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Synthesis, Anti-HIV, and Antifungal Activity of New Benzensulfonamides Bearing the 2,5-Disubstituted-1,3,4-Oxadiazole Moiety

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Synthesis, Anti–HIV, and Antifungal Activity of New Benzensulfonamides Bearing the 2,5-Disubstituted-1,3,4-Oxadiazole Moiety

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A series of novel chiral and achiral N-[1-(1,3,4-oxadiazol-2ylthio)alkyl]-4methyl/chloro/methoxybenzenesulfonamides **5a-l** were prepared by the reaction of 4-(4-methyl, chloro, methoxyphenylsulfonamido)alkyl carboxylic acid hydrazides **4a-l** with CS₂ and KOH. Another series of new secondary benzenesulfonamides **10a-j** and bis-benzenesulfonamides **11a-j** have been synthesized by a new approach using Et_3N and dimethylaminopyridine. All synthesized compounds were characterized by physical, microanalytical, and spectral data. Some of the synthesized compounds were screened in vitro for their anti-HIV and antifungal activities.

 $\label{eq:keywords} \begin{array}{ll} \mbox{Antifungal activity; anti-HIV activity; benezenesulfonamides chiral sulfonamides; $1,3,4-$ oxadiazole} \end{array}$

The 1,3,4-oxadiazole family attracts significant attention due to their chemotherapeutic importance.¹⁻⁶ Such compounds showed high

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activity by carrying the potential sulfonamide and free thiol residues. The sulfonamide moiety is a crucial functionality because of its wide variety of pharmacological, activities, such as antimicrobial, anti–HIV,⁷ insuline-releasing antidiabetic, carbonic anhydrase inhibitory,^{8.9} high ceiling diuretic, and antithyroid and antitumor activities.^{10–12} In addition, more recent articles have reported various sets of novel sulfonamide drugs, e.g., an inhibitor of membrane-bound human and bovine isozymes IV¹³ and sildenafil citrate (Viagra[®]) as a drug for treating male erectile dysfunction (ED).¹⁴ The second-generation antimitotic sulfonamide, ER-34410, is 2 to 3 times more potent than E7010 in a panel of various human tumor-cell lines in vitro and can be administered intravenously.¹⁵

Regarding the free thiol moiety (SH)/free mercaptoaryl group, it showed facil coordination with transition metal ions, such as Zn (ll), Cu (ll), and Fe (lll), giving products with highly physiological importance. A large number of metallo-enzymes incorporate Zn (ll) or Cu (ll) ions coordinated by one or several –SH groups belonging to Cys residues.^{1,15,16} Furthermore, the free SH has a strong nucleophilic character and can easily be derivatized by many electrophiles (E^+), such as haloacetates, maleimides, and activated sulfonyl groups, which show different physicochemical properties.¹⁶ The S-alkylation/arylation, Sacylation, or S-sulfonylation of the free SH is indeed of exceptional importance mainly for the design of novel chemotherapeutic agents.^{1,15} These biological data prompted us to synthesize some novel chiral and achiral 1,3,4-oxadiazoles-bearing sulfonamides and thiol residues compounds and evaluate their anti–HIV-1 and antifungal activities.

RESULTS AND DISCUSSION

Although a number of methods are available for the synthesis of sulfonamides, they are usually prepared from carboxylic acids/hydrazides¹⁷ and sulfonic acids/sulfonylchlorides¹⁸ as starting compounds. We report herein a novel approach using different chiral and achiral amino acids as a starting material (Scheme 1), together with a series of new benzenesulfonamides with 2,5-disubstituted-1,3,4-oxadiazole moiety via a new alternative approach (Scheme 2). The advantages of these methods include the availability of the starting materials with high yields of products.

Four amino acids, **1a–d**, were converted into their corresponding sulfonamides **2a–l** by a reaction with 4-methylbenzenesulfonylchloride, 4-chlorobenzenesulfonylchloride, and 4-methoxybenzene-sulfonyl chloride in an alkaline medium (Scheme 1) using standard methods.^{19a} Esterfication of **2a–l** with ethanol in an acidic medium afforded the



SCHEME 1 Reagents and conditions (i) aq. 5% NaOH, ether, 23°C, 6h; (ii) H_2SO_4 /ethanol, reflux; (iii) NH_2 - NH_2 · H_2O /ethanol reflux, 9 h; (iv) CS_2 /KOH, ethanol, reflux, 17 h.

esters **3a-d** following the literature method.^{19b} Treatment of **3a-d**, with 80% hydrazine hydrate, furnished the corresponding hydrazides **4a-l** in good yields. The sulfonamides bearing a 2,5-disubstituted-1,3,4-oxadiazole moiety **5a-l** were then prepared by the reaction of hydrazides **4a-l** with CS₂ and KOH employing the literature method.^{6,20}

The structures of the synthesized compounds were determined by the ¹H NMR, IR, and mass spectra, as well as the optical rotations (chiral



SCHEME 2 Conditions and reagents (i) *p*-NO₂-PhCOCl, CH₃CN, 23°C, 6 h; (ii) SOCl₂, reflux, 2 h; (iii) Pd/C (10%), ethanol, reflux, 9 h; (iv) Et₃N, DMAP, CHCl₃, 70°C, reflux 11 h.

compounds). Compound **5j** was selected for the spectroscopic analysis, since the analogues **5a–f** and **5k–l** showed a similar spectral pattern. The IR spectrum of **5j** revealed the presence of characteristic bands for -NH at 3282 cm⁻¹, 2551 cm⁻¹ for -SH, 1589 cm⁻¹ (C=N), and 1375 cm⁻¹ and 1126 cm⁻¹ for the $-SO_2$ functional group. The mass spectrum of **5j** showed a molecular ion peak at m/z 299 (M⁺, 45). The ¹H NMR spectrum of **5j** showed a multiplet signal at δ 4.57–4.65, characteristic for the chiral *CH*(Z) center, whereas the other protons were fully analyzed. To the best of our knowledge, **5g–i** are not reported in the literature. Meanwhile, the new sulfonamides **5a–f**, **5j–l**, and their corresponding intermediate compounds were prepared^{21,22} recently in our laboratory (Scheme 1).

Alternatively, hydrazides **6a–e** were converted into the *N,N*diacylhydrazines **7a–e** by treatment with 4-nitrobenzoylchloride in dry MeCN. Compounds **7a–e** were subjected to dehydrative cyclization in the presence of thionyl chloride to give **8a–e**.²³ The reduction of **8a–e** with Pd/C and hydrazine hydrate, following a reported method,²⁴ afforded the amino compounds **9a–e** in good yields. The treatment of **9a–e** with Et₃N and dimethylaminopyridine furnished, after purification, the corresponding sulfonamides **10a–e** and **11a–e** (Scheme 2).

Structures of the synthesized compounds were characterized by ¹H NMR, IR, and mass spectra. Compound **10a** was selected for the spectroscopic interpretation, whereas its analogs revealed similar spectral patterns. The IR spectrum of **10a** revealed the presence of characteristic bands for NH at 3266 cm⁻¹, 1589 cm⁻¹ for C=N, and 1379 cm⁻¹ and 1149 cm⁻¹ for SO₂ functional groups. The mass spectrum of **10a** showed a molecular ion peak at m/z 405 (M⁺). The ¹H NMR spectrum of **10a** demonstrated singlets at δ 2.44 and δ 2.84 that were attributed to CH₃-Ar, whereas the doublets at δ 7.26, 7.43, 7.49, 7.81, 8.06, and 8.20 ($J \sim 8.0$ Hz) belonged to aromatic protons. The NH signal appeared at δ 10.54, which exchanged with D₂O. The IR spectrum of *bis*-sulfonamide **11a** showed no signal for the NH group, whereas it showed a molecular ion peak at m/z 559 (M⁺).

ANTI-HIV ACTIVITY

Compounds **4k**, **5b**, **5c**, **5e**, **5f**, **5g**, **9a**, **9b**, **10a**, and **10f** were tested for their anti–HIV-1 and HIV-2 activity in vitro using III_B and ROD strains, respectively, in human T-lymphocyte (MT-4) cells. The results are summarized in Table I in which the data have been included for comparison purposes. Compound-induced cytotoxicity was also measured in MT-4 cells parallel with antiviral activity. None of the oxadiazole derivatives (sulfonamides bearing a 2,5-disubstituted-1,3,4-oxadiazole moiety) were found to inhibit HIV-1 and HIV-2 replication in vitro at EC₅₀ lower than the CC₅₀ in comparison to the antiviral agent efavirenz (EFV)²⁴ and azidothymidine (AZT).²⁵ On the other hand, **5g** showed IC₅₀ > 18.3 μ g/mL and induced cytopathicity in human MT-4 lymphocyte cells at nontoxic concentrations, with no selectivity (SI = 3). Meanwhile, it showed an unusual result by the higher value of anti–HIV-2 activity in comparison to anti–HIV activity with maximum protection 62.

The cavity on gp41 of HIV plays an important role in the viral replication process, which could hold a small molecule inhibitor. Nonreverse transcriptase inhibitors that would fit this cavity have been

Compound	$\mathrm{IC}_{50}(\mu\mathrm{g/mL})^c$ MT-4		$CC_{50}(\mu g/mL)^d$	SI^e	Max. Prot.	
		110	110	-		
4K I	IIB	>113	= 113	<1	1	
l	ROD	> 125	= 125	<1	2	
5b 1	II_B	> 70	=70	<1	4	
I	ROD	>74	=74	<1	5	
5c 1	II_B	> 110	= 110	<1	17	
I	ROD	> 125	= 125	<1	32	
5e l	IIB	> 122	= 122	<1	2	
1	ROD	> 125	= 125	<1	5	
5f 1	II_{B}	> 125	= 125	<1	1	
1	ROD	> 125	= 125	<1	24	
5g 1	II_{B}	>71	=71	<1	8	
1	ROD	= 18	= 63	= 3	62	
9a	II_{B}	> 22	= 22	<1	6	
]	ROD	> 35	= 35	<1	13	
9 b]	IIB	>98	= 99	<1	1	
1	ROD	>116	= 116	<1	5	
10a	Пъ	>89	= 89	<1	1	
1	ROD	>119	= 119	<1	2	
10f	ΠR	>94	=2.44	<1	1	
	ROD	>103	=103	<1	3	
EFV		40	0.003		0	
AZT		63	0.02			

TABLE I In vitro anti-HIV-1 a and HIV-2 b of Some NewOxadiazole Derivatives

^{*a*}Anti–HIV-1 activity measured with strain III_B .

^bAnti–HIV-2 activity measured with strain ROD.

 $^c\mathrm{Compound}$ concentration required to reduce the viability of mock-infected MT-4 cells by 50%.

^dCompound concentration required to achieve 50% protection of MT-4 cells from HIV-1 and 2 induced cytopathogenicity.

^eSI: Selectivity index (IC₅₀/CC₅₀).

identified as active precursors²⁶ to inhibit virus replication. Accordingly, our synthetic strategy for the synthesis of new oxadiazole derivatives bearing mercapto (-SH) moieties depends on this hypothesis. In conclusion, compounds having an oxadiazole backbone carrying thio congeners offer more opportunity for further antiviral investigation than amino alkyl groups.

Antifungal Activity

Invasive aspergillosis is one of the most common fungal infections in immunocompromised patients and carries high mortality rates.²⁷

	Compound No.								Standard
Name of Fungi	5b	5c	5e	5f	5g	5k	51	8a	Drug
Trichphyton longifusus	90	50	0	0	0	50	0	0	Miconazole
Candida albicans	0	0	0	0	0	0	0	0	Miconazole
Aspergillus flavus	100	0	50	0	0	0	50	0	Amphotericin
Microsporum canis	0	0	0	0	0	0	0	0	Miconazole
Fusarium solani	0	0	30	50	0	0	0	50	Miconazole
Candida glabrata	50	0	0	0	0	0	0	0	Miconazole

TABLE II Antifungal Activity of Some New Oxadiazole Derivativesand Inhibition Zones (%)

Conc. of sample 200 μ g/mL of DMSO at 27°C, incubation period 7 days.

Sulfonamides, especially sulfamethoxazole-trimethoprim, are antimicrobial agents frequently employed in AIDS patients to prevent bacterial and fungal infections.²⁸ Therefore, 16 selected representatives of newly synthesized sulfonamides and 1,3,4-oxadiazoles **5b**, **5c**, **5e**-**f**, **5g**, **5k**-**l**, **8a**, **8c**, **8e**, **10a**-**b**, **10e**, **11a**-**b**, and **11e** were screened in vitro for their antifungal activity against six species using the agar plate technique.²⁹ Linear growth of the fungus was obtained by measuring the diameter of the fungal colony after 7 days. The amount of growth inhibition in each case was calculated as percentage inhibition. The screening results are given in Tables II and III. It is worthwhile to note that compounds **5b**, **8e**, and **10e** exhibited significant antifungal activities, which might be attributed to the presence of a free SH at position 5 of the oxadiazole ring, as well as the NO₂ and Cl substituents of the 1,3,4-oxadiazole ring.

TABLE III Antifungal Activity of Some Synthesized Compounds andInhibition Zones (%)

	Compound No.								Standard
Name of Fungi	8c	8e	10a	10b	10e	11a	11b	11e	Drug
Trichphyton longifusus	35	0	50	0	90	0	0	0	Miconazole
Candida albicans	0	60	0	50	60	0	40	0	Miconazole
Aspergillus flavus	0	100	0	0	50	0	0	0	Amphotericin
Microsporum canis	40	90	0	60	40	0	0		Miconazole
Fusarium solani	40	0	0	40	0	50	0	40	Miconazole
Candida glabrata	0	0	0	0	0	0	0	0	Miconazole

Conc. of sample 200 μ g/mL of DMSO at 27°C, incubation period 7 days.

EXPERIMENTAL

General Procedure

Melting points were determined on a Gallenkamp melting-point apparatus and were uncorrected. Optical rotation data were recorded on a Perkin-Elmer 241 polarimeter. IR spectra were recorded in KBr disc on an FTIR model FTS 3000 MX spectrometer. Elemental analysis was performed on a Carlo Erba 1106 elemental analyzer. ¹H NMR (400 and 500 MHz) spectra were recorded on a Bruker NMR spectrophotometer, using tetramethylsilane (TMS) as internal standard with δ values and coupling constants in Hz. Mass spectra were recorded on a MAT 312 and MAT 311A mass spectrometer. TLC was performed on precoated silica gel 60 F₂₅₄ aluminum sheets (Merck, Darmstadt, Germany).

Preparation of the Sulfonamides 2a–I and the Corresponding Esters 3a–I

Compounds **2a–l** were prepared from the corresponding amino acids **1a–d** using 3 different sulfonyl chlorides, whereas the corresponding esters **3a–l** were prepared following the established procedure mentioned in the literature.^{19a,b} Compound **2c** [m.p. 149°C (72%), lit.^{19c} 149°C]. Compounds **2–8** were recrystallized from aq. Ethanol; meanwhile, compounds **10a–j** and **11a–j** were purified by TLC using ethyl acetate/pet. ether.

General Procedure for Preparation of Compounds 4a–I

A mixture of 3a (10 mmol) and hydrazine monohydrate (80%) in absolute EtOH (50 mL) was heated under reflux for 9 h. The solution was concentrated, and the precipitate was filtered, washed with water, and recrystallized from 60% aqueous ethanol. Hydrazides **4b–1** were prepared in a similar fashion.

4a. Yield: 76%, m.p. 92–94°C. ν_{max} (cm⁻¹) 3316, 3286 (NH), 1651 (C=O), 1365 (SO₂), 1147 (SO₂). ¹H NMR (acetone- d_6) δ 1.65–1.72 (m, 2H, CH₂), 2.5 (t, 2H, J=7.4 Hz, CH₂), 2.7 (t, 2H, J=6.6 Hz, CH₂), 2.4 (s, 3H, CH₃), 7.35 (d, 2H, J=8.0 Hz, ArH), 7.7 (d, 2H, J=8.0 Hz, ArH), 9.3 (br s., 2H, NH₂), 10.5 (br s., 1H, NH). EI-MS: m/z 271 (M⁺).

4b. Yield: 75%, m.p. 91–93°C. ν_{max} (cm⁻¹) 3377, 3285 (NH), 1671 (C=O), 1376, 1155 (SO₂). ¹H NMR (acetone- d_6) δ 1.66–1.75 (m, 2H, CH₂), 2.55 (t, 2H, J=7.4 Hz, CH₂), 7.45 (d, 2H, J=8.0 Hz, ArH), 7.89 (d, 2H, J=8.0 Hz, ArH), 9.61 (br s., 2H, NH), 11.29 (br s., 1H, NH). EI-MS: m/z 291 (M⁺).

4c. Yield: 62%, m.p. 110–112°C. ν_{max} (cm⁻¹) 3332, 3260 (NH), 1656 (C=O), 1372, 1161 (SO₂). ¹H NMR (acetone- d_6) δ 1.69–1.78 (m, 2H, CH₂), 2.84 (t, 2H, J=7.8 Hz, CH₂), 2.78 (t, 2H, J=6.9 Hz, CH₂), 7.25 (d, 2H, J=8.1 Hz, ArH), 7.59 (d, 2H, J=8.2 Hz, ArH), 9.57 (br s., 2H, NH₂), 10.75 (br s., 1H, NH). EI-MS: m/z 287 (M⁺).

4d. Yield: 83%, m.p. 156–158°C. ν_{max} (cm⁻¹) 3342, 3285 (NH), 1653 (C=O), 1365 (SO₂), 1149 (SO₂). ¹H NMR (acetone- d_6) δ 0.93 (dd, 3H, J = 7.4 Hz, J = 7.4 Hz, CH₃), 1.83–1.89 (m, 2H, CH₂), 2.38 (s, 3H, CH₃), 4.40 (dd, 1H, J = 7.5 Hz, J = 7.6 Hz, CH), 7.32 (d, 2H, J = 8.1 Hz, ArH), 7.76 (d, 2H, J = 8.0 Hz, ArH), 9.50, 10.70 (2xbr s., 2H, 2xNH). EI-MS: m/z 271 (M⁺).

4e. Yield: 85%, m.p. 161–163°C. ν_{max} (cm⁻¹) 3319, 3292 (NH), 1653 (C=O), 1365, 1149 (SO₂). ¹H NMR (acetone- d_6) δ 0.98 (dd, 3H, J=7.2 Hz, CH₃), 1.82–1.92 (m, 2H, CH₂), 4.38 (t, 1H, J=7.5 Hz, CH), 7.65 (d, 2H, J=8.0 Hz, ArH), 8.01 (d, 2H, J=8.0 Hz, ArH), 9.72 (br s., 2H, NH₂), 11.25 (br s., 1H, NH). EI-MS m/z: 291 (M⁺).

4f. Yield: 65%, m.p. 165–167°C. ν_{max} (cm⁻¹) 3297, 3242 (NH), 1671 (C=O), 1375, 1166 (SO₂). ¹H NMR (acetone- d_6) δ 0.89 (t, 3H, J=7.4 Hz, CH₃), 1.84–1.89 (m, 2H, CH₂), 3.91 (s, 3H, OCH₃), 4.37 (t, 3H, J=7.4 Hz, CH₃), 7.12 (d, 2H, J=8.2 Hz, ArH), 7.72 (d, 2H, J=8.2 Hz, ArH), 9.75 (br s., 2H, NH₂), 10.75 (br s., 1H, NH). EI-MS: m/z 287 (M⁺).

4g. Yield: 61%, m.p. 114–116°C. ν_{max} (cm⁻¹) 3365, 3282 (NH), 1675 (C=O), 1367, 1155 (SO₂).¹H NMR (acetone- d_6) δ 2.03(s, 3H, CH₃S), 2.12–2.24 (m, 2H, CH₂), 2.52–2.59 (m, 2H, CH₂), 2.38 (s, 3H, CH₃), 4.68 (dd, 1H, J=8.0 Hz, J=8.0 Hz, CH), 7.35 (d, 2H, J=8.0 Hz, ArH), 7.68 (d, 2H, J=8.0 Hz, ArH), 9.30 (br s., 2H, NH₂), 10.51 (br s., 1H, NH). EI-MS: m/z 317 (M⁺).

4h. Yield: 55%, m.p. 121–123°C. ν_{max} (cm⁻¹) 3342, 3271 (NH), 1672 (C=O), 1375, 1167 (SO₂). ¹H NMR (acetone- d_6) δ 2.11 (s, 3H, CH₃S), 2.15–2.27 (m, 2H, CH₂), 2.56–2.63 (m, 2H, CH₂), 4.65 (dd, 1H, J=8.2 Hz, J=8.2 Hz, CH), 7.57 (d, 2H, J=8.2 Hz, ArH), 7.91 (d, 2H, J=8.2 Hz, ArH), 9.57(br s., 2H, NH₂), 11.27 (br s., 1H, NH). EI-MS: m/z 337 (M⁺).

4j. Yield: 81%, m.p. 151–153°C. ν_{max} (cm⁻¹) 3366, 3251 (NH), 1675 (C=O), 1378, 1165 (SO₂). EI-MS: m/z 257 (M⁺).

4k. Yield: 89%, m.p. 155–157°C. ν_{max} (cm⁻¹) 3375, 3281 (NH), 1671 (C=O), 1369, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 1.25 (d, 3H, J =7.0 Hz, CH₃), 4.73–4.81 (m, 1H, *CH), 7.55 (d, 2H, J = 8.0 Hz, ArH), 7.80 (d, 2H, J = 8.0 Hz, ArH), 9.12 (br s., 2H, NH₂), 9.47, 10.38 (2xbr s., 2H, 2xNH). EI-MS: m/z 277 (M⁺).

4l. Yield: 64%, m.p. 160–162°C. ν_{max} (cm⁻¹) 3388, 3282 (NH), 1672 (C=O), 1375, 1166 (SO₂). ¹H NMR (acetone- d_6) δ 1.35 (**d**, 3H, J = 7.4 Hz, CH₃), 3.91 (s, 3H, OCH₃), 4.55–4.63 (m, 1H, CH), 7.12 (d, 2H, J = 8.0 Hz,

ArH), 7.66 (d, 2H, J = 8.0 Hz, ArH), 9.45 (br s., 2H, NH₂), 10.92 (br s., 1H, NH). EI-MS: m/z 273 (M⁺).

General Procedure for Preparation of Compounds 5a–I

To a solution of 4a (5.5 mmol) in absolute EtOH (80 mL) was added CS_2 (6.6 mmol), followed by an addition of aq. solution of KOH (10 mL, 5.5 mmol). The reaction mixture was stirred for 15 min and then refluxed for 17 h. The solution was concentrated, diluted with water, and acidified with 4N HCl to pH 2–3. The solid obtained was filtered, washed with water, and recrystallized from 60% aqueous EtOH. Compounds **5b–l** were synthesized in a similar manner.

5a. Yield: 85%, m.p. 145–147°C. ν_{max} (cm⁻¹) 3206 (NH), 2564 (SH), 1589 (C=N), 1379 (SO₂ asym), 1179 (SO₂ sym). ¹H NMR (acetone- d_6) δ 1.89–1.96 (m, 2H, CH₂), 2.4 (s, 3H, CH₃), 2.8 (t, 2H, J=7.4 Hz, CH₂), 3.04 (t, 2H, J=6.6 Hz, CH₂), 7.38 (d, 2H, J=8.10 Hz, ArH), 7.72 (d, 2H, J=8.2 Hz, ArH), 12.8 (bs, 1H, NH). Anal. calcd. for C₁₂H₁₅O₃N₃S₂ (313.39): C, 45.99; H, 4.82; N, 13.41. Found: C, 45.71; H, 4.49; N, 13.22. EI-MS: m/z 313(M⁺).

5b. Yield: 85%, m.p. 171–172°C. ν_{max} (cm⁻¹) 3287 (NH), 2545 (C=N), 1375, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 1.92–1.98 (m, 2H, CH₂), 2.80 (t, 2H, J=7.5 Hz, CH₂), 3.09 (t, 2H, J=6.7 Hz, CH₂), 7.63 (d, 2H, J=8.1 Hz, ArH), 7.87 (d, 2H, J=8.2 Hz, ArH), 12.80 (br s.,1H, NH). Anal. calcd. for C₁₁H₁₂O₃N₃S₂Cl (333.79): C, 39.58; H, 3.62; N, 12.59. Found: C, 39.68; H, 3.74; N, 12.77. EI-MS: m/z 335 (M⁺).

5c. Yield: 87%, m.p. 159–161°C. ν_{max} (cm⁻¹) 3216 (NH), 2548 (SH), 1589 (C=N), 1369, 1179 (SO₂). ¹H NMR (acetone- d_6) δ 1.89–1.96 (m, 2H, CH₂), 2.79 (t, 2H, J = 6.5 Hz, CH₂), 3.00 (q, 2H, J = 6.7 Hz, CH₂), 3.88 (s, 3H, OCH₃), 7.07 (d, 2H, J = 8.1 Hz, ArH), 7.76 (d, 2H, J = 8.2 Hz, ArH) 12.92(br s., 1H, NH). Anal. calcd. for C₁₂H₁₅O₄N₃S₂ (329.39): C, 43.76; H, 4.60; N, 12.76. Found: C, 43.44; H, 4.56; N, 12.87. EI-MS: m/z 330 (M⁺).

5d. Yield: 87%, m.p. 205–205°C, $[\alpha]_D = +44^\circ$ (c = 1.05, acetone). ν_{max} (cm⁻¹) 3266 (NH), 2565 (SH), 1582 (C=N), 1356, 1145 (SO₂). ¹H NMR (acetone- d_6) δ 0.92 (t, 3H, J = 7.4 Hz, CH₃), 1.82–1.90 (m, 2H, CH₂), 2.38 (s, 3H, CH₃), 4.38 (dd, 1H, J = 7.5 Hz, J = 7.6 Hz, CH), 7.32 (d, 2H, J = 8.1 Hz, ArH), 7.66 (d, 2H, J = 8.2 Hz, ArH), 12.7 (br s., 1H, NH). Anal. calcd. for C₁₂H₁₅O₃N₃O₃S₂ (313.39): C, 45.99; H, 4.82; N, 13.41. Found: C, 45.81; H, 4.56; N, 13.26. EI-MS: m/z 313 (M⁺).

5e. Yield: 81%, m.p. 191–192°C, $[\alpha]_D = +24^\circ$ (c = 0.60, acetone). ν_{max} (cm⁻¹) 3233 (NH), 2545 (SH), 1589 (C=N), 1365, 1149 (SO₂). ¹H NMR (acetone- d_6) δ 0.94 (t, 3H, J = 7.4 Hz, CH₃), 1.84–1.90 (m, 2H, CH₂), 4.39 (dd, 1H, J = 7.8 Hz, J = 7.5 Hz, CH), 7.61 (d, 2H, J = 8.0 Hz, ArH), 7.85

(d, 2H, J = 8.0 Hz, ArH) 12.89 (br s., 1H, NH). Anal. calcd. for $C_{11}H_{12}O_3$ ClN₃S₂ (333.79): C, 39.58; H, 3.62; N, 12.59. Found: C, 39.59; H, 3.65; N, 12.20. EI-MS: m/z 332/334 (M⁺).

5f. Yield: 91%, m.p. 211–213°C, $[\alpha]_D = +43^\circ$ (c = 1.04, acetone). ν_{max} (cm⁻¹) 3266 (NH), 2565 (SH), 1582 (C=N), 1356, 1145(-SO₂). ¹H NMR (acetone- d_6) δ 0.92 (t, 3H, J=7.5 Hz, CH₃), 1.82–1.89 (m, 2H, CH₂), 3.86 (s, 3H, OCH₃), 4.36 (dd, 1H, J=7.6 Hz, J=7.7 Hz, CH), 7.01 (d, 2H, J=8.0 Hz, ArH), 7.71 (d, 2H, J=8.2 Hz, ArH). Anal. calcd. for C₁₂H₁₅O₄N₃S₂ (329.39): C, 43.76; H, 4.60; N, 12.76; Found: C, 43.56; H, 4.37; N, 12.78. EI-MS: m/z 330 (M⁺).

5g. Yield: 61%, m.p. 163–165°C, $[\alpha]_D = +42^\circ$ (c = 1.02, acetone). ν_{max} (cm⁻¹) 3275 (NH), 2550 (SH), 1589 (C=N), 1351, 1161 (SO₂). ¹H NMR (acetone- d_6) δ 2.01 (s, 3H, CH₃S), 2.08–2.15 (m, 2H, CH₂), 2.39 (s, 3H, CH₃-Ar), 2.50–2.59 (m, 2H, CH₂), 4.69 (dd, 1H, J=8.1 Hz, J=8.0 Hz, CH), 7.35 (d, 2H, J=8.0 Hz, ArH), 7.67 (d, 2H, J=8.1 Hz, ArH), 12.88 (br s., 1H, NH). Anal. calcd. for C₁₃H₁₇O₃N₃S₃ (359.35): C, 43.42; H, 4.77; N, 11.69. Found: C, 43.16; H, 4.85; N, 11.53. EI-MS: m/z 359 (M⁺).

5h. Yield: 67%, m.p. 171–172°C, $[\alpha]_D = +45^{\circ}$ (c = 1.07, acetone). ν_{max} (cm⁻¹) 3235 (NH), 1586 (C=N), 2553 (SH), 1379, 1167 (SO₂). ¹H NMR (acetone- d_6) δ 2.01 (s, 3H, CH₃S), 2.09–2.15 (m, 2H, CH₂), 2.48–2.57 (m, 2H, CH₂), 4.73 (dd, 1H, J = 8.0 Hz, J = 8.0 Hz, CH), 7.57 (d, 2H, J = 8.1 Hz. ArH), 7.83 (d, 2H, J = 8.1 Hz, ArH), 12.86 (br s., 1H, NH). Anal. calcd. for C₁₂H₁₄O₃Cl N₃S₃ (379.89): C, 37.94; H, 3.72; N, 11.06. Found: C, 37.65; H, 3.72; N, 11.14. EI-MS: m/z 378/380 (M⁺).

5i. Yield: 65%, m.p. 158–160°C, $[\alpha]_D = +29^\circ$ (c = 0.65, acetone). ν_{max} (cm⁻¹) 3271 (NH), 1585 (C=N), 1357, 1166 (SO₂). ¹H NMR (acetoned₆) δ 2.02 (s, 3H, CH₃S), 2.07–2.14 (m, 2H, CH₂), 2.50–2.58 (m, 2H, CH₂), 3.88 (s, 3H, OCH₃), 4.37 (dd, 1H, J=8.0 Hz, J=8.0 Hz, CH), 7.01 (d, 2H, J=8.1 Hz, ArH), 7.69 (d, 2H, J=8.2 Hz, ArH), 12.89 (br s., 1H, NH). Anal. calcd. for C₁₃H₁₇O₄N₃S₃ (375.34): C, 41.57; H, 4.57; N, 11.21. Found: C, 41.75; H, 4.66; N, 11.36. EI-MS: m/z 375 (M⁺).

5j. Yield: 83%, m.p. 205–207°C, $[\alpha]_D = +23^\circ$ (c = 0.55, acetone). ν_{max} (cm⁻¹) 3282 (NH), 2551 (SH), 1589 (C=N), 1375, 1126 (SO₂). ¹H NMR (acetone- d_6) δ 1.46 (d, 3H, CH₃), 2.40 (s, 3H, CH₃), 4.57–4.65 (m, 1H, CH), 7.34 (d, 2H, J=8.2 Hz, ArH), 7.68 (d, 2H, J=8.2 Hz, ArH), 12.85 (br s., 1H, NH). Anal. calcd. for C₁₁H₁₃O₃N₃S₂(299.36): C, 44.13; H, 4.38; N, 14.04; Found: C, 44.07; H, 4.43; N, 14.31. EI-MS: m/z 299 (M⁺).

5k. Yield: 90%, m.p. 172–174°C, $[\alpha]_D = +42^{\circ}$ (c = 1.0, acetone). ν_{max} (cm⁻¹) 3285 (NH), 2550 (SH), 1611 (C=N), 1356 (SO₂ asym), 1149 (SO₂ sym). ¹H NMR (acetone- d_6) δ 1.51 (d, 3H, J=7.0 Hz, CH₃), 4.73–4.65 (m, 1H, CH), 7.58 (d, 2H, J=8.0 Hz, CH₂), ArH, 7.83 (d, 2H, J=8 Hz, ArH), 12.86 (br s., 1H, NH). Anal. calcd. for C₁₀H₁₀O₃ClN₃S₂ (319.78):

C, 37.56; H, 3.15; N, 13.14. Found: C, 37.74; H, 2.88; N, 13.10. EI-MS: m/z 318/320 (M⁺).

51. Yield 79%, m.p. 177–179°C, $[\alpha]_D = +44^{\circ}$ (c = 1.0, acetone). ν_{max} (cm⁻¹) 3266 (NH), 2550 (SH), 1586 (C=N), 1371, 1162 (SO₂). ¹H NMR (acetone- d_6) δ 1.53 (d, 3H, J=7.2 Hz, CH₃), 3.89 (s, 3H, OCH₃), 4.74–4.65 (m, 1H, CH), 7.52(d, 2H, J=8.1 Hz, ArH), 7.76 (d, 2H, J=8.1 Hz, ArH), 12.85(br s., 1H, NH). Anal. calcd. for C₁₁H₁₃O₄N₃S₂ (315.36): C, 41.90; H, 4.21; N, 13.32. Found: C, 42.13; H, 4.20; N, 13.22. EI-MS: m/z 315 (M⁺).

General Procedure for Preparation of *N*,*N*[′]-Diacylhydrazines 7a–e

To a suspension of **6a–e** (5.0 mmol) in dry acetonitrile (50 mL) was added, in portion, 4-nitrobenzoyl chloride (5.1 mmol), and the reaction mixture was stirred for 5–7 h at 23°C. The solution was concentrated, and the solid product was filtered and recrystallized from aqueous EtOH to afford **7a–e**. Compound **7a** (83%) had m.p. 241–243°C (lit.² 273–275°C, 67%).

7b. Yield: 91%, m.p. 231–233°C. ν_{max} (cm⁻¹) 3181 (NH), 3011 (ArH), 1655 (C=O).

7c. Yield: 82%, m.p. 180–182°C. ν_{max} (cm⁻¹) 3217 (NH), 3037 (ArH), 1649 (C=O).

7d. Yield: 79%, m.p. 216–218°C. ν_{max} (cm⁻¹) 3207 (NH), 3017 (ArH), 1647 (C=O).

7e. Yield: 90%, m.p. 277–279°C. ν_{max} (cm⁻¹) 3241 (NH), 3017 (ArH), 1643 (C=O).

General Procedure for Preparation of 2,5-Disubstituted 1,3,4-Oxadiazoles (8a–e)

A mixture of N, N'-diacylhydrazines **7a–e** (2.0 mmol) and thionyl chloride (10 mL) was heated under reflux for 2 h. After cooling, the resulting mixture was poured onto crushed ice and stirred vigorously. The solid product thus obtained was filtered off, washed with water, and recrystallized from aqueous ethanol to afford **8a–e**.

8a. Yield: 71%, m.p. 183–185°C. ν_{max} (cm⁻¹) 1601 (C=N), 1275 (Ar-NO₂). ¹H NMR (DMSO- d_6) δ 2.44 (s, 3H, CH₃-Ar), 7.27 (d, 2H, J=8.0 Hz, ArH), 7.44 (d, 2H, J=8.0 Hz, ArH), 8.32 (d, 2H, J=8.2 Hz, ArH), 8.42 (d, 2H, J=8.2 Hz, ArH). EI-MS: m/z 281 (M⁺).

8b. Yield: 91%, m.p. 193–195°C. ν_{max} (cm⁻¹) 1603 (C=N), 1271 (Ar-NO₂). ¹H NMR (DMSO- d_6) δ 3.81 (s, 3H, OCH₃), 7.29–7.89 (m, 6H, ArH), 8.21 (d, 2H, J=7.2 Hz, ArH). EI-MS: m/z 297 (M⁺).

8c. Yield: 91%, m.p. 189–191°C. ν_{max} (cm⁻¹) 1621 (C=N), 1277(Ar-NO₂). ¹H NMR (DMSO- d_6) δ 3.79 (s, 9H, OCH₃), 6.95 (s, 2H, ArH), 7.96 (d, 2H, J=8.0 Hz, ArH), 8.34 (d, 2H, J=8.0, ArH). EI-MS: m/z 357 (M⁺).

8d. Yield: 91%, m.p. 176–177°C. ν_{max} (cm⁻¹) 1621, (C=N), 1271 (Ar-NO₂). ¹H NMR (DMSO- d_6) δ 7.65–7.91 (m, 6H, ArH), 8.32 (d, 2H, J = 8.0 Hz, ArH). EI-MS: m/z 301 (M⁺).

8e. Yield, 83%, m.p. 210–212°C. IR (ν , cm⁻¹): 1621 (C=N), 1271 (Ar-NO₂). ¹H NMR (DMSO- d_6) δ 7.66 (d, 2H, J=7.1 Hz, ArH), 8.13–8.25 (m, 6H, ArH). EI-MS: m/z 301 (M⁺).

General Procedure for Preparation of Compounds (9a-e)

To a suspension of **8a–e** (1.63 mmol) in EtOH (80 mL) containing 10% Pd/C (0.03 g) was added 10 mL of 80% hydrazine monohydrate dropwise at 85°C, followed by heating under reflux for 25 h. After cooling, the mixture was filtered, and the filtrate was evaporated to dryness. The crude product was recrystallized from EtOH to give **9a–e**.

9a. Yield: 81%, m.p. 191–193°C, ν_{max} (cm⁻¹) 3454, 3348 (NH), 1606, 1581 (C=N). ¹H NMR (DMSO- d_6) δ 2.38 (s, 3H, CH₃-Ar), 6.75 (d, 2H, J=8.1 Hz, ArH), 7.26 (d, 2H, J=8.1 Hz, ArH), 7.8 (d, 2H, J=8.1 Hz, ArH), 7.96 (d, 2H, J=8.2 Hz, ArH). EI-MS: m/z 251 (M⁺).

9b. Yield: 89%, m.p. 205–207°C, ν_{max} (cm⁻¹) 3452, 3338 (NH), 1602, 1582 (C=N). ¹H NMR (DMSO- d_6) δ 3.89 (s, 3H, OCH₃), 6.72 (d, 2H, J = 8.0 Hz, ArH), 7.30 (d, 2H, J = 8.0 Hz, ArH), 7.73 (d, 2H, J = 7.7 Hz, ArH), 7.92 (d, 2H, J = 7.8 Hz, ArH). EI-MS: m/z 267 (M⁺).

9c. Yield: 93%, m.p. 197–199°C. ν_{max} (cm⁻¹) 3399, 3348 (NH), 1586, 1561 (C=N). ¹H NMR (DMSO- d_6) δ 3.88 (s, 9H, OCH₃), 6.71 (d, 2H, J=8.5 Hz, ArH), 7.25 (s, 2H, ArH), 7.86 (d, 2H, J=8.5 Hz, ArH). EI-MS: m/z 327 (M⁺).

9d. Yield: 73%, m.p. 181–183°C. ν_{max} (cm⁻¹) 3394, 3318 (NH), 1596, 1561 (C=N). ¹H NMR (DMSO- d_6) δ 6.80 (d, 2H, J = 7.4 Hz, ArH), 7.91–8.14 (m, 6H, ArH). EI-MS: m/z 271(M⁺).

9e. Yield: 79%, m.p. 210–212°C. ν_{max} (cm⁻¹) 3424, 3338 (NH), 1606, 1582 (C=N). ¹H NMR (DMSO- d_6) δ 7.20 (d, 2H, J=8.0 Hz, ArH), 7.76 (d, 2H, J=8.0 Hz, ArH), 7.85 (d, 2H, J=8.1 Hz, ArH). EI-MS: m/z 271 (M⁺).

General Procedure for Preparation of Benzenesulfonamides Bearing 2,5-Disubstituted 1,3,4-Oxadiazoles (10a–j and 11a–j)

A mixture of **9a–e** (0.75 mmol), Et_3N (0.22 mmol), and a catalytic amount of DMAP (25 mg) was stirred in dry CH_3Cl (50 mL) for 15 min.

Sulfonyl chloride (1.5 mmol) was then added to the previously mentioned solution, and the mixture was refluxed for 5–9 h. The reaction mixture was washed with dilute HCl, brine solution, and water, and the organic layer was dried (Na₂SO₄), filtered, and evaporated to dryness. The residue was recrystallized from aq. EtOH. The sulfonamides **10a-j** and **11a-j** were separated by preparative TLC, using ethyl acetate/pet. ether as an eluent.

10a. Yield, 61%, m.p. 193–195°C. ν_{max} (cm⁻¹) 3266 (NH), 1589 (C=N), 1379, 1149 (SO₂). ¹H NMR (acetone- d_6) δ 2.44 (s, 3H, CH₃-Ar), 2.84 (s, 3H, CH₃-Ar), 7.26 (d, 2H, J=8.1 Hz, ArH), 7.43 (d, 2H, J=8.1 Hz, ArH), 7.49 (d, 2H, J=8.1 Hz, ArH), 7.81 (d, 2H, J=8.1, Hz, ArH), 8.06 (d, 2H, J=7.9 Hz, ArH), 8.20 (d, 2H, J=7.9 Hz, ArH), 10.54 (br s., 1H, NH). Anal. calcd. for C₂₂H₁₉O₃N₃S (405.47): C, 65.17; H, 4.72; N, 10.36. Found: C, 65.24; H, 4.71; N, 10.55. EI-MS: m/z 405 (M⁺).

10b. Yield: 51%, m.p. 190–191°C. ν_{max} (cm⁻¹) 3281 (NH), 1595 (C=N), 1365, 1149 (SO₂). 1089 (br s, NH). ¹H NMR (acetone- d_6) δ 2.49 (s, 3H, CH₃-Ar), 3.89 (s, 3H, OCH₃), 7.1 (d, 2H, J=7.8 Hz, ArH), 7.45 (d, 2H, J=7.9 Hz, ArH), 7.49 (d, 2H, J=8.0 Hz, ArH), 7.98 (d, 2H, J=8.1 Hz, ArH), 8.06 (d, 2H, J=8.0 Hz, ArH), 8.12 (d, 2H, J=8.1 Hz, ArH). Anal. calcd. for C₂₂H₁₉O₄N₃S (421.47): C, 62.71; H, 4.54; N, 9.97. Found: C, 62.85; H, 4.41; N, 9.66. EI-MS: m/z 421 (M⁺).

10c. Yield: 54%, m.p. 197–199°C. ν_{max} (cm⁻¹) 3298 (NH), 1598 (C=N), 1377, 1164 (SO₂). ¹H NMR (acetone- d_6) δ 2.45(s, 3H, CH₃-Ar), 3.91 (s, 9H, OCH₃), 5.74(s, 1H, NH), 7.25 (d, 2H, J=8.0 Hz, ArH), 7.41 (s, 2H, ArH), 7.50 (d, 2H, J=8.0 Hz, ArH), 8.16 (d, 2H, J=8.1 Hz, ArH), 8.22 (d, 2H, J=8.1 Hz, ArH). 10.84 (br s., 1H, NH). Anal. calcd. for C₂₄H₂₃O₆N₃S (481.28): C, 59.85; H, 4.82; N, 8.73. Found: C, 60.13; H, 4.62; N, 8.69. EI-MS: m/z 481 (M⁺).

10d. Yield: 63%, m.p. 187–188°C. ν_{max} (cm⁻¹) 3258 (NH), 1581 (C=N), 1357, 1149 (SO₂). ¹H NMR (acetone- d_6) δ 2.45 (s, 3H, CH₃), 7.48 (d, 2H, J=8.1 Hz, ArH), 7.59–8.08 (m, 9H, ArH) 8.14 (s, 1H, ArH). 10.88 (br s., 1H, NH). Anal. calcd. for C₂₁H₁₆O₃ClN₃S (425.89): C, 59.22; H, 3.81; N, 9.87. Found: C, 59.39; H, 3.75; N, 9.66. EI-MS: m/z 424/426 (M⁺).

10e. Yield: 53%, m.p. 183–185°C. ν_{max} (cm⁻¹) 3266 (NH), 1587 (C=N), 1351, 1161 (SO₂). ¹H NMR (acetone- d_6) δ 2.49 (s, 3H, CH₃-Ar), 7.17 (d, 2H, J=8.1 Hz, ArH), 7.31 (d, 2H, J=8.1 Hz, ArH), 7.51 (m, 4H, ArH), 7.78 (d, 2H, J=8.0 Hz, ArH), 8.10 (d, 2H, J=8.0 Hz, ArH). 10.91 (br s., 1H, NH). Anal. calcd. for C₂₁H₁₆O₃ClN₃S (425.89): C, 59.22; H, 3.81; N, 9.91. Found: C, 59.25; H, 3.90; N, 10.11. EI-MS: m/z 424/426 (M⁺).

10f. Yield: 61%, m.p. 194–195°C. ν_{max} (cm⁻¹) 3291 (NH), 1582 (C=N), 1372, 1166 (SO₂). ¹H NMR (acetone- d_6) δ 2.84 (s, 3H, CH₃-Ar), 3.88 (s, 3H, OCH₃), 6.92 (d, 2H, J=7.5 Hz, ArH), 7.41 (d, 2H, J=8.0 Hz, ArH),

7.49 (d, 2H, J=8.0 Hz, ArH), 7.78 (d, 2H, J=8.1 Hz, ArH), 7.97 (d, 2H, J=8.1 Hz, ArH), 8.06 (d, 2H, J=8.0 Hz, ArH). 10.74 (br s., 1H, NH). Anal. calcd. for $C_{22}H_{19}O_4N_3S$ (421.47): C, 62.71; H, 4.54; N, 9.97. Found: C, 62.33; H, 4.71; N, 10.33. EI-MS: m/z 421 (M⁺).

10g. Yield: 57%, m.p. 177–179°C. ν_{max} (cm⁻¹) 3289 (NH), 1592 (C=N), 1379, 1159 (SO₂). ¹H NMR (acetone- d_6) δ 3.88 (s, 6H, OCH₃), 6.91 (d, 4H, J = 7.5 Hz, ArH), 7.49 (d, 2H, J = 7.9 Hz, ArH), 7.91–8.05 (m, 6H, ArH), 10.89 (br s.,1H, NH). Anal. calcd. for C₂₂H₁₉O₅N₃S (435.47): C, 60.68; H, 4.41; N, 9.65. Found: C, 60.41; H, 4.63; N, 9.68. EI-MS. m/z 435 (M⁺).

10h. Yield: 41%, m.p. 187–189°C. ν_{max} (cm⁻¹) 3295 (NH), 1581 (C=N), 1378, 1167 (SO₂). ¹H NMR (acetone- d_6) δ 3.89 (s, 12H, OCH₃), 6.91 (d, 2H, J=7.6 Hz, ArH), 7.12 (d, 2H, J=7.6 Hz, ArH), 7.26 (s, 1H, ArH), 7.91 (d, 2H, J=8.1 Hz, ArH), 7.98 (d, 2H, J=8.1 Hz, ArH). 11.54 (br s. 1H, NH). Anal. calcd. for C₂₄H₂₃O₇N₃S₂(497.52): C, 57.94; H, 4.66; N, 8.45. Found: C, 57.70; H, 4.65; N, 8.18. EI-MS: m/z 497 (M⁺).

10i. Yield: 45%, m.p. 175–177°C. ν_{max} (cm⁻¹) 3266 (NH), 1592 (C=N), 1375, 1166 (SO₂). ¹H NMR (acetone- d_6) δ 3.86 (s, 3H, OCH₃), 7.02 (d, 2H, J=8.1 Hz, ArH), 7.48 (d, 2H, J=8.0 Hz, ArH), 7.76 (d, 2H, J=8.1 Hz, ArH), 7.61–7.90 (m, 5H, ArH), 8.13 (s, 1H, ArH). 11.14 (br s.,1H, NH). Anal. calcd. for C₂₁H₁₆O₄ClN₃S (441.89): C, 57.10; H, 3.65; N, 9.51. Found: C, 57.19; H, 3.68; N, 9.51. EI-MS: m/z 440/442 (M⁺).

10j. Yield: 48%, m.p. 195–196°C. ν_{max} (cm⁻¹) 3266 (NH), 1587 (C=N), 1351, 1161 (SO₂). ¹H NMR (acetone- d_6) δ 3.88 (s, 3H, OCH₃), 6.92 (d, 2H, J=7.4 Hz, ArH), 7.15 (d, 2H, J=7.4 Hz, ArH), 7.49 (d, 2H, J=8.1 Hz, ArH), 7.49 (d, 2H, J=8.1 Hz, ArH), 7.84 (d, 2H, J=7.8 Hz, ArH), 8.14 (d, 2H, J=7.8 Hz, ArH). 10.67 (br s., 1H, NH). Anal. calcd. for C₃₁H₂₉O₁₀N₃S₃ (441.89): C, 57.01; H, 3.65; N, 14.83. Found: C, 57.15; H, 3.67; N, 14.78. EI-MS: m/z 441 (M⁺).

11a. Yield: 79%, m.p. 214–216°C. ν_{max} (cm⁻¹) 1592 (C=N), 1369, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 2.49 (s, 6H, CH₃-Ar), 2.88 (s, 6H, 2CH₃-Ar-oxa), 7.27 (d, 2H, J=8.0 Hz, ArH), 7.44 (d, 4H, J=8.0 Hz, ArH), 7.49 (d, 4H, J=8.1 Hz, ArH), 7.80 (d, 4H, J=8.1 Hz, ArH), 8.07 (d, 4H, J=8.2 Hz, ArH), 8.19 (d, 4H, J=8.2 Hz, ArH). Anal. calcd. for C₂₉H₂₅O₅N₃S₂ (559.65). C, 62.24; H, 4.50; N, 7.51. Found: C, 62.20; H, 4.23; N, 7.31. EI-MS: m/z 559 (M⁺).

11b. Yield: 71%, m.p. 210–212°C. ν_{max} (cm⁻¹) 1586 (C=N), 1378, 1147 (SO₂). ¹H NMR (acetone- d_6) δ 2.48 (s, 6H, 2CH₃), 3.88 (s, 3H, OCH₃), 6.98 (d, 2H, J=7.9 Hz, ArH), 7.35 (d, 2H, J=7.9 Hz, ArH), 7.48 (d, 2H, J=8.0 Hz, ArH), 7.89 (d, 2H, J=8.1 Hz, ArH), 7.95 (d, 2H, J=8.1 Hz, ArH), 8.05 (d, 2H, J=8.0 Hz, ArH). Anal. calcd. for C₂₉H₂₅O₆N₃S₂ (575.65): C, 60.51; H, 4.38; N, 7.30. Found: C, 60.77; H, 4.19; N, 7.39. EI-MS m/z 575 (M⁺).

11c. Yield: 69%, m.p. 217–219°C. ν_{max} (cm⁻¹) 1595 (C=N), 1379, 1165 (SO₂).¹H NMR (acetone- d_6) δ 2.49 (s, 3H, CH₃-Ar), 3.90 (s, 9H, OCH₃), 7.23 (d, 2H, J=8.4 Hz, ArH), 7.40 (s, 2H, ArH), 7.49 (d, 2H, J=8.4 Hz, ArH), 8.14 (d, 2H, J=8.2 Hz, ArH), 8.21 (d, 2H, J=8.2 Hz, ArH). Anal. calcd. for C₃₁H₂₉O₈N₃S₂ (635.71): C, 58.57; H, 4.61; N, 6.61. Found: C, 58.28; H, 4.51; N, 6.40. EI-MS: m/z 635 (M⁺).

11d. Yield: 62%, m.p. 221–223°C. ν_{max} (cm⁻¹) 1589 (C=N), 1371, 1166 (SO₂). ¹H NMR (acetone- d_6) δ 2.49 (s, 6H, CH₃), 7.51 (d, 4H, J=8.1 Hz, ArH), 7.60–7.98 (m, 11H, ArH), 8.13 (s, 1H, ArH). Anal. calcd. for C₂₈H₂₂O₅ClN₃S₂ (579.07): C, 58.08; H, 3.83; N, 7.26. Found: C, 58.34; H, 3.85; N, 7.50. EI-MS: m/z 578/580 (M⁺).

11e. Yield: 63%, m.p. $214-215^{\circ}$ C. ν_{max} (cm⁻¹) 1585 (C=N), 1353, 1159 (SO₂). ¹H NMR (acetone- d_6) δ 2.42 (s, 6H, CH₃-Ar), 7.16 (d, 2H, J=8.0 Hz, ArH), 7.30 (d, 4H, J=7.9 Hz, ArH), 7.50 (m, 4H, ArH), 7.77 (d, 2H, J=7.7 Hz, ArH), 8.08 (d, 2H, J=7.9 Hz, ArH). Anal. calcd. for $C_{28}H_{22}O_5$ ClN₃S₂ (579.07): C, 58.77; H, 3.83; N, 7.31. Found: C, 58.56; H, 3.71; N, 7.29. EI-MS: m/z 578/580 (M⁺).

11f. Yield: 65%, m.p. 219–222°C. ν_{max} (cm⁻¹) 1583 (C=N), 1377, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 2.85 (s, 3H, CH₃-Ar), 3.89 (s, 6H, OCH₃), 6.93 (d, 4H, J=8.0 Hz, ArH), 7.15 (d, 2H, J=8.1 Hz, ArH), 7.46 (d, 2H, J=8.0 Hz, ArH), 7.93–7.98 (m, 8H, ArH). Anal. calcd. for C₂₉H₂₅O₇N₃S₂ (559. 59): C, 62.23; H, 4.50; N, 7.51. Found: C, 62.07; H, 4.51; N, 7.81. EI-MS: m/z 559 (M⁺).

11g. Yield: 72%, m.p. 207–209°C. ν_{max} (cm⁻¹) 1579 (C=N), 1355, 1161 (SO₂). ¹H NMR (acetone- d_6) δ 3.89 (s, 6H, OCH₃), 6.93 (d, 6H, J=7.2 Hz, ArH), 7.47 (d, 2H, J=7.5 Hz, ArH), 7.93–7.98 (m, 8H, ArH). Anal. calcd. for C₂₉H₂₅O₈N₃S₂ (607.65): C, 57.32; H, 4.15; N, 6.92. Found: C, 57.52; H, 4.18; N, 7.23. EI-MS: m/z 607 (M⁺).

11h. Yield: 69%, m.p. 219–220°C. ν_{max} (cm⁻¹) 1585 (C=N), 1375, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 3.90(s, 15H, OCH₃), 6.93 (d, 4H, J = 7.8 Hz, ArH), 7.13 (d, 2H J = 7.8 Hz, ArH), 7.26 (s, 1H, ArH), 7.78 (d, 2H, J = 8.0 Hz, ArH), 7.79 (d, 4H, J = 8.0 Hz, ArH). Anal. calcd. for C₃₁H₂₉O₁₀N₃S₃ (699.77): C, 53.21; H, 4.21; N, 6.01. Found: C, 53.51; H, 4.29; N, 5.94. EI-MS: m/z 699 (M⁺).

11i. Yield: 64%, m.p. 195–197°C. ν_{max} (cm⁻¹) 1582 (C=N), 1378, 1165 (SO₂). ¹H NMR (acetone- d_6) δ 3.89 (s, 6H, OCH₃), 6.92 (d, 4H, J=8.0 Hz, ArH), 7.12 (d, 2H, J=8.0 Hz, ArH), 7.75–7.95 (m, 10H, ArH). Anal. calcd. for C₂₈H₂₂O₇ClN₃S₂ (611.07): C, 55.04; H, 3.63; N, 6.80; S, 10.53 Found: C, 54.86; H, 3.57; N, 7.03. EI-MS: m/z 610/612 (M⁺).

11j. Yield: 75%, m.p. 230–232°C. ν_{max} (cm⁻¹) 1569 (C=N), 1365, 1148 (SO₂). ¹H NMR (acetone- d_6) δ 3.89 (s, 6H, OCH₃), 6.91 (d, 4H, J=7.0 Hz, ArH), 7.48 (d, 2H, J=7.1 Hz, ArH), 7.76–7.89 (m, 8H, ArH), 8.12

(d, 2H, J=7.5 Hz, ArH). Anal. calcd. for C₂₈H₂₂O₇ClN₃S₂ (611.07): C, 55.01; H, 3.62; N, 6.88. Found: C, 54.90; H, 3.61; N, 7.15. EI-MS: m/z 610/612 (M⁺).

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