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Tetrahedron 62 (2006) 11274–11281
Tetrahedron

# Synthesis of dispirooxindolecycloalka[*d*]pyrimidino[2,3-*b*]-thiazole pyrrolidine/thiapyrrolizidine ring systems

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Received 23 May 2006; revised 11 August 2006; accepted 1 September 2006
Available online 6 October 2006

**Abstract**—The synthesis of a new class of spirooxindolo pyrrolidines and spirooxindolo thiapyrrolizidines has been accomplished by a three component, one-pot 1,3-dipolar cycloaddition reaction. The cycloaddition was found to be highly regioselective.


## 1. Introduction

The azomethine ylide represents one of the most reactive and versatile classes of 1,3-dipoles and is readily trapped by a range of dipolarophiles forming substituted pyrrolidines.[1] The reactions of azomethine ylides have been studied more than any other dipoles due to their remarkable synthetic potentials.[2] Spiropyrrolidines and spiropyrrolizidines have gained much attention in recent years due to their interesting biological activities.[3,4] The synthesis of spirooxindole ring systems has also attracted considerable attention since they are the basic building units in many natural products like gelsemine, pseudotabersonine, morroniside, etc.[5] Molecules with the thiazolidine nucleus have shown a wide spectrum of bioactivities like anti-inflammatory and anti-hypertensive activities.[6,7] Apart from the well established pharmacological activities of the thiazolone ring fused to a cycloheptene system,[8] the pyrimidine ring fused with substituted seven- and eight-membered carbocycles has shown anticancer and herbicidal activities.[9–11]

Since we have been involved in [3+2] cycloaddition chemistry for some years[12,13] and some of our synthesized molecules have shown good biological activities,[14] we decided to synthesize some complex spiroheterocyclic ring systems incorporating the foresaid bioactive moieties anticipating an overall bioactivity. These complex spiroheterocycles are synthesized by reacting suitable non-stabilized azomethine ylides with various substituted (*E*)-arylmethylene derivatives of octahydro/decahydro cycloalka[*d*]thiazolo[3,2-*a*]-pyrimidine-3-ones.

*Keywords*: Azomethine ylide; Regioselective; Spiropyrrolidines; Spirothiapyrrolizidines.
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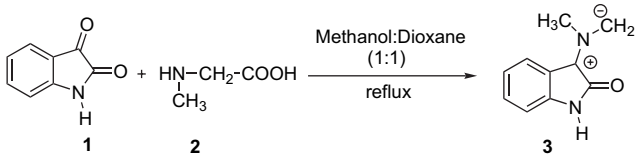
doi:10.1016/j.tet.2006.09.008

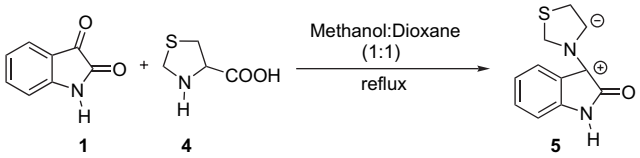
## 2. Results and discussion

Azomethine ylides can be prepared by several methods from easily available starting materials. Among the methods, the 'decarboxylation route' offers a general method in which an aldehyde or a ketone is reacted with α-amino acids.[15]

The in situ generated azomethine ylide is trapped by dipolarophiles to give cycloadducts. In our synthetic study, we have generated two types of azomethine ylides, namely cyclic and acyclic, by reacting *N*-methyl glycine **2** and L-thiazolidine-4-carboxylic acid **4** with isatin **1** (Schemes 1 and 2). The ylides so generated were reacted with arylidene octahydro/decahydro cycloalka[*d*]thiazolo[3,2-*a*]pyrimidine-3-ones as dipolarophiles to yield novel dispiropolycyclic complex heterocycles.

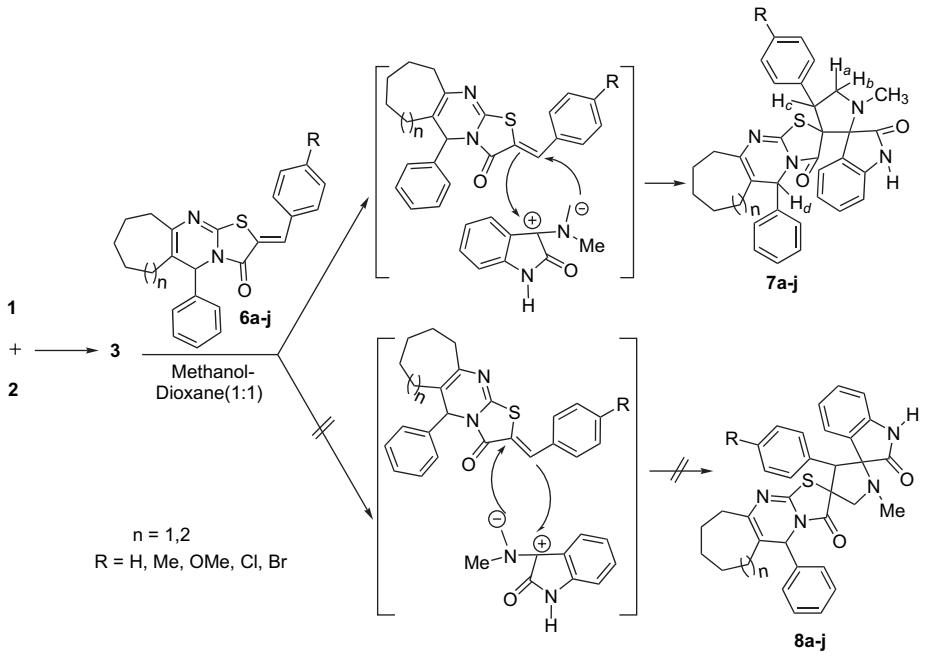



**Scheme 1**.




**Scheme 2**.

The required dipolarophiles **6a–j** were prepared in three steps by heating mono arylmethylene cycloalkanones with




**Scheme 3**.

thiourea in ethanolic potassium hydroxide giving cycloalka[*d*]pyrimidine-2-thiones, which were cyclized with monochloroacetic acid followed by condensation with various substituted benzaldehydes.[16,17]

When an equimolar mixture of isatin **1**, sarcosine **2** and dipolarophiles **6a–j** in methanol–dioxane (1:1) was heated to reflux, a series of novel spirooxindolo-spirothiazolo pyrimidino pyrrolidines **7a–j** were obtained in good yields (Scheme 3). The in situ generated *anti* 1,3-dipole[18,19] was trapped by conformationally restricted *S-cis* enone dipolarophiles to afford a series of cycloadducts.

A series of solvent systems such as methanol, acetonitrile and methanol–dioxane (1:1) were investigated to find the best reaction conditions. Among the solvents used, methanol–dioxane mixture (1:1) was found to be the best in terms of higher yields and shortest reaction times (Table 1). A single regioisomer was isolated in all the cases studied. No trace of the other regioisomers **8a–j** were found even after prolonged reaction times.

**Table 1**. Cycloaddition of ylides generated from isatin and sarcosine with the dipolarophiles

| Entry | Product | *n* | R | Yield (%) (A/B/C)[a] | Reaction time (h) (A/B/C)[a] |
|---|---|---|---|---|---|
| 1 | **7a** | 1 | H | 68/76/84 | 12/9/5 |
| 2 | **7b** | 1 | *p*-Me | 64/70/79 | 11/10/5 |
| 3 | **7c** | 1 | *p*-OMe | 69/72/79 | 14/11/5.5 |
| 4 | **7d** | 1 | *p*-Cl | 69/72/88 | 12/9/4.5 |
| 5 | **7e** | 1 | *p*-Br | 68/72/87 | 11.5/9/4 |
| 6 | **7f** | 2 | H | 63/74/87 | 10/9/4 |
| 7 | **7g** | 2 | *p*-Me | 70/73/83 | 13/10/4 |
| 8 | **7h** | 2 | *p*-OMe | 69/74/81 | 13/10/4.5 |
| 9 | **7i** | 2 | *p*-Cl | 69/74/81 | 11/9/3 |
| 10 | **7j** | 2 | *p*-Br | 69/74/88 | 12/10/3.5 |

[a] Solvent system: A=methanol, B=acetonitrile, C=methanol–dioxane (1:1).

The structure and regiochemistry of the products **7a–j** were established by IR, $^{1}H/^{13}C$ NMR spectroscopic and mass spectrometric studies. For instance, the IR spectrum of cycloadduct **7a** showed three characteristic peaks at 1721, 1712 and 3250 $cm^{-1}$ corresponding to the oxindole ring carbonyl, the thiazolidinone ring carbonyl and the secondary amide NH groups, respectively.

The $^{1}H$ NMR spectrum of **7a** displayed multiplets in the region $\delta$ 0.96–2.25 due to the cycloheptyl ring protons. A sharp singlet at $\delta$ 2.14 was accounted for the *N*-methyl protons. Three doublet of doublets appeared at $\delta$ 3.35, 4.06 and 3.96 for $H_a$ and $H_b$ of N–$CH_2$ protons and benzylic proton ($H_c$) of pyrrolidine ring, which explained the observed regiochemistry.

If the other regioisomer **8a** had formed then a singlet for the benzylic proton ($H_c$) and two doublets for the *N*-methylene ($H_a$ and $H_b$) protons would be observed. Also, the regiochemistries of the cycloadducts **7a**[20] and **7f**[21] were unambiguously corroborated by their X-ray crystallographic data (Figs. 1 and 2).

The signals appearing at $\delta$ 174.2 and 177.1 in the $^{13}C$ NMR spectrum reveal the presence of the thiazolone and the oxindole ring carbonyl groups, respectively. The two spiro quaternary carbons at C2 and C4 positions appeared at $\delta$ 79.7 and 70.7.

We performed a similar three component reaction in which the azomethine ylide **5** generated from L-thiazolidine 4-carboxylic acid **4** and isatin **1** was reacted with dipolarophiles **6a–j** to yield a series of novel dispiro-thio-pyrrolizidines **9a–j** in good yields. The products were formed by the regioselective cycloaddition of the ylide **5** across the exocyclic double bond of the dipolarophiles **6a–j** (Scheme 4). As in the case of the cycloaddition reactions described in

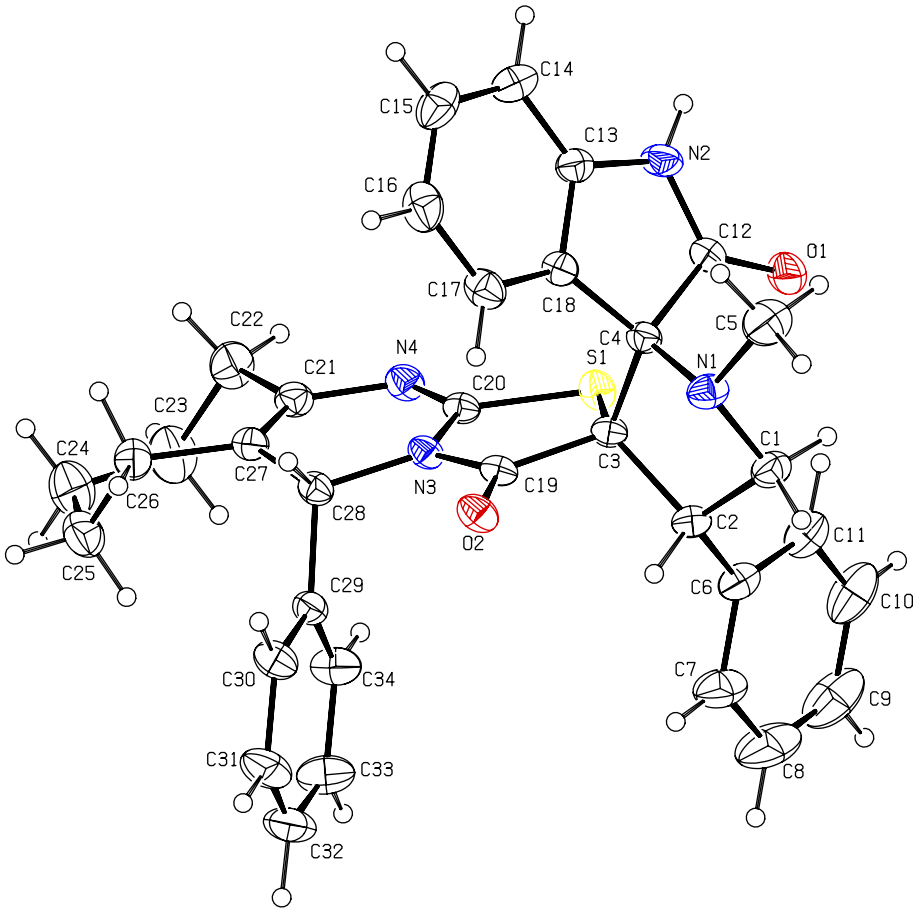



**Figure 1**. ORTEP diagram of **7a**.

Scheme 3, we noticed that the reaction proceeded to give the best yield of the products in methanol–dioxane (1:1) (Table 2).

The structure and stereochemistry of the cycloadducts **9a–j** were confirmed by their spectral data. Thus, the thiazolone keto carbonyl of **9a** exhibited a peak at 1710 $cm^{-1}$ in the IR spectrum showing an increase of 10 $cm^{-1}$ from the normal value observed for benzylidene pyrimidine thiazolo-3-one, indicating the loss of conjugation. Also, the IR spectrum showed characteristic absorption due to a secondary amide at 3250 $cm^{-1}$ and the oxindole carbonyl stretching band at 1720 $cm^{-1}$. In the $^1H$ NMR spectrum, apart from the multiplets observed for the cycloheptyl protons in the region $\delta$ 0.95 and 2.34, the benzylic proton on pyrrolidine ring $H_b$ appeared at $\delta$ 3.82 as a doublet and the $H_e$ and $H_f$ protons were seen as two doublets at $\delta$ 3.58 and 4.00, respectively. The $H_a$ proton was found as a multiplet in the region $\delta$ 4.95–4.99. The benzylic proton $H_g$ on the pyrimidine ring appeared at $\delta$ 5.04 as a singlet. In contrast, if **10a** was formed, the $H_b$ proton would appear as a singlet and the *N*–CH proton of the thiapyrrolizidine ring would manifest itself as a doublet of doublets. The $^{13}C$ NMR spectrum of **9a** showed peaks for two spiro quaternary carbons at $\delta$ 69.5 and 74.5. The carbonyl carbons resonated at $\delta$ 173.7 and 176.6. And the remaining signals for aromatic and aliphatic carbons confirmed the proposed structure. No trace of the other regioisomer **10a** was detected.

## 3. Conclusion

In conclusion, the synthesis of a series of novel dispirooxindolo pyrrolidines and dispirooxindolo thiapyrrolizidines has been achieved in a one-pot, three component cycloaddition reaction. It was observed that the non-stabilized azomethine ylide generated added regioselectively across the exocyclic double bonds of the dipolarophiles to give novel spiroheterocycles. The evaluation of the biological activities of the synthesized compounds is in progress. All of the cycloadducts have shown moderate to good activities against human pathogenic bacterias like *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Salmonella paratyphi* 'A', *Salmonella paratyphi* 'H', *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Escherichia coli* and fungi like *Candida albicans* and *Candida tropicalis*.

## 4. Experimental

### 4.1. General considerations

Infra red spectra were recorded on a Shimadzu IR-8300 series FT-IR spectrophotometer. $^1H$ NMR and $^{13}C$ NMR spectra were recorded on a JEOL 300 and JEOL 400 MHz instrument in $CDCl_3$ solvent with TMS as a standard. Mass spectra were recorded by JEOL-DX303 HF

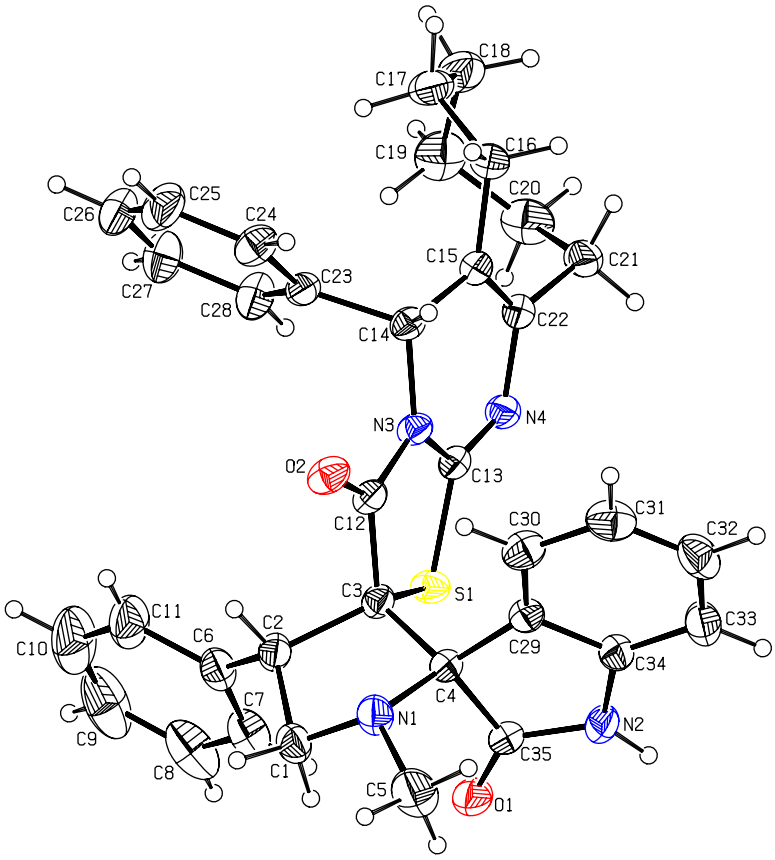
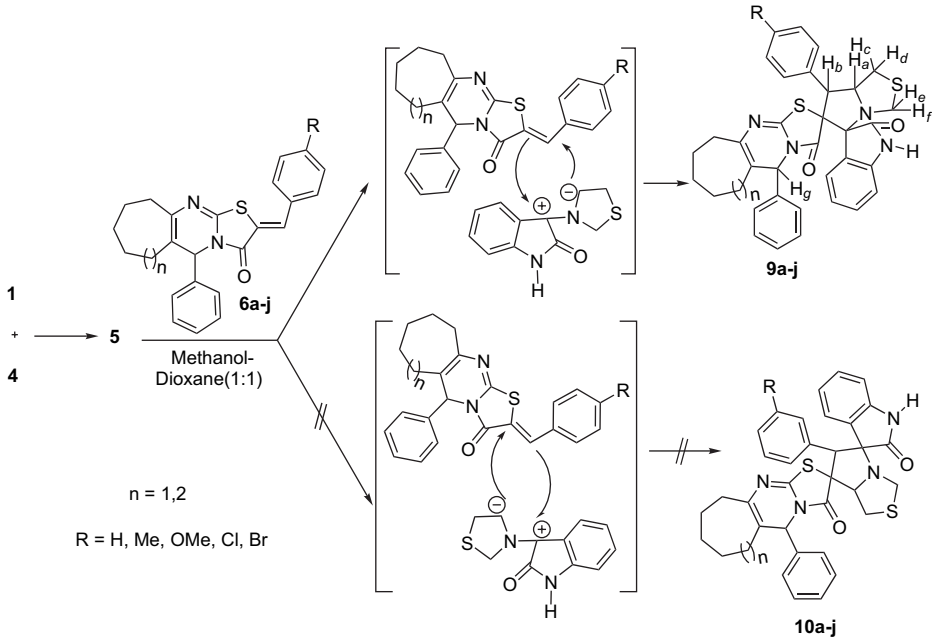



**Figure 2**. ORTEP diagram of **7f**.

mass Spectrometer. Elemental analyses were carried out by Perkin–Elmer CHNS 2400 instrument. X-ray diffraction data collection was performed by using Endraf-Nonius CHD4 diffractometer and Smart CCD Area diffractometer.

Column chromatography was performed on silica gel (ACME, 100–200 mesh). Routine monitoring of the reaction was made using thin layer chromatography developed on glass plates coated with silica gel-G (ACME) of 25 mm thickness and visualized with iodine.




**Scheme 4**.

**Table 2**. Cycloaddition of ylides generated from isatin and L-thiaproline with the dipolarophiles

| Entry | Product | *n* | R | Yield (%) (A/B/C)[a] | Reaction time (h) (A/B/C)[a] |
|---|---|---|---|---|---|
| 11 | **9a** | 1 | H | 66/70/80 | 13/10.5/4 |
| 12 | **9b** | 1 | *p*-Me | 67/77/80 | 14/11/4.5 |
| 13 | **9c** | 1 | *p*-OMe | 66/77/81 | 13/12/5 |
| 14 | **9d** | 1 | *p*-Cl | 68/72/83 | 12/10/3.5 |
| 15 | **9e** | 1 | *p*-Br | 69/73/85 | 12/9/3.5 |
| 16 | **9f** | 2 | H | 63/73/84 | 14/11/3.5 |
| 17 | **9g** | 2 | *p*-Me | 61/69/79 | 16/13/5 |
| 18 | **9h** | 2 | *p*-OMe | 64/70/79 | 15/13/5 |
| 19 | **9i** | 2 | *p*-Cl | 65/77/86 | 15/12/3.5 |
| 20 | **9j** | 2 | *p*-Br | 70/77/89 | 13/9/3.5 |

[a] Solvent system: A=methanol, B=acetonitrile, C=methanol–dioxane (1:1).

### 4.2. General procedure for the synthesis of cycloadducts 7a–j

A mixture of isatin **1** (0.176 g, 1.2 mmol), sarcosine **2** (0.106 g, 1.2 mmol) and 5-phenyl-2-(arylmethylene)-5,6,7,8,9,10-hexahydrocyclohepta/5,6,7,8,9,10,11-heptahydrocycloocta[*d*]thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones **6a–j** (1 mmol) in methanol–dioxane (1:1, 20 mL) was refluxed until the disappearance of the starting materials as shown by the TLC analysis ($R_f$=0.35–0.40). The reaction mixture was then concentrated in vacuo and extracted with water (50 mL) and dichloromethane (50 mL). The organic layer was washed with brine solution, dried with anhydrous sodium sulfate and concentrated in vacuo. The residue was purified by column chromatography with hexane–ethyl acetate (8:2) mixture to get compounds **7a–j** in good yields. The cycloadducts **7a** and **7f** were recrystallized from methanol by slow evaporation method for X-ray crystallographic analysis.

**4.2.1. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]-thiazolo[3,2-*a*]pyrimidin-3″-one-4-phenyl-pyrrolidine (7a).** Colourless solid (0.470 g, 84%). Mp 235–236 °C. IR (KBr): 3250, 2921, 1721, 1712, 1649, 1583 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.96–2.25 (m, 10H, cycloheptyl), 2.14 (s, 3H, N-Me), 3.35 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.96 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.06 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.02 (s, 1H, $H_d$), 6.72–7.40 (m, 14H, Ar-H), 8.46 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.4, 26.1, 30.8, 31.7, 35.3, 53.9, 57.7, 60.3, 70.7, 79.7, 110.0, 118.4, 123.0, 124.3, 127.6, 127.7, 128.3, 128.4, 128.5, 130.2, 130.2, 137.3, 139.1, 141.0, 142.7, 150.2, 174.2, 177.1. MS *m/z*: 560.7 ($M^+$). Anal. Calcd for $C_{34}H_{34}N_4O_2S$: C, 72.82; H, 5.75; N, 9.99. Found: C, 72.71; H, 5.68; N, 9.88.

**4.2.2. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-methyl)-phenyl-pyrrolidine (7b).** Fluffy white solid (0.454 g, 79%). Mp 230–231 °C. IR (KBr): 3245, 2921, 1719, 1710, 1652, 1583 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.77–2.28 (m, 10H, cycloheptyl), 2.16 (s, 3H, N-Me), 2.33 (s, 3H, $CH_3$), 3.38 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 4.00 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.06 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.04 (s, 1H, $H_d$), 6.74–7.40 (m, 13H, Ar-H), 8.75 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 21.1, 25.4, 26.1, 30.7, 30.9, 31.7, 34.2, 35.2, 35.5, 53.6, 57.7, 60.3, 70.8, 79.7, 110.0, 118.4, 122.9, 124.4, 127.6, 128.0, 128.3, 128.4, 129.2, 130.1, 134.2, 137.2, 139.2, 141.0, 142.7, 150.4, 174.3, 177.1. MS *m/z*: 574.6 ($M^+$). Anal. Calcd for $C_{35}H_{34}N_4O_2S$: C, 73.14; H, 5.96; N, 9.74. Found: C, 73.02; H, 5.89; N, 9.70.

**4.2.3. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-methoxy)phenyl-pyrrolidine (7c).** Colourless solid (0.466 g, 79%). Mp 202–204 °C. IR (KBr): 3240, 2931, 1720, 1710, 1649, 1581 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.78–2.20 (m, 10H, cycloheptyl), 2.16 (s, 3H, N-Me), 3.38 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.96 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.04 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 3.79 (s, 3H, OMe), 5.05 (s, 1H, $H_d$), 6.70–7.41 (m, 13H, Ar-H), 8.50 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.3, 26.1, 30.7, 31.6, 35.2, 35.5, 53.4, 55.1, 57.8, 60.2, 71.0, 79.5, 110.0, 113.7, 118.3, 122.9, 124.3, 127.6, 128.3, 128.4, 129.3, 130.1, 131.3, 139.1, 140.9, 142.7, 150.4, 158.8, 174.2, 177.2. MS *m/z*: 590.7 ($M^+$). Anal. Calcd for $C_{35}H_{36}N_4O_3S$: C, 71.16; H, 5.80; N, 9.48. Found: C, 71.22; H, 5.75; N, 9.40.

**4.2.4. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-chloro)-phenyl-pyrrolidine (7d).** Colourless solid (0.523 g, 88%). Mp 177–179 °C. IR (KBr): 3240, 2921, 1719, 1710, 1643, 1590 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.78–2.26 (m, 10H, cycloheptyl), 2.12 (s, 3H, N-Me), 3.31 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.93 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.00 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.00 (s, 1H, $H_d$), 6.70–7.33 (m, 13H, Ar-H), 8.50 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.4, 26.1, 30.8, 31.5, 31.6, 35.2, 35.5, 53.6, 57.6, 60.3, 70.3, 79.5, 110.2, 118.5, 123.1, 124.1, 127.7, 128.4, 128.5, 128.6, 128.6, 130.3, 131.6, 133.4, 135.8, 139.0, 141.0, 142.8, 150.1, 174.0, 177.2. MS *m/z*: 595.1 ($M^+$). Anal. Calcd for $C_{34}H_{31}N_4O_2SCl$: C, 68.69; H, 5.24; N, 9.41. Found: C, 68.60; H, 5.18; N, 9.34.

**4.2.5. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-bromo)-phenyl-pyrrolidine (7e).** Pale yellow powder (0.556 g, 87%). Mp 216–218 °C. IR (KBr): 3245, 2931, 1720, 1712, 1640, 1589 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.88–2.33 (m, 10H, cycloheptyl), 2.19 (s, 3H, N-Me), 3.40 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.94 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.06 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.11 (s, 1H, $H_d$), 6.77–7.47 (m, 13H, Ar-H), 8.73 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 21.0, 25.3, 26.1, 30.8, 31.6, 35.2, 35.5, 53.6, 57.5, 60.3, 70.2, 79.4, 110.1, 118.5, 121.7, 123.0, 124.1, 127.7, 128.4, 128.5, 128.6, 130.3, 131.5, 132.0, 136.3, 139.0, 141.0, 142.7, 149.9, 174.0, 177.1. MS *m/z*: 639.6 ($M^+$). Anal. Calcd for $C_{34}H_{31}N_4O_2SBr$: C, 63.84; H, 4.88; N, 8.76. Found: C, 63.90; H, 4.93; N, 8.83.

**4.2.6. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocyclo-octeno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-phenyl-pyrrolidine (7f).** Colourless solid (0.499 g, 87%). Mp 199–201 °C. IR (KBr): 3240, 2931, 1724, 1712, 1642,

1589 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.85–2.28 (m, 12H, cyclooctyl), 2.24 (s, 3H, N-Me), 3.47 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 4.06 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.26 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.04 (s, 1H, $H_d$), 6.74–7.40 (m, 14H, Ar-H), 8.20 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 25.8, 26.3, 28.4, 28.7, 29.0, 31.3, 35.4, 52.4, 58.0, 58.9, 70.8, 80.2, 109.9, 116.0, 122.8, 124.2, 125.4, 126.9, 127.7, 128.4, 128.5, 128.5, 128.7, 130.0, 130.2, 130.4, 137.8, 138.0, 140.1, 142.5, 150.8, 174.3, 177.0. MS *m/z*: 574.4 ($M^+$). Anal. Calcd for $C_{35}H_{34}N_4O_2S$: C, 73.14; H, 5.96; N, 9.74. Found: C, 73.06; H, 5.91; N, 9.68.

**4.2.7. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocyclooctено-[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-methyl)-phenyl-pyrrolidine (7g).** Fluffy white solid (0.488 g, 83%). Mp 221–223 °C. IR (KBr): 3245, 2921, 1720, 1711, 1643, 1596 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.88–2.27 (m, 12H, cyclooctyl), 2.23 (s, 3H, N-Me), 2.32 (s, 3H, Ar-$CH_3$), 3.45 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 4.03 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.22 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.03 (s, 1H, $H_d$), 6.73–7.82 (m, 13H, Ar-H), 8.84 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 21.1, 25.8, 26.3, 28.4, 28.7, 28.9, 31.3, 35.3, 52.0, 58.1, 58.8, 70.9, 80.1, 109.8, 115.9, 122.8, 124.3, 126.9, 127.6, 128.3, 128.4, 129.2, 130.1, 130.3, 134.7, 137.2, 138.0, 140.1, 142.4, 174.4, 176.9. MS *m/z*: 588.7 ($M^+$). Anal. Calcd for $C_{36}H_{36}N_4O_2S$: C, 73.43; H, 6.16; N, 9.50. Found: C, 73.38; H, 6.10; N, 9.40.

**4.2.8. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocyclooctено-[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-methoxy)-phenyl-pyrrolidine (7h).** Pale yellow powder (0.489 g, 81%). Mp 215–217 °C. IR (KBr): 3250, 2921, 1718, 1710, 1645, 1585 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.88–2.27 (m, 12H, cyclooctyl), 2.17 (s, 3H, N-Me), 3.80 (s, 3H, OMe), 3.45 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.97 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.20 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.04 (s, 1H, $H_d$), 6.79–7.42 (m, 13H, Ar-H), 8.33 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 25.8, 26.3, 28.4, 28.7, 29.0, 31.3, 35.3, 51.8, 55.2, 58.2, 58.8, 71.1, 80.0, 109.7, 113.9, 115.9, 122.8, 124.3, 127.0, 127.7, 128.3, 128.4, 129.8, 130.3, 131.3, 138.1, 140.1, 142.3, 158.9, 174.4, 176.8. MS *m/z*: 604.7 ($M^+$). Anal. Calcd for $C_{36}H_{36}N_4O_3S$: C, 71.49; H, 5.99; N, 9.26. Found: C, 71.58; H, 5.72; N, 9.11.

**4.2.9. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocyclooctено-[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-chloro)-phenyl-pyrrolidine (7i).** Fluffy white solid (0.493 g, 81%). Mp 209−211 °C. IR (KBr): 3240, 2920, 1724, 1712, 1640, 1590 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.85−2.26 (m, 12H, cyclooctyl), 2.22 (s, 3H, N-Me), 3.45 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.96 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.20 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.05 (s, 1H, $H_d$), 6.78–7.40 (m, 13H, Ar-H), 8.40 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 25.8, 26.3, 28.4, 28.9, 29.0, 31.2, 35.3, 52.0, 58.0, 59.0, 70.4, 80.0, 110.0, 116.1, 122.9, 124.0, 127.0, 127.7, 128.5, 128.7, 130.5, 131.6, 133.4, 136.2, 138.0, 140.0, 142.5, 150.6, 174.2, 177.1. MS *m/z*: 608.5 ($M^+$). Anal. Calcd for $C_{35}H_{33}N_4O_2SCl$: C, 69.00; H, 5.45; N, 9.19. Found: C, 69.11; H, 5.55; N, 9.12.

**4.2.10. 1-*N*-Methyl-spiro[2.3′]oxindole-spiro[3.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocyclooctено-[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-4-(*p*-bromo)-phenyl-pyrrolidine (7j).** White solid (0.575 g, 88%). Mp 207–209 °C. IR (KBr): 3270, 2921, 1720, 1710, 1649, 1596 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.85–2.26 (m, 12H, cyclooctyl), 2.26 (s, 3H, N-Me), 3.45 (dd, 1H, $H_a$, $J_1$=8.0 Hz, $J_2$=8.8 Hz), 3.98 (dd, 1H, $H_c$, $J_1$=8.8 Hz, $J_2$=10.0 Hz), 4.18 (dd, 1H, $H_b$, $J_1$=10.0 Hz, $J_2$=8.0 Hz), 5.06 (s, 1H, $H_d$), 6.74–7.45 (m, 13H, Ar-H), 8.75 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 24.9, 25.8, 26.3, 27.4, 28.3, 28.9, 29.0, 31.2, 35.5, 52.1, 57.9, 59.1, 70.3, 80.0, 110.1, 116.1, 121.7, 122.9, 123.9, 125.4, 126.9, 127.7, 128.7, 130.5, 131.6, 132.0, 136.8, 138.0, 140.0, 142.7, 150.6, 174.2, 177.2. MS *m/z*: 653.6 ($M^+$). Anal. Calcd for $C_{35}H_{33}N_4O_2SBr$: C, 64.31; H, 5.08; N, 8.57. Found: C, 64.23; H, 4.97; N, 8.49.

### 4.3. General procedure for the synthesis of cycloadducts 9a–j

A mixture of isatin **1** (0.176 g, 1.2 mmol), L-thiazolidine-4-carboxylic acid **4** (0.106 g, 1.2 mmol) and 5-phenyl-2-(arylmethylene)-5,6,7,8,9,10-hexahydrocyclohepta/5,6,7,8,9,10,11-heptahydrocycloocta[*d*]thiazolo[3,2-*a*]pyrimidin-3(2*H*)-ones **6a–j** (1 mmol) in methanol–dioxane (1:1, 20 mL) was refluxed until the disappearance of starting materials as shown by the TLC analysis ($R_f$=0.35–0.40). The reaction mixture was then concentrated in vacuo and extracted with water (50 mL) and dichloromethane (50 mL). The organic layer was washed with brine solution, dried with anhydrous sodium sulfate and concentrated in vacuo. The residue was purified by column chromatography with hexane–ethyl acetate (8:2) mixture to get compounds **9a–j** in good yields.

**4.3.1. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-phenyl-thiapyrrolizidine (9a).** Colourless solid (0.483 g, 80%). Mp 219–221 °C. IR (KBr): 3250, 2912, 1720, 1710, 1639, 1589 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.95–2.34 (m, 10H, cycloheptyl), 2.77 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.7 Hz), 2.92 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.7 Hz), 3.58 (d, 1H, $H_e$, $J$=5.8 Hz), 3.82 (d, 1H, $H_b$, $J$=9.7 Hz), 4.00 (d, 1H, $H_f$, $J$=5.8 Hz), 4.95–4.99 (m, 1H, $H_a$), 5.04 (s, 1H, $H_g$), 6.85–7.64 (m, 14H, Ar-H), 8.63 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 25.3, 26.1, 30.6, 31.6, 32.4, 35.5, 47.4, 58.6, 60.7, 69.5, 74.5, 110.4, 118.7, 122.8, 123.4, 127.9, 128.1, 128.5, 128.5, 128.6, 130.0, 130.6, 135.7, 139.3, 140.6, 142.4, 150.0, 173.7, 176.6. MS *m/z*: 604.0 ($M^+$). Anal. Calcd for $C_{35}H_{32}N_4O_2S_2$: C, 69.50; H, 5.33; N, 9.26. Found: C, 69.40; H, 5.47; N, 9.20.

**4.3.2. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-methyl)-phenyl-thiapyrrolizidine (9b).** White solid (0.495 g, 80%). Mp 212–214 °C. IR (KBr): 3286, 2921, 1720, 1712, 1644, 1587 $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 0.80–2.31 (m, 10H, cycloheptyl), 2.33 (s, 3H, Ar-$CH_3$), 2.70 (dd, 1H, $H_c$, $J_1$=6.9 Hz,

$J_2$=9.6 Hz), 2.92 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.58 (d, 1H, $H_e$, $J$=5.7 Hz), 3.80 (d, 1H, $H_b$, $J$=9.6 Hz), 4.01 (d, 1H, $H_f$, $J$=5.7 Hz), 4.92–4.99 (m, 1H, $H_a$), 5.03 (s, 1H, $H_g$), 6.76–7.57 (m, 13H, Ar-H), 8.65 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 22.1, 25.3, 26.1, 30.6, 31.6, 31.6, 32.4, 35.5, 47.4, 58.2, 60.6, 69.5, 74.6, 110.4, 118.6, 122.8, 123.5, 128.0, 128.1, 128.4, 128.5, 129.3, 129.8, 130.5, 132.6, 137.5, 139.3, 140.6, 142.3, 150.1, 173.7, 176.6. MS *m/z*: 618.5 ($M^+$). Anal. Calcd for $C_{36}H_{34}N_4O_2S_2$: C, 69.87; H, 5.53; N, 9.05. Found: C, 69.94; H, 5.59; N, 9.11.

**4.3.3. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-methoxy)-phenyl-thiapyrrolizidine (9c).** Pale yellow solid (0.488 g, 81%). Mp 191–193 °C. IR (KBr): 3286, 2922, 1720, 1713, 1640, 1595 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.80–2.33 (m, 10H, cycloheptyl), 2.70 (dd, 1H, $H_c$, $J_1$=6.9 Hz, $J_2$=9.6 Hz), 2.92 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.58 (d, 1H, $H_e$, $J$=5.7 Hz), 3.77 (d, 1H, $H_b$, $J$=9.6 Hz), 3.80 (s, 3H, Ar-$OCH_3$), 4.01 (d, 1H, $H_f$, $J$=5.7 Hz), 4.87–4.95 (m, 1H, $H_a$), 5.03 (s, 1H, $H_g$), 6.73–7.57 (m, 13H, Ar-H), 8.42 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.3, 26.1, 30.6, 31.7, 32.5, 35.6, 47.4, 55.1, 58.1, 60.0, 69.0, 74.1, 110.3, 114.0, 118.6, 122.8, 123.5, 127.7, 128.1, 128.5, 130.5, 131.1, 139.3, 140.6, 142.2, 159.5, 173.1, 176.9. MS *m/z*: 602.7 ($M^+$). Anal. Calcd for $C_{36}H_{34}N_4O_3S_2$: C, 71.73; H, 5.68; N, 9.29. Found: C, 71.64; H, 5.59; N, 9.21.

**4.3.4. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-chloro)-phenyl-thiapyrrolizidine (9d).** Pale yellow solid (0.530 g, 83%). Mp 217–219 °C. IR (KBr): 3286, 2922, 1720, 1713, 1640, 1595 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.80–2.32 (m, 10H, cycloheptyl), 2.68 (dd, 1H, $H_c$, $J_1$=6.9 Hz, $J_2$=9.6 Hz), 2.91 (dd, 1H, $H_d$, $J_1$=5.9 Hz, $J_2$=9.6 Hz), 3.58 (d, 1H, $H_e$, $J$=5.7 Hz), 3.77 (d, 1H, $H_b$, $J$=9.6 Hz), 4.02 (d, 1H, $H_f$, $J$=5.7 Hz), 4.86–4.94 (m, 1H, $H_a$), 5.06 (s, 1H, $H_g$), 6.77–7.57 (m, 13H, Ar-H), 8.74 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.3, 26.1, 30.6, 31.5, 31.6, 32.4, 35.4, 47.4, 58.2, 60.7, 69.5, 74.1, 110.5, 118.8, 122.9, 123.2, 128.1, 128.2, 128.6, 130.6, 131.3, 133.8, 134.2, 139.1, 140.6, 142.3, 149.7, 173.4, 176.5. MS *m/z*: 639.8 ($M^+$). Anal. Calcd for $C_{35}H_{31}N_4O_2S_2Cl$: C, 65.76; H, 4.88; N, 8.76. Found: C, 65.79; H, 4.80; N, 8.82.

**4.3.5. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″-hexahydrocyclohepteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-bromo)-phenyl-thiapyrrolizidine (9e).** Pale yellow solid (0.581 g, 85%). Mp 198–200 °C. IR (KBr): 3286, 2922, 1720, 1713, 1640, 1595 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.88–2.25 (m, 10H, cycloheptyl), 2.61 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.7 Hz), 2.83 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.7 Hz), 3.51 (d, 1H, $H_e$, $J$=5.8 Hz), 3.68 (d, 1H, $H_b$, $J$=9.7 Hz), 4.95 (d, 1H, $H_f$, $J$=5.8 Hz), 4.81–4.84 (m, 1H, $H_a$), 4.99 (s, 1H, $H_g$), 6.64–7.49 (m, 13H, Ar-H), 8.95 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 26.1, 30.6, 31.5, 32.4, 35.4, 47.5, 58.3, 60.7, 69.4, 74.0, 110.5, 118.8, 122.0, 122.8, 123.1, 128.1, 128.2, 128.6, 130.6, 131.7, 134.7, 139.1, 140.6, 142.4, 149.7, 173.4, 176.6. MS *m/z*: 683.6 ($M^+$). Anal. Calcd for $C_{35}H_{31}N_4O_2S_2Br$: C, 61.48; H, 4.56; N, 8.19. Found: C, 61.31; H, 4.49; N, 8.26.

**4.3.6. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocycloocteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-phenyl-thiapyrrolizidine (9f).** Yellow solid (0.519 g, 84%). Mp 198–200 °C. IR (KBr): 3250, 2930, 1720, 1710, 1640, 1595 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.85–2.18 (m, 12H, cyclooctyl), 2.75 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.7 Hz), 2.94 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.7 Hz), 3.60 (d, 1H, $H_e$, $J$=5.8 Hz), 3.90 (d, 1H, $H_b$, $J$=9.7 Hz), 3.97 (d, 1H, $H_f$, $J$=5.8 Hz), 4.76–4.85 (m, 1H, $H_a$), 5.00 (s, 1H, $H_g$), 6.82–7.49 (m, 14H, Ar-H), 8.63 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.7, 26.3, 28.4, 29.0, 31.2, 32.5, 32.6, 35.7, 46.7, 47.1, 57.0, 58.8, 59.3, 70.0, 74.7, 110.3, 116.1, 122.7, 123.2, 125.3, 127.2, 127.4, 127.9, 128.4, 128.7, 128.9, 129.8, 130.0, 130.8, 136.2, 140.1, 142.2, 150.6, 173.9, 176.5. MS *m/z*: 618.8 ($M^+$). Anal. Calcd for $C_{36}H_{34}N_4O_2S_2$: C, 69.87; H, 5.53; N, 9.05. Found: C, 69.80; H, 5.47; N, 8.98.

**4.3.7. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocycloocteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-methyl)-phenyl-thiapyrrolizidine (9g).** Fluffy white solid (0.499 g, 79%). Mp 203–205 °C. IR (KBr): 3260, 2912, 1720, 1712, 1643, 1593 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.97–2.18 (m, 12H, cyclooctyl), 2.33 (s, 3H, Ar-$CH_3$), 2.74 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.6 Hz), 2.94 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.61 (d, 1H, $H_e$, $J$=5.8 Hz), 3.91 (d, 1H, $H_b$, $J$=9.6 Hz), 3.99 (d, 1H, $H_f$, $J$=5.8 Hz), 4.95–4.99 (m, 1H, $H_a$), 5.04 (s, 1H, $H_g$), 6.85–7.64 (m, 13H, Ar-H), 8.63 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 21.1, 25.0, 25.7, 26.3, 27.0, 28.4, 28.8, 29.0, 31.3, 32.5, 35.8, 46.8, 47.1, 56.8, 58.8, 59.4, 61.7, 70.1, 74.8, 110.3, 116.1, 122.7, 123.3, 125.8, 127.4, 128.6, 129.4, 130.7, 133.2, 137.6, 140.2, 142.2, 150.7, 173.9, 176.5. MS *m/z*: 632.8 ($M^+$). Anal. Calcd for $C_{37}H_{33}N_4O_2S_2$: C, 69.74; H, 5.73; N, 8.85. Found: C, 69.66; H, 5.67; N, 8.77.

**4.3.8. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocycloocteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-methoxy)-phenyl-thiapyrrolizidine (9h).** Pale yellow fluffy solid (0.512 g, 79%). Mp 192–194 °C. IR (KBr): 3250, 2930, 1723, 1711, 1643, 1591 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.83–2.22 (m, 12H, cyclooctyl), 2.74 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.6 Hz), 2.95 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.61 (d, 1H, $H_e$, $J$=5.8 Hz), 3.82 (s, 3H, OMe), 3.88 (d, 1H, $H_b$, $J$=9.6 Hz), 4.02 (d, 1H, $H_f$, $J$=5.8 Hz), 4.80–4.89 (m, 1H, $H_a$), 5.02 (s, 1H, $H_g$), 6.80–7.52 (m, 13H, Ar-H), 8.70 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.7, 26.3, 28.3, 28.8, 29.0, 31.2, 32.5, 47.2, 55.1, 56.7, 59.4, 70.2, 74.9, 110.3, 114.0, 116.0, 122.6, 123.3, 127.4, 127.4, 128.3, 128.3, 128.5, 128.7, 130.6, 131.1, 137.8, 140.2, 142.3, 150.7, 159.1, 173.9, 176.7. MS *m/z*: 648.8 ($M^+$). Anal. Calcd for $C_{37}H_{36}N_4O_3S_2$: C, 68.49; H, 5.59; N, 8.63. Found: C, 68.40; H, 5.51; N, 8.67.

**4.3.9. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocycloocteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-chloro)-phenyl-thiapyrrolizidine (9i).** Fluffy white solid (0.531 g, 86%). Mp 220–221 °C. IR (KBr): 3150, 2920, 1724, 1710, 1643, 1590 cm$^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.83–2.24 (m, 12H, cyclooctyl), 2.72 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.6 Hz), 2.93 (dd,

1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.61 (d, 1H, $H_e$, $J$=5.8 Hz), 3.89 (d, 1H, $H_b$, $J$=9.6 Hz), 4.02 (d, 1H, $H_f$, $J$=5.8 Hz), 4.90–4.96 (m, 1H, $H_a$), 5.03 (s, 1H, $H_g$), 6.79–7.50 (m, 13H, Ar-H), 8.40 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 26.0, 26.5, 28.6, 29.2, 29.3, 30.3, 31.5, 32.7, 47.4, 57.1, 59.8, 70.3, 74.5, 110.7, 116.5, 123.0, 123.3, 127.8, 128.8, 128.9, 129.1, 131.0, 131.7, 134.1, 135.0, 138.1, 140.4, 142.7, 150.6, 174.0, 176.7. MS *m/z*: 653.3 ($M^+$). Anal. Calcd for $C_{36}H_{33}N_4O_2S_2Cl$: C, 66.19; H, 5.09; N, 8.57. Found: C, 66.11; H, 5.01; N, 8.48.

**4.3.10. Spiro[4.3′]oxindole-spiro[5.2″]-5″-phenyl-5″,6″,7″,8″,9″,10″,11″-heptahydrocycloocteno[1,2-*d*]thiazolo[3,2-*a*]pyrimidin-3″-one-6-(*p*-bromo)-phenyl-thiapyrrolizidine (9j).** Fluffy white solid (0.620 g, 89%). Mp 204–206 °C. IR (KBr): 3286, 2921, 1719, 1710, 1649, 1595 $cm^{-1}$. $^1$H NMR ($CDCl_3$): $\delta$ 0.91–2.20 (m, 12H, cyclooctyl), 2.72 (dd, 1H, $H_c$, $J_1$=6.8 Hz, $J_2$=9.6 Hz), 2.93 (dd, 1H, $H_d$, $J_1$=5.8 Hz, $J_2$=9.6 Hz), 3.62 (d, 1H, $H_e$, $J$=5.8 Hz), 3.87 (d, 1H, $H_b$, $J$=9.6 Hz), 4.03 (d, 1H, $H_f$, $J$=5.8 Hz), 4.92–4.95 (m, 1H, $H_a$), 5.03 (s, 1H, $H_g$), 6.84–7.50 (m, 13H, Ar-H), 8.91 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$): $\delta$ 25.7, 26.3, 28.3, 29.0, 29.1, 31.1, 32.5, 47.3, 57.0, 58.9, 59.6, 70.0, 74.1, 110.5, 116.3, 122.1, 122.8, 130.5, 130.8, 131.5, 131.8, 131.8, 132.0, 135.2, 137.8, 140.1, 142.4, 150.4, 173.7, 176.7. MS *m/z*: 697.7 ($M^+$). Anal. Calcd for $C_{36}H_{33}N_4O_2S_2Br$: C, 61.97; H, 4.76; N, 8.03. Found: C, 61.91; H, 4.68; N, 7.94.

## Acknowledgements

M.P. thanks Council of Scientific and Industrial Research (CSIR), New Delhi, India for the award of Senior Research Fellowship (SRF). Financial support from DST and DST-FIST, Department of Science and Technology, New Delhi, India is also gratefully acknowledged.

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