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

Hamdi M. Hassaneen,* Ahmad S. Shawali, Tayseer A. Abdallah, and Fatma M. Saleh

Department of Chemistry, Faculty of Science, University of Cairo, Giza, Egypt
E-mail: hamdi_251@yahoo.com

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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(3H)-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.

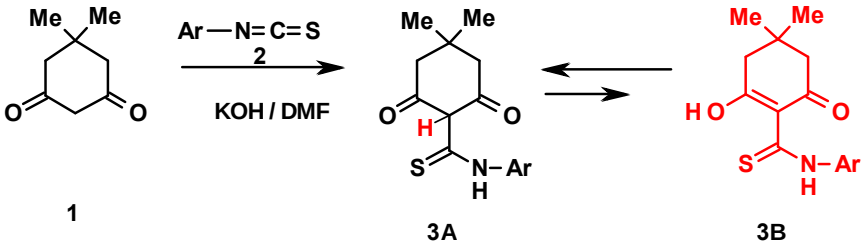
Keywords: Dimedone, thioanilide, enaminone, thiadiazole, hydrazonoyl halides

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, $2CH_3$) and 2.65 (4H, $2CH_2$) 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).



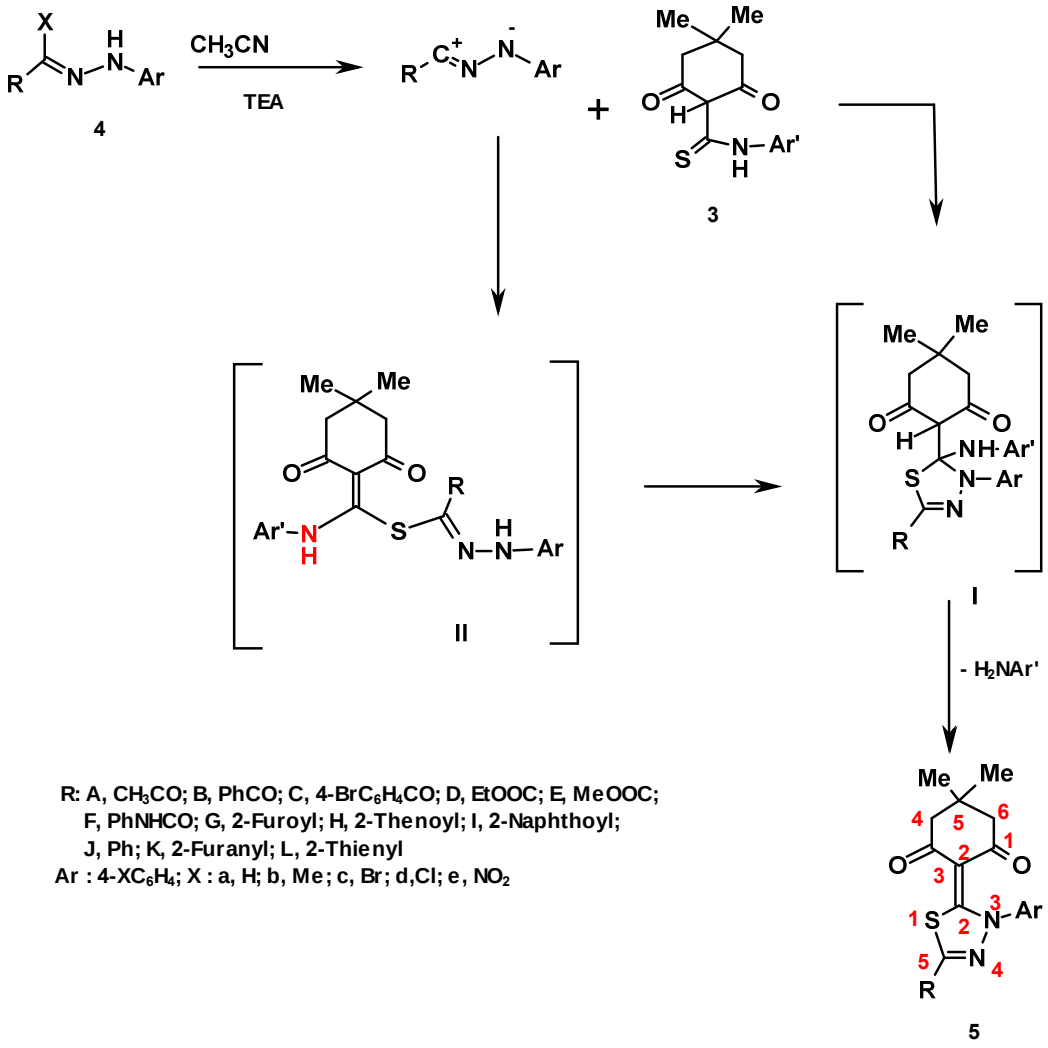
Ar = 4-XC_6H_4 ; X : a, H; b, Cl; c,Me

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 hydrazonoyl halides with other thioanilides.[21-23]

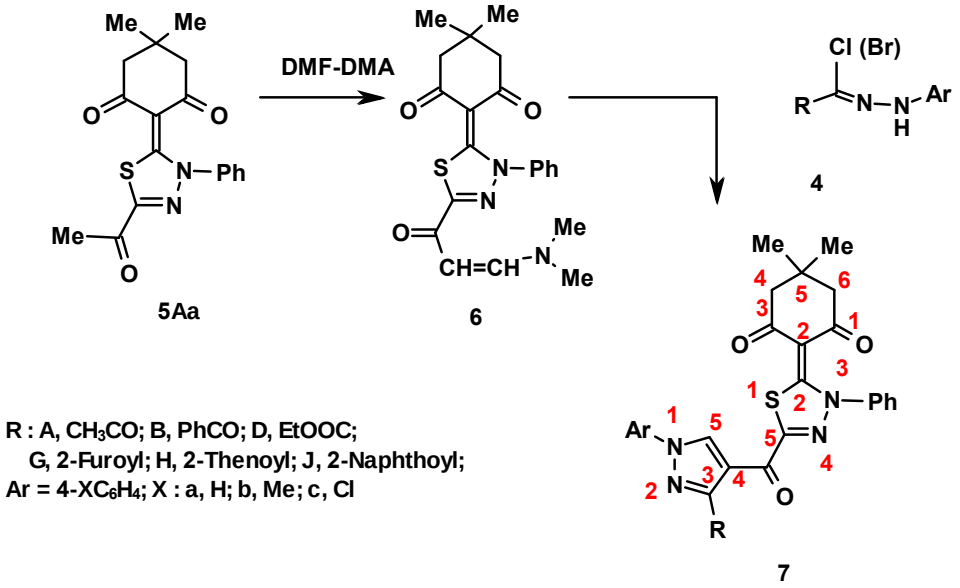


Scheme 2

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, $2CH_3$) and δ 2.23 (4H, $2CH_2$) and a singlet signal at 2.93–3.20 (6H, $N(CH_3)_2$). 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 ^{1}H 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 ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or [D_6] DMSO on a Varian Mercury VXR 300 spectrometer (300 MHz for ^{1}H 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 procedures [24-32]

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 dimedone 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 ^{o}C IR (ν_{max}, cm^{-1}): 3217 (NH), 1697 and 1664 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12 (6H, s, $2CH_3$), 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 ($C(CO)_2$), 120.7, 125.3, 127.1 and 128.9 (Ph), 187.9 (C=S), 190.2 (dimedone-CO), 199.0 (dimedone-CO). Anal. Calcd. for $C_{15}H_{17}NO_2S$ (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 ^{o}C IR (ν_{max}, cm^{-1}): 3210 (NH), 1695 and 1660 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.11 (6H, s, $2CH_3$), 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 $C_{15}H_{16}ClNO_2S$ (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 ^{o}C IR (ν_{max}, cm^{-1}): 3215 (NH), 1693 and 1662 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12 (6H, s, $2CH_3$), 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 ($\underline{CH_3}C_6H_4$), 27.7 (CH_3), 29.8 (CMe_2), 46.5 (CH_2), 52.2 (CH_2), 107.8 (1C, $C(CO)_2$), 125.1, 129.3, 134.8 and 136.8 (Ph), 188.4 (C=S), 191.0 (dimedone-CO), 198.9 (dimedone-CO). Anal. Calcd. for $C_{16}H_{19}NO_2S$ (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(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (5Aa). Yellow needles crystals, yield 1.56 g, 92%, mp 204-206 ^{o}C (CH_3CN); IR (ν_{max}, cm^{-1}): 1689 and 1652 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (6H, s, $2CH_3$), 2.36 (4H, s, $2CH_2$), 2.69 (3H, s, CH_3CO) and 7.27-7.40 (5H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.5 ($\underline{CH_3}CO$), 26.2 (CH_3), 30.9 (CMe_2), 52.0 (CH_2), 105.5 (1C, $\underline{C}(CO)_2$), 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 $C_{18}H_{18}N_2O_3S$ (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(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (5Ba). Orange needles crystals, yield 1.81 g, 88%, mp 210-212 ^{o}C (CH_3CN); IR (ν_{max}, cm^{-1}): 1649 and 1590 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (6H, s, $2CH_3$), 2.39 (4H, s, $2CH_2$) and 7.27-8.34 (10H, m, 2Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.7 (CH_3), 31.2 (CMe_2), 51.2 (CH_2), 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 $C_{23}H_{20}N_2O_3S$ (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(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (5Bd). Yellow needles crystals, yield 1.89 g, 85%, mp 260-262 ^{o}C (DMF-Ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.40 (4H, s, $2CH_2$) and 7.27-8.30 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.7 (CH_3), 31.1 (CMe_2), 51.4 (CH_2), 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 $C_{23}H_{19}ClN_2O_3S$ (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(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (5Ca). Yellow needles crystals, yield 2.21 g, 90%, mp 236-238 ^{o}C (DMF); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.00 (6H, s, $2CH_3$), 2.30 (4H, s, $2CH_2$) and 7.06-8.18 (9H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.9 (CH_3), 30.4 (CMe_2), 50.5 (CH_2), 104.9 (1C, $\underline{C}(CO)_2$), 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 $C_{23}H_{19}BrN_2O_3S$ (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 ^{o}C (CH_3CN); IR (ν_{max}, cm^{-1}): 1713 (COOEt), 1680 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (6H, s, $2CH_3$), 1.29-1.47 (3H, ^{3}J = 7.3 Hz, t, CH_3), 2.40 (4H, s, $2CH_2$), 4.05-4.25 (2H, ^{3}J = 7.3 Hz, q, CH_2) and 7.09-7.49 (5H, m, Ph). MS, *m/z* (%) =77 (100), 372 $[M]^+$ (33.1); Anal. Calcd. for $C_{19}H_{20}N_2O_4S$ (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 ^{o}C; (CH_3CN); IR (ν_{max}, cm^{-1}): 1710 (COOMe), 1685 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.00 (6H, s, $2CH_3$), 2.34 (4H, s, $2CH_2$), 4.00 (3H, s, OCH_3) and 6.90-7.30 (5H, m, Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.4 (CH_3), 30.8 (CMe_2), 51.6 (CH_2), 57.8 (CH_3O), 108.6 (1C, $\underline{C}(CO)_2$), 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 $C_{18}H_{18}N_2O_4S$ (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 ^{o}C (DMF); IR (ν_{max}, cm^{-1}): 3384 (NH), 1683 and 1646 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.38 (4H, s, $2CH_2$), 7.07-7.69 (10H, m) and 11.80 (1H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.9 (CH_3), 31.1 (CMe_2), 51.3 (CH_2), 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 $C_{23}H_{21}N_3O_3S$ (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 ^{o}C (DMF); IR (ν_{max}, cm^{-1}): 3380 (NH), 1680 and 1650 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (6H, s, $2CH_3$), 1.78 (3H, s, CH_3), 2.88-2.95 (4H, s, $2CH_2$), 7.12-7.39 (9H, m) and 11.74 (1H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2 ($\underline{CH_3}$-C_6H_4), 27.9 (CH_3), 31.2 (CMe_2), 51.2 (CH_2), 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 $C_{24}H_{23}N_3O_3S$ (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 ^{o}C (DMF-Ethanol); IR (ν_{max}, cm^{-1}): 3385 (NH), 1685 and 1661 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.39 (4H, s, $2CH_2$), 7.18-8.61 (9H, m) and 11.87 (1H, s, NH). MS, *m/z* (%) = 77 (100), 497 $[M]^+$ (25.4); Anal. Calcd. for $C_{23}H_{20}BrN_3O_3S$ (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 ^{o}C (DMF); IR (ν_{max}, cm^{-1}): 3382 (NH), 1680 and 1660 (C=O) cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.41 (4H, s, $2CH_2$), 7.22-7.67 (9H, m) and 11.90 (1H, s, NH). MS, *m/z* (%) = 55 (100), 453 $[M]^+$ (32.0); Anal. Calcd. for $C_{23}H_{20}ClN_3O_3S$ (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 ^{o}C (CH_3CN); IR (ν_{max},

cm^{-1}): 1695 and 1660 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.17 (6H, s, $2CH_3$), 2.39 (4H, s, $2CH_2$) and 6.62-7.92 (8H, m). MS, *m/z* (%) = 95 (100), 394 $[M]^+$ (7.01); Anal. Calcd. for $C_{21}H_{18}N_2O_4S$ (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 ^oC (DMF); IR (ν_{max}, cm^{-1}): 1660 and 1650 (C=O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.97 (6H, s, $2CH_3$), 2.29 (4H, s, $2CH_2$) and 7.32-8.42 (8H, m). ^{13}C NMR (75 MHz, DMSO): δ 28.0 (CH_3), 30.4 (CMe_2), 50.4 (CH_2), 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 $C_{21}H_{18}N_2O_3S_2$ (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 ^oC (DMF); IR (ν_{max}, cm^{-1}): 1665 and 1640 (C=O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 1.00 (6H, s, $2CH_3$), 2.32 (4H, s, $2CH_2$) and 7.28-8.42 (7H, m). ^{13}C NMR (75 MHz, DMSO): δ 28.0 (CH_3), 30.4 ($\underline{C}(CH_3)_2$), 50.5 (CH_2), 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 $C_{21}H_{17}ClN_2O_3S_2$ (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 ^oC (CH_3CN); IR (ν_{max}, cm^{-1}): 1648 and 1640 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.08 (6H, s, $2CH_3$), 2.43 (4H, s, $2CH_2$) and 7.11-9.00 (12H, m). MS, *m/z* (%) =127 (100), 454 $[M]^+$ (28.0); Anal. Calcd. for $C_{27}H_{22}N_2O_3S$ (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 ^oC (CH_3CN); IR (ν_{max}, cm^{-1}): 1660 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.36 (4H, s, $2CH_2$) and 7.27-7.91 (10H, m, 2Ph). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.4 (CH_3), 30.7 (CMe_2), 50.9 (CH_2), 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 $C_{22}H_{20}N_2O_2S$ (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-dimethyl cyclohexane-1,3-dione (5Ke). Beige blocks crystals, yield 1.63 g, 78%, mp 214-216 ^oC (CH_3CN); IR (ν_{max}, cm^{-1}): 1665 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.16 (6H, s, $2CH_3$), 2.41 (4H, s, $2CH_2$) and 6.60-8.34 (7H, m). MS, *m/z* (%) = 55 (100), 411 $[M]^+$ (45.16); Anal.

Calcd. for $C_{20}H_{17}N_3O_5S$ (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(3*H*)-ylidene) cyclohexane-1,3-dione (5Le). Yellow needles crystals, yield 1.75 g, 81%, mp 256-258 ^{o}C (DMF); IR (ν_{max}, cm^{-1}): 1660 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO): δ 0.98 (6H, s, $2CH_3$), 2.32 (4H, s, $2CH_2$) and 7.26-8.32 (7H, m). ^{13}C NMR (75 MHz, DMSO): δ 28.0 (CH_3), 30.5 (CMe_2), 50.4 (CH_2), 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 $C_{20}H_{17}N_3O_4S_2$ (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(3*H*)-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 compoud **6**. Red needles crystals, yield 11.12 g, 93%, mp 250-252 ^{o}C (DMF); IR (ν_{max}, cm^{-1}): 1635 and 1650 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO): δ 0.96 (6H, s, $2CH_3$), 2.23 (4H, s, $2CH_2$), 2.93 (3H, s, CH_3), 3.20 (3H, s, CH_3), 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). ^{13}C NMR (75 MHz, DMSO): δ 28.1 (CH_3), 30.3 (CMe_2), 37.3 (CH_3N), 45.1 (CH_3N), 50.6 (CH_2), 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 $C_{21}H_{23}N_3O_3S$ (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 hydrazonoyl halide **4 (**0.005 mol) in chloroform $CHCl_3$ (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-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Aa). Yellow needles crystals, yield 2.29 g, 89%, mp 192-194 ^{o}C (CH_3CN); IR (ν_{max}, cm^{-1}): 1702 and 1656 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 2.37 (4H, s, $2CH_2$), 2.59 (3H, s, CH_3CO), 7.27-7.75 (10H, m, 2Ph) and 8.55 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.1 (CH_3), 28.4 ($\underline{CH_3}CO$), 30.2 (CMe_2), 50.6 (CH_2), 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 ($COCH_3$), 193.8 (dimedone-CO). MS, *m/z* (%) = 213 (100), 512 $[M]^+$ (44.0); Anal. Calcd. for

$C_{28}H_{24}N_4O_4S$ (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)-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene) -5,5-dimethylcyclohexane-1,3-dione (7Ab). Yellow needles crystals, yield 2.23 g, 84%, mp 182 ^oC (CH_3CN); IR (ν_{max}, cm^{-1}): 1700 and 1660 (C=O) cm^{-1}. ^1H NMR (300 MHz, DMSO): δ 0.97 (6H, s, $2CH_3$), 2.31 (4H, s, $2CH_2$), 2.36 (3H, s, CH_3), 2.57 (3H, s, CH_3CO), 7.34-7.84 (9H, m, 2Ph) and 9.20 (1H, s, CH). ^{13}C NMR (75 MHz, DMSO): δ 20.5 ($\underline{CH_3}$-C_6H_4), 27.5 (CH_3), 28.0 (CH_3CO), 30.4 (CMe_2), 50.4 (CH_2), 105.0 (1C, $\underline{C}(CO)_2$), 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 $C_{29}H_{26}N_4O_4S$ (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)-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*) -ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Ac). Yellow needles crystals, yield 2.17 g, 79%, mp 204 ^oC (DMF); IR (ν_{max}, cm^{-1}): 1700 and 1658 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.04 (6H, s, $2CH_3$), 2.36 (4H, s, $2CH_2$), 2.56 (3H, s, CH_3CO), 7.27-7.71 (9H, m, 2Ph) and 8.55 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.7 (CH_3), 28.4 (CH_3CO), 30.8 (CMe_2), 51.0 (CH_2), 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 $C_{28}H_{23}ClN_4O_4S$ (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-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene] -5,5-dimethylcyclohexane-1,3-dione (7Ba). Yellow blocks crystals, yield 2.39 g, 83%, mp 240-242 ^oC (DMF); IR (ν_{max}, cm^{-1}): 1680 and 1660 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.03 (6H, s, $2CH_3$), 2.34 (4H, s, $2CH_2$), 7.08-8.05 (15H, m) and 8.75 (1H, s, CH). MS, *m/z* (%) =77 (100), 574 $[M]^+$ (16.5); Anal. Calcd. for $C_{33}H_{26}N_4O_4S$ (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)-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene)-5,5-dimethylcyclohexane-1,3-dione (7Bb). Yellow needles crystals, yield 2.30 g, 78%, mp 230-232 ^oC (DMF); IR (ν_{max}, cm^{-1}): 1678 and 1657 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.02 (6H, s, $2CH_3$), 2.33 (4H, s, $2CH_2$), 2.40 (3H, s, CH_3), 7.08-8.03 (14H, m) and 8.71 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.0 ($\underline{CH_3}$-C_6H_4), 28.4 (CH_3), 30.7 (CMe_2), 51.0 (CH_2), 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 $C_{34}H_{28}N_4O_4S$ (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-1*H*-pyrazole-3-carboxylate (7Da). Yellow needles crystals, yield 2.48 g, 91%, mp 182-184 ^oC (CH_3CN); IR (ν_{max}, cm^{-1}): 1739 (COOEt), 1671 and 1644 (C=O) cm^{-1}. ^1H

NMR (300 MHz, $CDCl_3$): δ 1.06 (6H, s, $2CH_3$), 1.25-1.30 (3H, *J* = 7.5 Hz, t, CH_3), 2.36 (s, 4H, $2CH_2$), 4.24-4.30 (2H, *J* = 7.5 Hz, q, CH_2), 7.27-7.74 (10H, m) and 8.64 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (CH_3CH_2), 26.8 (CH_3), 30.4 (CMe_2), 50.4 (CH_2), 61.8 (OCH_2CH_3), 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 $C_{29}H_{26}N_4O_5S$ (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)-1*H*-pyrazole-3-carboxylate (7Db). Yellow needles crystals, yield 2.41 g, 86%, mp 216 °C (CH_3CN); ^{1}H NMR (300 MHz, DMSO): δ 0.98 (6H, s, $2CH_3$), 1.12-1.17 (3H, *J* = 7.5 Hz, t, CH_3), 2.32 (3H, s, CH_3), 2.37 (4H, s, $2CH_2$), 4.13-4.20 (2H, *J* = 7.5 Hz, q, CH_2), 7.37-7.83 (9H, m) and 9.34 (1H, s, CH). ^{13}C NMR (75 MHz, DMSO): δ 13.7 (CH_3CH_2), 20.5 (CH_3-C_6H_4), 28.0 (CH_3), 30.5 (CMe_2), 50.4 (CH_2), 61.5 (OCH_2CH_3), 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 $C_{30}H_{28}N_4O_5S$ (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)-1*H*-pyrazole-3-carboxylate (7Dc). Yellow needles crystals, yield 2.40 g, 83%, mp 210 °C; (CH_3CN); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (6H, s, $2CH_3$), 1.23-1.28 (3H, *J* = 7.5 Hz, t, CH_3), 2.36 (s, 4H, $2CH_2$), 4.21-4.28 (2H, *J* = 7.5 Hz, q, CH_2), 7.27-7.70 (9H, m) and 8.62 (1H, s, CH).). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2 (CH_3CH_2), 28.7 (CH_3), 31.1 (CMe_2), 51.4 (CH_2), 62.4 (OCH_2Me), 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 $C_{29}H_{25}ClN_4O_5S$ (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-1*H*-pyrazole-4-carbonyl]-3-phenyl-1,3,4-thiadiazol-2(3*H*)-ylidene]-5,5-dimethylcyclohexane-1,3-dione (7Ga). Yellow needles crystals, yield 2.47 g, 87%, mp 242-244 °C (DMF); ^{1}H NMR (300 MHz, DMSO): δ 0.97 (6H, s, $2CH_3$), 2.30 (4H, s, $2CH_2$), 6.8-8.2 (13H, m) and 9.45 (1H, s, CH). ^{13}C NMR (75 MHz, DMSO): δ 28.0 (CH_3), 30.4 (CMe_2), 50.4 (CH_2), 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 $C_{31}H_{24}N_4O_5S$ (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)-1*H*-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}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (6H, s, $2CH_3$), 2.36 (4H, s, $2CH_2$), 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)-1*H*-pyrazole-4-carbonyl)-1,3,4-thiadiazol-2(3*H*)-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}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.03 (6H, s, $2CH_3$), 2.34 (3H, s, CH_3), 2.42 (4H, s, $2CH_2$), 7.10-8.04 (12H, m) and 8.62 (1H, s, CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.3 (CH_3-C_6H_4), 28.7 (CH_3), 31.0 (CMe_2), 51.4 (CH_2), 105.6 (1C, $\underline{C}(CO)_2$), 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)-1*H*-pyrazole-4-carbonyl)-3-phenyl-1,3,4-thiadiazol-2(3*H*)-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}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (6H, s, $2CH_3$), 2.31 (4H, s, $2CH_2$), 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-1*H*-pyrazole-4-carbonyl]-3-phenyl-1,3,4-thiadiazol-2(3*H*)-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}. ^{1}H NMR (300 MHz, DMSO): δ 0.94 (6H, s, $2CH_3$), 2.26 (4H, s, $2CH_2$), 7.02-8.64 (17H, m) and 9.53 (1H, s, CH). ^{13}C NMR (75 MHz, DMSO): δ 27.9 (CH_3), 30.4 (CMe_2), 50.4 (CH_2), 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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