

Synthesis and cycloaddition reactions of 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides with nitrilimines

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Abstract

A new series of 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides were prepared by reaction of aryl isothiocyanate with dimedone. Reaction of *N*-aryl-4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides with hydrazonoyl halides led to the formation of the corresponding thiadiazoles. Treatment of 2-[5-acetyl-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione with dimethylformamide dimethylacetal (DMF-DMA) in refluxing dioxane afforded (*E*)-2-[5-(3-(dimethylamino)acryloyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione. Reaction of the latter enaminone with hydrazonoyl halides yielded the corresponding 2-(1-aryl-3-substituted-pyrazol-4-carbonyl)-5-[3-phenyl-5-(5,5-dimethylcyclohexane-1,3-dione)-[1,3,4]-thiadiazole] derivatives. The structures of the new compounds were elucidated on the basis of their elemental analyses and spectral data.

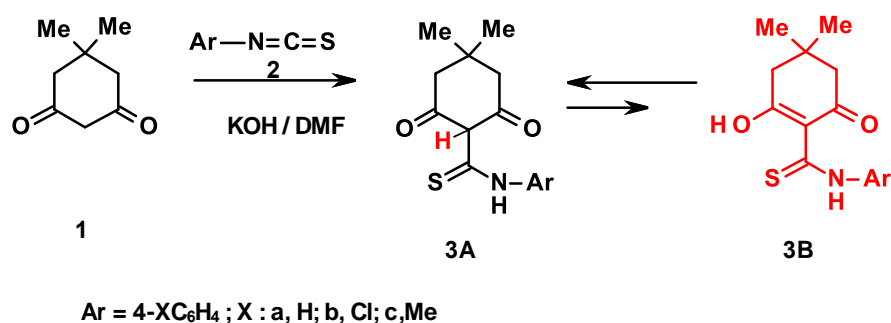
Keywords: Dimedone, thioanilide, enaminone, thiadiazole, hydrazonoyl halides

Introduction

A literature survey revealed that many substituted 1,3,4-thiadiazole derivatives exhibit wide range of biological activities such as antimicrobial, antituberculosis, antiviral, anti-inflammatory, anticancer, antidiabetic and anticonvulsant activities.¹ In the light of these activities and in continuation of our work dealing with chemistry of hydrazonoyl halides,¹⁻²⁰ it was thought interesting to synthesize new functionalized 1,3,4-thiadiazole derivatives and evaluate their pharmaceutical activities. The synthetic strategy adopted for the target compounds is based on reactions of hydrazonoyl halides with 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides **3** (Scheme 1). Such reactions have not been reported hitherto. Our interest in such a study is to shed some light on the site selectivity in the target cycloaddition reactions of nitrilimines to **3** as the latter compounds contain three dipolarophilic sites namely C=O, C=C and C=S groups.

Results and Discussion

The required 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides **3a-c** were prepared herein by reaction of 5,5-dimethylcyclohexane-1,3-dione **1** with each of aryl isothiocyanates **2a-c** in dimethylformamide in the presence of potassium hydroxide (Scheme 1). The structures of the products **3a-c** were substantiated by their microanalyses and spectral (MS, IR, NMR) data (see Experimental). For example, their IR spectra revealed, in each case, two carbonyl bands at ν 1696, 1664 cm^{-1} and NH band near ν 3217 cm^{-1} . Their ^1H NMR spectra showed, in addition to the aromatic protons multiplet, two characteristic singlet signals at δ 1.12 (6H, 2CH₃) and 2.65 (4H, 2CH₂) and two other singlet signals at δ 14.00 and 17.39 assignable to -NH and -OH protons, respectively. Such data indicate that compounds **3** in DCCl_3 , each exists as a mixture of two tautomeric forms **3A** and **3B** (Scheme 1).

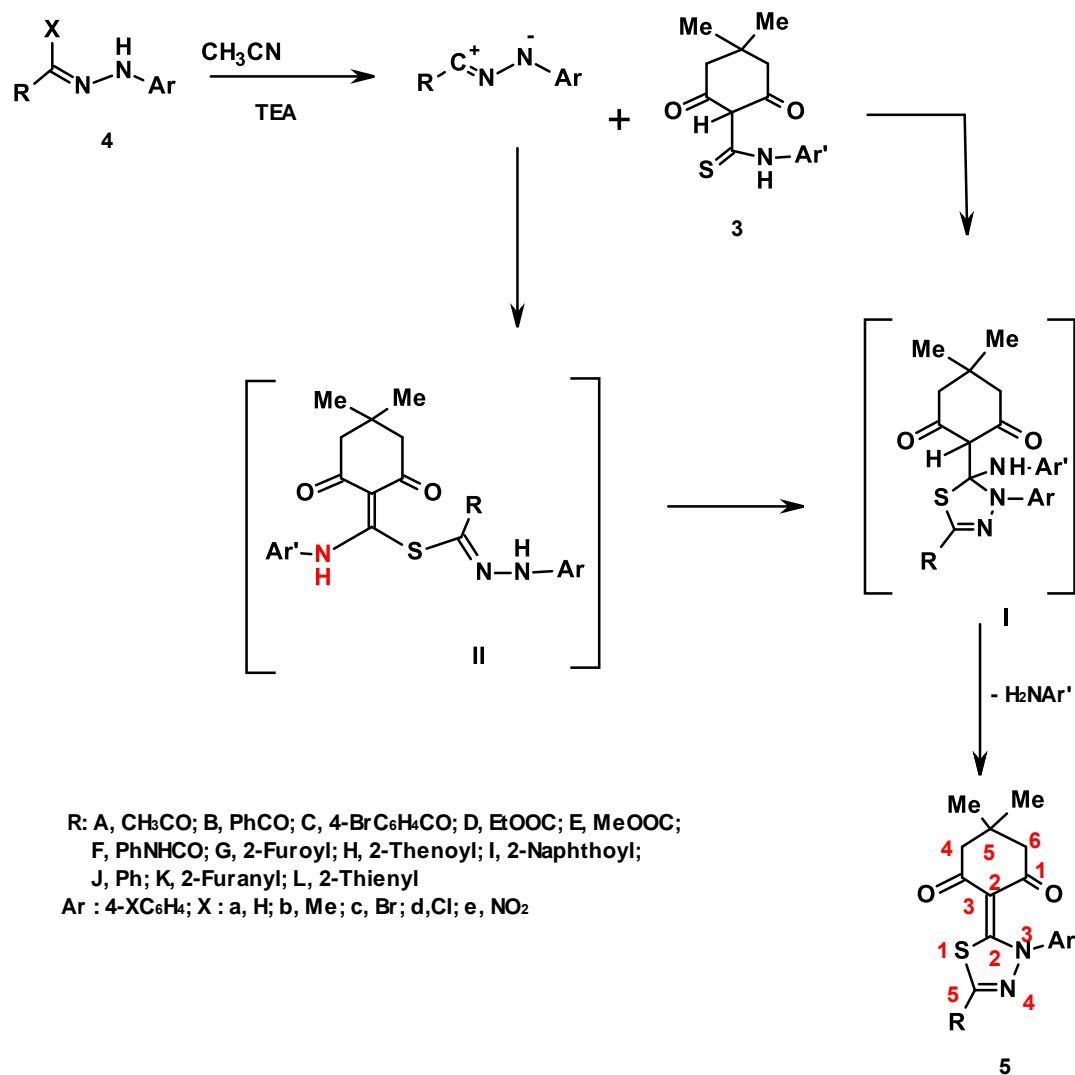


Scheme 1

Next, the reactions of **3** with the hydrazonoyl halides **4** were examined. In our hands, stirring of **3a** with each of the hydrazonoyl halides **4** in acetonitrile at room temperature in the presence of triethylamine as a base catalyst afforded, in each case, one isolable product as evidenced by TLC analysis of the crude product (Scheme 2). The structure of the isolated products proved to be **5** on the basis of both elemental and spectral (MS, IR, NMR) analyses (see Experimental) and by alternate synthesis as outlined below. For example, the IR spectra of the products **5** reveal, in each case, the presence of two carbonyl bands in the region ν 1713-1652 cm^{-1} .

Similar reactions of the appropriate hydrazonoyl halides **4** with each of **3b** and **3c** under the same reaction conditions afforded products that proved identical in all respects (mp, mixed mp, MS, IR and NMR spectra) with those obtained from reactions of **3a** and **4**. This finding indicates that the studied reactions of **3** with **4** involve the elimination of ArNH_2 molecule. To account for the formation of **5**, it is suggested as depicted in Scheme 2 that the reaction involves initially the formation of the intermediate cycloadduct **I** which undergoes *in situ* elimination of aniline molecule to give **5** as end products (Scheme 2). Alternatively, the reaction involves first the formation of the thiohydrazonate ester **II** which undergoes tandem *in situ* cyclization followed

by elimination of aniline molecule (Scheme 2). These two suggested pathways are consistent with other literature reports on reactions of hydrazoneyl halides with other thioanilides.²¹⁻²³

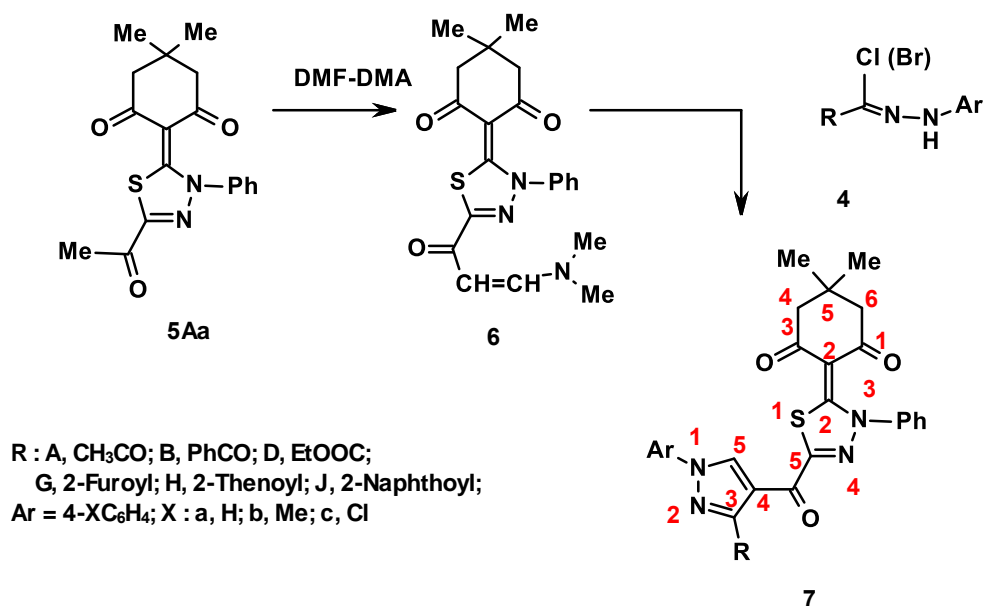


Scheme 2

Treatment of compound **5Aa** with dimethylformamide dimethylacetal (DMF-DMA) in refluxing dioxane, yielded the corresponding enaminone **6** (Scheme 3). The structure of the latter enaminone **6** was confirmed by its spectra and elemental analyses. For example, its IR spectrum showed two C=O bands in the region ν 1635–1650 cm⁻¹. In addition to the signals of the aromatic protons, its ¹H NMR spectrum revealed two singlet signals at δ 0.96 (6H, 2CH₃) and δ 2.23 (4H, 2CH₂) and a singlet signal at 2.93–3.20 (6H, N(CH₃)₂). Also, such spectrum showed two characteristic doublet signals at δ 5.77–5.81 (1H, d) and 7.88–7.90 (1H, d) with coupling

constant $J=13$ Hz assignable to the two olefinic protons. This coupling constant value indicates that the enaminone **6** has the *E*-configuration.

The reactions of the enaminone **6** as dipolarophile, with the nitrilimines generated *in situ* by base-catalyzed dehydrohalogenation of the hydrazonoyl halides **4**, were next examined (Scheme 3). In our hands, reaction of **6** with each of the hydrazonoyl halides **4** in refluxing chloroform in the presence of triethylamine yielded, in each case, a single product. The isolated products were identified, on the basis of their elemental analysis and spectral (IR, NMR and MS) data (Experimental Section), as the respective 2-(1-aryl-3-substituted-pyrazol-4-carbonyl)-5-[3-phenyl-5-(5,5-dimethylcyclohexane-1,3-dione)-[1,3,4]-thiadiazole] derivatives **7** (Scheme 3). For example, the ^1H NMR spectra of the products isolated products showed, in each case, a singlet signal (1H) in the region δ 8.52-9.53, which corresponds to the distinct H-5 proton of the pyrazole ring residue in such products.



Scheme 3

Experimental Section

General. Melting points were determined on a Stuart melting point apparatus and are uncorrected. The IR spectra were measured as KBr pellets on a FTIR Bruker-Vector 22 spectrophotometer. The ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 or $[\text{D}_6]$ DMSO on a Varian Mercury VXR 300 spectrometer (300 MHz for ^1H NMR and 75 MHz for ^{13}C NMR) using TMS as internal standard. Mass spectra were measured on a Shimadzu GCMS-Q-1000 EX mass spectrometer at 70 eV. The elemental analyses were carried out at the Microanalytical

Center, Cairo University using Automated analyzer CHNS, Vario EL III, Elementar, Germany. The hydrazonoyl halides **4** were prepared using the reported procedures²⁴⁻³²

General procedure for *N*-aryl 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamides (3a-c). 5,5-Dimethylcyclohexane-1,3-dione **1** (14.0 g, 0.1 mol) was added to a solution of potassium hydroxide (5.6 g, 0.1 mol) in dimethylformamide (100 mL). The mixture was stirred until dione dissolved. The appropriate aryl isothiocyanate **2** (0.1 mol) was then added to the reaction mixture. The reaction mixture was stirred overnight and then acidified with acetic acid. The solid formed was collected and crystallized from ethanol to give the corresponding thioamide **3**. The compounds **3a-c** prepared together with their physical constants are listed below.

***N*-phenyl 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamide (3a).** Yellow needles, yield 22.55 g, 82%, mp 140-141 °C IR (ν_{\max} , cm^{-1}): 3217 (NH), 1697 and 1664 (C=O) cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 1.12 (6H, s, 2 CH_3), 2.50 (2H, s, CH_2), 2.65 (2H, s, CH_2), 7.27-7.48 (5H, m, Ph), 14.00 (1H, s, NH) and 17.39 (1H, s, OH). ^{13}C NMR (75 MHz, CDCl_3): δ 27.3 (CH_3), 29.8 (CMe_2), 51.2 (CH_2), 108.1 ($\text{C}(\text{CO})_2$), 120.7, 125.3, 127.1 and 128.9 (Ph), 187.9 (C=S), 190.2 (dione-CO), 199.0 (dione-CO). Anal. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_2\text{S}$ (275): C, 65.44; H, 6.22; N, 5.09; S, 11.62%. Found: C, 65.70; H, 6.10; N, 4.80; S, 11.44%.

***N*-(4-Chlorophenyl) 4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamide (3b).** Yellow blocks crystals, yield 24.70 g, 80%, mp 160-162 °C IR (ν_{\max} , cm^{-1}): 3210 (NH), 1695 and 1660 (C=O) cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 1.11 (6H, s, 2 CH_3), 2.45 (2H, s, CH_2), 2.70 (2H, s, CH_2), 7.27-7.52 (4H, m, Ar), 14.01 (1H, s, NH) and 17.39 (1H, s, OH). Anal. Calcd. for $\text{C}_{15}\text{H}_{16}\text{ClNO}_2\text{S}$ (309): C, 58.15; H, 5.21; Cl, 11.44; N, 4.52; S, 10.35%. Found: C, 58.35; H, 5.10; Cl, 11.30; N, 4.43; S, 10.25%.

***N*-(*p*-Tolyl)-4,4-dimethyl-2,6-dioxocyclohexane-thiocarboxamide (3c).** Yellow needles crystals, yield 24.30 g, 84%, mp 92-94 °C IR (ν_{\max} , cm^{-1}): 3215 (NH), 1693 and 1662 (C=O) cm^{-1} . ^1H NMR (300 MHz, CDCl_3): δ 1.12 (6H, s, 2 CH_3), 2.37 (3H, s, CH_3), 2.47 (2H, s, CH_2), 2.63 (2H, s, CH_2), 7.21-7.40 (4H, m, Ar), 14.00 (1H, s, NH) and 17.41 (1H, s, OH). ^{13}C NMR (75 MHz, CDCl_3): δ 20.9 ($\text{CH}_3\text{C}_6\text{H}_4$), 27.7 (CH_3), 29.8 (CMe_2), 46.5 (CH_2), 52.2 (CH_2), 107.8 (1C, $\text{C}(\text{CO})_2$), 125.1, 129.3, 134.8 and 136.8 (Ph), 188.4 (C=S), 191.0 (dione-CO), 198.9 (dione-CO). Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_2\text{S}$ (289): C, 66.41; H, 6.62; N, 4.84; S, 11.08%. Found: C, 66.70; H, 6.51; N, 4.76; S, 10.87%.

General procedure for synthesis of 1,3,4-thiadiazole derivatives 5. A mixture of compound **3** (0.005 mol) and the appropriate hydrazonoyl halide **4** (0.005 mol) was dissolved in acetonitrile (50 mL). To the resulting solution triethylamine (2 mL) was added and reaction mixture was stirred for 2 h at room temperature. The resulting solid product that precipitated was collected, washed with ethanol and crystallized from a suitable solvent to afford the corresponding thiadiazole derivatives. The products **5** prepared together with their physical constants are listed below.

2-(5-Acetyl-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione

(5Aa). Yellow needles crystals, yield 1.56 g, 92%, mp 204-206 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1689 and 1652 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.04 (6H, s, 2CH₃), 2.36 (4H, s, 2CH₂), 2.69 (3H, s, CH₃CO) and 7.27-7.40 (5H, m, Ph). ¹³C NMR (75 MHz, CDCl₃): δ 25.5 (CH₃CO), 26.2 (CH₃), 30.9 (CMe₂), 52.0 (CH₂), 105.5 (1C, C(CO)₂), 121.2, 124.05, 128.20 and 158.8 (Ph), 142.99 (thiadiazole-C2), 164.8 (thiadiazole-C5), 190.52 (C=O, acetyl), 191.71 (dimedone-C=O). MS, m/z (%) = 77 (100), 342 [M]⁺ (71.9). Anal. Calcd. for C₁₈H₁₈N₂O₃S (342): C, 63.16; H, 5.30; N, 8.19; S, 9.34%. Found: C, 63.35; H, 5.24; N, 7.98; S, 9.25%.

2-(5-Benzoyl-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione

(5Ba). Orange needles crystals, yield 1.81 g, 88%, mp 210-212 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1649 and 1590 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.07 (6H, s, 2CH₃), 2.39 (4H, s, 2CH₂) and 7.27-8.34 (10H, m, 2Ph). ¹³C NMR (75 MHz, CDCl₃): δ 25.7 (CH₃), 31.2 (CMe₂), 51.2 (CH₂), 109.5 (1C, C(CO)₂), 116.5, 118.6, 121.6, 123.58, 125.8, 126.5, 129.0 and 159.0 (2Ph), 140.1 (thiadiazole-C2), 162.4 (thiadiazole-C5), 185.3 (Ph-C=O), 190.4 (dimedone-C=O). MS, m/z (%) = 105 (100), 404 [M]⁺ (27.0); Anal. Calcd. for C₂₃H₂₀N₂O₃S (404): C, 68.30; H, 4.98; N, 6.93; S, 7.93%. Found: C, 68.56; H, 4.88; N, 6.87; S, 7.81%.

2-[5-Benzoyl-3-(4-chlorophenyl)-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione

(5Bd). Yellow needles crystals, yield 1.89 g, 85%, mp 260-262 °C (DMF-Ethanol). ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.40 (4H, s, 2CH₂) and 7.27-8.30 (9H, m). ¹³C NMR (75 MHz, CDCl₃): δ 28.7 (CH₃), 31.1 (CMe₂), 51.4 (CH₂), 106.0 (1C, C(CO)₂), 117.0, 124.3, 128.2, 129.0, 129.7, 130.8, 134.9 and 159.9 (2Ph), 141.6 (thiadiazole-C2), 164.0 (thiadiazole-C5), 184.0 (Ph-C=O), 192.0 (dimedone-C=O). MS, m/z (%) = 105 (100), 438 [M]⁺ (18.2); Anal. Calcd. for C₂₃H₁₉ClN₂O₃S (438): C, 62.94; H, 4.36; Cl, 8.08; N, 6.38; S, 7.31%. Found: C, 63.10; H, 4.24; Cl, 7.97; N, 6.27; S, 7.19%.

2-[5-(4-Bromobenzoyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione

(5Ca). Yellow needles crystals, yield 2.21 g, 90%, mp 236-238 °C (DMF); ¹H NMR (300 MHz, CDCl₃): δ 1.00 (6H, s, 2CH₃), 2.30 (4H, s, 2CH₂) and 7.06-8.18 (9H, m). ¹³C NMR (75 MHz, CDCl₃): δ 26.9 (CH₃), 30.4 (CMe₂), 50.5 (CH₂), 104.9 (1C, C(CO)₂), 115.1, 122.7, 128.3, 129.4, 130.8, 131.7, 132.9 and 158.1 (2Ph), 142.5 (thiadiazole-C2), 162.7 (thiadiazole-C5), 182.4 (Ph-C=O), 190.6 (dimedone-C=O). MS, m/z (%) = 183 (100), 482 [M]⁺ (24.29); Anal. Calcd. for C₂₃H₁₉BrN₂O₃S (482): C, 57.15; H, 3.96; Br, 16.53; N, 5.80; S, 6.63%. Found: C, 57.37; H, 3.71; Br, 16.63; N, 5.78; S, 6.72%.

Ethyl 5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate

(5Da). Yellow blocks crystals, yield 1.78 g, 94%, mp 146-148 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1713 (COOEt), 1680 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.13 (6H, s, 2CH₃), 1.29-1.47 (3H, ³J = 7.3 Hz, t, CH₃), 2.40 (4H, s, 2CH₂), 4.05-4.25 (2H, ³J = 7.3 Hz, q, CH₂) and 7.09-7.49 (5H, m, Ph). MS, m/z (%) = 77 (100), 372 [M]⁺ (33.1); Anal. Calcd. for C₁₉H₂₀N₂O₄S (372): C, 61.27; H, 5.41; N, 7.52; S, 8.61%. Found: C, 61.45; H, 5.29; N, 7.46; S, 8.58%.

Methyl 5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (5Ea). Yellow blocks crystals, yield 1.44 g, 79%, mp 178-180 °C; (CH₃CN); IR (ν_{\max} , cm⁻¹): 1710 (COOMe), 1685 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.00 (6H, s, 2CH₃), 2.34 (4H, s, 2CH₂), 4.00 (3H, s, OCH₃) and 6.90-7.30 (5H, m, Ph). ¹³C NMR (75 MHz, CDCl₃): δ 27.4 (CH₃), 30.8 (CMe₂), 51.6 (CH₂), 57.8 (CH₃O), 108.6 (1C, C(CO)₂), 118.6 120.4, 130.2 and 154.9 (Ph), 145.4 (thiadiazole-C2), 161.6 (thiadiazole-C5), 167.4 (COOMe), 192.2 (dimedone-C=O). Anal. Calcd. for C₁₈H₁₈N₂O₄S (358): C, 60.32; H, 5.06; N, 7.82; S, 8.95%. Found: C, 60.51; H, 4.98; N, 7.75; S, 8.82%.

5-(4,4-Dimethyl-2,6-dioxocyclohexylidene)-N,4-diphenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (5Fa). Yellow needles crystals, yield 1.93 g, 91%, mp 220-222 °C (DMF); IR (ν_{\max} , cm⁻¹): 3384 (NH), 1683 and 1646 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.38 (4H, s, 2CH₂), 7.07-7.69 (10H, m) and 11.80 (1H, s, NH). ¹³C NMR (75 MHz, CDCl₃): δ 27.9 (CH₃), 31.1 (CMe₂), 51.3 (CH₂), 105.5 (1C, C(CO)₂), 119.2, 119.5, 122.0, 124.1, 126.8, 128.4, 136.4 and 156.9 (2 Ph), 143.1 (thiadiazole-C2), 162.7 (thiadiazole-C5), 167.4 (CONH), 191.8 (dimedone-C=O). MS, *m/z* (%) = 77 (100), 419 [M]⁺ (66.0); Anal. Calcd. for C₂₃H₂₁N₃O₃S (419): C, 65.85; H, 5.05; N, 10.02; S, 7.64%. Found: C, 66.01; H, 4.94; N, 9.98; S, 7.56%.

5-(4,4-Dimethyl-2,6-dioxocyclohexylidene)-N-phenyl-4-(p-tolyl)-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (5Fb). Yellow blocks crystals, yield 1.91 g, 87%, mp 208-210 °C (DMF); IR (ν_{\max} , cm⁻¹): 3380 (NH), 1680 and 1650 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.05 (6H, s, 2CH₃), 1.78 (3H, s, CH₃), 2.88-2.95 (4H, s, 2CH₂), 7.12-7.39 (9H, m) and 11.74 (1H, s, NH). ¹³C NMR (75 MHz, CDCl₃): δ 22.2 (CH₃-C₆H₄), 27.9 (CH₃), 31.2 (CMe₂), 51.2 (CH₂), 105.8 (1C, C(CO)₂), 120.1, 120.6, 121.2, 126.7, 128.0, 129.3, 131.4 and 155.8 (2Ph), 143.6 (thiadiazole-C2), 161.3 (thiadiazole-C5), 167.2 (CONH), 191.2 (dimedone-C=O). MS, *m/z* (%) = 91 (100), 433 [M]⁺ (47.31); Anal. Calcd. for C₂₄H₂₃N₃O₃S (433): C, 66.49; H, 5.35; N, 9.69; S, 7.40%. Found: C, 66.60; H, 5.25; N, 9.60; S, 7.36%.

4-(4-Bromophenyl)-5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-N-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (5Fc). Yellow blocks crystals, yield 2.03 g, 81%, mp 226-228 °C (DMF-Ethanol); IR (ν_{\max} , cm⁻¹): 3385 (NH), 1685 and 1661 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.39 (4H, s, 2CH₂), 7.18-8.61 (9H, m) and 11.87 (1H, s, NH). MS, *m/z* (%) = 77 (100), 497 [M]⁺ (25.4); Anal. Calcd. for C₂₃H₂₀BrN₃O₃S (497): C, 55.43; H, 4.04; Br, 16.03; N, 8.43; S, 6.43%. Found: C, 55.64; H, 3.94; Br, 15.97; N, 8.32; S, 6.35%.

4-(4-Chlorophenyl)-5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-N-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (5Fd). Pale yellow blocks crystals, yield 1.96 g, 85%, mp 254-256 °C (DMF); IR (ν_{\max} , cm⁻¹): 3382 (NH), 1680 and 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.41 (4H, s, 2CH₂), 7.22-7.67 (9H, m) and 11.90 (1H, s, NH). MS, *m/z* (%) = 55 (100), 453 [M]⁺ (32.0); Anal. Calcd. for C₂₃H₂₀ClN₃O₃S (453): C, 60.86; H, 4.44; Cl, 7.81; N, 9.26; S, 7.06%. Found: C, 61.02; H, 4.32; Cl, 7.76; N, 9.16; S, 6.96%.

2-[5-(Furan-2-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (5Ga). Brown needles crystals, yield 1.64 g, 82%, mp 230-232 °C (CH₃CN); IR (ν_{\max} ,

cm⁻¹): 1695 and 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.17 (6H, s, 2CH₃), 2.39 (4H, s, 2CH₂) and 6.62-7.92 (8H, m). MS, *m/z* (%) = 95 (100), 394 [M]⁺ (7.01); Anal. Calcd. for C₂₁H₁₈N₂O₄S (394): C, 63.94; H, 4.60; N, 7.10; S, 8.13%. Found: C, 64.08; H, 4.51; N, 7.10; S, 8.04%.

5,5-Dimethyl-2-[3-phenyl-5-(thiophene-2-carbonyl)-1,3,4-thiadiazol-2(3*H*)-ylidene]cyclohexane-1,3-dione (5Ha). Orange needles crystals, yield 1.84 g, 88%, mp 236-238 °C (DMF); IR (ν_{max}, cm⁻¹): 1660 and 1650 (C=O) cm⁻¹. ¹H NMR (300 MHz, DMSO): δ 0.97 (6H, s, 2CH₃), 2.29 (4H, s, 2CH₂) and 7.32-8.42 (8H, m). ¹³C NMR (75 MHz, DMSO): δ 28.0 (CH₃), 30.4 (CMe₂), 50.4 (CH₂), 105.0 (1C, C(CO)₂), 115.5, 122.8, 128.9, 135.2, 136.3, 137.4, 138.6 and 157.8 (Ph and thiophene), 142.6 (thiadiazole-C2), 162.4 (thiadiazole-C5), 174.6 (thiophene-CO), 190.6 (dimedone-C=O). MS, *m/z* (%) = 111 (100), 410 [M]⁺ (15.0); Anal. Calcd. for C₂₁H₁₈N₂O₃S₂ (410): C, 61.44; H, 4.42; N, 6.82; S, 15.62%. Found: C, 61.65; H, 4.33; N, 6.79; S, 15.49%.

2-[3-(4-Chlorophenyl)-5-(thiophene-2-carbonyl)-1,3,4-thiadiazol-2(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (5Hd). Yellow needles crystals, yield 1.89 g, 84%, mp 248-250 °C (DMF); IR (ν_{max}, cm⁻¹): 1665 and 1640 (C=O) cm⁻¹. ¹H NMR (300 MHz, DMSO): δ 1.00 (6H, s, 2CH₃), 2.32 (4H, s, 2CH₂) and 7.28-8.42 (7H, m). ¹³C NMR (75 MHz, DMSO): δ 28.0 (CH₃), 30.4 (C(CH₃)₂), 50.5 (CH₂), 105.0 (1C, C(CO)₂), 117.0, 124.5, 128.8, 132.8, 137.3, 138.4, 138.5 and 158.0 (Ph and thiophene), 141.3 (thiadiazole-C2), 162.6 (thiadiazole-C5), 174.5 (thiophene-CO), 190.7 (dimedone-C=O). MS, *m/z* (%) = 111 (100), 444 [M]⁺ (16.3); Anal. Calcd. for C₂₁H₁₇ClN₂O₃S₂ (444): C, 56.69; H, 3.85; Cl, 7.97; N, 6.30; S, 14.41%. Found: C, 56.91; H, 3.75; Cl, 7.85; N, 6.19; S, 14.31%.

2-(5-(2-Naphthoyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (5Ia). Yellow needles crystals, yield 2.14 g, 93%, mp 224-226 °C (CH₃CN); IR (ν_{max}, cm⁻¹): 1648 and 1640 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.08 (6H, s, 2CH₃), 2.43 (4H, s, 2CH₂) and 7.11-9.00 (12H, m). MS, *m/z* (%) = 127 (100), 454 [M]⁺ (28.0); Anal. Calcd. for C₂₇H₂₂N₂O₃S (454): C, 71.34; H, 4.88; N, 6.16; S, 7.05%. Found: C, 71.60; H, 4.71; N, 6.02; S, 6.98%.

2-(3,5-Diphenyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (5Ja). White needles crystals, yield 1.52 g, 80%, mp 188-190 °C (CH₃CN); IR (ν_{max}, cm⁻¹): 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.36 (4H, s, 2CH₂) and 7.27-7.91 (10H, m, 2Ph). ¹³C NMR (75 MHz, CDCl₃): δ 28.4 (CH₃), 30.7 (CMe₂), 50.9 (CH₂), 104.3 (C(CO)₂), 122.8, 127.0, 128.5, 128.6, 128.9, 129.2, 131.7 and 160.6 (Ph), 143.1 (thiadiazole-C2), 163.0 (thiadiazole-C5), 191.2 (dimedone-C=O). MS, *m/z* (%) = 77 (100), 376 [M]⁺ (34.23); Anal. Calcd. for C₂₂H₂₀N₂O₂S (376): C, 70.19; H, 5.35; N, 7.44; S, 8.52%. Found: C, 70.41; H, 5.24; N, 7.30; S, 8.41%.

2-(5-(Furan-2-yl)-3-(4-nitrophenyl)-1,3,4-thiadiazol-2(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (5Ke). Beige blocks crystals, yield 1.63 g, 78%, mp 214-216 °C (CH₃CN); IR (ν_{max}, cm⁻¹): 1665 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.16 (6H, s, 2CH₃), 2.41 (4H, s, 2CH₂) and 6.60-8.34 (7H, m). MS, *m/z* (%) = 55 (100), 411 [M]⁺ (45.16); Anal.

Calcd. for C₂₀H₁₇N₃O₅S (411): C, 58.38; H, 4.16; N, 10.21; S, 7.79%. Found: C, 58.40; H, 4.01; N, 10.13; S, 7.65%.

5,5-Dimethyl-2-(3-(4-nitrophenyl)-5-(thiophen-2-yl)-1,3,4-thiadiazol-2(3H)-ylidene)

cyclohexane-1,3-dione (5Le). Yellow needles crystals, yield 1.75 g, 81%, mp 256-258 °C (DMF); IR (ν_{\max} , cm⁻¹): 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, DMSO): δ 0.98 (6H, s, 2CH₃), 2.32 (4H, s, 2CH₂) and 7.26-8.32 (7H, m). ¹³C NMR (75 MHz, DMSO): δ 28.0 (CH₃), 30.5 (CMe₂), 50.4 (CH₂), 104.6 (C(CO)₂), 124.1, 124.3, 128.9, 129.5, 131.8, 146.1, 147.4 and 154.7 (Ar and thiadiazole-C2), 161.2 (thiadiazole-C5), 190.8 (dimedone-CO). MS, m/z (%) = 55 (100), 427 [M]⁺ (37.94); Anal. Calcd. for C₂₀H₁₇N₃O₄S₂ (427): C, 56.19; H, 4.01; N, 9.83; S, 15.00%. Found: C, 56.30; H, 3.92; N, 9.68; S, 14.87%.

(E)-2-(5-(3-(Dimethylamino)acryloyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-

dimethylcyclohexane-1,3-dione (6). To a compound 5Aa (10.3 g, 0.03 mole) in dioxane (50 mL), dimethylformamide dimethyl acetal (DMF-DMA) (4 mL, 0.03 mol) was added. The reaction mixture was refluxed for 6h. The solid product was collected and crystallized from DMF to afford compound 6. Red needles crystals, yield 11.12 g, 93%, mp 250-252 °C (DMF); IR (ν_{\max} , cm⁻¹): 1635 and 1650 (C=O) cm⁻¹. ¹H NMR (300 MHz, DMSO): δ 0.96 (6H, s, 2CH₃), 2.23 (4H, s, 2CH₂), 2.93 (3H, s, CH₃), 3.20 (3H, s, CH₃), 5.77-5.81 (1H, *J* 13 Hz, d, CH), 7.30-7.40 (5H, m, Ph) and 7.88-7.90 (1H, *J* 13 Hz, d, CH). ¹³C NMR (75 MHz, DMSO): δ 28.1 (CH₃), 30.3 (CMe₂), 37.3 (CH₃N), 45.1 (CH₃N), 50.6 (CH₂), 89.1 (CHCO), 104.3 (C(CO)₂), 122.6, 127.9, 128.5 and 155.1 (Ph), 142.7 (thiadiazole-C2), 162.5 (thiadiazole-C5), 164.0 (CH=CHCO), 175.2 (COCH), 190.2 (dimedone-CO). MS, m/z (%) = 98 (100), 397 [M]⁺ (11.0); Anal. Calcd. for C₂₁H₂₃N₃O₃S (397): C, 63.47; H, 5.83; N, 10.57; S 8.05%. Found: C, 63.69; H, 5.77; N, 10.43; S 7.98%.

General procedure for 2-(1-aryl-3-substituted-pyrazol-4-carbonyl)-5-(3-phenyl-5-(5,5-dimethylcyclohexane-1,3-dione)-[1,3,4]-thiadiazole derivatives (7). To a solution of the enaminone 6 (2 g, 0.005 mol) and the appropriate hydrazoneyl halide 4 (0.005 mol) in chloroform CHCl₃ (50 mL), triethylamine TEA (2 ml) was added. The reaction mixture was refluxed for 6 h. The solvent was evaporated then ethanol was added. The solid that precipitated was collected, washed with ethanol and crystallized from a suitable solvent to give the corresponding products 7. The compounds 7 prepared together with their physical constants are given below.

2-[5-(3-Acetyl-1-phenyl-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Aa). Yellow needles crystals, yield 2.29 g, 89%, mp 192-194 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1702 and 1656 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 2.37 (4H, s, 2CH₂), 2.59 (3H, s, CH₃CO), 7.27-7.75 (10H, m, 2Ph) and 8.55 (1H, s, CH). ¹³C NMR (75 MHz, CDCl₃): δ 27.1 (CH₃), 28.4 (CH₃CO), 30.2 (CMe₂), 50.6 (CH₂), 105.5 (C(CO)₂), 120.2, 121.5, 122.0, 128.4, 129.1, 130.3, 131.1 and 152.4 (2Ph), 132.2, 138.8 and 158.0 (pyrazole), 143.2 (thiadiazole-C2), 162.4 (thiadiazole-C5), 178.3 (CO), 191.8 (COCH₃), 193.8 (dimedone-CO). MS, m/z (%) = 213 (100), 512 [M]⁺ (44.0); Anal. Calcd. for

C₂₈H₂₄N₄O₄S (512): C, 65.61; H, 4.72; N, 10.93; S, 6.26%. Found: C, 65.82; H, 4.64; N, 10.81; S, 6.18%.

2-(5-(3-Acetyl-1-(p-tolyl)-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Ab). Yellow needles crystals, yield 2.23 g, 84%, mp 182 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1700 and 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, DMSO): δ 0.97 (6H, s, 2CH₃), 2.31 (4H, s, 2CH₂), 2.36 (3H, s, CH₃), 2.57 (3H, s, CH₃CO), 7.34-7.84 (9H, m, 2Ph) and 9.20 (1H, s, CH). ¹³C NMR (75 MHz, DMSO): δ 20.5 (CH₃-C₆H₄), 27.5 (CH₃), 28.0 (CH₃CO), 30.4 (CMe₂), 50.4 (CH₂), 105.0 (1C, C(CO)₂), 119.3, 119.5, 120.6, 122.8, 128.5, 128.9, 130.1 and 151.0 (Ar), 133.8, 138.0 and 157.9 (pyrazole), 142.5 (thiadiazole-C2), 162.7 (thiadiazole-C5), 178.6 (CO), 190.7 (COMe), 193.3 (dimedone-CO). Anal. Calcd. for C₂₉H₂₆N₄O₄S (526): C, 66.14; H, 4.98; N, 10.64; S, 6.09%. Found: C, 66.35; H, 4.88; N, 10.45; S, 5.89%.

2-(5-(3-Acetyl-1-(4-chlorophenyl)-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Ac). Yellow needles crystals, yield 2.17 g, 79%, mp 204 °C (DMF); IR (ν_{\max} , cm⁻¹): 1700 and 1658 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.04 (6H, s, 2CH₃), 2.36 (4H, s, 2CH₂), 2.56 (3H, s, CH₃CO), 7.27-7.71 (9H, m, 2Ph) and 8.55 (1H, s, CH). ¹³C NMR (75 MHz, CDCl₃): δ 27.7 (CH₃), 28.4 (CH₃CO), 30.8 (CMe₂), 51.0 (CH₂), 105.2 (C(CO)₂), 120.3, 121.2, 122.8, 128.9, 129.1, 129.9, 132.0 and 152.3 (Ar), 134.4, 137.1 and 156.1 (pyrazole), 142.8 (thiadiazole-C2), 164.6 (thiadiazole-C5), 178.0 (CO), 191.6 (COMe), 193.4 (dimedone-CO). Anal. Calcd. for C₂₈H₂₃ClN₄O₄S (546): C, 61.48; H, 4.24; Cl, 6.48; N, 10.24; S, 5.86%. Found: C, 61.69; H, 4.10; Cl, 6.34; N, 10.14; S, 5.78%.

2-[5-(3-Benzoyl-1-phenyl-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Ba). Yellow blocks crystals, yield 2.39 g, 83%, mp 240-242 °C (DMF); IR (ν_{\max} , cm⁻¹): 1680 and 1660 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.03 (6H, s, 2CH₃), 2.34 (4H, s, 2CH₂), 7.08-8.05 (15H, m) and 8.75 (1H, s, CH). MS, m/z (%) = 77 (100), 574 [M]⁺ (16.5); Anal. Calcd. for C₃₃H₂₆N₄O₄S (574): C, 68.97; H, 4.56; N, 9.75; S, 5.58%. Found: C, 69.10; H, 4.44; N, 9.68; S, 5.42%.

2-(5-(3-Benzoyl-1-(p-tolyl)-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Bb). Yellow needles crystals, yield 2.30 g, 78%, mp 230-232 °C (DMF); IR (ν_{\max} , cm⁻¹): 1678 and 1657 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.02 (6H, s, 2CH₃), 2.33 (4H, s, 2CH₂), 2.40 (3H, s, CH₃), 7.08-8.03 (14H, m) and 8.71 (1H, s, CH). ¹³C NMR (75 MHz, CDCl₃): δ 21.0 (CH₃-C₆H₄), 28.4 (CH₃), 30.7 (CMe₂), 51.0 (CH₂), 105.2 (C(CO)₂), 120.0, 121.0, 122.5, 128.4, 128.6, 128.9, 130.2, 130.3, 131.7, 133.6, 136.1 and 152.3 (Ar), 136.3, 138.7 and 159.1 (pyrazole), 142.6 (thiadiazole-C2), 164.3 (thiadiazole-C5), 176.9 (CO), 188.5 (COPh), 191.4 (dimedone-CO). Anal. Calcd. for C₃₄H₂₈N₄O₄S (588): C, 69.37; H, 4.79; N, 9.52; S, 5.45%. Found: C, 69.51; H, 4.42; N, 9.40; S, 5.39%.

Ethyl 4-[5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carbonyl]-1-phenyl-1H-pyrazole-3-carboxylate (7Da). Yellow needles crystals, yield 2.48 g, 91%, mp 182-184 °C (CH₃CN); IR (ν_{\max} , cm⁻¹): 1739 (COOEt), 1671 and 1644 (C=O) cm⁻¹. ¹H

NMR (300 MHz, CDCl₃): δ 1.06 (6H, s, 2CH₃), 1.25-1.30 (3H, J = 7.5 Hz, t, CH₃), 2.36 (s, 4H, 2CH₂), 4.24-4.30 (2H, J = 7.5 Hz, q, CH₂), 7.27-7.74 (10H, m) and 8.64 (1H, s, CH). ¹³C NMR (75 MHz, CDCl₃): δ 14.0 (CH₃CH₂), 26.8 (CH₃), 30.4 (CMe₂), 50.4 (CH₂), 61.8 (OCH₂CH₃), 105.5 (C(CO)₂), 119.9, 120.2, 123.5, 128.7, 129.5, 129.8, 130.8 and 151.2 (Ar), 134.5, 139.6 and 159.3 (pyrazole), 143.4 (thiadiazole-C2), 161.8 (thiadiazole-C5), 178.3 (CO), 189.4 (COOEt), 194.3 (dimedone-CO). MS, m/z (%) = 104 (100), 542 [M]⁺ (36.4); Anal. Calcd. for C₂₉H₂₆N₄O₅S (542): C, 64.19; H, 4.83; N, 10.33; S, 5.91%. Found: C, 64.38; H, 4.75; N, 10.28; S, 5.84%.

Ethyl 4-(5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carbonyl)-1-(p-tolyl)-1H-pyrazole-3-carboxylate (7Db). Yellow needles crystals, yield 2.41 g, 86%, mp 216 °C (CH₃CN); ¹H NMR (300 MHz, DMSO): δ 0.98 (6H, s, 2CH₃), 1.12-1.17 (3H, J = 7.5 Hz, t, CH₃), 2.32 (3H, s, CH₃), 2.37 (4H, s, 2CH₂), 4.13-4.20 (2H, J = 7.5 Hz, q, CH₂), 7.37-7.83 (9H, m) and 9.34 (1H, s, CH). ¹³C NMR (75 MHz, DMSO): δ 13.7 (CH₃CH₂), 20.5 (CH₃-C₆H₄), 28.0 (CH₃), 30.5 (CMe₂), 50.4 (CH₂), 61.5 (OCH₂CH₃), 105.1 (C(CO)₂), 119.7, 119.9, 122.7, 128.5, 128.8, 130.2, 133.6 and 157.9 (Ar), 135.9, 138.1 and 161.3 (pyrazole), 142.5 (thiadiazole-C2), 162.6 (thiadiazole-C5), 177.6 (CO), 180.0 (COOEt), 190.8 (dimedone-CO). Anal. Calcd. for C₃₀H₂₈N₄O₅S (556): C, 64.73; H, 5.07; N, 10.07; S, 5.76%. Found: C, 64.91; H, 4.95; N, 9.97; S, 5.61%.

Ethyl 1-(4-chlorophenyl)-4-(5-(4,4-dimethyl-2,6-dioxocyclohexylidene)-4-phenyl-4,5-dihydro-1,3,4-thiadiazole-2-carbonyl)-1H-pyrazole-3-carboxylate (7Dc). Yellow needles crystals, yield 2.40 g, 83%, mp 210 °C; (CH₃CN); ¹H NMR (300 MHz, CDCl₃): δ 1.04 (6H, s, 2CH₃), 1.23-1.28 (3H, J = 7.5 Hz, t, CH₃), 2.36 (s, 4H, 2CH₂), 4.21-4.28 (2H, J = 7.5 Hz, q, CH₂), 7.27-7.70 (9H, m) and 8.62 (1H, s, CH). ¹³C NMR (75 MHz, CDCl₃): δ 14.2 (CH₃CH₂), 28.7 (CH₃), 31.1 (CMe₂), 51.4 (CH₂), 62.4 (OCH₂Me), 105.7 (C(CO)₂), 121.0, 121.7, 122.8, 129.2, 129.4, 130.1, 132.1 and 146.4 (Ar), 134.7, 138.3 and 161.8 (pyrazole), 143.1 (thiadiazole-C2), 164.5 (thiadiazole-C5), 177.1 (CO), 188.0 (COOEt), 191.9 (dimedone-CO). Anal. Calcd. for C₂₉H₂₅ClN₄O₅S (576): C, 60.36; H, 4.37; Cl, 6.14; N, 9.71; S, 5.56%. Found: C, 60.67; H, 4.27; Cl, 6.02; N, 9.65; S, 5.41%.

2-[5-[3-(Furan-2-carbonyl)-1-phenyl-1H-pyrazole-4-carbonyl]-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Ga). Yellow needles crystals, yield 2.47 g, 87%, mp 242-244 °C (DMF); ¹H NMR (300 MHz, DMSO): δ 0.97 (6H, s, 2CH₃), 2.30 (4H, s, 2CH₂), 6.8-8.2 (13H, m) and 9.45 (1H, s, CH). ¹³C NMR (75 MHz, DMSO): δ 28.0 (CH₃), 30.4 (CMe₂), 50.4 (CH₂), 105.0 (1C, C(CO)₂), 113.2, 120.4, 122.6, , 120.0, 120.7, 123.6, 128.3, 128.4, 128.7, 129.8, 149.4 and 150.8 (Ar and furan), 133.9, 138.2 and 157.5 (pyrazole), 142.4 (thiadiazole-C2), 162.6 (thiadiazole-C5), 174.2 (CO), 177.7 (furan-CO), 190.7 (dimedone-CO). MS, m/z (%) = 95 (100), 564 [M]⁺ (19.4); Anal. Calcd. for C₃₁H₂₄N₄O₅S (564): C, 65.94; H, 4.28; N, 9.92; S, 5.68%. Found: C, 66.01; H, 4.14; N, 9.80; S, 5.57%.

5,5-Dimethyl-2-[3-phenyl-5-[1-phenyl-3-(thiophene-2-carbonyl)-1H-pyrazole-4-carbonyl]-1,3,4-thiadiazol-2(3H)-ylidene]cyclohexane-1,3-dione (7Ha). Yellow blocks crystals, yield 2.63 g, 90%, mp 228-230 °C (DMF); IR (ν_{\max} , cm⁻¹): 1690 and 1665 (C=O) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ 1.05 (6H, s, 2CH₃), 2.36 (4H, s, 2CH₂), 7.11-8.06 (13H, m) and 8.66 (1H, s,

CH). MS, m/z (%) = 111 (100), 580 $[M]^+$ (14.5); Anal. Calcd. for $C_{31}H_{24}N_4O_4S_2$ (580): C, 64.12; H, 4.17; N, 9.65; S, 11.04%. Found: C, 64.35; H, 4.02; N, 9.51; S, 10.98%.

5,5-Dimethyl-2-(3-phenyl-5-(3-(thiophene-2-carbonyl)-1-(p-tolyl)-1H-pyrazole-4-carbonyl)-1,3,4-thiadiazol-2(3H)-ylidene)cyclohexane-1,3-dione (7Hb). Yellow needles crystals, yield 2.60 g, 87%, mp 238 °C (DMF); IR (ν_{max} , cm^{-1}): 1687 and 1662 (C=O) cm^{-1} . 1H NMR (300 MHz, $CDCl_3$): δ 1.03 (6H, s, 2CH₃), 2.34 (3H, s, CH₃), 2.42 (4H, s, 2CH₂), 7.10-8.04 (12H, m) and 8.62 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3 (CH₃-C₆H₄), 28.7 (CH₃), 31.0 (CMe₂), 51.4 (CH₂), 105.6 (1C, $\underline{C}(\text{CO})_2$), 120.2, 121.3, 122.8, 128.5, 128.9, 129.1, 130.6, 131.9, 135.8, 136.3, 136.6 and 151.9 (Ar and thiophene), 139.0, 142.7 and 159.2 (pyrazole), 143.0 (thiadiazole-C2), 164.7 (thiadiazole-C5), 177.8 (CO), 180.7 (thiophene-CO), 191.8 (dimedone-CO). Anal. Calcd. for $C_{32}H_{26}N_4O_4S_2$ (594): C, 64.63; H, 4.41; N, 9.42; S, 10.78%. Found: C, 64.90; H, 4.30; N, 9.28; S, 10.67%.

2-(5-(1-(4-Chlorophenyl)-3-(thiophene-2-carbonyl)-1H-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Hc). Yellow blocks crystals, yield 2.59 g, 84%, mp 242 °C (DMF); IR (ν_{max} , cm^{-1}): 1690 and 1664 (C=O) cm^{-1} . 1H NMR (300 MHz, $CDCl_3$): δ 1.01 (6H, s, 2CH₃), 2.31 (4H, s, 2CH₂), 6.76-8.22 (12H, m) and 8.61 (1H, s, CH). Anal. Calcd. for $C_{31}H_{23}ClN_4O_4S_2$ (614): C, 60.53; H, 3.77; Cl, 5.76; N, 9.11; S, 10.43%. Found: C, 60.75; H, 3.68; Cl, 5.66; N, 9.05; S, 10.29%.

2-[5-[3-(2-Naphthoyl)-1-phenyl-1H-pyrazole-4-carbonyl]-3-phenyl-1,3,4-thiadiazol-2(3H)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Ja). Yellow needles crystals, yield 2.42 g, 77%, mp 222-224 °C (CH_3CN); IR (ν_{max} , cm^{-1}): 1675 and 1660 (C=O) cm^{-1} . 1H NMR (300 MHz, DMSO): δ 0.94 (6H, s, 2CH₃), 2.26 (4H, s, 2CH₂), 7.02-8.64 (17H, m) and 9.53 (1H, s, CH). ^{13}C NMR (75 MHz, DMSO): δ 27.9 (CH₃), 30.4 (CMe₂), 50.4 (CH₂), 105.0 (C(CO)₂), 120.0, 120.7, 122.5, 124.3, 127.0, 127.7, 128.2, 128.4, 128.7, 129.3, 129.8, 130.0, 132.0, 133.2, 133.9 and 151.9 (Ar), 135.5, 138.2 and 157.8 (pyrazole), 142.2 (thiadiazole-C2), 162.5 (thiadiazole-C5), 177.5 (CO), 188.5 (naphthalene-CO), 190.7 (dimedone-CO). MS, m/z (%) = 127 (100), 624 $[M]^+$ (51.2); Anal. Calcd. for $C_{37}H_{28}N_4O_4S$ (624): C, 71.14; H, 4.52; N, 8.97; S, 5.13%. Found: C, 71.29; H, 4.48; N, 8.85; S, 5.08%.

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