Synthesis of some novel spiro heterocycles- Part II

Venkatapuram Padmavathi,* Boggu Jagan Mohan Reddy, Akula Baliah, Adivireddy Padmaja, and Dandu Bhaskar Reddy

Department of Chemistry, Sri Venkateswara University, Tirupati-517 502, India
E-mail: vkpuram2001@yahoo.com

Abstract

A new class of spiro-pyrimidinones, pyrazolidinones and isoxazolidinones are prepared from 4-cyano-4-ethoxycarbonyl-piperidines / tetrahydropyrans / tetrahydrothiopyrans.

Keywords: Spiro-pyrimidinones, spiro-pyrazolidinones, spiro-isoxazolidinones, cyclocondensation

Introduction

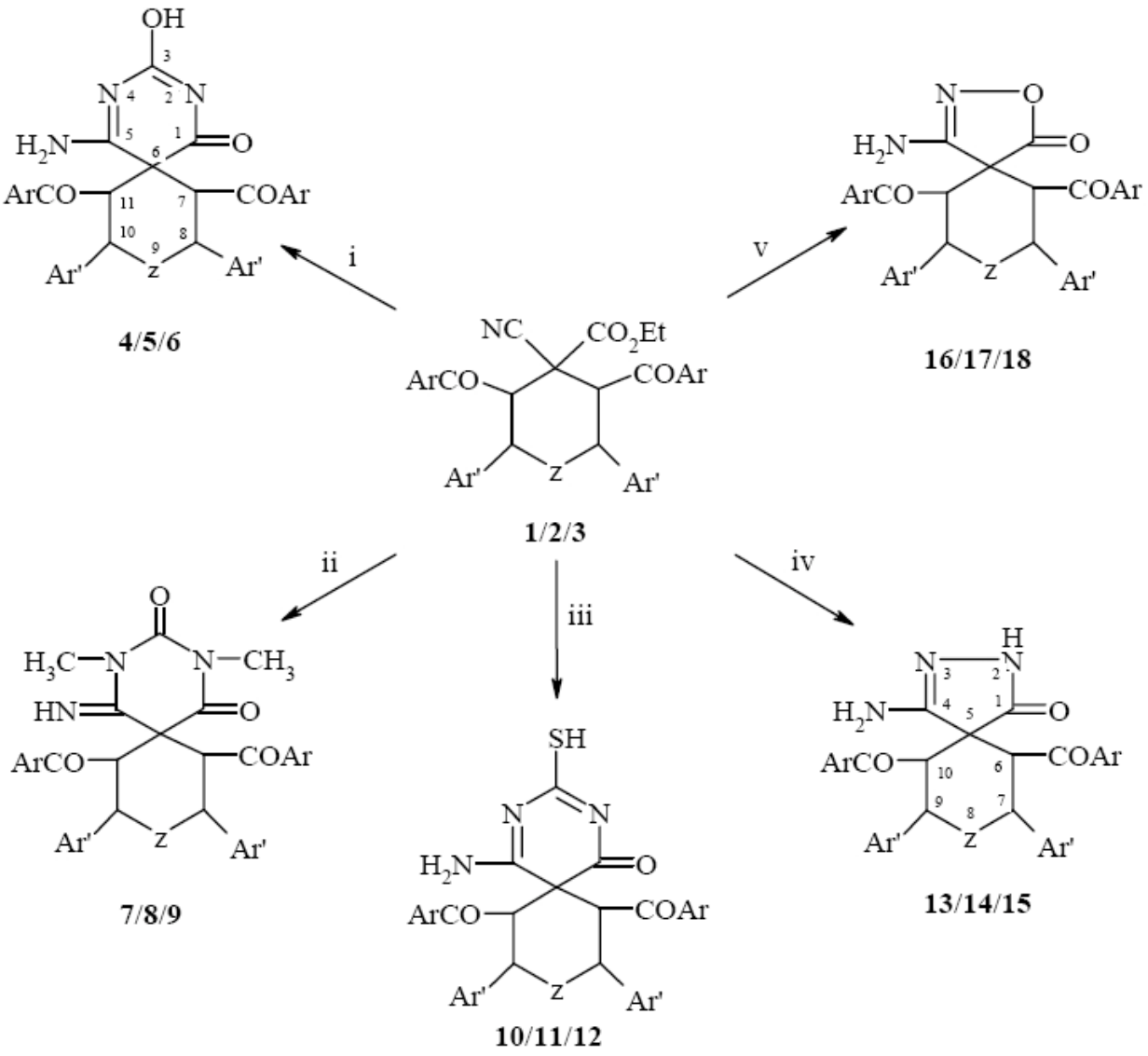
During the last one and half decades we have been actively involved in the synthesis of spiro heterocycles. In fact, a variety of compounds *viz*, spiro-pyrimidinetriones, pyrazolidinediones and isoxazolidinediones have been reported by exploiting the synthetic utility of bis chalcones and bis (styryl) sulfones via double Michael addition followed by reaction with different nucleophiles.[1-6] In continuation of our sustained interest in this field, new, versatile and multifunctional reactive intermediates 3,3-disubstituted 1,5-diaryl-1,5-pentanediones have been reported. These compounds were used as synthons to get a variety of spiro-heterocycles.[7,8] Furthermore, the active methylene group present in these compounds was subjected to Knoevenagel condensation with araldehydes under PTC conditions.[9] Incorporation of heteroatoms in these 3,3-disubstituted 2,4-diaroyl-1,5-diaryl-1,4-pentanedienes resulted 4,4disubstituted 3,5-diaroyl-2,6-diaryl-piperidines / pyrans / thiopyrans.[9] It is well documented that pyrazole, isoxazole, pyrimidine and thioxopyrimidine derivatives were prepared by treating gemdicarboxylates with hydrazine hydrate, hydroxylamine hydrochloride, urea and thiourea.[10-12] Adopting the same methodology, dimethyl 3,5-diaroyl-2,6-diaryl- piperidine / tetrahydropyran / tetrahydrothiopyran-4,4-dicarboxylates were used as synthons for spiro-pyrimidinetriones, thioxopyrimidinediones, pyrazolidinediones and isoxazolidinediones.[13] Encouraged by these results herein we report a new and novel class of spiro heterocycles from 3,5-diaroyl-2,6-diaryl4-cyano-4-ethoxycarbonyl- piperidines / tetrahydropyrans / tetrahydrothiopyrans.

Results and Discussion

The cyclocondensation of 3,5-diaroyl-2,6-diaryl-4-cyano-4-ethoxycarbonyl- piperidines **1**, 3,5diaroyl-2,6-diaryl-4-cyano-4-ethoxycarbonyl-tetrahydropyrans **2**, 3,5-diaroyl-2,6-diaryl-4-cyano4-ethoxycarbonyl-tetrahydrothiopyrans **3** with urea in the presence of NaOMe gave 5-amino7,11-diaroyl-8,10-diaryl-3-hydroxy-2,4,9-triazaspiro[5.5]undeca-2,4-dien-1-ones **4**, 5-amino7,11-diaroyl-8,10-diaryl-3-hydroxy-9-oxa-2,4-diazaspiro [5.5]undeca-2,4-dien-1-ones **5** and 5-amino-7,11-diaroyl-8,10-diaryl-3-hydroxy-9-thia-2,4-diazaspiro[5.5]undeca-2,4-dien-1-ones **6**.

Similar reaction with N,N'-dimethyl urea and thiourea afforded 7,11-diaroyl-8,10-diaryl-2,4dimethyl-5-imino-2,4,9-triaza-spiro[5.5]undecane-1,3-diones **7**, 7,11-diaroyl-8,10-diaryl-2,4dimethyl-5-imino-9-oxa-2,4-diazaspiro[5.5]undecane-1,3-diones **8**, 7,11-diaroyl-8,10-diaryl-2,4dimethyl-5-imino-9-thia-2,4-diazaspiro[5.5]undecane-1,3-diones **9** and 5-amino-7,11-diaroyl8,10-diaryl-3-mercapto-2,4,9-triazaspiro[5.5]undeca-2,4-dien-1-ones **10**, 5-amino-7,11-diaroyl8,10-diaryl-3-mercapto-9-oxa-2,4-diazaspiro[5.5]undeca-2,4-dien-1-ones **11**, 5-amino-7,11diaroyl-8,10-diaryl-3-mercapto-9-thia-2,4-diazaspiro[5.5]undeca-2,4-dien-1-ones **12**, respectively. Likewise, five membered spiro heterocycles, 4-amino-6,10-diaroyl-7,9-diaryl2,3,8-triazaspiro[4.5]deca-3-en-1-ones **13**, 4-amino-6,10-diaroyl-7,9-diaryl-8-oxa-2,3diazaspiro[4.5]deca-3-en-1-ones **14**, 4-amino-6,10-diaroyl-7,9-diaryl-8-thia-2,3diazaspiro[4.5]deca-3-en-1-ones **15** and 4-amino-6,10-diaroyl-7,9-diaryl-2-oxa-3,8diazaspiro[4.5]deca-3-en-1-ones **16**, 4-amino-6,10-diaroyl-7,9-diaryl-2,8-dioxa-3azaspiro[4.5]deca-3-en-1-ones **17**, 4-amino-6,10-diaroyl-7,9-diaryl-2-oxa-8-thia-3-azaspiro[4.5]deca-3-en-1-ones **18** were prepared by refluxing **1/2/3** with hydrazine hydrate and hydroxylamine hydrochloride, respectively (Scheme). The IR spectra of **4-6**, **10-18** displayed an absorption band in the region 3200-3330 cm^{-1}(NH_2). The compounds **4-6** showed an absorption band at 3410-3445 cm^{-1} (OH), while **10-12** a weak absorption band at 2550-2600 cm^{-1} (SH). Apart from these the compounds **4-15** exhibited an absorption band at 1665-1680 cm^{-1} (C=O of pyrimidine / pyrazole ring) while **16-18** at 1740-1750 cm^{-1} (C=O of isoxazole ring). However, all the compounds displayed an absorption band at 1640-1660 cm^{-1} (Ar-CO). In the ^{1}H NMR spectra of these compounds the methine protons displayed doublets at 4.29-5.45 ppm (C<u>H</u>Ar) and 3.73-4.34 ppm (C<u>H</u>COAr). The coupling constants J ~ 9.0 Hz indicates that they possess *trans* geometry. Thus the ^{1}H NMR spectra of **4–18** can be rationalized by presuming that the substituents in piperidine, tetrahydropyran and tetrahydrothiopyran rings are in true *cis*-1,3diequatorial arrangement in their preferred rigid chair conformation.14 The substituted pyrimidinone / pyrazolidinone / isoxazolidinone rings which are nearly planar would be perpendicular to the average plane of the heterocyclic rings (Figure).

All the compounds displayed a broad singlet at 6.69-10.12 (NH_2/NH), while **4-6** at 6.859.20 ppm (OH). The signals due to NH, NH2 and OH disappeared on deuteration. The compounds **7-9** showed a singlet at 2.70-2.75 (N-CH_3), while **10-12** at 1.37-1.42 ppm (SH).
The structures of all these compounds are also confirmed by ^{13}C NMR spectral data.



1,**4**,**7**,**10**,**13**,**16**; Z=NH
2,**5**,**8**,**11**,**14**,**17**; Z=O
3,**6**,**9**,**12**,**15**,**18**; Z=S

	Ar	Ar'
a	Ph	Ph
b	Ph	4-OMe.Ph
c	4-Cl.Ph	Ph

i) NH_2CONH_2 / Na OMe ii) $CH_3NHCONHCH_3$ / Na OMe
iii) NH_2CSNH_2 / Na OMe iv) $NH_2NH_2.H_2O$ / Na OMe v) $NH_2OH.HCl$ / Na OMe

Scheme 1

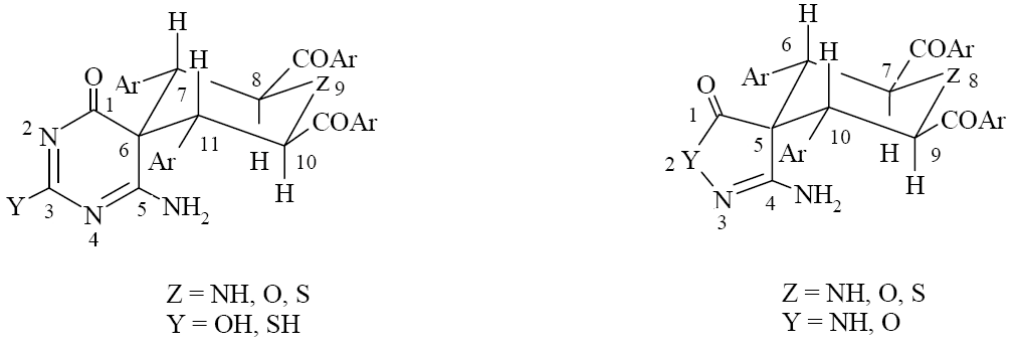


Figure 1

Conclusions

The versatility of olefinic and *gem*-cyano, ester functionalities in **1-3** thus forms the basis for the syntheses of novel spiro heterocycles by simple and well-versed methodology.

Antimicrobial activity

The compounds **4-18** were tested for their antimicrobial activity[15] at three different concentrations (25, 75 & 100 µg / disc). The antifungal activity was screened on *Fusarium solani*, *Curvularia lunata*, and *Aspergillus niger* using Nystatin (25 µg / disc) as a standard drug and the fungal cultures were grown on potato dextrose broth (PDA) at 25^0C for 3 d and finally spore suspension was adjusted to 10^6 spores/ml. All the compounds were also evaluated for antibacterial activity against *Staphylococcus aureus Bacillus subtilis* (Gram positive) and *Escherichia coli* (Gram negative) on nutrient agar plates at 37^0C for 24h using *Gentamycin* (25 µg / disc) as a reference drug. In general they showed more activity against Gram positive than Gram negative bacteria. Besides, they have also moderately inhibited the growth of fungi. Compounds **4, 6, 13** and **15** showed more inhibitory activity against both bacteria and fungi.

Experimental Section

General Procedures. Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 3:1). The IR spectra were recorded on a Perkin-Elmer grating infrared spectrometer, model 337 in KBr pellets. ^{1}H NMR spectra were recorded in $CDCl_3$ using 300 MHz on a Varian EM-360 spectrometer. ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian VXR spectrometer operating at 75.5 MHz. All chemical shifts were reported in ppm from TMS as an internal standard. The elemental analyses were performed at Punjab University, Chandigarh, India. The compounds 3,5-diaroyl-2,6-diaryl-4-cyano-4-ethoxycarbonyl-piperidines **1**, 3,5-diaroyl-2,6-diaryl-4-cyano-4-ethoxy-carbonyl-tetrahydropyrans **2**, 3,5-diaroyl-2,6-diaryl4-

cyano-4-ethoxycarbonyl-tetra-hydrothiopyrans 3 were prepared according to the literature procedure.[9]

5-Amino-7,11-diaroyl-8,10-diaryl-3-hydroxy-2,4,9-triazaspiro[5.5]undeca-2,4-dien-1-ones (4) / 5-amino-7,11-diaroyl-8,10-diaryl-3-hydroxy-9-oxa-2,4-diazaspiro[5.5] undeca-2,4-dien1-ones (5) / 5-amino-7,11-diaroyl-8,10-diaryl-3-hydroxy-9-thia-2,4-diazaspiro[5.5]undeca2,4-dien-1-ones (6). A mixture of **1** / **2** / **3** (0.526 / 0.607 / 0.628 g, 1 mmol), urea (0.090 g, 1.5 mmol), MeOH (20 mL) and 10% NaOMe (5 mL) was refluxed for 6-7 h. The solution was cooled and poured onto crushed ice containing HCl. The solid obtained was filtered, dried and recrystallized from MeOH.

4a. (0.373 g, 67%); mp 261-263°C; *Anal*. Calcd. $C_{34}H_{28}N_4O_4$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.49; H, 5.02; N, 10.17. IR (KBr, cm^{-1}) 3212 & 3264 (NH_2), 3300 (NH), 3420 (OH), 1640 (CO<u>Ar</u>), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.81 (2H, C_7 & C_{11}-H, d, *J* = 9.0 Hz), 4.59 (2H, C_8 & C_{10}-H, d, *J* = 9.0 Hz), 7.05-7.87 (20H, Ar-H, m), 6.69 (2H, bs, NH_2), 6.88 (1H, bs, OH) 10.12 (1H, bs, NH); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ36.3 (C-6), 44.7 (C-7 & C-11), 48.9 (C-8 & C-10), 159.6 (C-3), 164.0 (C-5), 200.7 (C=O), 204.0 (C-1).

4b. (0.382 g, 62%); mp 274-276°C; *Anal*. Calcd. $C_{36}H_{32}N_4O_6$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.22; H, 5.26; N, 9.18. IR (KBr, cm^{-1}) 3220& 3275 (NH_2), 3298 (NH), 3430 (OH), 1645 (CO<u>Ar</u>), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.69 (6H, s, Ar-OCH_3), 3.85 (d, C_7 & C_{11}-H, 2H, *J* = 9.2 Hz), 4.52 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.14-7.83 (18H, m, Ar-H), 6.71 (2H, NH_2, bs), 6.85 (1H, OH, bs), 10.08 (1H, NH, bs); ^{13}C-NMR 36.8 (C-6), 45.2 (C-7 & C-11), 49.0 (C-8 & C-10), 56.0 (OCH_3), 160.0 (C-3), 163.1 (C-5), 201.3 (C=O), 204.9 (C-1).

4c. (0.350 g, 59%); mp 278-280°C; *Anal*. Calcd. $C_{34}H_{26}C_{l2}N_4O_4$: C, 65.29; H, 4.19; N, 8.96. Found: C, 65.36; H, 4.15; N, 8.90. IR (KBr, cm^{-1}) 3222 & 3275 (NH_2), 3304 (NH), 3440 (OH), 1650 (CO<u>Ar</u>), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.86 (2H, C_7 & C_{11}-H, d, *J* = 9.0 Hz), 4.54 (2H, C_8 & C_{10}-H, d, *J* = 9.0 Hz), 7.12-7.81 (18H, Ar-H, m), 6.72 (2H, NH_2, bs), 6.87 (1H, OH, bs), 10.06 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 36.3 (C-6), 45.4 (C-7 & C-11), 49.4 (C-8 & C-10), 159.6 (C-3), 163.2 (C-5), 201.7 (C=O), 204.4 (C-1).

5a. (0.346 g, 68%); mp 290-292°C; *Anal*. Calcd. $C_{34}H_{27}N_3O_5$: C, 73.24; H, 4.88; N, 7.54. Found:C, 73.10; H, 4.82; N, 7.64. IR (KBr, cm^{-1}) 3200 & 3268 (NH_2), 3410 (OH), 1645 (CO<u>Ar</u>), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.90 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 5.43 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.20-7.90 (20H, Ar-H, m), 6.88 (2H, NH_2, bs), 8.34 (1H, OH, bs); ^{13}CNMR (75.5 MHz, $CDCl_3$) δ 37.1 (C-6), 45.5 (C-7 & C-11), 66.1 (C-8 & C-10), 159.2 (C-3), 163.1 (C-5), 201.7 (C=O), 202.6 (C-1).

5b. (0.401 g, 65%); mp 265-267°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_7$: C, 70.06; H, 5.05; N, 6.80.
Found: C, 70.17; H, 5.10; N, 6.89. IR (KBr, cm^{-1}) 3212 & 3278 (NH_2), 3420 (OH), 1640 (CO<u>Ar</u>), 1668 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.68 (6H, Ar-OCH_3, s), 3.85 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 5.40 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.18-7.88 (18H, Ar-H, m), 6.86 (2H, NH_2, bs), 8.32 (1H, OH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 37.4 (C-6), 45.4 (C-7 & C11), 56.0 (OCH_3), 65.6 (C-8 & C-10), 159.4 (C-3), 162.5 (C-5), 201.5 (C=O), 202.6 (C-1).

5c. (0.426 g, 66%); mp 274-276°C; *Anal*. Calcd. $C_{34}H_{25}C_{l2}N_3O_5$: C, 65.18; H, 4.02; N, 6.70. Found: C, 65.27; H, 4.05; N, 6.76. IR (KBr, cm^{-1}) 3215 & 3280 (NH_2), 3445 (OH), 1660 (COAr), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.87 (2H, C_7 & C_{11}-H, d, *J* = 9.4 Hz), 5.42 (2H, C_8 & C_{10}-H, d, *J* = 9.4 Hz), 7.1-7.87 (18H, Ar-H, m), 6.88 (2H, NH_2, bs), 8.24 (1H, OH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 36.5 (C-6), 47.0 (C-7 & C-11), 67.4 (C-8 & C10), 160.1 (C-3), 164.7 (C-5), 200.3 (C=O), 205.5 (C-1).
6a. (0.356 g, 62%); mp 272-274°C; *Anal*. Calcd. $C_{34}H_{27}N_3O_4S$: C, 71.19; H, 4.74; N, 7.32. Found: C, 71.11; H, 4.77; N, 7.28. IR (KBr, cm^{-1}) 3235 & 3300 (NH_2), 3415 (OH), 1640 (COAr), 1672 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.01 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 4.29 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 6.69 (2H, NH_2, bs), 7.08-7.90 (20H, Ar-H, m), 9.20 (1H, OH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 32.2 (C-8 & C-10), 38.2 (C-6), 45.9 (C-7 & C11), 161.9 (C-3), 162.7 (C-5), 201.1 (C=O), 203.6 (C-1).
6b. (0.374 g, 59%); mp 278-280°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_6S$: C, 68.23; H, 4.93; N, 6.63. Found: C, 68.12; H, 4.90; N, 6.70. IR (KBr, cm^{-1}) 3240 & 3305 (NH_2), 3420 (OH), 1645 (COAr), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.73 (6H, Ar-OCH_3, s), 4.04 (2H, C_7 & C_{11}-H, d, *J* = 9.5 Hz), 4.32 (2H, C_8 & C_{10}-H, d, *J* = 9.5 Hz), 6.73 (2H, NH_2, bs), 7.09-7.89 (18H, Ar-H, m), 9.16 (1H, OH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 30.8 (C-8 & C-10), 37.8 (C6), 45.2 (C-7 & C-11), 57.9 (OCH_3), 160.5 (C-3), 164.5 (C-5), 199.3 (C=O), 204.1 (C-1).
6c. (0.418 g, 65%); mp 262-264°C; *Anal*. Calcd. $C_{34}H_{25}C_{l2}N_3O_4S$: C, 63.55; H, 3.92; N, 6.54. Found: C, 63.61; H, 3.89; N, 6.50. IR (KBr, cm^{-1}) 3235 & 3310 (NH_2), 3440 (OH), 1655 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.07 (2H, C_7 & C_{11}-H, d, *J* = 9.3 Hz), 4.34 (2H, C_8 & C_{10}-H, d, *J* = 9.3 Hz), 6.70 (2H, NH_2, bs), 7.10-7.90 (18H, Ar-H, m), 9.14 (1H, OH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 30.4 (C-8 & C-10), 36.7 (C-6), 45.8 (C-7 & C11), 162.0 (C-3), 164.9 (C-5), 197.9 (C=O), 204.2 (C-1).

7,11-Diaroyl-8,10-diaryl-2,4-dimethyl-5-imino-2,4,9-triazaspiro[5.5]undecane-1,3-diones (7) / 7,11-diaroyl-8,10-diaryl-2,4-dimethyl-5-imino-9-oxa-2,4-diazaspiro[5.5] undecane-1,3diones (8) / 7,11-diaroyl-8,10-diaryl-2,4-dimethyl-5-imino-9-thia-2,4diazaspiro[5.5]undecane-1,3-diones (9). The compound **1** / **2** / **3** (0.526 / 0.607 / 0.628 g, 1 mmol), N,N'-dimethyl urea (0.089 g, 1 mmol), 10 % NaOMe (5 mL) in dry MeOH (20 mL) was refluxed for 9-13 h. Then, it was cooled and poured onto crushed ice containing conc. HCl. The separated solid was collected by filtration, dried and recrystallized from MeOH.
7a. (0.362 g, 62%); mp 266-268°C; *Anal*. Calcd. $C_{36}H_{32}N_4O_4$: C, 73.95; H, 5.51; N, 9.58. Found: C, 73.86; H, 5.50; N, 9.65. IR (KBr, cm^{-1}) 3305 (NH), 1650 (COAr), 1672 (CO at 1/1,3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.71 (6H, N-CH_3, s), 3.81 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 4.30 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.08-7.89 (20H, Ar-H, m), 9.24 (2H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 28.2 & 29.4 (N-CH_3), 34.3 (C-6), 42.7 (C-7 & C-11), 44.6 (C-8 & C-10), 158.0 (C-3), 164.0 (C-5), 176.8 (C-1), 200.7 (C=O).
7b. (0.387 g, 60%); mp 258-260°C; *Anal*. Calcd. $C_{38}H_{36}N_4O_6$: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.72; H, 5.58; N, 8.79. IR (KBr, cm^{-1}) 3312 (NH), 1645 (COAr), 1672 (CO at 1/1,3); ^{1}H-

NMR (300 MHz, $CDCl_3$) δ 2.70 (6H, NCH_3, s), 3.74 (6H, Ar-OCH_3, s), 3.83 (2H, C_7 & C_{11}-H, d, *J* = 9.4 Hz), 4.32 (2H, C_8 & C_{10}-H, d, *J* = 9.4 Hz), 7.15-7.89 (18H, Ar-H, m), 9.26 (2H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 29.7 & 28.2 (N-CH_3), 33.4 (C-6), 41.9 (C-7 & C-11), 45.0 (C-8 & C-10), 56.0 (OCH_3), 160.1 (C-3), 163.1 (C-5), 174.1 (C-1), 202.1 (C=O).

7c. (0.431 g, 66%); mp 264-266°C; *Anal*. Calcd. $C_{36}H_{30}Cl_2N_4O_4$: C, 66.16; H, 4.63; N, 8.57. Found: C, 66.08; H, 4.67; N, 8.63. IR (KBr, cm^{-1}) 3308 (NH), 1640 (COAr), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.72 (6H, N-CH_3, s), 3.82 (2H, C_7 & C_{11}-H, d, *J* = 9.3 Hz), 4.35 (2H, C_8 & C_{10}-H, d, *J* = 9.3 Hz), 7.16-7.91 (18H, Ar-H, m), 9.28 (2H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 28.9 & 28.8 (N-CH_3), 33.1 (C-6), 42.5 (C-7 & C-11), 45.4 (C-8 & C-10), 161.5 (C-3), 164.4 (C-5), 176.4 (C-1), 204.1 (C=O).

8a. (0.340 g, 58%); mp 189-191°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_5$: C, 73.83; H, 5.34; N, 7.17. Found: C, 73.93; H, 5.37; N, 7.12. IR (KBr, cm^{-1}) 3298 (NH), 1660 (COAr), 1668 (CO at 1/1,3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (6H, N-CH_3, s), 3.93 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 5.44 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.20-7.90 (20H, Ar-H, m), 9.19 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 29.9 & 28.5 (N-CH_3), 33.5 (C-6), 41.3 (C-7 & C-11), 65.9 (C-8 & C-10), 157.4 (C-3), 162.3 (C-5), 175.0 (C-1), 203.1 (C=O).

8b. (0.420 g, 64%); mp 200-202°C; *Anal*. Calcd. $C_{38}H_{35}N_3O_7$: C, 70.68; H, 5.46; N, 6.51. Found: C, 70.75; H, 5.42; N, 6.60. IR (KBr, cm^{-1}) 3286 (NH), 1650 (COAr), 1670 (CO at 1/1,3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.71 (6H, N-CH_3, s), 3.74 (6H, Ar-OCH_3, s), 3.92 (2H, C_7 & C_{11}-H, d, *J* = 9.4 Hz), 5.42 (2H, C_8 & C_{10}-H, d, *J* = 9.4 Hz), 7.18-7.90 (18H, Ar-H, m), 9.20 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 29.3 & 26.8 (N-CH_3), 34.3 (C-6), 42.1 (C-7 & C-11), 56.0 (OCH_3), 65.6 (C-8 & C-10), 156.7 (C-3), 163.3 (C-5), 175.4 (C-1), 205.3 (C=O).

8c. (0.410 g, 65%); mp 215-217°C; *Anal*. Calcd. $C_{36}H_{29}Cl_2N_3O_5$: C, 66.06; H, 4.47; N, 6.42. Found: C, 66.16; H, 4.45; N, 6.34. IR (KBr, cm^{-1}) 3304 (NH), 1640 (COAr), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.72 (6H, N-CH_3, s), 3.97 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 5.44 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.12-7.86 (18H, Ar-H, m), 9.23 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 29.3 & 28.0 (N-CH_3), 32.1 (C-6), 40.5 (C-7 & C-11), 66.7 (C-8 & C-10), 156.0 (C-3), 161.9 (C-5), 177.5 (C-1), 202.4 (C=O).

9a. (0.391 g, 65%); mp 255-257°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_4S$: C, 71.86; H, 5.19; N, 6.98. Found: C, 71.98; H, 5.13; N, 7.06. IR (KBr, cm^{-1}) 3306 (NH), 1645 (COAr), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.75 (6H, N-CH_3, s), 3.98 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 4.32 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.12-7.89 (20H, Ar-H, m), 9.09 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 28.1 & 29.7 (N-CH_3), 33.8 (C-8 & C-10), 36.5 (C-6), 43.5 (C-7 & C-11), 158.0 (C-3), 164.9 (C-5), 176.0 (C-1), 201.1 (C=O).

9b. (0.463 g, 70%); mp 283-285°C; *Anal*. Calcd. $C_{38}H_{35}N_3O_6S$: C, 68.97; H, 5.33; N, 6.35. Found: C, 69.06; H, 5.35; N, 6.30. IR (KBr, cm^{-1}) 3296 (NH), 1650 (COAr), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.72 (6H, N-CH_3, s), 3.77 (6H, Ar-OCH_3, s), 4.06 (2H, C_7 & C_{11}-H, d, *J* = 9.0 Hz), 4.32 (2H, C_8 & C_{10}-H, d, *J* = 9.0 Hz), 7.02-7.83 (18H, Ar-H, m), 9.24 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 28.9 & 29.2 (N-CH_3), 32.2 (C-8 & C-10), 35.8 (C-6), 42.9 (C-7 & C-11), 55.9 (OCH_3), 156.6 (C-3), 163.1 (C-5), 176.5 (C-1), 202.1 (C=O).

9c. (0.590 g, 68%); mp 295-297°C; *Anal*. Calcd. $C_{36}H_{29}C_{l2}N_3O_4S$: C, 64.48; H, 4.36; N, 6.27. Found: C, 64.42; H, 4.40; N, 6.37. IR (KBr, cm^{-1}) 3298 (NH), 1660 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.74 (6H, N-CH_3, s), 4.08 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 4.33 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.10-7.85 (18H, Ar-H, m), 9.28 (1H, NH, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 27.8 & 29.2 (N-CH_3), 34.7 (C-8 & C-10), 35.6 (C-6), 43.5 (C-7 & C-11), 154.7 (C-3), 163.6 (C-5), 174.8 (C-1), 202.5 (C=O).

5-Amino-7,11-diaroyl-8,10-diaryl-3-mercapto-2,4,9-triazaspiro[5.5]undeca-2,4-dien-1-ones (10) / 5-amino-7,11-diaroyl-8,10-diaryl-3-mercapto-9-oxa-2,4-diazaspiro[5.5] undeca-2,4dien-1-ones (11) / 5-amino-7,11-diaroyl-8,10-diaryl-3-mercapto-9-thia-2,4diazaspiro[5.5]undeca-2,4-dien-1-ones (12). A mixture of **1** / **2** / **3** (0.526 / 0.607 / 0.628 g, 1 mmol), thiourea (0.074 g, 1 mmol), MeOH (20 mL) and 10% NaOMe (5 mL) was refluxed for 11-13 h. The solution was cooled and poured onto crushed ice containing HCl. The solid obtained was filtered, dried and recrystallized from MeOH.

10a. (0.349 g, 61%); mp 208-210°C; *Anal*. Calcd. $C_{34}H_{28}N_4O_3S$: C, 71.31; H, 4.93; N, 9.78. Found: C, 71.25; H, 4.99; N, 9.70. IR (KBr, cm^{-1}) 3210 & 3275 (NH_2), 3312 (NH), 1640 (COAr), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.38 (1H, SH, s), 3.84 (2H, C_7 & C_{11}-H, d, *J* = 9.4 Hz), 4.57 (2H, C_8 & C_{10}-H, d, *J* = 9.4 Hz), 7.06-7.87 (20H, Ar-H, m), 9.23 (3H, NH, NH2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 35.1 (C-6), 42.6 (C-7 & C-11), 43.1 (C-8 & C10), 162.8 (C-3), 163.1 (C-5), 200.7 (C=O), 204.1 (C-1).

10b. (0.405 g, 64%); mp 198-200°C; *Anal*. Calcd. $C_{36}H_{32}N_4O_5S$: C, 68.34; H, 5.10; N, 8.85. Found: C, 68.43; H, 5.05; N, 8.92. IR (KBr, cm^{-1}) 3220 & 3268 (NH_2), 3300 (NH), 1645 (COAr), 1672 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.36 (1H, SH, s), 3.67 (6H, Ar-OCH_3, s), 3.82 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 4.55 (d, 2H, C_8 & C_{10}-H, *J* = 9.2 Hz), 7.05-7.88 (m, 18H, Ar-H), 9.25 (bs, 3H, NH, NH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 35.4 (C-6), 41.2 (C-7 & C-11), 43.6 (C-8 & C-10), 54.5 (OCH_3), 163.8 (C-3), 164.3 (C-5), 200.5 (C=O), 205.4 (C-1).

10c. (0.366 g, 57%); mp 226-228°C; *Anal*. Calcd. $C_{34}H_{26}C_{l2}N_4O_3S$: C, 63.65; H, 4.08; N, 8.73. Found: C, 63.58; H, 5.00; N, 8.69. IR (KBr, cm^{-1}) 3222 & 3270 (NH_2), 3315 (NH), 1650 (COAr), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.40 (1H, SH, s), 3.86 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 4.52 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.02-7.82 (18H, Ar-H, m), 9.27 (3H, NH, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 34.5 (C-6), 43.2 (C-7 & C-11), 43.9 (C-8 & C10), 164.7 (C-3), 165.3 (C-5), 202.0 (C=O), 203.5 (C-1).

11a. (0.356 g, 62%); mp 202-204°C; *Anal*. Calcd. $C_{34}H_{27}N_3O_4S$: C, 71.19; H, 4.74; N, 7.32. Found: C, 71.34; H, 4.70; N, 7.40. IR (KBr, cm^{-1}) 3255 & 3320 (NH_2), 1655 (COAr), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.39 (1H, SH, s), 3.75 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 5.42 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.19-7.91 (20H, Ar-H, m), 9.44 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 34.0 (C-6), 41.4 (C-7 & C-11), 65.8 (C-8 & C-10), 163.1 (C-3), 164.9 (C5), 201.0 (C=O), 203.7 (C-1).

11b. (0.400 g, 63%); mp 199-201°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_6S$: C, 68.23; H, 4.93; N, 6.63. Found: C, 68.33; H, 4.90; N, 6.70. IR (KBr, cm^{-1}) 3265 & 3325 (NH_2), 1640 (COAr), 1674 (CO

at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.37 (1H, SH, s), 3.69 (6H, Ar-OCH_3, s,), 3.73 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 5.45 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.15-7.69 (18H, Ar-H, m), 9.41 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 33.2 (C-6), 41.8 (C-7 & C-11), 57.7 (OCH_3), 66.0 (C-8 & C-10), 162.9 (C-3), 164.1 (C-5), 200.6 (C=O), 203.1 (C-1).

11c. (0.424 g, 66%); mp 216-218°C; *Anal*. Calcd. $C_{34}H_{25}C_{l2}N_3O_4S$: C, 63.55; H, 3.92; N, 6.54. Found: C, 63.50; H, 3.94; N, 6.60. IR (KBr, cm^{-1}) 3260 & 3330 (NH_2), 1660 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.36 (1H, SH, s), 3.72 (2H, C_7 & C_{11}-H, d, *J* = 9.2 Hz), 5.42 (2H, C_8 & C_{10}-H, d, *J* = 9.2 Hz), 7.12-7.69 (18H, Ar-H, m), 9.42 (2H, NH_2, bs); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 32.2 (C-6), 41.5 (C-7 & C-11), 65.8 (C-8 & C-10), 163.3 (C-3), 164.6(C-5), 201.4(C=O), 203.6(C-1).

12a. (0.360 g, 61%); mp 243-245°C; *Anal*. Calcd. $C_{34}H_{27}N_3O_3S_2$: C, 69.25; H, 4.61; N, 7.13. Found: C, 69.15; H, 4.58; N, 7.26. IR (KBr, cm^{-1}) 3250 & 3315 (NH_2), 1650 (COAr), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.41 (1H, SH, s), 4.01 (2H, C_7 & C_{11}-H, d, *J* = 9.3 Hz), 4.33 (2H, C_8 & C_{10}-H, d, *J* = 9.3 Hz), 7.06-7.88 (20H, Ar-H, m), 9.38 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 31.5 (C-8 & C-10), 36.4 (C-6), 42.8 (C-7 & C-11), 164.3 (C-3), 165.4 (C5), 201.2 (C=O), 204.1 (C-1).

12b. (0.448 g, 64%); mp 188-190°C; *Anal*. Calcd. $C_{36}H_{31}N_3O_5S_2$: C, 66.54; H, 4.81; N, 6.47. Found: C, 66.62; H, 4.85; N, 6.40. IR (KBr, cm^{-1}) 3240 & 3305 (NH_2), 1655 (COAr), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.40 (1H, SH, s), 3.69 (6H, Ar-OCH_3, s), 4.04 (2H, C_7 & C_{11}-H, d, *J* = 9.1 Hz), 4.32 (2H, C_8 & C_{10}-H, d, *J* = 9.1 Hz), 7.04-7.86 (18H, Ar-H, m), 9.35 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 32.1 (C-8 & C-10), 36.7 (C-6), 43.2 (C-7 & C-11), 55.9 (OCH_3), 162.3 (C-3), 166.4 (C-5), 200.2 (C=O), 202.4 (C-1).

12c. (0.425 g, 69%); mp 233-235°C; *Anal*. Calcd. $C_{34}H_{25}C_{l2}N_3O_3S_2$: C, 62.00; H, 3.83; N, 6.38. Found: C, 61.95; H, 3.85; N, 6.46. IR (KBr, cm^{-1}) 3242 & 3300 (NH2), 1655 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.38 (1H, SH, s), 4.05 (2H, C_7 & C_{11}-H, d, *J* = 9.0 Hz), 4.34 (2H, C_8 & C_{10}-H, d, *J* = 9.0 Hz), 7.15-7.91 (18H, Ar-H, m), 9.33 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 33.6 (C-8 & C-10), 35.9 (C-6), 41.3 (C-7 & C-11), 162.0 (C-3), 164.1 (C-5), 200.0 (C=O), 203.5 (C1).

4-Amino-6,10-diaroyl-7,9-diaryl-2,3,8-triazaspiro[4.5]deca-3-en-1-ones (13) / 4-amino6,10-diaroyl-7,9-diaryl-8-oxa-2,3-diazaspiro[4.5]deca-3-en-1-ones (14) / 4-amino-6,10diaroyl-7,9-diaryl-8-thia-2,3-diazaspiro[4.5]deca-3-en-1-ones (15). To a solution of **1** / **2** / **3** (0.526 / 0.607 / 0.628 g, 1 mmol) in MeOH (20 mL), 80% hydrazine hydrate (0.075 g, 1.5 mmol) and 10% NaOMe (5 mL) were added and refluxed for 4-5 h. The contents were cooled and poured onto crushed ice containing HCl. The separated solid was filtered, dried and recrystallized from 2-propanol.

13a. (0.317 g, 60%); mp 205-207°C; *Anal*. Calcd. $C_{33}H_{28}N_4O_3$: C, 74.98; H, 5.34; N, 10.60. Found: C, 74.90; H, 5.28; N, 10.69. IR (KBr, cm^{-1}) 3220 & 3280 (NH_2), 3340 (br, NH), 1640 (COAr), 1660 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.80 (2H, C_6 & C_{10}-H, d, *J* = 9.1 Hz), 4.58 (2H, C_7 & C_9-H, d, *J* = 9.1 Hz), 7.06-7.83 (20H, Ar-H, m), 9.26 (4H, 2NH, NH_2, bs);

^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 42.4 (C-6 & C-10), 43.9 (C-5), 44.6 (C-7 & C-9), 155.0 (C-4), 182.1 (C-1), 201.0 (C=O).

13b. (0.365 g, 62%); mp 198-199°C; *Anal*. Calcd. $C_{35}H_{32}N_4O_5$: C, 71.41; H, 5.48; N, 9.52. Found: C, 71.52; H, 5.52; N, 9.60. IR (KBr, cm^{-1}) 3225 & 3275 (NH_2), 3345 (br, NH), 1650 (COAr), 1665 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.68 (6H, Ar-OCH_3, s), 3.82 (2H, C_6 & C_{10}-H, d, *J* = 9.3 Hz), 4.54 (2H, C_7 & C_9-H, d, *J* = 9.3 Hz), 7.02-7.85 (18H, Ar-H, m), 9.28 (4H, 2NH, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 43.4 (C-6 & C-10), 44.3 (C-5), 46.6 (C-7 & C-9), 55.9 (OCH_3), 156.0 (C-4), 182.5 (C-1), 205.0 (C=O).

13c. (0.388 g, 65%); mp 215-217°C; *Anal*. Calcd. $C_{33}H_{26}C_{l2}N_4O_3$: C, 66.34; H, 4.39; N, 9.38. Found: C, 66.43; H, 4.36; N, 9.44. IR (KBr, cm^{-1}) 3218 & 3280 (NH_2), 3343 (NH), 1640 (COAr), 1670 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.86 (2H, C_6 & C_{10}-H, d, *J* = 9.4 Hz), 4.53 (2H, C_7 & C_9-H, d, *J* = 9.4 Hz), 7.08-7.91 (18H, Ar-H, m), 9.23 (4H, 2NH, NH_2, bs);^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 41.5 (C-6 & C-10), 44.3 (C-5), 46.2 (C-7 & C-9), 154.4 (C-4),181.2 (C-1), 202.5 (C=O).

14a. (0.339 g, 64%); mp 188-190°C; *Anal*. Calcd. $C_{33}H_{27}N_3O_4$: C, 74.84; H, 5.14; N, 7.93. Found: C, 74.92; H, 5.07; N, 7.88. IR (KBr, cm^{-1}) 3230 & 3285 (NH_2), 1645 (COAr), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.92 (2H, C_6 & C_{10}-H, d, *J* = 9.1 Hz), 5.45 (2H, C_7 & C_9-H, d, *J* = 9.1 Hz), 7.19-7.92 (20H, Ar-H & 3H, NH, NH_2, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) d41.8 (C-6 & C-10), 44.0 (C-5), 66.5 (C-7 & C-9), 153.5 (C-4), 181.8 (C-1), 203.9 (C=O).

14b. (0.389 g, 66%); mp 177-178°C; *Anal*. Calcd. $C_{35}H_{31}N_3O_6$: C, 71.29; H, 5.30; N, 7.13. Found: C, 71.20; H, 5.33; N, 7.23. IR (KBr, cm^{-1}) 3224 & 3292 (NH_2), 1640 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.74 (6H, Ar-OCH_3, s), 3.95 (2H, C_6 & C_{10}-H, d, *J* = 9.4 Hz), 5.42 (2H, C_7 & C_9-H, d, *J* = 9.4 Hz), 7.09-7.95 (18H, Ar-H & 3H, NH, NH_2, m); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 42.6 (C-6 & C-10), 43.9 (C-5), 55.2 (OCH_3), 64.8 (C-7 & C-9), 154.3 (C-4), 183.4 (C-1), 201.5 (C=O).

14c. (0.353 g, 59%); mp 194-196°C; *Anal*. Calcd. $C_{33}H_{25}C_{l2}N_3O_4$: C, 66.23; H, 4.21; N, 7.02. Found: C, 66.63; H, 4.25; N, 6.95. IR (KBr, cm^{-1}) 3228 & 3290 (NH_2), 1660 (COAr), 1675 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.92 (2H, C_6 & C_{10}-H, d, *J* = 9.1 Hz), 5.40 (2H, C_7 & C_9-H, d, *J* = 9.1 Hz), 7.10-7.96 (18H, Ar-H & 3H, NH, NH_2, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) d42.4 (C-6 & C-10), 45.9 (C-5), 63.4 (C-7 & C-9), 153.6 (C-4), 181.4 (C-1), 202.5 (C=O).

15a. (0.371 g, 68%); mp 185-187°C; *Anal*. Calcd. $C_{33}H_{27}N_3O_3S$: C, 72.64; H, 4.99; N, 7.70. Found: C, 72.70; H, 5.05; N, 7.78. IR (KBr, cm^{-1}) 3225 & 3295 (NH_2), 1640 (COAr), 1668 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.03 (2H, C_6 & C_{10}-H, d, *J* = 9.2 Hz), 4.33 (2H, C_7 & C_9-H, d, *J* = 9.2 Hz), 7.12-7.89 (20H, Ar-H & 3H, NH, NH_2, m,); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 30.6 (C-7 & C-9), 42.5 (C-6 & C-10), 44.1 (C-5), 153.7 (C-4), 180.5 (C-1), 202.3 (C=O).

15b. (0.367 g, 64%); mp 196-197°C; *Anal*. Calcd. $C_{35}H_{31}N_3O_5S$: C, 69.40; H, 5.16; N, 6.94. Found: C, 69.47; H, 5.14; N, 7.02. IR (KBr, cm^{-1}) 3230 & 3292 (NH_2), 1645 (COAr), 1676 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.72 (6H, Ar-OCH_3, s), 4.01 (2H, C_6 & C_{10}-H, d, *J* = 9.4 Hz), 4.32 (2H, C_7 & C_9-H, d, *J* = 9.4 Hz), 7.04-7.86 (18H, Ar-H & 3H, NH, NH_2, m); ^{13}C-NMR

(75.5 MHz, $CDCl_3$) δ 30.2 (C-7 & C-9), 41.9 (C-6 & C-10), 44.5 (C-5), 55.2 (OCH_3), 53.4 (C-4), 178.5 (C-1), 204.3 (C=O).

15c. (0.411 g, 67%); mp 169-171°C; *Anal*. Calcd. $C_{33}H_{25}C_{l2}N_3O_3S$: C, 64.50; H, 4.10; N, 6.84. Found: C, 64.45; H, 4.14; N, 7.00. IR (KBr, cm^{-1}) 3230 & 3295 (NH_2), 1660 (COAr), 1680 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.03 (2H, C_6 & C_{10}-H, d, *J* = 9.0 Hz), 4.29 (2H, C_7 & C_9-H, d, *J* = 9.0 Hz), 7.09-7.92 (18H, Ar-H & 3H, NH, NH_2, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) d31.1 (C-7 & C-9), 42.0 (C-6 & C-10), 43.7 (C-5), 154.9 (C-4), 182.5 (C-1), 201.8 (C=O).

4-Amino-6,10-diaroyl-7,9-diaryl-2-oxa-3,8-diazaspiro[4.5]deca-3-en-1-ones (16) / 4-amino6,10-diaroyl-7,9-diaryl-2,8-dioxa-3-azaspiro[4.5]deca-3-en-1-ones (17) / 4-amino-6,10diaroyl-7,9-diaryl-2-oxa-8-thia-3-azaspiro[4.5]deca-3-en-1-ones (18). A mixture of **1** / **2** / **3** (0.526 / 0.607 / 0.628 g, 1 mmol), hydroxylamine hydrochloride (0.0695 g, 1.5 mmol), MeOH (20 mL) and 10% NaOMe (5 mL) was refluxed for 4-5 h. It was cooled and poured onto crushed ice containing HCl. The solid obtained was filtered, dried and recrystallized from 2-propanol.

16a. (0.318 g, 60%); mp 196-198°C; *Anal*. Calcd. $C_{33}H_{27}N_3O_4$: C, 74.84; H, 5.14; N, 7.93. Found: C, 74.97; H, 5.09; N, 8.00. IR (KBr, cm^{-1}) 3214 & 3268 (NH_2), 3350 (NH), 1640 (COAr), 1740 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.82 (2H, C_6 & C_{10}-H, d, *J* = 9.0 Hz), 4.53 (2H, C_7 & C_9-H, d, *J* = 9.0 Hz), 7.12-7.79 (20H, Ar-H, m), 9.81 (3H, NH, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 36.6 (C-6 & C-10), 44.7 (C-7 & C-9), 49.5 (C-5), 163.4 (C-4), 181.0 (C-1), 203.2 (C=O).

16b. (0.336 g, 57%); mp 198-200°C; *Anal*. Calcd. $C_{35}H_{31}N_3O_6$: C, 71.29; H, 5.30; N, 7.13. Found: C, 71.21; H, 5.36; N, 7.20. IR (KBr, cm^{-1}) 3222 & 3275 (NH_2), 3347 (NH), 1645 (COAr), 1745 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.69 (6H, Ar-OCH_3, s), 3.83 (2H, C_6 & C_{10}-H, d, *J* = 9.3 Hz), 4.52 (2H, C_7 & C_9-H, d, *J* = 9.3 Hz), 7.08-7.79 (18H, Ar-H, m), 9.87 (3H, NH, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 37.8 (C-6 & C-10), 45.0 (C-7 & C-9), 48.2 (C-5), 55.8 (OCH_3), 162.1 (C-4), 182. 6 (C-1), 201.6 (C=O).

16c. (0.395 g, 66%); mp 175-176°C; *Anal*. Calcd. $C_{33}H_{25}C_{l2}N_3O_4$: C, 66.23; H, 4.21; N, 7.02. Found: C, 66.33; H, 4.18; N, 7.08. IR (KBr, cm^{-1}) 3218 & 3272 (NH_2), 3352 (NH), 1660 (COAr), 1750 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.87 (2H, C_6 & C_{10}-H, d, *J* = 9.4 Hz), 4.55 (2H, C_7 & C_9-H, d, *J* = 9.4 Hz), 7.16-7.81 (18H, Ar-H, m), 9.88 (3H, NH, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 37.4 (C-6 & C-10), 44.5 (C-7 & C-9), 47.8 (C-5), 163.2 (C-4),181.7 (C-1), 200.5 (C=O).

17a. (0.355 g, 65%); mp 205-206°C; *Anal*. Calcd. $C_{33}H_{26}N_2O_5$: C, 74.70; H, 4.94; N, 5.28. Found: C, 74.60; H, 4.90; N, 5.22. IR (KBr, cm^{-1}) 3235 & 3300 (NH_2), 1650 (COAr), 1744 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.27 (2H, C_6 & C_{10}-H, d, *J* = 9.2 Hz), 5.36 (2H, C_7 & C_9-H, d, *J* = 9.2 Hz), 7.19-7.83 (20H, Ar-H, m), 9.28 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 36.6 (C-6 & C-10), 48.4 (C-5), 65.2 (C-7 & C-9), 162.9 (C-4), 179.6 (C-1), 201.6 (C=O).

17b. (0.402 g, 68%); mp 221-223°C; *Anal*. Calcd. $C_{35}H_{30}N_2O_7$: C, 71.18; H, 5.12; N, 4.74. Found: C, 71.26; H, 5.10; N, 4.80. IR (KBr, cm^{-1}) 3232 & 3298 (NH_2), 1640 (COAr), 1748 (CO

at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.68 (6H, Ar-OCH_3, s), 4.25 (2H, C_6 & C_{10}-H, d, *J* = 9.1 Hz), 5.37 (2H, C_7 & C_9-H, d, *J* = 9.1 Hz), 7.03-7.80 (18H, Ar-H, m), 9.25 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 37.5 (C-6 & C-10), 47.8 (C-5), 55.8 (OCH_3), 65.4 (C-7 & C-9), 163.2 (C-4), 178.6 (C-1), 202.2 (C=O).

17c. (0.372 g, 62%); mp 214-216°C; *Anal*. Calcd. $C_{33}H_{24}C_{l2}N_2O_5$: C, 66.12; H, 4.04; N, 4.67. Found: C, 66.20; H, 4.08; N, 4.72. IR (KBr, cm^{-1}) 3235 & 3302 (NH_2), 1655 (COAr), 1750 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.34 (d, 2H, C_6 & C_{10}-H, *J* = 9.2 Hz), 5.42 (d, 2H, C_7 & C_9-H, *J* = 9.2 Hz), 7.13-7.79 (m, 18H, Ar-H), 9.32 (bs, 2H, NH_2); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 37.9 (C-6 & C-10), 48.4 (C-5), 66.4 (C-7 & C-9), 162.9 (C-4), 179.6 (C-1), 201.6 (C=O).

18a. (0.328 g, 60%); mp 182-184°C; *Anal*. Calcd. $C_{33}H_{26}N_2O_4S$: C, 72.51; H, 4.79; N, 5.12. Found: C, 72.64; H, 4.83; N, 5.24. IR (KBr, cm^{-1}) 3230 & 3304 (NH_2), 1645 (COAr), 1746 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.04 (2H, C_6 & C_{10}-H, d, *J* = 9.4 Hz), 4.33 (2H, C_7 & C_9-H, d, *J* = 9.4 Hz), 7.08-7.87 (20H, Ar-H, m), 9.29 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 31.3 (C-7 & C-9), 36.5 (C-6 & C-10), 49.1 (C-5), 162.9 (C-4), 179.6 (C-1), 203.8 (C=O).

18b. (0.376 g, 62%); mp 196-197°C; *Anal*. Calcd. $C_{35}H_{30}N_2O_6S$: C, 69.29; H, 4.98; N, 4.62. Found: C, 69.30; H, 4.95; N, 4.68. IR (KBr, cm^{-1}) 3231 & 3300 (NH_2), 1650 (COAr), 1742 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.78 (6H, Ar-OCH_3, s), 4.04 (2H, C_6 & C_{10}-H, d, *J* = 9.2 Hz), 4.35 (2H, C_7 & C_9-H, d, *J* = 9.2 Hz), 7.06-7.79 (18H, Ar-H, m), 9.32 (2H, NH_2, bs); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 32.1 (C-7 & C-9), 37.2 (C-6 & C-10), 50.4 (C-5), 56.8 (OCH_3), 163.3 (C-4), 180.2 (C-1), 201.5 (C=O).

18c. (0.400 g, 65%); mp 168-170°C; *Anal*. Calcd. $C_{33}H_{24}C_{l2}N_2O_4S$: C, 64.39; H, 3.93; N, 4.55. Found: C, 64.32; H, 3.97; N, 4.60. IR (KBr, cm^{-1}) 3236 & 3307 (NH_2), 1660 (COAr), 1745 (CO at 1/1,3); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.06 (2H, C_6 & C_{10}-H, d, *J* = 9.1 Hz), 4.38 (2H, C_7 & C_9-H, d, *J* = 9.1 Hz), 7.16-7.81 (18H, Ar-H, m), 9.30 (2H, NH_2, bs); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 32.4 (C-7 & C-9), 38.3 (C-6 & C-10), 50.8 (C-5), 164.8 (C-4), 182.7 (C-1), 202.5 (C=O).

Acknowledgements

The authors are thankful to CSIR, New Delhi, India for the financial assistance under major research project.

References

1. Bhaskar Reddy, D.; Padmavathi, V.; Ramana Reddy, P. V. *Indian J. Chem.* **1992**, *31B*, 774.
2. Bhaskar Reddy, D.; Padmavathi, V.; Seenaiah, B.; Padmaja, *A. Heteroatom Chem.* **1993**, *4*, 55.

3. Bhaskar Reddy, D.; Ramana Reddy, M.V.; Padmavathi, V. *Indian J. Chem.* **1998**, *37B*, 167.
4. Bhaskar Reddy, D.; Ramana Reddy, M. V.; Padmavathi, V. *Heteroatom Chem.* **1999**, *10*, 17.
5. Bhaskar Reddy, D.; Chandrasekhar Babu, N.; Padmavathi, V. *Heteroatom Chem.* **2001**, *12*, 131.
6. Bhaskar Reddy, D.; Chandrasekhar Babu, N.; Padmavathi, V. *J. Heterocycl. Chem.* **2001**, *38*, 769.
7. Padmavathi, V.; Balaiah, A.; Venugopal Reddy, K.; Padmaja, A.; Bhaskar Reddy, D. *Indian J. Chem.* **2002**, *41B*, 1670.
8. Padmavathi, V.; Balaiah, A.; Padmaja, A.; Bhaskar Reddy, D. *Phosphorus, Sulfur and Silicon* **2002**, *177*, 2791.
9. Padmavathi, V.; Jagan Mohan Reddy, B.; Rajagopala Sarma, M.; Padmaja, A. *Indian J. Chem.* **2004**, *43B*, 2459.
10. 10. Padmavathi, V.; Balaiah, A.; Ramana Reddy, T. V.; Jagan Mohan Reddy, B.; Bhaskar Reddy, D. *Heteroatom Chem.* **2003**, *14*, 513.
11. Padmavathi, V.; Balaiah, A.; Bhaskar Reddy, D. *J. Heterocycl. Chem.* **2002**, *39*, 649.
12. Padmavathi, V.; Balaiah, A.; Muralidhar Reddy, M.; Bhaskar Reddy, D. *Indian J. Chem.* **2003**, *42B*, 1519.
13. Padmavathi, V.; Jagan Mohan Reddy, B.; Padmaja, A.; Venugopal Reddy, K.; Rajagopala Sarma, M.; *Indian J. Chem.* **2004**, *43B*, 2628.
14. Bhaskar Reddy, D.; Somasekhar Reddy, A.; Padmavathi, V. *Indian J. Chem.* **1999**, *38*, 141.
15. Vincent, J. C.; Vincent, H. W.; *Proc. Soc. Expt. Biol. Med.* **1944**, *55*, 162.