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ORIGINAL ARTICLE

Synthesis of thia- and thioxo-tetraazaspiro[4.4]nonenones from nitrile imines and arylidenethiohydantoins

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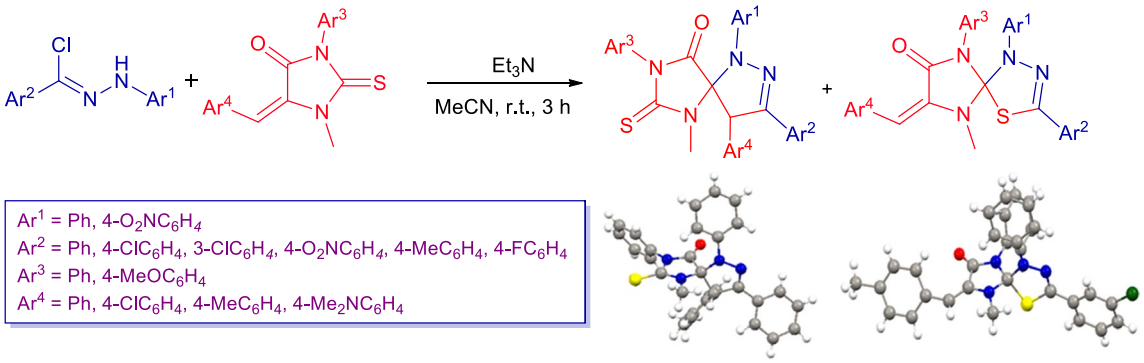
Abstract

5-Arylidene-1-methyl-2-thiohydantoins undergo [3+2]-cycloaddition reaction with nitrile imines, generated in situ from hydrazonyl chlorides, at C=C and C=S dipolarophiles in the thiohydantoin moiety to afford thioxo-tetraazaspiro[4.4]nonenones and thia-tetraazaspiro[4.4]nonenones in moderate to good yields. The stereochemistry of these spiroheterocycles has been confirmed by X-ray diffraction studies.

Graphic abstract



Keywords 1,3-Dipolar cycloaddition · Nitrile imines · Spirocycles · Thiohydantoins · Tetraazaspiro[4.4]nonenones

Introduction

The creation of molecular complexity and diversity in potential drug candidates and biologically important molecules from common starting materials is a challenge in modern organic chemistry from both academic and industrial viewpoints [1, 2]. A protocol to achieve these goals involves the use of molecular hybridization approach that involves coupling of different pharmacophores with varied bioactivities in one molecular framework. Such hybrid molecules have been used for treatment of metabolic disorders, malaria, inflammation, and ischemia [3, 4].

The construction of spirocycles, besides facilitating the expedient creation of chemical libraries of structurally diverse compounds, plays a key role in combinatorial synthesis. Interest in spirocyclic structures stems not only from their structural properties but also from their biological activities and their occurrence in a wide range of natural products [5–10].

Arylidene-thioxoimidazolidinone skeleton, commonly known as "arylidenethiohydantoin," is an important

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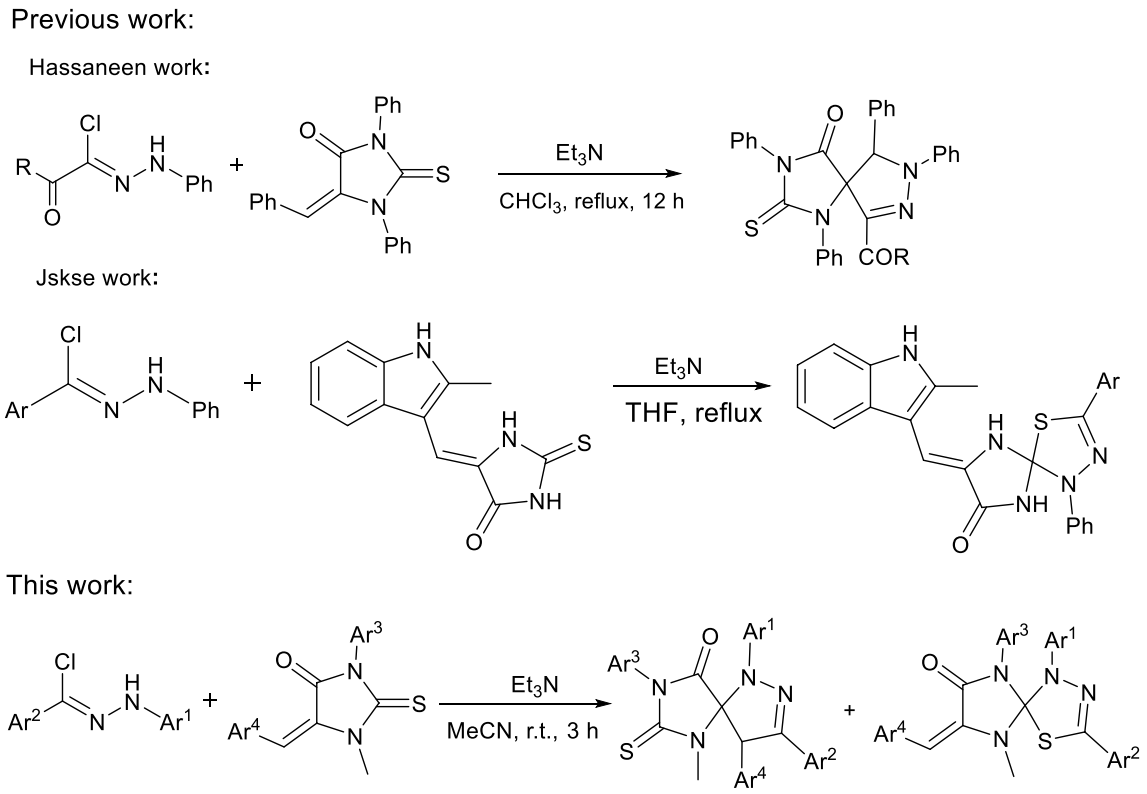
structural unit, which can be used as building blocks in spiroheterocycles preparation [11–14]. The cycloaddition reactions of nitrile imines with arylidenethiohydantoins afford nitrogen-containing spiroheterocycles.

Nitrile imines, generally prepared from hydrazonyl halides, are important transient 1,3-dipolar species and have been utilized as useful synthons of spiroheterocycles in organic synthesis [15–17]. In arylidenethiohydantoins, both the exocyclic C=C and C=S bonds could be considered as the potential dipolarophilic units. The 1,3-dipolar cycloaddition of nitrile imines to arylidenethiohydantoins is poorly studied in the literature. In 1995, Hassaneen et al. reported three examples of 1,3-dipolar cycloaddition of nitrile imines to arylidenethiohydantoins [18]. However, the reaction in these reported three examples was claimed to be chemoselective to the C=C dipolarophile (see Scheme 1). In 2007, Jakse et al. reported two examples of 1,3-dipolar cycloaddition of nitrile imines to arylidenethiohydantoins which were chemoselective to the C=S dipolarophile [19]. As a part of our interest in the cycloaddition reaction of nitrile imines with various dipolarophiles [20–23], we reinvestigated the 1,3-dipolar cycloaddition of nitrile imines to arylidenethiohydantoins using 5-arylidene-1-methyl-2-thiohydantoins **2** as potential reaction partners of nitrile imines **1**. As shown in Scheme 1, 1,3-dipolar cycloaddition reaction took place at the C=C and C=S dipolarophiles in the imidazole moiety to afford the corresponding spiroproducts.

Results and discussion

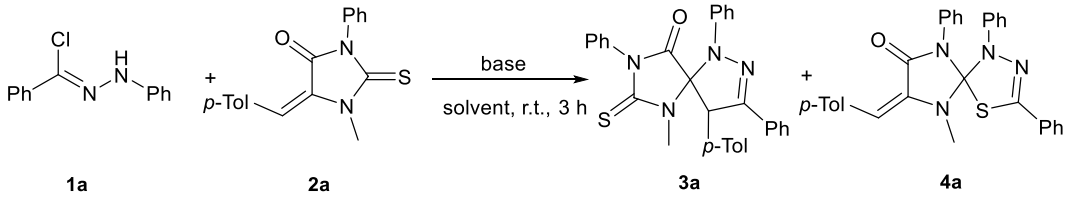
The 5-arylidene-1-methyl-2-thiohydantoins **2** were prepared by refluxing a mixture of benzaldehydes, appropriate isothiocyanates, and sarcosine in ethanol containing Et_3N, according to a previously reported method [12]. In a test experiment, we conducted the reaction between *N*-phenylbenzohydrazonyl chloride (**1a**) and 1-methyl-5-(4-methylbenzylidene)-3-phenyl-2-thioxoimidazolidin-4-one (**2a**) in the presence of Et_3N in MeCN at room temperature. After 3 h, two products, namely 6-methyl-1,3,8-triphenyl-7-thioxo-4-(*p*-tolyl)-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (**3a**) and 9-methyl-8-(4-methylbenzylidene)-1,3,6-triphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (**4a**), were isolated in 38% and 49% yields, respectively. Then, the reaction conditions, including the base and solvent, were optimized. As shown in Table 1, comparison of results obtained in the presence of different bases and solvents shows that Et_3N and MeCN were superior to the others.

With the optimal reaction conditions in hand, the scope of the substrates was investigated (see Table 2). Various



Scheme 1 Synthetic approaches to thia- and thioxo-tetraazaspiro[4.4]nonenones from hydrazonyl chlorides and arylidenethiohydantoins

Table 1 Optimization of the reaction conditions for the synthesis of spiroadducts **3a** and **4a**



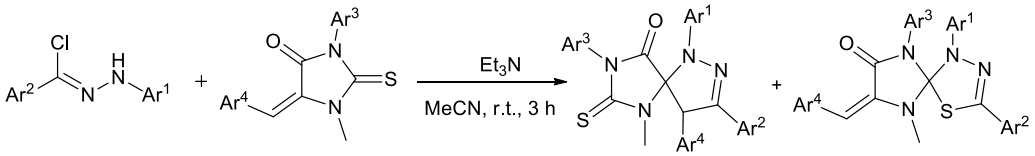
1a **2a** **3a** **4a**

Entry	Base	Solvent	Yield of **3a** (%)[a]	Yield of **4a** (%)[a]
1	Et_3N	MeCN	38	49
2	Et_3N	THF	29	41
3	Et_3N	DMSO	31	43
4	Et_3N	DMF	34	41
5	Et_3N	CH_2Cl_2	37	45
6	K_2CO_3	MeCN	36	46
7	DABCO	MeCN	35	40
8	DBU	MeCN	37	41
9	Cs_2CO_3	MeCN	36	47

Reactions conditions: **1a** (0.230 g, 1 mmol), **2a** (0.308 g, 1 mmol), base (0.101 g, 1 mmol), in solvent (5 mL) at r.t.

[a]Isolated yield

Table 2 Chemo- and regioselective synthesis of spirocycles **3** and **4**



1 **2** **3** **4**

Entry	Ar^1	Ar^2	Ar^3	Ar^4	Product	Yield of **3** (%)[a]	Yield of **4** (%)[a]
1	Ph	Ph	Ph	*p*-Me-C_6H_4	**3a, 4a**	38	49
2	Ph	Ph	Ph	*p*-Cl-C_6H_4	**3b, 4b**	40	43
3	Ph	*p*-F-C_6H_4	Ph	*p*-Cl-C_6H_4	**3c, 4c**	39	45
4	Ph	*p*-F-C_6H_4	Ph	*p*-Me-C_6H_4	**3d, 4d**	35	44
5	Ph	*p*-Cl-C_6H_4	Ph	*p*-Me-C_6H_4	**3e, 4e**	42	46
6	Ph	*p*-Cl-C_6H_4	Ph	*p*-Me_2N-C_6H_4	**–, 4f**	–	89
7	Ph	*m*-Cl-C_6H_4	Ph	*p*-Me-C_6H_4	**3g, 4g**	43	44
8	Ph	*m*-Cl-C_6H_4	Ph	*p*-Cl-C_6H_4	**3h, 4h**	41	45
9	Ph	*p*-O_2N-C_6H_4	Ph	*p*-Me-C_6H_4	**–, 4i**	–	79
10	Ph	*p*-Me-C_6H_4	Ph	*p*-Cl-C_6H_4	**3j, 4j**	43	45
11	*p*-O_2N-C_6H_4	Ph	*p*-MeO-C_6H_4	Ph	**–, 4k**	–	73

Reactions conditions: **1** (1 mmol), **2** (1 mmol), Et_3N (0.101 g, 1 mmol), in MeCN (5 mL) at r.t.

[a]Isolated yield

hydrazonyl chlorides having electron-donating or withdrawing groups at different positions of the benzene ring performed the reaction well to give products **3** and **4** in moderate to good yields. In general, substrates with electron-withdrawing groups on the benzene ring exhibited higher reactivity than those with electron-donating groups. Next, we carried out an investigation on precursors **2** with different substituents at 4-position of the aryl moiety. The electronic properties of the substituents on the benzene ring seem to have no significant effect on the reaction with the exception of 4-NMe_2 substituted precursor (**2i**), leading to product **4i**.

The structures of spiroadducts **3** and **4** resulting from the cycloaddition were deduced from their IR, ^{1}H NMR, and ^{13}C NMR spectra and their mass spectrometric data. The ^{13}C NMR spectra of **3a** and **4a** each exhibit 23 signals in agreement with the proposed structures. The mass spectra of products **3a** and **4a** displayed the molecular ion peak at $m/z = 502$. The regio- and the stereochemical outcome of the cycloaddition was furthermore ascertained by X-ray analysis of the crystal structure of cycloadducts **3a** and **4g,** whose ORTEP presentations are shown in Fig. 1. The same structures were assumed for the other derivatives on the basis of their NMR spectroscopic similarities. As shown by NMR and X-ray analysis, the regioisomeric configurations of cycloadducts **3** are opposite compared to the products reported by Hasseneen et al. (see Scheme 1).

To explain the formation of products **3** and **4,** the following mechanistic pathway is proposed (Scheme 1). The hydrazonyl chlorides **1**, under basic conditions, produce the nitrile imine species **5**. This 1,3-dipolar system undergoes chemoselective @@@[3+2]-cycloaddition reactions with the exocyclic C=C and C=S dipolarophiles of thiohydantoin **2** to afford thioxo-tetraazaspiro[4.4]nonenones **3** and thia-tetraazaspiro[4.4]nonenones **4**, respectively (Scheme 2).

Conclusion

In summary, we have reinvestigated the 1,3-dipolar cycloaddition of 5-arylidene-1-methyl-2-thiohydantoins as potential reaction partners of nitrile imines. The 1,3-dipolar cycloaddition reaction took place at both the C=C and C=S double bonds of thiohydantoin moiety to afford spiroadducts thioxo-tetraazaspiro[4.4]nonenones and thia-tetraazaspiro[4.4]nonenones in moderate to good yields. A range of thiohydantoins and nitrile imines are compatible with the mild reaction

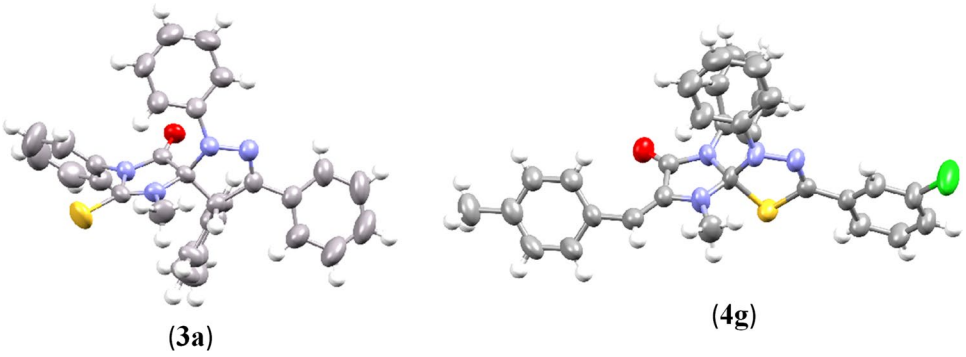
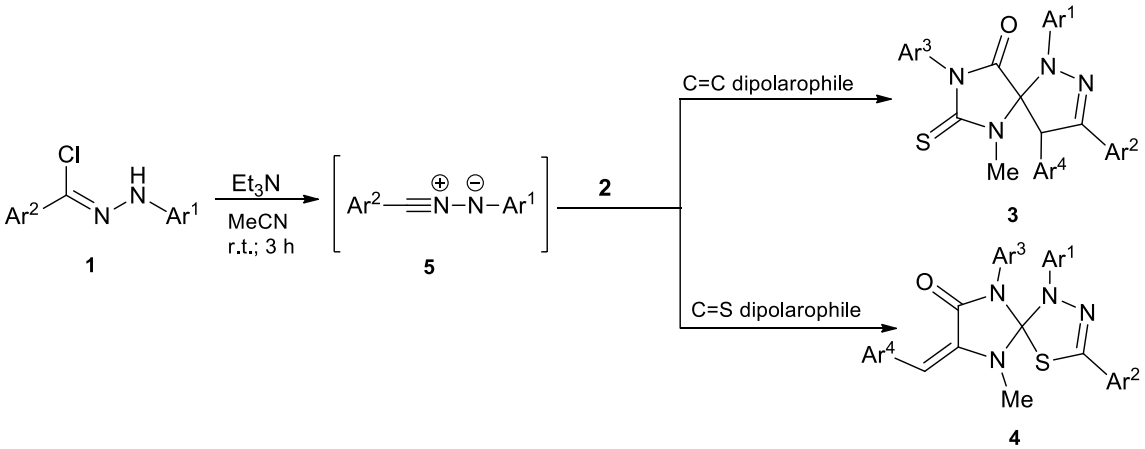


Fig. 1 Molecular structure and numbering scheme of **3a** and **4g**; the thermal ellipsoids are drawn at the 50% probability level



Scheme 2 Plausible mechanism for the formation of spiroheterocyclic systems **3** and **4**

conditions. Thus, the 1,3-dipolar cycloaddition reaction of nitrile imines is found to be chemoselective at both C=C and C=S dipolarophile moieties of arylidenethiohydantoins.

Experimental section

General remarks

All purchased solvents and chemicals were of analytical grade and used without further purification. Melting points were measured on an Electrothermal 9100 capillary melting point apparatus and are uncorrected. IR spectra were taken on a IR-460 Shimadzu spectrometer in KBr pellets and reported in cm^{-1}. The ^1H and ^{13}C spectra were obtained with a BRUKER DRX-500 AVANCE instrument using $CDCl_3$ as applied solvent and TMS as internal standard at 500.1 and 125.7 MHz, respectively. The chemical shift (δ) is given in ppm (s = singlet, d = doublet, t = triplet, brs = broad singlet, m = multiplet), coupling constant in Hz. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. X-Ray crystallographic analysis was performed with a STOE IPDS 2T diffractometer.

General procedure for the synthesis of compounds 3 and 4

A mixture of hydrazonyl chloride derivative **1** (1 mmol) and Et_3N (0.101 g, 1 mmol) in MeCN (3 mL) was stirred at r.t. for 15 min. Then, 5-arylidene-1-methyl-2-thiohydantoins **2** (1 mmol) was added to the above mixture, and the reaction was stirred at r.t. for 3 h. After completion of the reaction (the progress of the reaction was followed by TLC), the solvent was removed under reduced pressure. The crude residue was purified by column chromatography [silica gel (230–400 mesh; Merck, *n*-hexane/AcOEt 7:1] to give the products **3** and **4**. Retention factor (R_f) values of products **4** (R_f = 0.70–0.75) were found to be higher than those of compounds **3** (R_f = 0.60–0.65).

8-Methyl-1,3,6-triphenyl-7-thioxo-4-(*p*-tolyl)-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3a) Colorless powder; yield: 0.19 g (38%); mp: 143–145 °C; IR (KBr) (ν_{max}/cm^{-1}): 1749, 1660, 1595; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 2.33 (3 H, *s*, Me), 3.43 (3 H, *s*, Me), 5.20 (1 H, *s*, CH), 6.87 (2 H, *d*, ^3J = 7.4 Hz, CH), 7.07 (1 H, *t*, ^3J = 7.4 Hz, CH), 7.11–7.15 (4 H, *m*, CH), 7.19 (2 H, *d*, ^3J = 8.1 Hz, CH), 7.28 (2 H, *t*, ^3J = 7.2 Hz, CH), 7.34–7.37 (6 H, *m*, CH), 7.67 (2 H, *d*, ^3J = 7.4 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 29.8 (Me), 61.1 (CH), 89.5 (C), 115.5 (2 CH), 122.7 (CH), 126.7 (2 CH), 128.0 (2 CH), 128.4 (CH), 128.5 (CH), 128.6 (2 CH), 129.0 (2 CH), 129.4 (2 CH), 129.6 (2 CH), 129.7 (2 CH), 130.6 (C), 133.7 (C), 133.8 (C), 138.7 (C),142.7 (C), 148.4 (C=N), 166.8 (C=O), 181.0 (C=S); MS (EI, 70 eV): *m/z* (%) = 502 (M^+, 1), 429 (8), 396 (5), 367 (22), 337 (42), 309 (23), 261 (15), 194 (60), 169 (10), 135 (22), 91 (100), 51 (15); Anal. Calcd for $C_{31}H_{26}N_4OS$ (502.63): C, 74.08; H, 5.21; N, 11.15%. Found: C, 74.44; H, 5.23; N, 11.47%.

4-(4-Chlorophenyl)-6-methyl-1,3,8-triphenyl-7-thioxo-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3b) Colorless powder; yield: 0.21 g (40%); mp: 91–93 °C; IR (KBr) (ν_{max}/cm^{-1}): 1756, 1586, 1520; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 3.42 (3 H, *s*, Me), 5.17 (1 H, *s*, CH), 6.89 (2 H, *d*, ^3J = 7.4 Hz, CH), 7.08 (1 H, *t*, ^3J = 7.3 Hz, CH), 7.16–7.18 (4 H, *m*, CH), 7.32 (2 H, *d*, ^3J = 8.3 Hz, CH), 7.33–7.37 (5 H, *m*, CH),. 7.38–7.41 (3 H, *m*, CH), 7.63 (2 H, *d*, ^3J = 7.3 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 29.9 (Me), 60.7 (CH), 89.1 (C), 115.7 (2 CH), 123.1 (CH), 126.6 (2 CH), 127.7 (2 CH), 128.7 (2 CH), 129.1 (2 CH), 129.2 (CH), 129.3 (2 CH), 129.6 (2 CH), 129.6 (2 CH), 130.1 (C), 130.7 (C), 130.8 (CH), 132.5 (C), 135.0 (C),142.4 (C), 147.8 (C=N), 166.8 (C=O), 180.9 (C=S); MS (EI, 70 eV): *m/z* (%) = 522 (M^+, 1), 449 (9), 416 (50), 357 (60), 329 (15), 381 (100), 281 (18), 227 (14), 194 (60), 169 (55), 150 (11), 133 (48), 107 (8), 91 (100), 64 (3); Anal. Calcd for $C_{30}H_{23}ClN_4OS$ (522.13): C, 68.89; H, 4.43; N, 10.71%. Found: C, 68.98; H, 4.45; N, 10.97%.

4-(4-Chlorophenyl)-3-(4-fluorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3c) Colorless powder; yield: 0.21 g (39%); mp: 149–151 °C; IR (KBr) (ν_{max}/cm^{-1}): 1758, 1597,1500; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 3.43 (3 H, *s*, Me), 5.14 (1 H, *s*, CH), 6.85 (2 H, *d*, ^3J = 7.3 Hz, CH), 7.04 (2 H, *t*, ^3J = 8.6 Hz, CH), 7.08 (1 H, *t*, ^3J = 7.4 Hz, CH), 7.15–7.17 (4 H, *m*, CH), 7.32 (2 H, *d*, ^3J = 8.4 Hz, CH), 7.36 (2 H, *d*, ^3J = 7.4 Hz, CH), 7.38–7.40 (3 H, *m*, CH), 7.61 (2 H, *d*, ^3J = 8.6 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 29.9 (Me), 60.6 (CH), 89.3 (C), 115.7 (2 CH), 115.9 (*d*, $^2J_{C\text{-}F}$ = 21.4 Hz), 123.2 (CH), 126.8 (*d*, $^4J_{C\text{-}F}$ = 3.8 Hz), 127.8 (2 CH), 128.5 (*d*, $^3J_{C\text{-}F}$ = 8.8 Hz), 129.2 (2 CH), 129.3 (2 CH), 129.6 (4 CH), 130.4 (C), 130.8 (CH), 132.5 (C), 135.2 (C), 142.4 (C), 146.9 (C=N), 163.4 (*d*, $^1J_{C\text{-}F}$ = 250 Hz), 166.6 (C=O), 181.0 (C=S); MS (EI, 70 eV): *m/z* (%) = 540 (M^+, 1), 328 (50), 271 (13), 212 (15), 150 (100), 123 (53), 77 (80), 51 (25); Anal. Calcd for $C_{30}H_{22}ClFN_4OS$ (540.12): C, 66.60; H, 4.10; N, 10.36%. Found: C, 66.91; H, 4.12; N, 10.75%.

3-(4-Fluorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-4-(*p*-tolyl)-1,2,6,8 tetraazaspiro[4.4]non-2-en-9-one (3d) Colorless powder; yield: 0.18 g (35%); mp: 162–164 °C; IR (KBr) (ν_{max}/cm^{-1}): 1756, 1598, 1494; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 2.33 (3 H, *s*, Me), 3.45 (3 H, *s*,

Me), 5.17 (1 H, *s*, CH), 6.83 (2 H, *d*, ^3J = 6.5 Hz, CH), 7.02 (2 H, *t*, ^3J = 8.6 Hz, CH), 7.06 (1 H, *t*, ^3J = 7.6 Hz, CH), 7.10 (2 H, *d*, ^3J = 7.9 Hz, CH), 7.14–7.17 (4 H, *m*, CH), 7.34–7.38 (5 H, *m*, CH), 7.64 (2 H, *d*, ^3J = 8.6 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_H = 2.87 (3 H, *s*, Me), 5.78 (1 H, *s*, CH), 7.07 (2 H, *t*, ^3J = 8.6 Hz, Ar), 7.12 (1 H, *m*, Ar), 7.23 (2 H, *d*, ^3J = 8.2 Hz, Ar), 7.30 (5 H, *m*, Ar), 7.36 (4 H, *m*, Ar), 7.56 (2 H, *d*, ^3J = 8.7 Hz, Ar), 7.78 (2 H, *d*, ^3J = 8.6 Hz, Ar); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.2 (Me), 29.8 (Me), 60.9 (CH), 89.7 (C), 115.5 (2 CH), 115.8 (*d*, $^2J_{C\text{-}F}$ = 22.7 Hz), 122.8 (CH), 126.8 (*d*, $^4J_{C\text{-}F}$ = 2.8 Hz), 127.9 (2 CH), 128.6 (*d*, $^3J_{C\text{-}F}$ = 8.8 Hz), 128.7 (C), 129.0 (2 CH), 129.2 (2 CH), 129.4 (CH), 129.6 (2 CH), 129.8 (2 CH), 132.7 (C), 138.9 (C), 142.7 (C), 147.4 (C=N), 163.3 (*d*, $^1J_{C\text{-}F}$ = 250 Hz), 166.7 (C=O), 181.1 (C=S); MS (EI, 70 eV): *m/z* (%) = 520 (M^+, 1), 428 (20), 368(9), 353 (50), 325 (8), 148 (70), 120 (100), 105 (25); Anal. Calcd for $C_{31}H_{25}FN_4OS$ (520.17): C, 71.52; H, 4.84; N, 10.76%. Found: C, 71.85; H, 4.86; N, 10.95%.

3-(4-Chlorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-4-(*p*-tolyl)-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3e) Colorless powder; yield: 0.23 g (42%); mp: 149–151 °C; IR (KBr) (ν_{max}/cm^{-1}): 1760, 1596, 1500; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.33 (3 H, *s*, Me), 3.44 (3 H, *s*, Me), 5.16 (1 H, *s*, CH), 6.82 (2 H, *d*, ^3J = 6.5 Hz, CH), 7.05–7.09 (3 H, *m*, CH), 7.13–7.17 (4 H, *m*, CH), 7.30 (2 H, *d*, ^3J = 8.6 Hz, CH), 7.34–7.37 (5 H, *m*, CH), 7.58 (2 H, *d*, ^3J = 8.6 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.2 (Me), 29.8 (Me), 60.7 (CH), 89.7 (C), 115.5 (2 CH), 122.9 (CH), 127.8 (2 CH), 127.9 (2 CH), 128.6 (C), 128.9 (2 CH), 129.0 (2 CH), 129.1 (C), 129.2 (2 CH), 129.3 (CH), 129.6 (2 CH), 129.8 (2 CH), 132.6 (C), 135.3 (C), 138.9 (C),142.6 (C), 147.3 (C=N), 166.7 (C=O), 181.1 (C=S); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 370(9), 281 (50), 182 (8), 143 (70), 106 (100), 91 (25), 77 (10), 43 (4); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.76; H, 4.71; N, 10.78%.

3-(3-Chlorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-4-(*p*-tolyl)-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3g) Colorless powder; yield: 0.23 g (43%); mp: 131–132 °C; IR (KBr) (ν_{max}/cm^{-1}): 1749, 1594, 1492; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.33 (3 H, *s*, Me), 3.43 (3 H, *s*, Me), 5.15 (1 H, *s*, CH), 6.86 (2 H, *d*, ^3J = 6.5 Hz, CH), 7.06–7.10 (3 H, *m*, CH), 7.15 (2 H, *d*, ^3J = 8.3 Hz, CH), 7.17 (2 H, *d*, ^3J = 8.6 Hz, CH), 7.23 (1 H, *t*, ^3J = 8.6 Hz, CH),. 7.31 (1 H, *d*, ^3J = 8.0 Hz, CH), 7.35–7.38 (6 H, *m*, CH), 7.79 (1 H, *s*, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 29.8 (Me), 60.7 (CH), 89.6 (C), 115.6 (2 CH), 123.1 (CH), 124.8 (CH), 126.4 (CH), 127.9 (2 CH), 128.3 (C), 128.5 (CH), 129.0 (2 CH), 129.1 (CH), 129.2 (CH), 129.3 (2 CH), 129.6 (2 CH), 129.8 (2 CH), 132.4 (C), 132.6 (C), 134.7 (C), 138.9 (C), 142.4 (C), 147.0 (C=N), 166.6 (C=O), 181.1 (C=S); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 427 (10), 308 (40), 228 (80), 130 (50), 91 (100), 64 (10); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.74; H, 4.72; N, 10.80%.

3-(3-Chlorophenyl)-4-(4-chlorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3h) Colorless powder; yield: 0.23 g (41%); mp: 153–155 °C; IR (KBr) (ν_{max}/cm^{-1}): 1752, 1593, 1493; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 3.42 (3 H, *s*, Me), 5.14 (1 H, *s*, CH), 6.87 (2 H, *d*, ^3J = 7.4 Hz, Ar), 7.10 (1 H, *t*, ^3J = 7.4 Hz, Ar), 7.16–7.18 (4 H, *m*, Ar), 7.25 (1 H, *d*, ^3J = 7.9 Hz, Ar), 7.32–7.36 (5 H, *m*, Ar), 7.37–7.40 (4 H, *m*, Ar), 7.76 (1 H, *s*, Ar); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 29.7 (Me), 60.3 (CH), 89.3 (C), 115.8 (2 CH), 123.4 (CH), 124.7 (CH), 126.4 (CH), 127.9 (2 CH), 128.5 (CH), 128.6 (C), 129.2 (2 CH), 129.4 (2 CH), 129.5 (2 CH), 129.7 (2 CH), 129.9 (CH), 130.2 (CH), 132.1 (C), 132.5 (C), 134.9 (C), 135.2 (C), 142.2 (C), 147.5 (C=N), 166.5 (C=O), 180.9 (C=S); MS (EI, 70 eV): *m/z* (%) = 556 (M^+, 1), 483 (11), 450 (13), 391 (50), 363 (10), 315 (12), 295 (100), 228 (30), 169 (46), 150 (21), 133 (63), 91 (100), 64 (8); Anal. Calcd for $C_{30}H_{22}Cl_2N_4OS$ (556.09): C, 64.63; H, 3.98; N, 10.05%. Found: C, 64.88; H, 4.01; N, 10.46%.

4-(4-Chlorophenyl)-6-methyl-1,8-diphenyl-7-thioxo-3-(*p*-tolyl)-1,2,6,8-tetraazaspiro[4.4]non-2-en-9-one (3j) Colorless powder; yield: 0.23 g (43%); mp: 163–165 °C; IR (KBr) (ν_{max}/cm^{-1}): 1757, 1596, 1498; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.36 (3 H, *s*, Me), 3.40 (3 H, *s*, Me), 5.14 (1 H, *s*, CH), 6.89 (2 H, *d*, ^3J = 7.6 Hz, CH), 7.06 (1 H, *t*, ^3J = 7.4 Hz, CH), 7.14–7.18 (5 H, *m*, CH), 7.31 (2 H, *d*, ^3J = 8.4 Hz, CH), 7.34–7.37 (3 H, *m*, CH), 7.38–7.40 (3 H, *m*, CH), 7.51 (2 H, *d*, ^3J = 8.2 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.4 (Me), 29.9 (Me), 60.8 (CH), 89.1 (C), 115.6 (2 CH), 122.9 (CH), 126.6 (2 CH), 127.9 (2 CH), 128.4 (CH) 128.5 (C), 129.1 (2 CH), 129.2 (2 CH), 129.5 (2 CH), 129.6 (2 CH), 130.8 (2 CH), 132.0 (C), 132.1 (C), 134.9 (C), 139.9 (C), 142.5 (C), 148.0 (C=N), 166.1 (C=O), 180.9 (C=S); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 363 (8), 350 (10), 322 (22), 134 (25), 106 (100), 91 (10), 59 (23); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.77; H, 4.73; N, 10.69%.

(*E*)-9-Methyl-8-(4-methylbenzylidene)-1,3,6-triphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4a) Colorless powder; yield: 0.25 g (49%); mp: 145–147 °C; IR (KBr) (ν_{max}/cm^{-1}): 1723, 1633, 1595; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.36 (3 H, *s*, Me), 2.86 (3 H, *s*, Me), 5.85 (1 H, *s*, CH), 7.11 (1 H, *t*, ^3J = 7.2 Hz, CH), 7.15 (2 H, *d*, ^3J = 7.4 Hz, CH), 7.26–7.30 (3 H, *m*, CH), 7.32–7.40 (4 H, *m*, CH), 7.49 (2 H, *d*, ^3J = 7.2 Hz, CH), 7.56–7.59 (3 H, *m*, CH), 7.70 (2

H, *t*, ^3J = 8.2 Hz, CH), (2 H, *d*, ^3J = 7.2 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 28.6 (Me), 108.6 (CH), 116.4 (C) 117.3 (2 CH), 123.1 (CH), 126.0 (2 CH), 128.1 (2 CH), 128.4 (CH), 128.5 (CH), 128.6 (2 CH), 128.7 (2 CH), 129.0 (2 CH), 129.3 (2 CH), 129.6 (C), 129.8 (2 CH), 131.1 (C), 132.0 (C), 132.1 (C), 133.7 (C),137.0 (C), 141.5 (C=N), 160.7 (C=O); MS (EI, 70 eV): *m/z* (%) = 502 (M^+, 1), 318 (8), 305 (10), 274 (22), 218 (25), 100 (23), 72 (100), 59 (23); Anal. Calcd for $C_{31}H_{26}N_4OS$ (502.63): C, 74.08; H, 5.21; N, 11.15%. Found: C, 74.35; H, 5.25; N, 11.36%.

(*E*)-8-(4-Chlorobenzylidene)-9-methyl-1,3,6-triphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4b) Colorless powder; yield: 0.22 g (43%); mp: 91–93 °C; IR (KBr) (ν_{max}/cm^{-1}): 1726, 1593, 1491; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 5.77 (1 H, *s*, CH), 7.11 (1 H, *t*, ^3J = 7.1 Hz, CH), 7.16 (2 H, *d*, ^3J = 8.0 Hz, CH), 7.24 (2 H, *d*, ^3J = 8.2 Hz, CH), 7.28–7.31 (3 H, *m*, CH), 7.33–7.36 (4 H, *m*, CH), 7.39 (2 H, *d*, ^3J = 7.7 Hz, CH), 7.51 (2 H, *d*, ^3J = 8.5 Hz, CH), 7.75 (2 H, *d*, ^3J = 8.1 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 28.6 (Me), 106.7 (CH), 116.1 (C) 117.4 (2 CH), 123.3 (CH), 126.1 (2 CH), 126.2 (CH), 126.9 (CH), 127.2 (C), 128.0 (2 CH), 128.1 (2 CH), 128.6 (2 CH), 128.8 (C), 129.1 (2 CH), 129.4 (2 CH), 129.5 (C), 129.8 (C), 131.2 (2 CH), 132.6 (C), 141.0 (C),141.4 (C=N), 160.6 (C=O); MS (EI, 70 eV): *m/z* (%) = 522 (M^+, 1), 413(9), 327 (15), 194 (100), 165 (35), 139 (40), 111 (20), 91 (90), 64 (4); Anal. Calcd for $C_{30}H_{23}ClN_4OS$ (522.13): C, 68.89; H, 4.43; N, 10.71%. Found: C, 69.21; H, 4.46; N, 10.96%.

(*E*)-8-(4-Chlorobenzylidene)-3-(4-fluorophenyl)-9-methyl-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4c) Colorless powder; yield: 0.24 g (45%); mp: 149–151 °C; IR (KBr) (ν_{max}/cm^{-1}): 1733, 1596, 1493; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.87 (3 H, *s*, Me), 5.78 (1 H, *s*, CH), 7.07 (2 H, *t*, ^3J = 8.6 Hz, CH), 7.12 (1 H, *m*, CH), 7.24 (2 H, *d*, ^3J = 8.2 Hz, CH), 7.28–7.33 (5 H, *m*, CH), 7.34–7.37 (4 H, *m*, CH), 7.56 (2 H, *d*, ^3J = 8.7 Hz, CH), 7.78 (2 H, *d*, ^3J = 8.6 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 28.6 (Me), 106.9 (CH), 115.7 (*d*, $^2J_{C\text{-}F}$ = 22.2 Hz), 116.5 (C), 117.3 (2 CH), 123.3 (CH), 127.7 (*d*, $^4J_{C\text{-}F}$ = 3.2 Hz), 127.8 (*d*, $^3J_{C\text{-}F}$ = 8.6 Hz), 128.0 (2 CH), 128.1 (2 CH), 128.7 (CH), 129.1 (2 CH), 129.4 (2 CH), 131.2 (2 CH), 131.9 (C), 132.5 (C), 132.6 (C), 133.4 (C), 139.9 (C), 141.3 (C=N), 160.5 (C=O),163.4 (*d*, $^1J_{C\text{-}F}$ = 250 Hz); MS (EI, 70 eV): *m/z* (%) = 540 (M^+, 1), 431(8), 327 (15), 296 (10), 212 (60), 162 (40), 135 (35), 119 (10), 91 (100), 51 (20); Anal. Calcd for $C_{30}H_{22}ClFN_4OS$ (540.12): C, 66.60; H, 4.10; N, 10.36%. Found: C, 66.93; H, 4.13; N, 10.76%.

(*E*)-3-(4-Fluorophenyl)-9-methyl-8-(4-methylbenzylidene)-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4d) Colorless powder; yield: 0.23 g (44%); mp: 161–164 °C; IR (KBr) (ν_{max}/cm^{-1}): 1725, 1600, 1493; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.37 (3 H, *s*, Me), 2.87 (3 H, *s*, Me), 5.87 (1 H, *s*, CH), 7.07 (2 H, *t*, ^3J = 8.6 Hz, CH), 7.11 (1 H, *t*, ^3J = 7.1 Hz, CH), 7.16 (2 H, *d*, ^3J = 8.1 Hz, CH), 7.25 (2 H, *d*, ^3J = 8.3 Hz, CH), 7.29–7.33 (3 H, *m*, CH), 7.35 (2 H, *t*, ^3J = 7.7 Hz, CH), 7.39 (2 H, *d*, ^3J = 8.1 Hz, CH), 7.57 (2 H, *d*, ^3J = 8.5 Hz, CH), 7.76 (2 H, *d*, ^3J = 8.1 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 28.6 (Me), 108.8 (CH), 115.7 (*d*, $^2J_{C\text{-}F}$ = 22.1 Hz), 116.7 (C), 117.3 (2 CH), 123.1 (CH), 127.7 (*d*, $^4J_{C\text{-}F}$ = 3.2 Hz), 127.8 (*d*, $^3J_{C\text{-}F}$ = 8.4 Hz), 128.2 (2 CH), 128.5 (CH), 128.7 (2 CH), 129.1 (2 CH), 129.4 (2 CH), 129.9 (2 CH), 131.0 (2 C), 133.7 (C), 137.1 (C), 139.9 (C), 141.4 (C=N), 160.7 (C=O),163.4 (*d*, $^1J_{C\text{-}F}$ = 250.7 Hz); MS (EI, 70 eV): *m/z* (%) = 520 (M^+, 1), 411 (13), 307(8), 212 (80), 183 (8), 130 (30), 91 (100), 64 (15); Anal. Calcd for $C_{31}H_{25}FN_4OS$ (520.17): C, 71.52; H, 4.84; N, 10.76%. Found: C, 71.87; H, 4.86; N, 10.93%.

(*E*)-3-(4-Chlorophenyl)-9-methyl-8-(4-methylbenzylidene)-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4e) Colorless powder; yield: 0.25 g (46%); mp: 149–151 °C; IR (KBr) (ν_{max}/cm^{-1}): 1721, 1635, 1591; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.36 (3 H, *s*, Me), 2.86 (3 H, *s*, Me), 5.87 (1 H, *s*, CH), 7.11 (1 H, *t*, ^3J = 7.1 Hz, CH), 7.16 (2 H, *d*, ^3J = 8.0 Hz, CH), 7.24 (2 H, *d*, ^3J = 8.2 Hz, CH), 7.28–7.31 (3 H, *m*, CH), 7.33–7.36 (4 H, *m*, CH), 7.39 (2 H, *d*, ^3J = 7.7 Hz, CH), 7.51 (2 H, *d*, ^3J = 8.5 Hz, CH), 7.75 (2 H, *d*, ^3J = 8.1 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 28.7 (Me), 108.9 (CH), 116.8 (C), 117.3 (2 CH), 123.3 (CH), 127.2 (2 CH), 128.2 (2 CH), 128.5 (CH), 128.7 (2 CH), 128.8 (2 CH), 129.1 (2 CH), 129.4 (2 CH), 129.9 (2 CH), 130.0 (C), 130.9 (C), 131.0 (C), 133.6 (C), 135.4 (C), 137.1 (C), 139.9 (C), 141.4 (C=N), 160.7 (C=O); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 370(9), 281 (50), 182 (8), 143 (70), 106 (100), 91 (25), 77 (10), 43 (4); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.76; H, 4.73; N, 10.72%.

(*E*)-3-(4-Chlorophenyl)-8-(4-(dimethylamino)benzylidene)-9-methyl-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4f) Colorless powder; yield: 0.50 g (89%); mp: 181–183 °C; IR (KBr) (ν_{max}/cm^{-1}): 1720, 1651, 1601, 1489; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.79 (3 H, *s*, Me), 2.98 (6 H, *s*, 2 Me), 6.67 (2 H, *d*, ^3J = 8.7 Hz, CH), 6.71 (1 H, *s*, CH), 7.13 (2 H, *d*, ^3J = 8.5 Hz, CH), 7.28–7.30 (3 H, *m*, CH), 7.32–7.35 (5 H, *m*, CH), 7.38–7.40 (4 H, *m*, CH), 7.50 (2 H, *d*, ^3J = 8.5 Hz, CH); ^{13}C NMR (125.7 MHz,

$CDCl_3$): δ_C = 31.5 (Me), 40.4 (2 Me), 104.9 (CH), 111.6 (2 CH), 117.2 (2 CH), 117.9 (C), 123.2 (CH), 127.2 (2 CH), 127.9 (2 CH), 128.4 (CH), 128.7 (2 CH), 129.1(2 CH), 129.4 (2 CH), 129.5 (C), 129.9 (C), 130.5 (2 CH), 131.3 (C), 134.1 (C), 135.3 (C), 139.8 (C), 141.4 (C=N), 149.5 (C), 162.6 (C=O); MS (EI, 70 eV): *m/z* (%) = 565 (M^+, 1), 394(9), 334 (50), 319 (8), 232 (70), 106 (100), 91 (25), 77 (10), 59 (4); Anal. Calcd for $C_{32}H_{28}ClN_5OS$ (565.17): C, 67.89; H, 4.99; N, 12.37%. Found: C, 68.19; H, 5.02; N, 12.67%.

(*E*)-3-(3-Chlorophenyl)-9-methyl-8-(4-methylbenzylidene)-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4g) Colorless powder; yield: 0.24 g (44%); mp: 131–133 °C; IR (KBr) (ν_{max}/cm^{-1}): 1718, 1639, 1591, 1552; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.38 (3 H, *s*, Me), 2.87 (3 H, *s*, Me), 5.89 (1 H, *s*, CH), 7.13 (1 H, *t*, ^3J = 7.2 Hz, Ar), 7.17 (2 H, *d*, ^3J = 8.0 Hz, Ar), 7.26 (2 H, *d*, ^3J = 6.8 Hz, Ar), 7.29 (1 H, *t*, ^3J = 7.1 Hz, Ar), 7.30–7.34 (4 H, *m,* Ar),. 7.37 (2 H, *t*, ^3J = 7.8 Hz, Ar), 7.41–7.44 (3 H, *m*, Ar), 7.63 (1 H, *s*, Ar), 7.77 (2 H, *d*, ^3J = 8.1 Hz, Ar); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 28.7 (Me), 109.0 (CH), 116.8 (C), 117.4 (2 CH), 123.4 (CH), 124.2 (CH), 125.8 (CH), 128.2 (2 CH), 128.6 (C), 128.7 (2 CH), 129.1 (2 CH), 129.4 (2 CH), 129.5 (CH), 129.8 (CH), 129.9 (2 CH), 130.9 (C), 131.0 (C), 133.2 (C),133.6 (C), 134.7 (C), 137.1 (C), 139.5 (C), 141.3 (C=N), 160.7 (C=O); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 456(5), 427 (7), 401 (15), 371 (8), 308 (90), 279 (10), 228 (60), 130 (80), 91 (100), 51 (3); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.69; H, 4.72; N, 10.90%.

(*E*)-8-(4-Chlorobenzylidene)-3-(3-chlorophenyl)-9-methyl-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4h) Colorless powder; yield: 0.25 g (45%); mp: 153–155 °C; IR (KBr) (ν_{max}/cm^{-1}): 1725, 1634, 1593; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.87 (3 H, *s*, Me), 5.79 (1 H, *s*, CH), 7.13 (1 H, *m*, CH), 7.23 (2 H, *d*, ^3J = 7.9 Hz, CH), 7.28 (2 H, *d*, ^3J = 8.5 Hz, CH), 7.30–7.32 (4 H, *m*, CH), 7.36–7.38 (5 H, *m*, CH), 7.41 (1 H, *d*, ^3J = 8.5 Hz, CH), 7.60 (1 H, *s*, CH), 7.78 (2 H, *d*, ^3J = 8.5 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 28.7 (Me), 107.1 (CH), 116.5 (C), 117.5 (2 CH), 123.6 (CH), 124.2 (CH), 125.8 (CH), 128.0 (2 CH) 128.1 (2 CH), 128.7 (CH), 129.2 (2 CH), 129.4 (2 CH), 129.5 (CH), 129.8 (CH), 131.2 (2 CH), 131.9 (C), 132.4 (C), 132.7 (C), 133.0 (C), 133.4 (C), 134.7 (C), 139.5 (C), 141.2 (C=N), 160.5 (C=O); MS (EI, 70 eV): *m/z* (%) = 556 (M^+, 1), 339 (11), 311 (13), 300 (21), 252 (10), 100 (50), 72 (100), 59 (44); Anal. Calcd for $C_{30}H_{22}Cl_2N_4OS$ (556.09): C, 64.63; H, 3.98; N, 10.05%. Found: C, 64.97; H, 4.01; N, 10.45%.

(*E*)-9-Methyl-8-(4-methylbenzylidene)-3-(4-nitrophenyl)-1,6-diphenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4i) Yellow powder; yield: 0.43 g (79%); mp: 155–157 °C; IR (KBr) (ν_{max}/cm^{-1}): 1722, 1639, 1594, 1547; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.37 (3 H, *s*, Me), 2.89 (3 H, *s*, Me), 5.92 (1 H, *s*, CH), 7.17 (2 H, *d*, ^3J = 8.0 Hz, CH), 7.23 (2 H, *d*, ^3J = 6.5 Hz, Ar CH), 7.31 (2 H, *d*, ^3J = 7.6 Hz, CH), 7.34–7.37 (3 H, *m,* CH),. 7.40–7.43 (3 H, *m*, CH), 7.72 (2 H, *d*, ^3J = 8.6 Hz, CH), 7.77 (2 H, *d*, ^3J = 8.1 Hz, CH), 8.22 (2 H, *d*, ^3J = 8.7 Hz, CH);^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.3 (Me), 28.8 (Me), 109.6 (CH), 117.4 (C), 117.7 (2 CH), 123.9 (2 CH), 124.0 (CH), 126.5 (2 CH), 128.2 (2 CH) 128.5 (CH), 128.7 (2 CH), 129.2 (2 CH), 129.5 (2 CH), 129.9 (2 CH), 130.7 (C), 130.8 (C), 133.7 (C), 133.8 (C), 137.4 (C), 138.6 (C), 140.9 (C=N), 147.8 (C), 160.6 (C=O); MS (EI, 70 eV): *m/z* (%) = 547 (M^+, 1), 448 (6), 420 (10), 353 (22), 309 (25), 252 (10), 140 (100), 125 (50), 73 (41), 45 (22); Anal. Calcd for $C_{31}H_{25}N_5O_3S$ (547.17): C, 67.99; H, 4.60; N, 12.79%. Found: C, 68.36; H, 4.63; N, 12.95%.

(*E*)-8-(4-Chlorobenzylidene)-9-methyl-1,6-diphenyl-3-(*p*-tolyl)-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4j) Colorless powder, yield: 0.24 g (45%); mp: 163–165 °C; IR (KBr) (ν_{max}/cm^{-1}): 1723, 1633, 1595, 1491; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 2.38 (3 H, *s*, Me), 2.86 (3 H, *s*, Me), 5.77 (1 H, *s*, CH), 7.11 (1 H, *t*, ^3J = 7.0 Hz, CH), 7.19 (2 H, *d*, ^3J = 8.0 Hz, CH), 7.25 (2 H, *d*, ^3J = 8.3 Hz, CH), 7.28–7.31 (4 H, *m*, CH), 7.33–7.38 (5 H, *m*, CH), 7.48 (2 H, *d*, ^3J = 8.1 Hz, NH), 7.79 (2 H, *d*, ^3J = 8.5 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 21.4 (Me), 28.6 (Me), 106.6 (CH), 116.0 (C), 117.3 (2 CH), 123.1 (CH), 125.9 (2 CH), 128.0 (2 CH), 128.1 (2 CH) 128.6 (CH), 129.1 (2 CH), 129.3 (2 CH), 129.4 (2 CH), 131.2 (2 CH), 132.1 (C), 132.5 (C), 132.6 (C), 133.5 (C), 133.7 (C), 140.0 (C), 141.2 (C), 141.5 (C=N), 160.6 (C=O); MS (EI, 70 eV): *m/z* (%) = 536 (M^+, 1), 463 (8), 401 (22), 371 (22), 328 (28), 208 (100), 165 (25), 150 (30), 123 (15), 91 (90), 64 (10); Anal. Calcd for $C_{31}H_{25}ClN_4OS$ (536.14): C, 69.33; H, 4.69; N, 10.43%. Found: C, 69.64; H, 4.72; N, 10.72%.

(*E*)-8-Benzylidene-6-(4-methoxyphenyl)-9-methyl-1-(4-nitrophenyl)-3-phenyl-4-thia-1,2,6,9-tetraazaspiro[4.4]non-2-en-7-one (4k) Colorless powder, yield: 0.41 g (73%); mp: 179–181 °C; IR (KBr) (ν_{max}/cm^{-1}): 1724, 1649, 1598, 1544; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H = 3.12 (3 H, *s*, Me), 3.72 (3 H, *s*, Me), 5.87 (1 H, *s*, CH), 6.72 (2 H, *d*, ^3J = 7.5 Hz, CH), 7.26 (2 H, *d*, ^3J = 7.6 Hz, CH), 7.30–7.36 (3 H, *m*, CH), 7.46–7.51 (5 H, *m*, CH), 7.58 (2 H, *d*, ^3J = 7.5 Hz, CH), 7.87 (2 H, *d*, ^3J = 8.9 Hz,CH), 8.29 (2 H, *d*, ^3J = 8.9 Hz, CH); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C = 28.7 (Me), 55.7 (Me), 109.6 (CH), 114.9 (2 CH), 117.4 (C), 117.7 (2 CH), 123.9 (2 CH), 124.0 (CH), 126.5 (2 CH), 128.2 (2 CH) 128.5 (CH), 128.7 (2 CH), 129.2 (2 CH), 129.5 (2 CH), 130.7 (C), 130.8 (C), 133.8 (C), 137.4 (C), 138.6 (C), 140.9 (C=N), 147.8 (C), 157.7 (C), 160.6 (C=O); MS (EI, 70 eV): *m/z* (%) = 563 (M^+, 1), 363 (8), 350 (10), 322 (22), 263 (25),

100 (100), 91 (10), 72 (27); Anal. Calcd for $C_{31}H_{25}N_5O_4S$ (563.63): C, 66.06; H, 4.47; N, 12.43%. Found: C, 66.41; H, 4.49; N, 12.83%.

X-ray crystal structure determination of 3a and 4g

Crystallographic data for the structure **3a** and **4g** have been deposited with the Cambridge Crystallographic Data Centre with CCDC–1874156 and CCDC-1881806 which contain the supplementary crystallographic data for compounds **3a** and **4g**, respectively. Copies of the data can be obtained, free of charge, on application to the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail:deposit@ccdc.cam.ac.uk).

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