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REGIOSELECTIVE SYNTHESIS OF THE NOVEL *N*₄-SUBSTITUTED PYRAZOLO[4,5-*e*][1,2,4]THIADIAZINES AS POTENT HIV-1 NNRTIs

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Abstract – A new ring system of 7-methylpyrazolo[4,5-*e*][1,2,4]thiadiazine (**5**) was synthesized. Starting from **5** a series of novel mono *N*₄-substituted derivatives (**6**) were prepared regioselectively and evaluated as potent HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs).

INTRODUCTION

Benzene- and heterocycle-fused thiadiazine derivatives bearing the sulfamido moiety have become of particular interest to chemists and biologists because of their broad spectrum of biological activities and potential pharmacological applications. 1,2,4-Benzothiadiazines, such as chlorothiazide and diazoxide, are widely used in clinic as diuretic and antihypertensive drugs respectively.^{1,2} Heterocycle fused thiadiazine derivatives, such as pyridothiadiazine, pyrazinothiadiazine, imidazothiadiazine and triazolothiadiazines, have shown unique potentialities for treatment of cerebro- and cardiovascular diseases,³ cognitive disorder,⁴ cancers, viral and bacterial infections.^{5,6}

Recently, we reported the design and synthesis of the new ring systems of heterocycle-fused 1,2,4-thiadiazines.⁷ Biological evaluation found that 2,4-disubstituted thieno[3,4-*e*][1,2,4]thiadiazine derivatives (TTDs) were potential HIV-1 non-nucleoside reverse transcriptase inhibitors (HIV-1 NNRTIs). The prototype compounds QM96639, QM96539 together with the newly discovered lead compound QM96652 showed high activity and selectivity against HIV-1 replication in MT-4 cell at low concentration ranges (IC₅₀ 0.05~0.10 μM) (**Figure 1**).^{8,9}

In continuation of our research, we undertook a study of the pyrazole series, specifically regarding the 7-methylpyrazolo[4,5-*e*][1,2,4]thiadiazines, a new regioisomer of 6-methylpyrazolo[4,5-*e*][1,2,4]-thiadiazines that previously reported by Vega and coworkers,⁸ because of the known thiophene-pyrazole

bioisosterism.¹⁰ In addition, structure activity relationships (SARs) study of these kinds of compounds had revealed that the active anti-HIV-1 agents were the N_2 , N_4 -disubstituted thienothiadiazines, while the mono N_2 -substituted derivatives were inactive. Substituents containing π -electrons in the N_4 side chain were also essential to preserve the anti-HIV activity.⁸ Although a general SARs has been established, a systematic understanding of the SARs is still needed to know if the mono N_4 -substituted thienothiadiazines are active HIV-1 NNRTIs, which prompted us to prepare the mono N_4 -substituted derivatives (**Figure 1**). The synthesis of 7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine framework and its novel mono N_4 -substituted derivatives by regioselective alkylation, as well as their inhibitory activities against HIV-1 reverse transcriptase(RT), are reported in this paper.

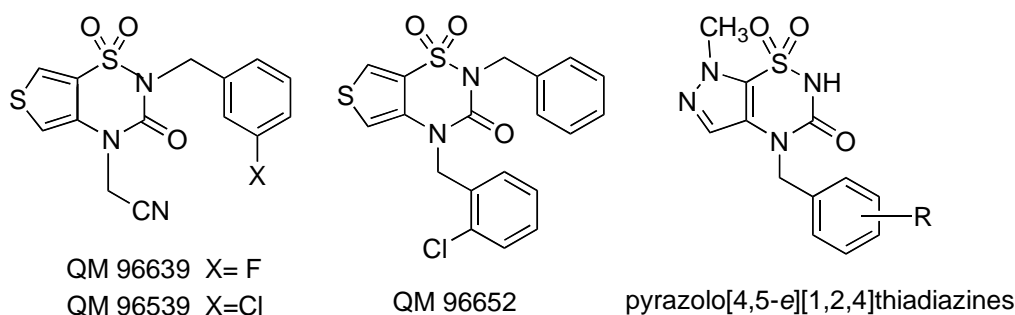


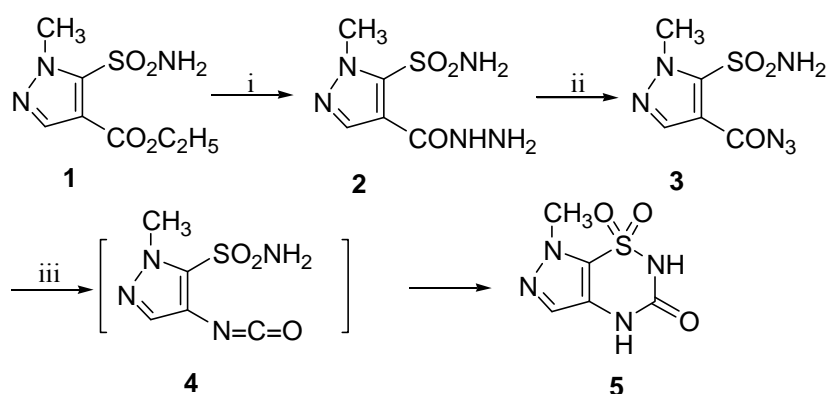
Figure 1. Lead compounds of 2,4-disubstituted thieno[3,4-*e*][1,2,4]thiadiazines (TTDs) and 4-substituted-7-methylpyrazolo[4,5-*e*][1,2,4]thiadiazines

RESULTS AND DISCUSSION

The nucleus ring of 7-methylpyrazolo[4,5-*e*][1,2,4]thiadiazine-1,1,3(2*H*,4*H*)trioxide (**5**) was prepared in similar manner to the thiophene and the regioisomeric pyrazole series^{7,8}, which was started from hydrazinolysis of the ethyl 1-methyl-5-sulfamoylpyrazole-4-carboxylate (**1**), a commercially available product, with hydrazine hydrate in refluxing ethanol, forming the hydrazide (**2**) in excellent yield. Carboxyazide (**3**) was obtained by the reaction of compound (**2**) with sodium nitrite in diluted hydrochloric acid under the temperature of 10°C, which is pure enough as a white solid for the next step of the ring closure reaction without further purification. Subsequently, by refluxing compound (**3**) in anhydrous toluene, a classical Curtius rearrangement was carried out through the intermediacy of isocyanate (**4**) to afford the new regioisomer (**5**) in good yield (**Scheme 1**).

Structural assignments for this nuclear ring (**5**) were based on its ¹H- and ¹³C-NMR, IR and MS spectral analysis. It exhibited the characteristic strong bands of the SO₂ groups at 1326 and 1186cm⁻¹ in IR spectrum and showed a broad signal at low field (11.49ppm), corresponding to protons exchangeable with deuterium by D₂O addition in the ¹H-NMR spectrum, which was assigned to the NH groups. The molecular ion fragment well matched its molecular weight in the MS. The structure was further confirmed by HMBC spectrum for long-distance proton/carbon correlation, in which N_4 -H (11.56ppm)

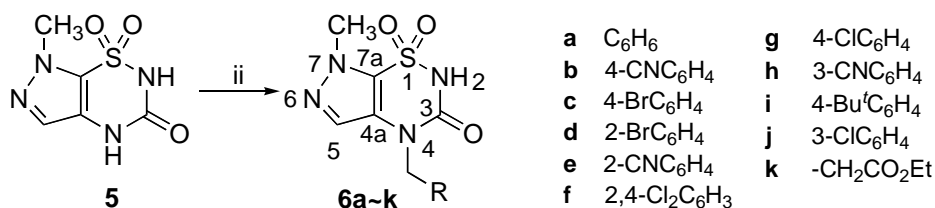
showed cross-peaks with C-3 (152.4ppm), C-4a (124.3ppm), C-5 (125.3ppm) and C-7a (123.4ppm), respectively. This information indicated the presented sequence of C and N atoms in the nuclear ring.



Scheme 1. Reagents: (i) $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O} / \text{EtOH}$; (ii) $\text{NaNO}_2, 2\text{M HCl}$; (iii) $\Delta / \text{toluene}$

The mono N_4 -substituted pyrazolo[4,5-*e*][1,2,4]thiadiazine (**6**) were prepared starting from the nuclear ring (**5**) with 2 equiv of sodium hydride in DMF solvent under 10°C , followed by addition of one equiv of alkyl halides at 80°C for 2-8 h, regioselectively achieving the mono N_4 -substituted products (**6**) in 50-65% yields (**Scheme 2**).

The site of alkylation was determined from the chemical shift of the CH_2 signal and by means of NOE experiments and sequences of HMBC for long-distance proton/carbon correlation. It was shown that the N_4 - CH_2 correlated exclusively with both quaternary carbons C-3 and C-4a, which is different from the N_2 - CH_2 that only would correlate with C-3.



Scheme 2. Reagents: $\text{NaH} / \text{RCH}_2\text{X} (2:1)$, DMF, 80°C

The mechanism of the regioselective alkylation at N_4 -position of the nuclear ring (**5**) is due to the N_2 and N_4 dianions formation by bis-deprotonation with sodium hydride and the delocalization of the two negative charges with the 3-carbonyl group, which diminish the nucleophilicity of N_2 anion. Also we speculated that the relatively high steric hindrance given by the 1-sulfonyl and 3-carbonyl groups resisted the alkylation at N_2 site. Therefore, the mono N_4 -substitution is the preferential product under these conditions.

The anti-HIV-1 activities of N_4 -substituted derivatives (**6**) were tested by evaluation of their inhibition against HIV-1 reverse transcriptase (RT). IC_{50} values of the tested compounds were determined. The

results showed that only compounds (**6c**) and (**6g**) exhibited activities to inhibit the HIV-1 RT with IC₅₀ values of 50μM and 80μM respectively, which further indicated the necessity of N₄-substituents for preserving the anti-HIV-1 activity of the hetero[4,5-*e*][1,2,4]thiadiazines. The anti-HIV-1 activities screening in cell lines are under way.

EXPERIMENTAL

All melting points were determined on a micromelting point apparatus and are uncorrected. ¹H-NMR and ¹³C-NMR spectra were obtained on a Bruker Avance-600 (600MHz) in the indicated solvent. Chemical shifts are expressed in δ units and TMS as internal reference. Infrared spectra (IR) were recorded with a Nexus 470FT-IR Spectrometer. Mass spectra were taken on a LC Autosampler Device: Standard G1313A instrument and elemental analysis was recorded with Elementar Analysensysteme Vario EI III. Flash column chromatography was performed on column packed with silica gel 60(230-400mesh). Solvents were reagent grade and when necessary, were purified and dried by the standard methods. Concentration of the reaction solutions involved the use of a rotary evaporator at reduced pressure.

1-Methyl-5-sulfamoylpyrazole-4-carbohydrazide (2) A mixture solution of 1-methyl-5-aminopyrazoloformate (**1**) (5.1g, 22mmol) and hydrazine hydrate (3.8g, 66mmol, 3eq) in 25mL ethanol was refluxed for 10h. When the reaction was completed, the solvent was evaporated under reduced pressure. The residue was purified by recrystallization from ethanol. White crystals, yield: 2.9g(61.7%), mp166-168°C. IR (KBr, cm⁻¹): 3376-3194(NH); 3097(Pyr-CH); 2960(CH₃); 1627(C=O); 1360, 1177(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 9.76(s, 1H, CONH₂); 8.02(s, 2H, SO₂NH₂); 7.89(s, 1H, Pyr-H, CH); 4.55(s, 2H, CONH₂); 4.05(s, 3H, CH₃). MS(EI) m/z: 220.1(M +1).

1-Methyl-5-sulfamoylpyrazole-4-carboxyazide (3) To a solution of compound (**2**) (2.19g, 10mmol) in 50mL of 2N hydrochloric acid was added dropwise a solution of sodium nitrite (98%, 0.85mg, 1.2mmol) in 2mL of water, keeping the reaction temperature below 10 °C. The reaction mixture was still stirred in this temperature for 2h, and the precipitate was filtered off, washed thoroughly with cold water and dried under vacuum as white solid (2.3g, 78.3%). The obtained compound was pure enough to be used in the following step. IR (KBr, cm⁻¹): 2149, 1216(N₃).

7-Methyl-1,1,3-trioxo-2H,4H-pyrazolo[4,5-*e*][1,2,4]thiadiazine (5) A suspension solution of (**3**) (8.8g, 40mmol) in dry toluene (100mL) was refluxed for 7h (keep from moisture). The precipitate was filtered, and recrystallized from ethanol to give white solid 6.78g (84%), mp 216 °C (dec). IR (KBr, cm⁻¹): 3244, 3152(NH); 3014(Pyr-CH); 1692(C=O); 1342, 1141(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 11.49(s, 1H, exchanged with deuterium by D₂O addition, NH); 7.40(s, 1H, Pyr-CH); 3.94(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 152.4(C=O), 125.3(C-5), 124.3(C-4a), 123.4(C-7a), 38.3(CH₃). MS(EI) m/z: 202.2(M⁺). *Anal.* Calcd for C₅H₆N₄O₃S: C, 29.70; H, 2.99; N, 27.71. Found: C 29.76; H 3.03; N 27.66.

General Procedure for the Preparation of *N*₄-Substituted-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine Derivatives (6a-k). To a solution of compound (5) (1eq) in dry DMF (1mmol:4mL) was added sodium hydride(60% dispersion in mineral oil, 2 equiv.) in portions, under inert atmosphere (N₂) and keeping the temperature below 10°C. After 15 minutes stirring, the alkyl halide(1eq) was added dropwise to. The mixture was stirred at room temperature for 20 min., then 30-80°C for 8-12h (checked by TLC), then neutralized with dilute hydrochloric acid (pH 4-6). After the solvent was evaporated under reduced pressure, the crude product was separated by flash column chromatography and purified by recrystallization.

4-Benzyl-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6a) Compound (5) and benzyl bromide at 30°C for 10h gave compound (6a), which separated by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purified by recrystallization from ethanol as white solid. Yield: 65%. mp 187°C. IR (KBr, cm⁻¹): 3430(NH), 3032(Ar-H), 1594(C=O), 1342, 1141(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 7.29-7.18 (m, 5H, Ar-H); 7.09 (s, 1H, Pyr-H); 4.90(s, 2H, CH₂); 3.83(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 152.3(C₃=O), 138.7(C-1'), 128.5, 128.2(2C), 127.1(2C), 126.7(C-5), 125.7(C-4a), 123.7(C-7a), 46.8(CH₂), 37.5(CH₃). MS(EI) m/z: 292.4(M⁺).

4-(4-Cyanobenzyl)-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6b) Compound (5) and 4-cyanobenzyl chloride at 30-40°C for 10h and separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) gave compound (6b) as white solid. Yield: 55%. mp 244°C. IR (KBr, cm⁻¹): 3461(NH), 2236(CN), 1598(C=O); 1338, 1143(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 7.74(d, 2H, *J*= 8.0Hz, Ar-H); 7.41(d, 2H, *J*= 8.0Hz, Ar-H); 7.12(s,1H, Pyr-H); 4.97(s, 2H, CH₂); 3.84(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 152.0(C=O), 144.8(C-1'), 132.2(2C), 128.2(C-5), 127.9(2C), 125.8 (C-4a), 123.5(C-7a), 118.8, 109.6(CN), 46.7(CH₂), 37.5(CH₃). MS(EI) m/z: 318.0(M+1).

4-(4-Bromobenzyl)-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6c) Compound (5) and 4-bromobenzyl bromide at 30°C for 10h and purification by flash column chromatography (CH₂Cl₂/CH₃OH 3:1) and purification by recrystallization from ethanol gave compound (6c) as white solid. Yield: 60%. mp 240°C. IR (KBr, cm⁻¹): 3201(NH), 1593(C=O); 1323, 1136(SO₂). ¹H-NMR(DMSO-*d*₆) δ: 7.47(d, 2H, *J*= 8.32Hz, Ar-H); 7.20(d, 2H, *J*= 8.28Hz, Ar-H); 7.14(s,1H, Pyr-H); 4.85(s, 2H, CH₂); 3.82(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 152.2(C=O), 138.4(C-1'), 131.3(2C), 129.5(2C), 128.4(C-5), 125.7(C-4a), 123.7(C-7a), 119.9, 46.3(CH₂), 37.6(CH₃). MS(EI) m/z: 371.2(M⁺).

4-(2-Bromobenzyl)-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6d) Compound (5) and 2-bromobenzyl bromide at at 30°C for 10h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 3:1) and purification by recrystallization from ethanol gave compound (6d) as white solid. Yield: 56%. mp 135°C. IR(KBr, cm⁻¹): 3189(NH), 3059(Pyr-CH), 1594(C=O); 1324, 1136(SO₂). ¹H-NMR(DMSO-*d*₆) δ: 7.62(d, 1H, *J*=7.96Hz, Ar-H); 7.27(t, 1H, *J*=7.36Hz, Ar-H); 7.17(t, 1H, *J*=7.42Hz,

Ar-H); 6.99 (s, 1H, Pyr-H); 6.81(d, 1H, $J=7.57\text{Hz}$, Ar-H); 4.88(s, 2H, CH₂); 3.86(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ : 152.1(C=O), 137.0(C-1'), 132.6, 128.7, 128.4(C-5), 127.8, 127.0, 125.8(C-4a), 123.5(C-7a), 122.0, 47.5(CH₂), 37.7(CH₃). MS(EI) m/z : 371.3(M⁺).

4-(2-Cyanobenzyl)-7-methyl-1,1,3-trioxo-2H,4H-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6e) Compound (5) and 2-cyanobenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from AcOEt/hexane gave compound (6e) as white solid. Yield: 50%. mp 132°C. IR(KBr, cm⁻¹): 3208(NH), 2208(CN), 1596(C=O); 1330, 1138(SO₂). ¹H-NMR(DMSO-*d*₆) δ : 7.83(d, 1H, $J=7.63\text{Hz}$, Ar-H); 7.60(t, 1H, $J=7.60\text{Hz}$, Ar-H); 7.42(t, 1H, $J=7.56\text{Hz}$, Ar-H); 7.17(s, 1H, Pyr-H); 7.04(d, 1H, $J=7.9\text{Hz}$, Ar-H); 5.07(s, 2H, CH₂); 3.87(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ : 152.0 (C=O), 142.6(C-1'), 133.5, 133.0, 128.5(C-5), 127.7, 126.3, 125.8(C-4a), 123.5(C-7a), 117.5, 110.3(CN), 45.6(CH₂), 37.7(CH₃). MS(EI) m/z : 318.4(M+1).

4-(2,4-Dichlorobenzyl)-7-methyl-1,1,3-trioxo-2H,4H-pyrazolo[4,5-*e*][1,2,4]thiadiazine(6f) Compound (5) and 2,4-dichlorobenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from ethanol gave compound (6f) as white solid. Yield: 54%. mp 250°C. IR(KBr, cm⁻¹): 3206(NH), 1594(C=O); 1327, 1137(SO₂). ¹H-NMR (DMSO-*d*₆) δ : 7.61(d, 1H, $J=1.79\text{Hz}$, Ar-H); 7.35(dd, 1H, $J=1.71, 8.4\text{Hz}$, Ar-H); 7.04(s, 1H, Py-H); 6.84(d, 1H, $J=8.4\text{Hz}$, Ar-H); 4.90(s, 2H, CH₂); 3.86(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ : 151.9(C=O), 135.0(C-1'), 132.7, 132.0, 128.8, 128.4, 128.3(C-5), 127.5, 125.9(C-4a), 123.5(C-7a), 44.7(CH₂), 37.7(CH₃). MS(EI) m/z : 361.2(M⁺).

4-(4-Chlorobenzyl)-7-methyl-1,1,3-trioxo-2H,4H-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6g) Compound (5) and 4-chlorobenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from ethanol gave compound (6g) as white solid. Yield: 51%. mp 218°C. IR (KBr, cm⁻¹): 3200(NH), 1592(C=O); 1327, 1135(SO₂). ¹H-NMR(DMSO-*d*₆) δ : 7.34(d, 2H, $J= 8.4\text{Hz}$, Ar-H); 7.33(d, 2H, $J= 8.4\text{Hz}$, Ar-H); 7.14(s, 1H, Pyr-H); 4.86(s, 2H, CH₂); 3.82(s, 3H, CH₃). ¹³C-NMR(DMSO-*d*₆) δ : 152.1(C₃=O), 137.9(C-1'), 131.3, 128.9(2C), 128.3(C-5), 128.1(2C), 125.8(C-4a), 123.5(C-7a), 46.2(CH₂), 37.5(CH₃). MS(EI) m/z : 327.3(M +1).

4-(3-Cyanobenzyl)-7-methyl-1,1,3-trioxo-2H,4H-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6h) Compound (5) and 3-cyanobenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from AcOEt/hexane gave compound (6h) as white solid. Yield: 57%. mp 134°C. IR(KBr, cm⁻¹): 3202(NH), 2231(CN), 1594(C=O); 1342, 1141(SO₂). ¹H-NMR(DMSO-*d*₆) δ : 7.69-7.50(4H, Ar-H); 7.23(s, 1H, Pyr-H); 4.92(s, 2H, CH₂); 3.83(s, 3H, CH₃). ¹³C-NMR(DMSO-*d*₆) δ : 152.2(C₃=O), 140.7(C-1'), 132.2, 130.8(2C), 129.7, 128.3(C-5), 125.8(C-4a), 123.7(C-7a), 118.9, 111.3(CN), 46.3(CH₂), 37.6(CH₃). MS(EI) m/z : 318.3(M +1).

4-(4-*t*-Butyl)benzyl-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6i) Compound (5) and 4-*t*-butylbenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from AcOEt/hexane gave compound (6i) as white solid. Yield: 51%. mp 205°C. IR (KBr, cm⁻¹): 3225(NH), 1591(C=O); 1329, 1135(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 7.29(d, 2H, *J*= 8.23Hz, Ar-H); 7.17(d, 2H, *J*= 8.18Hz, Ar-H); 7.13(s, 1H, Pyr-H); 4.83(s, 2H, CH₂); 3.82(s, 3H, Pyr-CH₃), 1.23(s, 9H, -C(CH₃)₃). ¹³C-NMR(DMSO-*d*₆) δ: 152.2(C=O), 149.1, 135.8(C-1'), 128.6(C-5), 126.9(2C), 125.8(C-4a), 124.9(2C), 123.7(C-7a), 46.4(CH₂), 37.4(Pyr-CH₃), 34.1(-C(CH₃)₃), 31.2(-C(CH₃)₃). MS(EI) *m/z*: 349.2(M+1).

4-(3-Chlorobenzyl)-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6j) Compound (5) and 3-chlorobenzyl chloride at 50-60°C for 24h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from AcOEt/hexane gave compound (6j) as white solid. Yield: 47%. mp 194°C. IR (KBr, cm⁻¹): 3422(NH), 1595(C=O); 1335, 1141(SO₂). ¹H-NMR (DMSO-*d*₆) δ: 7.33-7.22(4H, Ar-H); 7.18(s, 1H, Pyr-H); 4.88(s, 2H, CH₂); 3.83(s, 3H, CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 152.1(C=O), 141.5, 133.0, 130.2, 128.3(C-5), 126.9, 126.8, 125.8, 125.7, 123.6(C-7a), 46.4(CH₂), 37.5(CH₃). MS(EI) *m/z*: 327.3(M+1).

4-(Ethoxycarbonylmethyl)-7-methyl-1,1,3-trioxo-2*H*,4*H*-pyrazolo[4,5-*e*][1,2,4]thiadiazine (6k) Compound (5) and ethyl bromoacetate at 30°C for 10h, separation by flash column chromatography (CH₂Cl₂/CH₃OH 4:1) and purification by recrystallization from AcOEt/hexane gave compound (6k) as white solid. Yield: 50%. mp 300°C. IR (KBr, cm⁻¹): 3441(NH), 3111(Pyr-H), 1732(-CH₂C=O), 1602(C₃=O); 1360, 1144(SO₂). ¹H-NMR(DMSO-*d*₆) δ: 7.22(s, 1H, Pyr-H); 4.38(s, 2H, -CH₂C=O); 4.08(q, 2H, *J*=7Hz, -OCH₂CH₃), 3.84(s, 3H, Pyr-CH₃), 1.18(t, 3H, *J*=7Hz, -OCH₂CH₃). ¹³C-NMR (DMSO-*d*₆) δ: 169(-CH₂C=O), 151(C₃=O), 128(C-5), 125(C-4a), 123(C-7a), 60(-OCH₂CH₃), 45(-CH₂C=O), 37(Pyr-CH₃), 14(-OCH₂CH₃). MS(EI) *m/z*: 289.2(M+1).

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