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# Synthesis of nitrogen-containing dispiroheterocycles (IV) using nitrilimines

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**Abstract:** A number of new substituted 1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetra-deca-2,10-dienes have been obtained from the reaction of 1,4-cyclohexanedione hydrazones having acetyl, benzoyl, ethoxycarbonyl and methoxycarbonyl groups with appropriate nitrilimines. The microanalysis and spectral data of the synthesized compounds are in full agreement with their molecular structure. The microbial features of the synthesized compounds were studied by a known method.

**Keywords:** Dispiroheterocycles; 1,4-cyclohexanedione hydrazones; nitrilimines; 1,3-dipolar cycloaddition. 

## 1. Introduction

Many spirocompounds were found to possess antimicrobial,[1] antitumor[2] activities and display modest inhibition of human peptidyl prolyl cis/trans isomerase Pin1.[3] Moreover, spirocompounds were found to exhibit vasodilation activities.[4] The most developed procedure for construction of spirocompounds depends mainly on 1,3-dipolar cycloadditions to exocyclic double bonds.[5] Recently, we described a versatile and efficient one-pot synthesis of hexa and octaazadispiroheterocyclic compounds utilizing 1,4-cyclohexanedione oxime or methyl hydrazones and nitrilimines, generated in situ from the corresponding hydrazonoyl halides by the action of a suitable base.[6,7]

On continuation of our research on the construction of spiroheterocyclic systems by means of the nitrilimine 1,3-dipolar cycloaddition methodology,[8-11] we reported here the reaction of C-substituted-N-arylnitrilimines **2** with 1,4-cyclohexanedione hydrazones **3** in an attempt to synthesize the hitherto unknown hexaazadispiroheterocyclic compounds **5a-p** with the aim of investigating their biological activities.

## 2. Results and discussion

The hydrazonoyl halides **1a-j** were prepared by a modified literature procedure[12-18] and the nitrilimines **2** were generated *in situ* from **1** by reaction with triethylamine ($Et_3N$). The non isolable nitrilimines **2** reacted readily with 1,4-cyclohexanedione hydrazones **3** (Y = COMe, COPh, COOMe, and COOEt) affording the five-membered dispiroheterocycles, 4,12-diacetyl, 4,12-diethoxycarbonyl and 4,12-dimethoxycarbonyl amino-1,2,4,9,10,12-hexaazaspiro[4.2.4.2]tetradeca-2,10-dienes **5a-p** as cyclo-addition products instead of the dispirotetrazine cyclocondensation products **4a-p (Figure 1).** The structures of the synthesized compounds **5a-p** are confirmed by IR, 1H, $^{13}C$ NMR and MS spectral

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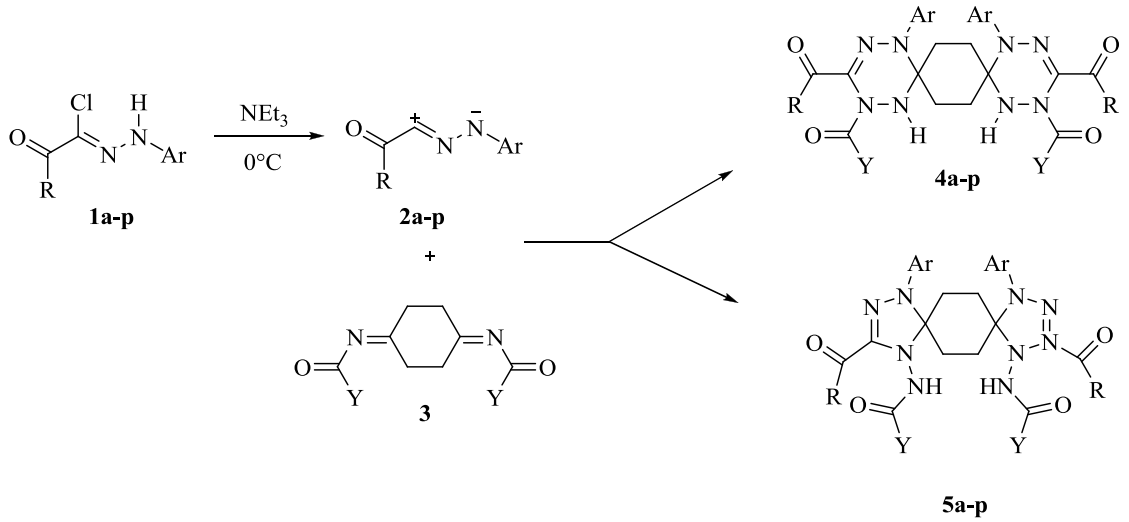
data, and are further supported by correct elemental microanalysis and given in the experimental section.

It is worth mentioning that, the dispirotetrazines were obtained from the reaction of nitrilimines with 1,4-cyclohexanedione methyl hydrazone[1]. This can be explained on the basis of the weak nucleophilicity of the nitrogen atom of the hydrazones carrying the acetyl, benzoyl, ethoxycarbonyl and methoxycarbonyl groups in comparison to that of the nitrogen atom carrying the methyl group in methyl hydrazone.




Y= Me, Ph, OMe, OEt
Ar= 4-X-$C_6H_4$
R/X/Y= **a:** Me/Cl/Me; **b:** Me/Br/Me; **c:** Me/Cl/OMe; **d:** Me/Cl/OEt; **e:** Ph/Cl/Me; **f:** Ph/Cl/Ome
**g:** PhNH/Cl/Me; **h:** PhNH/H/Me; **i:** PhNH/Cl/Ome; **j:** PhNH/Me/Me; **k:** PhNH/Me/OEt;
**l:** 2-$CH_4O$-/Cl/OMe; **m:** 2-$C_4H_3S$-/Cl/OMe; **n:** $C_{10}H_7$-/Cl/Me; **o:** $C_{10}H_7$-/Cl/Ome; **p:**$C_{10}H_7$-/Cl/OEt

**Figure 1.** Synthetic pathway for the preparation of dispiro compounds **5a-p.**

## *2.1. Spectral data analysis:*

The IR spectra for **5a-p** showed the presence of NH absorption bands in the region 3330-3320 $cm^{-1}$, in addition to the characteristic bands in the region 1690-1650 $cm^{-1}$ for C=O and NH-C=O groups. Their $^1H$ NMR spectra revealed, besides aromatic protons at 8.5-7.1 ppm, a $D_2O$-exchangeble singlet signal in the region 9.6-9.4 ppm assignable to the amide NH of the five-membered dispiro compounds **5a-p**. The NH of the tetrazine structures **4a-p** is expected to resonate at 4-5 ppm. The entire $^1H$ NMR data are presented in the experimental section.

The $^{13}C$ NMR spectra showed all the signals expected for the proposed structures and, in particular, the C-5 and C-8 signals (spiro carbons) were found at about 97-89 ppm. This is similar to reported values for spiro carbons flanked by two nitrogen atoms in five-membered heterocycles,[9-11] which provides strong evidence in support of the structures **5a-p** rather than the six-membered structure **4a-p**, which is expected to have a C-6 and C-9 signal at about 70 ppm[2], The signal at about 147 ppm was attributed to the C=N of the triazole ring. This assignment is in good agreement with literature data for azomethine carbons. The complete $^{13}C$ NMR data are presented in the experimental section. Further work on the structures of the synthesized compounds is underway. The electron impact (EI) mass spectra displayed the correct molecular ions ($M^{+\cdot}$) in accordance with the suggested structures. The base peak in all these compounds was that of the conjugated vinyl triazole cation **(Figure 2)**, this fragmentation pattern is well known for cycloalkanones.[19]

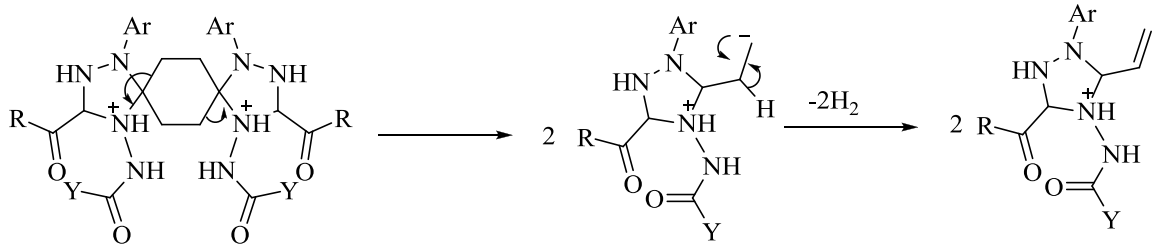



**Figure 2.** The main fragmentation of compounds **5a-p**.

## 3. Antimicrobial activity

Some of synthesized compounds were screened in vitro for their antimicrobial activity against a variety of bacterial strains such as *Euterococci, Escherichia coli*, *Staphylococcus aureus*, *Klebsiella spp*, *Proteus spp*, and fungi such as *Aspergillus niger*, *Candida albicans*, employing the nutrient agar disc diffusion method[20-22] at 10 mg/mL concentration in dimethyl formamide (DMF) by measuring the average diameter of the inhibition zone in mm. The results showed that all the tested compounds exhibited a marked degree of activity against bacteria and fungi compared with well known antibacterial and antifungal substances such as tetracycline and fluconazole. According to NCCLS (2004), zones of inhibition for tetracycline and fluconazole < 14 mm were considered resistant, between 15 and 18 mm were considered weakly sensitive and > 19 mm were considered sensitive. Also, the results showed the degree of inhibition varied with the tested compounds (Table 2).

**Table 2.** Antimicrobial screening results of the tested compounds*.

| Comp. No. | Antibacterial activity | | | | | Antifungal activity | |
|---|---|---|---|---|---|---|---|
| | ***Eutero-cocci*** | ***E. coli*** | ***Staph. aureus*** | ***Klebsiella spp*** | ***Proteus spp*** | ***Candida albicans*** | ***Aspergillus niger*** |
| **5a** | 12 | 14 | 16 | 10 | 9 | 16 | 16 |
| **5c** | 16 | 16 | 14 | 13 | 12 | 17 | 14 |
| **5e** | 14 | 12 | 10 | 11 | 14 | 18 | 18 |
| **5g** | 11 | 17 | 14 | 17 | 12 | 16 | 10 |
| **5i** | 15 | 15 | 18 | 18 | 18 | 9 | 13 |
| **5k** | 12 | 11 | 12 | 16 | 15 | 12 | 11 |
| **5l** | 17 | 18 | 15 | 13 | 18 | 14 | 17 |
| **5m** | 13 | 16 | 16 | 16 | 14 | 17 | 13 |
| **5o** | 11 | 14 | 12 | 10 | 13 | 15 | 12 |
| DMF | - | - | - | - | - | - | - |

*Calculated as average of three values.

## 4. Experimental Section

All melting points were determined on an A. Krüss Melting Point Meter equipped with a thermometer and are uncorrected. The IR spectra were measured as potassium bromide pellets using a Satellite 3000 Mid infrared spectrophotometer. The $^{1}$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AM 300 MHz spectrometer at room temperature in DMSO-$d_6$ solution using tetramethylsilane (TMS) as internal reference. Chemical shifts were recorded as δ values in parts per millions (ppm)

downfield from internal TMS. Electron impact (EI) mass spectra were run on a Shimadzu GCMS-QP1000 EX spectrometer at 70 eV. Elemental analyses were performed at Cairo University, Egypt. The hydrazonoyl halides **1**[12-18] and 1,4-cyclohexanedione hydrazones **3**[23] were prepared according to literature procedures. Tetrahydrofuran (THF) and triethylamine were purchased from Avocado Research Chemicals, England, and used without further purification.

*4.1. General procedure for reaction of nitrilimines 2 with 1,4-cyclohexanedione hydrazones (3):*

Triethylamine (0.05 mol, 7 mL) in tetrahydrofuran (10 mL) was added dropwise to stirred mixture of 1,4-cyclohexanedione hydrazones **3** (0.025 mol) and the appropriate hydrazonoyl halides **1** (0.05 mol) in tetrahydrofuran (100 mL) at 0 $^{o}$C. The reaction temperature was allowed to rise slowly to room temperature and stirring was continued overnight. The precipitated salts were filtered off and the solvent was then evaporated. The residue was washed with water (3x50 mL) and in few cases the gummy products were triturated with ethanol (10-15 mL). The crude solid product was collected and recrystallized from ethanol to give the desired compounds. The following compounds were synthesized using this method:

*4.1.1 3,11-Diacetyl-4,12-diacetylamino-1,9-di(4-chlorophenyl)-1,2,4,9,10,12-hexaazadispiro-4.2.4.2] tetradeca-2,10-diene (5a):* Yield 57%, m.p. 180-182 $^{o}$C. IR (KBr, ν, cm$^{-1}$):3385 (NH), 1678 (C=O), 1622 (C=N). $^{1}$H NMR (DMSO-d$_6$) (δ, ppm): 9.44 (s, 2H, 2NH), 7.42-7.12 (m, 8H, arom. protons), 2.48 (s, 6H, 2CH$_3$), 2.44 (6H, 2CH$_3$), 2.17-2.03 (m, 8H, 4CH$_2$). $^{13}$C NMR (DMSO-d$_6$) (δ, ppm): 189.65 (C=O), 147.95 (C=N), 141.46-120.18 (arom. carbons), 87.45 (spiro carbons), 35.07, 34.83 (2CH$_2$), 26.45, 26.32 (2CH$_3$). MS: *m/z* = 612/610 (M$^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{28}H_{30}Cl_2N_8O_4$ (Mw 613.50): C, 54.8; H, 4.9 N, 18.3%. Found: C, 55.15; H, 4.80; N, 18.38%.

*4.1.2 3,11-Diacetyl-4,12-diacetylamino-1,9-di(4-bromophenyl)-1,2,4,9,10,12-hexaazadispiro-4.2.4.2]-tetradeca-2,10-diene (5b):* Yield 54%, m.p. 186-188 $^{o}$C. IR (KBr ν, cm$^{-1}$): 3385 (NH), 1676 (C=O), 1620 (C=N). $^{1}$H NMR (DMSO-d$_6$) (δ, ppm): 9.42 (s, 2H, 2NH), 7.48-7.14 (m, 8H, arom. protons), 2.47 (s, 6H, 2CH$_3$), 2.44 (6H, 2CH$_3$), 2.16-2.01 (m, 8H, 4CH$_2$). $^{13}$C NMR (DMSO-d$_6$) (δ, ppm): 189.71 (C=O), 147.96 (C=N), 141.94-121.10 (arom. carbons), 87.22 (spiro carbons), 35.10, 34.86 (2CH$_2$), 26.48, 26.31 (2CH$_3$). MS: *m/z* = 700/798 (M$^{+\cdot}$, Bromine isotopes). Anal. Calcd for $C_{28}H_{30}Br_2N_8O_4$ (Mw 702.40): C, 47.9; H, 4.3; N, 16.0%. Found: C, 47.75; H, 4.12; N, 15.90%.

*4.1.3 3,11-Diacetyl-1,9-di(4-chlorophenyl)-4,12-dimethoxycarbonyl-1,2,4,9,10,12-hexaazadispiro-[4.2.4.2]tetradeca-2,10-diene (5c):* Yield 50%, m.p. 173-175 $^{o}$C. IR (KBr ν, cm$^{-1}$): 3380 (NH), 1720 (C=O), 1625 (C=N). $^{1}$H NMR (DMSO-d$_6$) (δ, ppm): 9.60 (s, 2H, 2NH), 7.57-7.20 (m, 8H, arom. protons), 3.74 (s, 6H, 2OCH$_3$), 2.47 (s, 6H, 2CH$_3$), 2.18-2.04 (m, 8H, 4CH$_2$); $^{13}$C NMR (DMSO-d$_6$) (δ, ppm): 156.69 (O-C=O), 147.90 (C=N), 141.90-121.16 (arom. carbons), 88.95 (spiro carbons), 54.32 (OCH$_3$), 35.56, 34.72 (2CH$_2$), 26.48 (CH$_3$).. MS: *m/z* = 644/642 (M$^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{28}H_{30}Cl_2N_8O_6$ (Mw 645.49): C, 52.1; H, 4.7; N, 17.4%. Found: C, 51.85; H, 4.55; N, 17.60%.

*4.1.4 3,11-Diacetyl-4,12-diethoxycarbonylamino-1,9-di(4-chlorophenyl)-1,2,4,9,10,12-hexaazadispiro-[4.2.4.2]tetradeca-2,10-diene (5d):* Yield 52%, m.p. 179-181 $^{o}$C. IR (KBr ν, cm$^{-1}$): 3365 (NH), 1665 (C=O), 1618 (C=N). $^{1}$H NMR (DMSO-d$_6$) (δ, ppm): 9.66 (s, 2H, 2NH), 8.46-7.26 (m, 8H, arom. protons), 4.24-4.04 (q, 2H, OCH$_2$, *J = 7 Hz*), 2.00-1.95 (m, 8H, 4CH$_2$), 1.26-1.13 (t, 3H, CH$_3$, *J = 7 Hz*). $^{13}$C NMR (DMSO-d$_6$) (δ, ppm): 184.86 (C=O), 148.10 (C=N), 142.15-121.19 (arom. carbons), 91.50 (spiro carbons), 61.3 (OCH$_2$), 35.54, 34.76 (2CH$_2$), 26.48, 13.8 (2CH$_3$).. MS: *m/z* = 672/670 (M$^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{30}H_{34}Cl_2N_8O_6$ (Mw 673.55): C, 53.4; H, 5.1; N, 16.6%. Found: C, 53.65; H, 4.88; N, 16.45%.

*4.1.5 4,12-Diacetylamino-3,11-dibenzoyl-1,9-di(4-chlorophenyl)-1,2,4,9,10,12-hexazadispiro[4.2.4.2]-tetradeca-2,10-diene (5e):* Yield 57%, m.p. 196-198 $^{o}$C. IR (KBr ν, cm$^{-1}$): 3375, 3248 (NH), 1655 (C=O), 1615 (C=N). $^{1}$H NMR (DMSO-d$_6$) (δ, ppm): 9.70 (s, 2H, 2NH), 7.76-7.03 (m, 18H, arom. protons), 2.47 (s, 6H, 2CH$_3$), 2.13-2.06 (m, 8H, 4CH$_2$). $^{13}$C NMR (DMSO-d$_6$) (δ, ppm): 159.36 (C=O), 147.86 (C=N), 141.43-121.10 (arom. carbons), 89.52 (spiro carbons), 35.50, 34.90 (2CH$_2$), 26.31 (CH$_3$). MS: *m/z* =

736/734 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{38}H_{34}Cl_2N_8O_4$ (Mw 737.63): C, 61.9; H, 4.6; N, 15.2%. Found: C, 62.20; H, 4.75; N, 14.05%.

*4.1.6 3,11-Dibenzoyl-1,9-di(4-chlorophenyl)-4,14-dimethoxycarbonylamino-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,10-diene (5f):* Yield 55%, m.p. 201-203 °C. IR (KBr ν, $cm^{-1}$): ν 3380, 3257 (NH), 1654 (C=O), 1612 (C=N) $cm^{-1}$. $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.65 (s, 2H, 2NH), 7.78-7.15 (m, 18H, arom. protons), 3.75 (s, 6H, $2OCH_3$), 2.11-2.05 (m, 8H, $4CH_2$). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.40 (C=O), 147.84 (C=N), 141.62-116.50 (arom. carbons), 89.60 (spiro carbons), 54.36 ($OCH_3$), 35.26, 34.90 ($2CH_2$). MS: *m/z* = 768/766 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{38}H_{34}Cl_2N_8O_6$ (Mw 769.63): C, 59.3; H, 4.5; N, 14.6%. Found: C, 59.05; H, 4.64; N, 14.42%.

*4.1.7 4,12-Diacetylamino-1,9-di(4-chlorophenyl)-3,11-diphenylaminocarbonyl-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,12-diene (5g):* Yield 59%, m.p. 191-193 °C. IR (KBr ν, $cm^{-1}$): 3380, 3260 (NH), 1655 (C=O), 1612 (C=N). $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.67 (s, 2H, 2NH), 8.89 (s, 2H, 2PhNH), 7.80-7.13 (m, 18H, arom. protons), 2.46 (s, 6H, $2CH_3$), 2.10-2.04 (m, 8H, $4CH_2$). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.24 (C=O), 147.90 (C=N), 141.55-119.94 (arom. carbons), 89.65 (spiro carbons), 35.50, 34.96 ($2CH_2$), 26.40 ($CH_3$). MS: *m/z* = 766/764 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{38}H_{36}Cl_2N_{10}O_4$ (Mw 767.66): C, 59.5; H, 4.7; N, 18.2%. Found: C, 59.35; H, 4.55; N, 18.32%.

*4.1.8 4,12-Diacetylamino-1,9-diphenyl-3,11-diphenylaminocarbonyl-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,12-diene (5h):* Yield 51%, m.p. 196-198 °C. IR (KBr ν, $cm^{-1}$): 3380, 3260 (NH), 1655 (C=O), 1612 (C=N) $cm^{-1}$. $^1$H NMR (DMSO-d6) (δ, ppm): 9.67 (s, 2H, 2NH), 8.88 (s, 2H, 2PhNH), 7.80-7.13 (m, 20H, arom. protons), 2.46 (s, 6H, $2CH_3$), 2.10-2.04 (m, 8H, $4CH_2$). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.24 (C=O), 147.90 (C=N), 141.55-119.94 (arom. carbons), 89.65 (spiro carbons), 35.50, 34.96 ($2CH_2$), 26.38 ($CH_3$). MS: *m/z* = 698 ($M^{+\cdot}$). Anal. Calcd for $C_{38}H_{38}N_{10}O_4$ (Mw 698.77): C, 65.3; H, 5.5; N, 20.0%. Found: C, 65.47; H, 5.36; N, 19.87%.

*4.1.9 1,9-Di(4-chlorophenyl)-4,12-Dimethoxycarbonylamino-3,11-diphenylaminocarbonyl-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,12-diene (5i):* Yield 57%, m.p. 171-173 °C. IR (KBr ν, $cm^{-1}$): 3380, 3260 (NH), 1655 (C=O), 1612 (C=N). $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.67 (s, 2H, 2NH), 8.89 (s, 2H, 2PhNH), 7.80-7.13 (m, 18H, arom. protons), 3.76 (s, 6H, $2OCH_3$), 2.10-2.04 (m, 8H, $4CH_2$). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.24 (C=O), 147.90 (C=N), 141.55-119.94 (arom. carbons), 89.65 (spiro carbons), 35.50, 34.96 ($2CH_2$), 54.36 ($OCH_3$). MS: *m/z* = 798/796 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{38}H_{36}N_{10}Cl_2O_6$ (Mw 799.68): C, 57.08; H, 4.54; N, 17.52%. Found: C, 56.85; H, 4.36; N, 17.38%.

*4.1.10 4,12-Diacetylamino-1,9-di(4-methylphenyl)-3,11-diphenylaminocarbonyl-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,12-diene (5j):* Yield 53%, m.p. 181-183 °C. IR (KBr ν, $cm^{-1}$): 3380, 3260 (NH), 1655 (C=O), 1612 (C=N). $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.67 (s, 2H, 2NH), 8.87 (s, 2H, 2PhNH), 7.80-7.13 (m, 18H, arom. protons), 2.46 (s, 6H, $2CH_3$), 2.26 (s, 6H, $2CH_3$), 2.10-2.04 (m, 8H, $4CH_2$). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.24 (C=O), 147.90 (C=N), 141.55-119.94 (arom. carbons), 89.65 (spiro carbons), 35.50, 34.96 ($2CH_2$), 26.31 ($CH_3$), 23.40 ($CH_3$). MS: *m/z* = 758 ($M^{+\cdot}$). Anal. Calcd for $C_{40}H_{42}N_{10}O_6$ (Mw 758.84): C, 63.31; H, 5.58; N, 18.46%. Found: C, 63.05; H, 5.66; N, 18.32%.

*4.1.11 4,12-Diethoxycarbonylamino-1,9-di(4-methylphenyl)-3,11-diphenylaminocarbonyl-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,12-diene (5k):* Yield 56%, m.p. 177-179 °C. IR (KBr ν, $cm^{-1}$): 3380, 3260 (NH), 1655 (C=O), 1612 (C=N). $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.67 (s, 2H, 2NH), 8.89 (s, 2H, 2PhNH), 7.80-7.13 (m, 18H, arom. protons), 4.22-4.03 (q, 2H, $OCH_2$, *J = 7 Hz*), 2.26 (s, 6H, $2CH_3$), 2.10-2.04 (m, 8H, $4CH_2$), 1.26-1.14 (t, 3H, $CH_3$, *J = 7 Hz*). $^{13}$C NMR (DMSO-$d_6$) (δ, ppm): 159.24 (C=O), 147.90 (C=N), 141.55-119.94 (arom. carbons), 89.65 (spiro carbons), 61.37 ($OCH_2$), 35.52, 34.98 ($2CH_2$), 23.40 ($CH_3$), 13.78 ($CH_3$). MS: *m/z* = 786 ($M^{+\cdot}$). Anal. Calcd for $C_{42}H_{46}N_{10}O_6$ (Mw 786.90): C, 64.11; H, 5.89; N, 17.80%. Found: C, 64.35; H, 5.76; N, 17.62%.

*4.1.12 4,12-Diacetylamino-1,9-di(4-chlorophenyl)-3,11-di(2-furoyl)-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,10-di-ene (5l):* Yield 58%, m.p. 194-196 °C. IR (KBr ν, $cm^{-1}$): 3370 (NH), 1665 (C=O), 1615 (C=N). $^1$H NMR (DMSO-$d_6$) (δ, ppm): 9.48 (s, 2H, 2NH), 7.80-7.16 (m, 14H, arom.

protons), 2.46 (s, 6H, $2CH_3$), 2.16-2.10 (m, 8H, $4CH_2$); $^{13}C$ NMR (DMSO-$d_6$) (δ, ppm): 174.56 (C=O), 148.25 (C=N), 143.20-121.58 (arom. carbons), 94.85 (spiro carbons), 35.41, 34.83 ($2CH_2$), 26.28 (CH3). MS: *m/z* = 748/746 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{34}H_{30}Cl_2N_8O_8$ (Mw 749.52): C, 54.48; H, 4.03; N, 14.95%. Found: C, 63.00; H, 3.90; N, 13.45%.

*4.1.13 1,9-Di(4-chlorophenyl)-4,12-dimethoxycarbonylamino-3,11-di(2-thenoyl)-1,2,4,9,10,12-hexaaza-dispiro[4.2.4.2]tetradeca-2,10-diene (5m):* Yield 50%, m.p. 184-186 °C. IR (KBr ν, $cm^{-1}$): 3375 (NH), 1660 (C=O), 1610 (C=N). $^1H$ NMR (DMSO-$d_6$) (δ, ppm): 9.45 (s, 2H, 2NH), 7.84-7.12 (m, 14H, arom. protons), 3.77 (s, 6H, $2OCH_3$), 2.15-2.06 (m, 8H, $4CH_2$); $^{13}C$ NMR (DMSO-$d_6$) (δ, ppm): 175.82 (C=O), 148.30 (C=N), 143.73-121.68 (arom. carbons), 94.64 (spiro carbons), 54.34 (OCH3), 35.35, 34.66 ($2CH_2$). MS: *m/z* = 780/778 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{34}H_{30}Cl_2N_8O_6S_2$ (Mw 781.70): C 52.24, H 3.87, N 14.33%. Found: C 60.80, H, 3.85; N, 13.02%.

*4.1.14 4,12-Diacetylamino-1,9-di(4-chlorophenyl)-3,11-di(2-naphthoyl)-1,2,4,9,10,12-hexaazadispiro-[4.2.4.2]tetradeca-2,10-diene (5n):* Yield 54%, m.p.189-191 °C. IR (KBr ν, $cm^{-1}$): 3365 (NH), 1650 (C=O), 1605 (C=N). $^1H$ NMR (DMSO-$d_6$) (δ, ppm): 9.63 (s, 2H, 2NH), 8.45-7.22 (m, 22H, arom. protons), 2.10-2.03 (m, 8H, $4CH_2$). $^{13}C$ NMR (DMSO-$d_6$) (δ, ppm): 184.56 (C=O), 148.32 (C=N), 142.12-120.86 (arom. carbons), 91.63 (spiro carbons), 35.30, 34.75 ($2CH_2$), 26.31 ($CH_3$). MS: *m/z* = 836/834 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{46}H_{38}Cl_2N_8O_4$ (Mw 837.77): C, 65.95; H, 4.57; N, 13.38%. Found: C, 69.60; H, 4.35; N, 11.76%.

*4.1.15 1,9-Di(4-Chlorophenyl)-4,12-dimethoxycarbonylamino-3,11-di(2-naphthoyl)-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,10-diene (5o):* Yield 52%, m.p. 187-189 °C. IR (KBr ν, $cm^{-1}$): 3365 (NH), 1650 (C=O), 1605 (C=N). $^1H$ NMR (DMSO-$d_6$) (δ, ppm): 9.62 (s, 2H, 2NH), 8.45-7.22 (m, 22H, arom. protons), 3.75 (s, 6H, $2OCH_3$), 2.10-2.03 (m, 8H, $4CH_2$). $^{13}C$ NMR (DMSO-d6) (δ, ppm): 184.56 (C=O), 148.32 (C=N), 142.12-120.86 (arom. carbons), 91.63 (spiro carbons), 54.32 (OCH3), 35.30, 34.75 (2CH2). MS: *m/z* = 868/866 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{46}H_{38}Cl_2N_8O_6$ (Mw 869.77): C, 63.52; H, 4.40; N, 12.88%. Found: C, 69.60; H, 4.35; N, 11.76%.

*4.1.16 1,9-Di(4-Chlorophenyl)-4,12-diethoxycarbonylamino-3,11-di(2-naphthoyl)-1,2,4,9,10,12-hexa-azadispiro[4.2.4.2]tetradeca-2,10-diene (5p):* Yield 56%, m.p. 206-208 °C. IR (KBr ν, $cm^{-1}$): 3365 (NH), 1650 (C=O), 1605 (C=N). $^1H$ NMR (DMSO-d6) (δ, ppm): 9.62 (s, 2H, 2NH), 8.45-7.22 (m, 22H, arom. protons), 4.18-4.01 (q, 2H, $OCH_2$, *J = 7 Hz*), 2.10-2.03 (m, 8H, $4CH_2$), 1.23-1.11 (t, 3H, $CH_3$, *J = 7 Hz*). $^{13}C$ NMR (DMSO-d6) (δ, ppm): 184.56 (C=O), 148.32 (C=N), 142.12-120.86 (arom. carbons), 91.63 (spiro carbons), 61.32 ($OCH_2$), 35.30, 34.75 ($2CH_2$), 13.74 ($CH_3$). MS: *m/z* = 896/894 ($M^{+\cdot}$, Chlorine isotopes). Anal. Calcd for $C_{48}H_{42}Cl_2N_8O_6$ (Mw 897.83): C, 64.21; H, 4.72; N, 12.48%. Found: C, 69.60; H, 4.35; N, 11.76%.

## 5. Conclusion

In summary, the nitrilimines **1** reacted with 1,4-cyclohexanedione hydrazones **3** to form a new dispiroheterocyles, 4,12-diacetyl, 4,12-diethoxycarbonyl and 4,12-dimethoxycarbonylamino-1,2,4,9,10,12-hexaazadispiro[4.2.4.2]tetradeca-2,10-dienes **5a-p**. Nine of the synthesized compounds were screened for their biological activities and displayed weak antibacterial and antifungal activities. The results confirm that the antimicrobial activity is strongly dependent on the size of compounds and the nature of the substituents at triazole moieties.

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