Synthesis of a New Class of Sulfone Linked Bisheterocycles

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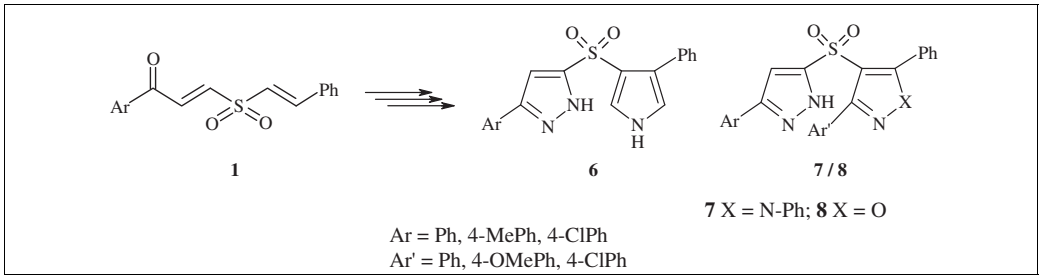

A new class of sulfone linked bisheterocycles—pyrrolyl pyrazoles, bispyrazoles, and pyrazolyl isoxazoles—were prepared from 1-aroyl-2-styrylsulfonylethenes, and the products were characterized by spectral parameters and elemental analyses.

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INTRODUCTION

Among different heterocycles, the chemistry and pharmacological relevance of five membered heterocycles has received much attention [1]. In fact, pyrazole and isoxazole derivatives have gained importance because of their various chemotherapeutic properties, viz. bacteriostatic, antibiotic, analgesic, anti-inflammatory, antifungal, and antiviral [2–7]. Celecoxib, a pyrazole derivative, and Valdecoxib, an isoxazole derivative are now widely used as anti-inflammatory drugs [8]. Among the different methods for the synthesis of pyrazolines and isoxazolines, the 1,3-dipolar cycloaddition of an ylide onto an alkene in a 3 + 2 manner is a facile one [9]. In addition, pyrroles are important class of heterocyclic compounds and are structural units found in several natural products [10], organic material [11], and bioactive molecules [12]. Pyrroles also play a crucial role in nonlinear optical materials and in supramolecular chemistry [13]. Classical methods for their preparation include the Knorr [14], Hantzsch [15], and Paal–Knorr condensation reactions [16] or by transition metal catalyzed reactions [17]. In fact, the development of practical methods for the preparation of differently substituted bisheterocycles has become an important and critical goal in organic synthesis. In continuation of our efforts to develop bisheterocyclic systems from the multifunctional synthetic intermediate 1-aroyl-2-styrylsulfonylethene [18], the present work has been taken up.

RESULTS AND DISCUSSION

The synthetic intermediate 1-aroyl-2-styrylsulfonylethene (**1**) was prepared by passing vinyl chloride gas into aroyl chloride under Friedel–Craft's conditions followed by condensation with sodium styryl sulfinate [19]. The reaction of **1** with hydrazine hydrate in ethanol resulted in 4,5-dihydro-3-aryl-5-(styrylsulfonyl)-1*H*-pyrazole (**2**) (Scheme 1). The ^{1}H-NMR spectrum of **2a** displayed an AMX splitting pattern for pyrazoline ring protons exhibiting three double doublets at δ 5.92 (H_A), 3.34 (H_M), and 3.08 ppm (H_X). The coupling constant values J_{AM} = 12.6 Hz, J_{MX} = 10.6 Hz, and J_{AX} = 5.5 Hz show that H_A and H_M are *cis*; H_A and H_X are *trans*; and H_M and H_X are *geminal*. In addition, a doublet observed at δ 6.65 ppm was assigned to H_C, whereas the signal due to H_D merged with aromatic protons [18]. The coupling constant value J = 14.2 Hz indicated their *trans* geometry.

The olefin moiety in **2** was used to develop different heterocyclic rings such as pyrroles, pyrazoles, and isoxazoles by using 1,3-dipolar cycloaddition reagents, viz. TosMIC [20], nitrile imines, and nitrile oxides [21]. The compound **2** was treated with TosMIC in the presence of sodium hydride in a mixture of ether and DMSO. The solid obtained was identified as 3-aryl-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (**3**). The ^{1}H-NMR spectrum of **3b** showed two singlets at δ 6.87 and 7.11 ppm due to $C_{2'}$–H and $C_{5'}$–H of pyrrole ring, apart from signals due to pyrazoline and aromatic protons. Similarly, 1,3-dipolar cycloaddition reaction of **2** with nitrile imines and nitrile oxides generated from araldehyde phenylhydrazones and araldoximes in the presence of chloramine-T in methanol resulted in 3-aryl-5-(4′,5′-dihydro-1′,5′-diphenyl-3′-aryl-1′*H*-pyrazol-4′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (**4**) and 3-aryl-5-(4′,5′-dihydro-3′-aryl-5′-phenylisoxazol-4′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (**5**), respectively (Scheme 1). The ^{1}H-NMR spectra of **4a** and **5a** displayed two doublets at

Scheme 1. i) N_2H_4. H_2O, EtOH; ii) TosMIC, NaH, Et_2O + DMSO; iii) Ar'-CH=NNHPh, Chloramine-T.$3H_2O$, MeOH; iv) Ar'-CH = NOH, Chloramine-T.$3H_2O$, MeOH; v) Chloranil, Xylene. a) Ar = Ph; b) Ar = 4-MePh; c) Ar = 4-ClPh, a) Ar' = Ph; b) Ar' = 4-OMePh; c) Ar' = 4-ClPh.

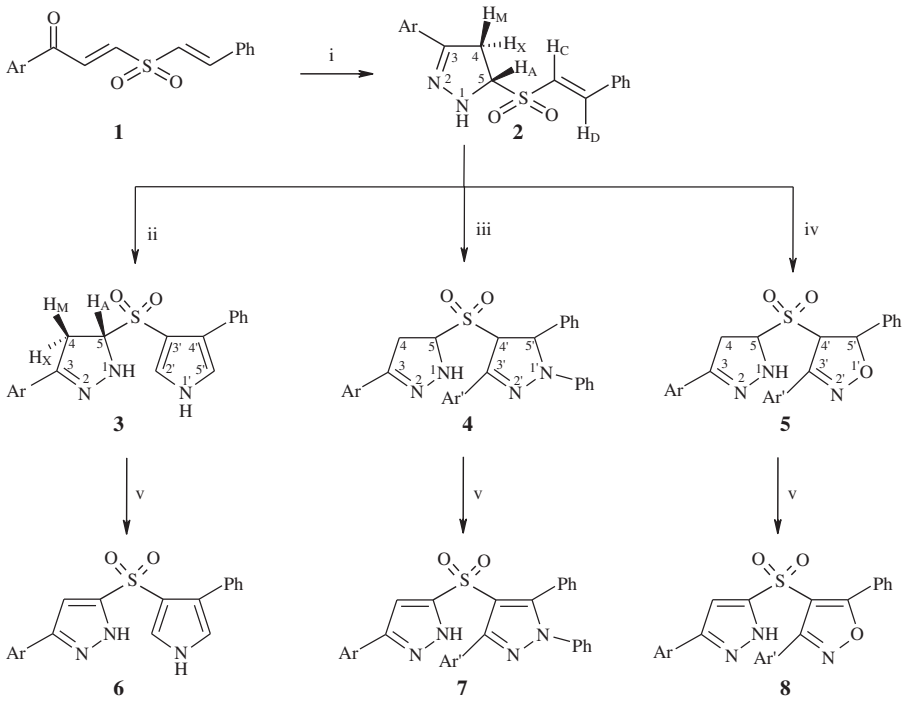

Table 1

Physical and analytical data of compounds **3–8**.

						Analysis %		
						Calcd/found		
Compound	Mp (°C)	Ar	Ar′	Yield %	Mol. formula	C	H	N
3a	147–149	C_6H_5	–	75	$C_{19}H_{17}N_3O_2S$	64.93	4.87	11.95
						64.79	4.92	12.03
3b	153–155	4-MeC_6H_4	–	69	$C_{20}H_{19}N_3O_2S$	65.73	5.23	11.49
						65.62	5.17	11.55
3c	172–174	4-ClC_6H_4	–	76	$C_{19}H_{16}ClN_3O_2S$	59.14	4.18	10.88
						59.21	4.11	10.93
4a	197–199	C_6H_5	C_6H_5	68	$C_{30}H_{26}N_4O_2S$	71.12	5.17	11.05
						71.22	5.12	11.14
4b	185–187	4-MeC_6H_4	4-OMeC_6H_4	72	$C_{32}H_{30}N_4O_3S$	69.79	5.49	10.17
						69.87	5.53	10.25
4c	204–206	4-ClC_6H_4	4-ClC_6H_4	75	$C_{30}H_{24}Cl_2N_4O_2S$	62.63	4.20	9.73
						62.49	4.27	9.62
5a	165–167	C_6H_5	C_6H_5	66	$C_{24}H_{21}N_3O_3S$	66.85	4.90	9.73
						66.65	4.98	9.64
5b	171–173	4-MeC_6H_4	4-OMeC_6H_4	65	$C_{26}H_{25}N_3O_4S$	65.66	5.29	8.83
						65.63	5.36	8.89
5c	194–196	4-ClC_6H_4	4-ClC_6H_4	69	$C_{24}H_{19}Cl_2N_3O_3S$	57.63	3.82	8.39
						57.71	3.75	8.45
6a	166–168	C_6H_5	–	70	$C_{19}H_{15}N_3O_2S$	65.31	4.32	12.02
						65.20	4.39	12.09
6b	175–177	4-MeC_6H_4	–	71	$C_{20}H_{17}N_3O_2S$	66.09	4.71	11.56
						66.00	4.65	11.50

(*Continued*)

Table 1
(Continued)

Compound	Mp (°C)	Ar	Ar′	Yield %	Mol. formula	Analysis % Calcd/found C	H	N
6c	183–185	4-ClC_6H_4	–	75	$C_{19}H_{14}ClN_3O_2S$	59.45	3.67	10.94
						59.37	3.60	10.88
7a	212–214	C_6H_5	C_6H_5	69	$C_{30}H_{22}N_4O_2S$	71.69	4.41	11.14
						71.55	4.48	11.03
7b	232–234	4-MeC_6H_4	4-$OMeC_6H_4$	74	$C_{32}H_{26}N_4O_3S$	70.30	4.79	10.24
						70.19	4.83	10.32
7c	225–227	4-ClC_6H_4	4-ClC_6H_4	72	$C_{32}H_{20}Cl_2N_4O_2S$	63.09	3.54	9.80
						62.91	3.48	9.75
8a	198–200	C_6H_5	C_6H_5	71	$C_{24}H_{17}N_3O_3S$	67.43	4.00	9.82
						67.52	3.93	9.94
8b	217–219	4-MeC_6H_4	4-$OMeC_6H_4$	74	$C_{26}H_{21}N_3O_4S$	66.22	4.48	8.91
						66.31	4.42	8.99
8c	225–227	4-ClC_6H_4	4-ClC_6H_4	76	$C_{24}H_{15}Cl_2N_3O_3S$	58.07	3.04	8.46
						58.18	3.10	8.55

δ 5.21 and 5.19 ppm and 5.58 and 5.78 ppm, which were assigned to H-4′ and H-5′, the two methine protons of the pyrazoline and isoxazoline rings. The coupling constant value $J = 6.2$ Hz showed that they are in a *trans* geometry. The compounds **3**, **4**, and **5** upon oxidation with chloranil in xylene gave the corresponding pyrazoles and isoxazoles, 3-aryl-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-1*H*-pyrazole (**6**), 3-aryl-5-(1′,5′-diphenyl-3′-aryl-1′*H*-pyrazol-4′-ylsulfonyl)-1*H*-pyrazole (**7**), and 3-aryl-5-(3′-aryl-5′-phenylisoxazol-4′-ylsulfonyl)-1*H*-pyrazole (**8**). The disappearance of signals due to pyrazoline/isoxazoline ring protons in the ^{1}H-NMR spectra of **6–8** confirms their formation. The structures of **2–8** were further confirmed by ^{13}C-NMR spectra.

CONCLUSION

A new class of sulfone linked bisheterocycles—pyrrolyl pyrazoles, bispyrazoles, and pyrazolyl isoxazoles—were prepared from 1-aroyl-2-styrylsulfonylethenes, adopting the 1,3-dipolar cycloaddition methodology using TosMIC, nitrile imines, and nitrile oxides.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus (India) and are uncorrected (Table 1). The purity of the compounds was checked by TLC (silica gel H, British Drug Houses Ltd., ethyl acetate/hexane, 3:1). The IR spectra were recorded on a Thermo Nicolet IR 200 FTIR spectrometer (Thermo Electron Scientific, Madison, WI) as KBr pellets, and the wave numbers were given in cm^{-1} (Table 2). The ^{1}H-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer (Oxford Instruments, England) at λ-300 MHz (Table 3). The ^{13}C-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 75.5 MHz (Table 3). All chemical shifts were reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer (Waltham, MA). The starting compounds 1-aroyl-2-styrylsulfonylethene (**1**) and 4,5-dihydro-3-aryl-5-(styrylsulfonyl)-1*H*-pyrazole (**2**) were prepared as per the literature procedure [18].

3-Aryl-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (3): general procedure. An equimolar mixture (1 mmol) of TosMIC and **2** in Et_2O/DMSO (10 mL 2:1) was added dropwise to a stirred suspension of NaH (50 mg) in dry Et_2O (10 mL) at room temperature. The stirring was

Table 2
IR data of compounds **2–8**.

Compound	IR (cm^{-1}) SO_2		C=C	C=N	NH
2a	1121	1333	1615	1575	3335
2b	1129	1336	1618	1571	3339
2c	1140	1340	1620	1585	3345
3a	1135	1341	1625	1576	3290
3b	1130	1346	1632	1580	3295
3c	1123	1332	1640	1570	3291
4a	1141	1340	–	1585	3335
4b	1132	1338	–	1582	3329
4c	1134	1336	–	1576	3330
5a	1128	1330	–	1575	3334
5b	1126	1342	–	1580	3340
5c	1130	1337	–	1577	3335
6a	1140	1342	1632	1574	3330
6b	1134	1339	1639	1570	3295
6c	1120	1333	1629	1572	3330
7a	1139	1330	1624	1583	3340
7b	1127	1335	1635	1578	3336
7c	1130	1340	1628	1571	3331
8a	1135	1345	1636	1582	3298
8b	1132	1338	1635	1585	3336
8c	1126	1333	1627	1576	3340

Table 3

^{1}H-NMR and ^{13}C-NMR data of compounds **2–8**.

Compound	^{1}H-NMR (δ, ppm)	^{13}C-NMR (δ, ppm)	Solvent
2a	3.08 (dd, 1H, H_X J_{MX} = 10.6, J_{AX} = 5.5 Hz), 3.34 (dd, 1H, H_M), 5.92 (dd, 1H, H_A, J_{AM} = 12.6 Hz), 6.65 (d, 1H, Hc, J_{CD} = 14.2 Hz), 7.00–7.62 (m, 11H, Ar–H and H_D), 10.23 (bs, 1H, NH)	40.2 (C-4), 80.1 (C-5), 132.2 (C-1′), 137.2 (C-2′), 156.5 (C-3), 128.2, 129.6, 130.8, 131.3, 132.5, 133.1, 133.6, 134.2 (aromatic carbons)	$CDCl_3$
2b	2.25 (s, 3H, Ar–CH_3), 3.03 (dd, 1H, H_X, J_{MX} = 10.4, J_{AX} = 5.3 Hz), 3.38 (dd, 1H, H_M), 5.98 (dd, 1H, H_A, J_{AM} = 12.1 Hz), 6.68 (d, 1H, Hc, J_{CD} = 14.1 Hz), 7.02–7.68 (m, 9H, Ar–H and H_D), 10.16 (bs, 1H, NH)	21.2 (Ar–CH_3), 39.4 (C-4), 80.4 (C-5), 132.9 (C-1′), 138.2 (C-2′), 155.9 (C-3), 127.8, 128.9, 130.3, 131.7, 132.9, 133.8, 134.0, 134.9 (aromatic carbons)	$CDCl_3$
2c	3.20 (dd, 1H, H_X. J_{MX} = 17.6, J_{AX} = 4.5 Hz), 3.48 (dd, 1H, H_M), 5.87 (dd, 1H, H_A, J_{AM} = 12.4 Hz), 7.04 (d, 1H, Hc, J_{CD} = 14.4 Hz), 7.09–7.71 (m, 9H, Ar–H and H_D), 9.98 (bs, 1H, NH)	38.7 (C-4), 78.9 (C-5), 133.4 (C-1′), 139.7 (C-2′), 156.7 (C-3), 127.0, 127.4, 128.3, 129.5, 131.3, 134.2, 135.7, 136.2 (aromatic carbons)	$CDCl_3$
3a	3.06 (dd, 1H, H_X, J_{MX} = 15.5, J_{AX} = 4.9 Hz), 3.64 (dd, 1H, H_M), 5.99 (dd, 1H, H_A, J_{AM} = 16.8 Hz), 6.91 (s, 1H, $C_{2'}$–H), 7.08, (s, 1H, $C_{5'}$–H) 7.11–7.62 (m, 10H, Ar–H), 8.86 (bs, 1H, NH), 10.14 (bs, 1H, NH)	41.4 (C-4), 76.2 (C-5), 118.2 (C-4′), 120.7 (C-3′), 124.2 (C-2′), 125.7 (C-5′), 155.1 (C-3), 128.2, 129.4, 130.2, 131.7, 132.5, 133.1, 133.6, 134.2 (aromatic carbons)	DMSO-d_6
3b	2.32 (s, 3H, Ar–CH_3), 3.20 (dd, 1H, H_X, J_{MX} = 16.1, J_{AX} = 3.3 Hz), 3.83 (dd, 1H, H_M), 6.03 (dd, 1H, H_A, J_{AM} = 17.6 Hz), 6.87 (s, 1H, $C_{2'}$–H), 7.11 (s, 1H, $C_{5'}$–H), 7.14–7.75 (m, 9H, Ar–H), 8.74 (bs, 1H, NH), 10.17 (bs, 1H, NH)	21.1 (Ar–CH_3), 42.3 (C-4), 77.5 (C-5), 117.9 (C-4′), 121.2 (C-3′), 123.6 (C-2′), 124.9 (C-5′), 156.0 (C-3), 125.3, 126.9, 128.8, 129.6, 130.7, 131.0, 137.3, 138.9 (aromatic carbons)	DMSO-d_6
3c	3.14 (dd, 1H, H_X, J_{MX} = 16.7, J_{AX} = 4.3 Hz), 3.79 (dd, 1H, H_M), 5.82 (dd, 1H, H_A, J_{AM} = 17.1 Hz), 6.83 (s, 1H, $C_{2'}$–H), 7.12 (s, 1H, $C_{5'}$–H), 7.25–7.74 (m, 9H, Ar–H), 8.91 (bs, 1H, NH), 10.02 (bs, 1H, NH)	41.9 (C-4), 76.9 (C-5), 116.4 (C-4′), 120.5 (C-3′), 122.9 (C-2′), 123.6 (C-5′), 155.1 (C-3), 128.1, 129.2, 130.9, 131.9, 132.8, 133.0, 133.8, 137.2 (aromatic carbons)	DMSO-d_6
4a	3.08 (dd, 1H, H_X, J_{MX} = 15.3, J_{AX} = 4.4 Hz), 3.51 (dd, 1H, H_M), 5.21 (d, 1H, $C_{4'}$–H, J = 6.2 Hz), 5.58 (d, 1H, $C_{5'}$–H, J = 6.2 Hz), 5.79 (dd, 1H, H_A, J_{AM} = 16.3 Hz), 7.10–7.69 (m, 20H, Ar–H), 10.15 (bs, 1H, NH)	40.8 (C-4), 63.7 (C-4′), 77.4 (C-5), 86.9 (C-5′), 154.2 (C-3′), 155.9 (C-3), 127.4, 128.9, 130.1, 131.4, 132.3, 133.6, 134.3, 134.9, 135.2, 137.0 (aromatic carbons)	$CDCl_3$
4b	2.26 (s, 3H, Ar–CH_3), 3.13 (dd, 1H, H_X. J_{MX} = 14.6, J_{AX} = 4.7 Hz), 3.81 (s, 3H, Ar–OCH_3), 3.58 (dd, 1H, H_M), 5.19 (d, 1H, $C_{4'}$–H, J = 6.4 Hz), 5.53 (d, 1H, $C_{5'}$–H, J = 6.4 Hz), 5.83 (dd, 1H, H_A, J_{AM} = 17.6 Hz), 7.08–7.76 (m, 18H, Ar–H), 10.21 (bs, 1H, NH)	21.6 (Ar–CH_3), 56.4 (Ar–OCH_3), 41.3 (C-4), 62.4 (C-4′), 78.0 (C-5), 87.2 (C-5′), 153.6 (C-3′), 156.3 (C-3), 128.6, 129.2, 131.9, 132.1, 133.2, 134.0, 134.7, 135.8, 136.4, 137.2 (aromatic carbons)	$CDCl_3$
4c	3.18 (dd, 1H, H_X. J_{MX} = 15.8, J_{AX} = 4.2 Hz), 3.63 (dd, 1H, H_M), 5.23 (d, 1H, $C_{4'}$–H, J = 6.7 Hz), 5.59 (d, 1H, $C_{5'}$–H, J = 6.7 Hz), 5.91 (dd, 1H, H_A, J_{AM} = 16.9 Hz), 7.14–7.87 (m, 18H, Ar–H), 10.12 (bs, 1H, NH)	40.6 (C-4), 63.6 (C-4′), 77.5 (C-5), 86.7 (C-5′), 154.8 (C-3′), 156.9 (C-3), 127.6, 128.7, 130.3, 132.8, 133.8, 134.5, 135.0, 136.9, 137.6, 138.9 (aromatic carbons)	$CDCl_3$
5a	3.16 (dd, 1H, H_X. J_{MX} = 14.0, J_{AX} = 4.9 Hz), 3.73 (dd, 1H, H_M), 5.19 (d, 1H, $C_{4'}$–H, J = 5.7 Hz), 5.78 (d, 1H, $C_{5'}$–H, J = 5.7 Hz), 5.56 (d, 1H, H_A, J_{AM} = 16.6 Hz), 7.13–7.75 (m, 15H, Ar–H), 8.98 (bs, 1H, NH)	42.3 (C-4), 64.5 (C-4′), 78.7 (C-5), 85.8 (C-5′), 153.8 (C-3), 155.2 (C-3′), 125.5, 126.6, 128.7, 129.5, 130.3, 131.5, 137.3, 139.0 (aromatic carbons)	$CDCl_3$
5b	2.22 (s, 1H, Ar–CH_3), 3.77 (s, 3H, Ar–OCH_3), 3.12 (dd, 1H, H_X. J_{MX} = 14.6, J_{AX} = 4.6 Hz), 3.65 (dd, 1H, H_M), 5.21 (d, 1H, $C_{4'}$–H, J = 5.9 Hz), 5.69 (d, 1H, $C_{5'}$–H, J = 5.9 Hz), 5.79 (dd, 1H, H_A, J_{AM} = 17.2 Hz), 7.14–7.79 (m, 13H, Ar–H), 9.02 (bs, 1H, NH)	22.8 (Ar–CH_3), 57.2 (Ar–OCH_3), 42.0 (C-4), 63.8 (C-4′), 77.4 (C-5), 87.2 (C-5′), 154.6 (C-3′), 155.1 (C-3), 128.0, 129.1, 130.7, 131.8, 132.2, 135.0, 135.6, 136.9 (aromatic carbons)	$CDCl_3$
5c	3.10 (dd, 1H, H_X. J_{MX} = 14.2, J_{AX} = 4.1 Hz), 3.62 (dd, 1H, H_M), 5.24 (d, 1H, $C_{4'}$–H, J = 5.4 Hz), 5.71 (d, 1H, $C_{5'}$–H, J = 5.4 Hz), 5.81 (d, 1H, H_A, J_{AM} = 17.5 Hz), 7.12–7.83 (m, 13H, Ar–H), 10.14 (bs, 1H, NH)	41.9 (C-4), 62.5 (C-4′), 76.9 (C-5), 86.7 (C-5′), 155.0 (C-3′), 156.6 (C-3), 128.7, 129.4, 129.9, 130.5, 131.2, 132.7, 133.3, 134.6, 137.9 (aromatic carbons)	$CDCl_3$
6a	6.81 (s, 1H, C_2–H), 6.92 (s, 1H, C_5–H), 7.11–7.64 (m, 11H, Ar–H and C_4–H), 8.84 (bs, 1H, NH), 10.04 (bs, 1H, NH)	117.4 (C-4′), 121.3 (C-3′), 123.2 (C-2′), 124.6 (C-5′), 138.2 (C-4), 152.2 (C-5), 156.0 (C-3), 127.4, 129.0, 131.9, 132.3, 133.8, 134.0, 133.7 134.1 (aromatic carbons)	DMSO-d_6
6b	2.23 (s, 3H, Ar–CH_3), 6.76 (s, 1H, $C_{2'}$–H), 6.88 (s, 1H, $C_{5'}$–H), 7.15–7.71 (m, 10H, Ar–H and C_4–H), 8.93 (bs, 1H, NH), 10.13 (bs, 1H, NH)	22.4 (Ar–CH_3), 116.8 (C-4′), 120.7 (C-3′), 122.8 (C-2′), 124.1 (C-5′), 137.7 (C-4), 151.4 (C-5), 155.8 (C-3), 128.1, 129.7, 130.7, 131.1, 132.7, 133.4, 134.2, 135.2 (aromatic carbons)	DMSO-d_6
6c	6.72 (s, 1H, C_2–H), 6.96 (s, 1H, C_5–H), 7.18–7.82 (m, 10H, Ar–H and C_4–H), 8.89 (bs, 1H, NH), 10.08 (bs, 1H, NH)	115.4 (C-4′), 121.5 (C-3′), 123.3 (C-2′), 124.9 (C-5′), 138.6 (C-4), 152.8 (C-5), 156.4 (C-3), 128.7, 130.1,	DMSO-d_6

(*Continued*)

Table 3
(Continued)

Compound	^{1}H-NMR (δ, ppm)	^{13}C-NMR (δ, ppm)	Solvent
		131.4, 132.5, 133.0, 134.6, 135.0 135.6 (aromatic carbons)	
7a	7.09–7.72 (m, 21H, Ar–H and C_4–H), 8.30 (bs, 1H, NH)	145.4 (C-3′), 148.2 (C-4′), 152.8 (C-5′), 138.6 (C-4), 153.6 (C-5), 155.2 (C-3), 127.8, 128.4, 129.7, 131.0, 132.9, 133.4, 134.0, 134.9, 135.9, 136.7 (aromatic carbons)	$CDCl_3$
7b	2.27 (s, 3H, Ar–CH_3), 3.78 (s, 3H, Ar–OCH_3), 7.16–7.79 (m, 19H, Ar–H and C_4–H), 8.14 (bs, 1H, NH)	21.8 (Ar–CH_3), 57.4 (Ar–OCH_3), 144.8 (C-3′), 149.7 (C-4′), 153.5 (C-5′), 137.9 (C-4), 154.3 (C-5), 156.9 (C-3), 127.3, 127.8, 128.2, 129.4, 131.9, 133.9, 134.2 135.3, 136.2 (aromatic carbons)	$CDCl_3$
7c	7.06–7.85 (m, 19H, Ar–H and C_4–H), 8.32 (bs, 1H, NH)	145.4 (C-3′), 147.8 (C-4′), 154.7 (C-5′), 138.2 (C-4), 155.7 (C-5), 156.6 (C-3), 127.9, 128.7, 129.1, 130.4, 132.3, 134.7, 135.6 137.4, 137.9 (aromatic carbons)	$CDCl_3$
8a	6.99–7.68 (m, 16H, Ar–H and C_4–H), 8.97 (bs, 1H, NH)	144.7 (C-3′), 149.6 (C-4′), 153.4 (C-5′), 137.6 (C-4), 154.8 (C-5), 156.8 (C-3), 127.2, 128.9, 131.4, 132.7, 134.3, 135.7, 136.0, 136.5 (aromatic carbons)	$CDCl_3$
8b	2.25 (s, 3H, Ar–CH_3), 3.71 (s, 3H, Ar–OCH_3), 7.04–7.74 (m, 14H, Ar–H and C_4–H), 8.83 (bs, 1H, NH)	21.9 (Ar–CH_3), 58.3 (Ar–OCH_3), 143.8 (C-3′), 148.3 (C-4′), 154.4 (C-5′), 136.4 (C-4), 155.3 (C-5), 157.5 (C-3), 128.5, 129.2, 131.9, 132.2, 133.7, 134.0, 135.2 136.5 (aromatic carbons)	$CDCl_3$
8c	7.12–7.81 (m, 14H, Ar–H and C_4–H), 8.74 (bs, 1H, NH)	145.2 (C-3′), 147.1 (C-4′), 155.2 (C-5′), 137.8 (C-4), 156.5 (C-5), 157.8 (C-3), 128.8, 129.4, 130.4, 131.7, 133.6, 135.8, 136.2, 137.8 (aromatic carbons)	$CDCl_3$

continued for 24 h and diluted with water. It was extracted with ether, and the organic layer was dried over anhydrous sodium sulfate. Removal of the solvent under vacuum gave crude product, which was purified by filtration through a column of silica gel (BDH, 60–120 mesh) with hexane/EtOAc (3:1) as eluent.

3-Aryl-5-(4′,5′-dihydro-1′,5′-diphenyl-3′-aryl-1′*H*-pyrazol-4′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (4): general procedure. A mixture of **2** (1 mmol), araldehyde phenylhydrazone (1.2 mmol), and chloramine-T (1.2 mmol) 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 and brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. Recrystallization of crude product from ethanol resulted in pure compound.

3-Aryl-5-(4′,5′-dihydro-3′-aryl-5′-phenylisoxazol-4′-ylsulfonyl)-4,5-dihydro-1*H*-pyrazole (5): general procedure. The compound **2** (1 mmol), araldoxime (1.2 mmol), and chloramine-T (2 mmol) in methanol (20 mL) were refluxed for 16–18 h on a water bath. 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 and brine and dried over anhydrous sodium sulfate. The solvent was removed *in vacuo*. The solid obtained was purified by recrystallization from ethanol.

3-Aryl-5-(4′-phenyl-1′*H*-pyrrol-3′-ylsulfonyl)-1*H*-pyrazole (6): general procedure. A solution of **3** (1 mmol) and chloranil (1.1 mmol) in xylene (10 mL) was refluxed for 20–24 h. Then the reaction mixture was treated with a 5% NaOH solution. The organic layer was separated and repeatedly washed with water. It was then dried over anhydrous sodium sulfate, and the solvent was removed on a rotary evaporator. The resultant solid was purified by recrystallization from methanol.

3-Aryl-5-(1′,5′-diphenyl-3′-aryl-1′*H*-pyrazol-4′-ylsulfonyl)-1*H*-pyrazole (7) and 3-aryl-5-(3′-aryl-5′-phenylisoxazol-4′-ylsulfonyl)-1*H*-pyrazole (8): general procedure. A solution of **4/5** (1 mmol) and chloranil (2.2 mmol) in xylene (10 mL) was refluxed for 24–28 h. Then, it was treated with 5% NaOH solution. The organic layer was separated, washed with water, and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The solid obtained was purified by recrystallization from 2-propanol.

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