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Synthesis, Characterization of Diethylamino Benzylidene-5-Methyl-2-Phenyl-Pyrazol-3-One Substituted 1,2,3-Triazoles and Evaluation of their Anti-Microbial Activity

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ABSTRACT

A new series of (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (5a-l) have been synthesized by the reaction of (Z)-4-(4-(diethylamino)-2-(prop-2-yn-1-yloxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one with different aromatic azides. Chemical structures of all the new compounds were established by IR, ¹H-NMR, ¹³C NMR, MS and elemental data. The Compounds 5a-l were evaluated for their antibacterial activity against Gram-positive bacteria viz *Bacillus subtilis* (MTCC 441), *Bacillus sphaericus* (MTCC 11), *Staphylococcus aureus* (MTCC 96), and Gram-negative bacteria viz *Pseudomonas aeruginosa* (MTCC 741), *Klebsiella aerogenes* (MTCC 39), *Chromobacterium violaceum* (MTCC 2656). Amongst them, compounds containing 5b [1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl], 5d [1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl], 5j [1-(3-acetylphenyl)], 5k [1-(4-acetylphenyl)-1H-1,2,3-triazol-4-yl] and 5l [4-(diethylamino)-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl))] were showed notable antibacterial activity, almost equal /more than the activity of the standard drug Streptomycin. Further, the compounds 5a-l were also tested for their antifungal activity against *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185), and *Trichophyton mentagrophytes* (IFO 40996). Most of these new compounds showed substantial activity against test bacteria and fungi and appear as prospective molecules for further evolution.

Keywords: Synthesis (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one; Antibacterial activity; Antifungal activity

INTRODUCTION

Heterocyclic compounds constitute the largest and most varied family of organic compounds [1]. It is well known that heterocyclic compounds are widely distributed in nature and are essential for life activities of plants and animals. They play a vital role in the metabolism of all living cells, for example the vitamins and co-enzyme precursors thiamine, riboflavin etc. Some of these are natural products, for example antibiotics such as penicillin and cephalosporin etc [2]. In particular, they are described as inhibitors of protein synthesis, antibacterial, antifungal, anticancer, antidepressant, anti-inflammatory, antituberculosis, antioxidant as well as antiviral agents [3].

Pyrazoles have illustrious history; in 1883, a German chemist Ludwig Knorr was the first to discover antipyretic action of pyrazole derivative in men, he named the compound antipyrine.

When he attempted to synthesize quinoline derivatives with antipyretic activity, accidentally obtained antipyrine (2,3-dimethyl-1-phenyl-3-pyrazolin-5-one) which has analgesic, antipyretic and antirheumatic activity; which stimulated interest in pyrazole chemistry [4].

Pyrazolones are five membered nitrogen containing heterocyclic compounds, where pyrazolone ring system represents an important class of compounds not only for their theoretical interest but also for their bio-activity. The 3-pyrazolone and 5-pyrazolone are most dominant classes having importance in pharmaceutical industry [5].

In our current research study, the 3-Methyl-1-Phenylpyrazol-5-one derivatives have been the subject of many research studies due to varieties of potential biological activities such as antimicrobial antiviral such as antimicrobial antiviral, antitumor, antihistaminic, antidepressant, antiinflammatory, anticancer, antioxidant, anticonvulsant, antidiabetic activities, and cytotoxic activities. The pyrazolone derivatives constitute an important moiety of numerous pharmaceuticals, agrochemicals, dyes and pigments, chelating and extracting agent. Pyrazolone can be considered as intermediate compound for the synthesis of various cyclic compounds of high biological activity [6-9].

The present examination distribute with the synthesis of some new (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **5a-l** in good yields, from (Z)-4-(4-(diethylamino)-2-(prop-2-yn-1-yloxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **4**. The antibacterial and antifungal activities of the compounds **5a-l** have also been estimated.

RESULTS AND DISCUSSION

Inspired by the growing importance and the wide range biological applications of (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one containing frameworks, we have developed an efficient easy synthesis of hybrid molecules containing Diethyl amino benzylidene-5-methyl-2-phenyl-pyrazol-3-one substituted 1,2,3-triazoles frameworks. (Figure 1)

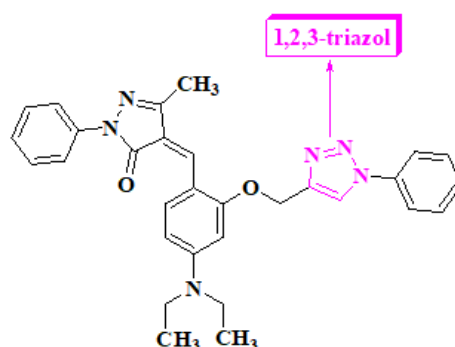
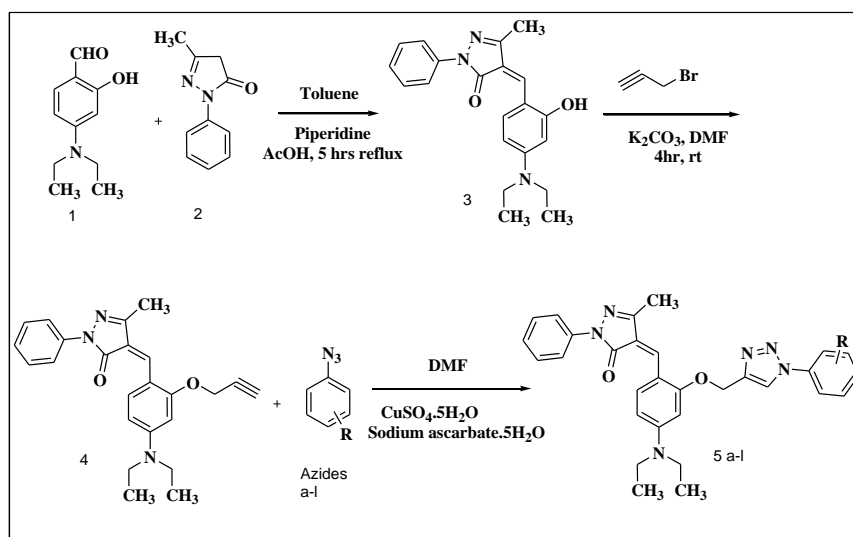


Figure 1: Structure of the final target compounds **5a-l**.

Synthetic route for the (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**5a-l**) were summarized in scheme 1. The 1,2,3-triazole tethered pyrazol-3-one core nucleus was constructed from commercially available compounds. The synthesis was started in between cyclocondensation with the 4-(diethylamino)-2-hydroxybenzaldehyde (**1**) and 5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**2**) in presence of Piperidine few drops AcOH in toluene solvent for 5r reflux to afford (Z)-4-(4-(diethylamino)-2-hydroxybenzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**3**) and confirms by NMR data of at 9.8ppm signal disappear in compound **3**. propargylation of 2-hydroxybenzylidene using propargyl bromide in DMF and dry K_2CO_3 rt for 3-4 hrs to yield (Z)-4-(4-(diethylamino)-2-(prop-2-yn-1-yloxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**4**) confirms by disappears signal of -OH group in NMR and IR respectively which on further click reaction of substituted aryl azides at the terminal alkyne position to provide (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (**5a-l**). The structures of all the latest synthesized products were confirmed IR, 1H -NMR, ^{13}C -NMR, MS and elemental analysis, obtained products in high yields (80-90%).

In the IR spectra of synthesized final compound **5a-l**, the alkyne C-H stretching frequency converted alkene C-H frequency in triazole ring those are $3380cm^{-1}$ and $3336cm^{-1}$ respectively, confirms the alkyne converted to triazole ring by click reaction it's also supported by 1H -NMR data signal appears at 8.55ppm confirms triazole ring formation (Scheme-1).



Scheme-1: Synthetic route for the (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one.

Antibacterial Activity

All the synthesized compounds **5a-l** were assayed for their antibacterial activity in opposition to Gram-positive bacteria viz *Bacillus subtilis*(MTCC 441), *Bacillus sphaericus* (MTCC 11), *Staphylococcus aureus* (MTCC 96), and Gram-negative bacteria viz. *Pseudomonas aeruginosa* (MTCC 741), *Klebsiella aeroge*(MTCC 39), *Chromobacterium violaceum* (MTCC 2656) by disc diffusion method[10], and the data of mean inhibition zone reported in **Table-1**. All assays incorporate the solvent and reference controls. Standard drug used as streptomycin.

The exploration of screening data antibacterial activity discloses that almost all synthesized compounds **5a-l** are potent and exhibit tolerable to marvelous antibacterial activity. Amidst them, compounds containing **5b**[1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl], **5d** [(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)], **5j** [(1-(3-acetylphenyl)-1,2,3-triazol-4-yl)], **5k** [-((1-(4-acetylphenyl)-1H-1,2,3-triazol-4-yl)] and **5l** [(4-(diethylamino)-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl))] moiety exhibit noteworthy antibacterial activity, almost equal/greater than the activity compare to standard drug streptomycin.

Antifungal Activity

All the synthesized compounds **5a-l** were assayed for their antifungal activity in opposition to Gram-positive bacteria viz *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185), and *Trichophyton mentagrophytes* (IFO 40996) in dimethyl sulfoxide (DMSO) by disc diffusion method. Amphotericin B was used as a standard drug and the data of mean inhibition zone (MZI) reported in **Table-2**. MZI data measured and compared with controls, the MZI values of the compounds screened.

The exploration of screening data antifungal activity discloses that almost all synthesized compounds **5a-l** are potent and exhibit tolerable to marvelous antifungal activity. Amidst them, compounds containing **5b**[1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl], **5d** [(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)], **5j** [(1-(3-acetylphenyl)-1,2,3-triazol-4-yl)], **5k** [-((1-(4-acetylphenyl)-1H-1,2,3-triazol-4-yl)] and **5l** [(4-(diethylamino)-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl))] moiety exhibit noteworthy antifungal activity, almost equal/greater than the activity compare to standard drug streptomycin.

Table 1: Antibacterial Activity of Compounds 5a-l.

Compound	Mean zone inhibition (MZI) ^a in 100 µg/mL					
	<i>B. subtilis</i>	<i>B. sphaericus</i>	<i>S. aureus</i>	<i>P. aeruginosa</i>	<i>K. aerogenes</i>	<i>C. violaceum</i>
6.3a	19	16	17	20	25	23
6.3b	29	26	25	21	25	23
6.3c	12	14	13	16	17	16
6.3d	32	29	32	23	29	26
6.3e	21	22	20	18	13	14
6.3f	20	10	11	14	16	17
6.3g	18	20	16	16	20	21
6.3 h	16	22	21	20	23	18
6.3i	19	20	23	20	26	23
6.3j	32	26	27	20	28	23
6.3k	33	26	28	22	26	22
6.3l	30	26	28	20	26	23
Streptomycin	31	27	26	19	27	24

^aValues are mean (n = 3).

Table 2: Antifungal Activity of Compounds 6.3a-l.

Compound	Mean zone inhibition (MZI) ^a in 100 µg/mL			
	<i>C. albicans</i>	<i>A. fumigatus</i>	<i>T. rubrum</i>	<i>T. mentagropytes</i>
6.3a	16	15	14	18
6.3b	28	24	15	28
6.3c	21	18	20	18
6.3d	28	26	26	26
6.3e	21	22	22	24

6.3f	16	15	16	12
6.3g	18	18	18	20
6.3h	21	20	22	23
6.3i	20	19	10	25
6.3j	28	24	23	25
6.3k	28	24	23	26
6.3l	30	26	25	26
Amphotericin B	29	25	24	27
^a Values are mean (n = 3)				

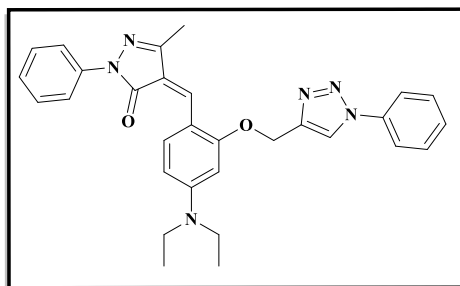
CONCLUSIONS

A new sequence of (Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one 5a-l has been synthesized and appraise for their antimicrobial activity against Gram-Positive, Gram-negative bacteria and fungi. Most of the compounds exhibit a average degree of antimicrobial activity. Amidst them, compounds consists 5b[1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl], 5d [(1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)], 5j [(1-(3-acetylphenyl)-1,2,3-triazol-4-yl)], 5k [-(1-(4-acetylphenyl)-1H-1,2,3-triazol-4-yl)] and 5l [(4-(diethylamino)-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl))] moiety showed average or more activity against standard drug streptomycin, Amphotericin respectively and emerged as potential molecules for further evaluation.

EXPERIMENTAL

Reagents were of commercial grade and were used as supplied or were prepared according to procedures described in literature. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel F254 plates from Merck, and compounds visualized either by exposure to UV light. Chromatographic columns 70–230 mesh silica gel for separations were used. Melting points were determined on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The ¹H NMR, ¹³C NMR spectra were recorded on a Varian Gemini spectrometer (300 MHz for ¹H and 75 MHz for ¹³C). Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (J) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 CHN elemental analyzer, were within ± 0.4% of theory.

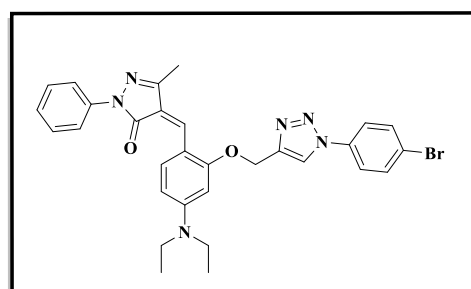
4.1.(Z)-4-(4-(diethylamino)-2-((1-phenyl-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9a):



Mol. Formula: C₃₀H₃₀N₆O₂
Exact Mass: 506
M.P.: 226-228

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.55 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.74 (d, 1H), 7.59 – 7.35 (m, 8H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 163.60, 157.88, 152.53, 152.37, 146.65, 137.34, 135.73, 132.42, 129.38, 128.26, 126.92, 126.02, 120.14, 119.16, 118.62, 118.52, 118.51, 116.72, 107.55, 98.12, 58.52, 43.84, 13.23, 11.67.

4.2.(Z)-4-(2-((1-(4-bromophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-(diethylamino) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9b):

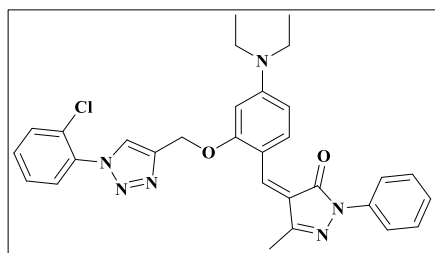


Mol. Formula: C₃₀H₂₉BrN₆O₂
Exact Mass: 584
M.P.: 214-216

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.55 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.70 – 7.58 (m, 4H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, Common NMR Solvents) δ 163.55, 157.83, 152.48, 152.32, 146.60, 137.29, 134.45, 132.97, 132.37, 128.21, 125.97, 120.83, 119.14,

118.98, 118.57, 118.47, 118.46, 116.67, 107.50, 98.07, 58.47, 43.79, 13.18, 11.62.

4.3. (Z)-4-(2-((1-(2-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-(diethylamino) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9c):



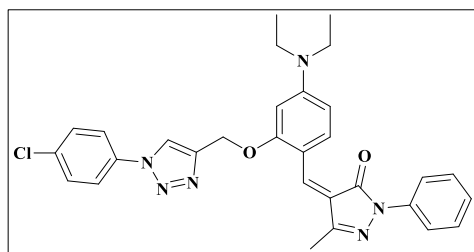
Mol. Formula: C₃₀H₂₉ClN₆O₂

Exact Mass: 540

M.P.: 220-222

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.55 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.64 – 7.58 (m, 2H), 7.55 – 7.48 (m, 2H), 7.43 (dd, 1H), 6.83 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 163.59, 157.87, 152.52, 152.36, 145.53, 137.33, 134.99, 132.41, 130.93, 128.25, 128.16, 127.50, 127.10, 126.01, 120.39, 119.19, 118.61, 118.51, 118.50, 116.71, 107.54, 98.11, 58.68, 43.83, 13.22, 11.66.

4.4. (Z)-4-(2-((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-(diethylamino) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9d):



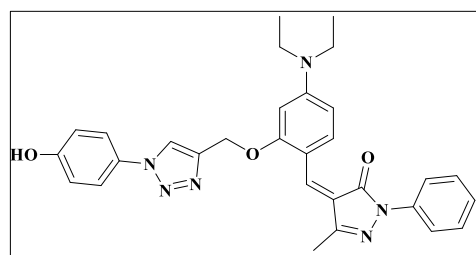
Mol. Formula: C₃₀H₂₉ClN₆O₂

Exact Mass: 540

M.P.: 228-230

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.55 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.70 (m, 3H), 7.55 – 7.48 (m, 2H), 7.48 – 7.39 (m, 3H), 6.83 (d, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 163.60, 157.88, 152.53, 152.37, 146.65, 137.34, 134.18, 134.07, 132.42, 129.66, 128.26, 126.02, 121.53, 119.19, 118.62, 118.52, 118.51, 116.72, 107.55, 98.12, 58.52, 43.84, 13.23, 11.67.

4.5. (Z)-4-(4-(diethylamino)-2-((1-(4-hydroxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9e):



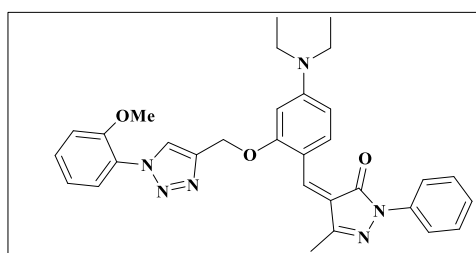
Mol. Formula: C₃₀H₃₀N₆O₃

Exact Mass: 522

M.P.: 208-210

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.12 (s, 1H), 8.54 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.66 (m, 3H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 6.97 – 6.90 (m, 2H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 163.57, 157.85, 156.08, 152.50, 152.34, 146.62, 137.31, 132.39, 128.94, 128.23, 125.99, 121.35, 119.49, 118.59, 118.49, 118.48, 116.71, 116.69, 107.52, 98.09, 58.49, 43.81, 13.20, 11.64.

4.6. (Z)-4-(4-(diethylamino)-2-((1-(2-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9f):



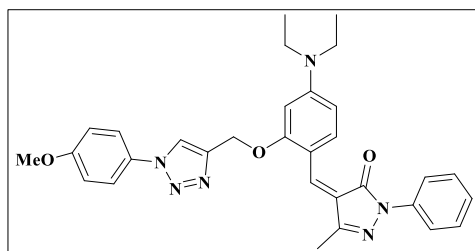
Mol. Formula: C₃₁H₃₂N₆O₃

Exact Mass: 536

M.P.: 214-216

^1H NMR (500 MHz, DMSO- d_6) δ 8.44 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.69 (m, 2H), 7.55 – 7.48 (m, 2H), 7.46 – 7.37 (m, 2H), 7.18 (td, $J = 7.2, 1.4$ Hz, 1H), 7.05 (d, $J = 1.2$ Hz, 1H), 6.83 (d, $J = 2.2$ Hz, 1H), 6.50 (d, $J = 2.2$ Hz, 1H), 5.36 (s, 2H), 3.84 (s, 3H), 3.47 (q, $J = 6.9$ Hz, 6H), 2.30 (s, 3H), 1.12 (t, $J = 7.0$ Hz, 5H); ^{13}C NMR (125 MHz, DMSO- d_6) 163.59, 157.87, 153.17, 152.52, 152.36, 145.29, 137.33, 132.41, 128.25, 127.95, 126.18, 126.01, 124.19, 119.23, 119.04, 118.61, 118.51, 118.50, 116.71, 113.36, 107.54, 98.11, 58.68, 55.04, 43.83, 13.22, 11.66.

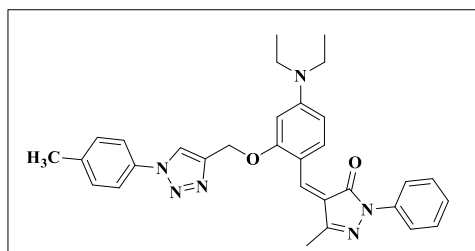
4.7. (Z)-4-(4-(diethylamino)-2-((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methoxy)+benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9g):



Mol. Formula: $\text{C}_{31}\text{H}_{32}\text{N}_6\text{O}_3$
Exact Mass: 536
M.P.: 230-232

^1H NMR (500 MHz, DMSO- d_6) δ 8.53 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.74 (d, $J = 8.1$ Hz, 1H), 7.66 – 7.59 (m, 2H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 7.06 – 6.99 (m, 2H), 6.83 (d, $J = 2.2$ Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.76 (s, 3H), 3.47 (q, $J = 6.9$ Hz, 4H), 2.30 (s, 3H), 1.12 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 163.57, 159.17, 157.85, 152.50, 152.34, 146.62, 137.31, 132.39, 130.07, 128.23, 125.99, 121.41, 119.49, 118.59, 118.49, 118.48, 116.69, 114.64, 107.52, 98.09, 58.49, 54.64, 43.81, 13.20, 11.64.

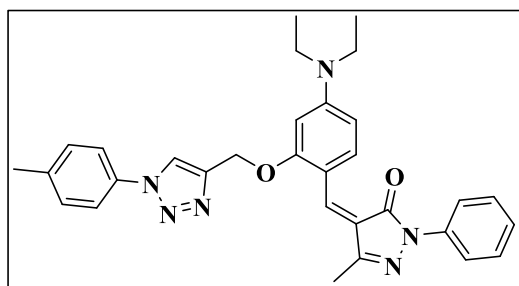
4.8. (Z)-4-(4-(diethylamino)-2-((1-(o-tolyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9h):



Mol. Formula: $\text{C}_{31}\text{H}_{32}\text{N}_6\text{O}_2$
Exact Mass: 520
M.P.: 218-220

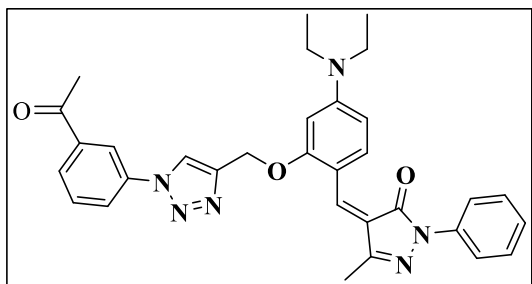
^1H NMR (500 MHz, DMSO- d_6) δ 8.57 (t, $J = 1.0$ Hz, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.66 (m, 2H), 7.55 – 7.48 (m, 2H), 7.46 – 7.38 (m, 2H), 7.29 – 7.19 (m, 2H), 6.83 (d, $J = 2.2$ Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, $J = 6.9$ Hz, 6H), 2.31 (s, 5H), 1.12 (t, $J = 7.0$ Hz, 5H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 163.60, 157.88, 152.53, 152.37, 146.04, 137.34, 135.88, 132.42, 132.09, 130.33, 128.26, 127.91, 126.78, 126.02, 119.96, 119.07, 118.62, 118.52, 118.51, 116.72, 107.55, 98.12, 58.69, 43.84, 16.83, 13.23, 11.67.

4.9. (Z)-4-(4-(diethylamino)-2-((1-(p-tolyl)-1H-1,2,3-triazol-4-yl)methoxy)benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9i):

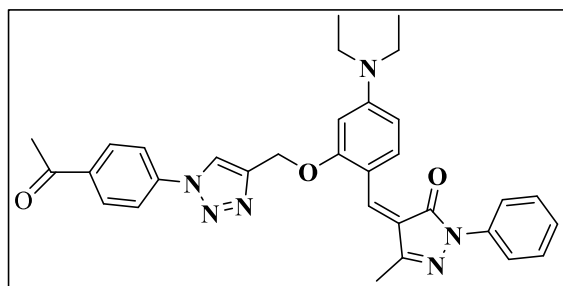


Mol. Formula: $\text{C}_{31}\text{H}_{32}\text{N}_6\text{O}_2$
Exact Mass: 520
M.P.: 222-224

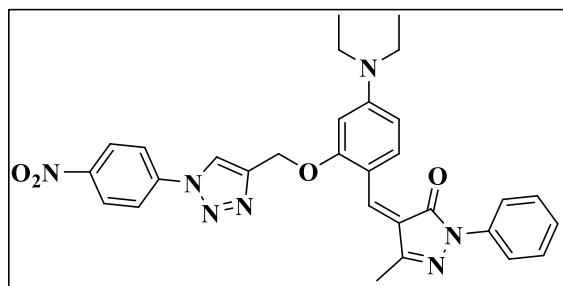
^1H NMR (500 MHz, DMSO- d_6) δ 8.57 (s, 1H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.66 (m, 2H), 7.55 – 7.48 (m, 2H), 7.46 – 7.38 (m, 2H), 7.29 – 7.19 (m, 2H), 6.83 (d, $J = 2.2$ Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, $J = 6.9$ Hz, 4H), 2.31 (s, 6H), 1.12 (t, $J = 7.0$ Hz, 6H); ^{13}C NMR (125 MHz, DMSO- d_6) δ 163.76, 158.04, 152.69, 152.53, 146.81, 137.50, 136.66, 134.11, 132.58, 130.02, 128.42, 126.18, 119.80, 119.31, 118.78, 118.68, 118.67, 116.88, 107.71, 98.28, 58.68, 44.00, 20.56, 13.39, 11.83.

4.10. (Z)-4-(2-((1-(3-acetylphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-(diethylamino) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9j):**Mol. Formula:** C₃₂H₃₂N₆O₃**Exact Mass:** 548**M.P.:** 216-218

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.64 (s, 1H), 8.15 (s, 1H), 7.87 – 7.77 (m, 4H), 7.76 – 7.65 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.62 (s, 3H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 196.82, 163.60, 157.88, 152.53, 152.37, 146.66, 137.55, 137.34, 137.02, 132.42, 129.17, 128.26, 126.02, 125.51, 121.46, 118.99, 118.77, 118.62, 118.52, 118.51, 116.72, 107.55, 98.12, 58.52, 43.84, 26.03, 13.23, 11.67.

4.11. (Z)-4-(2-((1-(4-acetylphenyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-(diethylamino) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9k):**Mol. Formula:** C₃₂H₃₂N₆O₃**Exact Mass:** 548**M.P.:** 206-208

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.59 (s, 1H), 7.95 – 7.89 (m, 2H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.76 – 7.72 (m, 3H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.56 (s, 3H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 196.11, 163.63, 157.91, 152.56, 152.40, 146.68, 137.57, 137.37, 134.77, 132.45, 129.96, 128.29, 126.05, 119.42, 119.22, 118.65, 118.55, 118.54, 116.75, 107.58, 98.15, 58.55, 43.87, 25.76, 13.26, 11.70.

4.12. (Z)-4-(4-(diethylamino)-2-((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methoxy) benzylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (4.9l):**Mol. Formula:** C₃₀H₂₉N₇O₄**Exact Mass:** 551**M.P.:** 216-218

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.57 (s, 1H), 8.37 – 8.30 (m, 2H), 7.97 – 7.90 (m, 2H), 7.87 – 7.81 (m, 2H), 7.79 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.46 – 7.39 (m, 1H), 6.83 (d, *J* = 2.2 Hz, 1H), 6.50 (s, 1H), 5.36 (s, 2H), 3.47 (q, *J* = 6.9 Hz, 4H), 2.30 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 163.57, 157.85, 152.50, 152.34, 148.92, 146.62, 138.87, 137.31, 132.39, 128.23, 125.99, 125.30, 120.50, 119.64, 118.59, 118.49, 118.48, 116.69, 107.52, 98.09, 58.49, 43.81, 13.20, 11.64.

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