Synthesis and X-Ray Characterization of 2,5,6-Trisubstituted Imidazo[2,1-*b*][1,3,4]thiadiazole Derivatives

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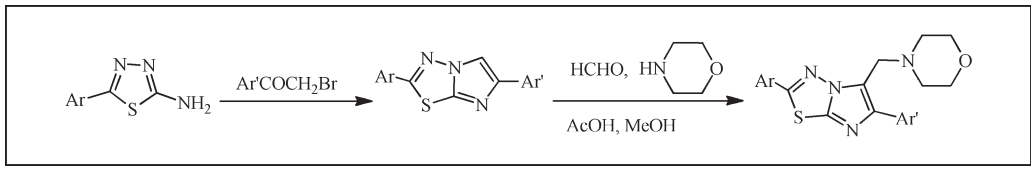

A series of 2,5,6-trisubstituted imidazo[2,1-*b*][1,3,4]thiadiazoles *via* Mannich reaction of imidazo[2,1-*b*][1,3,4]thiadiazoles with morpholine and formaldehyde were synthesized. Structures of all the newly synthesized compounds are well supported by spectral data such as IR, NMR, Mass, and Elemental analysis. Compound **3a** has been confirmed by X-ray diffraction studies.

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INTRODUCTION

Imidazo[2,1-*b*]-1,3,4-thiadiazole derivatives have been of interest to the medicinal chemists for many years because of their anticancer [1], antitubercular [2], antibacterial [3], antifungal [4], analgesic [5], and antisecretory [6] activities. Moreover, much interest has also been focused on the anti-inflammatory [7], cardiotonic [8], diuretic [9], herbicidal [10] activities displayed by compounds incorporating this heterocyclic system. Because the imidazo[2,1-b]-1,3,4-thiadiazole system is similar in part to Levamisole, a well-known immunomodulator [11], the possibility of reducing the harmful effects of the cytotoxic agents on the immune system also appears to be very attractive.

Biheterocycles containing benzofuran, pyridine, thiadiazoles, and chromone rings have been found to exhibit antimicrobial, psychotropic, and anti-inflammatory activities [12]. It has been envisaged that these two active pharmacophores, if linked together would generate novel molecular templates which are likely to exhibit interesting biological properties in animal models. For example, it has been shown that some of methylene bridged benzofuranylimidazo[2,1-b][1,3,4]thiadiazoles can increase both analgesic and anti-inflammatory activities [13].

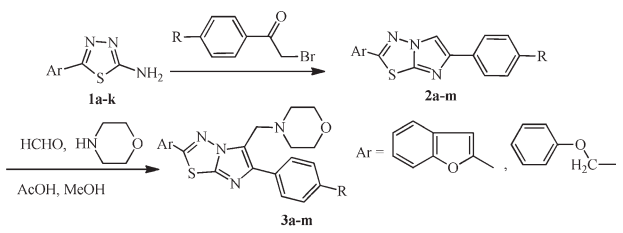
Recently, we have reported the synthesis of some 2-aryloxymethylene-6-arylimidazoimidazo[2,1-*b*]-1,3,4-thiadiazole under microwave irradiation [14]. In continuation of our interest on biologically active compounds such as benzofuran derivatives [15], imidazo[2,1-*b*]-1,3,4-thiadiazole derivatives [14], we herein wish to report an expeditious, one-pot method for the preparation of a series of new 2,5,6-trisubstituted imidazo[2,1-*b*][1,3,4]thiadiazoles *via* Mannich reaction of imidazo[2,1-*b*][1,3,4]thiadiazole (**2**) with morpholine and formaldehyde (Scheme 1).

RESULTS AND DISCUSSION

Synthesis. The synthesis of imidazo[2,1-b][1,3,4]thiadiazole is reported many years ago [16]. In this article, the synthesis of the basic nucleus imidazo[2,1-*b*][1,3,4]thiadiazole is brought about by the condensation of 2-amino-1,3,4-thiadiazole (**1**) with α-bromoarylketone under microwave irradiation in ethanol [14], Mannich reaction of imidazo[2,1-*b*][1,3,4]thiadiazole (**2**) with morpholine and formaldehyde in methanol in the presence of acetic acid yielded corresponding products (**3**). Generally, 5-(morpholin-4-ylmethyl)-6-arylimidazo[2,1-*b*][1,3,4]thiadiazoles could be prepared in good yields via Mannich reaction of 2-(aryloxymethyl)-6-phenylimidazo[2,1-b][1,3,4]thiadiazoles with morpholine and formaldehyde. In fact, when using 2-benzofuranyl-6-arylimidazo[2,1-b]-1,3,4-thiadiazoles **(2k–m)** as substrates, lower yields of products **3k–m** resulted.

Spectroscopic characterization. The formation of Mannich bases imidazothiadiazole derivatives (**3**) were confirmed by the absence of imidazole proton in the ^{1}H NMR spectra. A singlet and two triplets were observed

Scheme 1



Ar = $C_6H_5OCH_2$ **3a**, 2-$CH_3C_6H_4OCH_2$ **3b**, 3-$CH_3C_6H_4OCH_2$ **3c**, 4-$CH_3C_6H_4OCH_2$ **3d**, 4-$CH_3OC_6H_4OCH_2$ **3e**, 2-$ClC_6H_4OCH_2$ **3f**, 4-$ClC_6H_4OCH_2$ **3g**, 2,4-$Cl_2C_6H_3OCH_2$ **3h**, 3-$NO_2C_6H_4OCH_2$ **3i**, 4-$NO_2C_6H_4OCH_2$ **3j**, 2-benzofuranyl **3k-3m**; R = H (**3a-3k**), 4-Cl (**3l**), 4-Br (**3m**).

around δ 4.00, δ 2.30, and δ 3.70, which were assigned to methylene protons and morpholine protons, respectively. Formation of Mannich bases was further confirmed by their ^{13}C NMR and mass spectra. The single crystal X-ray crystallography of product **3a** also confirmed the structures of obtained products (Fig. 1, CCDC Deposit no. 644233).

Molecular and crystal structure of 2-phenyloxymethyl-5-(morpholin-4-ylmethyl)-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole 3a. Compound **3a** crystallized in the centrosymetric space group P21/c with one molecule per asymmetric unit. The ORTEP view of the molecule **3a** with the atomic numbering scheme is given in Figure 1.

In conclusion, 2,5,6-trisubstituted imidazo[2,1-*b*][1,3,4]thiadiazole derivatives *via* Mannich reaction of imidazo[2,1-*b*][1,3,4]thiadiazole (**2**) with morpholine and formaldehyde were synthesized. A new crystal 2-phenyloxymethyl-5-(morpholin-4-ylmethyl)-6-phenylimidazo[2,1-*b*][1,3,4]thiadiazole has been obtained by slow evaporation of ethanol. Detailed crystal structure analysis has been performed to identify the molecular arrangement. Spectral analyses have also been carried out.

EXPERIMENTAL

All reagents were obtained commercially and used without further purification. Melting points were determined on an XT-4 electrothermal micromelting point apparatus and uncorrected. IR spectra were recorded using KBr pellets on a Nicolet AVATAR 360 FTIR spectrophotometer. NMR spectra were recorded at 400 (^1H) and 100 (^{13}C) MHz, respectively, on a Varian Mercury plus-400 instrument using $CDCl_3$ and DMSO-d_6 as solvent and TMS as internal standard. Elemental analyses were performed on a Carlo-Erba 1106 Elemental Analysis instrument. Mass spectra were recorded on a ZAB-HS spectrometer. The single crystal X-ray data collections of compounds **3a** was caried out on a Bruker Smart Apex CCD area detector using a graphite monochromated MoKα radiation (λ = 0.71073 Å) at 20°C. 2-Aryoxylmethylene-6-arylimidazo[2,1-b]-1,3,4-thiadiazoles (**2a–j**) were prepared according to our previous procedures [14].

General procedure for 2-(2-benzofuranyl)-6-arylimidazo[2,1-b]-1,3,4-thiadiazole (2k–m). A mixture of 2-amino-5-(2-benzofuranyl)-1,3,4-thiadiazole (5 mmol) and ω-bromoacetophenone (5 mmol) dissolved in ethanol (10 mL) was stirred at refluxing for 24 h. Completion of the reaction was monitored by TLC using ethyl acetate, acetone, and petroleum ether (1:1:2) as eluent. The solution was concentrated, and the residue was recrystallized from DMF-EtOH to give compounds **2k–m**.

2k: m.p. 240–242°C, yield: 75%. IR (KBr) ν: 3108, 1622 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 7.32 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.35 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.44 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.55 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.66–7.74 (m, 5H, Ph-H), 8.10 (s, 1H, imidazole). Anal. Calcd. For $C_{18}H_{11}N_3OS$: C, 68.12; H, 3.49; N, 13.24. Found: C, 67.97; H, 3.42; N, 13.17. MS (FAB) *m/z*: 317 (M^+).

2l: m.p. 242–244°C, yield: 70%. IR (KBr) ν: 3100, 1623 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 7.35 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.46 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.55 (t, 1H, *J* = 8.0 Hz, Ar-H), 7.61 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.69 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.72 (t, 1H, *J* = 7.2 Hz, Ar-H), 7.73–7.75 (m, 2H, Ar-H), 8.08 (s, 1H, imidazole-H). Anal. Calcd. For $C_{18}H_{10}ClN_3OS$: C, 61.45; H, 2.87; N, 11.94. Found: C, 61.62; H, 2.93; N, 11.84. MS (FAB) *m/z*: 351 (M^+).

2m: m.p. 268–270°C, yield: 79%. IR (KBr) ν: 3076, 1612 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) δ = 7.36 (d, 1H, *J* = 8.0 Hz, Ar-H), 7.50 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.55 (d, 1H, *J* = 7.2 Hz, Ar-H), 7.64 (s, 1H, Ar-H), 7.67–7.69 (m, 2H, Ar-H), 7.71–7.74 (m, 2H, Ar-H), 8.07 (s, 1H, imidazole-H). Anal. Calcd. For $C_{18}H_{10}BrN_3OS$: C, 65.69; H, 5.75; N, 13.32. Found: C, 65.52; H, 5.81; N, 13.24. MS (FAB) *m/z*: 395 (M^+).

General procedure for the preparation of 2,5,6-trisubstituted imidazo[2,1-*b*][1,3,4]thiadiazoles (3a–m). A mixture of 2-aryloxymethyl-6-arylimidazo[2,1-b][1,3,4]-thiadiazole (**2a–m**) (1 mmol), morpholine (1.2 mmol), formalin (1 mL), and acetic acid (1 mL) in methanol (10 mL) was refluxed for 8 h. The resulting mixture was cooled to room temperature and concentrated. The resulting crystals were collected by filtration and recrystallized from ethanol to give the products (**3a–m**).

3a: m.p. 130–132°C, Yield 82%. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.53 (t, *J* = 4.0 Hz, 4H, CH_2NCH_2), 3.69 (t, *J* = 4.0 Hz, 4H, CH_2OCH_2), 3.90 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 7.00–7.05 (m, 3H, Ar-H), 7.30–7.34 (m, 3H, Ar-H), 7.43 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.95 (t, 2H, *J* = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.60, 157.19, 145.02, 143.85, 134.41, 129.71, 128.43, 127.62, 127.40, 122.35, 119.91, 114.91, 66.90, 65.33, 53.05, 51.26. Anal. Calcd. For $C_{22}H_{22}N_4O_2S$: C, 65.00; H, 5.46; N, 13.78. Found: C, 64.82; H, 5.52; N, 13.65. MS (FAB) *m/z*: 407 $(M+1)^+$.

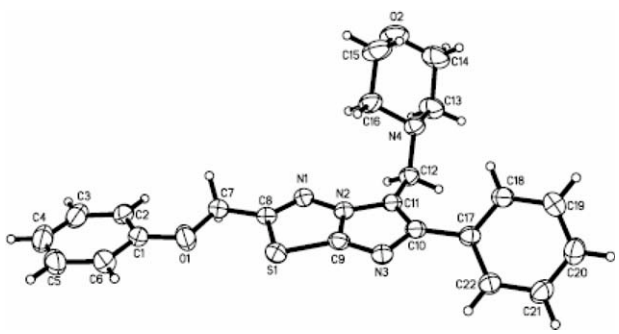


Figure 1. ORTEP diagram of compound **3a**.

3b: m.p. 120–122°C, Yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.30 (s, 3H, CH_3), 2.54 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.69 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.91 (s, 2H, CH_2), 5.35 (s, 2H, CH_2O), 6.93–7.10 (m, 4H, Ar-H), 7.33 (t, J = 8.0 Hz, 1H, Ar-H), 7.44 (d, J = 7.6 Hz, 2H, Ar-H), 7.96 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.96, 157.05, 145.15, 143.88, 134.40, 130.19, 129.91, 128.49, 127.69, 126.46, 124.95, 122.45, 119.91, 114.91, 66.92, 65.65, 53.12, 51.38, 12.24. Anal. Calcd. For $C_{23}H_{24}N_4O_2S$: C, 65.69; H, 5.75; N, 13.32. Found: C, 65.58; H, 5.81; N, 13.40. MS (FAB) m/z: 421 $(M+1)^+$.

3c: m.p. 142–144°C, Yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.31 (s, 3H, CH_3), 2.54 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.69 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.91 (s, 2H, CH_2), 5.35 (s, 2H, CH_2O), 6.88–7.15 (m, 4H, Ar-H), 7.35 (t, J = 8.0 Hz, 1H, Ar-H), 7.43 (d, J = 7.6 Hz, 2H, Ar-H), 7.95 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.96, 157.05, 145.15, 143.88, 138.09, 134.40, 129.91, 129.41, 128.49, 127.69, 122.36, 119.89, 113.80, 111.21, 66.92, 65.65, 53.12, 51.38, 21.15. Anal. Calcd. For $C_{23}H_{24}N_4O_2S$: C, 65.69; H, 5.75; N, 13.32. Found: C, 65.76; H, 5.67; N, 13.20. MS (FAB) m/z: 421 $(M+1)^+$.

3d: m.p. 152–154°C, Yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.31 (s, 3H, CH_3), 2.54 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.70 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 6.91 (d, J = 8.0 Hz, 2H, Ar-H), 7.12 (d, J = 8.0 Hz, 2H, Ar-H), 7.34 (t, J = 8.0 Hz, 1H, Ar-H), 7.44 (d, 2H, J = 7.6 Hz, Ar-H), 7.95 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.96, 157.36, 145.07, 143.83, 134.49, 131.86, 130.19, 128.49, 127.69, 127.46, 119.94, 114.90, 66.98, 65.64, 53.11, 51.32, 20.51. Anal. Calcd. For $C_{23}H_{24}N_4O_2S$: C, 65.69; H, 5.75; N, 13.32. Found: C, 65.52; H, 5.81; N, 13.24. MS (FAB) m/z: 421 $(M+1)^+$.

3e: m.p. 118–120°C, Yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.54 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.71 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.76 (s, 3H, CH_3O), 3.92 (s, 2H, CH_2), 5.38 (s, 2H, CH_2O), 6.85–7.06 (m, 4H, Ar-H), 7.33 (t, J = 8.0 Hz, 1H, Ar-H), 7.42 (d, 2H, J = 7.6 Hz, Ar-H), 7.96 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.98, 153.36, 150.18, 145.07, 143.83, 134.49, 130.03, 128.49, 127.69, 119.94, 115.41, 115.12, 66.98, 65.64, 53.11, 51.32, 53.86. Anal. Calcd. For $C_{23}H_{24}N_4O_3S$: C, 63.28; H, 5.54; N, 12.83. Found: C, 63.13; H, 5.47; N, 12.69. MS (FAB) m/z: 436 (M^+).

3f: m.p. 136–138°C, Yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.52 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.68 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.92 (s, 2H, CH_2), 5.35 (s, 2H, CH_2O), 6.91–7.16 (m, 3H, Ar-H), 7.28 (d, J = 8.0 Hz, H, Ar-H), 7.36 (d, J = 8.0 Hz, 1H, Ar-H), 7.45 (d, J = 7.6 Hz, 2H, Ar-H), 7.99 (d, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.97, 157.05, 145.15, 143.88, 134.40, 129.91, 129.32, 128.49, 127.69, 127.46, 122.86, 122.45, 119.91, 115.61, 66.92, 65.65, 53.12, 51.38. Anal. Calcd. For $C_{22}H_{21}ClN_4O_2S$: C, 59.92; H, 4.80; N, 12.71. Found: C, 60.07; H, 4.90; N, 12.84. MS (FAB) m/z: 441 $(M+1)^+$.

3g: m.p. 133–134°C, Yield 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.53 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.69 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.90 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 6.95 (d, J = 8.0 Hz, 2H, Ar-H), 7.29–7.35 (m, 3H, Ar-H), 7.43 (d, J = 7.6 Hz, 2H, Ar-H), 7.95 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.99, 157.33, 145.07, 143.83, 134.48, 129.79, 129.28, 128.49, 127.69, 126.55, 119.94, 115.59, 66.91, 65.64, 53.07, 51.32. Anal. Calcd. For $C_{22}H_{21}ClN_4O_2S$: C, 59.92; H, 4.80; N, 12.71. Found: C, 60.10; H, 4.87; N, 12.80. MS (FAB) m/z: 440 (M^+).

3h: m.p. 167–168°C, Yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.51 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.68 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.90 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 6.91–7.17 (m, 2H, Ar-H), 7.31–7.35 (m, 2H, Ar-H), 7.42 (d, J = 7.6 Hz, 2H, Ar-H), 7.95 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.99, 157.11, 145.15, 143.81, 134.40, 131.41, 129.32, 128.49, 128.19, 128.02, 127.66, 124.86, 119.91, 117.61, 66.92, 65.65, 53.12, 51.40. Anal. Calcd. For $C_{22}H_{20}Cl_2N_4O_2S$: C, 55.58; H, 4.24; N, 11.79. Found: C, 55.74; H, 4.29; N, 11.67. MS (FAB) m/z: 475 $(M+1)^+$.

3i: m.p. 162–164°C, Yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.52 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.69 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.91 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 7.33–7.87 (m, 7H, Ar-H), 7.96 (t, 2H, J = 7.2 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 160.96, 158.01, 149.32, 145.15, 143.88, 134.40, 129.99, 129.41, 128.49, 127.61, 120.36, 119.89, 113.80, 111.13, 66.89, 65.64, 53.22, 51.32. Anal. Calcd. For $C_{22}H_{21}N_5O_4S$: C, 58.52; H, 4.69; N, 15.51. Found: C, 58.38; H, 4.80; N, 15.39. MS (FAB) m/z: 451 (M^+).

3j: m.p. 188–189°C, Yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.54 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.70 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.92 (s, 2H, CH_2), 5.36 (s, 2H, CH_2O), 7.27 (d, J = 8.0 Hz, 2H, Ar-H), 7.33 (t, J = 8.0 Hz, 1H, Ar-H), 7.44 (d, 2H, J = 7.6 Hz, Ar-H), 7.95 (t, 2H, J = 7.2 Hz, Ar-H), 8.22 (d, 2H, J = 8.0 Hz, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.85, 160.79, 145.07, 143.89, 140.66, 134.69, 129.11, 128.52, 127.72, 122.00, 119.94, 114.99, 66.89, 65.66, 53.20, 51.32. Anal. Calcd. For $C_{22}H_{21}N_5O_4S$: C, 58.52; H, 4.69; N, 15.51. Found: C, 58.71; H, 4.53; N, 15.40. MS (FAB) m/z: 451 (M^+).

3k: m.p. 206–208°C, Yield 79%. IR (KBr) ν: 2988, 1620, 1475, 794 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.49 (t, J = 4.5 Hz, 4H, CH_2NCH_2), 3.57 (t, J = 4.5 Hz, 4H, CH_2OCH_2), 3.92 (s, 2H, CH_2), 7.33 (d, 1H, J = 7.6 Hz, Ar-H), 7.39 (d, 1H, J = 7.2 Hz, Ar-H), 7.44–7.48 (m, 2H, Ar-H), 7.51 (d, 1H, J = 7.2 Hz, Ar-H), 7.79 (d, 2H, J = 8.6 Hz, Ar-H), 7.89–7.98 (m, 3H, Ar-H). Anal. Calcd. For $C_{23}H_{20}N_4O_2S$: C, 66.33; H, 4.84; N, 13.45. Found: C, 66.49; H, 4.92; N, 13.60. MS (FAB) m/z: 417 $(M+1)^+$.

3l: m.p. 220–222°C, Yield 73%. IR (KBr) ν: 2960, 1612, 1450, 748 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.50 (t, J = 4.5 Hz, 4H, CH_2NCH_2), 3.59 (t, J = 4.5 Hz, 4H, CH_2OCH_2), 3.92 (s, 2H, CH_2), 7.31 (d, 1H, J = 7.6 Hz, Ar-H), 7.41 (d, 1H, J = 7.2 Hz, Ar-H), 7.46 (d, 1H, J = 8.0 Hz, Ar-H), 7.50 (d, 1H, J = 8.0 Hz, Ar-H), 7.77 (d, 2H, J = 8.0 Hz, Ar-H), 7.86–7.97 (m, 3H, Ar-H). Anal. Calcd. For $C_{23}H_{19}ClN_4O_2S$: C, 61.26; H, 4.25; N, 12.42. Found: C, 61.10; H, 4.18; N, 12.35. MS (FAB) m/z: 451 $(M+1)^+$.

3m: m.p. 210–212°C, Yield 74%. IR (KBr) ν: 2928, 1600, 1469, 760 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 2.52 (t, J = 4.0 Hz, 4H, CH_2NCH_2), 3.55 (t, J = 4.0 Hz, 4H, CH_2OCH_2), 3.90 (s, 2H, CH_2), 7.35 (d, 1H, J = 8.0 Hz, Ar-H), 7.42 (d, 2H, J = 8.0 Hz, Ar-H), 7.49 (d, 1H, J = 7.2 Hz, Ar-H), 7.52 (d, 1H, J = 7.2 Hz, Ar-H), 7.65 (d, 1H, J = 8.4 Hz, Ar-H), 7.85–7.99 (m, 3H, Ar-H). Anal. Calcd. For

$C_{23}H_{19}BrN_4O_2S$: C, 55.76; H, 3.87; N, 11.31. Found: C, 55.95; H, 3.97; N, 11.45. MS (FAB) *m/z*: 495 $(M+1)^+$.

Crystal structure determination of compound 3a. X-ray quality crystals of the colorless title compound **3a** were obtained by crystallization from EtOH solution. The diffraction data were collected with a Bruker Smart Apex CCD area detector using a graphite monochromated MoKα radiation ($\lambda = 0.71073$ Å) at 20°C. The data collection and processing were performed using program SMART and SAINT [17]. The structure solution, refinement, and geometrical calculations were carried out through SHELX TL [18]. All hydrogen atoms were added theoretically. Crystallographic data for the structure analysis has been deposited at the Cambridge Crystallographic Data Centre, CCDC No. 644233 for **3a**. Copies of these information can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (44) 01223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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