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Ionic liquid promoted spiroannulation *via* hetero-Michael addition and intramolecular heterocyclisation

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A sequential efficient method for the synthesis of novel spiro-5-thiazolidin-2-one-indolo[1,5]benzothiazepine from readily available isatin, 4-thioxothiazolidin-2-one and 2-aminothiophenol is reported. The synthesis involves formation of *N*-methyl-3-(2-oxo-4-thioxothiazolidinon-5-ylidene)-1,3-dihydro indol-2-one by [bmIm]OH promoted Knoevenagel condensation of 4-thioxo-2-thiazolidinone with isatin. The Knoevenagel product on ionic liquid promoted thia-Michael addition with 2-aminothiophenol and intramolecular cyclocondensation yielded the title compounds with high atom economy. The ionic liquid, [bmIm]OH was recovered completely and recycled thrice for the synthesis with no appreciable decrease in the efficiency of the process. The whole sequence of reactions proceeded with quantitative transformation of reactants into spiro [1,5]benzothiazepine at ambient temperature. The sequential reaction pathway is supported by the isolation of the thia-Michael adduct of the knoevenagel product with 2-aminothiophenol and quantitative conversion of the adduct into the final products under the same reaction conditions.

Introduction

Spiro-cyclics have attracted attention due to their unique structural properties and reactivity pattern. Five and six-membered rings containing spiro-3-indole derivatives exhibit enhanced biological activities[1–3] and are extensively studied,[4–7] but those incorporating a seven membered thiazepine moiety have so far received little attention.[8] The well known drugs Thiazesim[9] and Diltiazem[10] as calcium channel blockers have a [1,5]benzothiazepine skeleton. The literature records show that annulated [1,5]benzothiazepines have been found to display a wide range of pharmacological properties.[11–15] Therefore, [1,5]benzothiazepines with spiro-heterocyclics appear to be an attractive scaffold to be utilized for exploiting chemical diversity and generating a drug-like library to screen for lead candidates. Along with indoles and [1,5]benzothiazepines, a wide spectrum of pharmacological activities are also associated with thiazolidinones.[16]

Spirocyclic structures are found in a wide range of natural alkaloids.[17–23] The complexity of these ring structures is represented by the quaternary carbon centre and two fused rings. Syntheses of spirocyclics by alkylation, rearrangement, cycloaddition, or cleavage of bridged system, suffer from drawbacks such as functional group incompatibility at one or more stages.[24] 1,4 Conjugate addition on quaternary carbon followed by cyclocondensation is one of the most common methods for constructing a spirocentre (Fig. 1). Spiro annulation *via* 1,4-conjugate addition has been shown for the synthesis of the core structure of alkaloid manzamine A.[25]

Design and development of reaction sequences leading to a highly selective approach to complex molecular moieties, particularly spirocyclics, while combining structural diversity, versatility and eco-compatiblility, are great challenges for synthetic chemists in the context of sustainable green chemistry.[26–28]

Recently, ionic liquids (IL) have received growing attention due to their tunable features, complete recovery, reusability, negligible vapour pressure, wide solvating capability, multiple bond forming efficiency and many other green credentials as alternative reaction media to molecular solvents, catalysts and reagents.[29–31] Basic ionic liquid [bmim]OH has been previously used for catalyzing a number of reactions such as Knoevenagel condensation, Michael addition,[32a–d] *etc.*

Knoevenagel condensation followed by hetero-Michael addition *viz.* aza-Michael, thia-Michael, oxa-Michael *etc.*, has considerably attracted attention as a versatile, expeditious and cost-effective

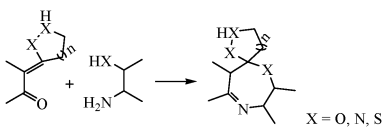

Fig. 1 Strategy for construction of spirocycles *via* 1,4-conjugate addition and subsequent heterocyclisation.

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strategy for the synthesis of heterocycles for drug discovery processes. Furthermore, utilization of a variety of heteroatoms in hetero-Michael addition broadens its applicability as an efficient and atom-economic route for the construction of carbon–heteroatom bonds in the synthesis of heterocyclic rings.

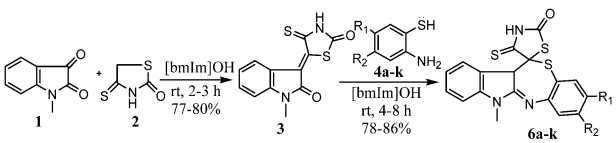
Owing to the chemical and biological interests of spiro [1,5]benzothiazepines, the need for developing new and efficient approaches for their synthesis with additional functional groups for further modification still remains an attractive goal.

Prompted by the green credentials of task specific ionic liquids (TSILs) and to avoid the drawbacks in construction of spirocyclics as well as in continuation of our work on the development of simple, efficient, versatile synthetic methodologies for biodynamic heterocyclic scaffolds,[32–38] we herein report 1,4-conjugate addition and subsequent intramolecular cyclocondensation as an expeditious strategy for the construction of novel spiro-5-thiazolidinone indolo[1,5]benzothiazepine based on Knoevenagel condensation and hetero-Michael addition in ionic liquid (Scheme 1).

In order to achieve our objective efficiently and expeditiously, we utilized [bmIm]OH as an alternative reaction medium as well as promoter. The strategy involves the initial reaction of isatin **1** with 4-thioxo-2-thiazolidin-2-one **2** in [bmIm]OH without using any base which resulted in the formation of *N*-methyl-3-(2-oxo-4-thioxo-thiazolidinon-5-ylidene)-1,3-dihydroindol-2-one **3**, having an α,β-unsaturated (enone) moiety. [bmIm]OH promoted Knoevenagel condensation gave *N*-methyl-3-(2-oxo-4-thioxothiazolidinon-5-ylidene)-1,3-dihydroindol-2-one in good yield (76–80%). The enone **3** on hetero-Michael addition and subsequent intramolecular cyclocondensation afforded **6(a–k)** with excellent yield (78–86%; Scheme 2).

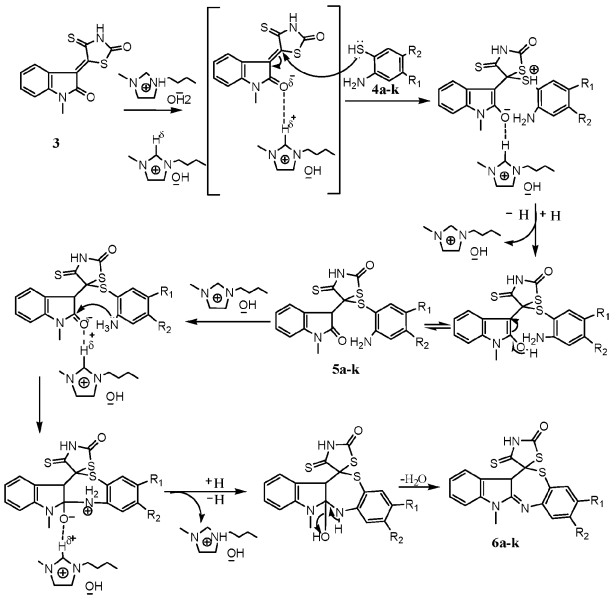
N-Methyl-3-(2-oxo-4-thioxothiazolidinon-5-ylidene)-1,3-dihydro indol-2-one was initially obtained in 60 to 65% yield by base-promoted Knoevenagel condensation of isatin with 4-thioxothiazolidin-2-one in ethanol under reflux for 8 to 10 h. However, when Knoevenagel condensation was done by using [bmIm]OH without base, the product was obtained in 77–80% yield at room temperature by stirring for 2 to 3 h.

In order to make the synthesis of 6 more expeditious and facile, we turned our attempt to investigate the optimization of reaction conditions with regard to solvent, base, time and yield of product. Herein, isatin **1**, 4-thioxothiazolidin-2-one **2** and **4**



4, 5, 6	R_1	R_2	4, 5, 6	R_1	R_2
a	H	H	g	CF_3	H
b	OCH_3	H	h	H	NO_2
c	Cl	H	i	H	Cl
d	Br	H	j	H	CF_3
e	F	H	k	H	OC_2H_5
f	CH_3	H			

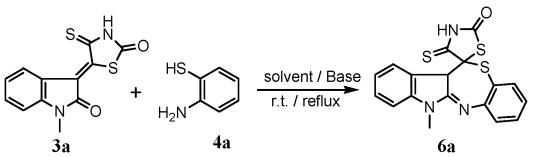
Scheme 1 Ionic liquid catalysed synthesis of spiro-5-thiazolidinone-indolo[1,5]benzothiazepine.

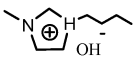
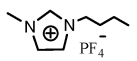
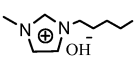
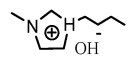
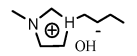
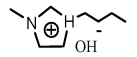
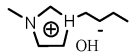


Scheme 2 Plausible mechanism for the formation of spiro-5-thiazolidinone indolo[1,5]benzothiazepine.

(R_1 = H, R_2 = H) were chosen as model reagents for the synthesis of representative compound **6a** and the reaction was performed at room temperature or under reflux (Table 1).

Table 1 Optimization of reaction conditions for the synthesis of spiro-5-thiazolidinone-indolo[1,5]benzothiazepine



Entry	Solvent	Mol%	Temp	Base	Time (h)	Yield[a] (%)
1	MeOH	—	Reflux	NaOH	10	40
2	DCM	—	Reflux	NaOH	10	32
3	THF	—	Reflux	NaOH	10	28
4		20	Room temp	—	6	80
5		20	Room temp	—	10	76
6		20	Room temp	—	10	71
7		20	Room temp	—	10	78
8		15	Room temp	—	6	75
9		25	Room temp	—	6	80
10		20	Room temp	—	8	80
11		20	60 °C	—	6	80

[a] Yield of isolated and purified products.

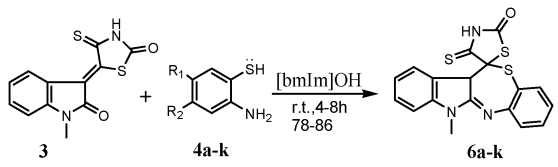
Methanol, DCM, THF and several imidazolium-based ionic liquids, with varying alkyl substituents and counter anions, were used as solvents and [bmIm]OH was found to be the most efficient solvent and catalyst (Table 1, entry 4) in the reported synthetic protocol.

The optimum catalyst loading for [bmIm]OH was found to be 20 mol%. By decreasing the amount of catalyst to 15 from 20% relative to substrate, the yield of product **6a** is reduced (Table 1, entry 8), however, by increasing the amount of catalyst from 20 to 25 mol%, no appreciable change in the yield of product was observed (Table 1, entry 9). However, low performance at high temperature in the presence of base was observed by methyl alcohol (Table 1, entry 1) whereas DCM and THF could not do well (Table 1, entries 2 and 3). With MeOH, DCM and THF, the product was obtained under reflux in the presence of a base, NaOH. It was also observed that a higher reaction temperature when [bmIm]OH was used as solvent and catalyst led to no appreciable effect on the yield (Table 1, entry 11).

Next, in order to investigate the substrate scope of the reaction, a variety of 2-aminothiophenols were used as dinucleophiles employing the present optimized reaction conditions. The yield and reaction were found to be fairly equal and good (Table 2). The highest yield was 86% of **6b** (Table 2, entry 2). The present optimized synthesis was accomplished by stirring the Knoevenagel product of isatin **1** with 4-thioxothiazolidin-2-one **2**, 2-amino thiophenol **4** and [bmIm]OH at room temperature for 4–8 h. Isolation and recrystallisation afforded the hitherto unknown spiro-5-thiazolidinonindolo[1,5]benzothiazepine in 78–86% yield (Table 2).

The formation of **6** may be rationalized by the attack of the more nucleophilic sulphur atom of 2-aminothiophenol at the β-carbon of the α,β-unsaturated carbonyl moiety of **3** leading to the formation of adduct **5** which undergoes intramolecular nucleophilic attack of the relatively more nucleophilic nitrogen atom of the amino group of 2-aminothiophenol on the carbonyl group at C_2 of the *N*-methyl-3-(2-oxo-4-thioxothiazolidinon-5-ylidene)-1,3-dihydroindol-2-one and subsequent dehydration yielded compound **6** in 78–86% yield. These conclusions are based on the observation that the intermediate compound **5** could be isolated and converted into the corresponding spiro [1,5]benzothiazepine in quantitative yield. The ionic liquid [bmIm]OH was easily recycled after the reaction and reused

Table 2 Ionic liquid [bmIm]OH promoted synthesis of spiro-5-thiazolidino-indolo[1,5]benzothiazepine (**6a–k**)



3 **4a-k** **6a-k**

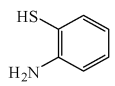
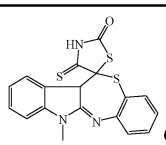
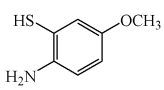
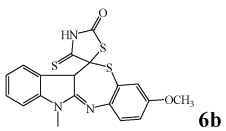
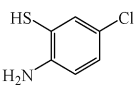
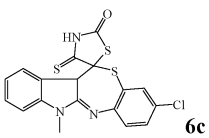
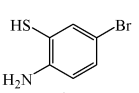
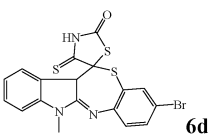
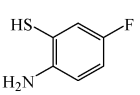
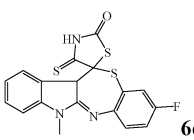
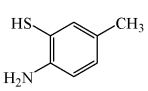
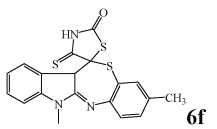
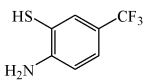
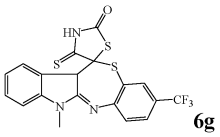
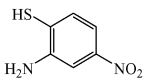
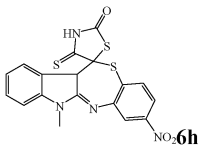
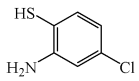
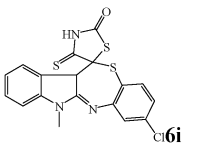
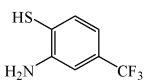
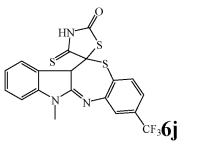
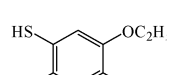
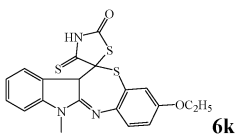
Entry	4	6	Time (h)	Yield[a,b] (%)
1	 **4a**	 **6a**	6	80
2	 **4b**	 **6b**	4	86
3	 **4c**	 **6c**	7	78
4	 **4d**	 **6d**	8	79
5	 **4e**	 **6e**	8	78

Table 2 (*continued*)

Entry	4	6	Time (h)	Yield[a,b] (%)
6	 **4f**	 **6f**	5	84
7	 **4g**	 **6g**	8	78
8	 **4h**	 **6h**	8	78
9	 **4i**	 **6i**	7	78
10	 **4j**	 **6j**	8	78
11	 **4k**	 **6k**	5	85

[a] Stirring time at room temperature. [b] Yield of isolated and purified products.

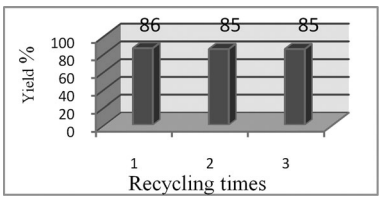


Fig. 2 Recyclability of [bmIm]OH.

three times without any loss in activity. Even after three cycles, the product **6a** was obtained in almost the same yield (Fig. 2).

In summary, we have developed an efficient method for the synthesis of potentially pharmaceutically important spiro-[1,5]-benzothiazepines from readily available substrates. Easy recovery of ionic liquid and its reuse without any appreciable decrease in yield of product and its activity, operational simplicity of the procedure and enhancement of product yield are some advantages over conventional processes and are some additional attributes of the protocol in the context of green chemistry.

Experimental

General

All chemicals were used as received without further purification. NMR spectra were recorded on a Bruker Avance DPX-400400 FT spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS as an internal reference. Mass spectra were recorded on a JEOL SX-102 (FAB) mass spectrometer at 70 eV. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyzer. Silica gel-G was used for TLC. Melting points were determined by open glass capillary method and are uncorrected.

Preparation of [bmIm]OH

The task specific basic ionic liquid was synthesized according to a reported procedure.[32a] Solid KOH (2.3 g, 40 mmol) was added to a solution of [bmIm]Br (8.8 g, 40 mmol) in dry CH_2Cl_2 (20 mL), and the mixture was stirred vigorously at room temperature for 10 h. The precipitated KBr was filtered off, and the filtrate was evaporated to leave the crude [bmIm]OH as a viscous liquid that was washed with ether (2 × 20 mL) and dried at 90 °C for 10 h to prepare the pure ionic liquid for use.

N-Methyl-3-(2-oxo-4-thioxo-thiazolidin-5-ylidene)-1,3-dihydro-indol-2-one (3): Procedure

A mixture of isatin **1** (2.0 mmol), 4-thioxothiazolidin-2-one **2** (2.0 mmol) and [bmIm]OH (0.4 mmol) was stirred at room temperature for (2–4) h. After completion of the reaction as indicated by TLC, 20 mL of water was added to the reaction mixture and stirred well. The product was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 to afford the crude product and recrystallized from ethanol to obtain analytically pure compound **3** (80%). After isolation of the product, the remaining aqueous layer containing the ionic liquid was washed with ether (2 × 10 mL) to remove any organic impurities and filtered. The filtrate was extracted with dichloromethane (2 × 10 mL), dried over $MgSO_4$ and evaporated under reduced pressure to afford [bmIm]OH, which was reused thrice in subsequent runs without further purification.

Compound 3

Brownish solid: 441 mg (80%), mp 290–292 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0 (s, 1H, -NH-), 6.95–7.59 (m, 4H, Ar-H), 2.79(s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 192, 169, 162.3, 150, 135.9, 134, 128, 126.8, 126.4, 124, 120.3, 35.0, EIMS: (*m*/*z*): 276 (M^+). Anal. calcd. For $C_{12}H_8N_2O_2S_2$: C, 52.16; N, 10.14; H, 2.92. Found: C, 52.19; N, 10.15; H, 2.90.

Spiro-5-thiazolidinonindolo [1,5]benzothiazepine: general procedure

A mixture of *N*-methyl-3-(2-oxo-4-thioxo-thiazolidin-5-ylidene)-1,3-dihydro-indol-2-one (2 mmol) **3**, 2-aminothiophenol (2 mmol) **4(a–k)** and [bmIm]OH (0.4 mmol) was stirred at room temperature for 4–10 h at rt. After completion of the reaction as indicated by TLC, 20 mL of water was added and the product was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under reduced pressure to afford the crude product and recrystallized from ethanol to afford an analytically pure compound **6a–k**. The ionic liquid [bmIm]OH was recovered by following the same procedure as above.

Charaterization of 5a

Brownish solid: 641 mg (80%) mp 285–287 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.36–7.19(m, 8H, Ar-H), 4.2(s, 1H), 4.1(s, 2H, NH_2), 2.79(s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 171.3, 169, 144.7, 142.1, 130.9, 127.8, 127.7, 127.5, 125.8, 124.5, 122.2, 120.8 118.8, 115.4, 87.3, 54.6, 35.2. EIMS: (*m*/*z*): 401 (M^+). Anal. calcd. For $C_{18}H_{15}N_3O_2S_3$: C, 53.84; N, 10.47; H, 3.77. Found: C, 53.85; N, 10.48; H, 3.75.

Compound 6a

Brownish solid: 613 mg (80%), mp 245–247 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.2 (m, 8H, Ar-H), 3.2(s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 147.1, 142.9, 129.1, 128.7, 128, 127.2, 126.5, 126.2, 124.0, 122.2, 117, 112.2, 82.8, 47.6, 35.6. EIMS: (*m*/*z*): 383 (M^+). Anal. calcd. For $C_{18}H_{13}N_3OS_3$: C, 56.37; N, 10.96; H, 3.42. Found: C, 56.39; N, 10.95; H, 3.40.

Compound 6b

Brownish solid: 710 mg (86%), mp 261–263 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.1 (m, 7H, Ar-H), 3.73 (s, 3H, OCH_3), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 160.7, 142.9, 139.4, 130.1, 128.7, 126.5, 124.0, 123.2, 117, 113.5, 112.2, 111.8, 82.8, 56.0, 47.6, 35.6. EIMS: (*m*/*z*): 413(M^+). Anal. calcd. For $C_{19}H_{15}N_3O_2S_3$: C, 55.18; N, 10.16; H, 3.66. Found: C, 55.15, N, 10.19, H, 3.64.

Compound 6c

Brownish solid: 650 mg (78%), mp 212–214 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.2 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 145.2, 142.9, 132.5, 130.5, 128.7, 128.3, 126.6, 126.5, 124.0, 123.6, 117, 112.2, 82.8, 47.6, 35.6. EIMS: (m/z): 417, 419 (M^+, M^{+2}). Anal. calcd. For $C_{18}H_{12}ClN_3OS_3$: C, 51.73; N, 10.05; H, 2.89. Found: C, 51.74; N, 10.07; H, 2.84.

Compound 6d

Brownish solid: 728 mg (79%), mp 201–203 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.3 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 146.1, 142.9, 131.3, 131.2, 129.5, 128.7, 126.5, 124.4, 124.0, 121.8, 117, 112.2, 82.8, 47.6, 35.6. EIMS: (m/z): 461, 463 (M, M^{+2}). Anal. calcd. For $C_{18}H_{12}BrN_3OS_3$: C, 46.75; N, 9.09; H, 2.62. Found: C, 46.77; N, 9.06; H, 2.64.

Compound 6e

Brownish solid: 625 mg (78%), mp 192–194 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0 (s, 1H, -NH-), 6.4–7.1 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 160.8, 142.9, 142.7, 130.7, 128.7, 126.5, 124.0, 123.8, 117, 114.9, 113.2, 112.2, 82.8, 47.6, 35.6. EIMS: (m/z): 401 (M^+). Anal. calcd. For $C_{18}H_{12}FN_3OS_3$: C, 53.85; N, 10.47; H, 3.01. Found: C, 53.87; N, 10.45; H, 3.02.

Compound 6f

Brownish solid: 667 mg (84%), mp 250–252 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.0 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79(s, 3H, -CH_3) 2.35(s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 144.1, 142.9, 136.4, 129.0, 128.7, 128.6, 126.9, 126.5, 124.0, 122.1, 117, 112.2, 82.8, 47.6, 35.6 , 20.5. EIMS: (m/z): 397 (M^+). Anal. calcd. For $C_{19}H_{15}N_3OS_3$: C, 57.40; N, 10.57; H, 3.80. Found: C, 57.43; N, 10.55; H, 3.81.

Compound 6g

Brownish solid: 703 mg (78%), 218–220 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.4 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 150.4, 142.9, 129.7, 129.4, 128.7, 126.5, 124.0, 123.0, 122.5, 118.9, 117, 112.2, 82.8, 47.6, 35.6. EIMS: (m/z): 451 (M^+). Anal. calcd. For $C_{19}H_{12}F_3N_3OS_3$: C, 50.54; N, 9.31; H, 2.68. Found: C, 50.57; N, 9.30; H, 2.65.

Compound 6h

Brownish solid: 668 mg (78%), mp 219–221 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–8.1 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 148.0, 146.1, 142.9, 135.2, 128.8, 128.7, 126.5, 124.0, 122.3, 117.3,117, 112.2, 82.8, 47.3, 35.6. EIMS: (m/z): 428 (M^+). Anal. calcd. For $C_{18}H_{12}N_4O_3S_3$: C, 50.45; N, 13.07; H, 2.82. Found: C, 50.43; N, 13.05; H, 2.81.

Compound 6i

Brownish solid: 650 mg (78%), mp 208–210 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H, -NH-), 6.4–7.2 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 148.5, 142.9, 131.5, 129.3, 128.7, 127.6, 127.2, 126.5, 124.0, 122.6, 117, 112.2, 82.8, 47.6, 35.6. EIMS: (m/z): 417, 419 (M, M^{+2}). Anal. calcd. For $C_{18}H_{12}ClN_3OS_3$: C, 51.73; N, 10.05; H, 2.89. Found: C, 51.74; N, 10.07; H, 2.84.

Compound 6j

Brownish solid: 703 mg (78%), mp 214–216 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0(s, 1H,-NH-), 6.4–7.3 (m, 7H, Ar-H), 3.2 (s, 1H), 2.79 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 147.4, 142.9, 132.4, 128.7, 128.7, 126.5, 124.0, 124.0, 119.3, 119.0, 117, 112.2, 82.8, 47.2, 35.6. EIMS: (m/z): 451 (M^+). Anal. calcd. For $C_{19}H_{12}F_3N_3OS_3$: C, 50.54; N, 9.31; H, 2.68. Found: C, 50.57; N, 9.30; H, 2.65.

Compound 6k

Brownish solid: 726 mg (85%), mp 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ: 8.0 (s, 1H, -NH-), 6.4–7.1 (m, 7H, Ar-H), 3.98 (q, 2H), 3.2 (s, 1H), 2.79 (s, 3H, -CH_3), 1.13 (t, 3H). ^{13}C NMR (100 MHz, $CDCl_3$/TMS) δ: 205, 169, 164, 157.5, 142.9, 138.7, 129.7, 126.5, 124.0, 123, 117, 113.6, 112.2, 112, 82.8, 65.7, 46.6, 35.6. EIMS: (m/z): 427 (M^+). Anal. calcd. For $C_{20}H_{17}N_3O_2S_3$: C, 56.18; N, 9.83; H, 4.01. Found: C, 56.16; N, 9.86; H, 4.03.

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