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Research Article

DESIGN, SYNTHESIS, CHARACTERIZATION AND PHARMACOLOGICAL ACTIVITY OF SOME NEW 1,3,4-OXADIAZOLE BASED 1,3,5-TRIAZINANONES

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ABSTRACT

A new series of various novel 1,4-diphenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones 5a–n were synthesized in good to excellent yields from the raw materials, 2-amino, 5-phenyl-1,3,4-oxadiazole (1) and various benzaldehydes (2) and by involving benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (3) and (isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (4) as intermediates. The chemical structures of these compounds have been established by IR, ^{1}H, ^{13}C-NMR, Mass spectral data and elemental analysis. The newly synthesized compounds were used to evaluate their antimicrobial activity.

INTRODUCTION

1, 3, 4-Oxadiazoles are biologically active, synthetically useful and important heterocyclic compounds. Different classes of oxadiazole compounds possess an extensive spectrum of pharmacological activities such as antibacterial[1], antimalarial[2], anti-inflammatory[3], antifungal[4], anticonvulsant[5], analgesic[6] antimycobacterial[7], antitumor[8], herbicidal[9], vasodialatory[10], cytotoxic[11], hypolipidemic[12], ulcerogenic[13] and antiedema[14]. In the last few decades, the chemistry of triazole and their derivatives has received considerable attention owing to their synthetic and effective biological importance. For example, a large number of 1,2,4-triazole-containing ring system have been incorporated into a wide variety of biological activities such as antibacterial[15], antifungal[16], antitubercular[17], antimycobacterial [18], anticancer[19], antiviral[20].

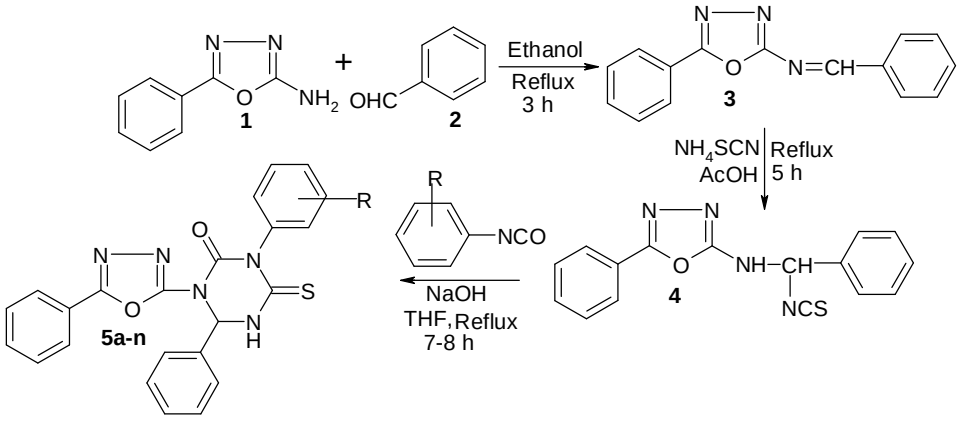
RESULTS AND DISCUSSION

The therapeutic importance of these rings prompted us to develop selective molecules in which a substituent could be arranged in a pharmacophoric pattern to display higher pharmacological activities. Thus we have synthesized various novel 1,4-diphenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones 5a–n in good yields. The synthetic route leading to the title compounds is summarized in scheme 1. The initial intermediate, benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine 3 was prepared through condensation reaction of 2-amino, 5-phenyl-1,3,4-oxadiazole (1) with benzaldehyde (2) in presence of ethanol under reflux for 3 h. Compound 3 on subsequent reaction with ammonium thiocyante in refluxing acetic acid for 5 h afforded key intermediate, (isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (4). Further, the title compounds, 1,4-diphenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones (5a–n) have been synthesized through the ring closure reaction of compound 4 with various phenyl isocyanates on alkaline condition in refluxing tetrahydrofuran for 7-8 h. The chemical structures of all the newly synthesized

compounds were confirmed by their IR, ^{1}H, ^{13}C NMR, mass spectral data and elemental analysis. Further the compounds 5a–n were used to evaluate their antimicrobial activity.

ANTIMICROBIAL ACTIVITY

The *in vitro* antibacterial activity of 1,4-diphenyl-3-(5-phenyl-[1,3,4]oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones **5a–n** was determined using disc diffusion method [21] by measuring zone of inhibition in mm at concentration of 10 µg/disc against two gram-positive strains viz., *Staphylococcus aureus* and *Bacillus subtilis* and two gram-negative strains viz., *Escherichia coli* and *Pseudomonas aeruginosa*. The antifungal evaluation was carried out against fungal organisms namely *Candida albicans* and *Aspergillus niger* at concentration of 5 µg/disc. Standard antibacterial drug Ciprofloxacin (10 µg/disc) and antifungal drug Fluconazole (10 µg/disc) were also tested under similar conditions against these organisms. Each experiment was done in triplicate and the average reading was taken.



Scheme. 1: 5, R a = H, b = 4-OCH_3, c = 4-Cl, d = 4-CH_3, e = 4-Br, f = 3-Cl, 4-Cl, g = 4-CH_2Cl, h = 4-$CH(CH_3)_2$, i = 2-OCF_3, j = 4-OCF_3, k = 2-F, 3-CF_3, l = 2-CF_3, 4-F, m = 2-Cl, 4-CF_3, n = 2-Cl, 5-CF_3

Table 1: Antimicrobial activity of compounds 5a-n (Zone of inhibition in mm)

Compound Activity	Antibacterial activity			Antifungal Activity		
	S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*
5a	09	08	07	09	06	07
5b	15	16	13	15	12	12
5c	17	15	14	17	13	11
5d	15	13	16	13	10	14
5e	13	19	18	17	14	13
5f	12	20	13	19	12	12
5g	11	18	10	14	13	10
5h	14	12	18	12	15	16
5i	20	21	26	20	19	20
5j	24	23	28	20	24	22
5k	26	22	27	25	22	24
5l	21	26	24	21	24	19
5m	22	24	26	22	21	25
5n	19	22	24	24	26	22
Cipro.	26	26	28	25	-	-
Fluco.	-	-	-	-	26	25

Cipro. = Ciprofloxacin; Fluco. = Fluconazole

The investigation of antibacterial screening data revealed that all the tested compounds exhibited significant and interesting biological activity, however with a degree of variation. According to the results (Table 1), it is clear that, some of the compounds displayed excellent antimicrobial activity. Among the series of the screened compounds **5a–n**, the compound **5j** with 4-trifluoromethoxy phenyl ring against *E. coli*, compound **5k** with 2-fluoro, 3-trifluoromethyl phenyl moiety towards *S. aureus and P. Aeruginosa* and compound **5l** which bearing 4-fluor, 2-trifluoromethyl substituted phenyl group against *B. subtilis* are highly active at 26, 26 and 28 mm zone of inhibition respectively, which are equal to the standard drug Ciproflaxacin.

Compounds **5k** and **5l** are highly active against different organisms at 26 mm zone of inhibition, which is equal to both compounds. The compound **5j** with 4-trifluoromethoxy phenyl group, against *E. coli*, compound **5k** against *E.coli*, the compound **5m** with 2-chloro, 4-trifluoromethyl phenyl derivative towards *B. subtilis* and compound **5n** with 2-cloro, 5-trifluoroomethyl phenyl moiety against *P. aeruginosa* are also highly active, at 24, 27, 24 and 24 mm zone of inhibition respectively, and the activity of these compounds are almost equal to the standard. The remaining compounds showed moderate to good antibacterial activity against all the organisms employed.

The compounds **5m** against *A. niger* and compound **5n** against *C. albicans* displayed excellent antifungal activity at zone of inhibition 25 and 26 mm respectively which is also equal to standard drug Flucanazole. The compounds **5j** and **5l** towards *C. albicans* and compound **5k** against *A. niger* are also exhibited antifungal activity at 24, 24 and 24 mm zone of inhibition respectively, which are almost equal to the standard drug. The remaining compounds showed moderate to good activity against the test organisms. The antimicrobial activity is considerably affected by the presence of substituted groups on benzene ring, when compared to unsubstituted compound **5a**. It is interesting to note that, none of the compound is inactive against all the tested microorganisms and this remarkable property may achieve to the compounds due to the two active pharmacophores (oxadiazole and triazinanone) in a single molecular skeleton. The outstanding properties of this new class of antimicrobial substances deserve further investigation in order to clarify the mode of action at molecular level, responsible for the activity observed. More extensive study is also warranted to determine additional physicochemical and biological parameters to have a deeper insight into structure-activity relationship and to optimize the effectiveness of this series of molecules.

EXPERIMENTAL

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60–120 mesh. IR spectra were obtained on a PerkinElmer BX series FT-IR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a Varian 300 MHz spectrometer for ^{1}H NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

Synthesis of benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (3)

To a stirred solution of 2-amino, 5-phenyl-1,3,4-oxadiazole **1** (1 mmol) in ethanol (20 ml), was added a solution of benzaldehyde **2** (1 mmol) in ethanol (20 ml) over a period of 10 min. The reaction mixture was constantly stirred at reflux temperature for 3 h. After completion of the reaction, (monitored by TLC), the mixture on cooling afforded the solid, which was recrystallized from petroleum ether to give pure benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine **3** .

Synthesis of (isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (4)

To a stirred solution of benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine **3** (1 mmol) in acetic acid (20 ml), was added drop wise a solution of ammonium thiocyanate (1 mmol) dissolved in acetic acid (20 ml). The mixture was refluxed on constant stirring for 5 h. After completion of the reaction (monitored by TLC), the separated product was filtered, washed with water, dried, and recrytallized from ethanol to form pure (isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine **4**.

Synthesis of 1,4-diphenyl-3-(5-phenyl-1,4-Diphenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones (5a-n)

A mixture of suitable phenyl isocyanate (1 mmol) in THF (10 ml) was added to a solution of (isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine **4** (1 mmol) and NaOH (5%) in THF (10 ml) at reflux temperature. The reaction mixture was further refluxed with constant stirring for 7-8 h. After completion of the reaction, (monitored by TLC), the solvent on evaporation resulted the crude product, which was filtered and purified by recrystallization from ethanol to give 1,4-diphenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-ones **5a-n**.

PHYSICAL AND SPECTRAL DATA

Benzylidene-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (3)

Yellow solid, Yield: 77%, mp: 213–215; IR (KBr, cm^{-1}): υ 3054 (C–H Ar), 1636 (C=N), 1626, 1586 (C=C, Ar), 1136 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02–6.97 (m, 10H, Ar–H), 8.12 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 159.6, 154.2, 137.6, 133.7, 132.6, 131.2 (2), 130.2 (2), 129.6 (2), 127.6, 125.3 (2); MS:

m/z 249 (M^+); Elemental analysis: Calculated for $C_{15}H_{11}N_3O$: C-72.28, H-4.45, N-16.86, O-6.42. Found: C-70.36, H-4.02, N-15.74, O-5.89.

(Isothiocyanato-phenyl-methyl)-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-amine (4)

Pale yellow solid, Yield: 78%, mp: 202–204; IR (KBr, cm^{-1}): υ 3115 ((N–H), 3045 (C–H Ar), 1640 (C=N), 1621, 1578 (C=C, Ar), 1215 (C=S), 1124 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (bs, 1H, NH), 7.89–7.05 (m, 10H, Ar–H), 4.15 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 155.8, 152.4, 143.7, 138.2, 131.2 (2), 130.4, 129.5 (2), 127.3 (2), 125.1 (2), 123.4, 77.1; MS: *m/z* 308 (M^+); Elemental analysis: Calculated for $C_{16}H_{12}N_4OS$: C-62.32, H-3.92, N-18.17, O-5.19, S-10.40. Found: C-60.21, H-3.56, N-17.15, O-4.85, S-9.56.

[1,3,4]-Oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5a)

Orange solid, Yield: 73%, mp: 194–196; IR (KBr, cm^{-1}): υ 3119 ((N–H), 3048 (C–H Ar), 2938 (C–H), 1680 (C=O), 1642 (C=N), 1618, 1588 (C=C, Ar), 1218 (C=S), 1128 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09–6.98 (m, 15H, Ar–H), 6.43 (bs, 1H, NH), 4.21 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.3, 153.6, 149.2, 145.2, 142.0, 138.5, 136.7, 129.3 (2), 128.2 (2), 128.9, 127.6 (2), 126.3 (2), 125.4 (2), 124.5, 121.4, 120.8 (2), 75.4; MS: *m/z* 427 (M^+); Elemental analysis: Calculated for $C_{23}H_{17}N_5O_2S$: C-64.62, H-4.01, N-16.38, O-7.49, S-7.50. Found: C-62.36, H-9.65, N-15.48, O-6.98, S-9.84.

1-(4-Methoxy-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5b)

White solid, Yield: 78%, mp: 180–182; IR (KBr, cm^{-1}): υ 3135 ((N–H), 3045 (C–H Ar), 2932 (C–H), 1680 (C=O), 1644 (C=N), 1636, 1545 (C=C, Ar), 1220 (C=S), 1136 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95–6.98 (m, 10H, Ar–H), 7.52 (d, 2H, J = 7.5 Hz, Ar–H), 7.48 (d, 2H, J = 7.5 Hz, Ar–H), 6.39 (bs, 1H, NH), 4.19 (s, 1H, CH), 3.81 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.4, 156.4, 154.3, 143.6, 138.4, 131.2 (2), 130.2, 129.6 (2), 128.4, 127.9 (2), 127.2 (2), 126.3, 124.6, 122.3, 120.3 (2), 112.3 (2), 73.6, 53.1; MS: *m/z* 457 (M^+); Elemental analysis: Calculated for $C_{24}H_{19}N_5O_3S$: C-63.01, H-4.19, N-15.31, O-10.49, S-7.01. Found: C-61.25, H-3.96, N-14.58, O-9.67, S-6.58.

1-(4-Chloro-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5c)

Yellow solid, Yield: 72%, mp: 160–162; IR (KBr, cm^{-1}): υ 3112 ((N–H), 3036 (C–H Ar), 2924 (C–H), 1678 (C=O), 1638 (C=N), 1635, 1573 (C=C, Ar), 1212 (C=S), 1148 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, 2H, J = 7.2 Hz, Ar–H), 7.52 (d, 2H, J = 7.2 Hz, Ar–H), 7.96–7.02 (m, 10H, Ar–H), 6.45 (bs, 1H, NH), 4.23 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3, 155.0, 144.2, 139.4, 135.1, 133.6 (2), 131.0, 130.4 (2), 128.1 (2), 127.4, 126.3 (2), 125.7 (2), 124.6, 123.4, 122.8, 120.4 (2), 74.7; MS: *m/z* 461 (M^+); Elemental analysis: Calculated for $C_{23}H_{16}ClN_5O_2S$: C-59.80, H-3.49, Cl-7.68, N-15.16, O-6.93, S-6.94. Found: C-57.89, H-3.12, Cl-6.86, N-14.76, O-5.96, S-5.97.

1-(4-Methyl-phenyl)-4-(phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5d)

Yellow solid, Yield: 78%, mp: 191–193; IR (KBr, cm^{-1}): υ 3142 ((N–H), 3048 (C–H Ar), 2932 (C–H), 1684 (C=O), 1636 (C=N), 1635, 1572 (C=C, Ar), 1220 (C=S), 1128 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08–7.08 (m, 10H, Ar–H), 7.72 (d, 2H, J = 7.4 Hz, Ar–H), 7.65 (d, 2H, J = 7.4 Hz, Ar–H), 6.51 (bs, 1H, NH), 4.26 (s, 1H, CH), 2.51 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.1, 157.4, 152.8, 146.3, 142.7, 139.6, 136.8, 134.8, 133.4 (2), 131.2 (2), 130.8, 129.9 (2), 129.2 (2), 128.2 (2), 127.1, 122.5 (2), 75.6, 22.1; MS: *m/z* 441 (M^+); Elemental analysis: Calculated for $C_{24}H_{19}N_5O_2S$: C-65.29, H-4.34, N-15.86, O-7.25, S-7.26. Found: C-63.69, H-3.95, N-14.85, O-6.76, S-6.83.

1-(4-Bromo-phenyl)-4-(phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5e)

Orange solid, Yield: 76%, mp: 224–226; IR (KBr, cm^{-1}): υ 3115 ((N–H), 3058 (C–H Ar), 2930 (C–H), 1684 (C=O), 1632 (C=N), 1575 (C=C, Ar), 1226 (C=S), 1146 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12–7.09 (m, 10H, Ar–H), 7.66 (d, 2H, J = 7.0 Hz, Ar–H), 7.52 (d, 2H, J = 7.0 Hz, Ar–H), 6.49 (bs, 1H, NH), 4.24 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 155.4, 153.2, 148.2, 145.6, 139.8, 138.7, 134.5 (2), 132.5 (2), 130.2 (2), 127.5, 126.8 (2), 126.4 (2), 125.7, 122.8 (2), 116.5, 75.6; MS: *m/z* 506 (M^+); Elemental analysis: Calculated for $C_{23}H_{16}BrN_5O_2S$: C-54.55, H-3.18, Br-15.78, N-13.83, O-6.32, S-6.33. Found: C-52.36, H-2.95, Br-14.63, N-12.84, O-5.89, S-5.79.

1-(3,4-Dichloro-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5f)

Pale yellow solid, Yield: 72%, mp: 182–184; IR (KBr, cm^{-1}): υ 3138 ((N–H), 3045 (C–H Ar), 2926 (C–H), 1676 (C=O), 1650 (C=N), 648, 1575 (C=C, Ar), 1214 (C=S), 1132 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94–6.82 (m, 10H,

Ar–H), 7.74 (d, 1H, J = 7.6 Hz, Ar–H), 7.65 (d, 1H, J = 7.6 Hz, Ar–H), 7.51 (s, 1H, Ar–H), 6.39 (bs, 1H, NH), 4.19 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.2, 155.3, 152.6, 146.3, 141.4, 139.6, 137.3, 135.6, 133.2 (2), 131.0 (2), 130.9, 130.2, 129.5 (2), 128.4 (2), 127.4, 125.2, 123.5, 121.0, 71.2; MS: *m/z* 496 (M^+); Elemental analysis: Calculated for $C_{23}H_{15}Cl_2N_5O_2S$: C-55.65, H-3.05, Cl-14.28, N-14.11, O-6.45, S-6.46. Found: C-53.58, H-2.84, Cl-13.68, N-13.78, O-5.98, S-5.86.

1-(4-Chloromethyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5g)

White solid, Yield: 77%, mp: 170–172; IR (KBr, cm^{-1}): υ 3148 ((N–H), 3050 (C–H Ar), 2924 (C–H), 1684 (C=O), 1652 (C=N), 1618, 1574 (C=C, Ar), 1224 (C=S), 1128 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89–7.05 (m, 10H, Ar–H), 7.68 (d, 2H, J = 7.6 Hz, Ar–H), 7.52 (d, 2H, J = 7.6 Hz, Ar–H), 6.39 (bs, 1H, NH), 4.18 (s, 1H, CH), 2.69 (s, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.3, 154.2, 152.4, 147.6, 145.6, 140.2, 138.4, 134.6 (2), 133.4, 131.2 (2), 130.8, 129.4 (2), 128.6 (2), 126.7 (2), 125.4, 121.5 (2), 71.2, 52.6; MS: *m/z* 475 (M^+); Elemental analysis: Calculated for $C_{24}H_{18}ClN_5O_2S$: C-60.56, H-3.81, Cl-7.45, N-14.71, O-6.72, S-6.74. Found: C-58.36, H-3.12, Cl-6.84, N-13.68, O-5.86, S-5.87.

1-(4-Isopropyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5h)

Brown solid, Yield: 75%, mp: 188–190; IR (KBr, cm^{-1}): υ 3128 ((N–H), 3048 (C–H Ar), 2930 (C–H), 1678 (C=O), 1648 (C=N), 1636, 1574 (C=C, Ar), 1220 (C=S), 134 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06–6.94 (m, 10H, Ar–H), 7.68 (d, 2H, J = 7.5 Hz, Ar–H), 7.57 (d, 2H, J = 7.5 Hz, Ar–H), 6.38 (bs, 1H, NH), 4.25 (s, 1H, CH), 2.68 (m, 1H, CH), 2.34 (d, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.8, 156.8, 153.4, 147.6, 145.4, 143.7, 135.7, 139.7, 133.4 (2), 131.8 (2), 130.4, 129.7 (2), 128.6 (2), 127.4, 126.5 (2), 123.6 (2), 72.8, 31.7, 26.3 (2); MS: *m/z* 469 (M^+); Elemental analysis: Calculated for $C_{26}H_{23}N_5O_2S$: C-66.50, H-4.94, N-14.91, O-6.81, S-9.83. Found: C-64.23, H-4.12, N-13.25, O-5.98, S-8.74.

4-Phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-1-(2-trifluoromethyl-phenyl)-[1,3,5]-triazinan-2-one (5i)

Orange solid, Yield: 77%, mp: 166–168; IR (KBr, cm^{-1}): υ 3135 ((N–H), 3048 (C–H Ar), 2932 (C–H), 1688 (C=O), 1636 (C=N), 1636, 1575 (C=C, Ar), 1226 (C=S), 1142 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.21–7.12 (m, 10H, Ar–H), 7.78 (d, 2H, J = 7.8 Hz, Ar–H), 7.67 (d, 2H, J = 7.8 Hz, Ar–H), 6.38 (bs, 1H, NH), 4.14 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6, 157.8, 154.2, 152.3, 146.3, 144.7, 141.8, 136.4 (2), 132.7 (2), 130.5, 129.8 (2), 128.7 (2), 125.4, 124.3,123.7, 122.1, 121.4, 121.0, 114.6, 77.8; MS: *m/z* 511 (M^+); Elemental analysis: Calculated for $C_{24}H_{16}F_3N_5O_3S$: C-56.62, H-3.15, F-11.14, N-13.69, O-9.38, S-6.27. Found: C-54.36, H-2.87, F-10.68, N-12.78, O-8.85, S-5.94.

4-Phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-1-(4-trifluoromethyl-phenyl)-[1,3,5]-triazinan-2-one (5j)

Pale yellow solid, Yield: 78%, mp: 220–222; IR (KBr, cm^{-1}): υ 3145 ((N–H), 3035 (C–H Ar), 2926 (C–H), 1690 (C=O), 1640 (C=N), 1645, 1565 (C=C, Ar), 1212 (C=S), 1132 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05–7.10 (m, 14H, Ar–H), 6.34 (bs, 1H, NH), 4.14 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.5, 157.4, 154.2, 152.6, 148.5, 141.8, 136.3, 133.5 (2), 131.5, 127.8 (2), 126.3, 125.7 (2), 124.5 (2), 122.8, 123.4, 121.4 (2), 114.8 (2), 71.2; MS: *m/z* 511 (M^+); Elemental analysis: Calculated for $C_{24}H_{16}F_3N_5O_3S$: C-56.36, H-3.15, F-11.14, N-13.69, O-9.38, S-6.27. Found: C-54.26, H-2.98, F-10.68, N-12.87, O-8.87, S-5.87.

1-(4-Fluoro-2-trifluoromethyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5k)

Yellow solid, Yield: 76%, mp: 184–186; IR (KBr, cm^{-1}): υ 3128 ((N–H), 3042 (C–H Ar), 2928 (C–H), 1682 (C=O), 1636 (C=N), 1636, 1574 (C=C, Ar), 1216 (C=S), 1134 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06–6.98 (m, 13H, Ar–H), 6.52 (bs, 1H, NH), 4.28 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.4, 153.2, 151.3, 150.8, 148.6, 144.2, 136.7, 134.3 (2), 131.7 (2), 129.8 (2), 128.5 (2), 127.8, 125.7, 124.5, 124.2, 123.2, 122.7, 118.4, 108.2, 70.5; MS: *m/z* 513 (M^+); Elemental analysis: Calculated for $C_{24}H_{15}F_4N_5O_2S$: C-56.14, H-2.94, F-14.80, N-13.64, O-6.23, S-6.24. Found: C-52.45, H-2.25, F-12.65, N-11.87, O-4.98, S-5.25.

1-(2-Fluoro-3-trifluoromethyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5l)

Brown solid, Yield: 70%, mp: 156–158; IR (KBr, cm^{-1}): υ 3138 ((N–H), 3044 (C–H Ar), 2938 (C–H), 1690 (C=O), 1638 (C=N), 1638, 1570 (C=C, Ar), 1225 (C=S), 1147 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86–6.84 (m, 10H, Ar–H), 7.65 (d, 1H, J = 7.8 Hz, Ar–H), 7.58 (d, 1H, J = 7.8 Hz, Ar–H), 7.52 (s, 1H, Ar–H), 6.54 (bs, 1H, NH), 4.26 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 154.8, 153.7, 152.5, 149.7, 146.4, 137.2, 135.0 (2), 131.7 (2), 130.7 (2),

129.4 (2), 128.2, 127.1, 125.6, 125.0, 124.2, 123.6, 119.4, 110.2, 69.4; MS: *m/z* 513 (M^+); Elemental analysis: Calculated for $C_{24}H_{15}F_4N_5O_2S$: C-56.14, H-2.94, F-14.80, N-13.64, O-6.23, S-6.24. Found: C-54.36, H-2.64, F-13.78, N-12.58, O-5.87, S-5.97.

1-(2-Chloro-4-trifluoromethyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5m)

Orange solid, Yield: 74%, mp: 168–170; IR (KBr, cm^{-1}): υ 3136 ((N–H), 3032 (C–H Ar), 2941 (C–H), 1686 (C=O), 1642 (C=N), 1628, 1572 (C=C, Ar), 1221 (C=S), 1132 (C-O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96–6.89 (m, 10H, Ar–H), 7.69 (d, 1H, J = 7.4 Hz, Ar–H), 7.62 (d, 1H, J = 7.4 Hz, Ar–H), 7.54 (s, 1H, Ar–H), 6.58 (bs, 1H, N–H), 4.39 (s, 1H, C–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.2, 152.3, 150.7, 149.7, 147.2, 145.1, 134.6, 133.1 (2), 130.2 (2), 128.7 (2), 127.4 (2), 126.8, 124.1, 123.2, 122.8, 121.7, 120.4, 116.7, 106.2, 68.1; MS: *m/z* 529 (M^+); Elemental analysis: Calculated for $C_{24}H_{15}ClF_3N_5O_2S$: C-54.40, H-2.85, Cl-6.69, F-10.76, N-13.22, O-6.04, S-6.05. Found: C-50.36, H-2.12, Cl-5.24, F-8.94, N-11.65, O-5.21, S-5.02.

1-(2-Chloro-5-trifluoromethyl-phenyl)-4-phenyl-3-(5-phenyl-[1,3,4]-oxadiazol-2-yl)-6-thioxo-[1,3,5]-triazinan-2-one (5n)

Yellow solid, Yield: 72%, mp: 220–222; IR (KBr, cm^{-1}): υ 3125 ((N–H), 3038 (C–H Ar), 2932 (C–H), 1678 (C=O), 1645 (C=N), 1628, 1574 (C=C, Ar), 1223 (C=S), 1141 (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04–7.06 (m, 13H, Ar–H), 6.54 (bs, 1H, NH), 4.32 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.2, 150.4, 148.7, 147.6, 146.7, 141.5, 134.8, 132.7 (2), 130.3 (2), 126.7 (2), 125.7 (2), 124.2, 123.6, 122.4, 121.7, 120.5, 119.8, 115.4, 103.7, 67.3; MS: *m/z* 529 (M^+); Elemental analysis: Calculated for $C_{24}H_{15}ClF_3N_5O_2S$: C-54.40, H-2.85, Cl-6.69, F-10.76, N-13.22, O-6.04, S-6.05. Found: C-52.12, H-2.45, Cl-5.98, F-9.84, N-12.25, O-5.78, S-5.69.

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