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Chemoselective Synthesis of Thieno[3,2-*c*][1,8]naphthyridin-4(5*H*)-ones by Tandem Cyclization

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ABSTRACT: *A number of the thieno[3,2-c][1,8]-naphthyridin-4(5H)-ones are chemoselectively synthesized from 4-(4′-aryloxybut-2′-ynylthio)-1-phenyl-1,8-naphthyridin-2(1H)-ones in 82–90% yield by the formation of sulfoxide, followed by [2,3] and [3,3]sigmatropic rearrangement and an intramolecular Michael addition.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:87–92, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20234

INTRODUCTION

1,8-Naphthyridin-2-ones and their derivatives are known to possess anti-inflammatory, antiallergic, potent gastric antisecretary, antitumor, and broncodilator properties [1–3]. 1-Phenyl-4-hydroxy-1,8-naphthyridin-2(1*H*)-one and its derivatives have been used as antiallergic agent [4]. 2-Oxo-1,8-naphthyridin-3-carboxylic acid derivatives possess potent gastric antisecretary properties and anti-inflammatory activities [5,6]. A series of novel imidazo[4,5-*c*][1,8]naphthyridin-4(5*H*)-ones exhibited potent bronchodilator activity [7]. The construction of the five-membered heterocyclic ring in benzo(*b*)-thiophenes and indoles through sulfoxide [8–10] and amine oxide [11–13] rearrangement, respectively was reported by Majumdar and Thyagaranjan. This protocol when applied to selenium analogues [14] proceeded with different results. Recently, we have reported some applications of sulfoxide [15–18] and amine oxide [19–22] rearrangement in heterocyclic substrates for the synthesis of tricyclic skeleton. Some fused tricyclic derivatives of naphthyridinones are known to possess a wide spectrum of medicinal properties [23], and this prompted us to undertake the study on the synthesis of some tricyclic compounds having 1,8-naphthyridine skeleton. Here we report the results of our investigation.

RESULTS AND DISCUSSION

The starting materials for this investigation, 4-(4′-aryloxybut-2′-ynylthio)-1-phenyl-1,8-naphthyridin-2(1*H*)-ones **5a–f**, were synthesized by the phase-transfer catalyzed alkylation of 4-mercapto-1-phenyl-1,8-naphthyridin-2(1*H*)-ones **3** with 1-aryloxy-4-chlorobut-2-ynes **4a–f** in 65–75% yield. 4-Mercapto-1-phenyl-1,8-naphthyridin-2(1*H*)-one **3** was prepared in situ from 1-phenyl-4-tosyloxy-1,8-naphthyridin-2(1*H*)-one **2**, which in turn was prepared from 1-phenyl–4-hydroxy-1,8-naphthyridin-2(1*H*)-one **1**. 1-Phenyl-4-hydroxy-1,8-naphthyridin-2(1*H*)-one **1** was prepared by the procedure described by Sherlock et al. [4] (Scheme 1).

Compounds **5a–f** were all solids and characterized from their elemental analyses and spectroscopic data.

Substrates **5a–f** contain a suitably placed alkynyl segment so as to allow the occurrence of a [2,3]

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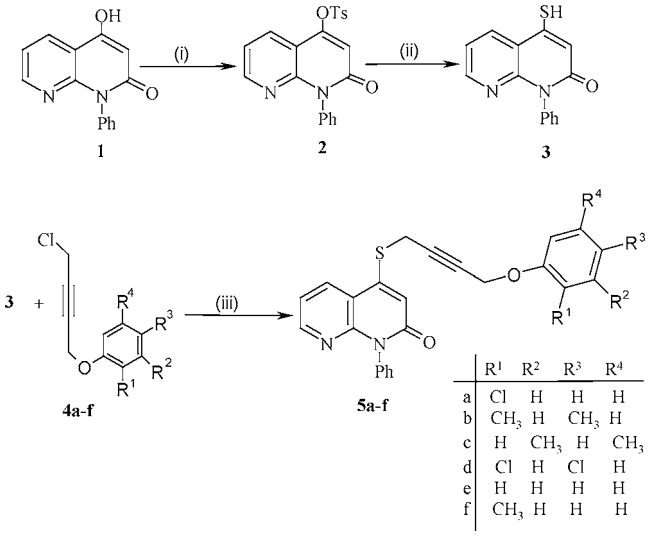
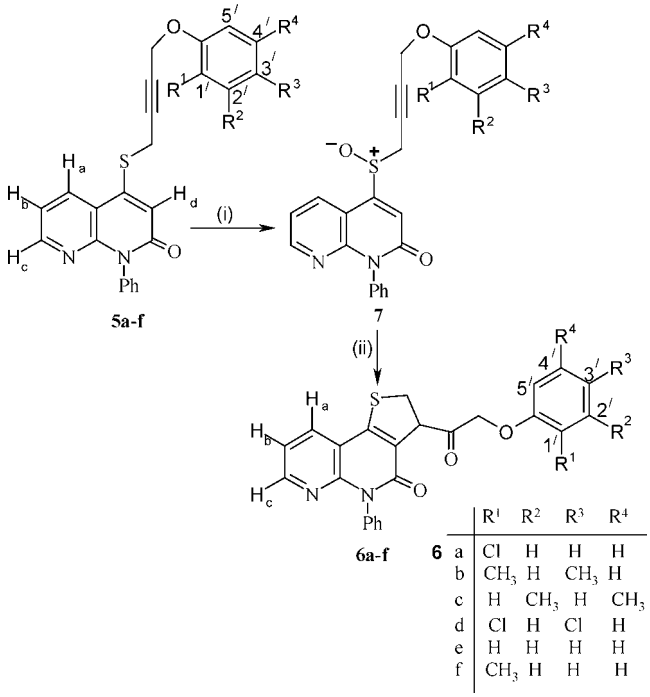


SCHEME 1 Reagents and reaction condition: (i) TsCl, Pyridine, Stirr., rt., 30 min. (ii) NaSH, dry EtOH, 0-5°C, Stirr., 5 h (iii) Aqueous NaOH, $CHCl_3$, BTEAC, Stirr., 8-10 h.



SCHEME 2 Reagents and reaction condition: (i) *m*-CPBA, dichloromethane, 0-5°C, 30 min (ii) Dichloromethane, reflux, 1 h.

sigmatropic rearrangement in the corresponding sulfoxides. With this in view, compound **5a** was treated with *m*-chloroperoxybenzoic acid (*m*-CPBA) at 0–5°C in CH_2Cl_2 solution over 0.5 h. The formation of the sulfoxide was indicated by a single spot (TLC monitoring, $R_f = 0.4$ in petroleum ether:ethyl acetate (70:30) % (v/v)) and disappearance of the starting sulfide. The sulfoxides are quite susceptible to rearrangement and rearranges even during the work up process of the reaction mixture. Therefore, no attempt was made to isolate the sulfoxide, and the reaction mixture was directly subjected to thermal rearrangement without further purification. The reaction mixture was then refluxed in CH_2Cl_2 for 1 h to give a solid, which was characterized from its elemental analysis and spectroscopic data to be **6a**. The ^{1}H NMR spectrum of compound **6a** displayed a multiplet at δ 3.78–3.84, indicating the presence of two $-SCH_2$ protons. The ring juncture proton appeared as one-proton double doublet at δ 5.07–5.11 ($J = 7.2$, 9.6 Hz). Two one-proton doublets at δ 4.96 ($J =$ 16 Hz) and δ 5.00 ($J = 16$ Hz) showed the presence of aryloxy methylene protons adjacent to ketonic carbonyl group. The remaining substrates **5b–f** were also similarly subjected to sulfoxide rearrangement to furnish the products **6b–f** (Scheme 2).

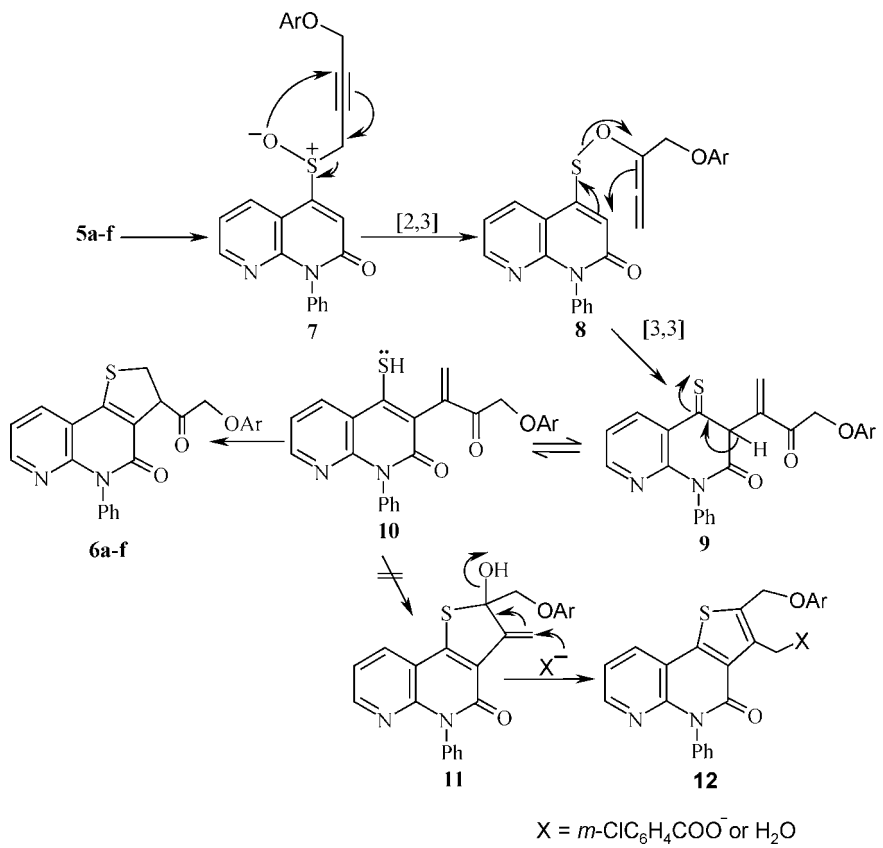
The formation of products **6** from **5** may be mechanistically interpreted as depicted in Scheme 3. Initial [2,3] sigmatropic rearrangement of the sulfoxides **7** gives the allenyl intermediates. Occurrence of [3,3] sigmatropic rearrangement in **8** may generate the intermediates **9**, which may then undergo tautomerization to **10**. Intermediates **10** possess a nucleophilic —SH functionality favorably juxtaposed to an α,β-enone moiety so as to allow an internal Michael-type addition to produce compounds **6**.

Another mode of cyclization of intermediate **10** could have occurred. —SH function could have delivered its nucleophilic attack to the carbonyl carbon of the enone moiety, leading to the allylic alcohol **11**. S_N2' attack of water or *m*-chlorobenzoate ion on **11** might have given to compound **12**. However, we could not obtain this compound **12** in any of the cases.

This method is found to be general for the chemoselective synthesis of thieno[3,2-*c*][1,8]naphthyridin-4(5*H*)-ones in excellent yield. This is a very mild and direct method for the synthesis of this potentially bioactive polyheterocycles by using sulfoxide rearrangement methodology.

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). ^{1}H NMR (300, 400, 500,



SCHEME 3 Mechanism of formation of products thieno[3,2-*c*][1,8]naphthyridin-4(5*H*)-ones **6a–f** from the sulfides **5a–f**.

600 MHz) and ^{13}C NMR (75.5, 125.7 MHz) spectra were recorded on a Bruker DPX-300, Vaian-400 MHz FT NMR, Bruker DPX-500 and Varian-600 MHz spectrometers in $CDCl_3$ (chemical shifts in δ) with TMS as internal standard. Elemental analyses and mass spectra were recorded on a Leco 932 CHNS analyzer and on a JEOL JMS-600 instrument, respectively. ^{1}H 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 TLC. Petroleum ether refers to the fraction boiling between 60 and 80°C.

The 1-aryloxy-4-chlorobut-2-ynes **4a–f** were prepared according to the published procedure [24].

General Procedure for the Preparation of 1-Phenyl-4-tosyloxy-1,8-naphthyridin-2(1H)-one **2**

1-Phenyl-4-hydroxy-1,8-naphthyridin-2(1*H*)-one (2.38 g, 10 mmol) was dissolved in dry pyridine (20 mL) and toluene-4-sulfonyl chloride (1.9 g, 10 mmol) was added to the solution and the mixture was shaken for about 30 min at room temperature. The reaction mixture was then poured into crushed ice and left overnight. The precipitate was filtered, washed with water, and dried. The solid was recrystallized from methanol to give a white solid **2** (3.71 g, 95%).

Compound **2**. Yield 95%, solid, m.p. 206–208°C; IR (KBr) ν_{max}: 3057, 1666, 1584, 1440 cm^{-1}; UV (EtOH), λ_{max}: 222, 328 nm; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.48 (s, 3H, —CH_3), 6.50 (s, 1H, =CH), 7.16–7.25 (m, 4H, ArH), 7.40–7.43 (d, 1H, J = 8.4 Hz, ArH), 7.49–7.58 (m, 3H, ArH), 7.91–7.3 (d, 2H, J = 8.4 Hz, ArH), 8.14–8.16 (dd, 1H, J = 1.6, 8 Hz, ArH), 8.46–8.47 (dd, 1H, J = 1.6, 3.6 Hz, ArH).

General Procedure for the Preparation of 4-Mercapto-1-phenyl-1,8-naphthyridin-2(1H)-one **3**

1-Phenyl-4-tosyloxy-1,8-naphthyridin-2(1*H*)-one (0.75 g, 2 mmol) was dissolved in dry ethanol (100 mL) and anhydrous NaOH (0.56 g, 10 mmol) was added to it at 0–5°C with constant stirring. The

reaction mixture was allowed to attain room temperature and stirred for 5 h. The alcohol was removed under reduced pressure in vacuum. Ice-cold 50% aqueous HCl was added to the reaction mixture to maintain the pH ~2. The reaction mixture was extracted in chloroform (2 × 50 mL); the extract was washed with water (2 × 25 mL) and dried (Na_2SO_4). Organic layer was evaporated under reduced pressure to get the crude product **3** and this crude product **3** was used in the subsequent phase-transfer catalyzed reaction without further purification.

General Procedure for the Preparation of 4-(4′-Aryloxybut-2′-ynylthio)-1-phenyl-1,8-naphthyridin-2(1H)-one **5a–f**

To a mixture of 4-mercapto-1-phenyl-1,8-naphthyridin-2(1*H*)-one **3** (0.5 g, 2 mmol) and 1-aryloxy-4-chloro-2-butyne **4a–f** (2.4 mmol) was added a solution of benzyltriethyl ammonium chloride (BTEAC) in 1% aqueous NaOH (50 mL), and the mixture was stirred at room temperature for about 8–10 h. The reaction mixture was then diluted with water (100 mL), and the organic layer was extracted with chloroform (3 × 25 mL). The organic layer was repeatedly washed with saturated brine and dried (Na_2SO_4). The solvent was removed and the viscous mass was chromatographed over silica gel using petroleum ether:ethyl acetate (3:1) as eluant to afford the products **5a–f**.

Compound **5a**. Yield 70%, solid, m.p. 151–153°C; IR (KBr) ν_{max}: 2951, 1651, 1579, 1481, 1402 cm^{-1}; UV (EtOH) λ_{max}: 222, 282, 309, 326 nm; ^1H NMR (600 MHz, $CDCl_3$): δ_H 3.86 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.80 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.71 (s, 1H, =CH, H_d), 6.89–6.92 (dt, 1H, $J = 1.2$, 7.8 Hz, C4′-H), 7.04–7.05 (dd, 1H, $J = 1.8$, 7.8 Hz, C5′-H), 7.15–7.17 (dd, 1H, $J = 4.2$, 7.8 Hz, H_b), 7.19–7.22 (dt, 1H, $J = 1.2$, 7.8 Hz, C3′-H), 7.27–7.28 (m, 2H, ArH), 7.34–7.35 (dd, 1H, $J = 1.8$, 7.8 Hz, C2′-H), 7.48–7.51 (m, 1H, ArH), 7.56–7.59 (m, 2H, ArH), 8.10–8.12 (dd, 1H, $J = 1.3$, 7.8 Hz, H_a), 8.45–8.46 (dd, 1H, $J = 1.2$, 4.2 Hz, H_c); MS (*m*/*z*): 434, 432 (M^+). Anal. Calcd for $C_{24}H_{17}N_2O_2SCl$: C, 66.58; H, 3.93; N, 6.47%. Found: C, 66.32; H, 4.05; N, 6.67%.

Compound **5b**. Yield 70%, solid, m.p. 118–120°C; IR (KBr) ν_{max}: 2919, 1646, 1580, 1504, 1433 cm^{-1}; UV (EtOH) λ_{max}: 222, 282, 308, 326 nm; ^1H NMR (300 MHz, $CDCl_3$): δ_H 2.19 (s, 3H, $-CH_3$), 2.22 (s, 3H, $-CH_3$), 3.86 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.70 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.73 (s, 1H, =CH, H_d), 6.78–6.94 (m, 3H, ArH), 7.14–7.18 (dd, 1H, $J = 3.2$, 7.8 Hz, H_b), 7.26–7.28 (m, 2H, ArH), 7.47–7.60 (m, 3H, ArH), 8.11–8.13 (d, 1H, $J = 7.9$ Hz, H_a), 8.45–8.46 (d, 1H, $J = 3.2$ Hz, H_c); MS (*m*/*z*): 426 (M^+). Anal. Calcd for $C_{26}H_{22}N_2O_2S$: C, 73.23; H, 5.16; N, 6.57%. Found: C, 73.01; H, 4.94; N, 6.79%.

Compound **5c**. Yield 65%, solid, m.p. 118–120°C; IR (KBr) ν_{max}: 2951, 1648, 1579, 1436 cm^{-1}; UV (EtOH) λ_{max}: 205, 221, 310, 326 nm; ^1H NMR (600 MHz, $CDCl_3$): δ_H 2.26 (s, 6H, $-CH_3$), 3.87 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.68 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.57–6.61 (m, 3H, ArH), 6.72 (s, 1H, =CH, H_d), 7.15–7.17 (dd, 1H, $J = 4.8$, 7.8 Hz, H_b), 7.26–7.28 (m, 2H, ArH), 7.48–7.51 (m, 2H, ArH), 7.56–7.58 (m, 1H, ArH), 8.11–8.13 (dd, 1H, $J = 1.2$, 7.8 Hz, H_a), 8.45–8.46 (dd, 1H, $J = 1.8$, 4.8 Hz, H_c); MS (*m*/*z*): 426 (M^+). Anal. Calcd for $C_{26}H_{22}N_2O_2S$: C, 73.23; H, 5.16; N, 6.57%. Found: C, 73.44; H, 5.01; N, 6.38%.

Compound **5d**. Yield 65%, solid, m.p. 120–122°C; IR (KBr) ν_{max}: 2934, 1651, 1581, 1481 cm^{-1}; UV (EtOH) λ_{max}: 205, 222, 294, 312, 328 nm; ^1H NMR (500 MHz, $CDCl_3$): δ_H 3.85 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.79 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.71 (s, 1H, =CH, H_d), 6.97–6.99 (d, 1H, $J = 8.2$ Hz, C4′-H), 7.15–7.18 (dd, 2H, $J = 3.3$, 7.8 Hz, C5′-H, H_b), 7.25–7.28 (m, 2H, ArH), 7.34–7.35 (d, 1H, $J = 2.3$ Hz, C2′-H), 7.48–7.51 (t, 1H, $J = 7.4$ Hz, ArH), 7.56–7.59 (t, 2H, $J = 7.5$ Hz, ArH), 8.09–8.11 (dd, 1H, $J = 1.0$, 7.8 Hz, H_a), 8.46–8.47 (d, 1H, $J = 3.3$ Hz, H_c); MS (*m*/*z*): 470, 468, 466 (M^+) Anal. Calcd for $C_{24}H_{16}N_2O_2SCl_2$: C, 61.67; H, 3.42; N, 5.99%. Found: C, 66.84; H, 3.49; N, 5.73%.

Compound **5e**. Yield 75%, solid, m.p. 155–157°C; IR (KBr) ν_{max}: 2938, 1642, 1579, 1432 cm^{-1}; UV (EtOH) λ_{max}: 221, 269, 277, 311, 326 nm; ^1H NMR (500 MHz, $CDCl_3$): δ_H 3.86 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.72 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.72 (s, 1H, =CH, H_d), 6.93–6.96 (m, 3H, ArH), 7.14–7.16 (dd, 1H, $J = 4.6$, 7.9 Hz, H_b), 7.25–7.29 (m, 4H, ArH), 7.48–7.51 (t, 1H, $J = 7.3$ Hz, ArH), 7.56–7.59 (t, 2H, $J = 1.5$, 7.9 Hz, ArH), 8.10–8.12 (dd, 1H, $J = 1.5$, 7.9 Hz, H_a), 8.45–8.46 (dd, 1H, $J = 1.5$, 4.6 Hz, H_c); MS (*m*/*z*): 398 (M^+) Anal. Calcd for $C_{24}H_{18}N_2O_2S$: C, 72.36; H, 4.52; N, 7.03%. Found: C, 72.17; H, 4.39; N, 7.25%.

Compound **5f**. Yield 65%, solid, m.p. 138–140°C; IR (KBr) ν_{max}: 2939, 1666, 1578, 1493 cm^{-1}; UV (EtOH) λ_{max}: 221, 282, 309, 327 nm; ^1H NMR (600 MHz, $CDCl_3$): δ_H 2.22 (s, 3H, $-CH_3$), 3.86 (t, 2H, $J = 2$ Hz, $-SCH_2$), 4.73 (t, 2H, $J = 2$ Hz, $-OCH_2$), 6.73 (s, 1H, =CH), 6.85–6.91 (m, 2H, ArH), 7.11–7.13 (m, 1H, ArH), 7.15–7.17 (dd, 1H, $J = 4.6$, 7.9 Hz, H_b) 7.26–7.28 (m, 2H, ArH), 7.48–7.51 (m, 2H, ArH), 7.56–7.59 (m, 2H, ArH), 8.11–8.13 (dd, 1H, $J = 1.2$, 7.2 Hz, H_a), 8.45–8.46 (dd, 1H, $J = 1.2$, 4.2 Hz, H_c);

MS (*m*/*z*) = 412 (M^+). Anal. Calcd for $C_{25}H_{20}N_2O_2S$: C, 72.81; H, 4.85; N, 6.79%. Found: C, 72.62; H, 4.97; N, 6.91%.

General Procedure for the Oxidation and Rearrangement of 4-(4′-Aryloxybut-2′-ynylthio)-1-phenyl-1,8-naphthyridin-2(1H)-one **5a–f**

A solution of *m*-CPBA (0.24 mmol, 0.08 g (50%)) in dichloromethane (30 mL) was slowly added to a well-stirred solution of the sulfide **5a–f** (0.24 mmol) in dichloromethane (30 mL) at 0–5°C over a period of 15 min. The reaction mixture was stirred at room temperature for an additional 30 min. Then the reaction mixture was refluxed for 1 h. The resulting solution was then washed with 10% aqueous Na_2CO_3 (3 × 25 mL), brine (25 mL), and dried (Na_2SO_4). Removal of dichloromethane furnished the crude product, which was purified by column chromatography over silica gel. Elution of the column with petroleum ether:ethyl acetate (5:1) mixture gave the pure compound **6a–f**.

Compound **6a**. Yield 88%, solid, m.p. 196–198°C; IR (KBr) ν_{max}: 2951, 1725, 1643, 1582, 1484 cm^{-1}; UV (EtOH) λ_{max}: 220 281, 331 nm; ^1H NMR (500 MHz, $CDCl_3$): δ_H 3.78–3.84 (m, 2H, $-SCH_2$), 4.96 (d, 1H, J = 16 Hz, $-OCH_2$), 5.00 (d, 1H, J = 16 Hz, $-OCH_2$), 5.07–5.11 (dd, 1H, J = 7.6, 9.6 Hz, ring juncture H), 6.86–6.88 (d, 1H, J = 8.3 Hz, ArH), 6.90–6.93 (t, 1H, J = 7.5 Hz, ArH), 7.14–7.25 (m, 4H, ArH), 7.34–7.36 (d, 1H, J = 7.8 Hz, ArH), 7.46–7.49 (t, 1H, J = 7.4 Hz, ArH), 7.53–7.58 (t, 2H, J = 7.3 Hz, ArH), 7.81–7.83 (dd, 1H, J = 1.2, 7.7 Hz, H_a), 8.47–8.48 (dd, 1H, J = 1.3, 4.5 Hz, H_c); ^{13}C NMR (125 MHz, $CDCl_3$): 35.54, 54.5, 74.01, 113.00, 114.06, 118.83, 122.80, 123.24, 127.50, 128.27, 129.08, 129.35, 129.87, 130.87, 135.19, 137.09, 151.13, 151.37, 153.71, 154.58, 159.55, 204.59; MS (*m*/*z*): 450, 448 (M^+). Anal. Calcd for $C_{24}H_{17}N_2O_3SCl$: C, 64.21; H, 3.79; N, 6.24%. Found: C, 64.37; H, 3.64; N, 6.04%.

Compound **6b**. Yield 85%, solid, m.p. 142–144°C; IR (KBr) ν_{max}: 2923, 1731, 1646, 1582, 1503, 1441 cm^{-1}; UV (EtOH) λ_{max}: 221, 280, 331 nm; ^1H NMR (400 MHz, $CDCl_3$): δ_H 2.24 (s, 6H, $-CH_3$) 3.64–3.80 (m, 2H, $-SCH_2$), 4.85 (d, 1H, J = 16 Hz, $-OCH_2$), 4.93 (d, 1H, J = 16 Hz, $-OCH_2$) 5.01–5.05 (dd, 1H, J = 7.2, 9.6 Hz, ring juncture H), 6.58–6.60 (d, 1H, J = 8 Hz, ArH), 6.87–6.89 (d, 1H, J = 8 Hz, ArH), 6.95 (d, 1H, J = 1 Hz, ArH), 7.16–7.19 (dd, 1H, J = 4.8, 7.6 Hz, H_b) 7.24–7.25 (m, 2H, ArH), 7.47–7.55 (m, 3H, ArH), 7.80–7.82 (d, 1H, J = 7.6 Hz, H_a), 8.47–8.48 (d, 1H, J = 4.8 Hz, H_c); ^{13}C NMR (100 MHz, $CDCl_3$): 16.45, 20.65, 35.42, 54.03, 73.47, 111.27, 112.77, 118.59, 126.70, 127.28, 127.49, 128.88, 129.16, 129.67, 130.83, 132.04, 134.96, 136.89, 150.93, 151.13, 154.00, 154.21, 159.30, 205.80; MS (*m*/*z*): 442 (M^+). Anal. Calcd for $C_{26}H_{22}N_2O_3S$: C, 70.58; H, 4.97; N, 6.33%. Found: C, 70.76; H, 5.06; N, 6.21%.

Compound **6c**. Yield 90%, solid, m.p. 212–214°C; IR (KBr) ν_{max}: 2914, 1726, 1647, 1597, 1581, 1445 cm^{-1}; UV (EtOH) λ_{max}: 221, 280, 329 nm; ^1H NMR (300 MHz, $CDCl_3$): δ_H 2.22 (s, 6H, $-CH_3$), 3.63–3.83 (m, 2H, $-SCH_2$), 4.94–4.99 (m, 3H, $-OCH_2$, ring juncture H), 6.51 (s, 2H, ArH), 6.60 (s, 1H, ArH), 7.16–7.25 (m, 3H, ArH), 7.48–7.57 (m, 3H, ArH), 7.81–7.83 (d, 1H, J = 7.5 Hz, H_a), 8.47–8.48 (d, 1H, J = 2.9 Hz, H_c); MS (*m*/*z*): 442 (M^+). Anal. Calcd for $C_{26}H_{22}N_2O_3S$: C, 70.58; H, 4.97; N, 6.33%. Found: C, 70.41; H, 4.82; N, 6.55%.

Compound **6d**. Yield 90%, solid, m.p. 198–200°C; IR (KBr) ν_{max}: 2917, 1724, 1644, 1581, 1483 cm^{-1}; UV (EtOH) λ_{max}: 221, 281, 293, 332 nm; ^1H NMR (300 MHz, $CDCl_3$): δ_H 3.69–3.89 (m, 2H, $-SCH_2$), 4.97–5.11 (m, 3H, $-OCH_2$, ring juncture H), 6.81–6.84 (d, 1H, J = 8.7 Hz, C5′-H), 7.09–7.36 (m, 4H, ArH), 7.50–7.57 (m, 4H, ArH), 7.82–7.85 (d, 1H, J = 7.4 Hz, H_a), 8.45–8.49 (d, 1H, J = 4.4 Hz, H_c); MS (*m*/*z*): 486, 484, 482 (M^+). Anal. Calcd for $C_{24}H_{16}N_2O_3SCl_2$: C, 59.62; H, 3.31; N, 5.79%. Found: C, 59.79; H, 3.42; N, 6.01%.

Compound **6e**. Yield 82%, solid, m.p. 216–218°C; IR (KBr) ν_{max}: 2914, 1722, 1646, 1582, 1445 cm^{-1}; UV (EtOH) λ_{max}: 221, 280, 330 nm; ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.65–3.83 (m, 2H, $-SCH_2$), 4.96–5.03 (m, 3H, $-OCH_2$, ring juncture H), 6.88–6.90 (d, 1H, J = 8.4 Hz, C5′-H), 6.94–6.98 (t, 1H, J = 7.7 Hz, C3′-H), 7.01–7.03 (d, 1H, J = 8 Hz, C1′-H), 7.16–7.31 (m, 4H, ArH), 7.46–7.61 (m, 4H, ArH), 7.81–7.83 (dd, 1H, J = 1.6, 7.6 Hz, H_a), 8.47–8.48 (dd, 1H, J = 1.2, 4.4 Hz, H_c); MS (*m*/*z*): 414 (M^+). Anal. Calcd for $C_{24}H_{18}N_2O_3S$: C, 69.56; H, 4.34; N, 6.76%. Found: C, 69.81; H, 4.12; N, 6.59%.

Compound **6f**. Yield 85%, solid, m.p. 172–174°C; IR (KBr) ν_{max}: 2914, 1723, 1645, 1603, 1580, 1445 cm^{-1}; UV (EtOH) λ_{max}: 220, 280, 328 nm; ^1H NMR (300 MHz, $CDCl_3$): δ_H 2.28 (s, 3H, $-CH_3$), 3.64–3.83 (m, 2H, $-SCH_2$), 4.89–5.07 (m, 3H, $-OCH_2$, ring juncture H), 6.69–6.72 (d, 1H, J = 8.1 Hz, C5′-H), 6.86–6.90 (t, 1H, J = 7.3, 14.6 Hz, C4′-H), 7.07–7.23 (m, 5H, ArH), 7.46–7.58 (m, 3H, ArH), 7.81–7.83 (dd, 1H, J = 1.2, 7.5 Hz, H_a), 8.48–8.49 (dd, 1H, J = 1.2, 3.0 Hz, H_c); MS (*m*/*z*): 428 (M^+). Anal. Calcd for

$C_{25}H_{20}N_2O_3S$: C, 70.09; H, 4.67; N, 6.54%. Found: C, 70.21; H, 4.74; N, 6.72%.

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