E,*E*-Bis(Styryl)Sulfones—Synthons for a New Class of Bis(heterocycles)

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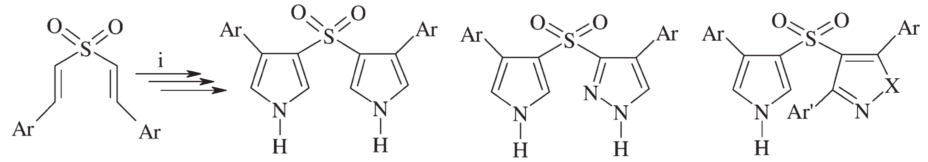

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8; X = N-Ph, 9; X= O

A new class of bis heterocycles having two different heterocyclic rings *viz*., pyrroles in combination with pyrazolines and isoxazolines were synthesized. All the compounds were characterized by elemental and spectral analysis.

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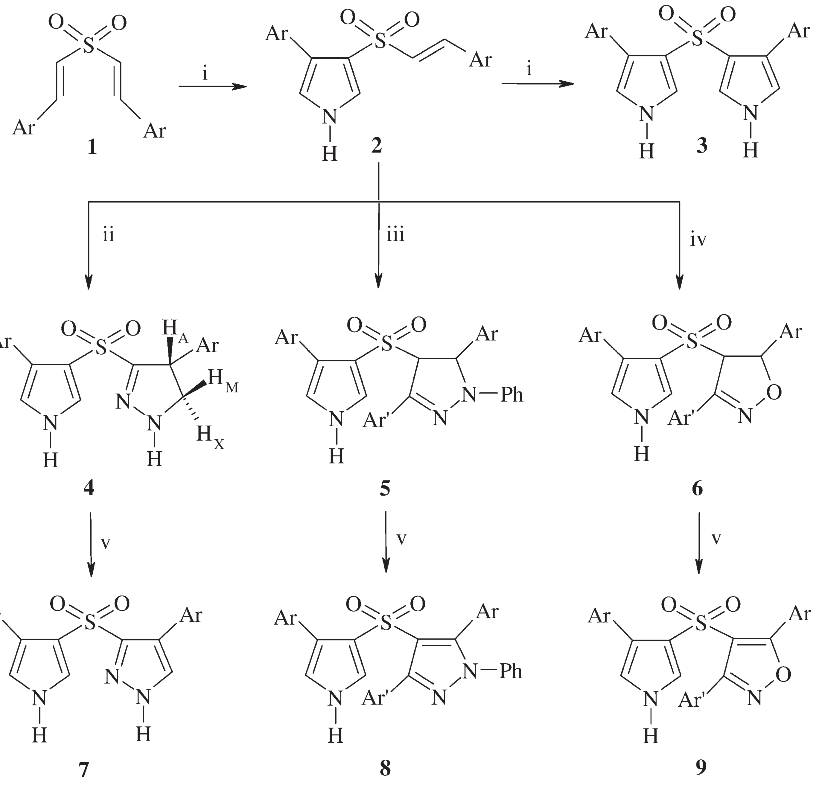
INTRODUCTION

Heterocyclic chemistry has attracted a lot of interest during recent years as many useful drugs have emerged in this branch. In fact, the development of simple, facile, and efficient synthetic methodologies for the development of five membered heterocycles has been a challenging task in organic synthesis. Amongst five membered heterocycles, pyrroles, pyrazoles, and isoxazoles have gained importance because of their varied physiological activities. As constituents of cytotoxic drugs, such as netrospin and distamycin, 4-aminopyrrole-2-carboxylates, have been used as the main compounds in the construction of a diverse series of DNA-binding ligands exhibiting antibiotic, antiviral, and oncolytic properties [1]. The related 3-amino pyrroles also exhibit anticonvulsant activity by blocking sodium channels [2]. In addition, pyrazolines and isoxazolines have gained importance due to their various chemotherapeutic properties. In fact, Celecoxib, a pyrazole derivative and Valdecoxib, an isoxazole derivative, have been widely used in the market as anti-inflammatory drugs [3]. Hence, it was considered worthwhile to prepare molecules having both pyrrole and pyrazole/isoxazole rings. In the literature, 3,4-disubstituted pyrroles were reported either by coupling imines and nitroalkanes or by using Friedel-Craft's acylation in the presence of an electron-withdrawing group on the pyrrole nitrogen or on 3,4-silylated precursors [4]. However, these synthetic routes were often complicated and limited to only some substituents. Previously, 3,4-disubstituted pyrroles were synthesized from Michael acceptors and tosylmethyl isocyanide (TosMIC) [5]. Following this synthetic methodology, we have reported recently a new regioselective one step procedure using phenyl vinyl sulfone, aryl styryl sulfones, benzyl styryl sulfones and TosMIC, leading to a series of 3,4-disubstituted pyrroles in good yields [6]. Similarly, pyrazolines and isoxazolines were prepared by 1,3-dipolar cycloaddition of an ylide to an alkene involving the 3+2 cycloaddition principle [7]. Among the ylides, diazomethane, nitrile imines, and nitrile oxides were used extensively as reactive intermediates. These nitrile imines and nitrile oxides can be generated by the dehydrogenation of araldehyde phenylhydrazones and araldoximes with lead tetraacetate [8], mercury acetate [9], 1-chlorobenzotriazole [10], chloramine-T [11] etc. Use of the latter for *in situ* generation of dipolar reagents has enthused many organic chemists. In fact, we have reported the 1,3-dipolar cycloaddition reaction of Chloramine-T catalysed dipolar reagents with variety of activated mono and bis(olefins) [12]. Apart from these, bis heterocycles, bis pyrroles and pyrrolyl pyrazoles were prepared from 1-arylsulfonyl-2-styrylsulfonyl ethenes by 1,3-dipolar cycloaddition methodology [13]. The present communication deals with the synthesis of hitherto unknown sulfonelinked bis (heterocycles) having pyrrole together with pyrazole or

Scheme 1



i) TosMIC / NaH/ Et_2O + DMSO ii) CH_2N_2 / Et_2O
iii) Ar'-CH=NNHPh / Chloramine-T.$3H_2O$ / MeOH
iv) Ar'-CH=NOH / Chloramine-T.$3H_2O$ / MeOH
v) Chloranil / Xylene

	Ar	Ar'
2a/3a/4a/7a	C_6H_5	-
2b/3b/4b	4-OMeC_6H_4	-
2c/3c/4c	4-ClC_6H_4	-
5a/6a/ 8a/ 9a	C_6H_5	C_6H_5
5b/6b	4-OMeC_6H_4	C_6H_5
5c/6c	C_6H_5	4-ClC_6H_4
5d/6d	4-ClC_6H_4	4-ClC_6H_4

isoxazole units, from 1,3-dipolar cycloaddition of TosMIC, nitrile imines and nitrile oxides to sulfonyl activated olefins.

RESULTS AND DISCUSSION

The synthetic scheme was based on the reactivity of *E*,*E*-bis(styryl)sulfone (**1**) towards 1,3-dipolar reagents *viz.*, TosMIC, diazomethane, nitrile imines and nitrile oxides. When **1** was treated with TosMIC in the presence of sodium hydride in a mixture of ether and dimethylsulfoxide, a solid was obtained which was identified as 4-aryl-3-(2′-arylethenesulfonyl)-1*H*-pyrrole (**2**) by spectral studies (Scheme 1; Table 1). Compound **2a** exhibited two singlets at δ 6.85 and 7.48 ppm, assigned to C_2-H and C_5-H of pyrrole ring protons. Two doublets were observed at δ 6.96 and 7.63 ppm corresponding to olefinic protons, in addition to the signals of aromatic protons (Table 3). The ^{13}C nuclear mass spectroscopy (NMR) spectra of **2a** showed signals at δ 119.8, 125.7, 125.9, and 127.3 for pyrrole ring carbons, C-4, C-3, C-5, C-2 and at δ 124.2, 141.3 ppm for olefinic carbons, C-1′, C-2′ (Table 3). Thus the formation of **2** indicates that the reaction was regiospecific. Attempts to prepare bis (4-aryl-1*H*-pyrrol-3-yl)sulfone (**3**) by treating **1** with

Table 1

Physical and analytical data of compounds **2–9**.

Compound	Mp (°C)	Yield (%)	Ar	Ar'	Molecular formula	Analysis % calculated/ found		
						C	H	N
2a	221–223	72	C_6H_5	–	$C_{18}H_{15}NO_2S$ (309.40)	69.88	4.89	4.53
						69.80	4.94	4.50
2b	243–245	69	4-OMeC_6H_4	–	$C_{20}H_{19}NO_4S$ (369.45)	65.02	5.18	3.79
						64.92	5.24	3.85
2c	265–267	66	4-ClC_6H_4	–	$C_{18}H_{13}Cl_2NO_2S$ (378.29)	57.15	3.46	3.70
						57.08	3.44	3.67
3a	232–234	76	C_6H_5	–	$C_{20}H_{16}N_2O_2S$ (348.43)	68.94	4.63	8.04
						68.85	4.68	8.11
3b	225–227	80	4-OMeC_6H_4	–	$C_{22}H_{20}N_2O_4S$ (408.48)	64.69	4.93	6.86
						64.76	4.96	6.92
3c	270–272	82	4-ClC_6H_4	–	$C_{20}H_{14}Cl_2N_2O_2S$ (417.32)	57.56	3.38	6.71
						57.50	3.35	6.66
4a	242–244	68	C_6H_5	–	$C_{19}H_{17}N_3O_2S$ (351.43)	64.94	4.87	11.96
						65.00	4.92	12.05
4b	230–232	70	4-OMeC_6H_4	–	$C_{21}H_{21}N_3O_4S$ (411.49)	61.29	5.14	10.21
						61.37	5.20	10.33
4c	256–258	65	4-ClC_6H_4	–	$C_{19}H_{15}Cl_2N_3O_2S$ (420.33)	54.29	3.60	9.99
						54.20	3.58	10.08
5a	282–284	68	C_6H_5	C_6H_5	$C_{31}H_{25}N_3O_2S$ (503.63)	73.93	5.00	8.34
						74.00	5.06	8.27
5b	270–272	64	4-OMeC_6H_4	C_6H_5	$C_{33}H_{29}N_3O_4S$ (563.68)	70.32	5.18	7.45
						70.43	5.14	7.38
5c	288–290	71	C_6H_5	4-ClC_6H_4	$C_{31}H_{24}ClN_3O_2S$ (538.07)	69.20	4.49	7.81
						69.27	4.53	7.92
5d	296–298	65	4-ClC_6H_4	4-ClC_6H_4	$C_{31}H_{22}Cl_3N_3O_2S$ (606.96)	61.34	3.65	6.92
						61.25	3.69	7.00
6a	277–278	70	C_6H_5	C_6H_5	$C_{25}H_{20}N_2O_3S$ (428.52)	70.07	4.70	6.54
						70.14	4.68	6.60
6b	264–266	65	4-OMeC_6H_4	C_6H_5	$C_{27}H_{24}N_2O_5S$ (488.57)	66.38	4.95	5.73
						66.32	5.00	5.67
6c	252–254	68	C_6H_5	4-ClC_6H_4	$C_{25}H_{19}ClN_2O_3S$ (462.96)	64.86	4.14	6.05
						64.78	4.10	6.13
6d	280–282	72	4-ClC_6H_4	4-ClC_6H_4	$C_{25}H_{17}Cl_3N_2O_3S$ (531.85)	56.46	3.22	5.27
						56.52	3.18	5.22
7a	274–276	66	C_6H_5	-	$C_{19}H_{15}N_3O_2S$ (349.42)	65.31	4.33	12.02
						65.26	4.31	12.12
8a	296–298	65	C_6H_5	C_6H_5	$C_{31}H_{23}N_3O_2S$ (501.61)	74.23	4.62	8.38
						74.33	4.67	8.46
9a	287–289	68	C_6H_5	C_6H_5	$C_{25}H_{18}N_2O_3S$ (426.50)	70.40	4.25	6.57
						70.52	4.28	6.51

two equivalents of TosMIC were not successful. However, **3** was obtained by treating **2** with one equivalent of TosMIC, as confirmed by NMR spectroscopy. Compound **3a** exhibited two sharp singlets at δ 6.84 and 7.08 ppm corresponding to $C_{2,2'}$-H and $C_{5,5'}$-H. The ^{13}C NMR spectra of **3a** exhibited signals at 119.2 (C-4,4′), 122.6 (C-3,3′), 126.2 (C-5,5′), 127.4 (C-2,2′). This indicates that the molecule was highly symmetrical.

The olefin in **2** was utilized in the synthesis of pyrazolines and isoxazolines. When **2** was subjected to 1,3-dipolar cycloaddition reaction with diazomethane, (4′-aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfone (**4**) was obtained (Scheme 1; Table 1). The ^{1}H NMR spectra of **4a** showed an *AMX* splitting pattern of the pyrazoline ring protons at δ 4.48 (H_A), 3.86 (H_M) and 3.48 ppm (H_X) respectively, in addition to the signals of the pyrrole ring protons. The observed coupling constant values $J_{AM} = 12.6$, $J_{AX} = 5.5$ and $J_{MX} = 10.0$ Hz indicated that H_A and H_M were *cis*, H_A and H_X were *trans* and H_M and H_X were *geminal*. The ^{13}C NMR spectrum of **4a** exhibited signals at δ 46.9, 57.2, 119.4, 120.3, 124.8, 125.6 and 152.3 ppm for the carbons C-4′, C-5′, C-4, C-3, C-5, C-2, and C-3′, respectively (Table 2).

In addition, the reaction of **2** with nitrile imines and nitrile oxides generated from araldehyde phenylhydrazones and araldoximes in the presence of chloramine-T resulted in (1′,3′,5′-triaryl-4′,5′-dihydro-1′*H*-pyrazol-4′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfones (**5**) and (3′,5′-diaryl-

Table 2

Infrared data of compounds **2–9**.

Compound	IR (KBr) cm^{-1}			
	SO$_2$	C=C	C=N	NH
2a	1130, 1300	1635	–	3175
2b	1145, 1297	1632	–	3170
2c	1132, 1295	1630	–	3180
3a	1140, 1294	–	–	3182
3b	1128, 1305	–	–	3168
3c	1124, 1296	–	–	3172
4a	1125, 1325	–	1570	3185
4b	1132, 1320	–	1575	3180
4c	1128, 1325	–	1572	3190
5a	1126, 1295	–	1558	3195
5b	1130, 1292	–	1568	3188
5c	1132, 1304	–	1560	3178
5d	1125, 1310	–	1562	3182
6a	1140, 1305	–	1574	3200
6b	1135, 1315	–	1562	3205
6c	1124, 1296	–	1578	3210
6d	1132, 1315	–	1566	3205
7a	1120, 1300	1625	1573	3198
7b	1124, 1298	1628	1558	3186
7c	1128, 1310	1630	1574	3198

4′,5′-dihydroisoxazol-4′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfone (**6**), respectively (Scheme 1; Table 1). The ^{1}H NMR spectrum of **5a** and **6a** displayed two doublets at δ 5.25, 5.19 and 5.63, 5.67 ppm, respectively, which were assigned to C$_{4'}$-H and C$_{5'}$-H, the two methine protons of the pyrazoline and isoxazoline rings. The *J* values indicated that they were in *trans* geometry (Table 3). The ^{13}C NMR spectra of **5a** and **6a** displayed signals at 63.0, 64.9 (C-4′), 87.4, 83.7 (C-5′), 119.2, 119.4 (C-4), 121.0, 121.9 (C-3), 124.4, 124.3 (C-5), 126.8, 126.3 (C-2) and 154.9, 151.7 (C-3′), respectively (Table 3). Compounds **4a**, **5a** and **6a** on oxidation with chloranil in xylene, gave the corresponding pyrazoles and isoxazoles **7a**, **8a** and **9a**. The disappearance of two doublets corresponding to pyrazoline/isoxazoline ring protons in the ^{1}H NMR spectra confirmed their formation.

CONCLUSION

A simple dipolarophile, bis(styryl)sulfone was exploited to get a new and novel sulfone-linked bis(heterocycles) containing two different heterocyclic rings adopting simple and versatile 1,3-dipolar cycloaddition methodology.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by thin layer chromatography (Silica gel H, BDH, ethyl acetate-hexane, 1:3). The infrared (IR) spectra were recorded on a Thermo Nicolet IR 200 FT-IR in 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 are reported in δ (ppm) using TMS as an internal standard. Elemental analyses were performed using Perkin-Elmer 240C elemental analyser. The starting substrates *E,E*-bis(styryl)sulfones were prepared according to the literature procedure [14]. Araldehyde phenylhydrazones and araldoximes were prepared by standard procedures [15].

4-Aryl-3-(2-arylethenesulfonyl)-1*H*-pyrroles (2). ***General procedure.*** A mixture of TosMIC (5 mmol) and **1** (5 mmol) in Et$_2$O/DMSO (2:1) was added dropwise under stirring to a suspension of NaH (50 mg) in Et$_2$O (10 mL) at room temperature. Stirring was continued for about 6 h. Then it was diluted with H$_2$O and extracted with Et$_2$O. The ethereal layer was dried over anhydrous Na$_2$SO$_4$. The solvent was removed *in vacuo*. The resultant solid was purified by recrystallization from MeOH.

Bis(4-aryl-1*H*-pyrrol-3yl)-sulfones (3). ***General procedure.*** A mixture of TosMIC (5 mmol) and **2** (5 mmol) in Et$_2$O/DMSO (2:1) was added dropwise under stirring to a suspension of NaH (50 mg) in Et$_2$O (10 mL) at room temperature. Stirring was continued for about 7 h. Then, H$_2$O was added and the product was extracted with Et$_2$O and dried over anhydrous Na$_2$SO$_4$. The solvent was removed *in vacuo*. The resultant solid was purified by column chromatography [Silica gel, hexane-ethyl acetate (1:4)].

(4′-Aryl-4′,5′-dihydro-1′*H*-pyrazol-3′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfones (4). ***General procedure.*** To a cooled solution of **2** (5 mmol) in CH$_2$Cl$_2$ (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 48–56 h. The solvent was removed under reduced pressure. The resultant solid was purified by recrystallization from MeOH.

(1′,3′,5′-Triaryl-4′,5′-dihydro-1′*H*-pyrazol-4′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfones (5). ***General procedure.*** A mixture of **2** (1 mmol), araldehyde phenylhydrazone (2 mmol) and chloramine-T (2 mmol) in MeOH (20 mL) was refluxed for 20–22 h. over a water bath. The precipitated inorganic salts were filtered off. The filtrate was concentrated and the residue was extracted with CH$_2$Cl$_2$. The organic phase was washed with water, brine and dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure. Recrystallization of the crude product from ethanol resulted in pure **5**.

(3′,5′-Diaryl-4′,5′-dihydro-isoxazol-4′-yl)-(4-aryl-1*H*-pyrrol-3-yl)-sulfones (6). ***General procedure.*** A mixture of **2** (1 mmol), araldoxime (2 mmol) and chloramine-T (2 mmol) in MeOH (20 mL) was refluxed for 16–18 h. over a water bath. The precipitated inorganic salts were filtered off. The filtrate was concentrated and the residue was extracted with CH$_2$Cl$_2$. The organic phase was washed with water, brine and dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure. Recrystallization of the crude product from ethanol resulted in pure **6**.

(4′-Phenyl-1′*H*-pyrazol-3′-yl)-(4-phenyl-1*H*-pyrrol-3-yl)-sulfone (7a)/(4-phenyl-1*H*-pyrrol-3-yl)-(1′,3′,5′-triphenyl-1′*H*-pyrazol-4′-yl)-sulfone (8a)/(3′,5′-diphenyl-isoxazol-4′-yl)-(4-phenyl-1*H*-pyrrol-3-yl)-sulfone (9a). ***General procedure.*** A solution of **4a**/**5a**/**6a** (1 mmol) and chloranil (1.04 mmol) in

Table 3

^1H and ^{13}C NMR data of compounds **2–9**.

Compound	^1H NMR ($CDCl_3$/DMSO-d_6) δ, ppm	^{13}C NMR ($CDCl_3$/DMSO-d_6) δ, ppm
2a	6.85 (s, 1H, C_2-H), 6.96 (d, 1H, C_1'-H, J = 15.6 Hz), 7.48 (s, 1H, C_5-H), 7.15-7.62 (m, 10H, Ar-H), 7.63 (d, 1H, C_2'-H, J = 15.6 Hz), 9.04 (bs, 1H, NH)	119.8 (C-4), 124.2 (C-1′), 125.7 (C-3), 125.9 (C-5), 127.3 (C-2), 141.3 (C-2′)
2b	3.72 (s, 6H, Ar-OCH_3), 6.79 (s, 1H, C_2-H), 6.89 (d, 1H, C_1'-H, J = 16.2 Hz), 7.41 (s, 1H, C_5-H), 6.95-7.58 (m, 8H, Ar-H), 7.65 (d, 1H, C_2'-H, J = 16.2 Hz), 9.12 (bs, 1H, NH)	55.2 (Ar-OCH_3), 118.7 (C-4), 123.6 (C-1′), 124.9 (C-3), 125.6 (C-5), 126.8 (C-2), 140.3 (C-2′)
2c	6.88 (s, 1H, C_2-H), 6.89 (d, 1H, C_1'-H, J = 16.3 Hz), 7.45 (s, 1H, C_5-H), 7.24-7.59 (m, 8H, Ar-H), 7.60 (d, 1H, C_2'-H, J = 16.3 Hz), 9.11 (bs, 1H, NH)	119.6 (C-4), 124.6 (C-1′), 125.8 (C-3), 126.3 (C-5), 127.6 (C-2), 140.3 (C-2′)
3a	6.84 (s, 2H, $C_{2,2}'$-H), 7.08 (s, 2H, $C_{5,5}'$-H), 7.02-7.48 (m, 10H, Ar-H), 9.05 (bs, 2H, NH)	122.6 (C-3,3′), 119.2 (C-4,4′), 126.2 (C-5,5′), 127.4 (C-2,2′)
3b	3.69 (s, 6H, Ar-OCH_3), 6.88 (s, 2H, $C_{2,2}'$-H), 7.06 (s, 2H, $C_{5,5}'$-H), 6.95-7.45 (m, 8H, Ar-H), 9.12 (bs, 2H, NH)	121.9 (C-3,3′), 55.5 (Ar-OCH_3), 118.6 (C-4,4′), 125.8 (C-5,5′), 127.6 (C-2,2′)
3c	6.89 (s, 2H, $C_{2,2}'$-H), 7.11 (s, 2H, $C_{5,5}'$-H), 7.15-7.44 (m, 8H, Ar-H), 9.11 (bs, 2H, NH)	122.5 (C-3,3′), 120.2 (C-4,4′), 124.6 (C-5,5′), 127.8 (C-2,2′)
4a	3.48 (dd, 1H, H_X, J_{AX} = 5.5, J_{MX} = 10.0 Hz), 3.86 (t, 1H, H_M) 4.48 (dd, 1H, H_A, J_{AM} = 12.6 Hz), 6.85 (s, 1H, C_2-H), 7.14-7.32 (m, 10H, Ar-H), 7.74 (s, 1H, C_5-H), 8.26 (bs, 1H, NH), 10.45 (bs, 1H, NH)	46.9 (C-4′), 57.2 (C-5′), 119.4 (C-4), 120.3 (C-3), 124.8 (C-5), 125.6 (C-2), 152.3 (C-3′)
4b	3.46 (dd, 1H, H_X, J_{AX} = 5.7, J_{MX} = 10.1 Hz), 3.67 (s, 6H, Ar-OCH_3), 3.89 (t, 1H, H_M), 4.45 (dd, 1H, H_A, J_{AM} = 12.8 Hz), 6.81 (s, 1H, C_2-H), 7.01-7.32 (m, 8H, Ar-H), 7.73 (s, 1H, C_5-H), 8.23 (bs, 1H, NH), 10.52 (bs, 1H, NH)	46.8 (C-4′), 55.3 (Ar-OCH_3), 56.4 (C-5′), 118.3 (C-4), 119.6 (C-3), 123.6 (C-5), 125.7 (C-2), 151.6 (C-3′)
4c	3.54 (dd, 1H, H_X, J_{AX} = 5.7, J_{MX} = 10.2 Hz), 3.84 (t, 1H, H_M), 4.45 (dd, 1H, H_A, J_{AM} = 12.9 Hz), 6.81 (s, 1H, C_2-H), 7.12-7.45 (m, 8H, Ar-H), 7.69 (s, 1H, C_5-H), 8.23 (bs, 1H, NH), 10.45 (bs, 1H, NH)	47.2 (C-4′), 56.8 (C-5′), 119.2 (C-4), 119.9 (C-3), 122.8 (C-5), 126.4 (C-2), 152.3(C-3′)
5a	5.25 (d, 1H, C_4'-H, J = 7.8 Hz), 5.63 (d, 1H, C_5'-H, J = 7.2 Hz), 6.79 (s, 1H, C_2-H), 6.85 (s, 1H, C_5-H), 7.22-7.54 (m, 20H, Ar-H), 8.85 (bs, 1H, NH)	63.6 (C-4′), 87.4 (C-5′), 119.2 (C-4), 121.0 (C-3), 124.4 (C-5), 126.8 (C-2), 154.9 (C-3′)
5b	3.74 (s, 6H, Ar-OCH_3), 5.27 (d, 1H, C_4'-H, J = 6.6 Hz), 5.63 (d, 1H, C_5'-H, J = 6.6 Hz), 6.74 (s, 1H, C_2-H), 6.87 (s, 1H, C_5-H), 7.04-7.83 (m, 18H, Ar-H), 8.86 (bs, 1H, NH)	55.2 (Ar-OCH_3), 64.8 (C-4′), 87.3 (C-5′), 120.4 (C-4), 121.6 (C-3), 123.8 (C-2), 127.2 (C-5), 154.8 (C-3′)
5c	5.24 (d, 1H, C_4'-H, J = 6.9 Hz), 5.62 (d, 1H, C_5'-H, J = 6.9 Hz), 6.73 (s, 1H, C_2-H), 6.85 (s, 1H, C_5-H), 7.12-7.80 (m, 19H, Ar-H), 8.91 (bs, 1H, NH)	62.8 (C-4′), 85.9 (C-5′), 118.6 (C-4), 122.6 (C-3), 123.8 (C-2), 125.8 (C-5), 154.6 (C-3′)
5d	5.26 (d, 1H, C_4'-H, J = 6.4 Hz), 5.65 (d, 1H, C_5'-H, J = 6.4 Hz), 6.76 (s, 1H, C_2-H), 6.92 (s, 1H, C_5-H), 7.18-7.82 (m, 17H, Ar-H), 8.93 (bs, 1H, NH)	63.9 (C-4′), 84.6 (C-5′), 119.3 (C-4), 121.8 (C-3), 124.6 (C-2), 124.9 (C-5), 153.7 (C-3′)
6a	5.19 (d, 1H, C_4'-H, J = 5.9 Hz), 5.67 (d, 1H, C_5'-H, J = 5.9 Hz), 6.76 (s, 1H, C_2-H), 6.85 (s, 1H, C_5-H), 7.08-7.93 (m, 15H, Ar-H), 8.83 (bs, 1H, NH)	64.9 (C-4′), 83.7 (C-5′), 119.4 (C-4), 121.9 (C-3), 124.3 (C-5), 126.3 (C-2), 151.7 (C-3′)
6b	3.74 (s, 6H, Ar-OCH_3), 5.21 (d, 1H, C_4'-H, J = 5.8 Hz), 5.66 (d, 1H, C_5'-H, J = 5.8 Hz), 6.75 (s, 1H, C_2-H), 6.87 (s, 1H, C_5-H), 7.01-7.94 (m, 13H, Ar-H), 8.86 (bs, 1H, NH)	55.6 (Ar-OCH_3), 63.6 (C-4′), 84.5 (C-5′), 118.7 (C-4), 122.3 (C-3), 125.7 (C-5), 126.7 (C-2), 152.6 (C-3′)
6c	5.23 (d, 1H, C_4'-H, J = 6.0 Hz), 5.72 (d, 1H, C_5'-H, J = 6.0 Hz), 6.74 (s, 1H, C_2-H), 6.83 (s, 1H, C_5-H), 7.14-7.92 (m, 14H, Ar-H), 8.91 (bs, 1H, NH)	64.6 (C-4′), 83.3 (C-5′), 119.8 (C-4), 122.6 (C-3), 125.5 (C-5), 126.1 (C-2), 153.8 (C-3′)
6d	5.24 (d, 1H, C_4'-H, J = 5.7 Hz), 5.70 (d, 1H, C_5'-H, J = 5.7 Hz), 6.78 (s, 1H, C_2-H), 6.86 (s, 1H, C_5-H), 7.18-7.89 (m, 12H, Ar-H), 8.94 (bs, 1H, NH)	64.7 (C-4′), 83.9 (C-5′), 119.6 (C-4), 121.8 (C-3), 125.3 (C-5), 125.9 (C-2), 152.7 (C-3′)
7a	6.36 (bs, 1H, NH), 6.75 (s, 1H, C_2-H), 6.94 (s, 1H, C_5-H), 6.96-7.84 (m, 11H, C_5'-H & Ar-H), 8.94 (bs, 1H, NH).	116.8 (C-4), 122.3 (C-3), 125.8 (C-5), 127.6 (C-2), 134.7 (C-5′), 140.9 (C-4′), 156.8 (C-3′)
8a	6.76 (s, 1H, C_2-H), 6.83 (s, 1H, C_5-H), 7.10-8.02 (m, 20H, Ar-H), 8.83 (bs, 1H, NH)	118.3 (C-4), 124.6 (C-3), 125.3 (C-5), 126.5 (C-2), 144.8 (C-3′), 147.8 (C-4′), 150.4 (C-5′)
9a	6.76 (s, 1H, C_2-H), 6.86 (s, 1H, C_5-H), 7.02-7.94 (m, 15H, Ar-H), 8.92 (bs, 1H, NH)	117.3 (C-4), 122.6 (C-3), 125.6 (C-5), 127.8 (C-2), 146.3 (C-4′), 147.4 (C-3′), 152.5 (C-5′)

xylene (10 mL) was refluxed for 30–35 h. Then it was treated with 5% sodium hydroxide solution. The organic layer was separated and repeatedly washed with water, dried over anhydrous Na_2SO_4 and was removed on a rotary evaporator. The solid obtained was purified by recrystallization in isopropanol to give pure **7a/8a/9a** respectively.

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