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Cite this: *RSC Advances*, 2012, **2**, 1432–1438

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PAPER

Solvent based selectivity in the synthesis of di(2-aryl-1*H*-3-indolyl) sulfides and 1-aryl-2-[(2-aryl-1*H*-3-indolyl)sulfanyl]-1-ethanones†

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Received 12th October 2011, Accepted 2nd November 2011
DOI: 10.1039/c1ra00878a

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The commendable product selectivity exhibited by the solvents during the reaction of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanones with phenylhydrazine hydrochloride yielding exclusively 1-aryl-2-[(2-aryl-1*H*-3-indolyl)sulfanyl]-1-ethanones in THF and di(2-aryl-1*H*-3-indolyl) sulfides in ethanol is described.

Introduction

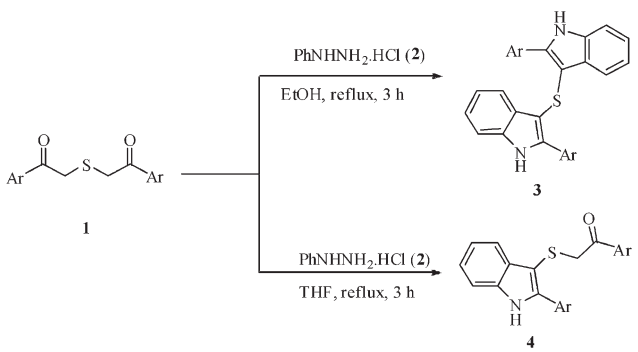
Indole nucleus is found in many medicinal compounds and hence is considered to be a very important heterocyclic moiety.[1] Indole and its derivatives possess a wide spectrum of biological activities including *anti*-inflammatory,[2] antimicrobial,[3] antibacterial,[4] anticonvulsant,[5] cardiovascular[6] and HIV-integrase inhibitor[7] characteristics.

The Fischer indolization of carbonyl synthons continues to maintain its prominent role as a route to indoles[8,9] and in synthetic combinatorial chemistry.[10] Though the Fischer method is the most widely used protocol for the synthesis of indoles, it suffers from low yields,[11] formation of side products and low regioselectivity in the case of unsymmetrical ketones.[11a–b,12] In contrast, the work described in the present investigation has achieved a remarkable selectivity yielding either mono- or bisindoles with the reaction medium determining the selectivity. It can be seen that protic solvents tend to favour the formation of bisindole, while aprotic solvents prefer to yield monoindole. Acetonitrile seems to be non selective.

Results and discussion

In continuation of our effort on the synthesis of diverse heterocyclic compounds[13] of biological significance, we herein report a very simple and highly selective method for the synthesis of di(2-aryl-1*H*-3-indolyl) sulfides and 1-aryl-2-[(2-aryl-1*H*-3-indolyl)sulfanyl]-1-ethanones by the reaction of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanones with phenylhydrazine hydrochloride in ethanol and THF respectively (Scheme 1). It is interesting that the natural product Echinosulfone A, a sulfone from the marine sponge, *Echinodictyum*[1e,14] has a bisindole core similar to that of di(2-aryl-1*H*-3-indolyl) sulphides generated during the present investigation.

A mixture of 2-[(2-oxo-2-phenylethyl)sulfanyl]-1-phenyl-1-ethanone **1a** (1 mmol) and phenylhydrazine hydrochloride **2** (2.5 mmol) when refluxed in ethanol (7 ml) gave di(2-phenyl-1*H*-3-indolyl) sulphide (**3a**) in 85% yield (Table 1). It is noteworthy that whatever be the mole ratio between 2-[(2-oxo-2-phenylethyl)sulfanyl]-1-phenyl-1-ethanone **1a** and phenylhydrazine hydrochloride **2** (1 : 1; 1 : 1.5; 1 : 2; 1 : 2.5), only the diheteroaryl sulphide and no mono indole was obtained. The best yield was obtained with a 1 : 2.5 ratio (Table 1). Under these optimized conditions for the generation of **3**, various substituted diketones **1** were selected to react with phenylhydrazine hydrochloride **2** to give different di(2-aryl-1*H*-3-indolyl) sulfides **3** in high yields (76–85%) within three hours (Table 2). The reaction proceeded efficiently, tolerating both electron donating and withdrawing substituents on the aromatic ring. When the reaction was performed in methanol, 2-propanol and ethylene glycol, the yield of **3a** decreased considerably (Table 1). When solvents like toluene, chloroform, dichloromethane and DMF were used, either a viscous mass with no recognisable products was obtained or the starting materials were recovered unchanged. A notable observation is that the reaction has led



Scheme 1 Synthesis of mono- and bisindoles.

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† Electronic Supplementary Information (ESI) available. See DOI: 10.1039/c1ra00878a/

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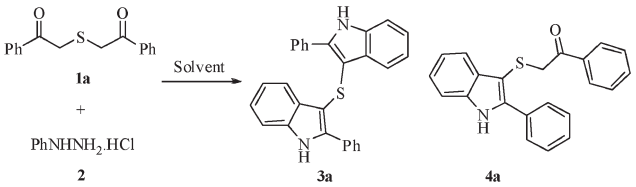
Table 1 Reaction of **1a** with **2** under different conditions



Entry	Solvent	Mole ratio, **1a**:**2**	Time (h)	Yield of **3a** (%)[a]	Yield of **4a** (%)[a]
1	EtOH	1 : 2.5	3	85	0
2	EtOH	1 : 2.0	3	76	0
3	EtOH	1 : 1.5	3.5	54	0
4	MeOH	1 : 2.5	3	72	0
5	2-Propanol	1 : 2.5	3	64	0
6	Ethylene glycol	1 : 2.5	3	61	0
7	DMF	1 : 2.5	5	0	0
8	Toluene	1 : 2.5	5	0	0
9	CH_3CN	1 : 2.5	5	21	32
10	$CHCl_3$	1 : 2.5	5	0	0
11	CH_2Cl_2	1 : 2.5	5	0	0
12	THF	1 : 1.0	3	0	72
13	THF	1 : 1.5	3	0	82
14	THF	1 : 2.0	3	0	81
15	THF	1 : 2.5	3.5	0	82

[a] Isolated yield after purification by column chromatography.

to a mixture of **3a** and **4a**, when the reaction was investigated in acetonitrile (Table 1).

Interestingly, when this reaction between **1a** and **2** was performed in THF in different mole ratios (1 : 1; 1 : 1.5; 1 : 2 and 1 : 2.5), only the monoindole, 1-phenyl-2-[(2-phenyl-1*H*-3-indolyl)sulfanyl]-1-ethanone **4a** was obtained in good yield (Table 1).

The cleanest conversion and highest yield of **4a** was achieved when 1.5 equiv of the phenylhydrazine hydrochloride for 1.0 equivalent of 2-[(2-oxo-2-phenylethyl)sulfanyl]-1-phenyl-1-ethanone **1a** was used. This protocol for **4a** was used to generate a range of monoindoles **4a–f** in 78–85% isolated yield (Table 2).

The structures of the isolated products bisindoles **3** and monoindoles **4** were deduced on the basis of IR, mass, ^{1}H NMR and ^{13}C NMR spectral studies. The structure of the symmetrical bisindoles **3** is in accord with the NMR spectroscopic data as illustrated for di[2-(4-methylphenyl)-1*H*-3-indolyl] sulphide **3b** (Fig. 1).

The ^{1}H NMR spectrum of **3b** has two triplets at 7.08 and 7.18 ppm (J = 7.5 Hz) which are assignable to H-5 and H-6 of the indole ring respectively. These protons show C,H-COSY correlation with C-5 at 120.2 and C-6 at 122.4 ppm. Both H-5 and H-6 protons further show HMBCs with C-3a at 131.2, C-7 at 111.3 ppm and C-7a at 136.1, C-4 at 119.3 ppm respectively. The H-4 hydrogen gives a doublet at 7.55 ppm (J = 7.5 Hz), which shows C,H-COSY correlation with the signal at 119.3 ppm assignable to C-4 and HMBCs with C-3 at 102.4, C-3a at 131.2, C-7a at 136.2, C-6 at 122.4 ppm (Fig. 1). The doublet at 7.37 ppm (J = 7.5 Hz) is due to H-7 hydrogen and is having HMBC correlation with C-3a at 131.2 and C-5 at 120.2 ppm. The H-7 further gives C,H-COSY correlation with the signal at 111.3 ppm due to C-7. The NH proton appeared as a singlet at 10.68 ppm. Bisindole **3b** shows absorption at 3374 cm^{-1} in its IR spectrum. There is neither the presence of carbonyl absorption band in IR nor any carbonyl signal in ^{13}C NMR spectrum.

The ^{1}H NMR spectrum of 1-(4-bromophenyl)-2-[2-(4-bromophenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (Fig. 2) **4d**, the H-5 and H-6 protons of the indole ring appeared as triplet of doublets at 7.15 and 7.22 ppm (J = 7.8, 1.2 Hz) respectively. These protons show C,H-COSY correlation with C-5 at

Table 2 Reaction of **1** with **2** in ethanol/THF under optimized conditions

		in EtOH		in THF	
Entry	Ar	Time (h)	Yield of **3** (%)[a]	Time (h)	Yield of **4** (%)[a]
a	C_6H_5	3	85	3	82
b	*p*-MeC_6H_4	3	81	3	79
c	*p*-ClC_6H_4	1	82	2.5	85
d	*p*-BrC_6H_4	1.5	79	2	82
e	*p*-PhC_6H_4	2	81	4	78
f	2-Naphthyl	1.5	76	3	79

[a] Isolated yield after purification by recrystallisation from ethyl acetate.

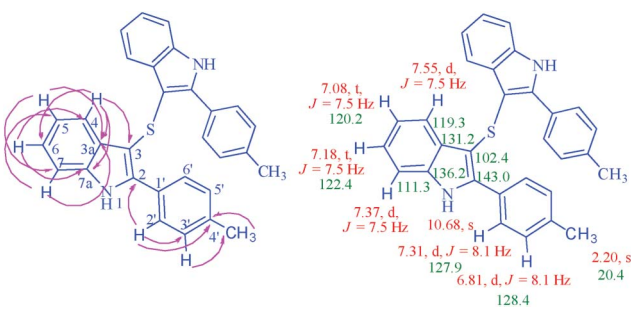


Fig. 1 Selected HMBCs and ^{1}H and ^{13}C chemical shifts in compound **3b**.

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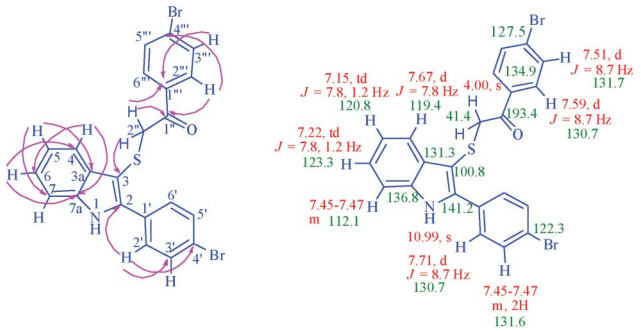
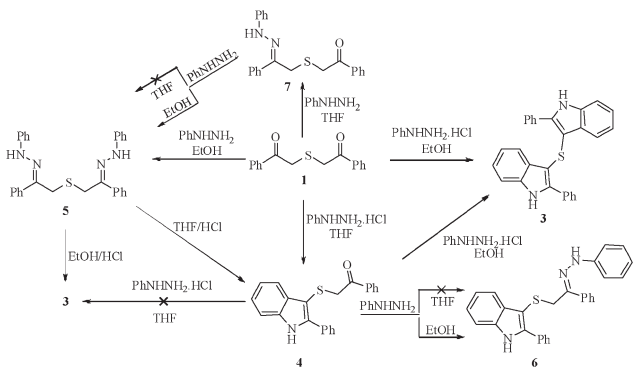


Fig. 2 Selected HMBCs and ^{1}H and ^{13}C chemical shifts in compound **4d**.

120.8 ppm and C-6 at 123.3 ppm respectively and they further show HMBCs with C-3a at 131.3 ppm, C-7 at 112.1 ppm and C-4 at 119.4 ppm, C-7a at 136.8 ppm. The H-4 proton appears as a doublet at 7.67 ppm (J = 7.8 Hz) which shows C,H-COSY correlation with the signal at 119.4 ppm assignable to C-4 and HMBCs with C-6 at 123.3, C-7a at 136.8 ppm (Fig. 2). The multiplet between 7.45 and 7.47 ppm is due to H-7 hydrogen. The NH proton appears as a singlet at 10.99 ppm. The formation of monoindole is confirmed by the CH_2 proton singlet at 4.00 ppm, which shows (i) C,H-COSY correlation with carbon signal at 41.4 ppm, due to C-2′′, (ii) HMBCs with C-3 at 100.8, carbonyl carbon at 193.4 ppm and C-1′′ at 134.9 ppm. Monoindole **4d** shows absorptions at 3345 (NH), 3051 (C–H) and 1656 (C=O) cm^{-1} indicating the presence of one indole ring and one carbonyl functionality. The mass spectrum of **4a** displayed the molecular ion [M-1] peak at m/z = 342.0 [calcd. 342.1].

The product selectivity of the reaction has been further explored by the experiments depicted in Scheme 2. When diphenacyl sulfide **1a** was allowed to react with phenylhydrazine in ethanol under reflux conditions for 30 min, it afforded bis (2-phenyl-2-(2-phenylhydrazono) ethyl)sulfane **5a**.[15] Bishydrazone **5a** subsequently reacted with con. HCl in ethanol yielding (82%) the bisindole **3a**. However, when **5a** was treated with HCl in THF medium, only the monoindole **4a** was obtained in 85% yield. It can be noticed that (i) the cyclization has occurred at one end and (ii) the phenylhydrazo group was hydrolyzed to ketone at the other end (Scheme 2). In a separate experiment, **4** was allowed to react with phenylhydrazine in ethanol, which yielded **6**.



Scheme 2 Effect of solvent on hydrazone and indole synthesis.

The second indolization of monoindole **4** can be effected in a facile manner with phenylhydrazine hydrochloride in ethanol medium (Table 3).

It is again interesting that the reaction of **1** with phenylhydrazine in THF yielded only the mono hydrazone **7**, (Table 4) which on further treatment with another mole of phenylhydrazine in ethanol, provided the bishydrazone **5**. But in THF medium, even after prolonged heating for 8 h, the mono hydrazone **7** did not react with another mole of phenylhydrazine (Scheme 2).

It is pertinent to note that simple 1,5-diketone **8**, on reaction with phenylhydrazine in ethanol, yielded mono and bis-indole derivatives depending on the proportion of reagents.[16] In the present investigation, the reaction of **8** with phenylhydrazine was attempted in THF medium. But the reaction has not given any desirable products (Scheme 3). Obviously the selectivity is more pronounced only in diaroyl sulphides, not in other 1,5-diketones.

The striking difference between the protic and aprotic solvents in dictating the course of the above reaction makes to believe that the reason for the observed selectivity is related to hydrogen bonding, assisted by sulfur. Probably in THF, the molecules prefer to have intermolecular hydrogen bonding between the carbonyl of one unit and the NH of the other, thus explaining the preferential formation of **4** or **7**. Hence in THF, the reactivity of carbonyl is reduced/prevented. In ethanol, this intermolecular hydrogen bonding may not be there, as ethanol can solvate the molecules. Thus in ethanol, the second carbonyl is as reactive as the first one as evident from the formation of **3**, **5** and **6**.

Conclusion

In conclusion, it is shown that solvent plays a vital role in deciding the course of the reaction between diphenacyl sulfide and phenylhydrazine/phenylhydrazine hydrochloride. The exclusive formation of either one or two indole rings with THF and ethanol illustrates the dramatic selectivity by the solvents in Fisher indole synthesis.

Experimental section

All melting points reported in this work were measured in open capillaries. The ^{1}H and ^{13}C NMR spectra have been measured at 300 and 75 MHz respectively using Bruker 300 MHz (Avance) instrument in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. Chemical shifts are reported as δ values (ppm). All one- and two-dimensional NMR spectra were obtained using standard Bruker software throughout. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. IR spectra were recorded on a JASCO FT IR instrument (KBr pellet).

General procedure for di(2-aryl-1*H*-3-indolyl) sulphide (3)

A mixture of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanone **1** (1 mmol) and phenylhydrazine hydrochloride **2** (2.5 mmol) in ethanol (7 ml) was refluxed for 3 h. After completion of the reaction, monitored by TLC, the mixture was poured into ice cold water and the solid separated was purified by recrystallisation from ethyl acetate.

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Table 3 Reaction of **4** with $PhNHNH_2$/$PhNHNH_2$.HCl in ethanol

Entry	Ar	Yield of **3** with $PhNHNH_2$.HCl (%)[a]	Yield of **6** with $PhNHNH_2$ (%)[a]
a	*p*-MeC_6H_4	79	81
b	*p*-ClC_6H_4	85	83
c	*p*-BrC_6H_4	83	80

[a] Isolated yield after purification by recrystallisation from ethyl acetate.

Di(2-phenyl-1*H*-3-indolyl) sulphide (3a)

Isolated as colorless solid; m.p. 132–133 °C; IR (KBr): 3380 (NH), 3054 (C–H) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 6.99 (t, 4H, *J* = 7.5 Hz, Ar–H), 7.09–7.27 (m, 12H, Ar–H), 7.57 (d, 2H *J* = 7.8 Hz, Ar–H), 8.10 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 104.0, 110.8, 120.0, 120.9, 123.1, 127.8, 127.9, 128.0, 130.7, 130.9, 135.4, 142.3. Anal. Calcd for $C_{28}H_{20}N_2S$: C, 80.74; H, 4.84; N, 6.73%. Found C, 80.69; H, 4.80; N, 6.77%.

Di[2-(4-methylphenyl)-1*H*-3-indolyl] sulphide (3b)

Isolated as colorless solid; m.p. 126–127 °C; IR (KBr): 3374 (NH), 3052 (C–H) cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 2.20 (s, 6H, CH_3), 6.81 (d, 4H, *J* = 8.1 Hz, Ar–H), 7.08 (t, 2H, *J* = 7.5 Hz, Ar–H), 7.18 (t, 2H , *J* = 7.5 Hz, Ar–H), 7.31 (d, 4H, *J* = 8.1 Hz, Ar–H), 7.37 (d, 2H, *J* = 7.5 Hz, Ar–H), 7.55 (d, 2H, *J* = 7.5 Hz, Ar–H), 10.68 (s, 2H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 20.4, 102.4, 111.3, 119.3, 120.2, 122.4, 127.9, 128.3, 128.4, 131.2, 136.2, 137.6, 143.0. Anal. Calcd for $C_{30}H_{24}N_2S$: C, 81.05; H, 5.44; N, 6.30%. Found C, 81.00; H, 5.41; N, 6.35%.

Di[2-(4-chlorophenyl)-1*H*-3-indolyl] sulphide (3c)

Isolated as colorless solid; m.p. 132–133 °C; IR (KBr): 3378 (NH), 3060 (C–H) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 6.92 (d, 4H, *J* = 8.4 Hz, Ar–H), 7.11 (d, 4H, *J* = 8.4 Hz, Ar–H), 7.15–7.22 (m, 2H , Ar–H), 7.26–7.27 (m, 4H, Ar–H), 7.62 (d, 2H, *J* = 8.1 Hz, Ar–H), 8.15 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 104.4, 110.9, 120.0, 121.2, 123.6, 128.1, 128.6, 129.0, 130.7, 134.0, 135.4, 140.9. Anal. Calcd for $C_{28}H_{18}Cl_2N_2S$: C, 69.28; H, 3.74; N, 5.77%. Found C, 69.25; H, 3.69; N, 5.81%.

Di[2-(4-bromophenyl)-1*H*-3-indolyl] sulphide (3d)

Isolated as colorless solid; m.p. 179–180 °C; IR (KBr): 3378 (NH), 3058 (C–H) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 7.06–7.26 (m, 14H, Ar–H), 7.62 (d, 2H, *J* = 7.8 Hz, Ar–H), 8.03 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 104.6, 111.0, 120.0, 121.3, 122.3, 123.7, 128.9, 129.5, 130.7, 131.0, 135.5, 140.8. Anal. Calcd for $C_{28}H_{18}Br_2N_2S$: C, 58.56; H, 3.16; N, 4.88%. Found C, 58.52; H, 3.13; N, 4.91%.

Table 4 Reaction of **1** with phenylhydrazine in ethanol/THF

Entry	Ar	Yield of **5** in EtOH (%)[a]	Yield of **7** in THF (%)[a]
a	C_6H_5	86	89
b	*p*-MeC_6H_4	87	92
c	*p*-ClC_6H_4	89	95
d	*p*-BrC_6H_4	89	93
e	*p*-$OMeC_6H_4$	86	90

[a] Isolated yield after purification by recrystallisation from ethanol.

Di[2-(biphenyl)-1*H*-3-indolyl] sulphide (3e)

Isolated as colorless solid; m.p. 166–167 °C; IR (KBr): 3384 (NH), 3058 (C–H) cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 7.08–7.19 (m, 4H, Ar–H), 7.28 (d, 4H, *J* = 7.5 Hz, Ar–H), 7.35 (d, 4H , *J* = 7.2 Hz, Ar–H), 7.44 (t, 4H, *J* = 7.2 Hz, Ar–H), 7.50–7.62 (m, 6H, Ar–H), 7.69–7.71 (m, 2H, Ar–H), 8.08 (d, 2H, *J* = 7.2 Hz, Ar–H), 10.79 (s, 2H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 102.9, 111.4, 119.3, 120.3, 122.7, 126.0, 126.5, 126.6, 127.3, 128.3, 128.6, 128.8, 130.0, 131.2, 136.3, 140.1, Anal. Calcd for $C_{40}H_{28}N_2S$: C, 84.47; H, 4.96; N, 4.93%. Found C, 84.42; H, 4.92; N, 4.98%.

Di[2-(2-naphthyl)-1*H*-3-indolyl] sulphide (3f)

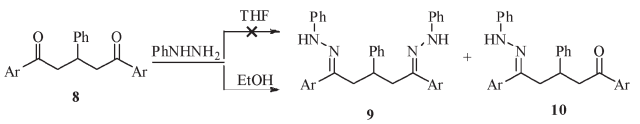
Isolated as colorless solid; m.p. 182-183 °C; IR (KBr): 3378 (NH), 3058 (C–H) cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 7.13–7.25 (m, 6H, Ar–H), 7.30–7.41(m, 6H, Ar–H), 7.49 (d, 2H, *J* = 8.7 Hz, Ar–H), 7.60 (dd, 2H, *J* = 8.4, 1.5 Hz, Ar–H), 7.68–7.42 (m, 4H, Ar–H), 7.90 (s, 2H, Ar–H), 10.86 (s, 2H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 103.2, 111.5, 119.4, 120.5, 122.8, 125.7, 125.8, 126.1, 127.1, 127.2, 127.3, 128.2, 128.5, 131.3, 132.8, 132.9, 136.4, 142.7. Anal. Calcd for $C_{36}H_{24}N_2S$: C, 83.69; H, 4.68; N, 5.42%. Found C, 83.64; H, 4.65; N, 5.46%.

General procedure for 1-aryl-2-[(2-aryl-1*H*-3-indolyl)sulfanyl]-1-ethanones (4)

A mixture of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanone **1** (1 mmol) and phenylhydrazine hydrochloride **2** (1.5 mmol) in THF (10 ml) was refluxed for 3 h. After completion of the reaction, monitored by TLC, the mixture was filtered to remove phenyl hydrazine hydrochloride and the filtrate was poured into ice cold water and the solid separated was purified by recrystallisation from ethyl acetate. Spectroscopic data for **4** are given below:

1-Phenyl-2-[(2-phenyl-1*H*-3-indolyl)sulfanyl]-1-ethanone (4a)

Isolated as colorless solid; m.p. 160–161 °C; IR (KBr): 3345 (NH), 3054 (C–H), 1654 (C=O), cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 4.09 (s, 2H, CH_2), 7.12 (td, 1H, *J* = 8.1, 1.2 Hz, Ar–H), 7.20 (td, 1H, *J* = 8.1, 1.2 Hz, Ar–H), 7.31–7.40 (m, 5H, Ar–H), 7.46 (d, 1H, *J* = 7.8 Hz, Ar–H), 7.51–7.56 (m, 1H, Ar–H), 7.65 (d, 1H, *J* = 7.8 Hz, Ar–H), 7.78 (dd, 2H, *J* = 8.1, 1.8 Hz, Ar–H), 7.86 (dd, 2H, *J* = 8.1, 1.8 Hz, Ar–H), 10.96 (s, 1H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 41.5, 100.0, 111.5, 118.9, 120.1, 122.5, 128.0,



Scheme 3 Effect of solvent on the reaction of phenylhydrazine with 1, 5-diketone **8**.

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128.1, 128.2, 128.3, 128.4, 131.0, 131.7, 132.7, 135.6, 136.1, 141.5, 194.1. *m/z* 342.0 [M-1] calcu. 342.1 [M-1]. Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08%. Found C, 76.91; H, 4.95; N, 4.13%.

1-(4-Methylphenyl)-2-[2-(4-methylphenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (4b)

Isolated as colorless solid; m.p. 153–154 °C; IR (KBr): 3344 (NH), 3052 (C–H), 1654 (C=O), cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ_H: 2.32 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.91 (s, 2H, CH_2), 7.03 (d, 2H, J = 8.1 Hz, Ar–H), 7.07 (d, 2H, J = 8.1 Hz, Ar–H), 7.12–7.16 (m, 2H, Ar–H), 7.18–7.23 (m, 1H, Ar–H), 7.52 (d, 2H, J = 8.1 Hz, Ar–H), 7.57 (d, 2H, J = 8.1 Hz, Ar–H), 7.64–7.67 (m, 1H, Ar–H), 8.65 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.2, 21.6, 41,9, 100.5, 111.2, 119.2, 120.6, 122.8, 128.1, 128.5, 128.7, 128.9, 129.0, 131.0, 133.0, 135.5, 138.1, 141.7, 143.6, 194.7. *m/z* 372.1 [M + 1] calcu. 372.1 [M + 1]. Anal. Calcd for $C_{24}H_{21}NOS$: C, 77.59; H, 5.70; N, 3.77%. Found C, 77.55; H, 5.65; N, 3.81%.

1-(4-Chlorophenyl)-2-[2-(4-chlorophenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (4c)

Isolated as colorless solid; m.p. 153–154 °C; IR (KBr): 3346 (NH), 3050 (C–H), 1656 (C=O), cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 4.02 (s, 2H, CH_2), 7.15 (t, 1H, J = 7.5 Hz, Ar–H), 7.22 (t, 1H, J = 7.5 Hz, Ar–H), 7.32–7.36 (m, 5H, Ar–H), 7.56 (d, 1H, J = 7.5 Hz, Ar–H), 7.67 (d, 2H, J = 8.4 Hz, Ar–H), 7.78 (d, 2H, J = 8.4 H), 10.93 (s, 1H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 40.9, 100.1, 111.6, 118.9, 120.4, 122.8, 128.1, 128.2, 128.3, 129.9, 130.1, 130.3, 130.8, 133.5, 133.9, 138.3, 140.7, 192.7. Anal. Calcd for$C_{22}H_{15}Cl_2NOS$: C, 64.08; H, 3.67; N, 3.40%. Found C, 64.04; H, 3.62; N, 3.43%.

1-(4-Bromophenyl)-2-[2-(4-bromophenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (4d)

Isolated as colorless solid; m.p. 164–165 °C; IR (KBr): 3345 (NH), 3051 (C–H), 1656 (C=O), cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 4.00 (s, 2H, CH_2), 7.15 (td, 1H, J = 7.8, 1.2 Hz, Ar–H), 7.22 (td, 1H, J = 7.8, 1.2 Hz, Ar–H), 7.45–7.47 (m, 3H, Ar–H), 7.51(d, 2H, J = 8.7 Hz, Ar–H), 7.59 (d, 2H, J = 8.7 Hz, Ar–H), 7.67 (d, 1H, J = 7.8 Hz, Ar–H), 7.71 (d, 2H, J = 8.7 Hz, Ar–H), 10.99 (s, 1H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 41.4, 100.8, 112.1, 119.4, 120.9, 122.2, 123.3, 127.5, 130.7 (2C), 131.1, 131.4, 131.6, 131.7, 135.0, 136.7, 141.2, 193.4. Anal. Calcd for $C_{22}H_{15}Br_2NOS$: C, 52.72; H, 3.02; N, 2.79%. Found C, 52.69; H, 3.00; N, 2.84%.

1-(Biphenyl)-2-[2-(biphenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (4e)

Isolated as colorless solid; m.p. 204–205 °C; IR (KBr): 3344 (NH), 3051 (C–H), 1660 (C=O), cm^{-1}; ^1H NMR (300 MHz, Acetone-d_6) δ_H: 4.07 (s, 2H, CH_2), 6.88 (td, 2H, J = 8.1, 0.9 Hz, Ar–H), 7.06 (td, 2H, J = 8.1, 0.9 Hz, Ar–H), 7.30–7.63 (m, 10H, Ar–H), 7.70–7.78 (m, 6H, Ar–H), 8.09 (d, 2H, J = 8.7 Hz, Ar–H), 10.79 (s, 1H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 41.3, 104.2, 111.3, 111.6, 119.0, 119.3, 119.8, 120.4, 122.3, 122.7, 126.1, 126.6, 126.7, 127.0, 127.4, 128.0, 128.4, 128.8 (2C), 129.0, 131.1, 131.4, 134.6, 136.3, 140.3, 193.5. Anal. Calcd for $C_{34}H_{25}NOS$: C, 82.39; H, 5.08; N, 2.83%. Found C, 82.36; H, 5.04; N, 2.87%.

1-(2-Naphthyl)-2-[2-(2-naphthyl)-1*H*-3-indolyl]sulfanyl-1-ethanone (4f)

Isolated as colorless solid; m.p. 172–173 °C; IR (KBr): 3348 (NH), 3052 (C–H), 1659 (C=O), cm^{-1}; ^1H NMR (300 MHz,Acetone-d_6) δ_H: 4.05 (s, 2H, CH_2), 7.11–7.26 (m, 3H, Ar–H), 7.33–7.42 (m, 3H, Ar–H), 7.47–7.53 (m, 4H, Ar–H), 7.59–7.64 (m, 4H, Ar–H), 7.67–7.83 (m, 3H, Ar–H), 7.88 (s, 1H, Ar–H), 10.69 (s, 1H, NH); ^{13}C NMR (75 MHz, Acetone-d_6) δ_C: 41.5, 103.0, 111.2, 111.6, 119.3, 119.7, 120.1, 120.4, 122.4, 122.9, 125.2, 125.9, 126.3, 126.4, 127.2, 127.3, 128.2, 128.6, 128.7 (2C), 129.4, 129.5, 130.4, 131.8 (2C), 132.7, 135.3, 136.7, 140.6, 192.7. Anal. Calcd for $C_{30}H_{21}NOS$: C, 81.23; H, 4.77; N, 3.16%. Found C, 81.18; H, 4.72; N, 3.21%.

General procedure for 1-aryl-2-(2-aryl-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenylhydrazone 5

A mixture of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanone **1** (1 mmol) and phenylhydrazine **2** (2.5 mmol) in ethanol (7 ml) was refluxed for 2–3 h. After completion of the reaction, monitored by TLC, the mixture was poured into ice cold water and the solid separated was purified by recrystallisation from ethanol. The spectral data for bisphenyl hydrazones are given below:

1-Phenyl-2-(2-phenyl-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenyl hydrazone (5a)

Isolated as colorless solid; m.p. 111–112 °C [reported 112–114 °C];[22] IR (KBr): 3283 (NH), 3054 (C–H), 1634 (C=N); ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.86 (s, 4H, CH_2), 6.89 (t, 2H, J = 7.2 Hz, Ar–H), 7.07 (d, 4H, J = 7.5 Hz, Ar–H), 7.19–7.36 (m, 10H, Ar–H), 7.77 (d, 4H, J = 7.2 Hz, Ar–H), 8.15 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.8, 113.5, 120.9, 125.2, 128.2, 128.6, 129.2, 137.5, 137.8, 144.5. Anal. Calcd for $C_{28}H_{26}N_4S$: C, 74.63; H, 5.82; N, 12.43%. Found C, 74.60; H, 5.78; N, 12.47%.

1-(4-Methylphenyl)-2-(2-(4-methylphenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenylhydrazone (5b)

Isolated as colorless solid; m.p. 121–122 °C [reported 121–124 °C];[22] IR (KBr): 3285 (NH), 3057 (C–H), 1633 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 2.33 (s, 6H, CH_3), 3.84 (s, 4H, CH_2), 6.87 (t, 2H, J = 7.2 Hz, Ar–H), 7.06 (d, 4H, J = 8.1 Hz, Ar–H), 7.18–7.27 (m, 8H, Ar–H), 7.65 (d, 4H, J = 8.1 Hz, Ar–H), 8.16 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.1, 25.9, 113.6, 120.6, 125.3, 128.3, 129.1, 129.2, 137.9, 138.0, 144.8. *m/z* 477.0 [M-1] calcu. 477.1 [M-1]. Anal. Calcd for $C_{30}H_{30}N_4S$: C, 75.28; H, 6.32; N, 11.71%. Found C, 75.25; H, 6.28; N, 11.75%.

1-(4-Chlorophenyl)-2-(2-(4-chlorophenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenylhydrazone (5c)

Isolated as colorless solid; m.p. 135–136 °C [reported 135–137 °C];[22] IR (KBr): 3280 (NH), 3055 (C–H), 1632 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.69 (s, 4H, CH_2), 6.93 (t, 2H, J = 7.2 Hz, Ar–H), 7.03 (d, 4H, J = 8.4 Hz, Ar–H), 7.20–7.32 (m, 8H, Ar–H), 7.64 (d, 4H, J = 8.4 Hz, Ar–H), 8.14 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.5, 113.6, 121.2, 126.4, 128.5, 128.7, 129.3, 136.1, 136.2, 144.3. Anal. Calcd for $C_{28}H_{24}Cl_2N_4S$:

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C, 64.74; H, 4.66; N, 10.79%. Found C, 64.70; H, 4.63; N, 10.83%.

1-(4-Bromophenyl)-2-(2-(4-bromophenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenylhydrazone (5d)

Isolated as colorless solid; m.p. 125–126 °C; IR (KBr): 3282 (NH), 3057 (C–H), 1634 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.79 (s, 4H, CH_2), 6.92 (t, 2H, J = 7.2 Hz, Ar–H), 7.03 (d, 4H, J = 8.4 Hz, Ar–H), 7.19–7.27 (m, 6H, Ar–H), 7.43 (d, 4H, J = 8.4 Hz, Ar–H), 7.59 (d, 2H, J = 8.4 Hz, Ar–H), 8.13 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.5, 113.6, 121.3, 126.7, 128.5, 129.3, 131.7, 136.1, 136.6, 144.2. *m/z* 604.8 [M-1] calcu. 605.0 [M-1]. Anal. Calcd for $C_{28}H_{24}Br_2N_4S$: C, 55.28; H, 3.98; N, 9.21%. Found C, 55.24; H, 3.95; N, 9.25%.

1-(4-Methoxyphenyl)-2-(2-(4-methoxyphenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 1-phenylhydrazone (5e)

Isolated as colorless solid; m.p. 119–120 °C; IR (KBr): 3282 (NH), 3055 (C–H), 1634 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.77 (s, 4H, CH_2), 3.80 (6H, OCH_3), 6.84 (t, 2H, J = 6.9 Hz, Ar–H), 7.05 (d, 4H, J = 8.4 Hz, Ar–H), 7.18–7.31 (m, 8H, Ar–H), 7.69 (d, 4H, J = 8.4 Hz, Ar–H), 8.05 (s, 2H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.7, 55.2, 113.5, 113.9, 120.5, 126.6, 129.1, 129.2, 137.9, 144.8, 159.6. *m/z* 511.2 [M + 1] calcu. 511.2 [M + 1]. Anal. Calcd for $C_{30}H_{30}N_4O_2S$: C, 70.56; H, 5.92; N, 10.97%. Found C, 70.52; H, 5.89; N, 11.01%.

General procedure for 1-aryl-2-(2-aryl-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone 7

A mixture of 2-[(2-oxo-2-arylethyl)sulfanyl]-1-aryl-1-ethanone (1 mmol) and phenylhydrazine (1.5 mmol) in THF (5 ml) was refluxed for 2–3 h. After completion of the reaction, monitored by TLC, the mixture was allowed to cool and then poured into ice cold water and the solid separated was purified by recrystallisation from ethanol.

1-Phenyl-2-(2-phenyl-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone (7a)

Isolated as colorless solid; m.p. 143–144 °C; IR (KBr): 3245 (NH), 3055 (C–H), 1674 (C=O), 1610 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.79 (s, 2H, CH_2), 3.83 (s, 2H, CH_2), 6.82–6.89 (m, 1H, Ar–H), 7.21 (d, 2H, J = 7.8 Hz, Ar–H), 7.28–7.34 (m, 6H, Ar–H), 7.41 (d, 2H, J = 8.4 Hz, Ar–H), 7.74 (d, 2H, J = 7.8 Hz, Ar–H), 7.79 (d, 2H, J = 8.4 Hz, Ar–H), 9.59 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.8, 36.8, 113.5, 120.8, 125.2, 127.7, 128.2, 128.5, 128.6, 128.8, 129.1, 133.9, 137.5, 137.7, 144.5, 195.2. *m/z* 359.1 [M-1] calcu. 359.1 [M-1]. Anal. Calcd for $C_{22}H_{20}N_2OS$: C, 73.30; H, 5.59; N, 7.77%. Found C, 70.26; H, 5.54; N, 7.80%.

1-(4-Methylphenyl)-2-(2-(4-methylphenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone (7b)

Isolated as colorless solid; m.p. 116-117 °C; IR (KBr): 3247 (NH), 3056 (C–H), 1674 (C=O), 1612 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 2.35 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.81 (s, 2H, CH_2), 3.86 (s, 2H, CH_2), 6.87 (t, 1H, J = 6.9 Hz, Ar–H), 7.20 (d, 2H, J = 8.1 Hz, Ar–H), 7.26–7.37 (m, 6H, Ar–H), 7.70 (d, 2H, J = 8.1 Hz, Ar–H), 7.89 (d, 2H, J = 8.1 Hz, Ar–H), 9.53 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.1, 21.7, 26.2, 36.7, 113.3, 120.0, 125.2, 128.8, 129.0, 129.1, 129.5, 132.6, 135.0, 137.7, 138.0, 145.0, 145.5, 194.9. Anal. Calcd for $C_{24}H_{24}N_2OS$: C, 74.19; H, 6.23; N, 7.21%. Found C, 74.16; H, 6.19; N, 7.25%.

1-(4-Chlorophenyl)-2-(2-(4-chlorophenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone (7c)

Isolated as colorless solid; m.p. 151–152 °C; IR (KBr): 3245 (NH), 3055 (C–H), 1672 (C=O), 1614 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.80 (s, 2H, CH_2), 3.87 (s, 2H, CH_2), 6.88–6.93 (m, 1H, Ar–H), 7.31–7.34 (m, 6H, Ar–H), 7.48 (d, 2H, J = 8.7 Hz, Ar–H), 7.72 (d, 2H, J = 8.7 Hz, Ar–H), 7.94 (d, 2H, J = 8.7 Hz, Ar–H), 9.52 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.0, 36.6, 113.4, 120.5, 126.5, 128.6, 129.0, 129.2, 129.3, 130.1, 133.3, 133.6, 136.2, 136.3, 145.1, 194.1. Anal. Calcd for $C_{22}H_{18}Cl_2N_2OS$: C, 61.54; H, 4.23; N, 6.52%. Found C, 61.50; H, 4.20; N, 6.56%.

1-(4-Bromophenyl)-2-(2-(4-bromophenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone (7d)

Isolated as colorless solid; m.p. 161–162 °C; IR (KBr): 3249 (NH), 3055 (C–H), 1675 (C=O), 1610 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.79 (s, 2H, CH_2), 3.86 (s, 2H, CH_2), 6.92 (tt, 1H, J = 8.1, 2.4 Hz, Ar–H), 7.27–7.35 (m, 4H, Ar–H), 7.47 (d, 2H, J = 8.7 Hz, Ar–H), 7.64 (d, 2H, J = 8.7 Hz, Ar–H), 7.65 (d, 2H, J = 8.7 Hz, Ar–H), 7.85 (d, 2H, J = 8.7 Hz, Ar–H), 9.50 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 25.9, 36.6, 113.4, 120.6, 121.9, 126.8, 129.2, 129.5, 130.2, 131.5, 132.3, 133.7, 136.3, 136.6, 145.0, 194.3. Anal. Calcd for $C_{22}H_{18}Br_2N_2OS$: C, 50.98; H, 3.50; N, 5.41%. Found C, 50.95; H, 3.46; N, 5.46%.

1-(4-Methoxyphenyl)-2-(2-(4-methoxyphenyl)-2-[2-phenylhydrazono]ethylsulfanyl)-1-ethanone (7e)

Isolated as colorless solid; m.p. 146–147 °C; IR (KBr): 3245 (NH), 3053 (C–H), 1675 (C=O), 1615 (C=N), cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.74 (s, 2H, CH_2), 3.77 (s, 2H, CH_2), 3.79 (s, 6H, OCH_3), 6.82–6.85 (m, 1H, Ar–H), 7.04 (d, 2H, J = 8.7 Hz, Ar–H), 7.24–7.30 (m, 4H, Ar–H), 7.67 (d, 2H, J = 9.0 Hz, Ar–H), 7.72 (d, 2H, J = 8.7 Hz, Ar–H), 7.92 (d, 2H, J = 9.0 Hz, Ar–H), 9.53 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 26.0, 36.4, 55.2, 55.3, 113.4, 113.9, 114.9, 120.4, 126.6, 129.1, 129.2, 131.0, 132.4, 137.9, 144.8, 159.7, 164.1, 193.7. Anal. Calcd for $C_{24}H_{24}N_2O_3S$: C, 68.55; H, 5.75; N, 6.66%. Found C, 68.51; H, 5.72; N, 6.70%.

General procedure for 1-(aryl)-2-[2-(aryl)-1*H*-3-indolyl]sulfanyl-1-ethanone 1-phenylhydrazone 6

A mixture of 1-aryl-2-[(2-aryl-1*H*-3-indolyl)sulfanyl]-1-ethanone **4** (1 mmol) and phenylhydrazine (1.5 mmol) in ethanol (10 ml) was refluxed for 2–3 h. After completion of the reaction, monitored by TLC, the mixture was poured into ice cold water and the solid separated was recrystallised from ethyl acetate to get pure product.

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1-(4-Methylphenyl)-2-[2-(4-methylphenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone 1-phenylhydrazone (6a)

Isolated as colorless solid; m.p. 145–146 °C; IR (KBr): 3375 (NH), 3272 (NH), 3045 (C–H), 1598 (C=N) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 2.31 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.84 (s, 2H, CH_2), 6.58 (d, 2H, J = 8.4 Hz, Ar–H), 6.79 (t, 1H, J = 7.5 Hz, Ar–H), 7.02 (d, 2H, J = 7.8 Hz, Ar–H), 7.08–7.16 (m, 4H, Ar–H), 7.28–7.35 (m, 3H, Ar–H), 7.43 (d, 2H, J = 8.1 Hz, Ar–H), 7.50 (d, 2H, J = 7.5 Hz, Ar–H), 7.54 (s, 1H, NH), 7.93 (m, 1H, Ar–H), 8.25 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 21.2, 21.3, 30.2, 100.5, 111.5, 113.1, 119.0, 119.9, 121.3, 123.2, 125.3, 128.2, 128.4, 128.7, 128.8, 129.3, 130.9, 134.9, 135.4, 137.4, 138.6, 140.6, 142.5, 145.1. Anal. Calcd for $C_{30}H_{27}N_3S$: C, 78.06; H, 5.90; N, 9.10%. Found C, 78.02; H, 5.85; N, 9.14%.

1-(4-Chlorophenyl)-2-[2-(4-chlorophenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone 1-phenylhydrazone (6b)

Isolated as colorless solid; m.p. 203–204 °C; IR (KBr): 3378 (NH), 3272 (NH), 3048 (C–H), 1598 (C=N) cm^{-1}; ^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.75 (s, 2H, CH_2), 6.46 (d, 2H, J = 8.4 Hz, Ar–H), 6.82 (t, 1H, J = 7.2 Hz, Ar–H), 7.05–7.21 (m, 7H, Ar–H), 7.28–7.34 (m, 5H, Ar–H, NH), 7.41 (d, 2H, J = 8.4 Hz, Ar–H), 7.93 (m, 1H, Ar–H), 8.18 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 28.9, 100.5, 111.8, 113.0, 120.4, 121.2, 121.6, 123.8, 126.3, 128.0, 128.6, 128.9, 129.2, 129.8, 130.8, 133.4, 134.6, 135.5, 135.7, 138.7, 141.6, 144.5. *m/z* 502.0 [M + 1] calcu. 502.0 [M + 1]. Anal. Calcd for $C_{28}H_{21}Cl_2N_3S$: C, 66.93; H, 4.21; N, 8.36%. Found C, 66.90; H, 4.17; N, 8.41%.

1-(4-Bromophenyl)-2-[2-(4-bromophenyl)-1*H*-3-indolyl]sulfanyl-1-ethanone 1-phenylhydrazone (6c)

Isolated as colorless solid; m.p. 179–180 °C; IR (KBr): 3376 (NH), 3271 (NH), 3048 (C–H), 1597 (C=N) cm^{-1};^1H NMR (300 MHz,$CDCl_3$) δ_H: 3.77 (s, 2H, CH_2), 6.47 (d, 2H, J = 7.5 Hz, Ar–H), 6.83 (t, 1H, J = 7.5 Hz, Ar–H), 7.16 (t, 1H, J = 7.5 Hz, Ar–H), 7.21–7.44 (m, 13H, Ar–H), 7.96 (m, 1H, Ar–H), 8.24 (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 28.8, 100.6, 111.8, 113.0, 119.0, 120.4, 121.6 (2C), 122.9, 123.8, 126.6, 129.0, 129.7, 130.0, 130.8, 130.9, 131.5, 135.5, 136.1, 138.6, 141.6, 144.5. *m/z* 589.9 [M + 1] calcu. 589.9 [M + 1]. Anal. Calcd for $C_{28}H_{21}Br_2N_3S$: C, 56.87; H, 3.58; N, 7.11%. Found C, 56.82; H, 3.54; N, 7.15%.

Acknowledgements

The authors thank DST, New Delhi for funds under IRHPA program towards high resolution NMR spectrometer to Madurai Kamaraj University and UGC, New Delhi for providing facilities to the Department of Industrial Chemistry of Alagappa University through SAP scheme. Financial support from UGC, New Delhi to NP is gratefully acknowledged.

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