derivatives are well known as medicinal compounds for their pharmaceutical and physiological activities [2]. Synthesis of oxygen-, nitrogen-, and sulfur-containing heterocyclic compounds [3] have received great attention in the field of synthetic organic chemistry and the synthesis of indole-annulated heterocyclic compounds are important as they are present in the wide range of natural products, many of which exhibit potent bioactivity [2,4]. The familiar bioactivity of various indole derivatives has drawn our interest to this area and we have tried to synthesize oxygen and sulfur containing indole derivatives. In this study after construction of a thiopyran ring fused with indole by means of *thio*-Claisen rearrangement [1,5] of the suitable sulfides we focused our attention to the synthesis of indole-annulated poly-heterocyclic compounds by acid catalyzed reaction of the enol ether [6–8]. Herein, we report the results of our investigation.

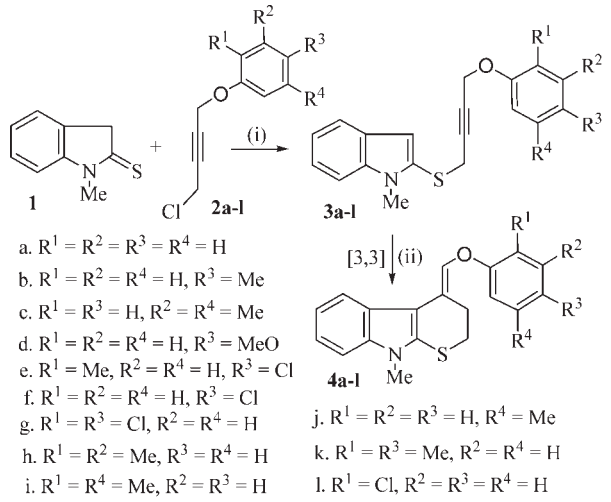
RESULTS AND DISCUSSION

The required precursors for our present study 4-(aryloxymethylene)-9-methyl-2,3,9-trihydrothiopyrano-[2,3-*b*] indoles (**4a-l**) were synthesized in 80–88% yield by the *thio*-Claisen rearrangement [5a] of 2-(4′-aryloxybut-2′-ynylthio)-1-methylindoles (**3a–l**) in refluxing chloro-benzene for 1 h. The compounds **3a–l** in turn were prepared in 90–94% yield by the reaction of 1-methyl-indoline-2-thione (**1**) and 1-aryloxy-4-chlorobut-2-yne (**2a–l**) under phase transfer catalysis (PTC) condition [5a,9] using benzyltriethyl ammonium chloride (BTEAC) as a phase transfer catalyst (Scheme 1).

A close examination of compounds **4** reveals that these are enol ethers and it is well known that enol ethers undergo hydrolysis in the presence of acid leading to the formation of corresponding aldehyde or ketone and alcohol or phenol [6–8]. With a view to hydrolyse the enol ether [8], compound **4a** was refluxed with conc. H_2SO_4 in dichloromethane-methanol-water mixture for 4 h. Three different products were obtained, a spiroheterocycle (**5a**, 11%), exocyclic double bond reduced product (**6a**, 42%) and a ketone (**7**, 8%) (Scheme 2).

The ^{1}H NMR spectrum of product **5a** showed two sets of one proton multiplets at δ 2.12–2.20 and 2.43–2.48 due to —$SCH_2C\mathbf{H}_2$ and another two sets of one proton multiplet at δ 3.11–3.15 and 3.19–3.23 due to —$SC\mathbf{H}_2$; two sets of one proton doublet at δ 4.40 (J = 9 Hz) and 4.65 (J = 9 Hz) due to —$OC\mathbf{H}_2$ (which are diastereotropic protons). ^{13}C NMR and DEPT-135 spectrum of **5a** indicates the presence of nineteen carbon atoms; among them one is CH_3, three are CH_2, eight are CH, and seven are

Scheme 1. Reagents and conditions: (i) 1% NaOH sol., DCM, BTEAC, stirring, 15 min., rt. (ii) Chlorobenzene, reflux, 1 h.



quaternary carbons. The ^{1}H NMR spectrum of product **6a** exhibited two sets of one proton multiplets at δ 2.09–2.20 and 2.60–2.67 due to —SCH$_2$C**H**$_2$, another two sets of one proton multiplets at δ 2.97–3.04 and 3.23–3.32 due to —SC**H**$_2$; one proton multiplet at δ 3.64–3.73 due to —CH$_2$C**H** at the asymmetric centre; one proton triplet at δ 3.86 (J = 9.4 Hz) and another one proton double of a doublet at δ 4.38 (J = 9.4, 3.9 Hz) due to —OC**H**$_2$ (diastereotropic protons). IR spectrum of compound **7** revealed a peak at 1719 cm^{-1} due to carbonyl group. ^{1}H NMR spectrum displayed to sets of two proton doublets at δ 6.93 (J = 8.7 Hz) and at δ 7.13 (J = 8.7 Hz) due to —SCH=C**H** and —SC**H**=CH, respectively.

The products **5a**, **6a**, and **7** were characterized from their elemental analyses and spectral data as 9′-methyl-2′,3′-dihydro-9′*H*-spiro{1-benzofuran-3,4′-thiopyrano[2,3-*b*]in-dole} (**5a**), 9-methyl-4-(phenyloxymethyl)-2,3,4,9-tetra-hydrothiopyrano[2,3-*b*]indole (**6a**) and 9-methyl-2,3,9-tri-hydrothiopyrano[2,3-*b*]indole-4-one (**7**). The product **5a** is the structural isomer of the spiroheterocyclic compound obtained by the aryl radical cyclization [5a] of the corresponding *o*-bromoenol ether.

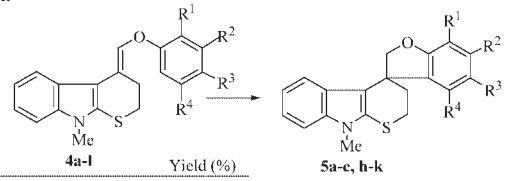
To generalize the reaction all the substrates **4b–l** were similarly treated. The spiroheterocyclic products **5b-c, h–k** were obtained in 28–60% yield, the products **6b–l** were isolated in 18–48% yield along with the product **7** (4–8%) (Scheme 2).

Formation of products **5** to **7** from compounds **4** by acid catalysis may be explained by the initial protonation of the enol ether double bond of **4** to form a latent carbonium ion **9**. The protonation of vinyl ether normally occurs at the remote position relative to the oxygen function [6,7]. But, here the more basic nitrogen function of the diene unit is the controlling site of protonation [8]. The potential carbonium ion **9** may undergo nucleophilic attack by the aromatic double bond (pathway a, Scheme 3) to give a resonance-stabilized carbocation **10**, which may then lose a proton to give spiroheterocyclic compounds **5**.

Intermediate **9** may also undergo nucleophilic attack by water molecule (pathway b, Scheme 3) followed by deprotonation and elimination of anisole **8** to give **13** which may then undergo double group transfer reaction [8,10] with **4** to give compound **6** and compound **7** (Scheme 3). Removal of the anisole (**8**) was demonstrated by the GC analysis of the crude reaction mixture after usual workup of the reaction mixture of compound **4a** (Compared with a standard sample of anisole). RT (min) of the standard sample of anisole was 2.762 whereas; the reaction mixture gave a peak at 2.802.

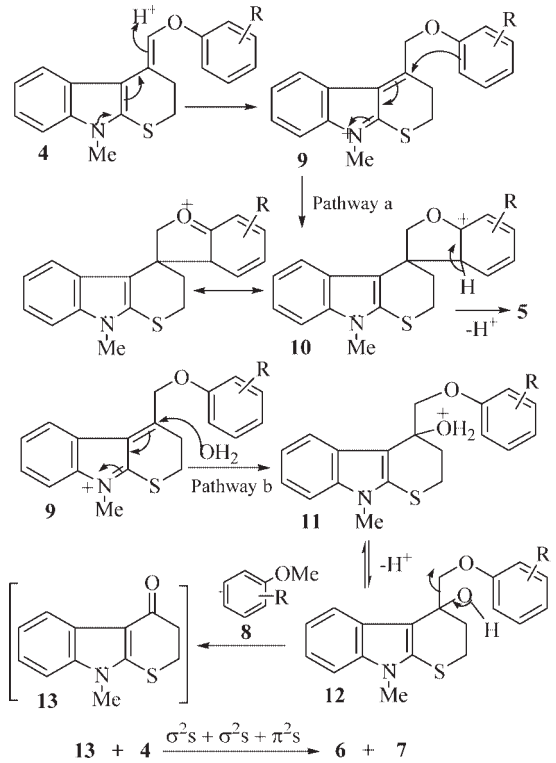
The nucleophilic attack by the aromatic double bond to the latent carbonium ion **9** becomes facile when the phenyl ring becomes electron rich. The unsubstituted phenyl ring participate in nucleophilic attack leads to only 11% spiroheterocyclic product **5a** but the presence of electron donating methyl group in the phenyl ring increases the yield of the product **5**. The dimethyl substituted phenyl ring gives higher yield of the product **5** and the yield markedly increased when the methyl group is present at the *o*-, *p*- position with respect to the participating carbon atom of the phenyl ring, *e.g*. **5c** was obtained in 60% yield. Product **5** was not obtained for *p*-methoxy substituted phenyl ring. The presence of the electron withdrawing chlorine atom at the phenyl ring inhibits the nucleophilic attack by the phenyl ring to the latent carbonium ion **9** and the spiroheterocyclic product for those cases were not obtained. The double group transfer reaction is possible in all cases irrespective of the substitution in the

Scheme 2. Reagents and conditions: DCM, MeOH, H_2SO_4, H_2O, reflux, 3–4 h.



4	Yield (%) 5	6	7
a. R^1 = R^2 = R^3 = R^4 = H	11	42	8
b. R^1 = R^2 = R^4 = H, R^3 = Me	28	32	6
c. R^1 = R^3 = H, R^2 = R^4 = Me	60	20	5
d. R^1 = R^2 = R^4 = H, R^3 = MeO	-	45	7
e. R^1 = Me, R^2 = R^4 = H, R^3 = Cl	-	46	8
f. R^1 = R^2 = R^4 = H, R^3 = Cl	-	45	7
g. R^1 = R^3 = Cl, R^2 = R^4 = H	-	48	8
h. R^1 = R^2 = Me, R^3 = R^4 = H	56	22	5
i. R^1 = R^4 = Me, R^2 = R^3 = H	58	18	4
j. R^1 = R^2 = R^3 = H, R^4 = Me	46	24	5
k. R^1 = R^3 = Me, R^2 = R^4 = H	34	30	6
l. R^1 = Cl, R^2 = R^3 = R^4 = H	-	42	7

Scheme 3



phenyl ring. Therefore, we obtained the products **6** and **7** in all the cases studied so far.

In conclusion the conditions under which the spiroheterocycles are formed is normally the usual ones for enol ether cleavage. From the experimental observation it is clear that the substituents on the phenyl ring seem to have a pronounced effect on the course of this reaction. We have developed an attractive strategy for the successful synthesis of spirocyclic indole annulated oxygen heterocyclic compounds having different connectivity between the furan and thiopyran ring with respect to the spirocyclic product obtained by the aryl radical cyclization [5a]. The methodology described here is synthetically useful and exhibits appreciable regioselectivity.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer (λ_{max} in cm^{-1}) on KBr disks. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer (λ_{max} in nm). ^1H NMR (300 MHz, 500 MHz) and ^{13}C NMR spectra were recorded on a Bruker DPX-300 and Bruker DPX-500 spectrometer in $CDCl_3$ (chemical shift in δ) with TMS as an internal standard. Elemental analyses were recorded on a Leco 932 CHNS analyzer instrument; mass spectra were recorded on JEOL JMS-600 and Q-Tof micro instrument. ^1H NMR and ^{13}C NMR spectra were recorded at the Indian Institute of Chemical Biology, Kolkata and Bose Institute, Kolkata. GC analysis was performed at IICB, Kolkata on a Hewlett-Packard 6890 puls fitted with FID. Silica gel [(60–120 mesh), (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 and 80°C.

General procedure for the synthesis of compounds 3a–l. To a mixture of 1-methylindoline-2-thione (1, 0.49 g, 3 mmol) and 1-aryloxy-4-chlorobut-2-yne (**2a**, 0.58 g, 3 mmol) in dichloromethane (30 mL) was added a solution of benzyl triethyl ammonium 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 an oily residue, which was subjected to column chromatography over silica gel (230–400 mesh). Elution of the column with petroleum ether-ethyl acetate (50:1) afforded compound **3a**. Compounds **3b–l** were prepared similarly.

Experimental data of compounds **3a–g** were published earlier [9].

1-Methyl-2-{4-(p-tolyloxy)but-2-ynylthio}-1H-indole (3h). Yield: 91%; Viscous liquid. IR (neat): ν_{max} = 1462, 2923 cm^{-1}. UV (EtOH): λ_{max} = 220, 290 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.16 (*s*, 3H, $ArCH_3$), 2.23 (*s*, 3H, $ArCH_3$), 3.44 (*s*, 2H, —SCH_2), 3.75 (*s*, 3H, —NCH_3), 4.59 (*s*, 2H, —OCH_2), 6.65–6.83 (*m*, 3H, ArH), 6.92 (s, 1H, =CH), 7.03–7.56 (*m*, 4H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.35; H, 6.36; N, 4.07%.

2-{4-(3,5-Dimethylphenoxy)but-2-ynylthio}-1-methyl-1H-indole (3i). Yield: 94%; Viscous liquid. IR (neat): ν_{max} = 1466, 2931 cm^{-1}. UV (EtOH): λ_{max} = 224, 287 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.30 (*s*, 3H, $ArCH_3$), 2.31 (*s*, 3H, $ArCH_3$), 3.43 (*s*, 2H, —SCH_2), 3.72 (*s*, 3H, —NCH_3), 4.55 (*s*, 2H, —OCH_2), 6.51–6.58 (*m*, 3H, ArH), 6.75 (*s*, 1H, =CH), 7.04–7.54 (*m*, 4H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.38; H, 6.21; N, 4.05%.

2-{4-(4-Chloro-2-methylphenoxy)but-2-ynylthio}-1-meth-yl-1-indole (3j). Yield: 89%; Viscous liquid. IR (neat): ν_{max} = 1456, 2930 cm^{-1}. UV (EtOH): λ_{max} = 219, 289 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.26 (*s*, 3H, $ArCH_3$), 3.46 (*s*, 2H, —SCH_2), 3.76 (*s*, 3H, —NCH_3), 4.58 (*s*, 2H, —OCH_2), 6.65–6.83 (*m*, 3H, ArH), 6.92 (*s*, 1H, =CH), 7.03–7.56 (*m*, 5H, ArH). MS: *m/z* = 321 (M^+). Anal. Calc. for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36%. Found: C, 74.58; H, 6.02; N, 4.25%.

2-{4-(2,4-Dichlorophenoxy)but-2-ynylthio}-1-methyl-1H-indole (3k). Yield: 94%; Viscous liquid. IR (neat): ν_{max} = 1459, 2919 cm^{-1}. UV (EtOH): λ_{max} = 217, 226, 286 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.16 (*s*, 3H, $ArCH_3$), 2.23 (*s*, 3H, $ArCH_3$), 3.44 (*s*, 2H, —SCH_2), 3.75 (*s*, 3H, —NCH_3), 4.59 (*s*, 2H, —OCH_2), 6.66–6.85 (*m*, 3H, ArH), 6.92 (*s*, 1H, =CH), 7.06–7.56 (*m*, 4H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.39; H, 6.22; N, 4.25%.2-{4-(2,3-dimethylphenoxy)but-2-ynylthio}-1-methyl-1H-indole (3l): Yield: 92%; Viscous liquid. IR (neat): ν_{max} = 1460, 2931 cm^{-1}. UV (EtOH): λ_{max} = 221, 289 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.44 (*s*, 2H, —SCH_2), 3.76 (*s*, 3H, —NCH_3), 4.73 (*s*, 2H, —OCH_2), 6.74 (*s*, 1H, =CH),

6.93–7.82 (*m*, 8H, ArH). MS: *m/z* = 341, 343 (M^+). Anal. Calc. for $C_{19}H_{16}ClNOS$: C, 66.75; H, 4.72; N, 4.10%. Found: C, 66.63; H, 4.80; N, 4.04%.

General procedure for the synthesis of compounds 4a–l. Compound **3a** (0.46 g, 1.5 mmol) was refluxed in chlorobenzene (10 mL) for 1 h. Then the crude mass was subjected to column chromatography over silica gel (60–120 mesh). Elution of the column with petroleum ether followed by petroleum ether-ethyl acetate (50:1) gave compound **4a** as white solid. Similarly, compounds **4b–l** were synthesized from **3b–l**.

9-Methyl-4-(phenoxymethylene)-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4a). Yield: 83%; White solid; mp 120–122°C. IR (KBr): ν_{max} = 1482, 2921, 3044 cm^{-1}. UV (EtOH): λ_{max} = 216, 230, 247, 257, 277, 308 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.06–3.08 (*m*, 2H, —SCH_2CH_2), 3.13–3.17 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 6.98–7.10 (*m*, 2H, ArH), 7.12 (*s*, 1H, =CH), 7.14–7.70 (*m*, 7H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 24.12, 27.81, 29.83, 108.48, 115.98, 116.40, 117.22, 118.82, 120.09, 120.90, 122.30, 124.77, 129.65, 132.99, 133.57, 137.55, 157.85. MS: *m/z* = 307 (M^+). Anal. Calc. for $C_{19}H_{17}NOS$: C, 74.23; H, 5.57; N, 4.56%. Found: C, 74.41; H, 5.49; N, 4.66%.

9-Methyl-4-(p-tolyloxymethylene)-,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4b). Yield: 83%; White solid; mp 122–124°C. IR (KBr): ν_{max} = 1466, 1499, 2916 cm^{-1}. UV (EtOH): λ_{max} = 205, 253, 277, 310 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.32 (*s*, 3H, $ArCH_3$), 3.08–3.11 (*m*, 2H, —SCH_2CH_2), 3.14–3.17 (*m*, 2H, —SCH_2), 3.65 (*s*, 3H, —NCH_3), 6.81–7.02 (*m*, 3H, ArH), 7.15 (*s*, 1H, =CH), 7.25–7.65 (*m*, 5H, ArH). MS: *m/z* = 321 (M^+). Anal. Calc. for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36%. Found: C, 74.88; H, 6.02; N, 4.48%.

4-{(3,5-Dimethylphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4c). Yield: 88%; White solid; mp 100–102°C. IR (KBr): ν_{max} = 1464, 2904, 3047 cm^{-1}. UV (EtOH): λ_{max} = 217, 247, 252, 257, 276, 307 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.29 (*s*, 3H, $ArCH_3$), 2.31 (*s*, 3H, $ArCH_3$), 3.03–3.07 (*m*, 2H, —SCH_2CH_2), 3.12–3.16 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 6.57–7.13 (*m*, 4H, ArH), 7.14 (*s*, 1H, =CH), 7.17–7.67 (*m*, 3H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C =21.33, 24.06, 27.81, 29.77, 108.43, 112.47, 113.70, 114.17, 116.87, 118.82, 120.02, 120.86, 123.30, 124.06, 133.80, 137.52, 139.46, 157.86. MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.35; H, 6.42; N, 4.22%.

4-{(4-Methoxyphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4d). Yield: 86%; White solid; mp 72–74°C. IR (KBr): ν_{max} = 1497, 2938 cm^{-1}. UV (EtOH): λ_{max} = 216, 252, 257, 276 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.06–3.08 (*m*, 2H, —SCH_2CH_2), 3.13–3.17 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 3.79 (*s*, 3H, —OCH_3), 6.86–7.09 (*m*, 4H, ArH), 7.11 (*s*, 1H, =CH), 7.13–7.64 (*m*, 4H, ArH). MS: *m/z* = 337 (M^+). Anal. Calc. for $C_{20}H_{19}NO_2S$: C, 71.19; H, 5.68; N, 4.15%. Found: C, 71.13; H, 5.72; N, 4.11%.

4{(4-chloro-2-methylphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4e). Yield: 84%; White solid; mp 122–124°C. IR (KBr): ν_{max} = 1477, 2922 cm^{-1}. UV (EtOH): λ_{max} = 212, 230, 256, 279, 311 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.31 (*s*, 3H, $ArCH_3$), 3.04–3.08 (*m*, 2H, —SCH_2CH_2), 3.14–3.17 (*m*, 2H, —SCH_2), 3.65 (*s*, 3H, —NCH_3), 6.96–6.99 (*m*, 1H, ArH), 7.10 (*s*, 1H, =CH), 7.12–7.63 (*m*, 6H, ArH). MS: *m/z* = 355, 357 (M^+). Anal. Calc. for $C_{20}H_{18}ClNOS$: C, 67.50; H, 5.10; N, 3.94%. Found: C, 67.38; H, 5.15; N, 3.85%.

4-{(4-Chlorophenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4f). Yield: 80%; White solid; mp 108–110°C. IR (KBr): ν_{max} = 1486, 2920 cm^{-1}. UV (EtOH): λ_{max} = 212, 219, 253, 278, 310 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.03–3.05 (*m*, 2H, —SCH_2CH_2), 3.14–3.16 (*m*, 2H, —SCH_2), 3.65 (*s*, 3H, —NCH_3), 7.03–7.05 (*m*, 2H, ArH), 7.11 (*s*, 1H, =CH), 7.13–7.63 (*m*, 6H, ArH). MS: *m/z* = 341, 343 (M^+). Anal. Calc. for $C_{19}H_{16}ClNOS$: C, 66.75; H, 4.72; N, 4.10%. Found: C, 66.85; H, 4.67; N, 4.21%.

4-{(2,4-Dichlorophenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4g). Yield: 85%; White solid; mp 116–118°C. IR (KBr): ν_{max} = 1474, 2928 cm^{-1}. UV (EtOH): λ_{max} = 211, 252, 280, 311 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.07–3.10 (*m*, 2H, —SCH_2CH_2), 3.14–3.18 (*m*, 2H, —SCH_2), 3.65 (*s*, 3H, —NCH_3), 6.96–7.07 (*m*, 1H, ArH), 7.10 (*s*, 1H, =CH), 7.14–7.62 (*m*, 6H, ArH). MS: *m/z* = 375, 377, 379 (M^+). Anal. Calc. for $C_{19}H_{15}Cl_2NOS$: C, 60.64; H, 4.02; N, 3.72%. Found: C, 60.48; H, 4.09; N, 3.65%

4-{(2,3-Dimethylphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4h). Yield: 86%; White solid; mp 114–116°C. IR (KBr): ν_{max} = 1466, 2918 cm^{-1}. UV (EtOH): λ_{max} = 206, 254, 276, 306 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.26 (*s*, 3H, $ArCH_3$), 2.31 (*s*, 3H, $ArCH_3$), 3.09–3.11 (*m*, 2H, —SCH_2CH_2), 3.14–3.18 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 6.87–7.08 (*m*, 3H, ArH), 7.11 (*s*, 1H, =CH), 7.13–7.65 (*m*, 4H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.39; H, 6.24; N, 4.29%.

4-{(2,5-Dimethylphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4i). Yield: 88%; White solid; mp 112–114°C. IR (KBr): ν_{max} = 1465, 2925 cm^{-1}. UV (EtOH): λ_{max} = 209, 253, 275, 307 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.29 (*s*, 3H, $ArCH_3$), 2.31 (*s*, 3H, $ArCH_3$), 3.06-3.10 (*m*, 2H, —SCH_2CH_2), 3.14–3.18 (*m*, 2H, —SCH_2), 3.66 (*s*, 3H, —NCH_3), 6.77–7.07 (*m*, 2H, ArH), 7.09 (*s*, 1H, =CH), 7.12–7.67 (*m*, 5H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.36; H, 6.19; N, 4.13%.

9-Methyl-4-(m-tolyloxymethylene)-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4j). Yield: 84%; White solid; mp 118–120°C. IR (KBr): ν_{max} = 1475, 2922 cm^{-1}. UV (EtOH): λ_{max} = 208, 252, 276, 308 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.32 (*s*, 3H, $ArCH_3$), 3.08–3.12 (*m*, 2H, —SCH_2CH_2), 3.14–3.18 (*m*, 2H, —SCH_2), 3.65 (*s*, 3H, -NCH_3), 6.81–7.04 (*m*, 3H, ArH), 7.15 (*s*, 1H, =CH), 7.23–7.63 (*m*, 5H, ArH). MS: *m/z* = 321 (M^+). Anal. Calc. for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36%. Found: C, 74.63; H, 6.03; N, 4.30%.

4-{(2,4-Dimethylphenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4k). Yield: 85%; White solid; mp 110–112°C. IR (KBr): ν_{max} = 1488, 2918 cm^{-1}. UV (EtOH): λ_{max} = 206, 254, 275, 305 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.29 (*s*, 3H, $ArCH_3$), 2.30 (*s*, 3H, $ArCH_3$), 3.08–3.10 (*m*, 2H, —SCH_2CH_2), 3.13–3.17 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 6.93–7.12 (*m*, 3H, ArH), 7.14 (*s*, 1H, =CH), 7.16–7.64 (*m*, 4H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.32; H, 6.42; N, 4.26%.

4-{(2-Chlorophenoxy)methylene}-9-methyl-2,3,4,9-tetrahydrothiopyrano[2,3-b]indole (4l). Yield: 82%; White solid; mp

98–100°C. IR (KBr): ν_{max} = 1471, 2920 cm^{-1}. UV (EtOH): λ_{max} = 216, 247, 252, 257, 278, 310 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 3.09–3.12 (*m*, 2H, —SCH_2CH_2), 3.14–3.17 (*m*, 2H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 6.87–6.95 (*m*, 1H, ArH), 7.12 (*s*, 1H, =CH), 7.13–7.64 (*m*, 7H, ArH). MS: *m/z* = 341, 343 (M^+). Anal. Calc. for $C_{19}H_{16}ClNOS$: C, 66.75; H, 4.72; N, 4.10%. Found: C, 66.87; H, 4.64; N, 4.05%.

General procedure for the acid catalyzed reaction of compounds 4a-l. To the dichloromethane (8.4 mL) solution of compound **4a** (0.3 g, 1 mmol), water (3 mL), methanol (13.5 mL) and concentrated sulfuric acid (2.3 mL) were added. The reaction mixture was then refluxed on water bath for 4 h, allowed to cool and extracted with dichloromethane (2 × 10 mL). The combined extract was washed with sodium bicarbonate solution (3 × 15 mL), water (3 × 15 mL), brine (15 mL) and dried (Na_2SO_4). After removal of the solvent the crude mass was subjected to column chromatography. Elution of the column with petroleum ether-ethyl acetate (50:1) on silica gel (60–120 mesh) afforded the compounds **5a**, **6a**, and **7**. Compounds **4b–l** were also treated similarly.

9′-Methyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5a). Yield: 11%; White solid; mp 156–158°C. IR (KBr): ν_{max} = 1479, 2898, 2918 cm^{-1}. UV (EtOH): λ_{max} = 233, 289, 297 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.12–2.20 (*m*, 1H, —SCH_2CH_2), 2.43–2.48 (*m*, 1H, —SCH_2CH_2), 3.11–3.15 (*m*, 1H, —SCH_2), 3.19–3.23 (*m*, 1H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 4.40 (d, 1H, *J* = 9 Hz, —OCH_2), 4.65 (d, 1H, *J* = 9 Hz, —OCH_2), 6.70–7.23 (*m*, 8H, ArH). ^{13}C NMR and DEPT-135 (75 MHz, $CDCl_3$): δ_C = 25.49 (CH_2), 30.21 (CH_3), 38.03 (CH_2), 46.65 (C), 82.63 (CH_2), 107.80 (C), 108.60 (CH), 110.32(CH), 118.93 (CH), 119.60 (CH), 120.89 (CH), 121.46 (CH), 124.72 (CH), 126.71 (C), 128.99 (CH), 131.86 (C), 134.54 (C), 137.87 (C), 160.17 (C). MS: *m/z* = 307 (M^+). Anal. Calc. for $C_{19}H_{17}NOS$: C, 74.23; H, 5.57; N, 4.56%. Found: C, 74.34; H, 5.66; N, 4.68%.

5,9′-Dimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5b). Yield: 28%; White solid; mp 114–116°C. IR (KBr): ν_{max} = 1466, 2920 cm^{-1}. UV (EtOH): λ_{max} = 234, 288, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.16 (*s*, 3H, ArCH_3), 2.38–2.42 (*m*, 1H, —SCH_2CH_2), 2.43–2.46 (*m*, 1H, —SCH_2CH_2), 3.11–3.16 (*m*, 1H, —SCH_2), 3.18–3.23 (*m*, 1H, —SCH_2), 3.65 (*s*, 3H, —NCH_3), 4.38 (d, 1H, *J* = 9 Hz, —OCH_2), 4.65 (d, 1H, *J* = 9 Hz, —OCH_2), 6.71–7.25 (*m*, 7H, ArH). MS: *m/z* = 321 (M^+). Anal. Calc. for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36%. Found: C, 74.92; H, 6.02; N, 4.28%.

4,6,9′-Trimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5c). Yield: 60%; White solid; mp 172–174°C. IR (KBr): ν_{max} = 1463, 2914 cm^{-1}. UV (EtOH): λ_{max} = 236, 289, 299 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.65 (*s*, 3H, ArCH_3), 2.14–2.23 (*m*, 1H, —SCH_2CH_2), 2.30 (*s*, 3H, ArCH_3), 2.33–2.40 (*m*, 1H, —SCH_2CH_2), 3.05–3.11 (*m*, 1H, —SCH_2), 3.17–3.26 (*m*, 1H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 4.33 (d, 1H, *J* = 9 Hz, —OCH_2), 4.52 (d, 1H, *J* = 9 Hz, —OCH_2), 6.41 (*s*, 1H, ArH), 6.59 (*s*, 1H, ArH), 6.78–7.23 (*m*, 4H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 17.27, 21.89, 25.69, 30.26, 34.75, 46.36, 82.26, 107.69, 108.47, 108.72, 118.44, 119.63, 120.89, 124.49, 127.15, 127.98, 131.08, 135.35, 137.75, 139.05, 160.61. MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.35; H, 6.20; N, 4.29%.

6,7,9′-Trimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5h). Yield: 56%; White solid; mp 154–156°C. IR (KBr): ν_{max} = 1462, 2929 cm^{-1}. UV (EtOH): λ_{max} = 225, 237, 288, 299 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.13–2.16 (*m*, 1H, —SCH_2CH_2), 2.23 (*s*, 3H, ArCH_3), 2.27 (*s*, 3H, ArCH_3), 2.40–2.42 (*m*, 1H, —SCH_2CH_2), 3.12–3.14 (*m*, 1H, —SCH_2), 3.15–3.18 (*m*, 1H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 4.39 (d, 1H, *J* = 9 Hz, —OCH_2), 4.63 (d, 1H, *J* = 9 Hz, —OCH_2), 6.62–7.24 (*m*, 6H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 12.10, 19.91, 25.47, 30.17, 37.95, 46.94, 82.38, 107.97, 108.49, 118.97, 119.12, 119.45, 120.76, 121.21, 122.79, 126.78, 131.32, 131.71, 137.55, 137.80, 158.64. MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.01; H, 6.38; N, 4.31%.

4,7,9′-Trimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5i). Yield: 58%; White solid; mp 170–172°C. IR (KBr): ν_{max} = 1466, 2920, 2941 cm^{-1}. UV (EtOH): λ_{max} = 224, 235, 288, 299 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.65 (*s*, 3H, ArCH_3), 2.18–2.22 (*m*, 1H, —SCH_2CH_2), 2.27 (*s*, 3H, ArCH_3), 2.35–2.42 (*m*, 1H, —SCH_2CH_2), 3.05–3.12 (*m*, 1H, —SCH_2), 3.18–3.27 (*m*, 1H, —SCH_2), 3.64 (*s*, 3H, —NCH_3), 4.35 (d, 1H, *J* = 9 Hz, —OCH_2), 4.53 (d, 1H, *J* = 9 Hz, —OCH_2), 6.48–7.23 (*m*, 6H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.30; H, 6.37; N, 4.26%.

4,9′-Dimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5j). Yield: 46%; White solid; mp 104–106°C. IR (KBr): ν_{max} = 1464, 2912 cm^{-1}. UV (EtOH): λ_{max} = 235, 288, 299 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.70 (*s*, 3H, ArCH_3), 2.16–2.25 (*m*, 1H, —SCH_2CH_2), 2.35–2.42 (*m*, 1H, —SCH_2CH_2), 3.15–3.19 (*m*, 1H, —SCH_2), 3.23–3.28 (*m*, 1H, —SCH_2), 3.66 (*s*, 3H, —NCH_3), 4.35 (d, 1H, *J* = 9 Hz, —OCH_2), 4.55 (d, 1H, *J* = 9 Hz, —OCH_2), 6.58–7.25 (*m*, 7H, ArH). MS: *m/z* = 321 (M^+). Anal. Calc. for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36%. Found: C, 74.92; H, 5.90; N, 4.29%.

5,7,9′-Trimethyl-3′,9′-dihydro-2H,2′H-spiro[benzofuran-3,4′-thiopyrano[2,3-b]indole] (5k). Yield: 34%; White solid; mp 158–160°C. IR (KBr): ν_{max} = 1466, 2909 cm^{-1}. UV (EtOH): λ_{max} = 225, 235, 290, 297 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.13 (*s*, 3H, ArCH_3), 2.18–2.23 (*m*, 1H, —SCH_2CH_2), 2.28 (*s*, 3H, ArCH_3), 2.36–2.47 (*m*, 1H, —SCH_2CH_2), 3.06–3.16 (*m*, 1H, —SCH_2), 3.17–3.27 (*m*, 1H, -SCH_2), 3.65 (*s*, 3H, —NCH_3), 4.36 d, 1H, *J* = 9 Hz, —OCH_2), 4.53 (d, 1H, *J* = 9 Hz, —OCH_2), 6.48–7.24 (*m*, 6H, ArH). MS: *m/z* = 335 (M^+). Anal. Calc. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18%. Found: C, 75.34; H, 6.22; N, 4.30%.

9-Methyl-4-(phenoxymethyl)-2,3,4,9-tetrahydrothiopy-rano[2,3-b]indole (6a). Yield: 42%; White solid; mp 90–92°C. IR (KBr): ν_{max} = 1469, 2912 cm^{-1}. UV (EtOH): λ_{max} = 224, 238, 279, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.09–2.20 (*m*, 1H, —SCH_2CH_2), 2.60–2.67 (*m*, 1H, —SCH_2CH_2), 2.97–3.04 (*m*, 1H, —SCH_2), 3.23–3.32 (*m*, 1H, —SCH_2), 3.61 (*s*, 3H, —NCH_3), 3.64–3.73 (*m*, 1H, —CH_2CH), 3.86 (*t*, 1H, *J* = 9.4 Hz, —OCH_2), 4.38 (dd, 1H, *J* = 9.4, 3.9 Hz, —OCH_2), 6.90–7.51 (*m*, 9H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 24.27, 25.59, 30.15, 32.04, 69.92, 105.45, 108.74, 115.01, 115.33, 117.12, 119.75, 120.90, 121.25, 128.14, 130.00, 131.01, 137.57, 159.40. MS: *m/z* 309 (M^+). Anal. Calc. for $C_{19}H_{19}NOS$: C, 73.75; H, 6.19; N, 4.53%. Found: C, 73.90; H, 6.24; N, 4.65%.

9-Methyl-4-(p-tolyloxymethyl)-2,3,4,9-tetrahydrothiopy-rano[2,3-b]indole (6b). Yield: 32%; Viscous liquid. IR (neat): ν_{max} = 1466, 2921 cm^{-1}. UV (EtOH): λ_{max} = 226, 238, 286, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.08–2.17 (*m*, 1H, —SCH_2CH_2), 2.27 (*s*, 3H, ArCH_3), 2.60–2.66 (*m*, 1H, —SCH_2CH_2), 2.96–3.01 (*m*, 1H, —SCH_2), 3.22–3.30 (*m*, 1H, —SCH_2), 3.60 (*s*, 3H, —NCH_3), 3.65–3.68 (*m*, 1H, —CH_2CH), 3.83 (*t*, 1H, *J* = 9.4 Hz, —OCH_2), 4.35 (dd, 1H, *J* = 9.4, 3.8 Hz, —OCH_2), 6.80–7.50 (*m*, 8H, Ar**H**). MS: *m*/*z* = 323 (M^+). Anal. Calc. for $C_{20}H_{21}NOS$: C, 74.27; H, 6.54; N, 4.33%. Found: C, 74.45; H, 6.59; N, 4.40%.

4-{(3,5-Dimethylphenoxy)methyl}-9-methyl-2,3,4,9-tetra-hydrothiopyrano[2,3-b]indole (6c). Yield: 20%; White solid; mp 92–94°C. IR (KBr): ν_{max} = 1464, 2919 cm^{-1}. UV (EtOH): λ_{max} = 224, 235, 255, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.05–2.19 (*m*, 1H, —SCH_2CH_2), 2.27 (*s*, 6H, ArCH_3), 2.59–2.67 (*m*, 1H, —SCH_2CH_2), 2.96–3.03 (*m*, 1H, —SCH_2), 3.23–3.32 (*m*, 1H, —SCH_2), 3.62 (*s*, 3H, —NCH_3), 3.65–3.71 (*m*, 1H, —CH_2CH), 3.83 (*t*, 1H, *J* = 9.4 Hz, —OCH_2), 4.35 (dd, 1H, *J* = 9.4, 3.8 Hz, —OCH_2), 6.56–7.51 (*m*, 7H, Ar**H**). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 21.83, 24.18, 25.47, 30.09, 31.97, 69.73, 105.47, 108.66, 112.70, 117.03, 119.65, 120.81, 122.93, 128.07, 130.92, 137.51, 139.67, 159.40. MS: *m*/*z* = 337 (M^+). Anal. Calc. for $C_{21}H_{23}NOS$: C, 74.74; H, 6.87; N, 4.15%. Found: C, 74.93; H, 6.94; N, 4.06%.

4-{(4-Methoxyphenoxy)methyl}-9-methyl-2,3,4,9-tetrahy-drothiopyrano[2,3-b]indole (6d). Yield: 45%; White solid; mp 62–64°C. IR (KBr): ν_{max} = 1467, 1510, 2924 cm^{-1}. UV (EtOH): λ_{max} = 226, 235, 240, 255, 261, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.09–2.19 (*m*, 1H, —SCH_2CH_2), 2.60–2.66 (*m*, 1H, —SCH_2CH_2), 2.97–3.04 (*m*, 1H, —SCH_2), 3.23–3.31 (*m*, 1H, —SCH_2), 3.61 (*s*, 3H, —NCH_3), 3.64–3.69 (*m*, 1H, —CH_2CH), 3.76 (*s*, 3H, —OCH_3), 3.82 (*t*, 1H, *J* = 9.4 Hz, —OCH_2), 4.33 (dd, 1H, *J* = 9.4, 3.8 Hz, —OCH_2), 6.80–7.50 (*m*, 8H, Ar**H**). MS: *m*/*z* = 339 (M^+). Anal. Calc. for $C_{20}H_{21}NO_2S$: C, 70.77; H, 6.24; N, 4.13%. Found: C, 70.65; H, 6.35; N, 4.21%.

4-{(4-Chloro-2-methylphenoxy)methyl}-9-methyl-2,3,4,9-tet-rahydrothiopyrano[2,3-b]indole (6e). Yield: 46%; Viscous liquid. IR (neat): ν_{max} = 1467, 1492, 2922 cm^{-1}. UV (EtOH): λ_{max} = 235, 289, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.02–2.19 (*m*, 1H, —SCH_2CH_2), 2.23 (*s*, 3H, ArCH_3), 2.58–2.65 (*m*, 1H, —SCH_2CH_2), 2.97–3.04 (*m*, 1H, —SCH_2), 3.23–3.31 (*m*, 1H, —SCH_2), 3.60 (*s*, 3H, —NCH_3), 3.67–3.73 (*m*, 1H, —CH_2CH), 3.82 (*t*, 1H, *J* = 9.2 Hz, —OCH_2), 4.35 (dd, 1H, *J* = 9.2, 3.8 Hz, —OCH_2), 6.66–7.48 (*m*, 7H, Ar**H**). MS: *m*/*z* = 357, 359 (M^+). Anal. Calc. for $C_{20}H_{20}ClNOS$: C, 67.12; H, 5.63; N, 3.91%. Found: C, 67.01; H, 5.50; N, 3.96%.

4-{(4-Chlorophenoxy)methyl}-9-methyl-2,3,4,9-tetrahy-dro-thiopyrano[2,3-b]indole (6f). Yield: 45%; White solid; mp 106–108°C. IR (KBr): ν_{max} = 1465, 1491, 2917 cm^{-1}. UV (EtOH): λ_{max} = 234, 290, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.09–2.21 (*m*, 1H, —SCH_2CH_2), 2.55–2.64 (*m*, 1H, —SCH_2CH_2), 2.98–3.05 (*m*, 1H, —SCH_2), 3.21–3.30 (*m*, 1H, —SCH_2), 3.61 (*s*, 3H, —NCH_3), 3.64–3.72 (*m*, 1H, —CH_2CH), 3.84 (*t*, 1H, *J* = 9.4 Hz, —OCH_2), 4.33 (dd, 1H, *J* = 9.4, 4 Hz, —OCH_2), 6.81–7.49 (*m*, 8H, Ar**H**). MS: *m*/*z* = 343, 345 (M^+). Anal. Calc. for $C_{19}H_{18}ClNOS$: C, 66.36; H, 5.28; N, 4.07%. Found: C, 66.52; H, 5.35; N, 3.97%.

4-{(2,4-Dichlorophenoxy)methyl}-9-methyl-2,3,4,9-tetrahy-drothiopyrano[2,3-b]indole (6g). Yield: 48%; White solid; mp 94–96°C. IR (KBr): ν_{max} = 1466, 1483, 2927 cm^{-1}. UV (EtOH): λ_{max} = 236, 294 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.14–2.25 (*m*, 1H, —SCH_2CH_2), 2.65–2.72 (*m*, 1H, —SCH_2CH_2), 3.00–3.07 (*m*, 1H, —SCH_2), 3.25–3.34 (*m*, 1H, —SCH_2), 3.62 (*s*, 3H, —NCH_3), 3.73–3.78 (*m*, 1H, —CH_2CH), 3.87 (*t*, 1H, *J* = 9.2 Hz, —OCH_2), 4.42 (dd, 1H, *J* = 9.2, 3.8 Hz, —OCH_2), 6.79–7.49 (*m*, 7H, Ar**H**). MS: *m*/*z* = 377, 379, 381 (M^+). Anal. Calc. for $C_{19}H_{17}Cl_2NOS$: C, 60.32; H, 4.53; N, 3.70%. Found: C, 60.44; H, 4.45; N, 3.81%.

4-{(2,3-Dimethylphenoxy)methyl}-9-methyl-2,3,4,9-tetra-hydrothiopyrano[2,3-b]indole (6h). Yield: 22%; White solid; mp 116–118°C. IR (KBr): ν_{max} = 1466, 2916 cm^{-1}. UV (EtOH): λ_{max} = 235, 239, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.12–2.14 (*m*, 1H, —SCH_2CH_2), 2.21 (*s*, 3H, ArCH_3), 2.28 (*s*, 3H, ArCH_3), 2.65–2.69 (*m*, 1H, —SCH_2CH_2), 2.98–3.03 (*m*, 1H, —SCH_2), 3.25–3.31 (*m*, 1H, —SCH_2), 3.62 (*s*, 3H, —NCH_3), 3.69–3.74 (*m*, 1H, —CH_2CH), 3.84 (*t*, 1H, *J* = 9.2 Hz, —OCH_2), 4.40 (dd, 1H, *J* = 9.2, 4 Hz, —OCH_2), 6.67–7.49 (*m*, 7H, Ar**H**). MS: *m*/*z* = 337 (M^+). Anal. Calc. for $C_{21}H_{23}NOS$: C, 74.74; H, 6.87; N, 4.15%. Found: C, 74.59; H, 6.95; N, 4.22%.

4-{(2,5-Dimethylphenoxy)methyl}-9-methyl-2,3,4,9-tetra-hydrothiopyrano[2,3-b]indole (6i). Yield: 18%; White solid; mp 72–74°C. IR (KBr): ν_{max} = 1464, 2924 cm^{-1}. UV (EtOH): λ_{max} = 239, 282, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.12–2.18 (*m*, 1H, —SCH_2CH_2), 2.23 (*s*, 3H, ArCH_3), 2.26 (*s*, 3H, ArCH_3), 2.64–2.70 (*m*, 1H, —SCH_2CH_2), 2.97–3.04 (*m*, 1H, —SCH_2), 3.25–3.34 (*m*, 1H, —SCH_2), 3.62 (*s*, 3H, —NCH_3), 3.69–3.75 (*m*, 1H, —CH_2CH), 3.83 (*t*, 1H, *J* = 9.3 Hz, —OCH_2), 4.39 (dd, 1H, *J* = 9.3, 3.6 Hz, —OCH_2), 6.62–7.51 (*m*, 7H, Ar**H**). MS: *m*/*z* = 337 (M^+). Anal. Calc. for $C_{21}H_{23}NOS$: C, 74.74; H, 6.87; N, 4.15%. Found: C, 74.92; H, 6.77; N, 4.06%.

9-Methyl-4-(m-tolyloxymethyl)-2,3,4,9-tetrahydrothio-pyrano[2,3-b]indole (6j). Yield: 24%; White solid; mp 86–88°C. IR (KBr): ν_{max} = 1464, 2922 cm^{-1}. UV (EtOH): λ_{max} = 235, 288, 299 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.07–2.15 (*m*, 1H, —SCH_2CH_2), 2.29 (*s*, 3H, ArCH_3), 2.57–2.63 (*m*, 1H, —SCH_2CH_2), 2.91–2.98 (*m*, 1H, —SCH_2), 3.19–3.27 (*m*, 1H, —SCH_2), 3.56 (*s*, 3H, —NCH_3), 3.64–3.67 (*m*, 1H, —CH_2CH), 3.83 (*t*, 1H, *J* = 9.3 Hz, —OCH_2), 4.34 (dd, 1H, *J* = 9.3, 3.7 Hz, —OCH_2), 6.70–7.49 (*m*, 8H, Ar**H**). MS: *m*/*z* = 323 (M^+). Anal. Calc. for $C_{20}H_{21}NOS$: C, 74.27; H, 6.54; N, 4.33%. Found: C, 74.13; H, 6.62; N, 4.45%.

4-{(2,4-Dimethylphenoxy)methyl}-9-methyl-2,3,4,9-tetra-hydrothiopyrano[2,3-b]indole (6k). Yield: 30%; White solid; mp 68–70°C. IR (KBr): ν_{max} = 1466, 2920 cm^{-1}. UV (EtOH): λ_{max} = 232, 286, 298 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.10–2.19 (*m*, 1H, —SCH_2CH_2), 2.24 (*s*, 6H, ArCH_3), 2.62–2.68 (*m*, 1H, —SCH_2CH_2), 2.94–3.01 (*m*, 1H, —SCH_2), 3.22–3.35 (*m*, 1H, —SCH_2), 3.58 (*s*, 3H, —NCH_3), 3.64–3.72 (*m*, 1H, —CH_2CH), 3.80 (*t*, 1H, *J* = 9.2 Hz, —OCH_2), 4.37 (dd, 1H, *J* = 9.2, 3.6 Hz, —OCH_2), 6.66–7.49 (*m*, 7H, Ar**H**). MS: *m*/*z* = 337 (M^+). Anal. Calc. for $C_{21}H_{23}NOS$: C, 74.74; H, 6.87; N, 4.15%. Found: C, 74.85; H, 6.97; N, 4.07%.

4-{(2-Chlorophenoxy)methyl}-9-methyl-2,3,4,9-tetrahy-dro-thiopyrano[2,3-b]indole (6l). Yield: 42%; White solid; mp 102–104°C. IR (KBr): ν_{max} = 1465, 2920 cm^{-1}. UV (EtOH): λ_{max} = 208, 222, 238, 300 nm. ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.14–2.25 (*m*, 1H, —SCH_2CH_2), 2.72–2.79 (*m*, 1H, —SCH_2CH_2), 3.00–3.07 (*m*, 1H, —SCH_2), 3.27–3.36 (*m*, 1H,

—SC**H**$_2$), 3.62 (*s*, 3H, —NC**H**$_3$), 3.76–3.85 (*m*, 1H, —CH$_2$C**H**), 3.88 (*t*, 1H, J = 9.2 Hz, —OC**H**$_2$), 4.48 (dd, 1H, J = 9.2, 3.6 Hz, —OC**H**$_2$), 6.80–7.56 (*m*, 8H, Ar**H**). MS: m/z = 343, 345 (M^+). Anal. Calc. for $C_{19}H_{18}ClNOS$: C, 66.36; H, 5.28; N, 4.07%. Found: C, 66.18; H, 5.35; N, 3.98%.

9-Methylthiopyrano[2,3-b]indol-4(9H)-one (7). Yield: 4–8%; Viscous liquid. IR (neat): ν_{max} = 1453, 1719, 2922 cm^{-1}. UV (EtOH): λ_{max} = 201, 229, 289 nm. ^{1}H NMR (300 MHz, $CDCl_3$): δ_H = 3.67 (*s*, 3H, —NC**H**$_3$), 6.93 (d, 1H, J = 8.7 Hz. —SCH=C**H**), 7.13 (d, 1H, J = 8.7 Hz. —SC**H**=CH), 7.32–7.60 (*m*, 4H, Ar**H**). MS: m/z = 215 (M^+). Anal. Calc. for $C_{12}H_9NOS$: C, 66.95; H, 4.21; N, 6.51%. Found: C, 67.11; H, 4.30; N, 6.44%.

GC analysis of Compound (8). The crude reaction mixture of compound **4a** after usual work up was injected into the column (oven temperature 40°-5-12C/mim-240-18). RT (min) of the standard sample of anisole was 2.762 whereas; the reaction mixture gave a peak at 2.802.

Acknowledgments. We thank the CSIR (New Delhi) for financial assistance. Two of us (S.A. and B. C) are grateful to UGC (New Delhi) and CSIR (New Delhi), respectively, for their fellowship. We also thank the DST (New Delhi) for providing UV–vis and IR spectrometers under DST-FIST program.

REFERNCES AND NOTES

[1] (a) Takada, S.; Makisumi, Y. Chem Pharm Bull 1984, 32, 872; (b) Takada, S.; Ishizuka, N.; Sasatani, T.; Makisumi, Y.; Jyoyama, H.; Hatakeyama, H.; Asanuma, F.; Hirose, K. Chem Pharm Bull 1984, 32, 877.

[2] (a) Sakabe, N.; Sendo, Y.; Iijima, I.; Ban, Y. Tetrahedron Lett 1969, 10, 2527; (b) Sundberg, R. J. The Chemistry of Indoles; Academic Press: New York, 1970, p 438; (c) Saxton, J. E. Indoles, Part 4; Wiley-Intersience: New York, 1983; (d) Nakashima, Y.; Kawashima, Y.; Amanuma, F.; Sota, K.; Tanaka, A.; Kameyama, T. Chem Pharm Bull 1984, 32, 4271; (e) Ohmoto, T.; Koike, K. Chem Pharm Bull 1984, 32, 170; (f) Shimizu, M.; Ishikawa, M.; Komoda, Y.; Nkajima, T.; Yamaguchi, K.; Yoneda, N. Chem Pharm Bull 1984, 32, 463; (g) Kamijo, S.; Yamamoto, Y. J Org Chem 2003, 68, 4764; (h) Hashimoto, Y.; Shudo, K.; Okamoto, T. Chem Pharm Bull 1984, 32, 4300; (i) Yamanaka, E.; One, M.; Kasamatsu, S.; Aimi, N.; Sakai, S. Chem Pharm Bull 1984, 32, 818; (j) Sakai, S.; Aimi, N.; Yamaguchi, K.; Hitotsuyonagi, Y.; Watanabe, C.; Yokose, K.; Koyama, Y.; Shudo, K.; Itai, A. Chem Pharm Bull 1984, 32, 354; (k) Endo, Y.; Shudo, K.; Furuhata, K.; Ogura, H.; Sakai, S.; Aimi, N.; Hitotsuyanagi, Y.; Koyama, Y. Chem Pharm Bull 1984, 32, 358; (l) Gul, W.; Hamann, M. T. Life Sci 2005, 78, 442; (m) Hoffmeister, D.; Keller, N. P. Nat Prod Rep 2007, 24, 393.

[3] (a) Dounay, A. B.; Overman, L. E. Chem Rev 2003, 103, 2945; (b) Castro, A. M. M. Chem Rev 2004, 104, 2939; (c) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. Tetrahedron 2004, 60, 6239; (d) Majumdar, K. C.; Mukhopadhyay, P. P.; Biswas, A. Tetrahedron Lett 2005, 46, 6655; (e) Escolano, C.; Jones, K. Tetrahedron Lett 2000, 41, 8951; (f) Zhang, W.; Pugh, G. Tetrahedron 2003, 59, 4337; (g) Majumdar, K. C.; Kundu, U. K.; Ghosh, S. Tetrahedron 2002, 58, 10309; (h) Majumdar, K. C.; Alam, S.; Muhuri, S. Lett Org Chem 2006, 3, 250; (i) Kobayashi, Y.; Fujimoto, T.; Fukuyama, T. J Am Chem Soc 1999, 121, 6501.

[4] (a) Sundberg, R. J. Indoles; Academic Press: London, 1996; (b) Bonjoch, J.; Bosch, J. Alkaloids 1996, 48, 75; (c) Hibino, S.; Choshi, T. Nat Prod Rep 2002, 19, 148 and earlier reviews in the series; (d) Joule, J. A. Science of Synthesis (Houben-Weyl, Methods of Molecular Transformations); Georg Thieme Verlag: Stuttgart, 2000, 10, 361; (e) O'Connor, S. E.; Maresh, J. J. Nat Prod Rep 2006, 23, 532. (f) Lachia, M.; Moody, C. J. Nat Prod Rep 2008, 25, 227. (g) Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. Nat Prod Rep 2006, 23, 26. (h) Morris, J. C.; Nicholasb, G. M.; Phillips, A. J. Nat Prod Rep 2007, 24, 87.

[5] (a) Majumdar, K. C.; Alam, S. Org Lett 2006, 8, 4059; (b) Majumdar, K. C.; Kundu, U. K.; Ghosh, S. K. Org Lett 2002, 4, 2629; (c) Majumdar, K. C.; Bandyopadhyay, A.; Biswas, A. Tetrahedron 2003, 59, 5289.

[6] (a) Kresge, A. J.; Chiang, Y. J Chem Soc B 1967, 53; (b) Fife, T. H. J Am Chem Soc 1965, 87, 1084; (c) Okuyama, T.; Fueno, T. Bull Chem Soc Jpn 1970, 40, 3256.

[7] (a) Johonson, R. A.; Morton, D. R.; Kinner, J. H.; Gorman, R. R.; McGuire, J. C.; Sun, F. F.; Whittaker, N.; Bunting, S.; Salmon, J.; Moncada, S.; Vane, J. R. Prostaglandins 1976, 12, 915; (b) Corey, E. J.; Keck, G. E.; Szekely, I. J Am Chem Soc 1977, 99, 2006; (c) Chiang, Y.; Cho, M. J.; Euser, B. A.; Kresge, A. J. J Am Chem Soc 1986, 108, 1492; (d) Halvarsson, T.; Bergman, N.-A. J Chem Soc Chem Commun 1989, 1219; (e) Halvarsson, T.; Bergman, N.-A. J Org Chem 1991, 56, 251.

[8] Majumdar, K. C.; Sarkar, S.; Bhattacharrya, T. Tetrahedron 2003, 59, 4309.

[9] Majumdar, K. C.; Alam, S. J Chem Res 2006, 289.

[10] (a) Woodward, R. B.; Hoffman, R. The Conservation of Orbital Symmetry; Academic Press: New York, 1970; (b) Hunig, S.; Muller, H. R.; Their, W. Angew Chem Int Ed 1965, 4, 271; (c) Doering Von, F.; Rosenthal, J. W. J Am Chem Soc 1967, 89, 4535.