Regioselective Synthesis of 4-Aryloxymethylene-2,3,5-trihydrothiopyrano[3,2-*b*]indoles by the *thio*-Claisen Rearrangement of 3-(4'-Aryloxybut-2'-ynylthio)indoles

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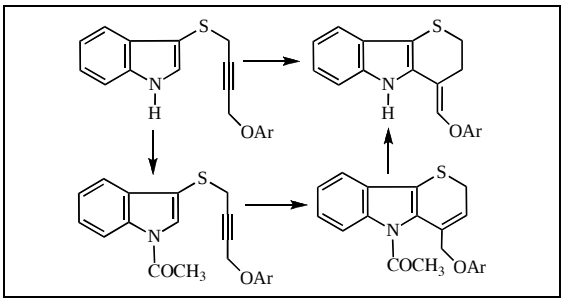

A number of new 4-aryloxymethylene-2,3,5-trihydrothiopyrano[3,2-*b*]indoles are regioselectively synthesized in 78-84% yield by the *thio*-Claisen rearrangement of 3-(4′-aryloxybut-2′-ynylthio)indoles. The endocyclic double bonded products are isolated by introducing electron withdrawing acetyl group at the indole nitrogen and also can be converted to the corresponding exocyclic isomers by deacetylation and subsequent heating.

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INTRODUCTION

Claisen rearrangement, since its discovery in 1912, has become a powerful method for carbon-carbon bond formation [1]. Much of its current popularity is due to the subsequent development of a series of new variants as well as its versatile application in the synthesis of various heterocycles using *oxy*- [2], *aza*- [3] and *thio*- [4,5] Claisen rearrangement. Synthesis of substituted indole derivatives has been a topic of great interest for many years because indole moiety is a key structural feature found in numerous natural products, many of which exhibit potent pharmacological activity [6]. Many indole derivatives are known to posses antitumor activity [7] such as indolocarbazole, staurosporine, K-252a, rebeccamycin *etc*., some tetrahydrothiopyrano[2,3-*b*]indole derivatives are known to have analgesic activity [8]. The tetrahydrothiopyrano[3,2-*b*]indole derivatives and their pharmaceutically acceptable salts are also useful as psychoanaleptic and nootropic drugs [9]. This prompted us to undertake a study on the *thio*-Claisen rearrangement of 3-(4'-aryloxybut-2'-ynylthio)indoles in order to achieve the synthesis of 4-aryloxymethylene-2,3,5-trihydrothiopyrano[3,2-*b*]indole derivatives. Herein we report the results of our study.

RESULTS AND DISCUSSION

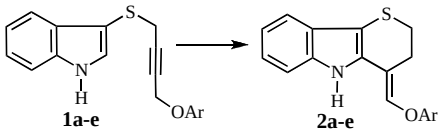
The required precursors 3-(4'-aryloxybut-2'-ynylthio)-indoles (**1a-e**) for our present study were synthesized in 90-95% yields by the reaction of S-[3-indolyl]isothiuronium iodide with an aquous solution of NaOH (10%) at 80-100°C for 10 minutes under nitrogen atmosphere followed by phase transfer catalyzed alkylation with different 1-aryloxy-4-chlorobut-2-ynes in the presence of catalytic amount of benzyltriethylammonium chloride (BTEAC) [10]. The S-[3-indolyl]isothiuronium iodide was in turn prepared by the reaction of indole with thiourea (1 equiv.) and one equivalent of iodine-potassium iodide reagent ($KI+I_2$) at 10°C with stirring for 1 h. The compounds **1a-e** were characterized from their spectral data and elemental analyses.

The substrate 3-(4'-aryloxybut-2'-ynylthio)indoles (**1a-e**) are unique in the sense that the molecules provide two different sites for [3,3] sigmatropic rearrangement, the but-2-ynylindole-3-yl sulfide moiety and arylprop-2-ynyl ether moiety. Our earlier observation in case of various systems [5] have shown that the [3,3] sigmatropic rearrangement is preferred at the propargyl vinyl thio-ether moiety over arylprop-2-ynyl ether moiety as the aromatic sextet would be disturbed in the transition state of the later. The present substrates **1a-e**, therefore, provide a scope for studying the competitive [3,3] sigmatropic rearrangement.

With this end in view the substrate 3-{4'-(2-methyl-phenyloxy)but-2'-ynylthio}indole (**1a**) was heated in chlorobenzene (132°C) under refluxing condition. TLC monitoring indicated the formation of a new product and the reaction was completed in 2 h. The product was isolated as viscous liquid in 80% yield. The IR spectrum of this product showed a peak at 3464 cm^{-1} due to N-H stretching. The ^1H NMR spectrum showed a three proton singlet at δ 2.34 due to ArCH_3, a two proton multiplet at δ

2.84-2.87 due to $-SCH_2CH_2$, another two proton multiplet at δ 3.09-3.11 due to $-SCH_2$, an one proton singlet at δ 6.39 due to vinylic proton =C*H*, of the exocyclic double bond, eight protons multiplet in the aromatic region at δ 7.04-7.48 and one proton broad singlet at δ 9.22 due to N-*H*. It was characterized from its spectral data and elemental analysis as 4-(2'-methylphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (**2a**) (**Scheme 1**).

Scheme 1



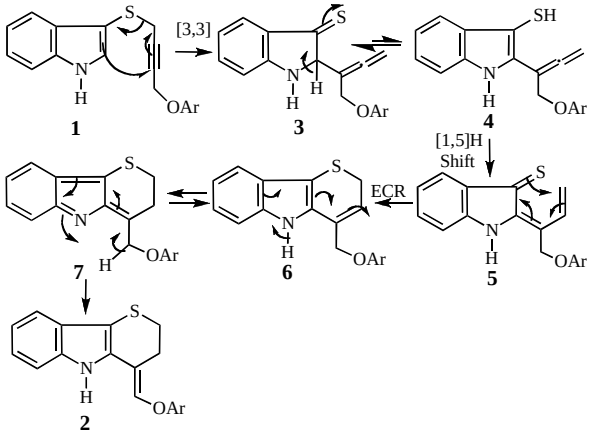
2	Ar	Yield (%)
a.	2-MeC_6H_4	80
b.	4-$MeOC_6H_4$	84
c.	4-MeC_6H_4	83
d.	2,4-$Me_2C_6H_3$	78
e.	2,3-$Me_2C_6H_3$	79

Regents and Conditions: Chlorobenzene, reflux, 2 h.

Encouraged by this result other substrates **1b-e** were also similarly treated to give the products **2b-e** in 78-84% yields (**Scheme 1**).

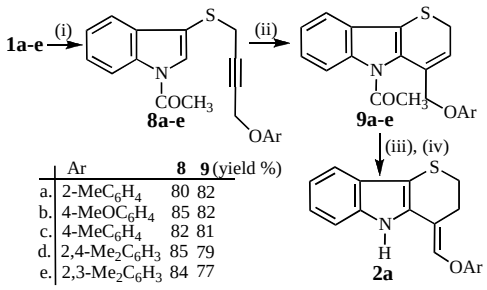
The formation of products **2** from **1** may be explained by an initial [3,3] sigmatropic rearrangement at but-2-ynylindol-3-yl sulfide moiety followed by rapid enolization to give the allenyl-ene-thiol intermediate (**4**), followed by [1,5] H shift and 6π-electrocyclic ring closure (ECR) to give endocyclic intermediate 4-aryloxymethyl-2,5-dihydrothiopyrano[3,2-*b*]indole (**6**, not isolated). These may then undergo thermal isomerisation to give products **2** (**Scheme 2**).

Scheme 2



We failed to isolate the intermediate **6** from the reaction mixture. We therefore, introduced an electron withdrawing acetyl group at the indole nitrogen of **1** in order to inhibit further thermal isomerisation of **6** during heating for the *thio*-Claisen rearrangement. The *N*-acetylation was carried out with acetyl chloride in presence of a catalytic amount of tetrabutyl ammonium hydrogen sluphate and powdered NaOH in dry dichloromethane to give 1-acetyl-3-(4'-aryloxybut-2'-ynylthio)indoles (**8a-e**, 80-85%) (**Scheme 3**).

Scheme 3



	Ar	8	9 (yield %)
a.	2-MeC_6H_4	80	82
b.	4-$MeOC_6H_4$	85	82
c.	4-MeC_6H_4	82	81
d.	2,4-$Me_2C_6H_3$	85	79
e.	2,3-$Me_2C_6H_3$	84	77

Regents and Conditions: (i) CH_3COCl, dry DCM, Bu_4NHSO_4, NaOH (powder), stirring, 1h, 0°C. (ii) Chlorobenzene, reflux, 2 h. (iii) CH_3ONa (1.5 equiv.), CH_3OH, -15°C, stirring, 1.5 h. (iv) Chlorobenzene, reflux, 1 h.

The compound 1-acetyl-3-{4'-(2-methylphenyloxy)but-2'-ynylthio}indole **8a** was refluxed in chlorobenzene. TLC indicated complete conversion in 2 h, but a structurally different product (*c.f.* **2a**) was obtained in 82% yield. The IR spectrum of the product clearly indicated the presence of carbonyl group at ν_{max} 1704 cm^{-1} and the ^1H NMR spectrum showed a three proton singlet at δ 2.07 due to $ArCH_3$, another three proton singlet at δ 2.64 due to $COCH_3$, a two proton doublet at δ 3.40 (J = 6.2 Hz) for $-SCH_2$, a two proton singlet at δ 4.87 due to $-OCH_2$ and an one proton triplet at δ 5.89 (J = 6.2 Hz) for =C*H*, confirmed the presence of endocyclic double bond, which was absent in the product **2a** and eight protons multiplet at δ 6.72-7.78 due to aromatic portons. This product was characterized by its spectral data and elemental analysis as 5-acetyl-4-(2'-methylphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (**9a**). To test the generality of the reaction, compounds **8b-e** were similarly treated to afford **9b-e** in 77-82% yields (**Scheme 3**). The compound **9a** in methanol was treated with sodium methoxide (1.5 equiv.) at -15°C with stirring for 1.5 h to effect deacetylation to give an unstable viscous liquid which was refluxed in chlorobenzene (132°C) for 1 h to afford a viscous liquid. This was found identical with product **2a** by comparison of its IR and NMR spectra as well as TLC behavior (**Scheme 3**). The exocyclic double bonded product **2a** was obtained from the endocyclic double bonded compound **9a**. Therefore it is shown that the *thio*-Claisen rearrangement of **1** passes through the initial formation of endocyclic double bonded intermediate **6** and then by thermal isomerization of **6** leading to the formation of exocyclic double bonded products **2**.

To conclude we have been successful in isolating the endocyclic double bonded intermediate by introducing electron withdrawing acetyl group at the indole nitrogen

and also succeeded to converting the endocyclic double bonded product to the exocyclic double bonded product by deacetylation and further heating. This also supports the described pathway for the formation of exocyclic double bonded product by the *thio*-Claisen rearrangement of the suitable sulfide *via* the endocyclic double bonded intermediate followed by thermal isomerisation. Methodology described here shows appreciable regioselectivity and synthetic utility for the synthesis of both exo- and endo-cyclic double bonded thiopyrano[3,2-*b*]-indole derivatives.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer (ν_{max} in cm^{-1}) using samples as neat liquids on KBr discs. ^1H NMR and ^{13}C NMR (300 MHz, 400 MHz, 500 MHz) spectra were recorded on a Bruker DPX-300, Varian-400 and Bruker DPX-500 spectrometer in $CDCl_3$ (chemical shift in δ) with TMS as internal standard. Mass spectra were recorded on a QTof-Micro and JEOL JMS600 instrument. 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°C to 80°C.

General procedure for the preparation of 3-(4′-aryloxy-but-2′-ynylthio)indoles (1a-e). S-[3-indolyl]isothiuron-ium iodide (0.96 g, 3 mmol) and 10% aq. NaOH solution (10 ml) were heated at 80-100°C for 10 minutes under nitrogen atmosphere and then 1-(2′-methyl)phenyloxy-4-chlorobut-2-yne (0.58 g, 3 mmol) in 10 ml CH_2Cl_2 was added to it followed by the addition of an aqueous solution of benzyltriethylammonium chloride (BTEAC, 0.25 g, 0.9 mmol). The reaction mixture was stirred at room temperature for 15 minutes. The CH_2Cl_2 layer was then washed with water (2x15 ml), brine (15 ml) and dried over Na_2SO_4. After evaporating CH_2Cl_2 at room temperature the crude mass was subjected to column chromatography over silicagel. Elution of the column with petroleum ether-ethyl acetate (15:1) on silica gel (60-120 mesh) afforded the compounds **1a** in 92% yield. Compounds **1b-e** were similarly obtained in 90-95% yields.

3-{4'-(2-Methylphenyloxy)but-2'-ynylthio}indole (1a). Yield: 92%, viscous liquid; ir (neat): 1466 (C-H bending), 2920 (C-H stretching), 3405 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.23 (s, 3H, ArC*H*$_3$), 3.40 (s, 2H, -SC*H*$_2$), 4.65 (s, 2H, -OC*H*$_2$), 6.78-7.22 (m, 6H, Ar*H*), 7.23 (s, 1H, =C*H*), 7.35-7.78 (m, 2H, Ar*H*), 8.06 (brs, 1H, N*H*); ms: m/z 307 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NOS$: C, 74.27; H, 5.54; N, 4.56. Found: C, 74.06; H, 5.68; N, 4.47.

3-{4'-(4-Methoxyphenyloxy)but-2'-ynylthio}indole (1b). Yield: 95%, viscous liquid; ir (neat): 1448 (C-H bending), 2915 (C-H stretching), 3398 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 3.50 (s, 2H, -SC*H*$_2$), 3.74 (s, 2H, -OC*H*$_3$), 4.64 (s, 2H, -OC*H*$_2$), 6.68-7.07 (m, 6H, Ar*H*), 7.16 (s, 1H, =C*H*), 7.23-7.54 (m, 2H, Ar*H*), 8.20 (brs, 1H, N*H*); ms: m/z 323 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NO_2S$: C, 70.59; H, 5.26; N, 4.33. Found: C, 70.66; H, 5.14; N, 4.24.

3-{4'-(4-Methylphenyloxy)but-2'-ynylthio}indole (1c). Yield: 94%, viscous liquid; ir (neat): 1450 (C-H bending), 2925 (C-H stretching), 3398 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.30 (s, 3H, ArC*H*$_3$), 3.41 (s, 2H, -SC*H*$_2$), 4.60 (s, 2H, -OC*H*$_2$), 6.78-7.21 (m, 6H, Ar*H*), 7.23 (s, 1H, =C*H*), 7.35-7.79 (m, 2H, Ar*H*), 8.11 (brs, 1H, N*H*); ms: m/z 307 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NOS$: C, 74.27; H, 5.54; N, 4.56. Found: C, 74.41; H, 5.63; N, 4.64.

3-{4'-(2,4-Dimethylphenyloxy)but-2'-ynylthio}indole (1d). Yield: 92%, viscous liquid; ir (neat): 1508 (C-H bending), 2911 (C-H stretching), 3405 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.23 (s, 3H, ArC*H*$_3$), 2.28 (s, 3H, ArC*H*$_3$), 3.41 (s, 2H, -SC*H*$_2$), 4.62 (s, 2H, -OC*H*$_2$), 6.69-7.22 (m, 5H, Ar*H*), 7.24 (s, 1H, =C*H*), 7.35-7.80 (m, 2H, Ar*H*), 8.09 (brs, 1H, N*H*); ms: m/z 321 (M^+). *Anal*. Calcd. for $C_{20}H_{19}NOS$: C, 74.77; H, 5.92; N, 4.36. Found: C, 74.60; H, 5.81; N, 4.48.

3-{4'-(2,3-Dimethylphenyloxy)but-2'-ynylthio}indole (1e). Yield: 90%, viscous liquid; ir (neat): 1460 (C-H bending), 2918 (C-H stretching), 3393 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.14 (s, 3H, ArC*H*$_3$), 2.28 (s, 3H, ArC*H*$_3$), 3.41 (s, 2H, -SC*H*$_2$), 4.63 (s, 2H, -OC*H*$_2$), 6.68-7.22 (m, 5H, Ar*H*), 7.24 (s, 1H, =C*H*), 7.35-7.80 (m, 2H, Ar*H*), 8.11 (brs, 1H, N*H*); ms: m/z 321 (M^+). *Anal*. Calcd. for $C_{20}H_{19}NOS$: C, 74.77; H, 5.92; N, 4.36. Found: C, 74.89; H, 5.92; N, 4.28.

General procedure for the preparation of compounds 2a-e. Compound **1a** (0.61 g, 2 mmol) was refluxed in chlorobenzene (8 ml) for 2 h. The reaction mixture was then subjected to column chromatography over silica gel (60-120 mesh) with petroleum ether followed by petroleum ether-ethyl acetate (10:1) to give compound **2a** as a viscous liquid in 80% yield. Compounds **2b-e** were similarly synthesized from compounds **1b-e** in 78-84% yields.

4-(2'-Methylphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (2a). Yield: 80%, viscous liquid; ir (neat): 1490 (C-H bending), 2921 (C-H stretching), 3464 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, ArC*H*$_3$), 2.84-2.87 (m, 2H, -SCH$_2$C*H*$_2$), 3.09-3.11 (m, 2H, -SC*H*$_2$), 6.39 (s, 1H, =C*H*), 7.04-7.48 (m, 8H, Ar*H*), 9.22 (brs, 1H, N*H*); ^{13}C nmr (125 MHz, $CDCl_3$): δ 16.83, 28.29, 29.58, 105.56, 109.84, 111.28, 116.95, 119.11, 119.96, 123.59, 124.44, 126.23, 127.79, 127.84, 128.21, 131.87, 136.14, 137.89, 155.84; ms: m/z 307 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NOS$: C, 74.27; H, 5.54; N, 4.56. Found: C, 74.05; H, 5.48; N, 4.39.

4-(4'-Methoxyphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (2b). Yield: 84%, viscous liquid; ir (neat): 1491 (C-H bending), 2923, 3056 (C-H stretching), 3402 (N-H) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.82-2.85 (m, 2H, -SCH$_2$C*H*$_2$), 3.07-3.11 (m, 2H, -SC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 6.34 (s, 1H, =C*H*), 6.88-7.49 (m, 8H, Ar*H*), 9.23 (brs, 1H, N*H*); ms: m/z 323 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NO_2S$: C, 70.59; H, 5.26; N, 4.33. Found: C, 70.48; H, 5.18; N, 4.42.

4-(4'-Methylphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (2c). Yield: 83%, viscous liquid; ir (neat): 1455 (C-H bending), 2922, 3055 (C-H stretching), 3462 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.41 (s, 3H, ArC*H*$_3$), 2.85-2.88 (m, 2H, -SCH$_2$C*H*$_2$), 3.10-3.12 (m, 2H, -SC*H*$_2$), 6.40 (s, 1H, =C*H*), 7.05-7.49 (m, 8H, Ar*H*), 9.27 (brs, 1H, N*H*); ms: m/z 307 (M^+). *Anal*. Calcd. for $C_{19}H_{17}NOS$: C, 74.27; H, 5.54; N, 4.56. Found: C, 74.08; H, 5.69; N, 4.61.

4-(2',4'-Dimethylphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (2d). Yield: 78%, viscous liquid; ir (neat): 1466 (C-H bending), 2935 (C-H stretching), 3388 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.29 (s, 3H, ArC*H*$_3$), 2.33 (s, 3H, ArC*H*$_3$), 2.84-2.87 (m, 2H, -SCH$_2$C*H*$_2$), 3.09-3.11 (m, 2H, -SC*H*$_2$), 6.35 (s, 1H, =C*H*), 6.93-7.47 (m, 7H, Ar*H*), 9.28 (brs, 1H, N*H*); ms: m/z 321 (M^+). *Anal*. Calcd. for $C_{20}H_{19}NOS$: C, 74.77; H, 5.92; N, 4.36. Found: C, 74.87; H, 6.11; N, 4.43.

4-(2',3'-Dimethylphenyloxymethylene)-2,3,5-trihydrothiopyrano[3,2-*b*]indole (2e). Yield: 79%, viscous liquid; ir (neat): 1468 (C-H bending), 2921, 3056 (C-H stretching), 3405 (N-H) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.31 (s, 3H, ArC*H*$_3$), 2.33 (s, 3H, ArC*H*$_3$), 2.84-2.87 (m, 2H, -SCH$_2$C*H*$_2$), 3.09-3.12 (m, 2H, -SC*H*$_2$), 6.35 (s, 1H, =C*H*), 6.95-7.49 (m, 7H, Ar*H*), 9.28 (brs, 1H, N*H*); ms: m/z 321 (M^+). *Anal.* Calcd. for $C_{20}H_{19}NOS$: C, 74.77; H, 5.92; N, 4.36. Found: C, 74.57; H, 5.85; N, 4.30.

General procedure for the preparation of Compounds 8a-e. Bu_4NHSO_4 (10 mg, 0.01 eqiv.) and NaOH (0.2 g, powder) were added to the dichloromethane solution (10 ml) of **1a** (0.61 g, 2 mmol) at 0°C, then a solution of acetyl chloride (0.24 g, 1.5 eqiv.) in dry dichloromethane (5 ml) was added to it drop wise and stirred for 1 h. The reaction mixture was washed with cold saturated Na_2CO_3 solution (2x15 ml), water (2x15 ml), brine (15 ml) and dried (Na_2SO_4) and then evaporated. Finally the crude reaction mixture was purified by column chromatography. Elution of the column with petroleum ether-ethyl acetate (9:1) on silica gel (60-120 mesh) afforded compound **8a**. Compounds **8b-e** were obtained by the same procedure from compounds **1b-e** in 80-85% yields.

1-Acetyl-3-{4'-(2-methylphenyloxy)but-2'-ynylthio}indole (8a). Yield: 80%, viscous liquid; ir (neat): 1370, 1440 (C-H bending), 1712 (C=O), 2925 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, ArC*H*$_3$), 2.49 (s, 3H, -COC*H*$_3$), 3.54 (s, 2H, -SC*H*$_2$), 4.64 (s, 2H, -OC*H*$_2$), 6.79-7.37 (m, 6H, Ar*H*), 7.53 (s, 1H, =C*H*), 7.67-8.42 (m, 2H, Ar*H*); ms: m/z 349 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_2S$: C, 72.21; H, 5.44; N, 4.01. Found: C, 72.44; H, 5.53; N, 3.89.

1-Acetyl-3-{4'-(4-methoxyphenyloxy)but-2'-ynylthio}indole (8b). Yield: 85%, viscous liquid; ir (neat): 1375, 1446 (C-H bending), 1713 (C=O), 2920 (C-H stretching) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.54 (s, 3H, -COC*H*$_3$), 3.53 (s, 2H, -SC*H*$_2$), 3.57 (s, 3H, -OC*H*$_3$), 4.56 (s, 2H, -OC*H*$_2$), 6.74-7.31 (m, 6H, Ar*H*), 7.58 (s, 1H, =C*H*), 7.68-8.43 (m, 2H, Ar*H*); ms: m/z 365 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_3S$: C, 69.04; H, 5.20; N, 3.84. Found: C, 69.22; H, 5.12; N, 3.93.

1-Acetyl-3-{4'-(4-methylphenyloxy)but-2'-ynylthio}indole (8c). Yield: 82%, viscous liquid; ir (neat): 1375, 1450 (C-H bending), 1708 (C=O), 2922 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.26 (s, 3H, ArC*H*$_3$), 2.50 (s, 3H, -COC*H*$_3$), 3.52 (s, 2H, -SC*H*$_2$), 4.59 (s, 2H, -OC*H*$_2$), 6.75-7.41 (m, 6H, Ar*H*), 7.54 (s, 1H, =C*H*), 7.66-8.44 (m, 2H, Ar*H*); ms: m/z 349 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_2S$: C, 72.21; H, 5.44; N, 4.01. Found: C, 72.25; H, 5.54; N, 4.12.

1-Acetyl-3-{4'-(2,4-dimethylphenyloxy)but-2'-ynylthio}indole (8d). Yield: 85%, viscous liquid; ir (neat): 1375, 1448 (C-H bending), 1712 (C=O), 2922 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.15 (s, 3H, ArC*H*$_3$), 2.23 (s, 3H, ArC*H*$_3$), 2.48 (s, 3H, -COC*H*$_3$), 3.53 (s, 2H, -SC*H*$_2$), 4.60 (s, 2H, -OC*H*$_2$), 6.68-7.41 (m, 5H, Ar*H*), 7.53 (s, 1H, =C*H*), 7.67-8.44 (m, 2H, Ar*H*); ms: m/z 363 (M^+). *Anal.* Calcd. for $C_{22}H_{21}NO_2S$: C, 72.73; H, 5.78; N, 3.86. Found: C, 72.54; H, 5.71; N, 3.92.

1-Acetyl-3-{4'-(2,3-dimethylphenyloxy)but-2'-ynylthio}indole (8e). Yield: 84%, viscous liquid; ir (neat): 1374, 1446 (C-H bending), 1713 (C=O), 2919 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.10 (s, 3H, ArC*H*$_3$), 2.24 (s, 3H, ArC*H*$_3$), 2.48 (s, 3H, -COC*H*$_3$), 3.53 (s, 2H, -SC*H*$_2$), 4.62 (s, 2H, -OC*H*$_2$), 6.68-7.41 (m, 5H, Ar*H*), 7.53 (s, 1H, =C*H*), 7.67-8.44 (m, 2H, Ar*H*); ms: m/z 363 (M^+). *Anal.* Calcd. for $C_{22}H_{21}NO_2S$: C, 72.73; H, 5.78; N, 3.86. Found: C, 72.85; H, 5.88; N, 3.81.

General procedure for the synthesis of Compounds 9a-e. Compound **8a** (0.52 g, 1.5 mmol) was refluxed in chlorobenzene (10 ml) for 2 h. Then the reaction mixture was subjected to column chromatography over silica gel (60-120 mesh). Elution of the column with petroleum ether followed by petroleum ether-ethylacetate (9:1) gave compound **9a** as viscous liquid in 82% yield. Compounds **9b-e** were similarly synthesized from **8b-e** in 77-82% yields.

5-Acetyl-4-(2'-methylphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (9a). Yield: 82%, viscous liquid; ir (neat): 1455 (C-H bending), 1704 (C=O), 2919, 3050 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.07 (s, 3H, ArC*H*$_3$), 2.64 (s, 3H, -COC*H*$_3$), 3.40 (d, 2H, J = 6.2 Hz, -SC*H*$_2$), 4.87 (s, 2H, -OC*H*$_2$), 5.89 (t, 1H, J = 6.2 Hz, =C*H*), 6.72-7.78 (m, 8H, Ar*H*); ms: m/z 349 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_2S$: C, 72.21; H, 5.44; N, 4.01. Found: C, 72.12; H, 5.57; N, 4.08.

5-Acetyl-4-(4'-methoxyphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (9b). Yield: 82%, viscous liquid; ir (neat): 1448 (C-H bending), 1703 (C=O), 2922, 3028 (C-H stretching) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$): δ 2.60 (s, 3H, -COC*H*$_3$), 3.31 (d, 2H, J = 6 Hz, -SC*H*$_2$), 3.65 (s, 3H, -OC*H*$_3$), 4.73 (s, 2H, -OC*H*$_2$), 5.78 (t, 1H, J = 6 Hz, =C*H*), 6.67-7.70 (m, 8H, Ar*H*); ms: m/z 365 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_3S$: C, 69.04; H, 5.20; N, 3.84. Found: C, 69.18; H, 5.34; N, 3.75.

5-Acetyl-4-(4'-methylphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (9c). Yield: 81%, viscous liquid; ir (neat): 1446 (C-H bending), 1704 (C=O), 2921, 3028 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.30 (s, 3H, ArC*H*$_3$), 2.66 (s, 3H, -COC*H*$_3$), 3.38 (d, 2H, J = 6 Hz, -SC*H*$_2$), 4.81 (s, 2H, -OC*H*$_2$), 5.85 (t, 1H, J = 6 Hz, =C*H*), 6.68-7.76 (m, 8H, Ar*H*); ms: m/z 349 (M^+). *Anal.* Calcd. for $C_{21}H_{19}NO_2S$: C, 72.21; H, 5.44; N, 4.01. Found: C, 72.35; H, 5.43; N, 3.92.

5-Acetyl-4-(2',4'-dimethylphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (9d). Yield: 79%, viscous liquid; ir (neat): 1456 (C-H bending), 1695 (C=O), 2916, 3020 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 2.01 (s, 3H, ArC*H*$_3$), 2.21 (s, 3H, ArC*H*$_3$), 2.64 (s, 3H, -COC*H*$_3$), 3.39 (d, 2H, J = 6.2 Hz, -SC*H*$_2$), 4.82 (s, 2H, -OC*H*$_2$), 5.88 (t, 1H, J = 6.2 Hz, =C*H*), 6.68-7.78 (m, 7H, Ar*H*); ms: m/z 363 (M^+). *Anal.* Calcd. for $C_{22}H_{21}NO_2S$: C, 72.73; H, 5.78; N, 3.86. Found: C, 72.56; H, 5.95; N, 3.90.

5-Acetyl-4-(2',3'-dimethylphenyloxymethyl)-2,5-dihydrothiopyrano[3,2-*b*]indole (9e). Yield: 77%, viscous liquid; ir (neat): 1455 (C-H bending), 1701 (C=O), 2918 (C-H stretching) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ_H 1.97 (s, 3H, ArC*H*$_3$), 2.19 (s, 3H, ArC*H*$_3$), 2.64 (s, 3H, -COC*H*$_3$), 3.40 (d, 2H, J = 6.2 Hz, -SC*H*$_2$), 4.83 (s, 2H, -OC*H*$_2$), 5.89 (t, 1H, J = 6.2 Hz, =C*H*), 6.72-7.77 (m, 7H, Ar*H*); ms: m/z 363 (M^+). *Anal.* Calcd. for $C_{22}H_{21}NO_2S$: C, 72.73; H, 5.78; N, 3.86. Found: C, 72.78; H, 5.90; N, 3.92.

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REFERENCES

[1] (a) Claisen, L. *Ber. Btsch. Chem. Ges* **1912**, *45*, 3157. (b) Castro, A. M. M. *Chem. Rev.* **2004**, *104*, 2939.

[2] (a) Majumdar, K. C.; De, R. N.; Khan, A. T.; Chattopadhyay, S. K. ; Dey, K.; Patra, A. *J. Chem. Soc., Chem. Commum.* **1988**, 777. (b) Subramanian, R. S.; Balasubramanian, K. K. *Tetrahedron Lett.* **1989**, *30*, 2297. (c) Majumdar, K. C.; Das, U. *J. Org. Chem.* **1998**, *63*, 9997. (d) Otter, B. A.; Suluja, S. S.; Fox, J. J. *J. Org. Chem.* **1972**, *37*, 2858. (e) Chattopadhyay, S. K.; Ghosh, D.; Biswas, T. *Synlett,* **2006**, 3358.

[3] (a) Kurth, J.; Decker, O. H. W. *J. Org. Chem.* **1985**, *50*, 5769. (b) Majumdar, K. C.; Bhattacharrya, T. *Synthesis* **2001**, 1568. (c) Majumdar, K. C.; Bhattacharrya, T. *Tetrahedron Lett.* **2001**, *42*, 4231. (d) Majumdar, K. C.; Ghosh, S. *Tetrahedron* **2001**, *57*, 1589.

[4] (a) Kwart, H.; Hackett, C. M. *J. Am. Chem. Soc.* **1962**, *84*, 1754. (b) Kwart, H.; George, T. J. *Chem. Commun.* **1970**, 433. (c) Kwart, H.; Schwartz, J. L. *J. Org. Chem.* **1974**, *39,* 1575. (d) Mohan, C.; Singh, P.; Mahajan, M. P. *Tetrahedron* **2005**, *61*, 10774.

[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. (d) Majumdar, K. C.; Jana, G. H. *Synthesis* **2001**, 924.

[6] (a) Lounasmaa, M.; Tolvanen, N. *Nat. Prod. Rep.* **2000**, *17*, 175. (b) Hibino, S.; Choshi, T. *Nat. Prod. Rep.* **2002**, *19*, 148. (c) Wacker, D. A.; Kasireddy, P. *Tetratedron lett.* **2002**, *43*, 5189. (d) Smart, B. P.; Oslund, R. C.; Walse, L. A.; Gelb, M. H. *J. Med. Chem.* **2006**, *49*, 2858. (e) Hino, T.; Nakagawa, M. *Alkaloids* **1998**, *34*, 1. (f) Sundberg, R. J. *Indoles*; Academic Press: London, 1996. (g) Yamanaka, E.; One, M.; Kasamatsu, S.; Aimi, N.; Sakai, S. *Chem. Pharm. Bull.* **1984**, *32*, 818. (h) Sakai, S.; Aimi, N.; Yamaguchi, K.; Hitotsuyonagi, Y.; Watanabe, C.; Yokose, K.; Koyama, Y.; Shudo, K.; Itai, A. *Chem. Pharm. Bull,* **1984**, ***32***, 354.

[7] (a) Haider, N.; Sotero, E. *Chem. Pharm. Bull.* **2002**, *50*, 1479 (b) Guillonneare, C.; Pierre, A.; Charton, Y.; Guilbaud, N.; Kraus-Berthier, I.; Leonce, S.; Michel, A.; Bisagni, I.; Atassi, G. *J. Med. Chem.* **1999**, *42*, 2191.

[8] (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.

[9] Makisumi, Y.; Satatani, T. United States Patent No. 4910318, March 20, 1990.

[10] (a) Harris, R. L. N. *Tetrahedron Lett.* **1969**, 4465. (b) Majumdar, K. C.; Alam, S.; Muhuri, S. *Lett. Org. Chem.* **2006**, *3*, 250.