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Synthesis Characterization and Anti-inflammation Activity of 1,3,4-Oxadiazole Derivatives

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Abstract

The paper presents the synthesis of 1,3,4-oxadiazol derivatives through the reaction between N'-(1-phenylethylidene) isonicotinohydrazide derivatives and oxoacetyl chloridein. The newly formed compounds have been characterized with the help of elemental analysis, condensation measurements, magnetic measurements and their structure configuration have been determined by various spectroscopic (IR, ^{1}H NMR, ^{13}C NMR, GCMS) techniques. These compounds were tested for their anti-inflammation potential.

Keywords: 1, 3, 4-Oxadiazole, Methyl 2-Hydroxybenzoate Derivatives, Hydrazine, Indoline-2-Carboxylic Acid, Biological Activity.

Introduction

Pharmaceutical Chemistry is a discipline at the intersection of chemistry. It involves the synthesis, development and characterization of new chemical suitable for therapeutic use. It is a part of pharmacology, this latter taken in its etymological sense 'pharmakon' + 'logs': study of drugs [1-5]. The activity of a given drug depends on a sequence of physio-chemical events that begin when the active molecule penetrates into the living organism and which culminates when the active molecule reaches its target and elicits the appropriate biological response. Classically it is admitted that three characteristic phases govern the biological activity of a drug in a living organism. A heterocyclic compound is a cyclic compound that has atoms of at least two different elements as members of its ring system (N and S) [5-7].

Review of Literature

Heterocyclic chemistry is the branch of chemistry dealing with the synthesis, properties, characterization and applications of ring compound containing at least one hetero atom in the ring system. The compound that contain, neither carbon nor hydrogen are often referred in organic chemistry as heteroatom. This is usually in comparison to the all-carbon Skelton, and does not prevent a compound such as borazine (which has no carbon atoms) from being labelled "heterocyclic"[8.9]. IUPAC recommends the Hantzsch-Widman nomenclature for naming heterocyclic compounds. 1,3,4-Oxadiazole containing an oxygen atom and two nitrogen atoms in a five membered ring. It is derived from furan by substitution of two methylene groups [10-12]. (=CH) with two pyridine type nitrogens (-N=) . There are three known isomers: 1,2,4-oxadiazole (2), 1,2,3-oxadiazole (3) and 1,2,5-oxadiazole [13]. However, 1,3,4-oxadiazole and 1,2,4-oxadiazole are better known heterocyclic compounds and widely used in current research because of their chemical and biological applicatios. Among heterocyclic compounds have many important construction motifs for the development of new biologically active compounds. 1,3,4-oxadiazole cores have a broad biological activity spectrum including antibacterial, antifungal, analgesic, anti-inflammatory, antiviral, anticancer, antihypertensive, anticonvulsant, and anti-diabetic properties [14,15]. They have also attracted interest in medicinal chemistry as surrogates (bioisosteres) for carboxylic acids, esters and carboxamides. The ability of 1,3,4-oxadiazole heterocyclic compounds is to undergo various chemical reactions has made them important role for new molecule planning because of their privileged structure. The synthesis of novel 1,3,4-oxadiazole derivatives, and investigation of their chemical properties and biological behavior has accelerated in the last two decades [16-19]. In recent years the number of scientific studies with these compounds has increased considerably. Considering the period from 2002 to 2015, the Scifinder Scholar database

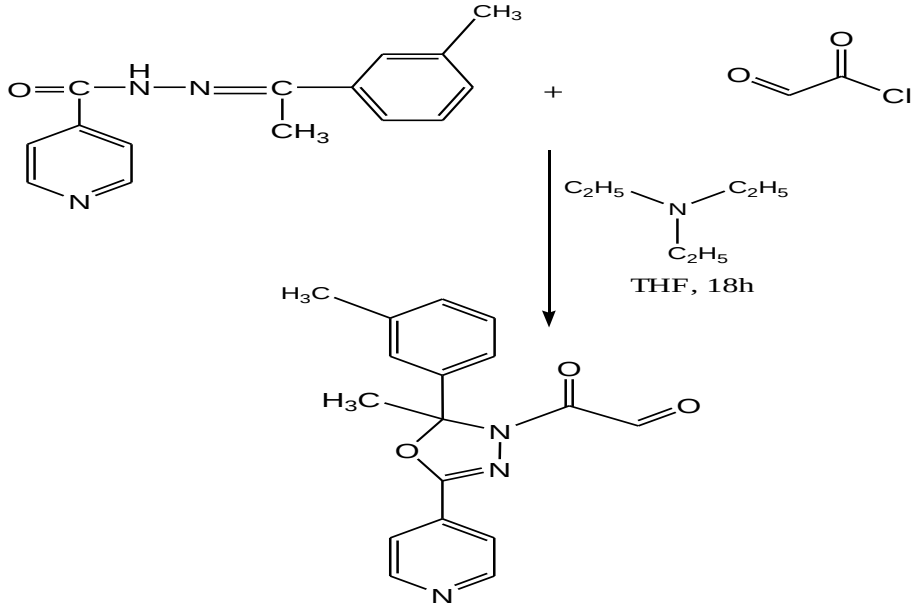
records 2,577 references to 1,3,4-oxadiazole, demonstrating its relevance for heterocyclic chemistry. Taking into account, the importance of these compounds of both heterocyclic and medicinal chemistry, we have decided to present the main synthesis approaches used for obtaining the heterocyclic nucleus, as well as the broad spectrum of pharmacological activities reported in the literature over the past years [20-22]. The pyrazole moiety into the 5-position of 1,3,4-oxadiazole, a series of novel 2-(thioether/sulfone)-5-pyrazolyl-1,3,4-oxadiazole derivatives were synthesized. Preliminary bioassays suggested that target compounds exhibited appreciable activity against pathogenic bacteria *Xanthomonas oryzae*pv. *oryzae* (*Xoo*) and five phytopathogenic fungi *in vitro*. Among them, the half-maximal effective concentration [23]

Aim of the Study

The aim of the present work is to prepare, characterize the chemical structure of the newly synthesized compounds and evaluate their anti-inflammation potential.

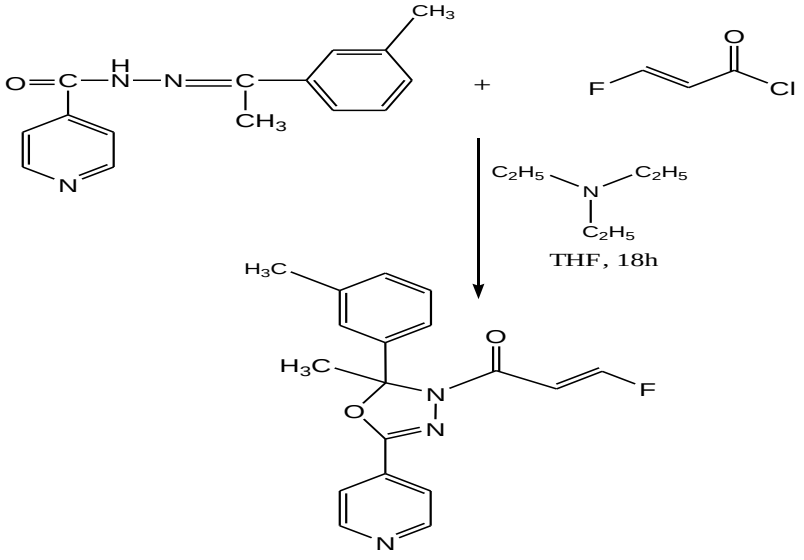
Experimental

2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4 oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



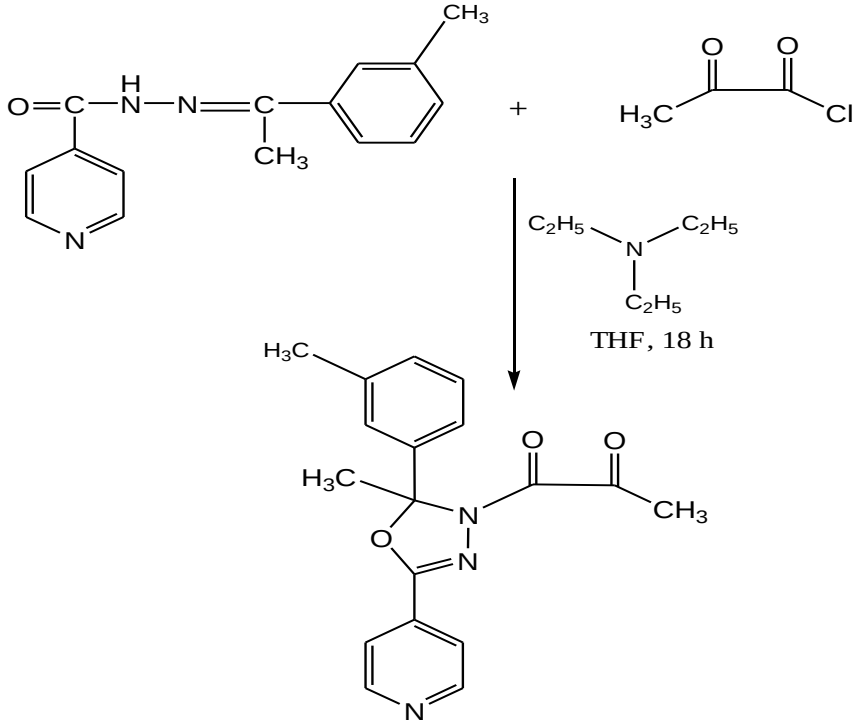
N'-(1-m-tolylethylidene)isonicotinohydrazide (0.152 g, 0.642 mmol) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.178 g, 0.608 mmol, 95%), colour as a yellow solid compound, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over anhydrous $CaCl_2$, calcu. C 66.01, H 4.89, N 13.58 found C 6.52, H 5.18, N 13.72 R*f* = 0.58, Mp 110 °C.

(E)-3-fluoro-1-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)prop-2-en-1-one.



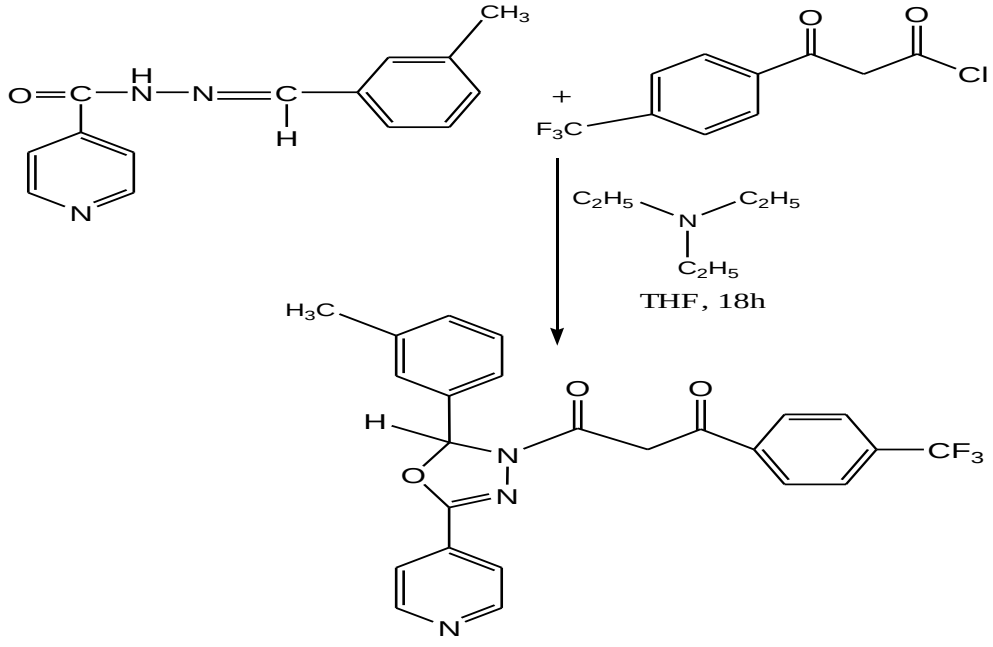
N'-(1-m-tolylethylidene) isonicotinohydrazide (0.115 g, 0.315 mmol) in THF react with (E)-3-floromoacryloyl chloride in the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce (E)-3-fluoro-1-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)prop-2-en-1-one (0.0981 g, 0.324 mmol, 82%) it is a yellow crystalline solid compound, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over anhydrous $CaCl_2$, calcu. C 66.45, H 4.96, N 12.92; found C 66.65, H 4.94, N 12.83 R*f* = 0.49 Mp 112 °C.

2-Methyl-1-(2-methyl-2-phenyl-5-(pyridin-4-yl)-1, 3, 4-oxadiazol-3(2*H*)-yl) prop-1, 2-dione



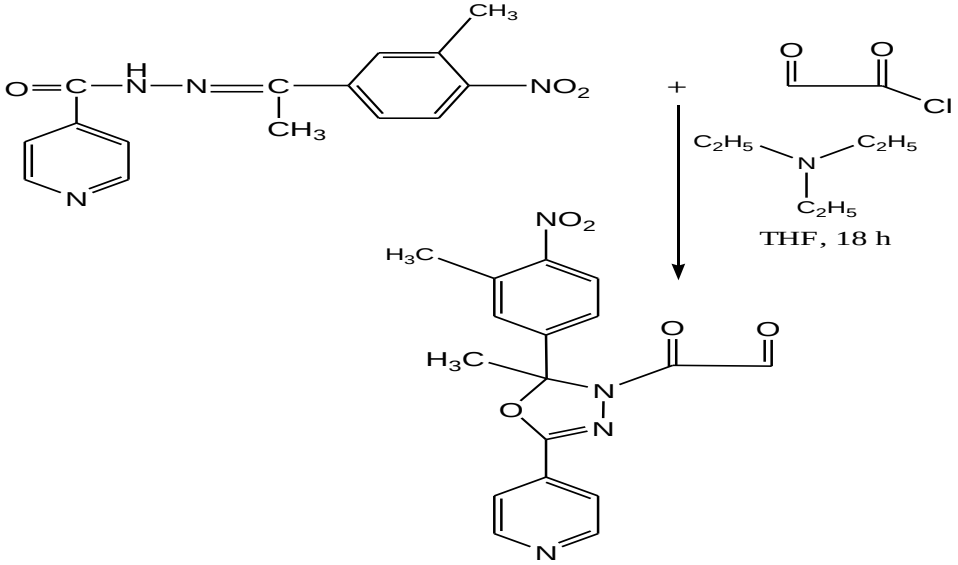
N'-(1-m-tolylethylidene)isonicotinohydrazide (0.212 g, 0.613 mmol) in THF react with 2-oxopropanoyl chloride in the presence of $(C_2H_5)_3N$ after refluxing the mixture for 18 hours it produce 1-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)propane-1,2-dione (0.189 g, 0.675 mmol, 88%) it is a colorless oil compound, calcu. C 66.86, H 5.30, N 13.00; found C 66.66, H 5.33, N 13.11 R*f* = 0.33.

1-(5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-3-(4-(trifluoromethyl)phenyl)propane-1,3-dione



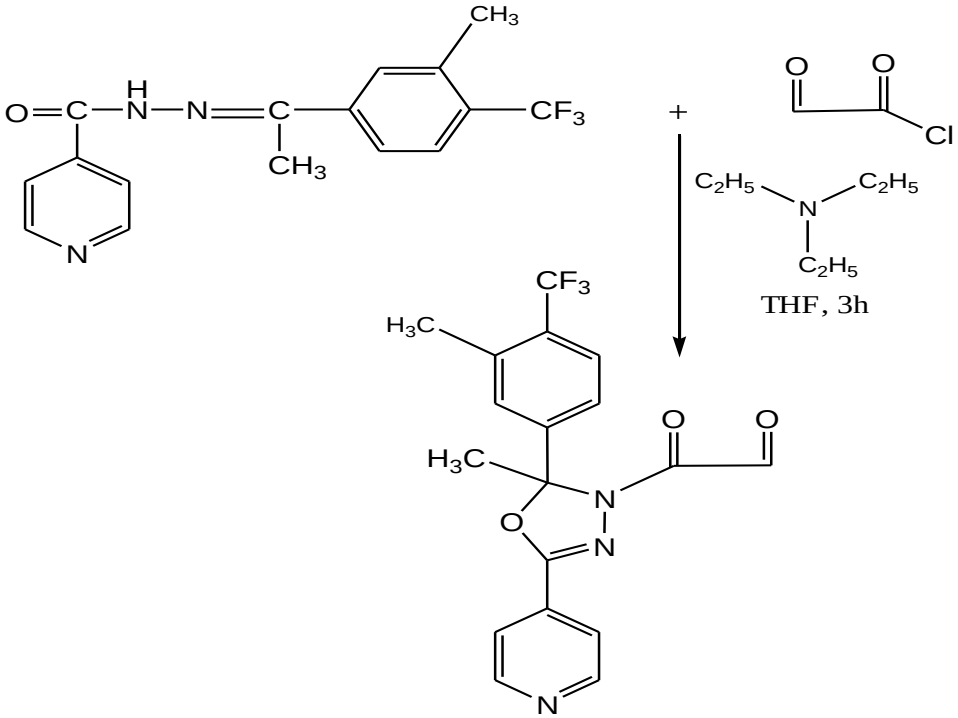
N'-(1-m-tolylmethylidene) isonicotinohydrazide (0.389 g, 0.108 mmol) in THF react with 3-oxo-3-(4-(trifluoromethyl) phenyl) propanoyl chloride in the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 1-(5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-3-(4-(trifluoromethyl)phenyl)propane-1,3-dione (0.894 g, 0.958 mmol, 59%) it is a yellow crystalline solid compound, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over anhydrous $CaCl_2$, calcu. C 63.57, H 4.00, N 9.27; found C 63.85, H 4.02, N 9.32 R*f* = 0.52 Mp 179 °C.

2-(2-methyl-2-(3-methyl-4-nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-(3-methyl-4-nitrophenyl)ethylidene) isonicotinohydrazide (0.121g, 0.415 mmol) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-2-(3-methyl-4-nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.132g, 0.105 mmol, 32%) it is a yellow oil, calcu.C 57.63, H 3.98, N 15.81; found C 57.65, H 3.89, N 15.88. R*f* = 0.42.

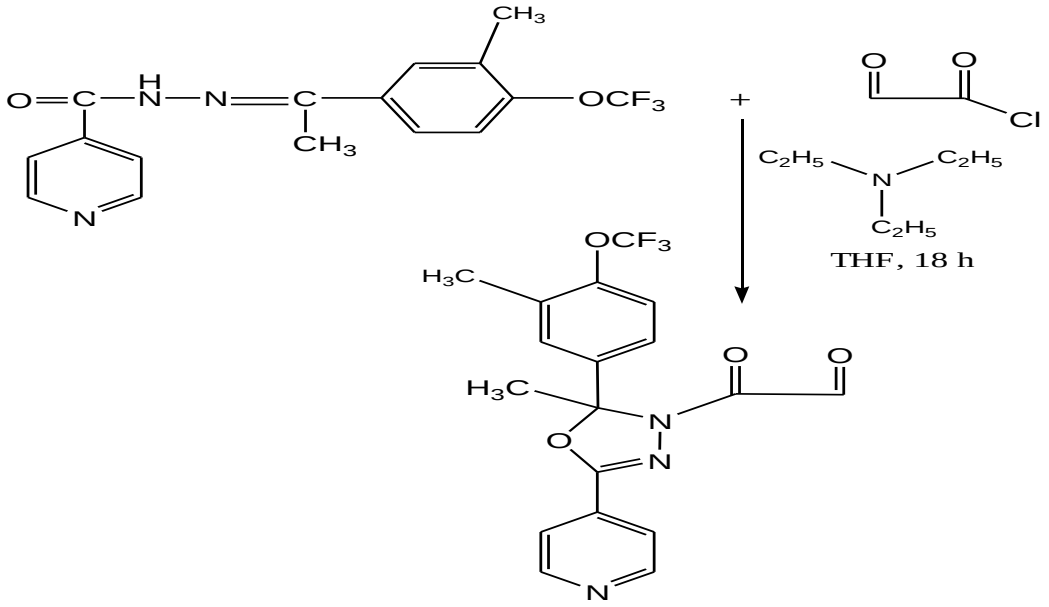
2-(2-methyl-2-(3-methyl-4-(trifluoromethyl) phenyl)-5-(pyridin-4-yl)-1, 3, 4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-(3-methyl-4-(trifluoromethyl) phenyl) ethylidene) isonicotinohydrazide (0.416 g, 0.998 mmol,) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction

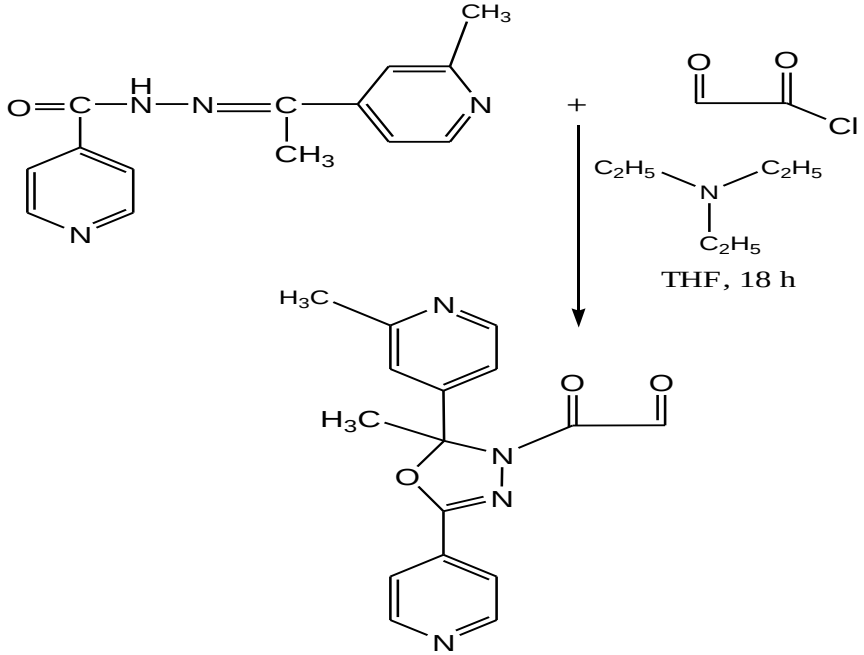
mixture for 18 hours it produce2-(2-methyl-2-(3-methyl-4-(trifluoromethyl)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.102 g, 0.0312 mmol, 24%) it is a yellow oil, calcu. C 57.30, H 3.74, N 15.11; found C 57.35, H 3.82, N 15.14. R*f* = 0.61.

2-(2-methyl-2-(3-methyl-4-(trifluoromethoxy) phenyl)-5-(pyridin-4-yl)-1, 3, 4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-(3-methyl-4-(trifluoromethoxy) phenyl) ethylidene)isonicotinohydrazide (0.114 g, 0.299 mmol,) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-2-(3-methyl-4-(trifluoromethoxy)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.107 g, 0.221 mmol, 61%) it is a yellow crystalline solid, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over anhydrous $CaCl_2$, calcu. C 54.97, H 3.59, N 10.68; found C 54.99, H 3.63, N 10.63 R*f* = 61., Mp 89 °C.

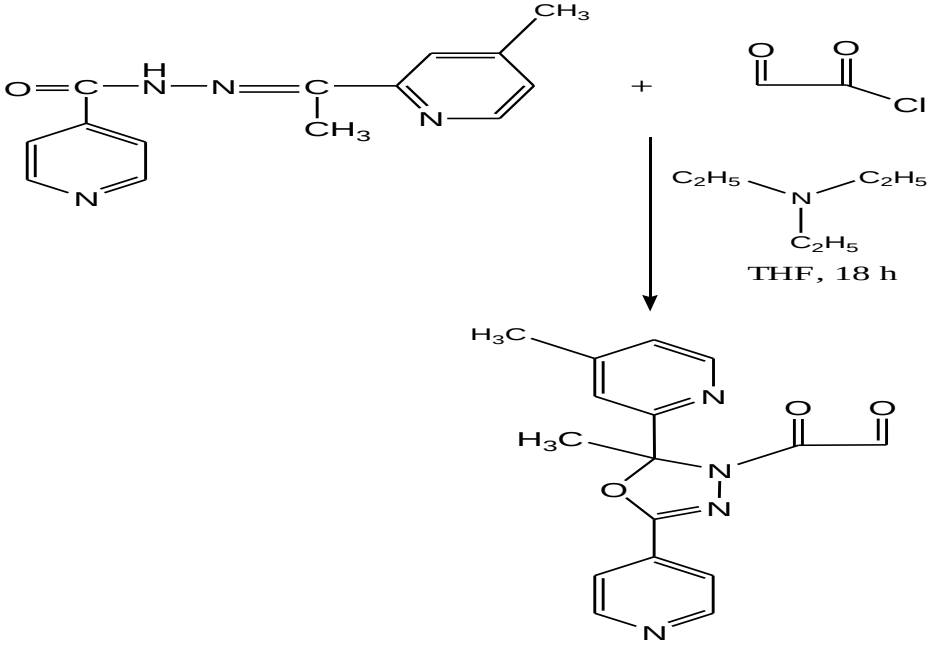
2-(2-methyl-2-(2-methylpyridin-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-(2-methylpyridin-4-yl)ethylidene) isonicotinohydrazide (0.216 g, 0.917 mmol) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-2-(2-methylpyridin-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.0834 g, 0.301 mmol, 27%) it is a white crystalline solid, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over

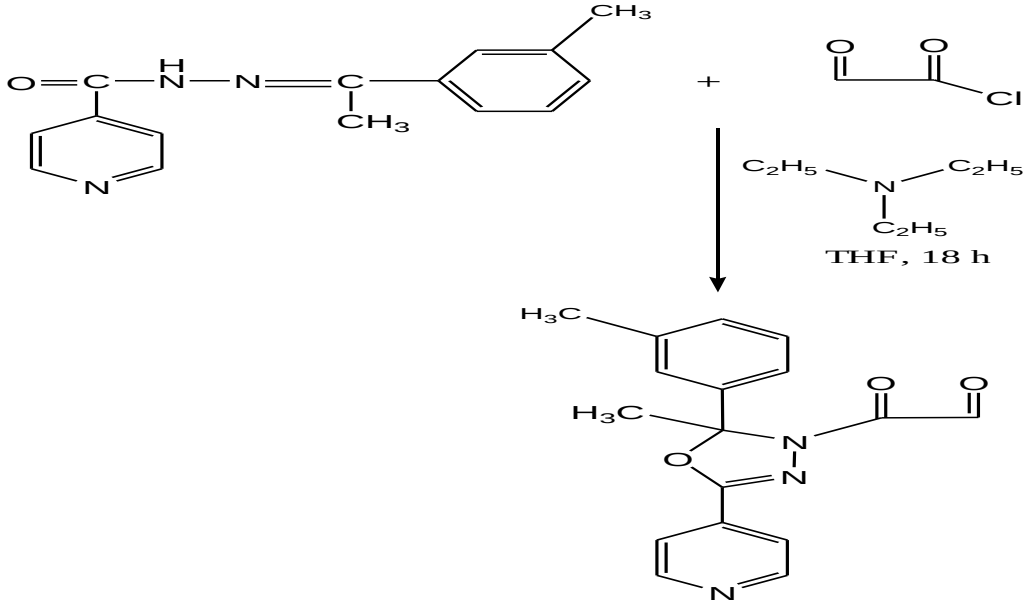
anhydrous $CaCl_2$calcu. C 61.93, H 4.55, N 18.06; found C 61.88, H 4.60, N 19.08 R*f* = 0.39; Mp 131°C.

2-(2-methyl-2-(4-methylpyridin-2-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-(4-methylpyridin-2-yl)ethylidene) isonicotinohydrazide (0.218 g, 0.913 mmol) in THF react with 2-oxoacetyl chloridein the presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-2-(4-methylpyridin-2-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.173 g, 0.515 mmol, 61%) it is a colorless oil, calcd. C 61.93, H 4.55, N 18.06; found C 61.91, H 4.52, N 18.08 R*f* = 0.46.

2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde



N'-(1-m-tolylethylidene)isonicotinohydrazide (0.218 g, 0.918 mmol) in THF react with 2-oxoacetyl chloride in presence of $(C_2H_5)_3N$ after refluxing the reaction mixture for 18 hours it produce 2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde (0.158g, 0.524 mmol, 61%) it is a brown crystalline solid, the product was purified on column chromatography and recrystallized from ethanol and dried under vacuum in a desiccator over anhydrous $CaCl_2$, calcu. C 66.01, H 4.89, N 13.58; found C 66.05, H 4.60, N 13.60. R*f* = 0.61 Mp 69 °C.

Result and Discussion

2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol- 3(2H)-yl)-2-oxoacetaldehyde

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.65 ppm (2 H, CH, Ar), 7.72 ppm (d, 2 H, CH, Ar), 7.61-7.53 ppm (m, 2 H, CH, Ar), 7.41-7.41 ppm (m, 3 H, CH, Ar), 7.24 ppm (dd, 1 H, CH), 6.39 ppm (dd, 1 H, CH), 5.68 ppm (dd, 1 H, CH), 2.34 ppm (s, 6H, CH_3) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 172.3, 161.1, 155.4, 141.5, 131.5, 121.3, 111.5, 105.4, 98.4, 88.6, 67.2, 48.7, 25.7 ppm.

IR (KBr): ν(H_2O) 3338, ν(NH_2) 3250, ν(C=O) 1712, ν(C=N) 1618, ν(N–N) 1122, ν(C–C) 761, ν(C=C, aromatic) 1544, ν(C–H, aromatic) 3042, ν(NH, hydrazide) 3155 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{18}H_{18}N_3O_2$: 308.12 $[M+H]^+$; found 308.18.

(E)-3-fluoro-1-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)prop-2-en-1-one.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.68 ppm (d, 2H, CH, Ar), 7.68 ppm (d, 2 H, CH, Ar), 7.48 ppm (m, 2 H, CH, Ar), 7.41 ppm (m, 3 H, CH, Ar), 6.89 ppm (m, 1 H, CH), 6.78 ppm (d, 1 H, CH), 2.34 ppm (s, 6 H, CH_3) 2.03 ppm (t, 3 H, CH_3).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 165.8, 155.9, 148.7, 133.6, 128.8, 119.4, 110.4, 98.5, 88.7, 72.9, 56.3, 48.8, 23.0, 19.2 ppm.

IR (KBr): ν(H_2O) 3388, ν(NH_2) 3280, ν(C=O) 1710, ν(C=N) 1616, ν(N–N) 1132, ν(C–C) 771, ν(C=C, aromatic) 1554, ν(C–H, aromatic) 3044, ν(NH, hydrazide) 3150 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{19}H_{20}N_3O_2$: 322.13 $[M+H]^+$; found 322.15.

2-Methyl-1-(2-methyl-2-phenyl-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)prop-1,2-dione.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.71 ppm (d, 2 H, CH, Ar), 7.69 ppm (d, 2 H, CH, Ar), 7.61-7.58 ppm (m, 2 H, CH, Ar), 7.55-7.99 ppm (m, 3 H, CH, Ar), 5.77 ppm (t, 1 H, CH), 5.59 ppm (t, 1 H, CH), 2.32 ppm (s, 6 H, CH_3), 2.10 ppm (t, 3 H, CH_3).

^{13}C-NMR (75 MHz, $CDCl_3$): δ = 166.9, 155.7, 151.6, 141.1, 128.4, 122.2, 119.3, 110.4, 98.5, 89.7, 76.1, 46.8, 22.6, 19.9 ppm.

IR (KBr): ν(H_2O) 3366, ν(NH_2) 3255, ν(C=O) 1712, ν(C=N) 1610, ν(N–N) 1133, ν(C–C) 781, ν(C=C, aromatic) 1544, ν(C–H, aromatic) 3040, ν(NH, hydrazide) 3141 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{19}H_{19}N_3O_2$: 321.13 $[M^+]$; found 321.18.

1-(5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-3-(4-(trifluoromethyl)phenyl)propane-1,3-dione

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.67 ppm (d, 2 H, CH, Ar), 7.69 ppm (d, 2 H, CH, Ar), 7.55 ppm (d, 1 H, CH), 7.62 ppm (m, 3 H, CH, Ar), 7.66 (d, 1 H, CH), 7.12 ppm (m, 1 H, CH, Ar), 7.98 (d, 1 H, CH, Ar), 7.32 (d, 1 H, CH), 6.92 (m, 3 H, CH, Ar), 2.40 ppm (s, 6 H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.4, 154.4, 149.3, 138.4, 131.4, 126.6, 112.3, 107.8, 78.5, 55.1, 32.2, 23.0 ppm.

IR (KBr): ν(H_2O) 3336, ν(NH_2) 3225, ν(C=O) 1722, ν(C=N) 1616, ν(N–N) 1122, ν(C–C) 771, ν(C=C, aromatic) 1534, ν(C–H, aromatic) 3041, ν(NH, hydrazide) 3144 cm^{-1}.

^{19}F-NMR (288 MHz, $CDCl_3$): δ = -65.7 ppm (s, CF_3).

FAB mas (EI-MS): m/z calcd for $C_{25}H_{21}F_3N_3O_2$: 452.14 $[M+H]^+$; found: 452.16.

2-(2-methyl-2-(3-methyl-4-nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.66 ppm (d, 2 H, CH, Ar), 8.14 ppm (d, 2 H, CH, Ar), 7.11 ppm (d, 2 H, CH, Ar), 7.34 ppm (d, 2 H, CH, Ar), 6.98 ppm (dd, 1 H, =CH), 6.33 (dd, 1 H, =CH), 5.44 (dd, 1 H, =CH), 2.37 ppm (s, 6 H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.8, 155.2, 149.5, 145.8, 134.8, 128.8, 119.2, 110.1, 98.8, 78.3, 54.7, 48.8, 23.0 ppm.

IR (KBr): ν(H_2O) 3356, ν(NH_2) 3233, ν(C=O) 1732, ν(C=N) 1633, ν(N–N) 1122, ν(C–C) 771, ν(C=C, aromatic) 1534, ν(C–H, aromatic) 3041, ν(NH, hydrazide) 3144 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{18}H_{17}N_4O_4$: 353.10 $[M+H]^+$; found 353.15.

2-(2-methyl-2-(3-methyl-4-(trifluoromethyl)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.55 ppm (d, 2 H, CH, Ar), 7.72-7.44 ppm (m, 6 H, CH, Ar), 7.22 ppm (dd, 1 H, =CH), 6.33 ppm (dd, 1 H, =CH), 5.52 ppm (dd, 1 H, CH), 2.33 ppm (s, 6 H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.7, 155.2, 149.4, 141.0, 129.9, 127.3, 123.3, 122.6, 113.7, 98.3, 78.5, 56.8, 45.6, 32.8, 22.9 ppm.

^{19}F-NMR (288 MHz, $CDCl_3$): δ = -63.3 ppm (CF_3).

IR (KBr): ν(H_2O) 3356, ν(NH_2) 3233, ν(C=O) 1732, ν(C=N) 1633, ν(N–N) 1122, ν(C–C) 771, ν(C=C, aromatic) 1534, ν(C–H, aromatic) 3041, ν(NH, hydrazide) 3144 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{19}H_{17}F_3N_3O_2$: 376.11 $[M+H]^+$; found 376.16.

2-(2-methyl-2-(3-methyl-4-(trifluoromethoxy)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.77 ppm (dd, 2H, CH, Ar), 7.62 ppm (dd, 2H, CH, Ar), 7.54 – 7.44 ppm (m, 2H, CH, Ar), 7.21 ppm (d, 2H, CH, Ar), 7.09 ppm (dd, 1H, =CH), 6.32 ppm (dd, 1H, =CH), 5.75 ppm (dd, 1H, =CH), 2.32 ppm (s, 6H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 164.6, 155.1, 148.8, 136.0, 133.0, 127.3, 124.2, 122.4, 119.6, 112.4, 98.6, 88.4, 79.6, 54.6, 45.6, 31.7, 23.0 ppm.

^{19}F-NMR (285 MHz, $CDCl_3$): δ = -55.9 ppm (s, CF_3).

IR (KBr): ν(H_2O) 3355, ν(NH_2) 3222, ν(C=O) 1729, ν(C=N) 1630, ν(N–N) 1133, ν(C–C) 762, ν(C=C, aromatic) 1544, ν(C–H, aromatic) 3044, ν(NH, hydrazide) 3148 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{19}H_{17}F_3N_3O_3$: 392.10 $[M+H]^+$; found 392.14.

2-(2-methyl-2-(2-methylpyridin-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.77 ppm (d, 2H, CH, Ar), 8.55 ppm (d, 2H, CH, Ar), 7.66 ppm (d, 2H, CH, Ar), 7.55 ppm (d, 2H, CH, Ar), 7.18 ppm (dd, 1H, =CH), 6.44 ppm (dd, 1H, =CH), 5.88 ppm (dd, 1H, =CH), 2.34 ppm (s, 6H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 168.7, 156.2, 151.4, 149.3, 145.5, 141.6, 139.6, 129.1, 119.3, 110.2, 98.4, 76.8, 56.9, 44.6, 36.6, 22.5 ppm.

IR (KBr): ν(H_2O) 3352, ν(NH_2) 3232, ν(C=O) 1739, ν(C=N) 1633, ν(N–N) 1122, ν(C–C) 772, ν(C=C, aromatic) 1554, ν(C–H, aromatic) 3034, ν(NH, hydrazide) 3118 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{17}H_{17}N_4O_2$: 319.11 $[M+H]^+$; found 319.16.

2-(2-methyl-2-(4-methylpyridin-2-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.77 ppm (d, 2H, CH, Ar), 8.66 ppm (dd, 1H, CH, Ar), 7.66 ppm (dd, 1H, CH, Ar), 7.67 ppm (d, 2H, CH, Ar), 7.44 ppm (d, 1H, CH, Ar), 7.19 ppm (d, 1H, CH, Ar), 7.27 ppm (dd, 10.4 Hz, 1H, =CH), 6.33 ppm (dd, 1H, =CH), 5.88 ppm (dd, 1H, =CH), 2.36 ppm (S, 6H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 166.6, 154.7, 151.5, 149.3, 145.6, 137.9, 135.4, 132.2, 126.4, 122.3, 119.6, 105.5, 102.5, 78.7, 55.7, 48.6, 31.6, 21.5 ppm.

IR (KBr): ν(H_2O) 3351, ν(NH_2) 3236, ν(C=O) 1733, ν(C=N) 1643, ν(N–N) 1132, ν(C–C) 792, ν(C=C, aromatic) 1564, ν(C–H, aromatic) 3055, ν(NH, hydrazide) 3122 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{17}H_{17}N_4O_2$: 309.11 $[M+H]^+$; found 309.17.

2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.75 ppm (d, CH, Ar), 7.71 ppm (d, 2H, CH, Ar), 7.55 ppm (dd, 2H, CH, Ar), 7.33 ppm (m, 3H, CH, Ar), 2.73 ppm (dq, 2H, CH_2), 2.31 ppm (s, 3H, CH_3), 1.19 ppm (t, 6H, CH_3).

^{13}C-NMR (100 MHz, $CDCl_3$): δ = 177.5, 155.6, 152.2, 148.8, 142.4, 139.3, 129.4, 123.6, 119.2, 104.5, 98.5, 87.5, 56.7, 44.6, 32.9, 27.7, 23.0, 8.4 ppm.

IR (KBr): ν(H_2O) 3349, ν(NH_2) 3230, ν(C=O) 1738, ν(C=N) 1638, ν(N–N) 1134, ν(C–C) 782, ν(C=C, aromatic) 1566, ν(C–H, aromatic) 3052, ν(NH, hydrazide) 3133 cm^{-1}.

FAB mas (EI-MS): m/z calcd for $C_{18}H_{20}N_3O_2$: 310.13 $[M+H]^+$; found 310.17.

Biological Activity (Anti-inflammation)

Inflammation was induced by the sub planter injection of 0.1 ml of a 10% carrageenin aqueous suspension in the hind paw of male rate weighing 120-125g. Volume of paws was measured by mercury displacement, and edema was considered as the volume recorded at 2, 3, 4 and 5 hrs after the carrageenin injection with values obtained immediately after the injection. In each assay one of the group received only the vehicle, while the other group were dosed by gastric gavages with 56 kg of the compound being tested, or with 3.0 or 5.0 mg/kg of idomethacin. Drugs were administered in a volume of 1 ml/100g one hour before the carrageenin injection. In each experiment there were three groups of seven animals each, one served as control for the other two groups values were expressed in percent of the initial value and control value were compared with those obtained in treated rates. Some newly synthesized compounds were screened for anti-inflammatory activity. Some of them show significant anti-inflammatory activity recorded in table 1.

Table 1: ALD 50 and Anti-Inflammatory Activity Data

Sr. No.	Name of Compound	Approximate		Anti-inflammation activity % of inhibition
		ALD50	Dose (mg/ kg) mice P.O.	
1	2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde	>1000	202	76
2	(E)-3-fluoro-1-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)prop-2-en-1-one.	682	202	81
3	2-Methyl-1-(2-methyl-2-phenyl-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2*H*)-yl)prop-1,2-dione.	827	170	79
4	1-(5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-3-(4-(trifluoromethyl)phenyl)propane-1,3-dione	683	200	81
5	2-(2-methyl-2-(3-methyl-4-nitrophenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde	827	175	64
6	2-(2-methyl-2-(3-methyl-4-(trifluoromethyl)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.	564	114 58 31	55 49 28
7	2-(2-methyl-2-(3-methyl-4-(trifluoromethoxy)phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.	827	167 43	41 29
8	2-(2-methyl-2-(2-methylpyridin-4-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde	683	138	20
9	2-(2-methyl-2-(4-methylpyridin-2-yl)-5-(pyridin-4-yl)-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde	827	167	50
10	2-(2-methyl-5-(pyridin-4-yl)-2-m-tolyl-1,3,4-oxadiazol-3(2H)-yl)-2-oxoacetaldehyde.	689	145	35

Conclusion

The newly synthesized compounds of 1,3,4-oxadiazol derivatives through the reaction between N'-(1-phenylethylidene)isonicotinohydrazide derivatives and oxoacetyl chloridein. These compounds $C_{19}H_{20}N_3O_2$, and $C_{25}H_{21}F_3N_3O_2$ were shows best their anti-inflammation potential.

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