Synthesis and Biological Activity of a New Class of Sulfone-Linked Pyrrolylpyrazoles and Pyrrolylisoxazoles from Methyl-3-aryl-2-(*E*-arylethenesulfonyl)acrylate

Venkatapuram Padmavathi,* Thunga Radha Lakshmi, Konda Mahesh, and Adivireddy Padmaja

Department of Chemistry, Sri Venkateswara University; Tirupati–517 502, India.
Received April 9, 2009; accepted August 18, 2009; published online August 31, 2009

A new class of sulfone-linked bis heterocycles, methyl-3-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (8), methyl-3-(1′-phenyl-3′,5′-diaryl-1′*H*-pyrazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (9) and methyl-3-(3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (10) were prepared by the regioselective reaction of methyl-3-aryl-2-(*E*-arylethenesulfonyl)acrylate (2) with tosylmethyl isocyanide followed by fuctionalization of olefin moiety with 1,3-dipolar reagents. The lead compounds were tested for their antimicrobial activity.

Key words pyrroly-pyrazole; isoxazole; 1,3-dipolar cycloaddition; antimicrobial activity

In recent years there has been an intense effort to develop biologically potent heterocycles. In fact, molecules containing five-membered heterocycles have elicited considerable interest with an astonishingly wide range of applications in synthetic organic chemistry. Amongst them pyrrole, pyrazole and isoxazole derivatives are important intermediates in organic synthesis and useful building blocks for biologically active compounds. Pyrroles are abundant as constituents of natural products and have broad synthetic utility in both materials science and medicine.[1—3] Pyrrole containing pharmaceuticals include the cholesterol lowering drug lipitor.[4] In addition, pyrazolines and isoxazolines have gained importance due to their various chemotherapeutic properties. In deed, Celecoxib a pyrazole derivative and Valdecoxib an isoxazole derivative are now widely used in the market as anti-inflammatory drugs.[5] Apart from varied biological properties the lability of 2-isoxazoline ring led to a variety of 1,3-bifunctionalized compounds such as α,β-aminoalcohols, β-hydroxyketones, 1,3-diketones, β-hydroxy nitriles, acids and esters which are used widely in the synthesis of a variety of natural products.[6—9] In the literature, multistep synthetic routes to 3,4-disubstituted pyrroles have been reported either by coupling of imines and nitroalkanes or by using Friedal-Craft's acylation in the presence of an electron-withdrawing group on the pyrrole nitrogen or on 3,4-silylated precursors.[10—12] 3,4-Disubstituted pyrroles have also been synthesized from Michael acceptors and tosylmethyl isocyanide (TosMIC).[13—16] Amongst different methods for the preparation of pyrazolines, isoxazolines, the 1,3-dipolar cycloaddition is the most important and versatile one. The dipolar reagents can be generated by the dehydrogenation of araldehyde hydrazones and araldoximes with lead tetracetate,[17] mercury acetate,[18] 1-chlorobenzotriazole,[19] chloramine-T (CAT)[20—25] *etc.* In fact, we have reported novel oxo-linked bis heterocycles by 1,3-dipolar cycloaddition of dipolar reagents *viz.*, TosMIC, diazomethane, nitrile imines and nitrile oxides to symmetrical and unsymmetrical bischalcones.[26,27] In our endeavour to prepare sulfone-linked bis heterocycles the present work has been taken up.

Chemistry The present communication deals with the reactivity of methyl-3-aryl-2-(*E*-arylethenesulfonyl)acrylate (**2**) towards TosMIC and 1,3-dipolar reagents *viz.*, diazomethane, nitrile imines and nitrile oxides (Chart 1). The compound **2** is prepared by the Knoevenagel condensation of *E*-styrylsulfonylacetic acid methyl ester (**1**) with araldehydes in the presence of piperidine in ethanol. The ^{1}H-NMR spectrum of **2a** displayed two doublets at 7.68, 6.58 for H_A and H_B and a singlet at 7.98 ppm for H_C. Apart from these another singlet is observed at 3.81 ppm for methoxy protons of carbomethoxy group. The compound **2** is treated with TosMIC in the presence of sodium hydride in a mixture of ether and DMSO. The solid obtained indicated two spots in TLC which are identified as methyl-3-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**3**) and methyl-4-aryl-3-(arylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (**4**) in minor and major amounts, respectively (Chart 1). However, repetition of this reaction with excess TosMIC resulted in **3** only. The compound **3a** showed four singlets at 7.19, 7.09, 6.78 and 7.01 ppm due to C_2-H, C_5-H, C_2′-H and C_5′-H of pyrrole ring protons and another singlet at 3.69 ppm due to methoxy protons of carbomethoxy group as well as signals due to aromatic protons. The compound **4a** exhibited two doublets at 7.72, 6.59 ppm due to H_A and H_B and three singlets at 7.14, 7.01 and 3.64 ppm due to C_2-H, C_5-H and methoxy protons of carbomethoxy group.

The olefin moiety in **4** is used to develop pyrazoline and isoxazoline rings by 1,3-dipolar cycloaddition of diazomethane, nitrile imines and nitrile oxides. Treatment of **4** with diazomethane at −20 to −15 °C for 48 h in the presence of triethylamine produced methyl-3-(4′,5′-dihydro-4′-aryl-1′*H*-pyrazol-3-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**5**). The ^{1}H-NMR spectrum of **5a** showed an AMX splitting pattern for pyrazoline ring protons exhibiting three double doublets at 4.57 (H_A), 4.24 (H_M) and 3.88 ppm (H_X) in addition to signals due to pyrrole ring, carbomethoxy and aromatic protons. The coupling constant values J_{AM}=12.0 Hz, J_{MX}=8.0 Hz and J_{AX}=4.0 Hz indicates that H_A, H_M are *cis*, H_A, H_X are *trans* and H_M, H_X are *geminal*.[20,21] The cyclocondensation of **4** with araldehyde phenylhydrazones in the presence of chloramine-T in methanol resulted in methyl-3-(4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-pyrazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**6**) (Chart 1). Similar reaction of **4** with araldoximes produced methyl-3-(4′,5′-dihydro-3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-

* To whom correspondence should be addressed. e-mail: vkpuram2001@yahoo.com

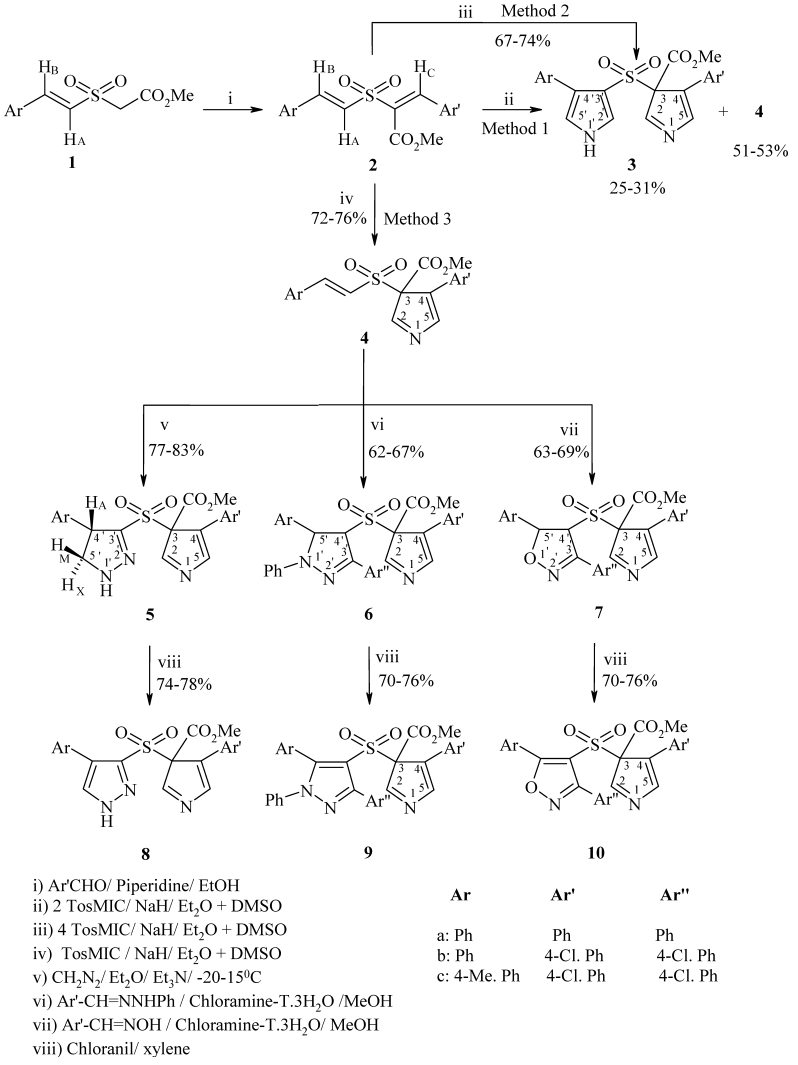

Chart 1

carboxylate (**7**). The ^{1}H-NMR spectra of **6a** and **7a** displayed two doublets at 5.21, 5.16 (C_4'-H) and at 5.58, 5.75 ppm (C_5'-H) in addition to signals due to other protons. The dehydrogenation of pyrazoline and isoxazoline rings in **5**, **6** and **7** is effected with chloranil in xylene. Thus the compounds methyl-3-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**8**), methyl-3-(1′-phenyl-3′,5′-diaryl-1′*H*-pyrazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**9**) and methyl-3-(3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**10**) are prepared (Chart 1). The absence of signals due to pyrazoline and isoxazoline ring protons indicated the formation of **8**, **9** and **10**. The structures of these compounds are further established by ^{13}C-NMR spectra.

Antimicrobial Testing The compounds **3**, **4**, **8**—**10** were tested for antimicrobial activity at two different concentrations 100 and 200 μg/ml. The antibacterial activity was screened against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Escherichia coli*, *Klebsiella pneumoniae* (Gram-negative bacteria) on nutrient agar plates at 37 °C for 24 h using chloramphenicol (25 μg per disc) as reference drug. The compounds were also evaluated for their antifungal activity against *Fusarium solani*, *Curvularia lunata* and *Aspergillus niger* using ketoconazole (25 μg per disc) as standard drug. Fungi cultures were grown on potato dextrose agar medium (PDA) at 25 °C for 3 d. The spore suspension was adjusted to 10^6 pores/ml at an mg/ml concentration by the Vincent and Vincent method.[28)]

The results of the compounds of preliminary antibacterial testing are shown in Table 1. The results revealed that the compounds **3a**—**c** and **4a**—**c** exhibited least activity against the Gram-positive bacteria and almost no activity against the Gram-negative bacteria. However, the other compounds showed higher inhibitory activity against the Gram-positive bacteria than that of the Gram-negative bacteria. The compounds **8b** and **10b** displayed excellent activity against the Gram-positive bacteria (inhibitory zone >34 mm) and good activity against Gram-negative bacteria (inhibitory zone >24 mm). Thus the compounds having pyrrole **8a**—**c** and isoxazole **10a**—**c** units exhibited good activity when compared with the compounds having pyrrole unit **3a**—**c** and **4a**—**c**. However, the compounds with tetrasubstituted pyrazole ring **9a**—**c** exhibited least activity against both bacteria. All the test compounds showed moderate to high inhibitory effect towards tested fungi. The presence of chloro substituent enhances the antimicrobial activity (Table 2).

The MIC values were determined as the lowest concentra-

Table 1. Antibacterial Activity of **3**, **4**, **8**—**10**

Compound	Concentration (μg/ml)	Zone of inhibition (mm) Gram (+)ve		Gram (−)ve	
		S. aureus	*B. subtilis*	*E. coli*	*K. pneumoniae*
3a	100	14	12	—	—
	200	17	14	10	10
3b	100	14	15	10	—
	200	18	17	12	11
3c	100	13	11	—	—
	200	15	14	—	—
4a	100	—	—	—	—
	200	10	—	—	—
4b	100	09	—	—	—
	200	12	11	—	—
4c	100	—	—	—	—
	200	09	—	—	—
8a	100	21	19	14	13
	200	25	23	18	17
8b	100	32	32	25	22
	200	38	36	27	26
8c	100	30	28	21	20
	200	34	32	25	23
9a	100	16	17	11	10
	200	18	19	14	13
9b	100	19	20	13	14
	200	22	23	15	16
9c	100	16	17	12	10
	200	19	18	14	13
10a	100	21	20	16	17
	200	24	23	18	19
10b	100	32	29	23	21
	200	36	34	25	24
10c	100	27	29	19	18
	200	30	32	22	21
Chloramphenicol	100	35	38	40	42
	200	39	41	44	45

Table 2. Antifungal Activity of **3**, **4**, **8**—**10**

Compound	Concentration (μg)	Zone of inhibition (mm)		
		F. solani	*C. lunata*	*A. niger*
3a	100	14	12	15
	200	17	14	18
3b	100	16	13	12
	200	19	16	16
3c	100	13	13	14
	200	15	16	16
4a	100	12	13	14
	200	16	16	17
4b	100	15	14	12
	200	17	16	15
4c	100	11	10	13
	200	14	12	17
8a	100	27	27	30
	200	32	33	34
8b	100	36	39	31
	200	39	41	34
8c	100	33	33	32
	200	35	37	36
9a	100	15	14	18
	200	20	19	22
9b	100	17	18	15
	200	22	23	18
9c	100	19	15	16
	200	20	22	20
10a	100	23	22	21
	200	27	26	25
10b	100	26	26	27
	200	30	29	31
10c	100	24	27	24
	200	27	30	29
Ketoconazole	100	38	41	36
	200	42	44	39

Table 3. Minimal Inhibitory Concentrations (MIC, μg/ml) of Compounds **8b** and **10b**

Compound	Minimal inhibitory concentration (MIC, μg/ml)						
	S. aureus	*B. subtilis*	*E. coli*	*K. pneumoniae*	*F. solani*	*C. lunata*	*A. niger*
8b	25	50	50	50	50	25	25
10b	50	100	100	100	100	100	100
Chloramphenicol	6.25	6.25	6.25	12.5	—	—	—
Ketoconazole	—	—	—	—	12.5	6.25	6.25

tion that completely inhibited visible growth of the microorganisms (Table 3). The structure–antimicrobial activity relationship of the tested compounds revealed that disubstituted pyrazole and trisubstituted isoxazole in combination with pyrrole displayed greater activity. The compounds having tetrasubstituted pyrazole with pyrrole exhibited least activity. The maximum activity was observed with the compounds **8b** and **10b**.

Conclusion

A new class of sulfone-linked bis heterocycles, methyl-3-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**8**), methyl-3-(1′-phenyl-3′,5′-diaryl-1′*H*-pyrazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**9**) and methyl-3-(3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (**10**) were prepared by the regioselective reaction of methyl-3-aryl-2-(*E*-arylethenesulfonyl)acrylate (**2**) with TosMIC followed by functionalization of olefin moiety towards 1,3-dipolar cycloaddition reaction with diazomethane, nitrile imines and nitrile oxides. The antimicrobial testing showed that the compounds **8b** and **10b** exhibited greater antimicrobial activity.

Experimental

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 3 : 1). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^{1}H-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM λ-300 MHz. The ^{13}C-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 75.5 MHz. All chemical shifts were reported in δ (ppm) using TMS as an

internal standard. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer. The starting compound *E*-styrylsulfonylacetic acid methyl ester (**1**) was prepared as per the literature procedure.[29]

General Procedure of Synthesis of Methyl-3-aryl-2-(*E*-arylethenesulfonyl)acrylate (2a—c) To an equimolar (0.01 mol) mixture of *E*-styrylsulfonylacetic acid methyl ester **1**, araldehyde and absolute ethanol (10 ml), piperidine (0.3 ml) was added and refluxed for 6—8 h. The solid separated on cooling was collected and recrystallized from 2-propanol.

Methyl-3-phenyl-2-(*E*-phenylethenesulfonyl)acrylate (**2a**): White solid, yield 66%, mp 97—99 °C; IR (KBr) cm^{-1}: 1733 (C=O), 1634 (C=C), 1332, 1131 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.81 (s, 3H, OCH_3), 6.58 (d, 1H, H_B, J=14.2 Hz), 7.68 (d, 1H, H_A, J=14.2 Hz), 7.98 (s, 1H, H_C), 7.11—7.59 (m, 10H, Ar, Ar′-H); ^{13}C-NMR ($CDCl_3$) δ: 54.8 (OCH_3), 125.4 (=$CHSO_2$), 129.7 (SO_2-C=(CO_2Me), 142.1 (=CH-Ar′), 145.4 (=CH-Ar), 172.4 (C=O), 128.6, 129.2, 129.4, 130.6, 131.8, 132.4, 131.9, 133.1 (aromatic carbons).

Methyl-3-(*p*-chorophenyl)-2-(*E*-phenylethenesulfonyl)acrylate (**2b**): White solid, yield 74%, mp 129—131 °C; IR (KBr) cm^{-1}: 1735 (C=O), 1632 (C=C), 1333, 1129 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.79 (s, 3H, OCH_3), 6.56 (d, 1H, H_B, J=14.1 Hz), 7.61 (d, 1H, H_A, J=14.1 Hz), 7.95 (s, 1H, H_C), 7.36—7.64 (m, 9H, Ar, Ar′-H); ^{13}C-NMR ($CDCl_3$) δ: 52.8 (OCH_3), 124.7 (=$CHSO_2$), 129.3 (SO_2-C=(CO_2Me), 142.8 (=CH-Ar′), 145.2 (=CH-Ar), 174.3 (C=O), 128.8, 129.4, 129.9, 131.4, 131.8, 132.0, 132.4, 132.8 (aromatic carbons).

Methyl-3-(*p*-chorophenyl)-2-(*E*-(*p*-methylphenyl)ethenesulfonyl)acrylate (**2c**): White crystals, yield 69%, mp 112—114 °C; IR (KBr) cm^{-1}: 1744 (C=O), 1636 (C=C), 1326, 1130 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 2.29 (s, Ar-CH_3), 3.82 (s, 3H, OCH_3), 6.68 (d, 1H, H_B, J=14.4 Hz), 7.67 (d, 1H, H_A, J=14.4 Hz), 7.89 (s, 1H, H_C), 7.26—7.55 (m, 8H, Ar, Ar′-H); ^{13}C-NMR ($CDCl_3$) δ: 21.6 (Ar-CH_3), 53.9 (OCH_3), 125.9 (=$CHSO_2$), 127.9 (SO_2-C=(CO_2Me), 143.9 (=CH-Ar′), 146.4 (=CH-Ar), 173.8 (C=O), 128.2, 128.8, 129.6, 130.4, 130.8, 131.6, 132.0, 135.4 (aromatic carbons).

General Procedure of Synthesis of Methyl-3-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (3) and Methyl-4-aryl-3-(arylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (4) (Method 1) A mixture of TosMIC (0.01 mol) and methyl 3-aryl-2-(*E*-arylethenesulfonyl)acrylate **2** (0.005 mol) in Et_2O–DMSO (2 : 1) was added dropwise under stirring to a suspension of NaH (50 mg) in Et_2O (10 ml) at room temperature and stirring was continued for 5—6 h. Then, water was added and extracted with Et_2O. The ethereal fraction was dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo*. The resulting mixture was separated by column chromatography (hexane–ethyl acetate; 4 : 1) and identified as methyl 3-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate **3** (minor) and methyl-4-aryl-3-(arylethenesulfonyl)-3*H*-pyrrole-3-carboxylate **4** (major).

General Procedure of Synthesis of Methyl-3-(4′-aryl-1′*H*-pyrrol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (3a—c) (Method 2) The compound **3** was also prepared by adding a mixture of TosMIC (0.02 mol) and methyl 3-aryl-2-(*E*-arylethenesulfonyl)acrylate **2** (0.005 mol) in Et_2O–DMSO (2 : 1) was added dropwise under stirring to a suspension of NaH (50 mg) in Et_2O (10 ml) at room temperature and stirring was continued for 5—6 h. Then, water was added and extracted with Et_2O. The ethereal fraction was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The resulting solid was purified by column chromatography (hexane–ethyl acetate; 4 : 1.5).

Methyl-3-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**3a**): Pale yellow solid, yield 70%, mp 156—158 °C; IR (KBr) cm^{-1}: 3320 (NH), 1736 (C=O), 1582 (C=N), 1330, 1126 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.69 (s, 3H, OCH_3), 6.78 (s, 1H, $C_{2'}$-H,) 7.01, 7.09 (s, 2H, $C_{5'}$-H, C_5-H), 7.19 (s, 1H, C_2-H), 7.21—7.62 (m, 10H, Ar, Ar′-H), 8.71 (br s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ: 53.2 (OCH_3), 76.8 (C-3), 117.5, 118.3 (C-4′, C-4), 121.6 (C-3′), 123.5, 125.2 (C-5′, C-5), 127.0, (C-2′) 157.8 (C-2), 164.2 (C=O), 128.6, 129.3, 130.2, 131.6, 132.3, 133.5, 134.6, 135.9 (aromatic carbons): *Anal.* Calcd for $C_{22}H_{18}N_2O_4S$: C, 65.01; H, 4.46; N, 6.89; Found: C, 65.12; H, 4.47; N, 6.93.

Methyl-3-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**3b**): Yellow solid, yield 67%, mp 174—176 °C; IR (KBr) cm^{-1}: 3323 (NH), 1738 (C=O), 1568 (C=N), 1339, 1126 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.74 (s, 3H, OCH_3), 6.85 (s, 1H, $C_{2'}$-H), 6.92, 7.06 (s, 2H, $C_{5'}$-H, C_5-H), 7.22 (s, 1H, $C_{2'}$-H), 7.26—7.63 (m, 9H, Ar, Ar′-H), 8.88 (br s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ: 53.8 (OCH_3), 77.6 (C-3), 116.2, 118.9 (C-4′, C-4), 120.8 (C-3′), 123.9, 126.4 (C-5′, C-5), 127.6, (C-2′) 157.4 (C-2), 165.7 (C=O), 128.0, 129.7, 130.3, 131.0, 131.9, 132.7, 133.7, 135.3 (aromatic carbons): *Anal.* Calcd for $C_{22}H_{17}ClN_2O_4S$: C, 59.93; H, 3.89; N, 6.35; Found: C, 59.97; H, 3.86; N, 6.39.

Methyl-3-(4′-(*p*-methylphenyl)-1′*H*-pyrrol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**3c**): Yellow solid, yield 74%, mp 149—151 °C; IR (KBr) cm^{-1}: 3342 (NH), 1744 (C=O), 1562 (C=N), 1128, 1333 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.21 (s, 3H, Ar-CH_3), 3.67 (s, 3H, OCH_3), 6.76 (s, 1H, $C_{2'}$-H), 6.89, 7.05 (s, 2H, $C_{5'}$-H, C_5-H), 7.17 (s, 1H, C_2-H) 7.21-7.68 (m, 8H, Ar, Ar′-H), 8.81 (br s, 1H, NH); ^{13}C-NMR (DMSO-d_6) δ: 22.4 (Ar-CH_3), 53.1 (OCH_3), 76.9 (C-3), 115.5, 117.1 (C-4′, C-4), 120.7 (C-3′), 124.3, 126.9 (C-5′, C-5), 124.3, (C-2′) 156.2 (C-2), 162.8 (C=O), 128.4, 129.6, 130.2, 131.9, 132.6, 133.2, 133.9, 136.6 (aromatic carbons): *Anal.* Calcd for $C_{23}H_{19}ClN_2O_4S$: C, 60.72; H, 4.21; N, 6.16; Found: C, 60.63; H, 4.16; N, 6.20.

General Procedure of Synthesis of Methyl-4-aryl-3-(arylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (4a—c) (Method 3) The compound **4** was also obtained by adding an equimolar (0.005 mol) mixture of 3-aryl-2-(*E*-arylethenesulfonyl)acrylate **2** and TosMIC in Et_2O–DMSO (2 : 1) dropwise under stirring to a suspension of NaH (25 mg) in Et_2O (6 ml) at room temperature. Stirring was continued for 4—5 h. Then, the contents were diluted with water and extracted with Et_2O. The ethereal layer was dried over anhydrous Na_2SO_4. The solvent was removed under vacuum. The resultant solid was purified by column chromatography (ethyl acetate/hexane, 1 : 4).

Methyl-4-phenyl-3-(phenylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (**4a**): Yellow solid, yield 72%, mp 133—135 °C; IR (KBr) cm^{-1}: 1731 (C=O), 1635 (C=C), 1569 (C=N), 1337, 1121 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.64 (s, 3H, OCH_3), 6.59 (d, 1H, H_B, J=14.1 Hz), 7.01 (s, 1H, C_5-H), 7.14 (s, 1H, C_2-H), 7.72 (d, 1H, H_A, J=14.1 Hz), 7.19—7.66 (m, 10H, Ar, Ar′-H); ^{13}C-NMR (DMSO-d_6) δ: 52.7 (OCH_3), 76.4 (C-3), 117.9 (C-4), 124.8 (C-5), 125.4 (=$CHSO_2$), 145.4 (=CH-Ar), 156.6 (C-2), 163.2 (C=O), 127.6, 129.1, 130.7, 131.4, 132.3, 133.0, 133.6, 134.2 (aromatic carbons): *Anal.* Calcd for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81; Found: C, 65.26; H, 4.69; N, 3.85.

Methyl-4-(*p*-chlorophenyl)-3-(phenylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (**4b**): Yellow solid, yield 76%, mp 146—148 °C; IR (KBr) cm^{-1}: 1748 (C=O), 1641 (C=C), 1572 (C=N), 1326, 1138 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.62 (s, 3H, OCH_3), 6.62 (d, 1H, H_B, J=14.0 Hz), 7.08 (s, 1H, C_5-H), 7.18 (s, 1H, C_2-H), 7.76 (d, 1H, H_A, J=14.0 Hz), 7.24—7.71 (m, 9H, Ar, Ar′-H); ^{13}C-NMR (DMSO-d_6) δ: 53.5 (–OCH_3), 77.9 (C-3), 117.0 (C-4), 125.9 (C-5), 124.1 (=$CHSO_2$), 145.9 (=CH-Ar), 157.0 (C-2), 162.5 (C=O), 128.6, 129.2, 129.9, 130.6, 131.9, 132.6, 133.4, 135.7 (aromatic carbons): *Anal.* Calcd for $C_{20}H_{16}ClNO_4S$: C, 59.78; H, 4.01; N, 3.49; Found: C, 59.84; H, 4.05; N, 3.46.

Methyl-4-(*p*-chlorophenyl)-3-(*p*-methylphenylethenesulfonyl)-3*H*-pyrrole-3-carboxylate (**4c**): Yellow solid, yield 75%, mp 157—159 °C; IR (KBr) cm^{-1}: 1731 (C=O), 1634 (C=C), 1565 (C=N), 1330, 1122 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.22 (s, 3H, Ar-CH_3), 3.69 (s, 3H, OCH_3), 6.59 (d, 1H, H_B, J=14.1 Hz), 6.99 (s, 1H, C_5-H), 7.11 (s, 1H, C_2-H), 7.71 (d, 1H, H_A, J=14.1 Hz), 7.22—7.69 (m, 8H, Ar, Ar′-H); ^{13}C-NMR (DMSO-d_6) δ: 22.6 (Ar-CH_3), 54.1 (OCH_3), 76.3 (C-3), 116.8 (C-4), 124.6 (C-5), 124.9 (=$CHSO_2$), 146.8 (=CH-Ar), 156.4 (C-2), 163.9 (C=O), 128.0, 129.4, 129.3, 130.9, 131.6, 132.3, 134.5, 135.9 (aromatic carbons): *Anal.* Calcd for $C_{21}H_{18}ClNO_4S$: C, 60.65; H, 4.36; N, 3.37; Found: C, 60.73; H, 4.41; N, 3.41.

General Procedure of Synthesis of Methyl-3-(4′,5′-dihydro-4′-aryl-1*H*-pyrazol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (5a—c) To a cooled solution of **4** (0.005 mol) in dichloromethane (20 ml), an ethereal solution of diazomethane (40 ml, 0.4 M) and triethylamine (0.12 g) were added. The reaction mixture was kept at −20 to −15 °C for 40—48 h. The solvent was removed under reduced pressure and the resultant solid was recrystsllized from 2-propanol.

Methyl-3-(4′,5′-dihydro-4′-phenyl-1*H*-pyrazol-3′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**5a**): Yellow solid, yield 82%, mp 169—171 °C; IR (KBr) cm^{-1}: 3347 (NH), 1742 (C=O), 1569 (C=N), 1336, 1131 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.75 (s, 3H, OCH_3), 3.88 (dd, 1H, H_X, J_{AX}=4.0 Hz, J_{MX}=8.0 Hz), 4.24 (dd, 1H, H_M, J_{AM}=12.0 Hz), 4.57 (dd, 1H, H_A), 7.04 (s, 1H, C_5-H), 7.17 (s, 1H, C_2-H), 7.25—7.61 (m, 10H, Ar, Ar′-H), 10.51 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$) δ: 49.9 (C-5′), 53.1 (OCH_3), 59.6 (C-4′), 77.4 (C-3), 117.4 (C-4), 125.3 (C-5), 150.5 (C-3′), 156.4 (C-2), 162.7 (C=O), 127.4, 128.1, 128.8, 129.3, 130.4, 131.3, 133.6, 134.2 (aromatic carbons): *Anal.* Calcd for $C_{21}H_{19}N_3O_4S$: C, 61.60; H, 4.68; N, 10.26; Found: C, 61.69; H, 4.72; N, 10.33.

Methyl-3-(4′,5′-dihydro-4′-phenyl-1*H*-pyrazol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**5b**): Yellow solid, yield 77%, mp 155—157 °C; IR (KBr) cm^{-1}: 3333 (NH), 1740 (C=O), 1583 (C=N), 1329, 1130 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.68 (s, 3H, OCH_3), 3.81 (dd, 1H, H_X, J_{AX}=3.9 Hz, J_{MX}=7.8 Hz), 4.21 (dd, 1H, H_M, J_{AM}=11.7 Hz), 4.51 (dd, 1H,

H_A), 6.98 (s, 1H, C_5-H), 7.13 (s, 1H, C_2-H), 7.22—7.73 (m, 9H, Ar, Ar′-H), 10.46 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$) δ: 50.5 (C-5′), 53.9 (OCH_3), 60.7 (C-4′), 76.3 (C-3), 116.8 (C-4), 124.7 (C-5), 151.7 (C-3′), 156.9 (C-2), 163.5 (C=O), 127.9, 128.0, 128.6, 129.2, 131.7, 132.8, 137.9, 138.2 (aromatic carbons): *Anal.* Calcd for $C_{21}H_{18}ClN_3O_4S$: C, 56.82; H, 4.09; N, 9.47; Found: C, 56.85; H, 4.07; N, 9.53.

Methyl-3-(4′,5′-dihydro-4′-(*p*-methylphenyl)-1*H*-pyrazol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**5c**): Yellow solid, yield 83%, mp 182—184 °C; IR (KBr) cm^{-1}: 3332 (NH), 1742 (C=O), 1575 (C=N), 1339, 1142 (SO_2); ^{1}H-NMR ($CDCl_3$+DMSO-d_6) δ: 2.31 (s, 3H, Ar-CH_3), 3.79 (s, 3H, OCH_3), 3.85 (dd, 1H, H_X, J_{AX}=4.3 Hz, J_{MX}=8.4 Hz), 4.23 (dd, 1H, H_M, J_{AM}=12.3 Hz), 4.54 (dd, 1H, H_A), 6.93 (s, 1H, C_5-H), 7.19 (s, 1H, C_2-H), 7.27—7.88 (m, 8H, Ar, Ar′-H), 10.11 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$+DMSO-d_6) δ: 22.4 (Ar-CH_3), 50.9 (C-5′), 54.2 (OCH_3), 61.2 (C-4′), 75.8 (C-3), 117.5 (C-4), 125.3 (C-5), 151.0 (C-3′), 155.8 (C-2), 162.3 (C=O), 128.5, 129.7, 130.8, 131.2, 132.9, 133.4, 135.4, 138.5 (aromatic carbons): *Anal.* Calcd for $C_{22}H_{20}ClN_3O_4S$: C, 57.70; H, 4.40; N, 9.18; Found: C, 57.60; H, 4.45; N, 9.24.

General Procedure of Synthesis of Methyl-3-(4′,5′-dihydro-1′-phenyl-3′,5′-diaryl-pyrazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (6a—c) A mixture of **4** (0.001 mol), araldehyde phenylhydrazone (0.0012 mol) and chloramine-T (0.0012 mol) in methanol (15 ml) was refluxed for 12—14 h. The precipitated inorganic salts were filtered off. The filtrate was concentrated and the residue was extracted with dichloromethane. The organic layer was washed with water, brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. Recrystallization of crude product from ethanol resulted in pure compound.

Methyl-3-(4′,5′-dihydro-1′,3′,5′-triphenyl-pyrazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**6a**): White solid, yield 67%, mp 202—204 °C; IR (KBr) cm^{-1}: 1749 (C=O), 1580 (C=N), 1328, 1123 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.68 (s, 3H, OCH_3), 5.21 (d, 1H, $C_{4'}$-H, J=6.5 Hz), 5.58 (d, 1H, $C_{5'}$-H, J=6.5 Hz), 7.02 (s, 1H, C_5-H), 7.16 (s, 1H, C_2-H), 7.19—7.79 (m, 20H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 53.3 (OCH_3), 62.4 (C-4′), 76.4 (C-3), 87.3 (C-5′), 116.8 (C-4), 126.6 (C-5), 155.8 (C-3′), 156.3 (C-2), 163.4 (C=O), 127.9, 128.3, 128.6, 129.3, 129.9, 130.4, 131.3, 132.9, 133.6, 134.6 (aromatic carbons): *Anal.* Calcd for $C_{33}H_{27}N_3O_4S$: C, 70.57; H, 4.85; N, 7.48; Found: C, 70.45; H, 4.91; N, 7.42.

Methyl-3-(4′,5′-dihydro-1′,5′-diphenyl-3′-(*p*-chlorophenyl)-pyrazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**6b**): White solid, yield 65%, mp 214—216 °C; IR (KBr) cm^{-1}: 1739 (C=O), 1567 (C=N), 1335, 1133 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.64 (s, 3H, OCH_3), 5.26 (d, 1H, $C_{4'}$-H, J=6.9 Hz), 5.62 (d, 1H, $C_{5'}$-H, J=6.9 Hz), 7.05 (s, 1H, C_5-H), 7.21 (s, 1H, C_2-H), 7.27—7.74 (m, 18H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 54.2 (OCH_3), 61.3 (C-4′), 76.9 (C-3), 86.7 (C-5′), 115.6 (C-4), 125.8 (C-5), 155.2 (C-3′), 157.4 (C-2), 162.9 (C=O), 128.1, 128.3, 129.4, 129.9, 130.9, 131.9, 132.1, 133.9, 134.8, 135.6 (aromatic carbons): *Anal.* Calcd for $C_{33}H_{25}Cl_2N_3O_4S$: C, 62.86; H, 4.00; N, 6.66; Found: C, 62.79; H, 4.05; N, 6.72.

Methyl-3-(4′,5′-dihydro-1′-phenyl-3′-(*p*-chlorophenyl)-5′-(*p*-methylphenyl)-pyrazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**6c**): White solid, yield 62 %, mp 235—237 °C; IR (KBr) cm^{-1}: 1748 (C=O), 1565 (C=N), 1336, 1135 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.23 (s, 3H, Ar-CH_3), 3.61 (s, 3H, OCH_3), 5.29 (d, 1H, $C_{4'}$-H, J=6.7 Hz), 5.68 (d, 1H, $C_{5'}$-H, J=6.7 Hz), 6.96 (s, 1H, C_5-H), 7.18 (s, 1H, C_2-H), 7.25—7.87 (m, 17H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 21.6 (Ar-CH_3), 53.9 (OCH_3), 61.6 (C-4′), 77.3 (C-3), 85.9 (C-5′), 114.7 (C-4), 126.3 (C-5), 155.9 (C-3′), 156.1 (C-2), 164.7 (C=O), 128.4, 128.8, 129.2, 129.4, 130.3, 131.6, 132.3, 132.1, 133.2, 136.9 (aromatic carbons): *Anal.* Calcd for $C_{34}H_{27}Cl_2N_3O_4S$: C, 63.35; H, 4.22; N, 6.52; Found: C, 63.41; H, 4.19; N, 6.57.

General Procedure of Synthesis of Methyl-3-(4′,5′-dihydro-3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (7a—c) A mixture of **4** (0.001 mol), araldoxime (0.0012 mol) and chloramine-T (0.0012 mol) in methanol (15 ml) was refluxed for 8—10 h. The precipitated inorganic salts were filtered off. The filtrate was concentrated and the residue was extracted with dichloromethane. The organic layer was washed with water, brine and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo*. The solid obtained was purified by recrystallization from ethanol.

Methyl-3-(4′,5′-dihydro-3′,5′-diphenylisoxazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**7a**): White solid, yield 69%, mp 197—199 °C; IR (KBr) cm^{-1}: 1742 (C=O), 1572 (C=N), 1325, 1138 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.72 (s, 3H, OCH_3), 5.16 (d, 1H, $C_{4'}$-H, J=5.6 Hz), 5.75 (d, 1H, $C_{5'}$-H, J=5.6 Hz), 6.99 (s, 1H, C_5-H), 7.10 (s, 1H, C_2-H), 7.15—7.76 (m, 15H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 54.3 (–OCH_3), 63.7 (C-4′), 76.6 (C-3), 84.3 (C-5′), 115.1 (C-4), 125.4 (C-5), 156.4 (C-3′), 156.7 (C-2), 163.9 (C=O), 128.1, 129.7, 130.9, 132.3, 132.9, 133.2, 134.6, 135.1 (aromatic carbons): *Anal.* Calcd for $C_{27}H_{22}N_2O_5S$: C, 66.65; H, 4.56; N, 5.76; Found: C, 66.72; H, 4.55; N, 5.82.

Methyl-3-(4′,5′-dihydro-3′-(*p*-chlorophenyl)-5′-phenylisoxazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**7b**): White solid, yield 63%, mp 169—171 °C; IR (KBr) cm^{-1}: 1743 (C=O), 1571 (C=N), 1317, 1140 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.75 (s, 3H, OCH_3), 5.22 (d, 1H, $C_{4'}$-H, J=5.8 Hz), 5.79 (d, 1H, $C_{5'}$-H, J=5.8 Hz), 7.02 (s, 1H, C_5-H), 7.18 (s, 1H, C_2-H), 7.22—7.89 (m, 13H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 53.2 (–OCH_3), 62.8 (C-4′), 75.8 (C-3), 83.8 (C-5′), 116.3 (C-4), 125.1 (C-5), 156.2 (C-3′), 157.8 (C-2), 162.7 (C=O), 128.1, 129.6, 131.9, 132.5, 134.2, 135.1, 136.8, 137.1 (aromatic carbons): *Anal.* Calcd for $C_{27}H_{20}Cl_2N_2O_5S$: C, 58.39; H, 3.63; N, 5.04; Found: C, 58.30; H, 3.67; N, 5.00.

Methyl-3-(4′,5′-dihydro-3′-(*p*-chlorophenyl)-5′-(*p*-methylphenyl)isoxazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**7c**): White solid, yield 67%, mp 222—224 °C; IR (KBr) cm^{-1}: 1746 (C=O), 1567 (C=N), 1321, 1131 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.27 (s, 3H, Ar-CH_3), 3.69 (s, 3H, OCH_3), 5.25 (d, 1H, $C_{4'}$-H, J=5.7 Hz), 5.77 (d, 1H, $C_{5'}$-H, J=5.7 Hz), 7.06 (s, 1H, C_5-H), 7.13 (s, 1H, C_2-H), 7.25—7.86 (m, 12H, Ar-H); ^{13}C-NMR (DMSO-d_6) δ: 22.7 (Ar-CH_3), 53.9 (OCH_3), 63.4 (C-4′), 75.0 (C-3), 82.5 (C-5′), 115.3 (C-4), 126.2 (C-5), 156.8 (C-3′), 158.1 (C-2), 163.3 (C=O), 128.6, 129.5, 130.9, 131.6, 132.3, 134.4, 136.5, 138.6 (aromatic carbons): *Anal.* Calcd for $C_{28}H_{22}Cl_2N_2O_5S$: C, 59.06; H, 3.89; N, 4.92; Found: C, 59.01; H, 3.87; N, 4.85.

General Procedure of Synthesis of Methyl-3-(4′-aryl-1′*H*-pyrazol-3′-ylsulfonyl)-4-aryl-3*H*-pyrrole-3-carboxylate (8a—c)/Methyl-3-(1′-phenyl-3′,5′-diaryl-1*H*-pyrazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (9a—c)/Methyl-3-(3′,5′-diarylisoxazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (10a—c) A solution of **5**/**6**/**7** (0.001 mol) and chloranil (0.0014 mol) in xylene (10 ml) was refluxed for 24—32 h. Then, the reaction mixture was treated with a 5% NaOH solution. The organic layer was separated and repeatedly washed with water. It was dried over anhydrous Na_2SO_4 and the solvent was removed on a rotary evaporator. The resultant solid was purified by recrystallization from 2-propanol.

Methyl-3-(4′-phenyl-1′*H*-pyrazol-3′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**8a**): White solid, yield 74%, mp 211—213 °C; IR (KBr) cm^{-1}: 3331 (NH), 1739 (C=O), 1574 (C=N), 1329, 1125 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.62 (s, 3H, –OCH_3), 6.99 (s, 1H, C_5-H), 7.19 (s, 1H, C_2-H), 7.21—7.65 (m, 11H, C_5′-H, Ar, Ar′-H), 8.98 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$) δ: 54.3 (OCH_3), 77.4 (C-3), 116.1 (C-4), 125.3 (C-5), 134.3 (C-5′), 138.6 (C-4′), 155.4 (C-3′), 157.6 (C-2), 162.9 (C=O), 128.2, 129.2, 130.6, 131.4, 132.0, 133.2, 134.5, 135.7 (aromatic carbons): *Anal.* Calcd for $C_{21}H_{17}N_3O_4S$: C, 61.90; H, 4.21; N, 10.31; Found: C, 61.96; H, 4.26; N, 10.38.

Methyl-3-(4′-phenyl-1′*H*-pyrazol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**8b**): White solid, yield 77%, mp 217—219 °C; IR (KBr) cm^{-1}: 3334 (NH), 1742 (C=O), 1570 (C=N), 1334, 1126 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 3.65 (s, 3H, OCH_3), 7.01 (s, 1H, C_5-H), 7.15 (s. 1H, C_2-H), 7.23—7.85 (m, 10H, C_5′-H, Ar, Ar′-H), 8.89 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$) δ: 53.6 (–OCH_3), 76.8 (C-3), 117.5 (C-4), 126.8 (C-5), 133.1 (C-5′), 138.7 (C-4′), 154.7 (C-3′), 156.6 (C-2), 163.7 (C=O), 128.1, 129.0, 129.8, 130.5, 131.1, 133.1, 134.9, 135.7 (aromatic carbons): *Anal.* Calcd for $C_{21}H_{16}ClN_3O_4S$: C, 57.08; H, 3.65; N, 9.51; Found: C, 57.12; H, 3.62; N, 9.47.

Methyl-3-(4′-(*p*-methylphenyl)-1′*H*-pyrazol-3′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**8c**): White solid, yield 78%, mp 236—238 °C; IR (KBr) cm^{-1}: 3339 (NH), 1748 (C=O), 1584 (C=N), 1331, 1139 (SO_2); ^{1}H-NMR ($CDCl_3$) δ: 2.27 (s, 3H, Ar-CH_3), 3.67 (s, 3H, OCH_3), 7.04 (s, 1H, C_5-H), 7.11 (s, 1H, C_2-H), 7.25—7.84 (m, 9H, C_5′-H, Ar, Ar′-H), 8.80 (br s, 1H, NH); ^{13}C-NMR ($CDCl_3$) δ: 22.4 (Ar-CH_3), 54.3 (–OCH_3), 76.2 (C-3), 118.2 (C-4), 125.6 (C-5), 132.5 (C-5′), 137.2 (C-4′), 155.9 (C-3′), 157.9 (C-2), 163.0 (C=O), 129.5, 130.9, 131.6, 132.3, 133.0, 134.9, 135.7, 136.1 (aromatic carbons): *Anal.* Calcd for $C_{22}H_{18}ClN_3O_4S$: C, 57.96; H, 3.98; N, 9.22; Found: C, 58.03; H, 3.94; N, 9.26.

Methyl-3-(1′,3′,5′-triphenyl-1*H*-pyrazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**9a**): Pale yellow solid, yield 78%, mp 221—223 °C; IR (KBr) cm^{-1}: 1739 (C=O), 1582 (C=N), 1327, 1135 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.64 (s, 3H, OCH_3), 6.99 (s, 1H, C_5-H), 7.17 (s, 1H, C_2-H), 7.19—7.79 (m, 20H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 53.9 (OCH_3), 77.4 (C-3), 116.3 (C-4), 124.7 (C-5), 145.4 (C-3′), 147.4 (C-4′), 150.6 (C-5′), 155.8 (C-2), 162.6 (C=O), 128.3, 128.7, 129.1, 130.5, 131.4, 132.0, 132.7, 133.0, 134.2 (aromatic carbons): *Anal.* Calcd for $C_{33}H_{25}N_3O_4S$: C, 70.82; H,

4.50; N, 7.51; Found: C, 70.86; H, 4.55; N, 7.49.

Methyl-3-(1′,5′-diphenyl-3′-(*p*-cholorophenyl)-1*H*-pyrazol-4′-ylsulfonyl)-4-(*p*-cholorophenyl)-3*H*-pyrrole-3-carboxylate (**9b**): Yellow solid, yield 70%, mp 252—254 °C; IR (KBr) cm^{-1}: 1736 (C=O), 1561 (C=N), 1321, 1137 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.73 (s, 3H, OCH_3), 6.96 (s, 1H, C_5-H), 7.12 (s, 1H, C_2-H), 7.21—7.85 (m, 18H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 54.2 (–OCH_3), 76.4 (C-3), 118.2 (C-4), 125.3 (C-5), 145.9 (C-3′), 147.9 (C-4′), 151.2 (C-5′), 157.8 (C-2), 163.9 (C=O), 128.4, 128.6, 129.5, 129.7, 130.3, 131.8, 132.3, 133.4, 133.9, 135.6, 136.1 (aromatic carbons): *Anal.* Calcd for $C_{33}H_{23}Cl_2N_3O_4S$: C, 63.06; H, 3.69; N, 6.69; Found: C, 63.00; H, 3.73; N, 6.73.

Methyl-3-(1′-phenyl-5′-(*p*-methylphenyl)-3′-(*p*-cholorophenyl)-1*H*-pyrazol-4′-ylsulfonyl)-4-(*p*-cholorophenyl)-3*H*-pyrrole-3-carboxylate (**9c**): Yellow solid, yield 76%, mp 285—287 °C; IR (KBr) cm^{-1}: 1748 (C=O), 1572 (C=N), 1339, 1145 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.22 (s, 3H, Ar-CH_3), 3.70 (s, 3H, –OCH_3), 6.99 (s, 1H, C_5-H), 7.19 (s, 1H, C_2-H), 7.26—7.89 (m, 17H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 53.7 (OCH_3), 76.8 (C-3), 118.7 (C-4), 126.1 (C-5), 146.3 (C-3′), 148.4 (C-4′), 150.6 (C-5′), 155.6 (C-2), 164.1 (C=O), 128.2, 128.6, 129.3, 130.4, 130.8, 131.2, 132.6, 133.9, 134.6, 135.5, 136.9, 137.3 (aromatic carbons): *Anal.* Calcd for $C_{34}H_{25}Cl_2N_3O_4S$: C, 63.55; H, 3.92; N, 6.54; Found: C, 63.49; H, 3.85; N, 6.62.

Methyl-3-(3′,5′-diphenylisoxazol-4′-ylsulfonyl)-4-phenyl-3*H*-pyrrole-3-carboxylate (**10a**): White solid, yield 70%, mp 218—220 °C; IR (KBr) cm^{-1}: 1741 (C=O), 1577 (C=N), 1332, 1134 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.69 (s, 3H, OCH_3), 6.96 (s, 1H, C_5-H), 7.11 (s, 1H, C_2-H), 7.19—7.74 (m, 15H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 54.3 (OCH_3), 77.0 (C-3), 117.9 (C-4), 126.6 (C-5), 146.6 (C-4′), 147.6 (C-3′), 153.1 (C-5′), 157.4 (C-2), 164.9 (C=O), 129.1, 130.5, 131.4, 132.0, 132.7, 133.0, 133.7 134.2 (aromatic carbons): *Anal.* Calcd for $C_{27}H_{20}N_2O_5S$: C, 66.93; H, 4.16; N, 5.78; Found: C, 66.97; H, 4.19; N, 5.83.

Methyl-3-(3′-(*p*-chlorophenyl)-5′-phenylisoxazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**10b**): White solid, yield 74%, mp 243—245 °C; IR (KBr) cm^{-1}: 1745 (C=O), 1570 (C=N), 1325, 1140 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 3.71 (s, 3H, CO_2CH_3), 7.04 (s, 1H, C_5-H), 7.17 (s, 1H, C_2-H), 7.25—7.82 (m, 13H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 53.9 (–OCH_3), 77.5 (C-3), 116.5 (C-4), 125.7 (C-5), 144.7 (C-4′), 147.3 (C-3′), 151.2 (C-5′), 156.7 (C-2), 163.3 (C=O), 128.6, 129.7, 130.3, 131.8, 132.3, 133.9, 135.6, 136.1 (aromatic carbons): *Anal.* Calcd for $C_{27}H_{18}Cl_2N_2O_5S$: C, 58.60; H, 3.28; N, 5.06; Found: C, 58.55; H, 3.24; N, 5.09.

Methyl-3-(3′-(*p*-chlorophenyl)-5′-(4-methylphenyl)isoxazol-4′-ylsulfonyl)-4-(*p*-chlorophenyl)-3*H*-pyrrole-3-carboxylate (**10c**): White solid, yield 76%, mp 267—269 °C; IR (KBr) cm^{-1}: 1743 (C=O), 1562 (C=N), 1327, 1137 (SO_2); ^{1}H-NMR (DMSO-d_6) δ: 2.27 (s, 3H, Ar-CH_3), 3.75 (s, 3H, CO_2CH_3), 7.00 (s, 1H, C_5-H), 7.12 (s, 1H, C_2-H), 7.19—7.84 (m, 12H, Ar, Ar′, Ar″-H); ^{13}C-NMR (DMSO-d_6) δ: 22.8 (Ar-CH_3), 54.5 (–OCH_3), 76.7 (C-3), 115.7 (C-4), 126.1 (C-5), 145.9 (C-4′), 147.9 (C-3′), 152.8 (C-5′) 156.1 (C-2), 162.6 (C=O), 128.1, 129.0, 129.8, 130.5, 131.1, 132.4, 133.1, 134.9 (aromatic carbons): *Anal.* Calcd for $C_{28}H_{20}Cl_2N_2O_5S$: C, 59.27; H, 3.55; N, 4.94; Found: C, 59.35; H, 3.50; N, 4.99.

Antimicrobial Testing The compounds **3**, **4**, **8**—**10** were dissolved in DMSO at different concentrations of 100, 200 and 800 μg/ml.

Antibacterial and Antifungal Assays Preliminary antimicrobial activity of compounds **3**, **4**, **8**—**10** was tested by agar disc-diffusion method. Sterile filter paper discs (6 mm diameter) moistened with the test compound solution in DMSO of specific concentration 100 μg and 200 μg/disc were carefully placed on the agar culture plates that had been previously inoculated separately with the microorganisms. The plates were incubated at 37 °C and the diameter of the growth inhibition zones were measured after 24 h in case of bacteria and after 48 h in case of fungi.

The MIC's of the compound assays were determined using microdilution susceptibility method. Chloramphenicol was used as reference antibacterial agent. Ketoconazole was used as reference antifungal agent. The test compounds, chloramphenicol and ketoconazole were dissolved in DMSO at concentration of 800 μg/ml. The two-fold dilution of the solution was prepared (400, 200, 100, …, 6.25 μg/ml). The microorganism suspensions were incubated at 36 °C for 24 and 48 h for bacteria and fungi, respectively. The minimum inhibitory concentrations of the compounds were recorded as the lowest concentration of each chemical compounds in the tubes with no turbidity (*i.e.* no growth) of inoculated bacteria/fungi.

Acknowledgements The Department of Science and Technology (DST), New Delhi, India, is gratefully acknowledged for its financial support.

References

1) Gribble G. W., "Comprehensive Heterocyclic Chemistry II," ed. by Katritzky A. R., Rees C. W., Scriven E. F. V., Storr R. C., Pergamon Press, Oxford, 1996, p. 207.
2) Loya S., Rudi A., Kashman Y., Hizi A., *Biochem. J.*, **85**, 344—347 (1999).
3) Boger D. L., Boyce C. W., Labroli M. A., Sehon C. A., Jin Q., *J. Am. Chem. Soc.*, **121**, 54—62 (1999).
4) Hansford K. A., Zanzarova V., Dorr A., Lubell W. D., *J. Comb. Chem.*, **6**, 893—898 (2004).
5) Dannahardt G., Kiefer W., Kramer G., Maehrlein S., Nowe U., Fiebich B., *Eur. J. Med. Chem.*, **35**, 499—510 (2000).
6) Jose B., Jesus J., Vicente, *J. Chem. Res.* (*s*), 464—466 (1980).
7) Stauart J. B., Christopher J. E., Paul S. G., Gregory W. S., *Tetraherdon Lett.*, **38**, 2175—2178 (1997).
8) Zhao B. X., Yu Y., Eguchi S., *Tetrahedron*, **52**, 12049—12060 (1996).
9) Shankar B. B., Girton D. Y. S., Ganguly A. K., *Tetrahedron Lett.*, **39**, 2447—2448 (1998).
10) Shiraishi H., Nishitani T., Nishihara T., Sakaguchi S., Ishii Y., *Tetrahedron*, **55**, 13957—13964 (1999).
11) Zelikin A., Shastri V. R., Langer R., *J. Org. Chem.*, **64**, 3379—3380 (1999).
12) Liu J. H., Chan H. W., Wong H. N. C., *J. Org. Chem.*, **65**, 3274—3283 (2000).
13) Van Leusen A. M., Siderius H., Hoogenboom B. E., Van Leusen D., *Terahedron Lett.*, 5337—5340 (1972).
14) Pavri N. P., Trudell M. L., *J. Org. Chem.*, **62**, 2649—2651 (1997).
15) Padmavathi V., Jagnan Mohan Reddy B., Padmaja A., *J. Heterocycl. Chem.*, **42**, 333—335 (2005).
16) Padmavathi V., Jagnan Mohan Reddy B., Rajagopala Sarma M., Thriveni P., *J. Chem. Res.* (*s*), 79—80 (2004).
17) Just G., Dhal K., *Tetrahedron*, **24**, 5251—5269 (1968).
18) Lokanath Rai K. M., Linganna N., Hassner A., Murthy C. A., *Org. Prep. Proc. Intl.*, **24**, 91—94 (1992).
19) Kim J. N., Ryu E. K., *Synth. Commun.*, **20**, 1373—1377 (1990).
20) Lokanath Rai K. M., Hassner A., *Indian J. Chem.*, **36B**, 242—245 (1997).
21) Lokanath Rai K. M., Hassner A., *Synth. Commun.*, **27**, 467—472 (1997).
22) Hassner A., Lokanath Rai K. M., *Synthesis*, 57—59 (1989).
23) Lokanath Rai K. M., Hassner A., *Synth. Commun.*, **19**, 2799—2807 (1989).
24) Padmavathi V., Sumathi R. P, Chandrasekhar Babu N., Bhaskar Reddy D., *J. Chem. Res.* (*s*), 610—611 (1999).
25) Padmavathi V., Sumathi R. P., Venugopal Reddy K., Somasekhar Reddy A., Bhaskar Reddy D., *Synth. Commun.*, **30**, 4007—4016 (2000).
26) Padmavathi V., Jagan Mohan Reddy B., Venkata Subbaiah D. R. C., *New. J. Chem.*, **28**, 1479—1483 (2004).
27) Padmavathi V., Jagan Mohan Reddy B., Chandra Obula Reddy B., Padmaja A., *Tetrahedron*, **61**, 2407—2411 (2005).
28) Vincent J. C., Vincent H. W., *Proc. Soc. Exp. Biol. Med.*, **55**, 162—164 (1944).
29) Bhaskar Reddy D., Muralidhar Reddy M., Subbaraju G. V., *Indian J. Chem.*, **34B**, 816—822 (1995).