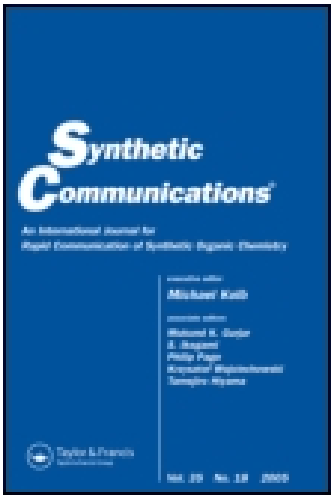

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Aluminium Chloride-Catalyzed Claisen Rearrangement: Synthesis of Polyheterocycles Containing Oxygen, Nitrogen, and Sulfur

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Aluminium Chloride–Catalyzed Claisen Rearrangement: Synthesis of Polyheterocycles Containing Oxygen, Nitrogen, and Sulfur

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Abstract: Synthesis of 1,8-naphthyridine-annulated polyheterocycles containing oxygen, nitrogen, and sulfur has been achieved by thionation and sequential Claisen rearrangement of 4-(4′-aryloxybut-2′-ynyloxy)-1-phenyl[1,8]-naphthyridin-2-ones first by heating in 1,2-dichlorobenzene for 1–2 h and then by anhydrous $AlCl_3$-catalyzed Claisen rearrangement in dichloromethane for 1 h.

Keywords: aluminium chloride, 1-aryloxy-4-chlorobut-2-yne, 1,8-naphthyridin-2-one, sequential Claisen rearrangement, *thio*-Claisen rearrangement

INTRODUCTION

Among the six isomeric naphthyridines, [1,8]naphthyridine derivatives have attracted considerable attention because of the exceptionally broad spectrum of their biological activities.[1] 4-Hydroxy-1-phenyl-1,8-naphthyridinone and its derivatives have been used as antiallergic agent,[2] anti-inflammatory,[3] and cytoprotective agents.[4] Thieno[2,3-*b*][1,8]naphthyridinones exhibiting antimicrobial and antitumor actions were synthesized from 2-mercapto derivatives of naphthyridinones.[5]

We have recently reported the synthesis of thieno-,[6] pyrano-,[7] and thiopyrano[8]-[1,8]naphthyridinone derivatives fused at the 3,4 position of the naphthyridine skeleton. Normally Claisen rearrangement of

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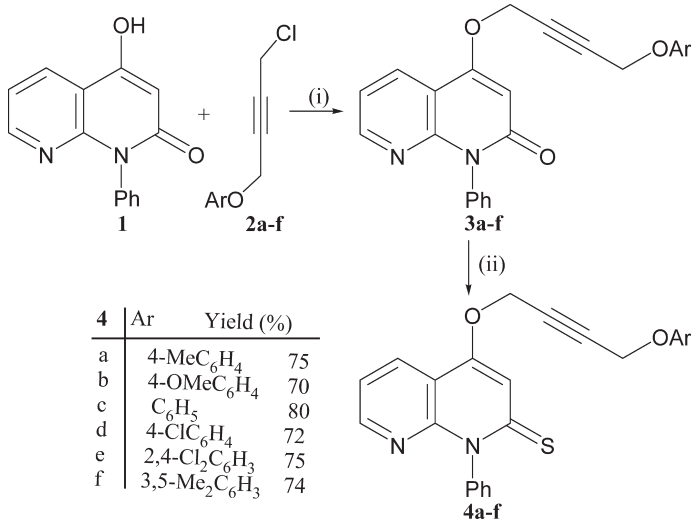
4-(4′-aryloxybut-2′-ynyloxy)-1-phenyl-[1,8]naphthyridinone is known to provide angularly fused pyrano-heterocycle.[7] The thionation of the amide carbonyl group of the naphthyridinone moiety is expected to change the mode of cyclization for the formation of new linearly fused heterocycle because sulfur has a much larger nucleophilic head compared to the oxygen.[9] Compounds containing five-membered heterocycles with a linearly fused 1,8-naphthyridine fragment and their antibacterial activity have been studied extensively.[10] However, there is no such report of thiopyrano fused linear heterocycle of 1,8-naphthyridine skeleton in the literature. Our continued interest in the synthesis of a hitherto unreported heterocyclic ring system by the application of [3,3] sigmatropic rearrangement led us to undertake a study of the sequential [3,3] sigmatropic rearrangement of 4-(4′-aryloxybut-2′-ynyloxy)-1-phenyl-1,8-naphthyridin-2-thione. Here, we report the results of our investigation.

RESULTS AND DISCUSSION

The required precursors, 4-(4′-aryloxybut-2′-ynyloxy)-1-phenyl-1,8-naphthyridin-2-thiones (**4a**–**f**), were synthesized in 72–80% yields from 4-hydroxy-1-phenyl-1,8-naphthyridin-2-one (**1**) and different 1-aryloxy-4-chlorobut-2-ynes (**2a**–**f**) by refluxing in dry acetone in the presence of anhydrous K_2CO_3 for 22–24 h followed by thionation with P_2S_5 in refluxing dry benzene for 1 h (Scheme 1). Disappearance of the carbonyl



4	Ar	Yield (%)
a	4-MeC_6H_4	75
b	4-$OMeC_6H_4$	70
c	C_6H_5	80
d	4-ClC_6H_4	72
e	2,4-$Cl_2C_6H_3$	75
f	3,5-$Me_2C_6H_3$	74

Scheme 1. Reagents and reaction conditions: (i) K_2CO_3, dry acetone, reflux, 22–24 h, (ii) P_2S_5, dry benzene, reflux, 1 h.

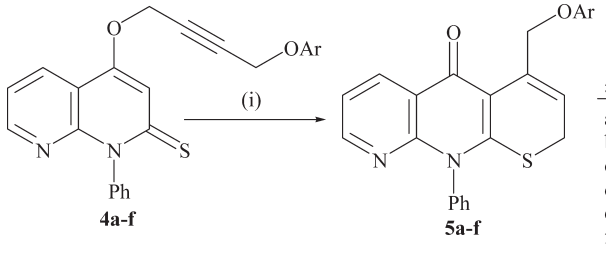
stretching in the compounds **4a–f** clearly indicates the transformation of -C═O to -C═S.

Compounds **4** contain the 4-(but-2-ynyloxy)-1-phenyl-1,8-naphthyridin-2-thione moiety as well as the arylprop-2-ynyl ether moiety and thus offer scope for two different [3,3] sigmatropic rearrangements. However, the Claisen rearrangement in the former moiety may be expected to require lower activation energy than the corresponding rearrangement of the arylprop-2-ynyl ether moiety as the aromatic sextet would be disturbed in the transition state of the latter.

The substrate **4a** was refluxed in *o*-dichlorobenzene, and the reaction was monitored by thin-layer chromatography (TLC). Complete conversion was achieved in 45 min, giving a yellow solid in 80% yield. Reappearance of the carbonyl stretching in the region 1715 cm^{-1} clearly indicates the presence of a carbonyl group. The ^1H NMR (500 MHz) showed signals at δ 2.27 (s, 3H, -C**H**$_3$), δ 3.29–3.30 (dt, $J = 1.1$ Hz, 6 Hz, 2H), δ 5.30–5.31(d, $J = 1.5$ Hz, 2H), and one proton triple triplet at δ 6.03–6.06 ($J = 1.7$ Hz, 6 Hz), indicating the formation of a six-membered thiopyran ring fused at the 2,3 position of the 1,8-naphthyridine nucleus. The product was characterized from its elemental analysis and spectroscopic data as **5a**. Compounds **4b–f** on similar treatment furnished products **5b–f** in 75–80% yield (Scheme 2).

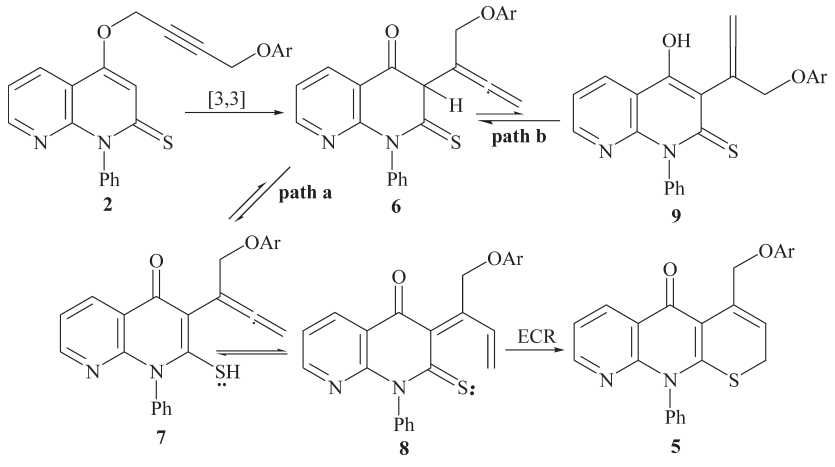
The formation of products **5** from the substrates **4** may be explained by considering an initial [3,3] sigmatropic rearrangement in substrates **4** to give allenyl-one-thione intermediates **6**, which can undergo enolization in two ways, either through path a or path b. Here, path a would be favored as the C═S bond is much more susceptible to enolization than the C═O bond. The rapid enolization of **6** may give the allenyl-ene-thiol intermediates **7**, followed by [1,5] hydrogen shift and 6π-electrocyclic ring closure (ECR), to afford products **5** (Scheme 3).

A close examination of the products **5** reveals that these products still contain an allyl aryl ether moiety well situated for the occurrence of a second Claisen rearrangement. However, this would require much higher temperature than the first Claisen rearrangement of compounds **4** because



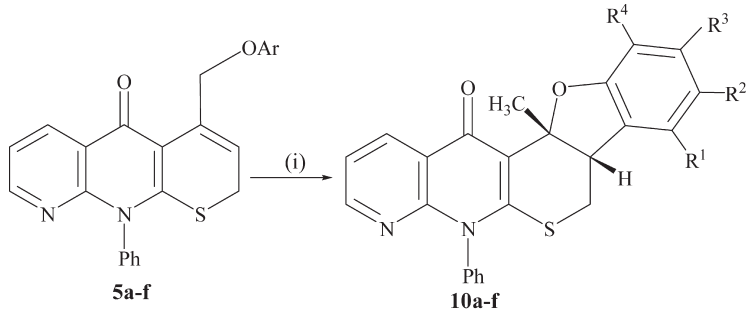
5	Ar	Yield (%)
a	4-MeC_6H_4	78
b	4-$OMeC_6H_4$	74
c	C_6H_5	72
d	4-ClC_6H_4	76
e	2,4-$Cl_2C_6H_3$	75
f	3,5-$Me_2C_6H_3$	70

Scheme 2. Reagents and reaction conditions: *o*dichlorobenzene, reflux, 1–2 h.



Scheme 3.

during this rearrangement the aromaticity of the aryl part will be disturbed. Compound **5a** was refluxed in *N,N*-diethyl aniline (216°C), but the substrate showed a tendency to decompose. Therefore, compound **5a** was subjected to Lewis acid–catalyzed Claisen rearrangement in the presence of anhydrous $AlCl_3$[11] in dry dichloromethane at room temperature for 1 h, and a white solid product **12a** was obtained in 80% yield (Scheme 4). Its ^{1}H NMR showed signals at δ 1.92 (s, 3H, -CH_3 at ring juncture), 2.31



10	R^1	R^2	R^3	R^4	Yield(%)
a	H	CH_3	H	H	80
b	H	OCH_3	H	H	70
c	H	H	H	H	72
d	H	Cl	H	H	75
e	Cl	H	Cl	H	78
f	H	CH_3	H	CH_3	71

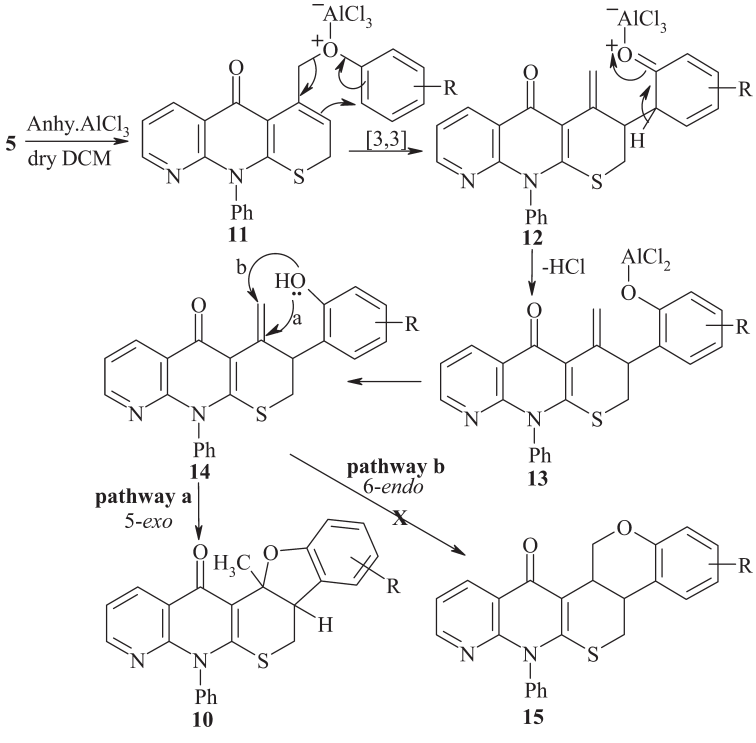
Scheme 4. Reagents adn reaction conditions: anhydrous $AlCl_3$, dry DCM, stirring, rt, 1–2 h.

(s, 3H, -CH_3), 2.72–2.77 (dd, $J = 11.8$ Hz, 13.1 Hz, 1H), 2.83–2.87 (dd, $J = 4$ Hz, 13.1 Hz, 1H), 3.28–3.32 (dd, $J = 4$ Hz, 11.6 Hz, 1H), indicating the formation of a furothiopyrano ring system. The product **12a** was characterized from its elemental analysis and spectroscopic data. Encouraged by this success, compounds **5b–f** were similarly treated, and the corresponding products **12b–f** were obtained in 70–80% yields.

The stereochemistry of the furothiopyran ring juncture of the product **10** can only be surmised from the molecular model (Dreiding model) of the molecule, which shows a strain-free cis arrangement (Scheme 4).

The formation of products **10** from **5** can be explained by the steps involving an initial charge-accelerated [3,3] sigmatropic rearrangement of **5** to **12** via an ether–$AlCl_3$ complex **11** that may pass through a charge delocalized transition state to give an intermediate, followed by rapid tautomerization and proton exchange to give the intermediate **14**, which may then undergo 5-*exo* cyclization, leading to the products **10** (Scheme 5).

In conclusion, we have executed the sequential Claisen rearrangement, a *thio*-Claisen, and a charge accelerated *oxy*-Claisen rearrangement. This methodology displays appreciable regioselectivity and represents a novel approach for



Scheme 5. Mechanism of anhyd. $AlCl_3$–catalyzed Claisen rearrangement.

the construction of a linearly fused pentacyclic heterocyclic ring system having a 1,8-naphthyridine skeleton, which may have potent biological activity.

EXPERIMENTAL

Melting points were determined in an open capillary and are uncorrected. 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). ^1H NMR (400 MHz, 500 MHz) and ^{13}C NMR (75.5 MHz) spectra were recorded on Bruker DPX-300, Varian-400 FT-NMR, and Bruker DPX-500 spectrometers in $CDCl_3$ (chemical shifts in δ) with TMS as internal standard. Mass spectra were recorded on a QTOF micromass instrument. ^1H NMR and ^{13}C NMR spectra were recorded at the Indian Institute of Chemical Biology, Kolkata, and Bose Institute, Kolkata. Silica gel [(60–120 mesh), Spectrochem, India] was used for chromatographic separation. Silica gel G [E-Merck (India)] was used for thin-layer chromatography (TLC). Petroleum ether refers to the fraction boiling between 60 and 80°C.

The 1-aryloxy-4-chlorobut-2-ynes **2(a–f)** were prepared according to the published procedure.[12]

General Procedure for the Preparation of Compounds 3a–f

A mixture of 1-aryloxy-4-chlorobut-2-ynes (**2a–f**) (10 mmol), 1-phenyl-4-hydroxy-1,8-naphthyridin-2(1*H*)-one (**1**) (2.38 g, 10 mmol), and anhydrous K_2CO_3 (3 g) was refluxed in dry acetone for 22–24 h. The reaction mixture was cooled and removal of the solvent from the filtrate gave a solid mass. This was subjected to column chromatography over silica gel. Elution of the column with petroleum ether–ethyl acetate (2:1) furnished compounds **3a–f**.

Compounds **3a–d** have been reported earlier.[7]

Data

Compound **3e**

Yield 55%; solid; mp 134–136°C; IR (KBr) ν_{max}: 2922, 1667, 1585; UV (EtOH), $\lambda_{max} = 317$, 293, 220 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.85$ (s, 2H, -OCH_2), 4.92 (s, 2H, -OCH_2), 6.22 (s, 1H, =CH), 6.99–7.01 (d, 1H, $J = 8.7$ Hz, ArH), 7.15–7.17 (dd, 1H, $J = 4.7$ Hz, 7.7 Hz, ArH), 7.20–7.22 (dd, 1H, $J = 2$ Hz, 8.6 Hz, ArH), 7.26–7.29 (m, 2H, ArH), 7.39 (s, 1H, ArH), 7.48–7.51 (t, 1H, $J = 7.3$ Hz, ArH), 7.56–7.59 (t, 2H, $J = 7.5$ Hz, ArH), 8.23–8.25 (d, 1H, $J = 7.7$ Hz, ArH), 8.47–8.48 (d, 1H, $J = 4.4$ Hz,

ArH); MS: $m/z = 451$, 453, 455 (M^+). Anal. calcd. for $C_{24}H_{16}N_2O_3Cl_2$: C, 63.87; H, 3.57; N, 6.21. Found: C, 63.88; H, 3.65; N, 6.31.

Compound **3f**

Yield 52%; solid; mp 144–146°C; IR (KBr) ν_{max}: 2913, 1643, 1611, 1593 cm^{-1}; UV (EtOH), $\lambda_{max} = 376$, 276, 218, 205 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 2.28$ (s, 6H, -CH_3), 4.73 (s, 2H, -OCH_2), 4.92 (s, 2H, -OCH_2), 6.22 (s, 1H, =CH), 6.58 (s, 1H, ArH), 6.64 (s, 1H, ArH), 7.13–7.15 (dd, 1H, $J = 4.7$ Hz, 7.8 Hz, ArH), 7.25–7.28 (m, 3H, ArH), 7.43–7.50 (t, 1H, $J = 7.4$ Hz, ArH), 7.55–7.58 (t, 2H, $J = 7.4$ Hz, ArH), 8.24–8.26 (dd, 1H, $J = 1.7$ Hz, 7.8 Hz, ArH), 8.45–8.47 (dd, 1H, $J = 1.7$ Hz, 4.6 Hz, ArH); MS: $m/z = 410$ (M^+). Anal. calcd. for $C_{26}H_{22}N_2O_3$: C, 76.08; H, 5.40; N, 6.82. Found: C, 76.22; H, 5.29; N, 6.94.

General Procedure for the Synthesis of Compounds 4a–f

A mixture of compounds **3a–f** (2 mmol) and P_2S_5 (3 mmol) was refluxed in anhydrous benzene (50 ml) on a water bath for 1 h. The reaction mixture was cooled, solid residue was extracted with benzene (3 × 25 ml), and the combined benzene layer was washed with water and dried (Na_2SO_4). Removal of solvent gave a gummy mass, which was chromatographed over silica gel. Compounds **4** were obtained when the column was eluted with 1:4 ethyl acetate–petroleum ether.

Data

Compound **4a**

Yield 75%; solid; mp 160–162°C; IR (KBr) ν_{max}: cm^{-1}; UV (EtOH), $\lambda_{max} = 377$, 277, 221, 201 nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta_H = 2.24$ (s, 3H, -CH_3), 4.78 (s, 2H, -OCH_2), 4.94 (s, 2H, -OCH_2), 6.85 (m, 2H, ArH), 7.11–7.23 (m, 5H, ArH), 7.27 (s, 1H, =CH), 7.48–7.51 (t, 1H, $J = 7.6$ Hz, ArH), 7.56–7.59 (t, 2H, $J = 7.6$ Hz, ArH), 8.26–8.29 (dd, 1H, $J = 1.6$ Hz, 8 Hz, ArH), 8.48–8.50 (dd, 1H, $J = 1.6$ Hz, 4.4 Hz, ArH); MS: $m/z = 412$ (M^+). Anal. calcd. for $C_{25}H_{20}N_2O_2S$: C, 72.79; H, 4.89; N, 6.79. Found: C, 72.65; H, 4.96; N, 6.68.

Compound **4b**

Yield 70%; solid; mp 156–158°C; IR (KBr) ν_{max}: 2925, 1643, 1601, 1596 cm^{-1}; UV (EtOH), $\lambda_{max} = 374$, 277, 219, 201 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 3.75$ (s, 3H, -OCH_3), 4.72 (t, 2H, $J = 1.6$ Hz,

-OCH_2), 4.94–4.95 (t, 2H, $J = 1.6$ Hz, -OCH_2), 6.83–6.96 (m, 2H, ArH), 6.90–6.93 (m, 2H, ArH), 7.21–7.25 (m, 3H, ArH), 7.29 (s, 1H, =CH), 7.50–7.53 (tt, 1H, $J = 1.1$ Hz, 7.4 Hz, ArH), 7.58–7.61 (m, 2H, ArH), 8.28–8.30 (dd, 1H, $J = 1.8$ Hz, 7.9 Hz, ArH), 8.51–8.52 (dd, 1H, $J = 1.8$ Hz, 4.6 Hz, ArH); MS: $m/z = 428$ (M^+). Anal. calcd. for $C_{25}H_{20}N_2O_3S$: C, 70.07; H, 4.70; N, 6.54. Found: C, 70.23; H, 4.64; N, 6.48.

Compound **4c**

Yield 80%; solid; mp 130–132°C; IR (KBr) ν_{max}: 2924, 2852, 1608, 1591 cm^{-1}; UV (EtOH), $\lambda_{max} = 381$, 277, 219, 206 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.78$ (s, 2H, -OCH_2), 4.95 (s, 2H, -OCH_2), 6.95–7.00 (m, 3H, ArH), 7.20–7.25 (m, 3H, ArH), 7.29 (s, 1H, =CH), 7.30–7.32 (m, 3H, ArH), 7.50–7.53 (m, 1H, ArH), 7.58–7.61 (m, 2H, ArH), 8.28–8.30 (ddd, 1H, $J = 0.8$ Hz, 1.8 Hz, 7.9 Hz, ArH), 8.51–8.52 (ddd, 1H, $J = 0.8$ Hz, 1.8 Hz, 4.6 Hz, ArH); MS: $m/z = 398$ (M^+). Anal. calcd. for $C_{24}H_{18}N_2O_2S$: C, 72.34; H, 4.55; N, 7.03. Found: C, 72.48; H, 4.42; N, 6.89.

Compound **4d**

Yield 72%; solid; mp 122–124°C; IR (KBr) ν_{max}: 2922, 2850,1608, 1591; UV (EtOH), $\lambda_{max} = 377$, 277, 220, 202 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.76$ (s, 2H, -OCH_2), 4.95 (s, 2H, -OCH_2), 6.89–6.91 (d, 2H, $J = 8.9$ Hz, ArH), 7.22–7.26 (m, 5H, ArH), 7.29 (s, 1H, =CH), 7.51–7.54 (t, 1H, $J = 7.4$ Hz, ArH), 7.59–7.62 (t, 2H, $J = 7.4$ Hz, ArH), 8.27–8.29 (dd, 1H, $J = 1.6$ Hz, 7.9 Hz, ArH), 8.52–8.53 (dd, 1H, $J = 1.6$ Hz, 4.5 Hz, ArH); MS: $m/z = 432$, 434 (M^+). Anal. calcd. for $C_{24}H_{17}N_2O_2SCl$: C, 66.58; H, 3.96; N, 6.47. Found: C, 66.84; H, 4.14; N, 6.69.

Compound **4e**

Yield 75%; solid; mp 130–132°C; IR (KBr) ν_{max}: 2964, 1606, 1596 cm^{-1}; UV (EtOH), $\lambda_{max} = 378$, 277, 218, 206 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.84$–4.85 (t, 2H, $J = 1.6$ Hz, -OCH_2), 4.95 (t, 2H, $J = 1.6$ Hz, -OCH_2), 6.99-7.01 (d, 1H, $J = 8.8$ Hz, ArH), 7.22–7.25 (m, 4H, ArH), 7.29 (s, 1H, =CH), 7.37 (d, 1H, $J = 2.5$ Hz, ArH), 7.51–7.54 (tt, 1H, $J = 1.1$ Hz, 7.4 Hz, ArH), 7.59–7.62 (m, 2H, ArH), 8.27–8.29 (dd, 1H, $J = 1.8$ Hz, 7.9 Hz, ArH), 8.52–8.53 (dd, 1H, $J = 1.8$ Hz, 4.6 Hz, ArH); MS: $m/z = 467$, 469, 471 (M^+). Anal. calcd. for $C_{24}H_{16}N_2O_2SCl_2$: C, 61.68; H, 3.45; N, 5.99. Found: C, 61.46; H, 3.48; N, 6.11.

Compound **4f**

Yield 74%; solid; mp 148-150°C; IR (KBr) ν_{max}: 2913, 1643, 1611, 1593 cm^{-1}; UV (EtOH), $\lambda_{max} = 376$, 276, 218, 205 nm; ^1H NMR

(500 MHz, $CDCl_3$): $\delta_H = 2.24$ (s, 3H, -CH_3), 2.27 (s, 3H, -CH_3), 4.73 (s, 2H, -OCH_2), 4.92 (s, 2H, -OCH_2), 6.58 (s, 1H, ArH), 6.64 (s, 1H, ArH), 7.13–7.15 (dd, 1H, $J = 4.6$ Hz, 7.3 Hz, ArH), 7.25–7.28 (m, 3H, ArH), 7.29 (s, 1H, =CH), 7.43–7.50 (t, 1H, $J = 7.4$ Hz, ArH), 7.55–7.58 (t, 2H, $J = 7.4$ Hz, ArH), 8.24–8.26 (dd, 1H, $J = 1.6$ Hz, 7.8 Hz, ArH), 8.45–8.47 (dd, 1H, $J = 1.6$ Hz, 4.6 Hz, ArH); MS: $m/z = 426$ (M^+). Anal. calcd. for $C_{26}H_{22}N_2O_2S$: C, 73.21; H, 5.20; N, 6.57. Found: C, 73.35; H, 5.16; N, 6.51.

General Procedure for the Synthesis of Compounds 5a–f

Compounds **4a–f** (500 mg) were refluxed in *o*-dichlorobenzene (5 ml) for 1–2 h. The reaction mixture was cooled and directly subjected to column chromatography over silica gel. *o*-Dichlorobenzene was eluted out with petroleum ether. All the compounds **5a–f** were obtained as white solids when the columns were eluted with 1:3 ethyl acetate-petroleum ether.

Data

Compound **5a**

Yield 78%; solid; mp 178–180°C; IR (KBr) ν_{max}: 2921, 2892, 1715, 1604, 1585 cm^{-1}; UV (EtOH), $\lambda_{max} = 350$, 281, 223, 206 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 2.27$ (s, 3H, -CH_3), 3.29–3.30 (dt, 2H, $J = 1.1$ Hz, 6 Hz, -SCH_2), 5.30–5.31 (d, 2H, $J = 1.5$ Hz, -OCH_2), 6.03–6.06 (tt, 1H, $J = 1.7$ Hz, 6 Hz, =CH), 6.78–6.90 (dt, 2H, $J = 2.8$ Hz, 8.5 Hz, ArH), 7.05–7.06 (d, 2H, $J = 8.1$ Hz, ArH), 7.28–7.30 (dd, 1H, $J = 4.5$ Hz, 7.8 Hz, ArH), 7.32–7.35 (m, 2H, ArH), 7.57–7.61 (m, 3H, ArH), 8.51-8.53 (dd, 1H, $J = 1.9$ Hz, 4.5 Hz, ArH), 8.69–8.71 (dd, 1H, $J = 1.9$ Hz, 7.8 Hz, ArH); MS: $m/z = 412$ (M^+), δ_C (75 MHz, $CDCl_3$): 20.60, 22.38, 29.17, 111.01, 115.09, 116.13, 119.22, 119.46, 129.46, 129.79, 130.01, 130.06, 131.90, 136.08, 138.35, 143.28, 150.43, 151.61, 152.55, 155.36, 173.80. Anal. calcd. for $C_{25}H_{20}N_2O_2S$: C, 72.79; H, 4.89; N, 6.79. Found: C, 72.98; H, 4.97; N, 6.83.

Compound **5b**

Yield 74%; solid; mp 158–160°C; IR (KBr) ν_{max}: 2929, 1721, 1647, 1614, 1589 cm^{-1}; UV (EtOH), $\lambda_{max} = 362$, 278, 205 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 3.28–3.29$ (d, 2H, $J = 6$ Hz, -SCH_2), 3.73 (s, 3H, -OCH_3), 5.27 (d, 2H, $J = 1.4$ Hz, -OCH_2), 6.02–6.05 (tt, 1H, $J = 1.5$ Hz, 6 Hz, =CH), 6.76–6.81 (dt, 2H, $J = 3.7$ Hz, 6.1 Hz, ArH), 6.90–6.93 (dt, 2H, $J = 3.7$ Hz, 6.1 Hz, ArH), 7.27–7.29 (dd, 1H, $J = 4.5$ Hz, 7.8 Hz, ArH), 7.31–7.34 (m, 2H, ArH), 7.56–7.61 (m, 3H, ArH), 8.50–8.52 (dd, 1H,

$J = 1.9$ Hz, 4.5 Hz, ArH), 8.68–8.70 (dd, 1H, $J = 1.9$ Hz, 7.9 Hz, ArH); MS: $m/z = 428$ (M^+). Anal. calcd. for $C_{25}H_{20}N_2O_3S$: C, 70.07; H, 4.70; N, 6.54. Found: C, 69.85; H, 4.62; N, 6.61.

Compound **5c**

Yield 72%; solid; mp 152–154°C; IR (KBr) ν_{max}: 2919, 1647, 1614, 1589 cm^{-1}; UV (EtOH), $\lambda_{max} = 356$, 279, 204 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 3.29–3.31$ (dt, 2H, $J = 1.1$ Hz, 6 Hz, -SCH_2), 5.34 (d, 2H, $J = 1.5$ Hz, -OCH_2), 6.04–6.07 (tt, 1H, $J = 1.7$ Hz, 6 Hz, =CH), 6.90–6.94 (tt, 1H, $J = 1$ Hz, 7.3 Hz, ArH), 6.97–7.00 (m, 2H, ArH), 7.24–7.36 (m, 5H, ArH), 7.57–7.62 (m, 3H, ArH), 8.52–8.53 (dd, 1H, $J = 1.9$ Hz, 4.5 Hz, ArH), 8.69–8.71 (dd, 1H, $J = 1.9$ Hz, 7.8 Hz, ArH); MS: $m/z = 398$ (M^+). Anal. calcd. for $C_{24}H_{18}N_2O_2S$: C, 72.34; H, 4.55; N, 7.03. Found: C, 72.52; H, 4.67; N, 7.11.

Compound **5d**

Yield 76%; solid; mp 196–198°C; IR (KBr) ν_{max}: 2972, 2937, 1732, 1617, 1593 cm^{-1}; UV (EtOH), $\lambda_{max} = 355$, 288, 266, 205 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 3.29–3.30$ (d, 2H, $J = 6$ Hz, -SCH_2), 5.36 (d, 2H, $J = 1.4$ Hz, -OCH_2), 6.07–6.10 (tt, 1H, $J = 1.6$ Hz, 6 Hz, =CH), 7.02–7.04 (d, 1H, $J = 8.8$ Hz, ArH), 7.15–7.17 (dd, 2H, $J = 2.5$ Hz, 8.8 Hz, ArH), 7.23–7.30 (m, 4H, ArH), 7.55–7.58 (m, 3H, ArH), 8.49–8.51 (dd, 1H, $J = 1.9$ Hz, 4.5 Hz, ArH), 8.68–8.70 (dd, 1H, $J = 1.9$ Hz, 7.8 Hz, ArH); MS: $m/z = 432$, 434 (M^+). Anal. calcd. for $C_{24}H_{17}N_2O_2SCl$: C, 66.58; H, 3.96; N, 6.47. Found: C, 66.79; H, 3.82; N, 6.29.

Compound **5e**

Yield 75%; solid; mp 170–172°C; IR (KBr) ν_{max}: 2918, 1721, 1608, 1588 cm^{-1}; UV (EtOH), $\lambda_{max} = 351$, 284, 206 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 3.32–3.33$ (d, 2H, $J = 6$ Hz, -SCH_2), 5.39 (d, 2H, $J = 1.4$ Hz, -OCH_2), 6.11–6.14 (tt, 1H, $J = 1.6$ Hz, 6 Hz, =CH), 7.02–7.04 (d, 1H, $J = 8.8$ Hz, ArH), 7.15–7.17 (dd, 2H, $J = 2.5$ Hz, 8.8 Hz, ArH), 7.29–7.34 (m, 3H, ArH), 7.58–7.61 (m, 3H, ArH), 8.52–8.54 (dd, 1H, $J = 1.9$ Hz, 4.5 Hz, ArH), 8.67–8.69 (dd, 1H, $J = 1.9$ Hz, 7.8 Hz, ArH); MS: $m/z = 467$, 469, 471 (M^+). Anal. calcd. for $C_{24}H_{16}N_2O_2SCl_2$: C, 61.68; H, 3.45; N, 5.99. Found: C, 61.46; H, 3.54; N, 6.08.

Compound **5f**

Yield 70%; solid; mp 182–184°C; IR (KBr) ν_{max}: 2929, 1717, 1608, 1588 cm^{-1}; UV (EtOH), $\lambda_{max} = 354$, 288, 205 nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta_H = 2.26$ (s, 6H, -OCH_3), 3.29–3.31 (d, 2H, $J = 5.6$ Hz, -SCH_2),

5.27 (s, 2H, -OCH_2), 6.06–6.07 (t, 1H, $J = 5.6$ Hz, =CH), 6.57 (s, 1H, ArH), 6.61 (s, 1H, ArH), 7.26–7.34 (m, 4H, ArH), 7.59–7.60 (m, 3H, ArH), 8.52–8.53 (d, 1H, $J = 3.9$ Hz, ArH), 8.71–8.73 (d, 1H, $J = 7.2$ Hz, ArH); MS: $m/z = 426$ (M^+). Anal. calcd. for $C_{26}H_{22}N_2O_2S$: C, 73.21; H, 5.20; N, 6.57. Found: C, 73.42; H, 5.11; N, 6.62.

General Procedure for the Preparation of 10a–f

Compounds (**5a–f**) (0.5 mmol) was dissolved in dry dichloromethane (10 ml), and anhydrous $AlCl_3$ (0.06 g, 0.5 mmol) was added to it. The reaction mixture was stirred at room temperature for 0.5–2.0 h. Crushed ice was added to the reaction mixture and was extracted with dichloromethane. The combined extracts were washed with water (20 ml) and brine (20 ml) and dried (Na_2SO_4). The solvent was removed, and the residual viscous mass was chromatographed over silica gel using ethyl acetate–petroleum ether (1.5:3.5) as eluant to afford the products **5a–f**.

Data

Compound **10a**

Yield 80%; solid; mp 138–140°C; IR (KBr) ν_{max}: 3013, 2926, 1620, 1592, 1471 cm^{-1}; UV (EtOH), $\lambda_{max} = 333$, 305, 289, 267, 207 nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta_H = 1.92$ (s, 3H, CH_3 of ring junction), 2.31 (s, 3H, CH_3) 2.72–2.79 (dd, 1H, $J = 11.8$ Hz, 13.1 Hz), 2.83–2.87 (dd, 1H, $J = 4$ Hz, 13.1 Hz), 3.28–3.32 (dd, 1H, $J = 4$ Hz, 11.6 Hz), 6.91–6.93 (d, 1H, $J = 8$ Hz, ArH), 7.01–7.03 (d, 1H, $J = 8$ Hz, ArH), 7.06 (s, 1H, ArH), 7.28–7.33 (m, 3H, ArH), 7.56–7.58 (m, 3H, ArH), 8.52–8.54 (dd, 1H, $J = 2$ Hz, 4.5 Hz, ArH), 8.78–8.79 (dd, 1H, $J = 2$ Hz, 7.8 Hz, ArH); MS: $m/z = 412$ (M^+). Anal. calcd. for $C_{25}H_{20}N_2O_2S$: C, 72.79; H, 4.89; N, 6.79. Found: C, 72.98; H, 4.74; N, 6.62.

Compound **10b**

Yield 70%; solid; mp 130–132°C; IR (KBr) ν_{max}: 2928, 2829, 1614, 1589, 1487 cm^{-1}; UV (EtOH), $\lambda_{max} = 333$, 301, 267, 206 nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta_H = 1.90$ (s, 3H, CH_3 of ring junction), 2.72–2.78 (t, 1H, $J = 12.8$ Hz), 2.82–2.86 (dd, 1H, $J = 3.8$ Hz, 13 Hz), 3.27–3.31 (dd, 1H, $J = 3.8$ Hz, 11.4 Hz), 3.75 (s, 3H, -OCH_3), 6.72–6.74 (dd, 1H, $J = 2$ Hz, 8.5 Hz, ArH), 6.80 (s, 1H, ArH), 6.89–6.92 (d, 1H, $J = 8.6$ Hz, ArH), 7.26–7.34 (m, 3H, ArH), 7.56–7.58 (m, 3H, ArH), 8.50 (d, 1H, $J = 3$ Hz, ArH), 8.76–8.78 (d, 1H, $J = 6.9$ Hz, ArH); MS: $m/z = 428$

(M^+). Anal. calcd. for $C_{25}H_{20}N_2O_3S$: C, 70.07; H, 4.70; N, 6.54. Found: C, 70.29; H, 4.78; N, 6.68.

Compound **10c**

Yield 72%; solid; mp 146–148°C; IR (KBr) ν_{max}: 2972, 2937, 1732, 1617, 1593, 1474 cm^{-1}; UV (EtOH), $\lambda_{max} = 335$, 306, 288, 266, 205 nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta_H = 1.94$ (s, 3H, CH_3 of ring junction), 2.74–2.80 (dd, 1H, $J = 11.8$ Hz, 13.1 Hz), 2.85–2.89 (dd, 1H, $J = 4$ Hz, 13.1 Hz), 3.34–3.38 (dd, 1H, $J = 4$ Hz, 11.6 Hz), 6.89–6.93 (t, 1H, $J = 7.3$ Hz, ArH), 7.02–7.04 (d, 1H, $J = 8$ Hz, ArH), 7.20–7.38 (m, 5H, ArH), 7.60–7.63 (m, 3H, ArH), 8.52–8.54 (dd, 1H, $J = 2$ Hz, 4.5 Hz, ArH), 8.79–8.81 (dd, 1H, $J = 2$ Hz, 7.8 Hz, ArH); MS: $m/z = 398$ (M^+). Anal. calcd. for $C_{24}H_{18}N_2O_2S$: C, 72.34; H, 4.55; N, 7.03. Found: C, 72.18; H, 4.57; N, 7.11.

Compound **10d**

Yield 75%; solid; mp 128-130°C; IR (KBr) ν_{max}: 2972, 2937, 1732, 1617, 1593, 1474 cm^{-1}; UV (EtOH), $\lambda_{max} = 335$, 306, 288, 266, 205 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 1.96$ (s, 3H, CH_3 of ring junction), 2.77–2.82 (dd, 1H, $J = 11.2$ Hz, 13 Hz), 2.83–2.87 (dd, 1H, $J = 4.2$ Hz, 13 Hz), 3.39–3.42 (dd, 1H, $J = 4.1$ Hz, 11 Hz), 7.09 (s, 1H, ArH), 7.28–7.35 (m, 5H, ArH), 7.57–7.61 (m, 3H, ArH), 8.49–8.51 (dd, 1H, $J = 1.8$ Hz, 4.4 Hz, ArH), 8.79–8.81 (dd, 1H, $J = 1.8$ Hz, 7.8 Hz, ArH); MS: $m/z = 432$, 434 (M^+). Anal. calcd. for $C_{24}H_{17}N_2O_2SCl$: C, 66.58; H, 3.96; N, 6.47. Found: C, 66.75; H, 4.05; N, 6.41.

Compound **10e**

Yield 78%; gummy mass; IR (KBr) ν_{max}: 2972, 2937, 1732, 1617, 1593, 1474 cm^{-1}; UV (EtOH), $\lambda_{max} = 335$, 306, 288, 266, 205 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 1.96$ (s, 3H, CH_3 of ring junction), 2.77–2.82 (dd, 1H, $J = 11.2$ Hz, 13 Hz), 2.83–2.87 (dd, 1H, $J = 4.2$ Hz, 13 Hz), 3.39–3.42 (dd, 1H, $J = 4.1$ Hz, 11 Hz), 7.09 (s, 1H, ArH), 7.28–7.35 (m, 4H, ArH), 7.57–7.61 (m, 3H, ArH), 8.49–8.51 (dd, 1H, $J = 1.8$ Hz, 4.4 Hz, ArH), 8.79–8.81 (dd, 1H, $J = 1.8$ Hz, 7.8 Hz, ArH); MS: $m/z = 467$, 469, 471 (M^+). Anal. calcd. for $C_{24}H_{16}N_2O_2SCl_2$: C, 61.68; H, 3.45; N, 5.99. Found: C, 61.91; H, 3.52; N, 6.08.

Compound **10f**

Yield 71%; gummy mass; IR (KBr) ν_{max}: 2928, 2829, 1614, 1589, 1487 cm^{-1}; UV (EtOH), $\lambda_{max} = 333$, 301, 267, 206 nm; ^1H NMR (500 MHz, $CDCl_3$): $\delta_H = 1.86$ (s, 3H, CH_3 of ring junction), 2.27 (s, 6H, CH_3) 2.61–2.67

(t, 1H, $J = 12.7$ Hz), 2.79–2.82 (dd, 1H, $J = 3.8$ Hz, 13 Hz), 3.23–3.26 (dd, 1H, $J = 3.8$ Hz, 12.4 Hz), 6.52 (s, 1H, ArH), 6.67 (s, 1H, ArH), 7.26–7.36 (m, 3H, ArH), 7.57–7.61 (m, 3H, ArH), 8.50–8.51 (dd, 1H, $J = 1.9$ Hz, 4.5 Hz, ArH), 8.76–8.78 (dd, 1H, $J = 1.9$ Hz, 7.8 Hz, ArH); MS: $m/z = 426$ (M^+). Anal. calcd. for $C_{26}H_{22}N_2O_2S$: C, 73.21; H, 5.20; N, 6.57. Found: C, 73.03; H, 5.28; N, 6.65.

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REFERENCES

1. (a) Litvinov, V. P.; Roman, S. V.; Dyachenko, V. D. *Russ. Chem. Rev.* **2000**, *69* (3), 201; (b) Litvinov, V. P. *Russ. Chem. Rev.* **2004**, *73* (7), 637.
2. Sherlock, M. H.; Kaminski, J. J.; Tom, W. C.; Lee, J. F.; Wong, S. C.; Kreutner, W.; Bryant, R. W.; McPhail, A. T. *J. Med. Chem.* **1998**, *31*, 2108.
3. (a) Santilli, A. A.; Scotese, A. C.; Bauer, R. F.; Bell, S. C. *J. Med. Chem.* **1987**, *30*, 2270; (b) Chen, K.; Kuo, S. C.; Hsieh, M. C.; Merger, A.; Lin, C. M.; Hamel, E.; Lee, K. H. *J. Med. Chem.* **1997**, *40*, 3049.
4. Blythin, D. J. Patent No. EP 127135, 1984, *Chem. Abstr.* 1985, 102, 166726.
5. Katsuhisa, N. Patent Abstracts of Japan, Pub. No. 03223289, 1991, 10.
6. Majumdar, K. C.; Islam, R. *Heteroatom. Chem.* **2007**, *1*, 87.
7. Majumdar, K. C.; Islam, R. *J. Heterocycl. Chem.* **2007**, *44*, 871.
8. Majumdar, K. C.; Islam, R. *Can. J. Chem.* **2006**, *84*, 1632.
9. Majumdar, K. C.; Ghosh, M.; Jana, M. *Synthesis* **2002**, 669.
10. (a) Suzuki, N.; Dohmori, R. *Chem. Pharm. Bull.* **1979**, *27*, 410; (b) Suzuki, N.; Tanaka, Y.; Dohmori, R. *Chem. Pharm. Bull.* **1980**, *28*, 235; (c) Suzuki, N. *Chem. Pharm. Bull.* **1980**, *28*, 761.
11. (a) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205; (b) Bates, D. K.; Janes, M. W. *J. Org. Chem.* **1978**, *43*, 3856; (c) Borgulya, J.; Madeja, R.; Fahrni, P.; Hansen, H. J.; Schmid, H.; Barner, R. *Helv. Chim. Acta* **1973**, *56*, 14.
12. (a) Majumdar, K. C.; Thyagarajan, B. S. *Int. J. Sulfur Chem.* **1972**, *2A*, 67; (b) Majumdar, K. C.; Thyagarajan, B. S. *Int. J. Sulfur Chem.* **1972**, *2A*, 93; (c) Hillard, J. B.; Reddy, K. V.; Majumdar, K. C.; Thyagarajan, B. S. *J. Heterocyc. Chem.* **1974**, *11*, 369.