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A novel method for the synthesis of dipyrromethanes by metal triflate catalysis

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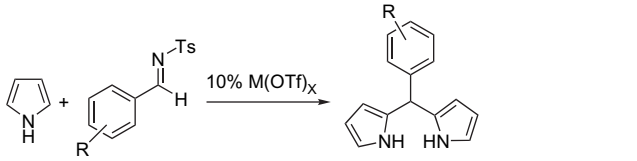
Abstract—5-Substituted dipyrromethanes were synthesized by the reaction of *N*-tosyl imines with excess pyrrole in the presence of metal triflates. Tripyrromethane and other oligomeric side products were not observed. High yields of 5-substituted dipyrromethanes were obtained for electron donating and withdrawing substituents by performing the reaction at two different temperatures. The new reaction procedure is simple and anhydrous conditions are not required.

1. Introduction

5-Substituted dipyrromethanes are important precursors for the synthesis of *meso*-substituted porphyrins, corroles, expanded and reduced porphyrins and related compounds such as dipyrrins, calixpyrroles and chlorins.[1] The first one-flask synthesis of dipyrromethanes was reported in 1994.[2] In the past decade, a number of methods have then been developed for the synthesis and purification of dipyrromethanes.[3] Almost all the methods consist of the condensation of an aldehyde and pyrrole in the presence of various acids such as $BF_3\cdot$etherate, trifluoroacetic acid (TFA), propionic acid and *p*-toluenesulfonic acid. These studies mostly afford moderate yields of *meso*-substituted dipyrromethanes. The yields are reduced due to the formation of oligomeric products, which make the purification of the dipyrromethanes from the reaction medium difficult.

Metal triflate catalyzed reactions are currently of great interest in organic chemistry. They have been used as water-stable and reuseable Lewis acids in several carbon–carbon bond forming reactions such as aldol, Michael, Diels–Alder and Friedel–Crafts acylation and alkylations.[4] Recently, we reported the metal triflate catalyzed addition of pyrroles to α,β-unsaturated esters.[5] We also examined the reactions of pyrrole with *N*-tosyl imines in the presence of catalytic amounts of metal triflates to obtain pyrrole-substituted sulfonamides.[6] In connection with this study, we report here a novel and an efficient method for preparing 5-substituted dipyrromethanes from the reaction of *N*-tosyl imines and excess pyrrole by using catalytic amounts of metal triflate (Scheme 1).



Scheme 1.

2. Results and discussion

Equimolar concentrations of pyrrole (**1**) and *N*-benzylidene-4-methylbenzenesulfonamide (**2a**) undergo a $Cu(OTf)_2$ catalyzed regioselective addition reaction in THF at rt to afford 4-methyl-*N*-(phenyl(1*H*-pyrrol-2-yl)methyl)benzenesulfonamide (**4a**). Increasing the molar ratio of pyrrole, to *N*-tosyl imine **2a**, to 2:1 gave **4a** in higher yield with the formation of 5-phenyldipyrromethane (**3a**) as a minor product.[6] After this examination, we focused on obtaining the 5-substituted dipyrromethane as the major product from the reaction of pyrrole and *N*-benzylidene-4-methylbenzenesulfonamide (**2a**). We performed the reaction of pyrrole with **2a** by using different pyrrole/*N*-tosyl imine ratios in the presence of copper triflate (10 mol %) at rt. Reactions with 10 and 20 equiv of pyrrole were carried out in THF, monitored with TLC and completed after 6 h, affording **3a**/**4a** with 34/37 and 40/32% yields, respectively (Scheme 2). When the reaction was performed with 40 equiv of pyrrole without solvent,

Keywords: Dipyrromethanes; Metal triflate; *N*-Tosyl imine; Pyrrole derivatives; Lewis acid catalysis.
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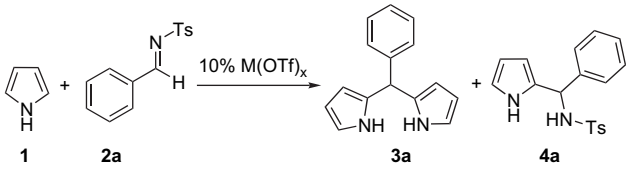
dipyrromethane was formed as the major product in 55% yield. Increasing the pyrrole equivalent did not obviously affect the yield of **3a**.



Scheme 2.

To investigate the effects of metal triflates, the reactions of pyrrole and *N*-benzylidene-4-methylbenzenesulfonamide (**2a**) were carried out in the presence of different metal triflates with excess pyrrole (40 equiv) at rt. Among all the metal triflates tested, $Gd(OTf)_3$ and $Cu(OTf)_2$ gave the highest yields of 5-phenyldipyrromethane (**3a**), 69 and 55%, respectively (Table 1).

Table 1. Effects of metal triflates on the synthesis of dipyrromethane **3a**[a]

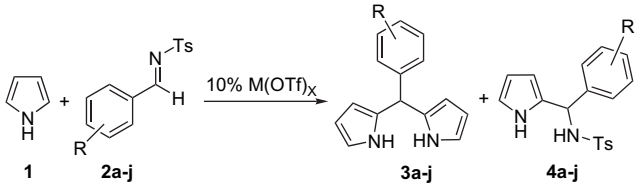
Entry	Catalyst	Yield (%)[b] **3a/4a**
1	$Cu(OTf)_2$	55/16
2	$Gd(OTf)_3$	69/20
3	$Yb(OTf)_3$	52/38
4	$Y(OTf)_3$	45/43
5	$La(OTf)_3$	34/53
6	$Zn(OTf)_2$	23/60
7	$Nd(OTf)_3$	14/72

[a] Reactions were carried out in excess pyrrole (40 equiv) as solvent at rt.
[b] Yield refers to pure product after column chromatography.

We continued to study the effect of substituents on the phenyl ring of the *N*-tosyl imines using $Cu(OTf)_2$ and $Gd(OTf)_3$ on the synthesis of 5-substituted dipyrromethanes. Reactions of *N*-tosyl imines (**2a–j**) and pyrrole with $Gd(OTf)_3$ catalyst gave 2-alkylated pyrrole sulfonamides (**4a–j**) in 10–85% yields and 5-substituted dipyrromethanes (**3a–j**) in 5–90% yields (Table 2). Similar results were obtained when $Cu(OTf)_2$ was used as the catalyst at rt; the corresponding pyrrole derivatives were obtained in 7–86% yields and dipyrromethanes in 5–85% yields. For both catalysts, formation of the products **3** and **4** is very sensitive to the nature of the substituents on *N*-tosyl imine. When the phenyl ring bears an electron donating substituent such as a methyl, hydroxy or methoxy, dipyrromethanes **3** are obtained in high yields (Table 2, entries 2–5). The reactions with electron withdrawing groups such as nitro, trifluoromethyl or halogens on the phenyl ring gave 5-substituted dipyrromethanes in lower yields at rt (Table 2, entries 6–10).

To improve the yields of dipyrromethane products having electron withdrawing substituents, reactions were carried out at 100 °C. It was observed that at high temperatures the yields of dipyrromethane products with electron withdrawing substituents and halogens increase dramatically (Table 2, entries 6–10). Dipyrromethanes with strongly electron withdrawing groups (nitro, trifluoromethyl) and halogens were synthesized in 68–79% yields with $Gd(OTf)_3$ and in 53–85% yields with $Cu(OTf)_2$. Despite this increase for electron withdrawing groups at 100 °C, yields for electron donating groups are lower. With this reaction protocol, we obtained high yields of dipyrromethanes for both types of

Table 2. Synthesis of 5-substituted dipyrromethanes by the reaction of pyrrole and different *N*-tosyl imines[a]



Entry	R	Catalyst $Gd(OTf)_3$ Yield (%)[b] **3/4**		Catalyst $Cu(OTf)_2$ Yield (%)[b] **3/4**		Compounds
		rt	100 °C	rt	100 °C	
1	H	69/20	65/17	55/16	48/10	**3a/4a**
2	4-CH_3O	83/10	64/15	85/8	45/19	**3b/4b**
3	2-CH_3O	71/17	61/21	55/20	48/35	**3c/4c**
4	4-CH_3	83/10	69/9	80/7	35/11	**3d/4d**
5	2-OH	90/—	44/—	77/—	27/—	**3e/4e**[c]
6	4-NO_2	5/85	79/8	7/78	72/9	**3f/4f**
7	4-CF_3	11/82	68/13	5/86	85/6	**3g/4g**
8	4-F	40/50	70/14	38/45	53/32	**3h/4h**
9	4-Cl	44/46	71/13	40/55	62/25	**3i/4i**
10	4-Br	20/71	74/12	38/53	74/14	**3j/4j**

[a] Reactions were carried out in excess pyrrole (40 equiv) as solvent.
[b] Yield refers to pure product after column chromatography.
[c] Addition product decomposed and could not be isolated by column chromatography.

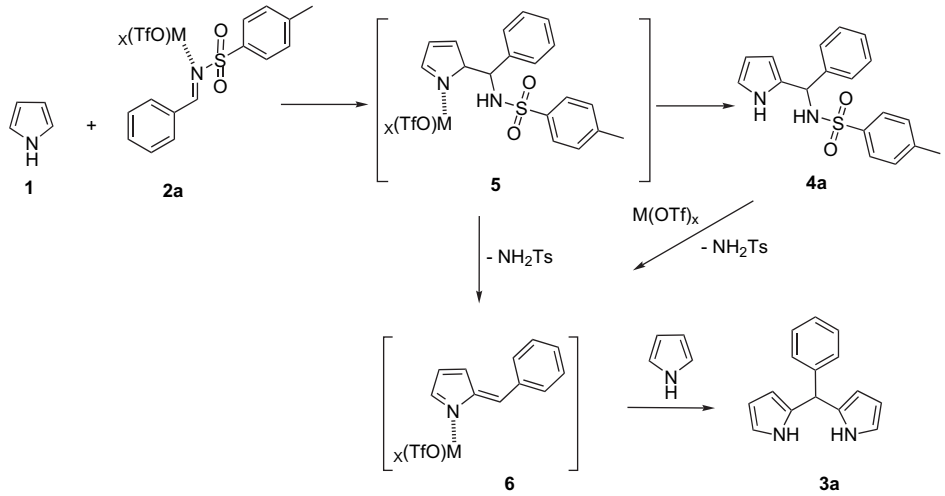
substituents only by performing the reaction at two different temperatures.

Structures of dipyrromethanes **3a–d**, **f**, **h–j** were confirmed by comparing their NMR spectra and melting points with those reported in literature.[2,7] Structures of **3e**, **g** and pyrrole derivatives **4a–j** were identified by ^1H NMR, ^{13}C NMR and elemental analysis. The position of the substituent was assigned by COSY spectra and by comparison of the ^1H NMR spectra with the known 2-alkylated pyrroles.[8]

The following reaction mechanism is proposed for the metal triflate catalyzed reaction of *N*-tosyl imine with pyrrole (Scheme 3). In the first step, *N*-tosyl imine is activated by the metal triflate. The addition of pyrrole to the activated imine complex affords structure **4a** through the intermediate **5**. Formation of dipyrromethane could be explained by the addition of a second pyrrole to the intermediate **6**, which is generated by the elimination of sulfonamide from intermediate **5** or compound **4a**. Structures like intermediate **6** are proposed by other researchers for the reaction of indole with imines, aldehydes and enones.[9] To support this proposed mechanism, the isolated product **4a** was reacted with excess pyrrole in the presence of metal triflate. Dipyrromethane was obtained as the main product after 6 h under the same conditions and *p*-toluenesulfonamide was isolated. The same reaction was performed without using the metal triflate and dipyrromethane formation was not observed. This examination shows that the metal triflate has a crucial role in the formation of dipyrromethane from **4a**.

3. Conclusion

In conclusion, a new and attractive synthetic method has been developed for the preparation of 5-substituted dipyrromethanes by the reaction of *N*-tosyl imine and pyrrole in the



Scheme 3.

presence of metal triflates. Tripyrromethane or any other oligomeric side products were not observed. The reaction procedure is simple and anhydrous conditions are not required. An advantage of this method is that high yields of 5-substituted dipyrromethanes with electron donating or withdrawing substituents can be obtained selectively only by tuning the reaction temperature.

4. Experimental

4.1. General

Commercially available reagents and solvents were used without further purification. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using $SiMe_4$ as an internal reference with Bruker Ultrashield FT NMR spectrometer. IR spectra were determined on an Unicam Mattson 1000 FT IR spectrometer. Melting points were recorded on Gallenkamp melting-point apparatus and are uncorrected. Thin-layer chromatography was performed with 60F silica gel plates and flash column chromatography by use of silica gel 60 F_{254} (230–400 mesh). The spots were visualized with UV light (λ=254 nm). *N*-Tosyl imines (**2a**–**j**) are synthesized in high yields by the reaction of *p*-toluenesulfonamide and aldehydes in the presence of *p*-toluenesulfonic acid.

4.2. Synthesis of dipyrromethanes (3) and 2-substituted pyrrole sulfonamides (4)

N-Tosyl imine (1 mmol) was dissolved in excess pyrrole (40 mmol) and then metal triflate (0.1 mmol) was added to the reaction mixture at the temperature indicated in Table 2. The reaction was monitored with TLC and completed after 6 h. Metal triflate was removed from the reaction medium by subjecting the mixture to a short flash silica gel chromatography using ethyl acetate as an eluent. The eluent was removed under reduced pressure and the residue was purified by flash silica gel chromatography.

4.2.1. 5-Phenyldipyrromethane (3a).[7a] Pale yellow crystals; mp: 100–101 °C, lit.: 100–101 °C; R_f 0.60 (1:3 EtOAc/hexane); IR (KBr) 3449, 2951, 1630, 1510, 1410, 1293, 1225, 1048, 760, 703, 607 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.49 (s, 1H, *meso*H), 5.92 (br s, 2H, 2C3-H), 6.14 (dd, *J* 2.8, 5.9, 2H, 2C4-H), 6.68 (dd, *J* 2.6, 4.2, 2H, 2C5-H), 7.22–7.35 (m, 5H, Ar-H), 7.88 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.10, 107.45, 108.75, 117.12, 127.03, 128.51, 128.68, 132.36, 142.23.

4.2.2. 5-(4-Methoxyphenyl)dipyrromethane (3b).[7a] Pale yellow powder; mp: 98–99 °C, lit.: 99 °C; R_f 0.47 (1:3 EtOAc/hexane); IR (KBr) 3405, 2964, 2936, 1616, 1507, 1457, 1299, 1245, 1175, 1103, 1027, 965, 838, 774, 720, 554 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H, OCH_3), 5.42 (s, 1H, *meso*H), 5.90–5.92 (m, 2H, 2C3-H), 6.14 (dd, *J* 2.8, 6.0, 2H, 2C4-H), 6.65–6.67 (m, 2H, 2C5-H), 6.85 (d, *J* 8.6, 2H, Ar-H), 7.14 (d, *J* 8.6, 2H, Ar-H), 7.82 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz): δ 43.21, 55.15, 107.27, 108.67, 114.03, 117.02, 129.44, 132.76, 134.29, 158.61.

4.2.3. 5-(2-Methoxyphenyl)dipyrromethane (3c).[7a] Pale yellow powder; mp: 114–115 °C, lit.: 115 °C; R_f 0.65 (1:3 EtOAc/hexane); IR (KBr) 3425, 1636, 1485, 1242, 1090, 1023, 966, 715, 555 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3H, OCH_3), 5.82 (s, 1H, *meso*H), 5.91 (br s, 2H, 2C3-H), 6.15 (d, *J* 2.5, 2H, 2C4-H), 6.63 (d, *J* 1.4, 2H, 2C5-H), 6.94–6.97 (m, 2H, Ar-H), 7.12 (d, *J* 6.8, 1H, Ar-H), 7.28 (t, *J* 7.8, 1H, Ar-H), 7.97 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.68, 55.74, 107.10, 108.70, 111.24, 116.67, 121.04, 128.07, 129.60, 131.14, 132.47, 156.73.

4.2.4. 5-(4-Methylphenyl)dipyrromethane (3d).[7b] Pale yellow crystals; mp: 110–111 °C, lit.: 110–111 °C; R_f 0.65 (1:3 EtOAc/hexane); IR (KBr) 3417, 2356, 1635, 1508, 1420, 1254, 1089, 1025, 964, 909, 790, 742, 509 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3), 5.44 (s, 1H, *meso*H), 5.91 (br s, 2H, 2C3-H), 6.13 (dd, *J* 2.8, 5.9, 2H, 2C4-H), 6.66 (dd, *J* 2.6, 4.2, 2H, 2C5-H), 7.10–7.15 (m, 4H, Ar-H), 7.85 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.18, 43.72, 107.32, 108.74, 116.99, 128.42, 129.38, 132.57, 136.42, 139.25.

4.2.5. 5-(2-Hydroxyphenyl)dipyrromethane (3e). Light brown oil; R_f 0.32 (1:3 EtOAc/hexane); IR (KBr) 3418, 2072, 1635, 1493, 1451, 1330, 1255, 1085, 1023, 909, 790, 741, 529 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.17

(br s, 1H, OH), 5.53 (s, 1H, *meso*H), 6.01 (br s, 2H, 2C3-H), 6.16 (dd, *J* 2.8, 5.9, 2H, 2C4-H), 6.70 (dd, *J* 2.6, 4.1, 2H, 2C5-H), 6.87–6.95 (m, 2H, Ar-H), 7.08–7.10 (m, 1H, Ar-H), 7.18–7.22 (m, 1H, Ar-H), 8.14 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.59, 107.22, 108.85, 117.89, 118.00, 121.63, 128.52, 128.81, 130.19, 130.78, 153.87. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.48; H, 6.03; N, 11.58.

4.2.6. 5-(4-Nitrophenyl)dipyrromethane (3f).[7a] Yellow powder; mp: 159–160 °C, lit.: 159–160 °C; R_f 0.48 (1:3 EtOAc/hexane); IR (KBr) 3394, 3359, 3101, 1595, 1512, 1348, 1114, 1027, 808, 735, 660, 568 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.59 (s, 1H, *meso*H), 5.88 (br s, 2H, 2C3-H), 6.18 (dd, *J* 2.8, 6.0, 2H, 2C4-H), 6.75 (dd, *J* 2.6, 4.2, 2H, 2C5-H), 7.39 (d, *J* 8.6, 2H, Ar-H), 7.98 (br s, 2H, 2N-H), 8.18 (d, *J* 8.8, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.87, 107.92, 108.95, 117.94, 123.80, 129.25, 130.76, 147.02, 149.66.

4.2.7. 5-(4-Trifluoromethylphenyl)dipyrromethane (3g). Yellow oil; R_f 0.47 (1:3 EtOAc/hexane); IR (KBr) 3448, 3401, 2980, 1618, 1416, 1326, 1164, 1124, 1067, 1019, 775, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.51 (s, 1H, *meso*H), 5.91 (br s, 2H, 2C3-H), 6.20 (dd, *J* 2.8, 6.0, 2H, 2C4-H), 6.67–6.69 (m, 2H, 2C5-H), 7.35 (d, *J* 8.3, 2H, Ar-H), 7.63 (d, *J* 8.1, 2H, Ar-H), 7.82 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.78, 107.84, 108.82, 117.66, 124.16 (q, $^1J_{C-F}$ 270.3), 125.54 (q, $^3J_{C-F}$ 3.7), 128.75, 129.29 (q, $^2J_{C-F}$ 32.2), 131.50, 146.28. Anal. Calcd for $C_{16}H_{13}F_3N_2$: C, 66.20; H, 4.51; N, 9.65. Found: C, 66.07; H, 4.70; N, 9.59.

4.2.8. 5-(4-Fluorophenyl)dipyrromethane (3h).[7a] Light brown crystals; mp: 80–81 °C, lit.: 81 °C; R_f 0.53 (1:3 EtOAc/hexane); IR (KBr) 3410, 2928, 1610, 1498, 1451, 1285, 1175, 1103, 960, 764, 554 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45 (s, 1H, *meso*H), 5.89 (br s, 2H, 2C3-H), 6.16 (dd, *J* 2.8, 5.8, 2H, 2C4-H), 6.66 (br s, 2H, 2C5-H), 7.00–7.05 (m, 2H, Ar-H), 7.16–7.20 (m, 2H, Ar-H), 7.81 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.28, 107.55, 108.79, 115.42 (d, $^2J_{C-F}$ 21.3), 117.34, 129.92 (d, $^3J_{C-F}$ 7.9), 132.24, 137.96 (d, $^4J_{C-F}$ 3.2), 161.85 (d, $^1J_{C-F}$ 244.5).

4.2.9. 5-(4-Chlorophenyl)dipyrromethane (3i).[7b] Pale yellow powder; mp: 112–113 °C, lit.: 112 °C; R_f 0.58 (1:3 EtOAc/hexane); IR (KBr) 3382, 2958, 2923, 2861, 1641, 1485, 1405, 1255, 1087, 1022, 767, 720, 550, 508 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.42 (s, 1H, *meso*H), 5.90 (br s, 2H, 2C3-H), 6.17 (dd, *J* 2.8, 5.8, 2H, 2C4-H), 6.66 (dd, *J* 2.6, 4.2, 2H, 2C5-H), 7.15 (d, *J* 8.4, 2H, Ar-H), 7.31 (d, *J* 8.4, 2H, Ar-H), 7.80 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.35, 107.61, 108.75, 117.42, 128.70, 129.74, 131.88, 132.81, 140.69.

4.2.10. 5-(4-Bromophenyl)dipyrromethane (3j).[2] Pale yellow powder; mp: 122–123 °C, lit.: 125–125.5 °C; R_f 0.59 (1:3 EtOAc/hexane); IR (KBr) 3374, 3098, 2957, 2920, 2861, 1707, 1481, 1400, 1083, 1021, 765, 720, 643, 544, 503 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.41 (s, 1H, *meso*H), 5.90 (br s, 2H, 2C3-H), 6.16 (dd, *J* 2.8, 5.9, 2H, 2C4-H), 6.66 (dd, *J* 2.6, 4.2, 2H, 2C5-H), 7.10 (d, *J* 8.4, 2H, Ar-H), 7.46 (d, *J* 8.4, 2H, Ar-H), 7.80 (br s, 2H, 2N-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.50, 107.65, 108.83, 117.44, 120.95, 130.17, 131.71, 131.77, 141.27.

4.2.11. 4-Methyl-*N*-(phenyl(1*H*-pyrrol-2-yl)methyl)-benzenesulfonamide (4a). White powder; mp: 132–133 °C; R_f 0.40 (1:3 EtOAc/hexane); IR (KBr): 3458, 2085, 1633, 1390, 1282, 1136, 1080, 1021, 689, 605, 531 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H, CH_3), 5.57–5.60 (m, 2H, C3-H, CH), 5.85 (d, *J* 9.9, 1H, SO_2NH), 5.97 (dd, *J* 2.8, 6.0, 1H, C4-H), 6.65 (dd, *J* 2.5, 4.0, 1H, C5-H), 7.09–7.20 (m, 7H, Ar-H), 7.53 (d, *J* 8.3, 2H, Ar-H), 8.76 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.49, 55.78, 108.20, 118.57, 127.16, 127.38, 127.57, 128.35, 129.05, 129.29, 130.53, 137.47, 138.89, 142.87. Anal. Calcd for $C_{18}H_{18}N_2O_2S$: C, 66.23; H, 5.56; N, 8.58; S, 9.82. Found: C, 66.12; H, 5.63; N, 8.40; S, 9.73.

4.2.12. *N*-((4-Methoxyphenyl)(1*H*-pyrrol-2-yl)methyl)-4-methylbenzenesulfonamide (4b). Colourless viscous oil; R_f 0.30 (1:3 EtOAc/hexane); IR (KBr): 3516, 2072, 1636, 1507, 1243, 1169, 1027, 762, 715, 556 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 5.50 (d, *J* 8.1, 1H, CH), 5.57–5.59 (m, 2H, SO_2NH, C3-H), 5.98 (dd, *J* 2.7, 6.0, 1H, C4-H), 6.67 (br s, 1H, C5-H), 6.70 (d, *J* 8.7, 2H, Ar-H), 7.02 (d, *J* 8.7, 2H, Ar-H), 7.14 (d, *J* 8.2, 2H, Ar-H), 7.55 (d, *J* 8.3, 2H, Ar-H), 7.84 (d, *J* 8.4, 2H, Ar-H), 8.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.55, 55.09, 55.53, 108.08, 108.19, 113.79, 118.51, 127.25, 128.04, 129.03, 130.90, 131.06, 137.54, 142.88, 159.19. Anal. Calcd for $C_{19}H_{20}N_2O_3S$: C, 64.02; H, 5.66; N, 7.86; S, 9.00. Found: C, 64.25; H, 5.63; N, 7.88; S, 9.08.

4.2.13. *N*-((2-Methoxyphenyl)(1*H*-pyrrol-2-yl)methyl)-4-methylbenzenesulfonamide (4c). Light brown powder; mp: 132–133 °C; R_f 0.34 (1:3 EtOAc/hexane); IR (KBr): 3440, 2954, 2835, 1638, 1491, 1453, 1328, 1247, 1156, 1092, 1023, 909, 790, 743, 664, 549 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 5.51 (br s, 1H, C3-H), 5.64 (d, *J* 9.3, 1H, CH), 5.90 (d, *J* 9.1, 1H, SO_2NH), 5.97 (dd, *J* 2.8, 5.8, 1H, C4-H), 6.70 (dd, *J* 2.5, 4.1, 1H, C5-H), 6.73 (d, *J* 8.3, 1H, Ar-H), 6.81 (t, *J* 7.4, 1H, Ar-H), 7.00 (dd, *J* 1.6, 7.5, 1H, Ar-H), 7.09 (d, *J* 8.2, 2H, Ar-H), 7.16–7.21 (m, 1H, Ar-H), 7.55 (d, *J* 8.2, 2H, Ar-H), 8.72 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.55, 53.85, 55.45, 107.04, 108.26, 111.21, 118.01, 120.87, 126.82, 127.22, 129.09, 129.60, 130.55, 137.86, 142.55, 156.76. Anal. Calcd for $C_{19}H_{20}N_2O_3S$: C, 64.02; H, 5.66; N, 7.86; S, 9.00. Found: C, 64.11; H, 5.81; N, 7.82; S, 8.75.

4.2.14. *N*-((1*H*-Pyrrol-2-yl)(*p*-tolyl)methyl)-4-methyl-benzenesulfonamide (4d). Light brown powder; mp: 96–97 °C; R_f 0.44 (1:3 EtOAc/hexane); IR (KBr): 3426, 2963, 2924, 2866, 2104, 1636, 1509, 1426, 1321, 1262, 1154, 1091, 1026, 910, 790, 722, 663, 563 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, CH_3), 2.43 (s, 3H, SO_2Ph-CH_3), 5.52 (d, *J* 8.2, 1H, CH), 5.58 (br s, 1H, C3-H), 5.62 (d, *J* 8.0, 1H, SO_2NH), 5.98 (dd, *J* 2.8, 5.7, 1H, C4-H), 6.66 (br s, 1H, C5-H), 7.00–7.02 (m, 4H, Ar-H), 7.13 (d, *J* 8.1, 2H, Ar-H), 7.55 (d, *J* 8.2, 2H, Ar-H), 8.62 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.15, 21.53, 55.64, 108.13, 108.17, 118.51, 127.24,

127.37, 129.06, 129.31, 130.78, 135.98, 137.27, 137.55, 142.83. Anal. Calcd for $C_{19}H_{20}N_2O_2S$: C, 67.03; H, 5.92; N, 8.23; S, 9.42. Found: C, 66.90; H, 5.95; N, 8.20; S, 9.37.

4.2.15. 4-Methyl-*N*-((4-nitrophenyl)(1*H*-pyrrol-2-yl)-methyl)benzenesulfonamide (4f). Light brown powder; mp: 153–154 °C; R_f 0.34 (1:3 EtOAc/hexane); IR (KBr): 3419, 1716, 1636, 1512, 1412, 1337, 1255, 1150, 1089, 1014, 909, 791, 741, 688, 549 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 3H, CH_3), 5.29 (br s, 1H, SO_2NH), 5.52 (br s, 1H, C3-H), 5.70 (br s, 1H, CH), 6.02 (dd, *J* 2.8, 6.0, 1H, C4-H), 6.76 (dd, *J* 2.6, 4.0, 1H, C5-H), 7.20 (d, *J* 8.0, 2H, Ar-H), 7.37 (d, *J* 8.6, 2H, Ar-H), 7.60 (d, *J* 8.3, 2H, Ar-H), 8.10 (d, *J* 8.7, 2H, Ar-H), 8.56 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.93, 55.06, 108.69, 119.38, 123.54, 127.15, 128.16, 128.99, 129.56, 134.98, 137.06, 143.78, 145.64. Anal. Calcd for $C_{18}H_{17}N_3O_4S$: C, 58.21; H, 4.61; N, 11.31; S, 8.63. Found: C, 58.00; H, 4.68; N, 11.38; S, 8.51.

4.2.16. *N*-((1*H*-Pyrrol-2-yl)(4-(trifluoromethyl)phenyl)-methyl)-4-methylbenzenesulfonamide (4g). White powder; mp: 113–114 °C; R_f 0.38 (1:3 EtOAc/hexane); IR (KBr): 3382, 3272, 3107, 3061, 2926, 2867, 1918, 1802, 1612, 1489, 1422, 1325, 1160, 1125, 1063, 1026, 915, 850, 792, 732, 665, 660, 555 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 3H, CH_3), 5.55 (br s, 1H, C3-H), 5.69 (d, *J* 8.6, 1H, CH), 6.00–6.03 (m, 2H, C4-H, SO_2NH), 6.69 (br s, 1H, C5-H), 7.07 (d, *J* 8.1, 2H, Ar-H), 7.24 (d, *J* 8.1, 2H, Ar-H), 7.39 (d, *J* 8.2, 2H, Ar-H), 7.47 (d, *J* 8.2, 2H, Ar-H), 8.86 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.32, 55.66, 108.36, 108.61, 119.15, 125.17 (q, $^3J_{C-F}$ 3.6), 127.05, 127.91, 129.39, 129.49, 129.90 (q, $^2J_{C-F}$ 32.2), 137.01, 142.49, 143.46. Anal. Calcd for $C_{19}H_{17}F_3N_2O_2S$: C, 57.86; H, 4.34; N, 7.10; S, 8.13. Found: C, 57.60; H, 4.32; N, 7.13; S, 7.99.

4.2.17. *N*-((4-Fluorophenyl)(1*H*-pyrrol-2-yl)methyl)-4-methylbenzenesulfonamide (4h). Colourless viscous oil; R_f 0.37 (1:3 EtOAc/hexane); IR (KBr): 3423, 2978, 2922, 2870, 1640, 1505, 1429, 1322, 1223, 1154, 1092, 1029, 915, 844, 774, 722, 664, 542 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H, CH_3), 5.54 (br s, 1H, C3-H), 5.57 (d, *J* 8.4, 1H, CH), 5.86 (d, *J* 8.4, 1H, SO_2NH), 5.98 (dd, *J* 2.7, 5.9, 1H, C4-H), 6.67 (dd, *J* 2.6, 4.1, 1H, C5-H), 6.84 (t, *J* 8.6, 2H, Ar-H), 7.07–7.13 (m, 4H, Ar-H), 7.52 (d, *J* 8.3, 2H, Ar-H), 8.77 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.50, 55.27, 108.25, 115.21 (d, $^2J_{C-F}$ 21.4), 118.81, 127.15, 129.10 (d, $^3J_{C-F}$ 8.1), 129.37, 130.31, 134.58 (d, $^4J_{C-F}$ 3.1), 137.35, 143.15, 162.21 (d, $^1J_{C-F}$ 245.7). Anal. Calcd for $C_{18}H_{17}FN_2O_2S$: C, 62.77; H, 4.98; N, 8.13; S, 9.31. Found: C, 62.40; H, 5.01; N, 8.05; S, 9.19.

4.2.18. *N*-((4-Chlorophenyl)(1*H*-pyrrol-2-yl)methyl)-4-methylbenzenesulfonamide (4i). Brown powder; mp: 115–116 °C; R_f 0.43 (1:3 EtOAc/hexane); IR (KBr): 3448, 3405, 2965, 2922, 2863, 1636, 1332, 1155, 1087, 1022, 805, 721, 662, 561 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 5.54–5.57 (m, 2H, C3-H, CH), 5.88 (d, *J* 8.5, 1H, SO_2NH), 5.98 (dd, *J* 2.7, 6.0, 1H, C4-H), 6.65–6.66 (m, 1H, C5-H), 7.05 (d, *J* 8.5, 2H, Ar-H), 7.11–7.13 (m, 4H, Ar-H), 7.49 (d, *J* 8.3, 2H, Ar-H), 8.79 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.53, 55.34, 108.27, 108.40, 118.91, 127.13, 128.44, 128.89, 129.40, 129.92, 133.60, 137.26, 137.32, 143.23. Anal. Calcd for $C_{18}H_{17}ClN_2O_2S$: C, 59.91; H, 4.75; N, 7.76; S, 8.89. Found: C, 59.67; H, 4.70; N, 7.82; S, 8.78.

4.2.19. *N*-((4-Bromophenyl)(1*H*-pyrrol-2-yl)methyl)-4-methylbenzenesulfonamide (4j). Brown powder; mp: 116–117 °C; R_f 0.42 (1:3 EtOAc/hexane); IR (KBr): 3388, 3275, 2961, 2921, 2862, 2756, 1691, 1596, 1484, 1432, 1323, 1154, 1088, 1025, 807, 663, 559 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 5.55–5.57 (m, 2H, C3-H, CH), 5.97–6.00 (m, 2H, SO_2NH, C4-H) 6.66 (dd, *J* 2.5, 4.0, 1H, C5-H), 6.98 (d, *J* 8.4, 2H, Ar-H), 7.10 (d, *J* 8.1, 2H, Ar-H), 7.26 (d, *J* 8.4, 2H, Ar-H), 7.47 (d, *J* 8.3, 2H, Ar-H), 8.83 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.55, 55.42, 108.27, 108.43, 118.94, 121.70, 127.11, 129.24, 129.41, 129.79, 131.38, 137.20, 137.77, 143.26. Anal. Calcd for $C_{18}H_{17}BrN_2O_2S$: C, 53.34; H, 4.23; N, 6.91; S, 7.91. Found: C, 53.67; H, 4.31; N, 6.84; S, 7.98.

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