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ORIGINAL PAPER

Synthesis and properties of 1-(3-(fluoromethyl and trifluoromethyl)phenyl)-5-oxopyrrolidine-3-carboxylic acid derivatives

Vytautas Mickevičius · Rita Vaickelionienė · Ilona Jonuškienė · Gema Mikulskienė · Kristina Kantminienė

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Abstract Condensation of 1-(3-(fluoromethyl and trifluoromethyl)phenyl)-5-oxopyrrolidine-3-carbohydrazides with aromatic aldehydes and acetone gave the corresponding hydrazones. Most of the reaction products are able to form isomers, because of the amide and azomethine structural units. The reactions of 1-aryl-4-hydrazinocarbonyl-2-pyrrolidinones with 2,4-pentanedione gave 3,5-dimethylpyrazole compounds and those with 2,5-hexanedione provided 1-substituted 2,5-dimethylpyrroles. Several oxadiazole derivatives were synthesized. The structures of the synthesized compounds were confirmed on the basis of their MS, IR, ^{1}H, and ^{13}C NMR spectra and by analytical methods. ^{13}C APT, ^{1}H/^{13}C 2D (HETCOR), and NOE (^{1}H) NMR techniques and molecular modeling were used for detailed structure examination. Complete NMR spectral assignment of the studied compounds was performed in order to evaluate their conformation, configuration, and substituent effects.

Keywords Hydrazides–hydrazones · Condensation · Rotamers · NMR spectroscopy · Molecular modeling

V. Mickevičius (✉) · R. Vaickelionienė · I. Jonuškienė
Department of Organic Chemistry,
Kaunas University of Technology, Radvilėnų pl. 19,
50254 Kaunas, Lithuania
e-mail: Vytautas.Mickevicius@ktu.lt

G. Mikulskienė
Department of Bioorganic Compounds Chemistry,
Institute of Biochemistry, Mokslininkų str.12,
08662 Vilnius, Lithuania

K. Kantminienė
Department of General Chemistry,
Kaunas University of Technology,
Radvilėnų pl. 19, 50254 Kaunas, Lithuania

Introduction

Amino acids, their derivatives, and products of their cyclization play an important role in the synthesis of biologically active compounds such as pharmaceuticals, protecting agents for field plants, and growth regulators.

Organic hydrazine compounds have been widely used as synthetic starting materials to construct various nitrogen-containing heterocycles. Hydrazides of carboxylic acids are used for the synthesis of hydrazones [1], pyrroles [2], pyrazoles [2], oxadiazoles [3–5], thiadiazoles [4, 6–8], and triazoles [3, 8]. Several of these compounds have analgesic, antitubercular, antidepressive, anticonvulsive, antitumor, and bactericidal activity.

Information about the structural features of these compounds can be obtained by use of the methods of NMR spectroscopic analysis [9]. Computer molecular modeling has provided insight into the structural basis of the title compounds [10]. Fluorine and trifluoromethyl groups attached to the benzene ring determine characteristic spin–spin splitting patterns and chemical shift effects [9]. The coupling constants between F–H and F–C nuclei are sensitive to the electronic effects of the substituents of the benzene ring [9–20]. The separate structural fragments of the study compounds have been widely investigated [21–40].

Signal doubling in the NMR spectra discloses the presence of rotamers or higher aggregates [9, 21, 22]. ^{1}H and ^{13}C NMR spectral data and the results of the MM2 and AM1 methods of modeling [10] have been used to elucidate the structures of the compounds in terms of *s-cis*/*s-trans* conformations and (*Z*)/(*E*) configurations [26–33]. The objectives of this work were the synthesis of 1-(3-(fluoromethyl and trifluoromethyl)phenyl)-5-oxopyrrolidine-3-carboxylic acid derivatives and investigation of their structures as a continuation of our earlier studies [34, 35].

Results and discussion

In this work, methyl 1-(3-fluorophenyl)-5-oxopyrrolidine-3-carboxylate (**2a**) and methyl 5-oxo-1-(3-(trifluoromethyl) phenyl)pyrrolidine-3-carboxylate (**2b**) were synthesized by esterification of carboxylic acids **1a** and **1b** with excess methanol under reflux in the presence of a catalytic amount of sulfuric acid. Reaction of esters **2a** and **2b** with hydrazine hydrate in 2-propanol under reflux gave 5-oxopyrrolidine-3-carbohydrazides **3a** and **3b**, which crystallized from the reaction mixture after cooling (Scheme 1). ^{1}H NMR spectra are most suitable for confirmation of the structures of **3a** and **3b**. The narrow singlets at ~3.69 ppm characteristic of $COOCH_3$ protons of **2a** and **2b** are absent in the ^{1}H NMR spectra of **3a** and **3b**. The broadened singlets at ~4.31 ppm assigned to the protons of the NH_2 group and signals at ~9.30 ppm assigned to protons of the CONH fragment of **3a** and **3b** prove the presence of the $CONHNH_2$ group in these compounds. IR spectra of these hydrazides showed $NHNH_2$ absorption at 3,313–3,284 cm^{-1}.

The structure of hydrazides **3a** and **3b** was also verified by their reaction with carbonyl compounds. Condensation of compounds **3** with aromatic aldehydes gave *N*′-benzylidene-1-(3-substituted phenyl)-5-oxopyrrolidine-3-carbohydrazides **4–10**. The reaction was carried out under reflux in 2-propanol or 1,4-dioxane.

Detailed analysis of the ^{1}H and ^{13}C NMR spectra of hydrazones **4–10** having different substitution patterns in the benzene ring was carried out. Considerable interest was focused on the ability to reveal the geometrical isomers originating from the azomethine group and on rotamer formation because of the restricted rotation of the amide group. NMR did not yield conclusive information about the conformations mentioned above, consequently molecular modeling data were also used. The total steric energies were obtained for all models of the available isomers of **4–10** using MM2 and AM1 methods. The dominant isomers were ascertained by comparison of the variations of tendencies of the obtained total steric energy values and distribution of the intensities of NH signals in the ^{1}H NMR spectra. The results of comparison led us to conclude that *s-cis*/(*Z*) and *s-trans*/(*E*) (*s-cis* and *s-trans*—amide rotamers, (*Z*) and (*E*)—azomethine geometrical isomers) isomers are favored in DMSO-d_6 solutions of **4–10**.

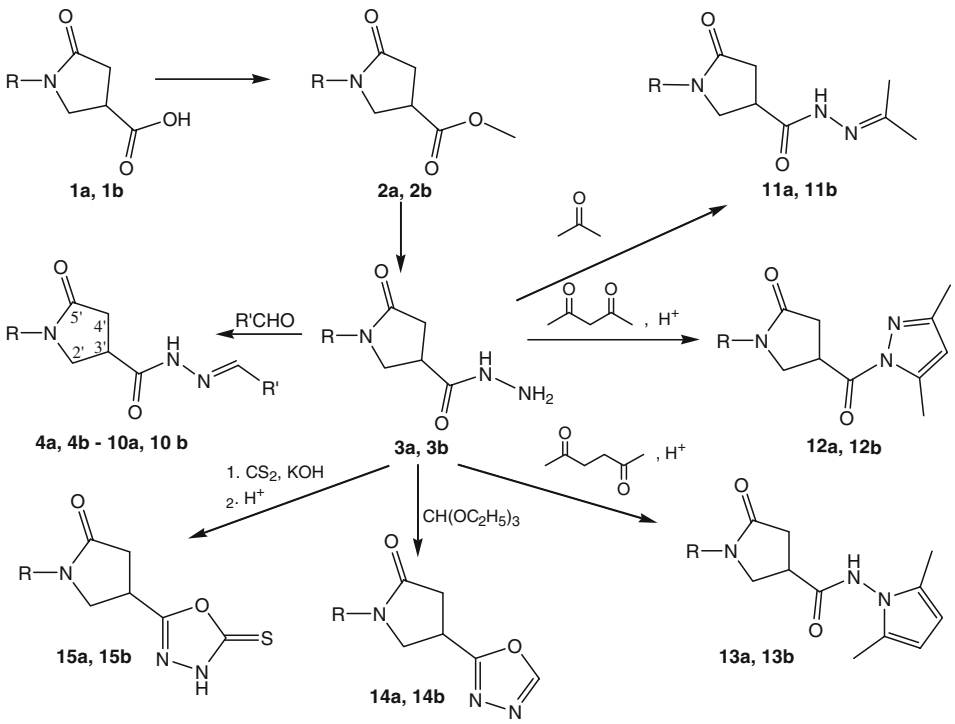
The presence of isomers was noticeable in the ^{1}H and ^{13}C NMR spectra for atoms separated by few bonds from the center of isomerism. The most informative signals for study of the isomers of **4–10** were NH group singlets which resonated at ~11.64 and ~11.70 ppm with the intensity ratio of 0.7:0.3, indicating the existence of *s-cis*/*s-trans* rotamers. The resonances of the N=CH fragments and CH groups of the pyrrolidinone ring with the same intensity ratio also showed the presence of the isomers. The ^{13}C NMR spectra of **4–10** exhibited double sets of resonances of CO, N=CH, pyrrolidinone ring carbons, and even some carbons (C-1, 2, 6) of the *N*-phenyl ring, because of restricted rotation around the CO–NH bond. The decay of the differences of the corresponding averaged chemical shifts of 4.97 ppm, 3.36 ppm (CO, N=CH), 1.97 ppm (C-3′), 0.73 ppm (C-4′), 0.48 ppm (C-2′), and 0.18 ppm (C-5′) demonstrates with certainty the presence of the center of isomerism. Such decay was not observed for the differences of the chemical shifts for carbons (C-1, 2, 6) of the *N*-phenyl ring.

Reaction of carbohydrazydes **3a** and **3b** with acetone under reflux was facile and provided the corresponding *N*′-isopropylidene hydrazides **11a** and **11b**. The formation of *s-cis*/*s-trans* rotamers in the ratio 0.5:0.5 was observed in the NMR spectra of **11a** and **11b**. The magnetic non-equivalence observed for both of the methyl groups is caused by the presence of the lone pair of the nitrogen atom in the azomethine group.

Reaction of carbohydrazides with β and γ diketones usually provides cyclic compounds. Condensation of hydrazides **3a** and **3b** with 2,4-pentanedione in 2-propanol in the presence of a catalytic amount of hydrochloric acid resulted in the formation of 1-substituted 4-((3,5-dimethylpyrazol-1-yl)carbonyl)pyrrolidin-2-ones **12a** and **12b**. The ^{13}C NMR spectra of these compounds exhibited three resonances at ~111.62, ~143.90, and ~152.17 ppm assigned to the pyrazole ring. The protons of CH and CH_3 groups resonated in the expected region of the ^{1}H NMR spectra and thus also confirmed the presence of the pyrazole moiety. The characteristic spin–spin coupling (^4J = 0.6 Hz) between CH and CH_3 (CH=C*CH*$_3$) groups was observed.

Condensation of hydrazides **3a** and **3b** with 2,5-hexanedione in 2-propanol in the presence of a catalytic amount of acetic acid resulted in the formation of *N*-(2,5-dimethyl-1*H*-pyrrol-1-yl)-1-(3-substituted phenyl)-5-oxopyrrolidine-3-carboxamides **13a** and **13b**. When hydrochloric acid was used as catalyst, the reaction mixture darkened and resinification occurred. The NMR spectra of **13a** and **13b** displayed the characteristic signals of the suggested structures. The intense singlets at 2.00 and 5.65 ppm (**a** and **b**) attributed to CH_3 and CH groups of the pyrrole ring were present in the ^{1}H NMR spectra. The double intensity resonances at ~10.91, ~103.06 and ~126.68 ppm in the ^{13}C NMR spectra pointed to the existence of the pyrrole ring. Despite the presence of the amide fragment, only the *s-cis* isomer with traces of the *s-trans* isomer were observed in the ^{1}H and ^{13}C NMR spectra of **13a** and **13b** in DMSO-d_6 solutions. The specific conformational behavior of rotation around the CO–NH bond was investigated using molecular

Scheme 1



a: R = 3-F-C_6H_4; **b**: R = 3-CF_3-C_6H_4

4: R' = C_6H_5; **5**: R' = 4-F-C_6H_4; **6**: R' = 4-Cl-C_6H_4;

7: R' = 4-Br-C_6H_4; **8**: R' = 4-$(CH_3)_2$N-C_6H_4; **9**: R' = 4-CH_3O-C_6H_4;

10: R' = 4-NO_2-C_6H_4

modeling techniques. The rotation barriers computed for the model **13a** were 117.50 kJ/mol (*s-cis*) and 62.37 kJ/mol (*s-trans*) and those for **13b** were 174.18 kJ/mol (*s-cis*) and 64.16 kJ/mol (*s-trans*). This allowed the conclusion that rotation around the CO–NH bond is highly restricted by the voluminous 2,5-dimethylpyrrole ring.

Monosubstituted oxadiazole derivatives can be obtained directly from acid hydrazides and ethyl orthoformate. 1,3,4-Oxadiazoles **14a** and **14b** were synthesized by heating hydrazides **3a** and **3b** under reflux in excess ethyl orthoformate. Formation of the five-membered oxadiazole ring was confirmed by the presence of a singlet (CH=N) at 9.25 ppm (**a** and **b**) in the ^{1}H NMR spectra and the resonances at ~154.97 and ~166.33 ppm, attributed to N=CH and N=C groups, in the ^{13}C NMR spectra. Hydrazinocarbonyl compounds also undergo reaction quite easily with carbon disulfide in the presence of potassium hydroxide. 1-Aryl-4-(4,5-dihydro-5-thioxo-1,3,4-oxadiazol-2-yl)pyrrolidin-2-ones **15a** and **15b** were synthesized from hydrazides **3a** and **3b** by the method described in literature [4]. Formation of the five-membered oxadiazole ring was confirmed by the presence of an NH singlet at ~14.50 ppm in the ^{1}H NMR spectra and the resonances at 163.77 and 178.02 ppm (**a** and **b**), ascribed to N=C and N-CS groups, in the ^{13}C NMR spectra.

The study compounds have F (compounds **a**) or a CF_3 group (compounds **b**) at the *m* position of the benzene ring. Because of the specific magnetic properties of the fluorine atom, spin–spin coupling (up to four bonds) was observed in the ^{1}H and ^{13}C NMR spectra. The splittings arising from the fluorine or trifluoromethyl group complicate analysis of the aromatic region of the NMR spectra. The multiplets of the aromatic resonances in the ^{1}H NMR spectra overlap and are insufficiently informative, whereas in the ^{13}C NMR spectra the multiplets are resolved. In the ^{13}C NMR spectra of compounds **a** atom C-3 resonated as a doublet centered at ~162.00 ppm with ^1J ~241.8 Hz and in the spectra of compounds **b** the C atom of the CF_3 group resonated as a quartet centered at ~121.84 ppm with ^1J ~272.0 Hz. ^2J values were different for C-2 (~26.5 Hz) and C-4 (~21.1 Hz), and ^3J values were different for C-1 (~10.9 Hz) and C-5 (~9.3 Hz) atoms in compounds **a**. These *J* values can be rationalized in terms of the substituent effects. The quartets of C-3 for all compounds **b** were centered at ~129.50 ppm with a ^2J value of

$\sim$31.8 Hz. It was noticed that ^3J was fully resolved only for **12b–15b**: its value for C-2 atoms centered at $\sim$115.76 ppm was $\sim$3.8 Hz and that for C-4 atoms centered at $\sim$120.46 ppm was $\sim$3.5 Hz. These multiplets for compounds **4b** and **9b** were not resolved because of the small ^3J values. For the rest of the **b**-type compounds ^3J values were measured only for C-2 atoms, whereas the resonances assigned to C-4 atoms were broadened and not resolved properly.

In conclusion, we have shown that fluorine-containing 1-aryl-5-oxopyrrolidine-3-carbohydrazides can be used as starting compounds in the synthesis of various hydrazones and azoles, which can have biological activity. The spectral and molecular modeling data were thoroughly analyzed to elucidate the structure and features of the synthesized compounds.

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova (300 MHz) spectrometer operating in Fourier transform mode with TMS as a internal standard. IR spectra were recorded on a Perkin–Elmer Spectrum BX FT-IR (KBr pellet) spectrometer. Mass spectra were obtained on a Waters ZQ 2000 spectrometer. Elemental analysis (C, H, N) was performed on an Elemental Analyzer CE-440, and results were found to be in good agreement (±0.2%) with calculated values. Melting points were determined on the Auto probe analyzer APA 1. Silica gel plates (Silufol UV-254) were used for analytical purposes.

Methyl 1-(3-fluorophenyl)-5-oxopyrrolidine-3-carboxylate (**2a**, $C_{12}H_{12}FNO_3$)

A mixture of 33.5 g 1-(3-fluorophenyl)-5-oxopyrrolidine-3-carboxylic acid (**1a**, 0.15 mol), 36.5 cm^3 methanol (0.90 mol), and 3 cm^3 sulfuric acid was stirred at reflux for 6 h, unreacted methanol was removed under reduced pressure, and 150 cm^3 10% Na_2CO_3 solution was added. The mixture was boiled then cooled. The crude product was isolated by filtration, washed with water, and dried. M.p.: 89–90 °C (from *n*-hexane to toluene); yield 99%; IR (KBr): $\bar{\nu}$ = 1,738 (C=O), 1,695 (C=O), 1,229 (OCH_3) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.70–2.89 (m, 2H, CH_2CO), 3.42–3.52 (m, 1H, CH), 3.68 (s, 3H, OCH_3), 3.96–4.12 (m, 2H, NCH_2), 6.94–7.68 (m, 4H, H_{ar}) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 34.70 (C-3′), 35.03 (C-4′), 49.64 (C-2′), 52.13 (OCH_3), 106.20 (d, $^2J_{C\text{-}F}$ = 26.5 Hz, C-2), 110.52 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 114.76 (br s, C-6), 130.30 (d, $^3J_{C\text{-}F}$ = 9.3 Hz, C-5), 140.57 (d, $^3J_{C\text{-}F}$ = 10.9 Hz, C-1), 162.00 (d, $^1J_{C\text{-}F}$ = 241.8 Hz, C-3), 171.96 (CONH), 172.93 (C-5′) ppm; MS (ESI, 20 eV): *m/z* (%) = 238 ([M + H]$^+$, 100).

Methyl 5-oxo-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3-carboxylate (**2b**, $C_{13}H_{12}F_3NO_3$)

A mixture of 54.6 g 5-oxo-1-(3-(trifluoromethyl)phenyl) pyrrolidine-3-carboxylic acid (**1b**, 0.20 mol), 48.6 cm^3 methanol (1.20 mol), and 3 cm^3 sulfuric acid was stirred at reflux for 6 h, unreacted methanol was removed under reduced pressure, and 150 cm^3 10% Na_2CO_3 solution was added. The mixture was boiled and cooled. The product was extracted with diethyl ether (3 × 150 cm^3), the combined organic layers were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to give resin residue **2b** in 70.9% yield. It was used for the synthesis of **3b**. R_f = 0.48 (acetone: *n*-hexane, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.75–2.86 (m, 2H, CH_2CO), 3.28–3.39 (m, 1H, CH), 3.70 (s, 3H, OCH_3), 3.96–4.09 (m, 2H, NCH_2), 7.36–7.87 (m, 3H, H_{ar}) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 35.02 (C-3′), 35.19 (C-4′), 49.68 (C-2′), 52.20 (OCH_3), 115.85 (q, $^3J_{C\text{–}F}$ = 3.1 Hz, C-2), 120.72 (br s, C-4), 122.33 (C-6), 121.84 (q, $^1J_{C\text{–}F}$ = 272.0 Hz, CF_3), 129.12 (C-5), 130.68 (q, $^2J_{C\text{-}F}$ = 33.2 Hz, C-3), 139.52 (C-1), 171.57 (CONH), 172.35 (C-5′) ppm.

*General procedure for preparation of 5-oxopyrrolidine-3-carbohydrazides **3a** and **3b***

A mixture of 47.45 g **2a** or 57.45 g **2b** (0.20 mol), 29.3 cm^3 hydrazine hydrate (0.60 mol), and 75 cm^3 2-propanol was heated under reflux for 1 h and cooled. Crystalline material **3** was isolated by filtration and purified.

1-(3-Fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**3a**, $C_{11}H_{12}FN_3O_2$)

M.p.: 204–205 °C (from 2-propanol); yield 87.7%; IR (KBr): $\bar{\nu}$ = 3,313 (NH), 3,170 (NH_2), 1,682 (C=O), 1,635 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.59–2.78 (m, 2H, CH_2CO), 3.11–3.21 (m, 1H, CH), 3.81–4.02 (m, 2H, NCH_2), 4.30 (s, 2H, NH_2), 6.93–7.69 (m, 4H, H_{ar}), 9.30 (s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 33.90 (C-3′), 35.89 (C-4′), 50.68 (C-2′), 106.11 (d, $^2J_{C\text{-}F}$ = 26.3 Hz, C-2), 110.44 (d, $^2J_{C\text{-}F}$ = 21.0 Hz, C-4), 114.68 (br s, C-6), 130.35 (d, $^3J_{C\text{-}F}$ = 9.4 Hz, C-5), 140.75 (d, $^3J_{C\text{-}F}$ = 10.9 Hz, C-1), 162.03 (d, $^1J_{C\text{-}F}$ = 241.7 Hz, C-3), 171.43 (CONH), 172.93 (C-5′) ppm; MS (ESI, 20 eV): *m/z* (%) = 238 ([M + H]$^+$, 100).

5-Oxo-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3-carbohydrazide (**3b**, $C_{12}H_{12}F_3N_3O_2$)

M.p.: 165–166 °C (from ethanol); yield 57.4%; IR (KBr): $\bar{\nu}$ = 3,323 (NH), 3,284 (NH_2), 1,687 (C=O), 1,637 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.63–2.70 (m, 2H, CH_2CO), 3.16–3.31 (m, 1H, CH), 3.91–4.12 (m, 2H, CH_2N), 4.33 (s, 2H, NH_2), 7.50–8.21 (m, 4H, H_{ar}), 9.32

(s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 33.63 (C-3′), 35.42 (C-4′), 50.21 (C-2′), 115.09 (q, $^3J_{C\text{-}F}$ = 3.0 Hz, C-2), 119.88 (br s, C-4), 122.24 (C-6), 123.84 (q, $^1J_{C\text{-}F}$ = 272.2 Hz, CF_3), 129.02 (q, $^2J_{C\text{-}F}$ = 31.5 Hz, C-3), 129.63 (C-5), 139.42 (C-1), 171.01 (CONH), 172.42 (C-5′) ppm; MS (ESI, 20 eV): *m/z* (%) = 288 ($[M + H]^+$, 100).

General procedure for preparation of N'-benzylidene-5-oxopyrrolidine-3-carbohydrazides ***4a–10a***

A mixture of the appropriate benzaldehyde (7.5 mmol), 1.19 g 5-oxopyrrolidine-3-carbohydrazide **3a** (5.0 mmol), and 10 cm^3 1,4-dioxane was heated under reflux for 3 h. After cooling the product was isolated by filtration, washed with 2-propanol, and dried.

N′-Benzylidene-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**4a**, $C_{18}H_{16}FN_3O_2$)
M.p.: 182–183 °C (from 1,4-dioxane); yield 83.7%; IR (KBr): $\bar{\nu}$ = 3,068 (NH), 2,966 (N=CH), 1,696 (C=O), 1,677 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.72–2.92 (m, 2H, CH_2CO), 3.30–3.41 (m, 0.3(1H), *s-cis*, CH), 3.96–4.19 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.93–7.73 (m, 9H, H_{ar}), 8.04, 8.22 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, N=CH), 11.62, 11.67 (2s, (0.7/03)(1H), *s-cis/s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.37, 34.33 (*s-cis/s-trans*, C-3′), 34.75, 35.47 (*s-cis/s-trans*, C-4′), 49.71, 50.18 (*s-cis/s-trans*, C-2′), 106.15 (d, $^2J_{C\text{-}F}$ = 26.4 Hz, *s-cis*, C-2), 106.25 (d, $^2J_{C\text{-}F}$ = 26.5 Hz, *s-trans*, C-2), 110.48 (d, $^2J_{C\text{-}F}$ = 21.0 Hz, C-4), 114.82 (br s, C-6), 126.92, 127.10 (C-2″, C-6″), 128.83 (C-3″, C-5″), 129.92, 130.14 (C-4″), 130.35 (d, $^3J_{C\text{-}F}$ = 9.5 Hz, C-5), 134.11 (C-1″), 140.73 (d, $^3J_{C\text{-}F}$ = 10.4 Hz, *s-cis*, C-1), 140.80 (d, $^3J_{C\text{-}F}$ = 10.8 Hz, *s-trans*, C-1), 143.37, 147.09 (*s-cis/s-trans*, N=CH), 162.08 (d, $^1J_{C\text{-}F}$ = 241.4 Hz, C-3), 168.59 (*s-cis*, CONH) 172.40, 172.60 (*s-cis/s-trans*, C-5′), 173.46 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 326 ($[M + H]^+$, 100).

N′-(4-Fluorobenzylidene)-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**5a**, $C_{18}H_{15}F_2N_3O_2$)
M.p.: 213–214 °C (from 1,4-dioxane); yield 90.9%; IR (KBr): $\bar{\nu}$ = 3,124 (NH), 2,971 (N=CH), 1,688 (C=O), 1,679 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71–2.93 (m, 2H, CH_2CO), 3.29–3.41 (m, 0.3(1H), *s-cis*, CH), 3.92–4.21 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.92–7.74 (m, 8H, H_{ar}), 8.03, 8.23 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, N=CH), 11.62, 11.69 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.62, 34.60 (*s-cis/s-trans*, C-3′), 35.02, 35.76 (*s-cis/s-trans*, C-4′), 49.99, 50.46 (*s-cis/s-trans*, C-2′), 106.17, 106.26 (2d, $^2J_{C\text{-}F}$ = 26.5 Hz, *s-cis/s-trans*, C-2), 110.50 (d, $^2J_{C\text{-}F}$ = 20.7 Hz, C-4), 114.86 (br s, C-6), 115.89 (d, $^2J_{C\text{-}F}$ = 22.0 Hz, C-3″, C-5″), 129.12 (d, $^3J_{C\text{-}F}$ = 8.5 Hz, *s-cis*, C-2″, C-6″), 129.29 (d, $^3J_{C\text{-}F}$ = 9.2 Hz, *s-trans*, C-2″, C-6″), 130.36 (d, $^3J_{C\text{-}F}$ = 9.4 Hz, C-5), 130.75 (d, $^4J_{C\text{-}F}$ = 2.0 Hz, C-1″), 140.74 (d, $^3J_{C\text{-}F}$ = 10.7 Hz, *s-cis*, C-1), 140.80 (d, $^3J_{C\text{-}F}$ = 10.9 Hz, *s-trans*, C-1), 142.60, 145.98 (*s-cis/s-trans*, N=CH), 162.09 (d, $^1J_{C\text{-}F}$ = 241.7 Hz, C-3), 163.01 (d, $^1J_{C\text{-}F}$ = 247.7 Hz, C-4″), 168.63 (*s-cis*, CONH), 172.42, 172.61 (*s-cis/s-trans*, C-5′), 173.46 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 344 ($[M + H]^+$, 100).

N′-(4-Chlorobenzylidene)-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**6a**, $C_{18}H_{15}ClFN_3O_2$)
M.p.: 225–226 °C (from 1,4-dioxane); yield 83.6%; IR (KBr): $\bar{\nu}$ = 3,130 (NH), 2,970 (N=CH), 1,681 (2×C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71–2.92 (m, 2H, CH_2CO), 3.30–3.41 (m, 0.3(1H), *s-cis*, CH), 3.95–4.18 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.93-7.76 (m, 8H, H_{ar}), 8.03, 8.21 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, N=CH), 11.68, 11.73 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.68, 34.67 (*s-cis/s-trans*, C-3′), 35.07, 35.80 (*s-cis/s-trans*, C-4′), 50.02, 50.48 (*s-cis/s-trans*, C-2′), 106.16, 106.25 (2d, $^2J_{C\text{-}F}$ = 26.5 Hz, (*s-cis/s-trans*, C-2), 110.49 (d, $^2J_{C\text{-}F}$ = 20.8 Hz, C-4), 114.76, 114.84 (2 br s, *s-cis/s-trans*, C-6), 128.58, 128.73 (C-2″, C-6″), 129.91 (C-3″, C-5″), 130.34 (d, $^3J_{C\text{-}F}$ = 9.2 Hz, C-5), 133.07 (C-1″), 134.35, 134.58 (C-4″), 140.72 (d, $^3J_{C\text{-}F}$ = 10.2 Hz, *s-cis*, C-1), 140.78 (d, $^3J_{C\text{-}F}$ = 11.3 Hz, *s-trans*, C-1), 142.46, 145.77 (*s-cis/s-trans*, N=CH), 162.08 (d, $^1J_{C\text{-}F}$ = 241.6 Hz, C-3), 168.70 (*s-cis*, CONH), 172.38, 172.56 (*s-cis/s-trans*, C-5′), 173.52 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 360 (M^+, 100), 362 ($[M + H + 1]^+$, 33).

N′-(4-Bromobenzylidene)-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**7a**, $C_{18}H_{15}BrFN_3O_2$)
M.p.: 223–224 °C (from 1,4-dioxane); yield 83.1%; IR (KBr): $\bar{\nu}$ = 3,132 (NH), 2,966 (N=CH), 1,690 (C=O), 1,670 (C=O), 514 (C–Br) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71–2.92 (m, 2H, CH_2CO), 3.30–3.40 (m, 0.3(1H), *s-cis*, CH), 3.95–4.18 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.93–7.73 (m, 8H, H_{ar}), 8.01, 8.19 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, N=CH), 11.68, 11.75 (2s, (0.7/0.3)(1H), *s-cis/s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.68, 34.67 (*s-cis/s-trans*, C-3′), 35.08, 35.80 (*s-cis/s-trans*, C-4′), 50.02, 50.48 (*s-cis/s-trans*, C-2′), 106.16 (d, $^2J_{C\text{-}F}$ = 26.8 Hz, *s-cis*, C-2), 106.25 (d, $^2J_{C\text{-}F}$ = 26.3 Hz, *s-trans*, C-2), 110.50 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 114.76, 114.86 (2 br s, *cis/s-trans*, C-6), 123.14, 123.41 (C-4″), 128.82, 128.93 (C-2″, C-6″), 30.36 (d, $^3J_{C\text{-}F}$ = 9.0 Hz, C-5), 131.82 (C-3″, C-5″), 133.41 (C-1″), 140.74 (d, $^3J_{C\text{-}F}$ = 11.4 Hz, *s-cis*, C-1), 140.79 (d, $^3J_{C\text{-}F}$ = 10.6 Hz, *s-trans*, C-1), 142.57, 145.85 (*s-cis/s-trans*, N=CH), 162.09 (d, $^1J_{C\text{-}F}$ = 241.5 Hz, C-3), 168.70

(*s-cis*, CONH), 172.38, 172.57 (*s-cis*/*s-trans*, C-5′), 173.52 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 404 (M^+, 95), 406 ($[M + H + 1]^+$, 100).

N′-(4-(Dimethylamino)benzylidene)-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carbohydrazide (**8a**, $C_{20}H_{21}FN_4O_2$)
M.p.: 229–230 °C (from 1,4-dioxane); yield 68.7%; IR (KBr): $\bar{\nu}$ = 3,084 (NH), 2,955 (N=CH), 1,690 (C=O), 1,664 (C=O), 1,613 ($N(CH_3)_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.72–2.93 (m, 2H, CH_2CO), 2.96 (s, 6H, $N(CH_3)_2$), 3.29–3.41 (m, 0.3(1H), *s-cis*, CH), 3.96–4.22 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.71–7.74 (m, 8H, H_{ar}), 7.90, 8.06 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, N=CH), 11.33, 11.38 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.63, 34.55 (*s-cis*/*s-trans*, C-3′), 35.05, 35.84 (*s-cis*/*s-trans*, C-4′), 50.09, 50.59 (*s-cis*/*s-trans*, C-2′), 39.78 ($N(CH_3)_2$), 106.13, 106.22 (d, $^2J_{C\text{-}F}$ = 26.3 Hz, *s-cis*/*s-trans*, C-2), 110.46 (d, $^2J_{C\text{-}F}$ = 21.0 Hz, C-4), 111.79 (C-3″, C-5″), 114.80 (br s, C-6), 121.31, 121.48 (C-1″), 128.18, 128.44 (C-2″, C-6″), 130.36 (d, $^3J_{C\text{-}F}$ = 9.5 Hz, C-5), 140.77 (d, $^3J_{C\text{-}F}$ = 11.4 Hz, *s-cis*, C-1), 140.83 (d, $^3J_{C\text{-}F}$ = 10.6 Hz, *s-trans*, C-1), 144.51, 147.86 (*s-cis*/*s-trans*, N=CH), 151.36, 151.53 (C-4″), 162.08 (d, $^1J_{C\text{-}F}$ = 241.3 Hz, C-3), 167.94 (*s-cis*, CONH), 172.51, 172.71 (*s-cis*/*s-trans*, C-5′), 172.81 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 369 ($[M + H]^+$, 100).

1-(3-Fluorophenyl)-N′-(4-methoxybenzylidene)-5-oxopyrrolidine-3-carbohydrazide (**9a**, $C_{19}H_{18}FN_3O_3$)
M.p.: 197–198 °C (from 1,4-dioxane); yield 85.6%; IR (KBr): $\bar{\nu}$ = 3,240 (NH), 3,087 (N=CH), 1,674 (C=O), 1,655 (C=O), 1,252 (OCH_3) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.69–2.91 (m, 2H, CH_2CO), 3.29–3.39 (m, 0.3(1H), *s-cis*, CH), 3.79, 3.80 (2s, 3H, *s-cis*/*s-trans*, OCH_3), 3.93–4.18 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.93–7.76 (m, 8H, H_{ar}), 8.03, 8.22 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, N=CH), 11.68, 11.73 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.63, 34.58 (*s-cis*/*s-trans*, C-3′), 35.04, 35.79 (*s-cis*/*s-trans*, C-4′), 50.04, 50.52 (*s-cis*/*s-trans*, C-2′), 55.23 (OCH_3), 106.07, 106.19 (d, $^2J_{C\text{-}F}$ = 26.4 Hz, *s-cis*/*s-trans*, C-2), 110.42 (d, $^2J_{C\text{-}F}$ = 21.0 Hz, C-4), 114.25 (C-3″, 5″), 114.75 (br s, C-6), 126.58, 126.65 (C-1″), 128.44, 128.66 (C-2″, 6″), 130.30 (d, $^3J_{C\text{-}F}$ = 9.2 Hz, C-5), 140.69, 140.76 (2d, $^3J_{C\text{-}F}$ = 10.6 Hz, *s-cis*/*s-trans*, C-1), 143.53, 146.91 (*s-cis*/*s-trans*, N=CH), 160.42, 160.81 (C-4″), 162.12 (d, $^1J_{C\text{-}F}$ = 241.3 Hz, C-3), 168.27 (*s-cis*, CONH), 172.38, 172.59 (*s-cis*/*s-trans*, C-5′), 173.13 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 356 ($[M + H]^+$, 100).

1-(3-Fluorophenyl)-N′-(4-nitrobenzylidene)-5-oxopyrrolidine-3-carbohydrazide (**10a**, $C_{18}H_{15}FN_4O_4$)
M.p.: 231–232 °C (from 1,4-dioxane); yield 88.6%; IR (KBr): $\bar{\nu}$ = 3,130 (NH), 2,976 (N=CH), 1,691 (C=O), 1,660 (C=O), 1,531 and 1,342 (NO_2) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.70–2.91 (m, 2H, CH_2CO), 3.28–3.39 (m, 0.3(1H), *s-cis*, CH), 3.92–4.20 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.92–8.31 (m, 9H, H_{ar} + N=CH), 11.90, 11.98 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.73, 34.75 (*s-cis*/*s-trans*, C-3′), 35.06, 35.78 (*s-cis*/*s-trans*, C-4′), 49.95, 50.41 (*s-cis*/*s-trans*, C-2′), 106.17 (d, $^2J_{C\text{-}F}$ = 26.7 Hz, *s-cis*, C-2), 106.21 (d, $^2J_{C\text{-}F}$ = 26.2 Hz, *s-trans*, C-2), 110.51 (d, $^2J_{C\text{-}F}$ = 20.8 Hz, C-4), 114.84 (br s, C-6), 124.01 (C-3″, C-5″), 127.86, 128.01 (C-2″, C-6″), 130.35 (d, $^3J_{C\text{-}F}$ = 9.5 Hz, C-5), 141.41 (C-1″), 140.72 (d, $^3J_{C\text{-}F}$ = 11.1 Hz, *s-cis*, C-1), 140.76 (d, $^3J_{C\text{-}F}$ = 10.5 Hz, *s-trans*, C-1), 141.42, 144.63 (*s-cis*/*s-trans*, N=CH), 147.69, 147.85 (C-4″), 162.09 (d, $^1J_{C\text{-}F}$ = 241.5 Hz, C-3), 169.08 (*s-cis*, CONH), 172.32, 172.50 (*s-cis*/*s-trans*, C-5′), 173.86 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 371 ($[M + H]^+$, 50).

General procedure for preparation of N′-benzylidene-5-oxopyrrolidine-3-carbohydrazides ***4b–10b***

A mixture of the appropriate benzaldehyde (7.5 mmol), 1.44 g 5-oxopyrrolidine-3-carbohydrazide **3b** (5.0 mmol), and 10 cm^3 1,4-dioxane was heated under reflux for 3 h. After cooling, the crude product was isolated by filtration and washed with 2-propanol.

N′-Benzylidene-5-oxo-1-(3-(trifluoromethyl)phenyl)-pyrrolidine-3-carbohydrazide (**4b**, $C_{19}H_{16}F_3N_3O_2$)
M.p.: 196–197 °C (from 1,4-dioxane); yield 64.0%; IR (KBr): $\bar{\nu}$ = 3,134 (NH), 2,979 (N=CH), 1,688 (2×C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.71–2.95 (m, 2H, CH_2CO), 3.29–3.41 (m, 0.3(1H), *s-cis*, CH), 4.02–4.25 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 7.04–8.22 (m, 9H, H_{ar} + 1H, N=CH), 11.62, 11.67 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.78, 34.73 (*s-cis*/*s-trans*, C-3′), 34.98 (C-4′), 49.92, 50.38 (*s-cis*/*s-trans*, C-2′), 115.66 (br s, C-2), 120.32 (br s, C-4), 122.78 (C-6), 123.67 (q, $^1J_{C\text{-}F}$ = 272.3 Hz, CF_3), 126.89, 127.07 (C-2″, C-6″), 128.81 (C-3″, C-5″), 128.81 (C-5), 129.76 (q, $^2J_{C\text{-}F}$ = 33.0 Hz, C-3), 130.02 (C-4″), 134.09 (C-1″), 139.82 (C-1), 143.73, 147.08 (*s-cis*/*s-trans*, N=CH), 168.50 (*s-cis*, CONH), 172.81, 172.93 (*s-cis*/*s-trans,* C-5′), 173.93 (*s-trans,* CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 376 ($[M + H]^+$, 100).

N′-(4-Fluorobenzylidene)-5-oxo-1-(3-(trifluoromethyl)-phenyl)pyrrolidine-3-carbohydrazide
(**5b**, $C_{19}H_{15}F_4N_3O_2$)
M.p.: 221–222 °C (from 1,4-dioxane); yield 99.7%; IR (KBr): $\bar{\nu}$ = 3,128 (NH), 2,968 (N=CH), 1,687 (C=O), 1,678 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.74–2.95 (m, 2H, CH_2CO), 3.33–3.43 (m, 0.3(1H),

s-cis, CH), 4.02–4.24 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 7.23–8.23 (m, 8H, H_{ar} + 1H, N=CH), 11.62, 11.67 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.79, 34.76 (*s-cis*/*s-trans,* C-3′), 35.02, 35.72 (*s-cis*/*s-trans,* C-4′), 49.95, 50.43 (*s-cis*/*s-trans,* C-2′), 115.67 (q, $^3J_{C\text{-}F}$ = 3.1 Hz, C-2), 115.87 (C-3″, C-5″), 120.29 (br s, C-4), 122.65, 122.74 (*s-cis*/*s-trans*, C-6), 124.09 (q, $^1J_{C\text{-}F}$ = 272.4 Hz, CF_3), 129.11 (d, $^3J_{C\text{-}F}$ = 8.9 Hz, *s-cis*, C-2″, C-6″), 129.28 (d, $^3J_{C\text{-}F}$ = 9.1 Hz, *s-trans*, C-2″, C-6″), 130.77 (C-5), 129.81 (q, $^2J_{C\text{-}F}$ = 29.0 Hz, C-3), 130.76 (br s, C-1″), 139.80 (br s, C-1), 142.55, 145.84 (*s-cis*/*s-trans*, N=CH), 163.01 (d, $^1J_{C\text{-}F}$ = 247.3 Hz, *s-cis*, C-4″), 163.16 (d, $^1J_{C\text{-}F}$ = 248.4 Hz, *s-trans*, C-4″), 168.60 (*s-cis*, CONH), 172.56, 172.75 (*s-cis*/*s-trans*, C-5′), 173.56 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 394 ($[M + H]^+$, 100).

N′-(4-Chlorobenzylidene)-5-oxo-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3-carbohydrazide
(**6b**, $C_{19}H_{15}ClF_3N_3O_2$)
M.p.: 238–239 °C (from 1,4-dioxane); yield 95.7%; IR (KBr): $\bar{\nu}$ = 3,132 (NH), 3,201 (N=CH), 1,688 (C=O), 1,667 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.74–2.95 (m, 2H, CH_2CO), 3.32–3.23 (m, 0.3(1H), *s-cis*, CH), 4.02–4.23 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 7.40–8.22 (m, 8H, H_{ar} + 1H, N=CH), 11.66, 11.73 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.74, 34.73 (*s-cis*/*s-trans*, C-3′), 34.97, 35.63 (*s-cis*/*s-trans*, C-4′), 49.88, 50.36 (*s-cis*/*s-trans*, C-2′), 115.51 (q, $^3J_{C\text{-}F}$ = 4.2 Hz, *s-cis*, C-2), 115.61 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, *s-trans*, C-2), 120.26 (br s, C-4), 122.63, 122.73 (*s-cis*/*s-trans*, C-6), 124.01 (q, $^1J_{C\text{-}F}$ = 272.4 Hz, CF_3), 128.54, 128.69 (C-2″, C-6″), 129.36 (d, $^2J_{C\text{-}F}$ = 31.7 Hz, C-3), 129.95 (C-3″, C-5″), 133.05 (C-1″), 134.32, 134.56 (C-4″), 139.74, 139.79 (C-1), 142.46, 145.77 (*s-cis*/*s-trans*, N=CH), 168.59 (*s-cis*, CONH), 172.57, 172.75 (*s-cis*/*s-trans*, C-5′), 173.45 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 410 ($[M + H]^+$, 100), 412 ($[M + H + 1]^+$, 33).

N′-(4-Bromobenzylidene)-5-oxo-1-(3-(trifluoromethyl)-phenyl)pyrrolidine-3-carbohydrazide
(**7b**, $C_{19}H_{15}BrF_3N_3O_2$)
M.p.: 200–201 °C (from 2-propanol); yield 91.5%; IR (KBr): $\bar{\nu}$ = 3,136 (NH), 2,978 (N=CH), 1,687 (C=O), 1,664 (C=O), 693 (C–Br) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.72–2.94 (m, 2H, CH_2CO), 3.31–3.43 (m, 0.3(1H), *s-cis*, CH), 4.01–4.23 (m, 0.7(1H), *s-trans*, CH + 2H, CH_2N), 7.47–8.21 (m, 8H, H_{ar} + 1H, N=CH), 11.67, 11.73 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.74, 34.73 (*s-cis*/*s-trans*, C-3′), 34.97, 35.63 (*s-cis*/*s-trans*, C-4′), 49.88, 50.35 (*s-cis*/*s-trans*, C-2′), 115.51 (q, $^3J_{C\text{-}F}$ = 4.3 Hz, *s-cis*, C-2), 115.61 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, *s-trans*, C-2), 120.22 (br s, C-4), 122.65, 122.74 (*s-cis*/*s-trans*, C-6), 123.09, 123.35 (C-4″), 124.04 (q, $^1J_{C\text{-}F}$ = 272.5 Hz, CF_3), 128.78, 128.92 (C-2″, C-6″), 129.35 (q, $^2J_{C\text{-}F}$ = 31.8 Hz, C-3), 129.97 (C-5), 131.78 (C-3″, C-5″), 133.38 (C-1″), 139.79 (C-1), 142.55, 145.84 (*s-cis*/*s-trans*, N=CH), 168.60 (*s-cis*, CONH), 172.56, 172,75 (*s-cis*/*s-trans*, C-5′), 173.46 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 454 (M^+, 97.5), 456 ($[M + H + 1]^+$, 100).

N′-(4-(Dimethylamino)benzylidene)-5-oxo-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3-carbohydrazide
(**8b**, $C_{21}H_{21}F_3N_4O_2$)
M.p.: 238–239 °C (from 1,4-dioxane); yield 91.0%; IR (KBr): $\bar{\nu}$ = 3,246 (NH), 2,931 (N=CH), 1,690 (C=O), 1,657 (C=O), 1,603 ($N(CH_3)_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.81–2.96 (m, 2H, CH_2CO), 2.97, 2.98 (2s, 6H, $N(CH_3)_2$), 3.31–3.43 (m, 0.3(1H), *s-cis*, CH), 4.13–4.25 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.72–8.31 (m, 8H, H_{ar} + 1H, N=CH), 11.33, 11.37 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.78, 34.68 (*s-cis*/*s-trans*, C-3′), 39.78 ($N(CH_3)_2$), 35.02, 35.75 (*s-cis*/*s-trans*, C-4′), 50.01, 50.52 (*s-cis*/*s-trans*, C-2′), 111.75 (C-3″, C-5″), 115.56 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, *s-cis*, C-2), 115.59 (q, $^3J_{C\text{-}F}$ = 3.5 Hz, *s-trans*, C-2), 120.22 (br s, C-4), 121.30, 121.46 (C-1″), 122.62, 122.69 (*s-cis*/*s-trans*, C-6), 124.05 (q, $^1J_{C\text{-}F}$ = 272.5 Hz, CF_3), 128.13, 128.39 (C-2″, C-6″), 129.35 (q, $^2J_{C\text{-}F}$ = 31.9 Hz, C-3), 129.97 (C-5), 139.77, 139.84 (*s-cis*/*s-trans*, C-1), 144.49, 147.88 (*s-cis*/*s-trans*, N=CH), 151.35, 151.51 (C-4″), 167.83 (*s-cis*, CONH), 172.73, 172.89 (*s-cis*/*s-trans*, C-5′), 173.73 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 419 ($[M + H]^+$, 100).

N′-(4-Methoxybenzylidene)-5-oxo-1-(3-(trifluoromethyl)-phenyl)pyrrolidine-3-carbohydrazide
(**9b**, $C_{20}H_{18}F_3N_3O_3$)
M.p.: 164–165 °C (from 2-propanol); yield 94.8%; IR (KBr): $\bar{\nu}$ = 3,211 (NH), 2,961 (N=CH), 1,688 (C=O), 1,678 (C=O), 1,607 (OCH_3) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.73–2.93 (m, 2H, CH_2CO), 3.30–3.41 (m, 0.3(1H), *s-cis*, CH), 3.78, 3.79 (2s, 3H, *s-cis*/*s-trans*, OCH_3), 4.01–4.23 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 6.96–8.23 (m, 8H, H_{ar} + 1H, N=CH), 11.50, 11.56 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.74, 34.68 (*s-cis*/*s-trans,* C-3′), 34.97, 35.69 (*s-cis*/*s-trans,* C-4′), 49.93, 50.43 (*s-cis*/*s-trans,* C-2′), 55.21 (OCH_3), 114.24 (C-3″, C-5″), 115.59 (br s, C-2), 120.18 (br s, C-4), 122.57 (C-5), 122.57 (C-6), 124.47 (q, $^1J_{C\text{-}F}$ = 272.6 Hz, CF_3), 126.66 (C-1″), 128.44 (C-2″, C-6″), 128.44 (C-5), 129.94 (C-3), 139.79 (C-1), 143.55, 146.91 (*s-cis*/*s-trans*, N=CH), 160.62, 160.81 (C-4″), 168.21 (*s-cis*, CONH), 172.64, 172.83 (*s-cis*/*s-trans*, C-5′), 173.09 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 406 ($[M + H]^+$, 100).

N′-(4-Nitrobenzylidene)-5-oxo-1-(3-(trifluoromethyl)-phenyl)pyrrolidine-3-carbohydrazide
(**10b**, $C_{19}H_{15}F_3N_4O_4$)
M.p.: 233–234 °C (from 1,4-dioxane); yield 97.5%; IR (KBr): $\bar{\nu}$ = 3,204 (NH), 2,976 (N=CH), 1,689 (C=O), 1,657 (C=O), 1,529 and 1,345 (NO_2) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.78–2.97 (m, 2H, CH_2CO), 3.30–3.46 (m, 0.3(1H), *s-cis*, CH), 4.04–4.26 (m, 0.7(1H), *s-trans*, CH + 2H, NCH_2), 7.48–8.43 (m, 8H, H_{ar} + 1H, N=CH), 11.90, 11.96 (2s, (0.7/0.3)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 32.78, 34.79 (*s-cis*/*s-trans,* C-3′), 34.93, 35.05 (*s-cis*/*s-trans,* C-4′), 49.82, 50.23 (*s-cis*/*s-trans,* C-2′), 115.61 (q, $^3J_{C\text{-}F}$ = 4.3 Hz, C-2), 120.32 (br s, C-4), 122.68, 122.80 (*s-cis*/*s-trans*, C-6), 123.72 (q″ $^1J_{C\text{-}F}$ = 272.4 Hz, CF_3), 123.99, 124.04 (C-3″, C-5″), 127.88, 128.01 (C-2″, C-6″), 129.37 (q, $^2J_{C\text{-}F}$ = 31.6 Hz, C-3), 129.99 (C-5), 139.70 (C-1), 140.38, 140.43 (C-1″), 141.42, 144.42 (*s-cis*/*s-trans,* N=CH), 147.73, 147.88 (C-4″), 168.97 (*s-cis*, CONH), 172.70 (C-5′), 173.81 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 421 ($[M + H]^+$, 100).

General procedure for preparation of N′-isopropylidene-5-oxopyrrolidine-3-carbohydrazides ***11a*** *and* ***11b***

A mixture of the appropriate hydrazide **3** (5.0 mmol) and 30 cm^3 acetone was heated under reflux for 3 h. When acetone was removed under reduced pressure the product crystallized.

1-(3-Fluorophenyl)-N′-isopropylidene-5-oxopyrrolidine-3-carbohydrazide (**11a**, $C_{14}H_{16}FN_3O_2$)
M.p.: 167–168 °C (from 1,4-dioxane); yield 76.5%; IR (KBr): $\bar{\nu}$ = 3,237 (NH), 1,694 (C=O), 1,657 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.87, 1.88 (2s, (0.5/0.5)(3H), (*Z*)/*s-cis*/*s-trans*, CH_3), 1.93 (s, 3H, (*E*)/*s-cis*/*s-trans*, CH_3), 2.63–2.83 (m, 2H, CH_2CO), 3.36–3.49 (m, 0.5(1H), *s-cis*, CH), 3.86–4.12 (m, 0.5(1H), *s-trans*, CH + 2H, NCH_2), 6.91–7.70 (m, 4H, H_{ar}), 10.25, 10.34 (2s, (0.5/0.5)(1H), *s-cis*/*s-trans*, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 17.16, 17.65 ((*Z*)/*s-cis*/*s-trans*, CH_3), 24.97, 25.27 ((*E*)/*s-cis*/*s-trans*, CH_3), 32.79, 34.14 (*s-cis*/*s-trans*, C-3′), 35.14, 36.00 (*s-cis*/*s-trans*, C-4′), 50.17, 50.83 (*s-cis*/*s-trans*, C-2′), 106.09 (d, $^2J_{C\text{-}F}$ = 26.3 Hz, *s-cis*, C-2), 106.21 (d, $^2J_{C\text{-}F}$ = 26.4 Hz, *s-trans*, C-2), 110.43 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 114.70, 114.80 (*s-cis*/*s-trans*, C-6), 130.33 (d, $^3J_{C\text{-}F}$ = 9.5 Hz, C-5), 140.70 (d, $^3J_{C\text{-}F}$ = 10.7 Hz, *s-cis*, C-1), 140.77 (d, $^3J_{C\text{-}F}$ = 10.9 Hz, *s-trans*, C-1), 151.35, 156.25 (*s-cis*/*s-trans*, C=N), 162.07 (d, $^1J_{C\text{-}F}$ = 241.7 Hz, C-3), 168.53 (*s-cis*, CONH), 172.60, 172.69 (*s-cis*/*s-trans*, C-5′), 173.56 (*s-trans*, CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 278 ($[M + H]^+$, 100).

N′-Isopropylidene-5-oxo-1-(3-(trifluoromethyl)-phenyl)pyrrolidine-3-carbohydrazide
(**11b**, $C_{15}H_{16}F_3N_3O_2$)
M.p.: 127–128 °C (from ethanol); yield 34.3%; IR (KBr): $\bar{\nu}$ = 3,266 (NH), 1,690 (C=O), 1,658 (C=O, N=C(CH_3)$_2$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.87, 1.88 (2s, (0.5/0.5)(3H), (*Z*)/*s-cis*/*s-trans*, CH_3), 1.94 (s, 3H, (*E*)/*s-cis*/*s-trans*, CH_3), 2.65–2.85 (m, 2H, CH_2CO), 3.39–3.51 (m, 0.5(1H), *s-cis*, CH), 3.90–4.17 (m, 0.5(1H), *s-trans*, CH + 2H, NCH_2), 7.48–8.20 (m, 4H, H_{ar}), 10.23, 10.34 (2s, (0.5/0.5)(1H), *s-cis*/*s-trans*, NH) ppm; MS (ESI, 20 eV): *m/z* (%) = 328 ($[M + H]^+$, 100).

General procedure for preparation of 4-((3,5-dimethyl-1H-pyrazol-1-yl)carbonyl)pyrrolidin-2-ones ***12a*** *and* ***12b***

A mixture of 1.19 g appropriate hydrazide **3** (5.0 mmol), 1.5 g 2,4-pentanedione (15.0 mmol), 15 cm^3 2-propanol, and 0.5 cm^3 hydrochloric acid was heated under reflux for 5 h, then cooled. The precipitate **12** was isolated by filtration and washed with 2-propanol.

4-((3,5-Dimethyl-1H-pyrazol-1-yl)carbonyl)-1-(3-fluorophenyl)pyrrolidin-2-one (**12a**, $C_{16}H_{16}FN_3O_2$)
M.p.: 133–134 °C (from 2-propanol); yield 59.8%; IR (KBr): $\bar{\nu}$ = 1,716 (C=O), 1,703 (C=O), 1,395 (2×CH_3) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.21 (s, 3H, CHC*CH*$_3$), 2.48 (d, 3H, ^4J = 0.6 Hz, HC = C*CH*$_3$), 2.81–2.98 (m, 2H, CH_2CO), 4.01–4.24 (m, 2H, NCH_2), 4.41–4.53 (m, 1H, CH), 6.23 (q, 1H, ^4J = 0.6 Hz, *HC* = CCH_3), 6.94–7.70 (m, 4H, H_{ar}) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 13.59 (CHC*CH*$_3$), 14.06 (HC = C*CH*$_3$), 35.23 (C-3′ + C-4′), 50.11 (C-2′), 106.32 (d, $^2J_{C\text{-}F}$ = 26.3 Hz, C-2), 110.60 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 111.63 (*HC* = CCH_3), 114.80 (br s, C-6), 130.36 (d, $^3J_{C\text{-}F}$ = 9.4 Hz, C-5), 140.61 (d, $^3J_{C\text{-}F}$ = 10.9 Hz, C-1), 143.90 (HC = *C*CH_3), 152.18 (CH*C*CH_3), 162.05 (d, $^1J_{C\text{-}F}$ = 241.7 Hz, C-3), 172.07 (C-5′), 172.50 (C=O) ppm.

4-((3,5-Dimethyl-1H-pyrazol-1-yl)carbonyl)-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (**12b**, $C_{17}H_{16}F_3N_3O_2$)
M.p.: 165–166 °C (from 2-propanol); yield 31.8%; IR (KBr): $\bar{\nu}$ = 1,723 (C=O), 1,712 (C=O), 1,382 (2×CH_3) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.21 (s, 3H, CHC*CH*$_3$), 2.49 (d, 3H, J = 0.6 Hz, HC = C*CH*$_3$), 2.88 (dd, 1H, J = 6.9 Hz, J = 17.3 Hz, CH_2CO), 2.95 (dd, 1H, J = 9.1 Hz, J = 17.3 Hz, CH_2CO), 4.11 (dd, 1H, J = 5.5 Hz, J = 10.0 Hz, CH_2N), 4.27 (dd, 1H, J = 8.9 Hz, J = 10.0 Hz, CH_2N), 4.51 (dddd, 1H, J = 5.5 Hz, J = 6.9 Hz, J = 8.9 Hz, J = 9.1 Hz, CH), 6.23 (q, 1H, J = 0.6 Hz, *HC*=CCH_3), 7.49–8.18 (m, 4H, H_{ar}) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): δ = 13.55

(CHC*CH*$_3$), 13.94 (HC=C*CH*$_3$), 35.08 (C-3′), 35.27 (C-4′), 50.00 (C-2′), 111.60 (*HC*=CCH$_3$), 115.71 (q, $^3J_{C\text{-}F}$ = 4.0 Hz, C-2), 120.36 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, C-4), 122.88, 122.22 ((*Z*)/(*E*), C-6), 123.22 (q, $J_{C\text{-}F}$ = 272.5 Hz, CF$_3$), 129.36 (q, $^2J_{C\text{-}F}$ = 31.8 Hz, C-3), 129.97 (C-5), 139.64 (C-1), 143.89 (HC=*C*CH$_3$), 152.16 (CH*C*CH$_3$), 172.27 (C-5′), 172.43 (CO) ppm.

N-(2,5-Dimethyl-1H-pyrrol-1-yl)-1-(3-fluorophenyl)-5-oxopyrrolidine-3-carboxamide (**13a**, $C_{17}H_{18}FN_3O_2$)

A mixture of 1.19 g **3a** (5.0 mmol), 1.17 cm^3 2,5-hexanedione (10 mmol), 20 cm^3 2-propanol, and 1 cm^3 acetic acid was heated under reflux for 6 h. After cooling, the precipitate of **13a** was isolated by filtration, and washed with a small amount of 2-propanol then diethyl ether.

M.p.: 176–177 °C (from 2-propanol); yield 64.8%; IR (KBr): $\bar{\nu}$ = 3,280 (NH), 1,693 (C=O), 1,671 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.00 (s, 6H, 2CH$_3$), 2.72–2.98 (m, 2H, CH$_2$CO), 3.36–3.53 (m, 1H, CH), 3.96–4.18 (m, 2H, NCH$_2$), 5.65 (s, 2H, CH-CH), 6.95–7.72 (m, 4H, H$_{ar}$), 10.94 (s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 10.94 (2CH$_3$), 33.91 (C-3′), 35.81 (C-4′), 50.33 (C-2′), 103.08 (2 CH$_3$C=*CH*), 106.17 (d, $^2J_{C\text{-}F}$ = 26.8 Hz, C-2), 110.57 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 114.82, 114.90 (*s-cis*/*s-trans*, C-6), 126.66 (2 CH$_3$*C*=CH), 130.30 (d, $^3J_{C\text{-}F}$ = 9.7 Hz, C-5), 140.55 (d, $^3J_{C\text{-}F}$ = 10.5 Hz, C-1), 162.08 (d, $^1J_{C\text{-}F}$ = 242.1 Hz, C-3), 171.76 (C-5′), 172.07 (CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 316 ([M + H]$^+$, 100).

N-(2,5-Dimethyl-1H-pyrrol-1-yl)-5-oxo-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3-carboxamide (**13b**, $C_{18}H_{18}F_3N_3O_2$)

A mixture of 1.44 g **3b** (5.0 mmol), 1.17 cm^3 2,5-hexanedione (10.0 mmol), 20 cm^3 2-propanol, and 1 cm^3 acetic acid was heated under reflux for 3 h. Solvent was removed under reduced pressure and the crude product obtained was boiled in 100 cm^3 water, isolated by filtration while hot, washed with water, and dried.

M.p.: 168–169 °C (from *n*-hexane to toluene); yield 64.1%; IR (KBr): $\bar{\nu}$ = 3,267 (NH), 1,713 (C=O), 1,673 (C=O), 1,340 (2×CH$_3$) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.00 (s, 6H, 2CH$_3$), 2.74–3.00 (m, 2H, CH$_2$CO), 3.37–3.55 (m, 1H, CH), 4.03–4.24 (m, 2H, NCH$_2$), 5.65 (s, 2H, CH-CH), 7.49–8.22 (m, 4H, H$_{ar}$), 10.95 (s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 10.89, 10.92 (2CH$_3$), 33.98 (C-3′), 35.73 (C-4′), 50.15 (C-2′), 103.04 (2 CH$_3$C=*CH*), 115.58 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, C-2), 120.30 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, C-4), 122.71 (C-6), 123.96 (q, $J_{C\text{-}F}$ = 272.4 Hz, CF$_3$), 126.69 (2 CH$_3$*C*=CH), 129.36 (q, $^2J_{C\text{-}F}$ = 31.7 Hz, C-3), 129.98 (C-5), 139.65 (C-1), 171.68 (C-5′), 172.26 (CONH) ppm; MS (ESI, 20 eV): *m/z* (%) = 366 ([M + H]$^+$, 100).

General procedure for preparation of oxadiazolylpyrrolidin-2-ones ***14a*** *and* ***14b***

A mixture of the appropriate hydrazide **3** (5.0 mmol), 13.34 g triethyl orthoformate (90.0 mmol), and 0.1 g toluenesulfonic acid was heated under reflux for 7 h, cooled, and diluted with 50 cm^3 *n*-hexane. The crystalline product **14** obtained was isolated by filtration and dried.

1-(3-Fluorophenyl)-4-(1,3,4-oxadiazol-2-yl)pyrrolidin-2-one (**14a**, $C_{12}H_{10}FN_3O_2$)

M.p.: 112–113 °C (from 2-propanol); yield 81.0%; IR (KBr): $\bar{\nu}$ = 1,689 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.88–3.13 (m, 2H, CH$_2$CO), 4.09–4.35 (m, 1H, CH + 2H, NCH$_2$), 6.96–7.68 (m, 4H, H$_{ar}$), 9.25 (s, 1H, N=CH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 27.52 (C-3′), 36.07 (C-4′), 50.60 (C-2′), 106.43 (d, $^2J_{C\text{-}F}$ = 26.4 Hz, C-2), 110.75 (d, $^2J_{C\text{-}F}$ = 21.1 Hz, C-4), 115.02 (d, $^4J_{C\text{-}F}$ = 1.8 Hz, C-6), 130.40 (d, $^3J_{C\text{-}F}$ = 9.4 Hz, C-5), 140.52 (d, $^3J_{C\text{-}F}$ = 10.8 Hz, C-1), 154.97 (N=CH), 162.06 (d, $^1J_{C\text{-}F}$ = 241.6 Hz, C-3), 166.34 (N=C), 171.34 (C-5′) ppm; MS (ESI, 20 eV): *m/z* (%) = 248 ([M + H]$^+$, 100).

4-(1,3,4-Oxadiazol-2-yl)-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (**14b**, $C_{13}H_{10}F_3N_3O_2$)

M.p.: 95–96 °C (from 2-propanol); yield 56.6%; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 2.90–3.15 (m, 2H, CH$_2$CO), 4.10–4.22 (m, 1H, CH + 2H, CH$_2$N), 7.50–8.16 (m, 4H, H$_{ar}$), 9.25 (br s, 1H, N=CH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d$_6$): δ = 27.53 (C-3′), 35.90 (C-4′), 50.45 (C-2′), 115.86 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, C-2), 120.58 (q, $^3J_{C\text{-}F}$ = 3.6 Hz, C-4), 123.01 (C-6), 124.04 (q, $^1J_{C\text{-}F}$ = 272.7 Hz, CF$_3$), 129.44 (q, $^2J_{C\text{-}F}$ = 33.0 Hz, C-3), 130.04 (C-5), 139.58 (C-1), 154.98 (CH=N), 166.31 (C=N), 171.90 (C-5′) ppm; MS (ESI, 20 eV): *m/z* (%) = 298 ([M + H]$^+$, 100).

General procedure for preparation of 4-(4,5-dihydro-5-thioxo-1,3,4-oxadiazol-2-yl)pyrrolidin-2-ones ***15a*** *and* ***15b***

A mixture of 1.19 g **3a** or 1.44 g **3b** (5.0 mmol), 0.38 g carbon disulfide (5.0 mmol), 25 cm^3 2-propanol, and 0.28 g 80% potassium hydroxide (5.0 mmol) was heated under reflux for 20 h. After evaporation, the residue was dissolved in water and acidified with hydrochloric acid. The crystalline product **15** obtained was isolated by filtration, washed with water, and dried.

4-(4,5-Dihydro-5-thioxo-1,3,4-oxadiazol-2-yl)-1-(3-fluorophenyl)pyrrolidin-2-one (**15a**, $C_{12}H_{10}FN_3O_2S$)

M.p.: 178–179 °C (from 2-propanol); yield 93.2%; IR (KBr): $\bar{\nu}$ = 3,118 (NH), 1,688 (C=O) cm^{-1}; ^{1}H NMR

(300 MHz, DMSO-d_6): $\delta = 2.83$–3.06 (m, 2H, CH_2CO), 3.91–4.01 (m, 1H, CH), 4.07–4.26 (m, 2H, NCH_2), 6.96–7.66 (m, 4H, H_{ar}), 14.48 (s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): $\delta = 27.80$ (C-3′), 35.22 (C-4′), 49.86 (C-2′), 106.46 (d, $^2J_{C\text{-}F} = 26.3$ Hz, C-2), 110.77 (d, $^2J_{C\text{-}F} = 21.1$ Hz, C-4), 115.05 (br s, C-6), 130.39 (d, $^3J_{C\text{-}F} = 9.4$ Hz, C-5), 140.47 (d, $^3J_{C\text{-}F} = 10.8$ Hz, C-1), 162.05 (d, $^1J_{C\text{-}F} = 242.2$ Hz, C-3), 163.77 (OC=N), 171.34 (C-5′), 178.02 (C=S) ppm; MS (ESI, 20 eV): *m/z* (%) = 280 ($[M + H]^+$, 100).

4-(4,5-Dihydro-5-thioxo-1,3,4-oxadiazol-2-yl)-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (**15b**, $C_{13}H_{10}F_3N_3O_2S$)

M.p.: 166–167 °C (from 2-propanol); yield 93.6%; IR (KBr): $\bar{\nu} = 3{,}097$ (NH), 1685 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): $\delta = 2.84$–3.08 (m, 2H, CH_2CO), 3.93–4.03 (m, 1H, CH), 4.14–4.32 (m, 2H, NCH_2), 7.50–8.14 (m, 4H, H_{ar}), 14.54 (s, 1H, NH) ppm; ^{13}C NMR (75.4 MHz, DMSO-d_6): $\delta = 27.82$ (C-3′), 35.04 (C-4′), 49.72 (C-2′), 115.88 (q, $^3J_{C\text{-}F} = 3.7$ Hz, C-2), 120.58 (q, $^3J_{C\text{-}F} = 3.0$ Hz, C-4), 124.04 (q, $^1J_{C\text{-}F} = 272.0$ Hz, CF_3), 123.03 (C-6), 129.01 (q, $^2J_{C\text{-}F} = 31.5$ Hz, C-3), 130.05 (C-5), 139.55 (C-1), 163.77 (OC=N), 171.71 (C-5′), 178.02 (C=S) ppm; MS (ESI, 20 eV): *m/z* (%) = 330 ($[M + H]^+$, 100).

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