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Full Paper

A Facile Eco-Friendly One-Pot Five-Component Synthesis of Novel 1,2,3-Triazole-Linked Pentasubstituted 1,4-Dihydropyridines and their Biological and Photophysical Studies

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An eco-friendly one-pot five-component synthesis of novel 1,2,3-triazole-linked pentasubstituted 1,4-dihydropyridines under ultrasonic and microwave irradiation in polyethylene glycol (PEG) 400 is described. All newly synthesised compounds were evaluated for antibacterial activity, antifungal activity, antioxidant activity, and photophysical properties. Antimicrobial activity was evaluated against six microbial strains. All compounds exhibited antifungal activity against *Aspergillus niger* and *Aspergillus flavus* and moderate antibacterial activity against Gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*). Antioxidant activity was evaluated using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay. All compounds showed good to moderate antioxidant activity. Furthermore all new compounds showed strong fluorescence in solution.

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Introduction

Multicomponent reactions (MCRs) offer valuable strategies for the rapid construction of molecules with high diversity, high intrinsic atom economy, and selectivity. In addition, simple reaction procedures, short reaction times, energy savings, high efficiency, and little to no waste production have led to sizeable efforts to design and implement MCRs in both academia and industry.[1] Development of novel MCRs for the synthesis of 'privileged medicinal scaffolds' with environmental benefits of using non-toxic reagents, green solvents, and alternative sources of energy, is a major challenge for modern drug discovery and green chemistry.

One of the 'privileged medicinal scaffolds' is a substituted 1,4-dihydropyridine (DHP) framework. DHPs are analogues of the nicotinamide adenine dinucleotide (NADH) coenzyme and have a wide range of biological activities including as a vasodilator, bronchodilator, antiatherosclerotic, antitumour, geroprotective, heptoprotective, antidiabetic, antibacterial, and antioxidant.[2–8] DHPs act as Ca^{2+} channel blockers enabling them to be important drugs in the treatment of cardiovascular disease including hypertension as exemplified by nifedipine and nicradipine.[9,10] Several DHPs with antiischemic activity can be used in the treatment of Alzheimer's disease.[11] 1,2,3-Triazoles are other privileged structures associated with a plethora of biological activities including anti-HIV,[12] antimicrobial,[13] antiviral,[14] antiproliferative,[15] antibiotics,[16] insecticides,[17] and fungicides.[18] In addition, they are also used as optical brighteners, dyes, light stabilisers, and corrosion-retarding agents.[19]

Use of ultrasonic and microwave (MW) irradiation as alternative sources of energy has proved to be one of the stepping stones towards green syntheses. Reactions under ultrasonic irradiation offer an advantage of enhanced reactivity and shorter reaction times by the process of acoustic cavitation.[20] MW-assisted organic synthesis offers higher yields of pure products, easier operation, and shorter reaction time as compared with traditional heating methods.[21] Replacement of hazardous volatile solvents with environmentally benign solvents is another aspect of green chemistry. Polyethylene glycol (PEG) is considered as an environmentally benign reaction medium since it is inexpensive, thermally stable, recoverable, biologically compatible, and non-toxic.[22]

Based on the aforementioned and in view of the emergence of resistance to several existing antimicrobial agents such as β-lactam antibiotics, macrolides, quinolones, and vancomycin, and further guided by the observation that the presence of two or more different heterocyclic moieties in a single molecule often enhances the biocidal profile remarkably, we investigated the green synthesis of novel 1,2,3-triazole-linked pentasubstituted DHPs by one-pot five-component reaction under ultrasonic irradiation at room temperature and also under MW irradiation. All newly synthesised compounds were evaluated for antibacterial activity, antifungal activity, antioxidant activity, and photophysical properties.

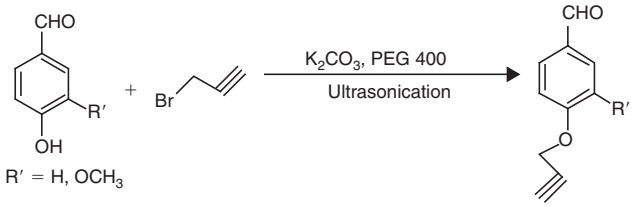
Results and Discussion

Chemistry

We describe herein an efficient one-pot five-component synthesis of novel 1,4-disubstituted-1,2,3-triazole-linked pentasubstituted DHPs using various substituted aryl azides, propargylated benzaldehyde derivatives, dimedone/cyclohexane-1,3-dione, ethyl acetoacetate, and ammonium acetate in the presence of 10 mol-% $CuSO_4{\cdot}5H_2O$ and 20 mol-% sodium ascrobate in PEG 400 as a reaction medium under ultrasonic irradiation at room temperature and under MW irradiation at 50°C.

First, 4-(prop-2-ynyloxy)benzaldehyde and 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde were synthesised by the reaction of 4-hydroxybenzaldehyde or 4-hydroxy-2-methoxybenzaldehyde with propargyl bromide in the presence of K_2CO_3 in PEG 400 as solvent under ultrasonic irradiation at room temperature, hitherto unreported in the literature, as outlined in Scheme 1.

The establishment of optimum reaction conditions for the one-pot five-component condensation was undertaken using 1-azido-4-bromobenzene (1.0 mmol), 5,5-dimethylcyclohexane-1,3-dione (dimedone) (1.0 mmol), 4-(prop-2-ynyloxy) benzaldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol), and ammonium acetate (1.5 mmol) as standard components for a model reaction. The model reactions were attempted in various solvents like ethanol, acetic acid, THF, DMF, acetonitrile, and PEG 400 in the presence of a catalytic amount of $CuSO_4{\cdot}5H_2O$ (10 mol-%) and sodium ascorbate (20 mol-%) as a reducing agent for the reduction of Cu^{II} to Cu^{I} under different conditions. However, best results were obtained when the reaction was carried out in PEG 400 as a medium under ultrasonic irradiation at room temperature. The reaction was complete in 25 min yielding 90 % of ethyl 4-(4-((1-(4-bromophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1a**) after work up (Scheme 2).



Scheme 1. Synthesis of propargylated benzaldehyde derivatives (PEG: polyethylene glycol).

This five-component reaction was not complete even after 150 min when attempted in ethanol under ultrasonic irradiation at room temperature and yielded only 44 % of the desired product **1a** (entry 1, Table 1). The reactions in other solvents, e.g. acetic acid, THF, DMF, and acetonitrile, under identical conditions required longer reaction times and gave inferior yields (entries 2–5, Table 1). So it can be inferred from Table 1, that PEG 400 is the most suitable reaction medium for this five component reaction. The reaction carried out in PEG 400 at room temperature by stirring in the absence of ultrasonic irradiation was not complete even after 180 min. It gave a mixture of products and only 40 % of the desired product **1a** (entry 7, Table 1) was obtained unlike the reaction under ultrasonic irradiation (entry 6, Table 1) which gave 90 % of **1a** in 25 min. Therefore, condensation of five components using $CuSO_4{\cdot}5H_2O$ (10 mol-%) and sodium ascorbate (20 mol-%) as catalysts in PEG 400 (5 mL) under ultrasonic irradiation at room temperature proved to be the optimum conditions.

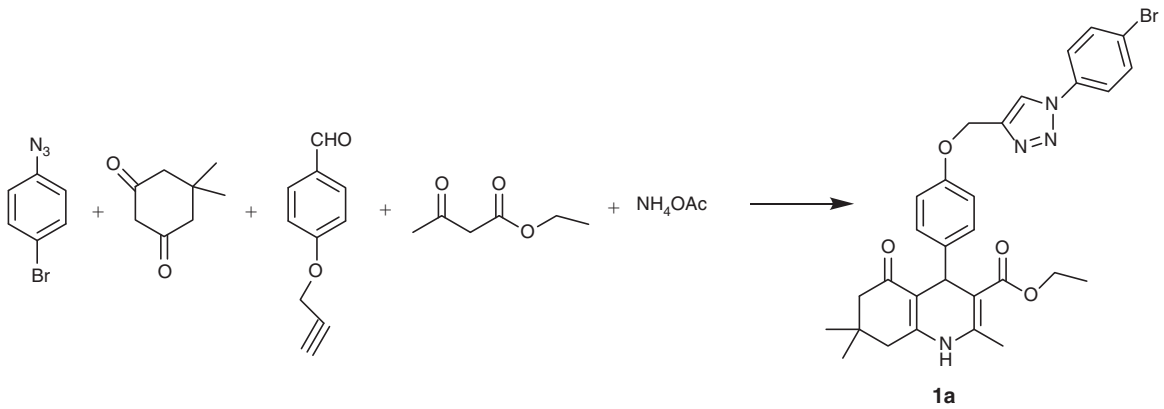
The scope of this novel five-component reaction was examined under optimised conditions by changing substrates. We observed that this five-component reaction is very general for both electron rich and electron deficient aromatic aryl azides which afforded the desired 1,2,3-triazole-linked DHPs in high yields (Table 2, method A, entries 1–9). Furthermore,

Table 1. Optimization of reaction conditions for the synthesis of 1a under ultrasonic irradiation

The reaction was carried out under ultrasonic irradiation using 1-azido-4-bromobenzene (1 mmol), 4-(prop-2-ynyloxy)benzaldehyde (1 mmol), dimedone (1 mmol), ethyl acetoacetate (1 mmol), and ammonium acetate (1.2 mmol) in presence of $CuSO_4{\cdot}5H_2O$ (10 mol-%) and sodium ascorbate (20 mol-%) as catalyst (PEG: polyethylene glycol)

Entry	Solvent	Time [min]	Yield [%]
1	Ethanol	150	44[A]
2	Acetic acid	150	79
3	THF	60	68
4	DMF	45	75
5	CH_3CN	80	66
6	PEG-400	25	90
7	PEG-400[B]	180	40[A,C]

[A]Incomplete reaction.
[B]The reaction was carried out using stirring at room temperature in absence of ultrasound irradiation.
[C]Mixture of products.



Scheme 2.

replacement of dimedone with cyclohexane-1,3-dione and (prop-2-ynyloxy)benzaldehyde with 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde under otherwise identical conditions afforded corresponding triazole-linked DHPs (Table 2, Method A, entries 10–16) in high yields. These results have been summarised in Table 2 (Method A).

The scope of this five-component condensation was also investigated under MW irradiation. The model reaction of 1-azido-4-bromobenzene (1.0 mmol), dimedone (1.0 mmol), 4-(prop-2-ynyloxy)benzaldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol), ammonium acetate (1.5 mmol), $CuSO_4{\cdot}5H_2O$ (10 mol-%), and sodium ascorbate (20 mol-%) in PEG 400 (3 mL) was attempted under MW irradiation under various conditions as outlined in Table 3. However, the best results were obtained when this five-component reaction was performed under MW irradiation (250 W) at 50°C in PEG 400 as it yielded 94 % of **1a** in 10 min and therefore this optimum condition was chosen for subsequent five-component condensations.

Various 1,2,3-triazole-linked pentasubstituted DHPs (**1a**–**1p**) were synthesised in high yield as listed in Table 2 (Method B) under these optimised conditions. The generalised reaction is shown in Scheme 3.

A plausible mechanism of this five-component reaction is shown in Scheme 4. The reaction sequence could proceed first by formation of a 1,2,3-triazole derivative by a Husigen 1,3-dipolar cycloaddition reaction between aryl azide and the propargylated benzaldehyde derivative, followed by the Hantzsch condensation reaction to afford the 1,4-disubstituted-1,2,3-triazole-linked DHPs. The formation of triazole by 1,3-dipolar cycloaddition of aryl azides to (prop-2-ynyloxy) benzaldehyde was distinctly observed in the reaction by comparing the TLC with an authentic sample and supports the proposed pathway.

We have also investigated the recyclability of the reaction medium, i.e. PEG 400, using the model reaction of 1-azido-4-bromobenzene, dimedone, 4-(prop-2-ynyloxy)benzaldehyde, ethyl acetoacetate, and ammonium acetate. After completion of the reaction, water (5 mL) was added to the reaction mixture. The precipitate formed was collected by vacuum filtration. The filtrate containing PEG 400 was rinsed with ether and vacuumed to dryness at 90°C for 2 h to remove any trapped moisture and was used for the next run. No appreciable loss in the yield of product **1a** was observed after three cycles: **1a** was obtained in 90 %, 88 %, and 87 % yield after the first, second, and third cycle, respectively.

Pharmacology

The antimicrobial activity of all new compounds (**1a**–**1p**) was evaluated by selecting six microbial strains on the basis of their clinical importance in causing diseases in humans. Two Gram-positive bacteria (*Staphylococcus aureus* MTCC 96 and *Bacillus subtilis* MTCC 121), two Gram-negative bacteria (*Escherichia coli* MTCC 1652 and *Pseudomonas aeruginosa* MTCC 741), and two fungi (*Aspergillus niger* and *Aspergillus flavus*) were used in the present study for evaluation of antimicrobial activity of all new compounds.

Antibacterial Activity

The antibacterial activity[23] of all compounds (**1a**–**1p**) was evaluated against both Gram-positive bacteria (*Staphylococcus aureus* MTCC 96 and *Bacillus subtilis* MTCC 121) as well as Gram-negative bacteria (*Escherichia coli* MTCC 1652 and

Table 3. Optimisation of reaction conditions for the synthesis of 1a under microwave irradiation

rt: room temperature, PEG: polyethylene glycol

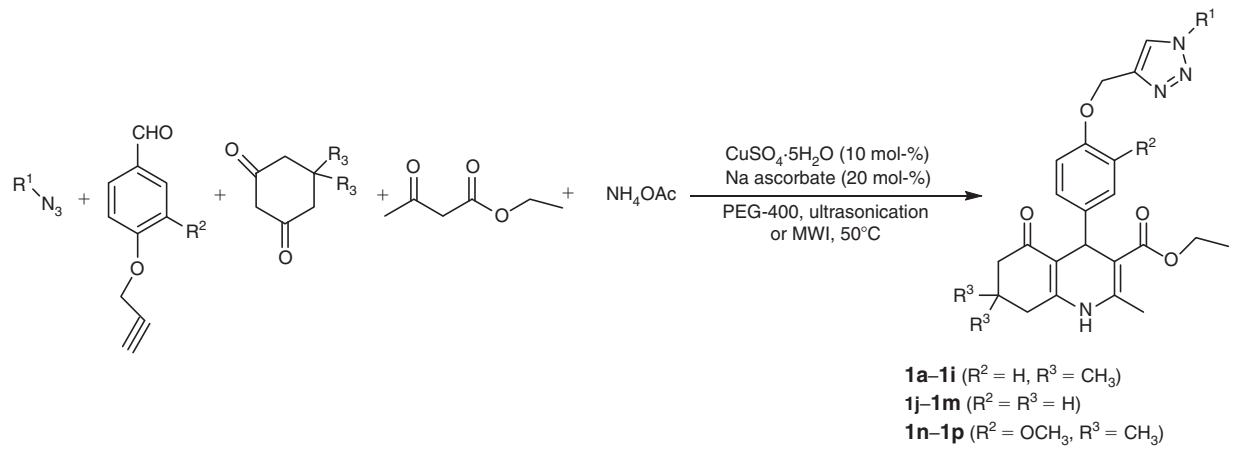
Entry	Solvent	Microwave power [W]	Temperature [°C]	Time [min]	Yield [%]
1	Ethanol	250	rt	45	60[A]
2	THF	250	rt	35	87
3	Acetic acid	250	rt	40	65[A]
4	PEG 400	250	rt	20	88
5	PEG 400	250	50	10	94
6	PEG 400	250	60	10	92
7	PEG 400	300	50	10	91

[A]Mixture of products.

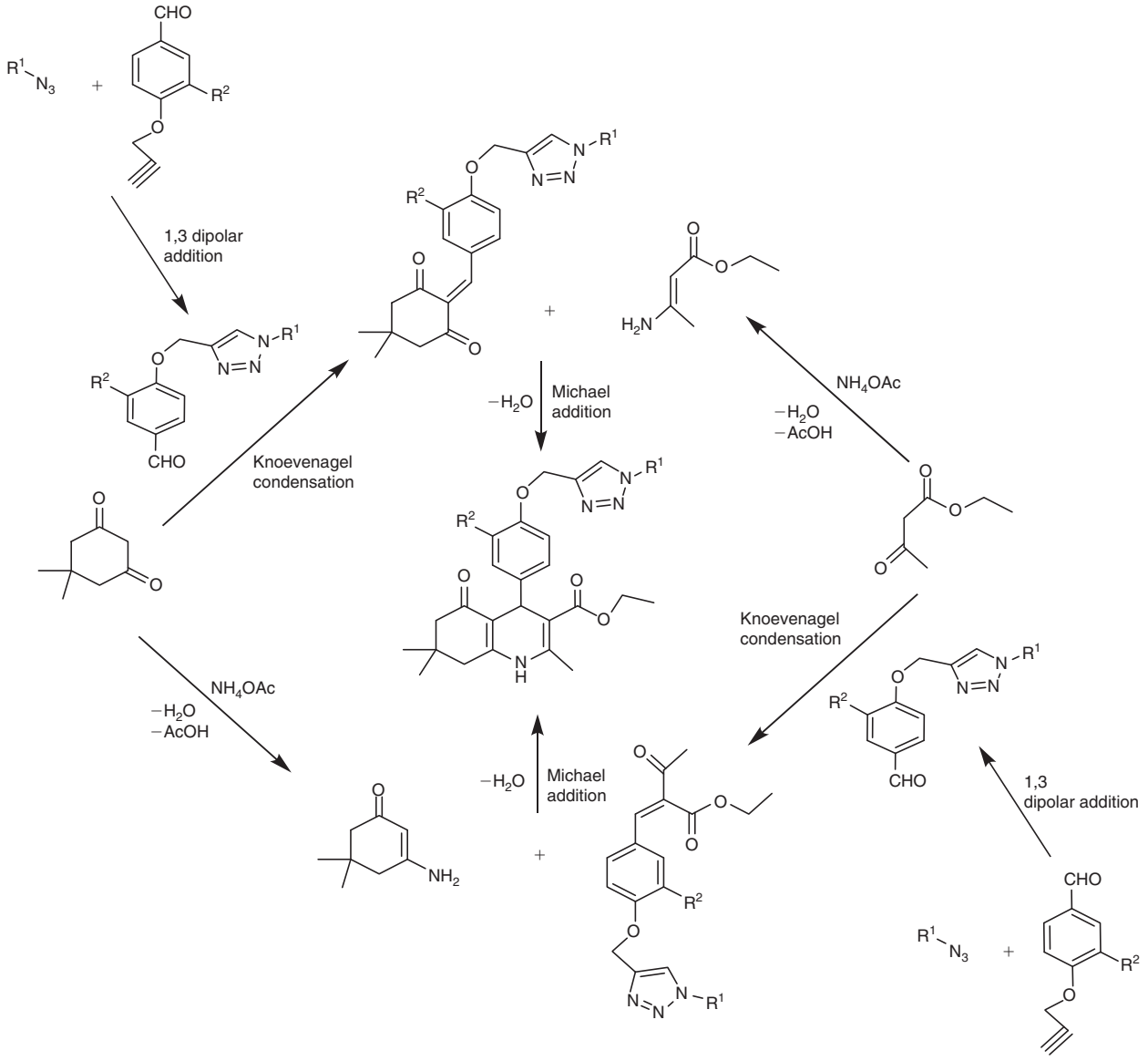
Table 2. One-pot five-component synthesis of triazole-linked pentasubstituted 1,4 dihydropyridines

Method A: reaction was carried under ultrasonic irradiation at room temperature; Method B: reaction was carried under microwave irradiation (250 W) at 50°C

Entry	R^1	R^2	R^3	Product	Method A		Method B	
					Time [min]	Yield [%]	Time [min]	Yield [%]
1	4-BrC_6H_4	H	CH_3	**1a**	25	90	10	94
2	4-MeC_6H_4	H	CH_3	**1b**	35	86	15	91
3	4-$MeOC_6H_4$	H	CH_3	**1c**	35	89	12	90
4	4-$NO_2C_6H_4$	H	CH_3	**1d**	25	93	10	91
5	4-FC_6H_4	H	CH_3	**1e**	35	92	18	94
6	4-F,3-ClC_6H_3	H	CH_3	**1f**	30	87	15	90
7	1-Naphthyl	H	CH_3	**1g**	40	91	15	95
8	C_6H_5	H	CH_3	**1h**	30	88	18	90
9	3-ClC_6H_4	H	CH_3	**1i**	35	86	15	94
10	4-$NO_2C_6H_4$	H	H	**1j**	40	90	12	91
11	4-MeC_6H_4	H	H	**1k**	45	91	15	92
12	4-$MeOC_6H_4$	H	H	**1l**	40	93	15	90
13	4-BrC_6H_4	H	H	**1m**	35	91	12	94
14	4-MeC_6H_4	OCH_3	CH_3	**1n**	30	92	15	93
15	4-$MeOC_6H_4$	OCH_3	CH_3	**1o**	45	88	18	90
16	4-BrC_6H_4	OCH_3	CH_3	**1p**	35	93	15	92



Scheme 3. One-pot five-component synthesis of 1,2,3 triazole-linked pentasubstituted 1,4-dihydropyridines (PEG: polyethylene glycol,))))): ultrasonication, MWI: microwave irradiation).



Scheme 4. A plausible mechanism for the synthesis of 1,2,3-triazole-linked dihydropyridines.

Pseudomonas aeruginosa MTCC 741) by an agar well diffusion method using ciprofloxacin as a standard. The results of the antimicrobial evaluation reveal that all compounds possessed variable antibacterial activity against Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*). However, none of the compounds exhibited activity against Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria. All compounds (**1a**–**1p**) showed a zone of inhibition ranging between 13.0 and 19.3 mm against the Gram positive bacteria as listed in Table S1 in the Supplementary Material. On the basis of the zone of inhibition produced, compound **1f** was found to be most effective against *B.subtilis* and *S. aureus*, with a zone of inhibition of 19.3 and 17.6 mm, respectively. Other compounds showed moderate antibacterial activity (Table S1, Figure S1).

The minimum inhibitory concentration (MIC) of all compounds (**1a**–**1p**) was measured against Gram positive bacteria, as shown in Table S2. The MIC of all compounds ranged between 64 and 512 $\mu g\,mL^{-1}$. Compound **1f** exhibited the lowest MIC of 64 $\mu g\,mL^{-1}$ against *B. subtilis* and *S. aureus* as compared with standard ciprofloxacin. The higher activity of compound **1f** could be due to the presence of fluorine at the *para* and chlorine at the *meta* position of the aromatic ring whereas compound **1e** with fluorine at the *para* position and compound **1i** with chlorine at the *meta* position showed lower activity compared with compound **1f**.

Antifungal Activity

Antifungal activity[24] of all compounds (**1a**–**1p**) was evaluated against *Aspergillus niger* and *Aspergillus flavus* using a poisoned food method. As shown in Table S3 and Figure S2, all compounds exhibited good antifungal activity as compared with standard fluconazole. Compounds **1f** and **1g** showed more than 50 % inhibition of mycelial growth against *Aspergillus niger* whereas compounds **1b**, **1f**, **1g**, and **1h** showed more than 50 % inhibition of mycelial growth against *Aspergillus flavus*.

Antioxidant Activity

The free radical antioxidant activity[25] of all compounds (**1a**–**1p**) was evaluated using a 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay at a concentration level of 0.8 and 0.4 $\mu M\,mL^{-1}$. All new compounds exhibited antioxidant activity comparable with the standard butylated hydroxytoulene (BHT). Compounds **1d** and **1n**–**1p** showed good antioxidant activity at higher concentration (0.8 $\mu mol\,mL^{-1}$) as compared with the standard BHT. Whereas other compounds at this concentration showed low to moderate antioxidant activity. Furthermore, at a lower concentration of 0.4 $\mu mol\,mL^{-1}$ compounds **1d** and **1n**–**1p** showed moderate antioxidant activity. It was observed that the antioxidant activity of triazole-linked pentasubstituted DHPs **1n**–**1p** was enhanced due to the presence of $R^2 = OCH_3$ at the phenyl ring attached to the DHP moiety. The results are summarised in Table S4 and Figure S3.

Photophysical Studies

The spectroscopic characteristics such as absorption maxima λ_{max} (nm), emission maxima λ_{em} (nm), and extinction coefficient (ε) of all compounds (**1a**–**1p**) were measured in methanol. All compounds showed absorption starting from 225 nm in the electronic absorption spectrum (Figure S4). The electronic absorption spectra of compounds **1a**–**1p** displayed three absorption maxima, band 1 in the region of 225–234 nm, band II in the region of 242–285 nm, and band III in the region of 362–369 nm and an emission maxima in the range of 441–451 nm. The spectroscopic characteristics are presented in Table S5.

The absorption band in the region of 242–285 nm is characteristic of cross conjugation and could be due to the presence of two carbonyl groups at position 3 and 5 in compounds **1a**–**1p** that would have created such a system.

The fluorescence spectra of all compounds **1a**–**1p** was also measured in methanol and showed strong fluorescence in solution. All compounds displayed almost similar fluorescence spectra in the range of 439–451 nm (Figure S5, Table S5). A fluorescence excitation wavelength (λ_{ext}) of 375 nm was used for all the compounds.

The influence of solvents on the fluorescence spectra of compound **1c** was measured in different solvents with varying polarity such as 1,4-dioxan, chloroform, methanol, acetonitrile, and dimethyl sulfoxide (Table S6). It can be inferred from Table S6 that compound **1c** displayed bathochromically shifted emission maxima in polar methanol as compared with non-polar 1,4-dioxan.

The effect of solvent polarity on the absorbance and fluorescence are the origin of the Stokes shift. The plot between orientation of polarisability (Δf) of solvents and the Stoke shift ($\Delta \nu$) is known as a Lippert–Mataga plot. The Lippert–Mataga plot for compound **1c** did not show any linear relationship (Figure S6) which indicates that no appreciable solvatochromism exists among polar solvents and solvent plays only a solvent specific role.

Furthermore, the effect of the *para* substituent in the phenyl ring of the 1,2,3-triazole on the fluorescence was also investigated. The plot between fluorescence emission maxima and *para* Hammett substitution constant for the phenyl ring attached to the 1,2,3-triazole did not show a linear relationship (Figure S7). Therefore it can be inferred from Figure S7 that fluorescence of the compounds is due directly to their framework and the substituent on the phenyl ring has little influence on fluorescence properties.

Conclusion

We have reported an efficient and environmentally benign synthesis of novel 1,2,3-triazole-linked pentasubstituted DHPs by a one-pot five-component reaction of aryl azides, propargylated benzaldehyde derivatives, dimedone/cyclohexane-1,3-dione, ethyl acetoacetate, and ammonium acetate in the presence of 10 mol-% $CuSO_4{\cdot}5H_2O$ and 20 mol-% sodium ascorbate in PEG 400 as a recyclable reaction medium under ultrasonic irradiation at room temperature and under MW irradiation at 50°C. All these compounds (**1a**–**1p**) were evaluated for antimicrobial activity against six microbial strains including four bacterial strains and two fungal strains. All compounds exhibited antifungal activity against *Aspergillus niger* and *Aspergillus. flavus* and moderate antibacterial activity against gram positive bacteria. Compound **1f** showed the best antifungal and antibacterial activity with an MIC of 64 $\mu g\,mL^{-1}$ against the Gram positive bacterial strains *B.subtilis* and *S. aureus* as compared with the standard ciprofloxacin and 55.8 % inhibition of mycelial growth against the fungal strain *Aspergillus flavus* and 51.1 % against *Aspergillus niger* as compared with the standard fluconazole. All compounds showed good antioxidant activity at a concentration of 0.8 $\mu mol\,mL^{-1}$ and a low antioxidant activity at a concentration of 0.4 $\mu mol\,mL^{-1}$. Compounds **1d**, **1n**, **1o**, and **1p** showed good antioxidant activity as

comparable to the standard BHT. Furthermore, the photophysical properties of all new compounds were also measured. All compounds showed a strong fluorescence in solution.

Experimental

All chemicals were available commercially and were purchased from Sigma–Aldrich and Spectrochem and were used as received. F_{254} precoated aluminium plates with silica gel 60 from Merck were used to monitor the reaction progress. An ultrasonic bath (54 kHz, 300 W, 3 L capacity) of Throughclean ultrasonic Pvt. Ltd (India) and a CEM discover MW reactor were used for reactions. Reported melting points are uncorrected. IR (KBr) spectra were recorded on a Perkin Elmer FTIR spectrophotometer and the values are expressed as ν_{max} in cm^{-1}. The NMR (^1H and ^{13}C) spectra were recorded on a Jeol JNM ECX-400P at 400 and 100 MHz, respectively. The chemical shift values are recorded on the δ scale and the coupling constants (J) are in Hertz. The mass spectra were recorded on an Agilent 6520 QTOF LCMS having an electrospray ionisation (ESI) source in positive mode. Elemental analyses were recorded on a VarioEL III elemental analyser in CHNS mode. UV-vis absorption spectra were recorded on an Analytikjena specord 250 spectrophotometer. The fluorescence spectra were measured using a Cary Eclipse Fluorescence spectrophotometer.

Procedure for Synthesis of 4-(Prop-2-ynyloxy)benzaldehyde and 3-Methoxy-4-(prop-2-ynyloxy)benzaldehyde

A mixture of 4-hydroxybenzaldehyde (1.0 mmol) (3-methoxy-4-hydroxybenzaldehyde (1.0 mmol)), propargyl bromide (1.2 mmol), K_2CO_3 (2 mmol), and PEG 400 (5 mL) was placed in a 50 mL round-bottomed flask. The reaction mixture was sonicated at room temperature for 30 min. After completion of reaction, as monitored by TLC using ethyl acetate/petroleum ether (40 : 60, v/v) as eluent, water (10 mL) was added to the reaction mixture. The precipitate formed was collected by vacuum filtration, washed with water to afford pure 4-(prop-2-ynyloxy) benzaldehyde (mp 80–82°C)[26] (3-methoxy-4-(prop-2-ynyloxy) benzaldehyde (mp 102–104°C))[27] in 94 % (92 %) yield.

*General Procedure for the Synthesis of 1,2,3-Triazole-Linked Pentasubstituted DHPs Under Ultrasonic Irradiation (Method A) (**1a**–**1p**)*

A mixture of 4-(prop-2-ynyloxy)benzaldehyde or 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde (1 mmol), substituted aryl azide (1 mmol), dimedone or cyclohexane-1,3-dione (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1.5 mmol), $CuSO_4 \cdot 5H_2O$ (10 mol-%), sodium ascorbate (20 mol-%), and PEG 400 (5 mL) was placed in a 50 mL round bottomed flask. The reaction mixture was sonicated for an appropriate time as mentioned in Table 2. The progress of the reaction was monitored by TLC using ethyl acetate/petroleum ether (60 : 40, v/v) as eluent. After completion of the reaction as indicated by TLC, water (10 mL) was added to the reaction mixture. The precipitate formed was collected by vacuum filtration and washed with water. The crude product so obtained, was purified by flash column chromatography over silica gel (230–400 mesh) using ethyl acetate/petroleum ether as eluent to afford pure products **1a**–**1p**.

*General Procedure for the Synthesis of 1,2,3-Triazole-Linked Pentasubstituted DHPs Under MW Irradiation (Method B) (**1a**–**1p**)*

A vial containing a mixture of 4-(prop-2-ynyloxy)benzaldehyde or 3-methoxy-4-(prop-2-ynyloxy)benzaldehyde (1 mmol), substituted aryl azide (1 mmol), dimedone or cyclohexane-1,3-dione (1 mmol), ethyl acetoacetate (1 mmol), ammonium acetate (1.5 mmol), $CuSO_4 \cdot 5H_2O$ (10 mol-%), sodium ascorbate (20 mol-%), and PEG 400 (3 mL) was sealed and placed in a CEM Discover MW reactor. The vial was subjected to MW irradiation, programmed at 50°C and 250 W. After completion of the reaction as indicated by TLC using ethyl acetate/petroleum ether (60 : 40, v/v) as eluent, the vial was cooled to room temperature and the contents were poured into water (10 mL). The precipitated solid was filtered off and washed with water. The crude product so obtained was purified by flash column chromatography over silica gel (230–400 mesh) using ethyl acetate/petroleum ether as eluent to afford pure products (**1a**–**1p**). All newly synthesised compounds were fully characterised on the basis of IR, UV, ^1H NMR and ^{13}C NMR spectra and high-resolution mass spectrometry.

*Spectroscopic Data of Compounds **1a**–**1p***

*Ethyl 4-(4-((1-(4-Bromophenyl)-1H-1,2,3-triazol-4-yl) methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1a**)*

Pale-yellow solid, mp 107°C, δ_H (400 MHz, $CDCl_3$) 8.01 (s, 1H, trizolyl-H), 7.63–7.58 (m, 4H, ArH), 7.20 (d, 2H, J 8.68, ArH), 6.79 (d, 2H, J 8.72, ArH), 6.63 (s, 1H, NH), 5.17 and 5.13 (AB system, J 12.36, 2H, $OCH_a.H_b$), 4.96 (s, 1H, CH), 4.04–3.99 (q, 2H, J 7.32, OCH_2), 2.30 (s, 3H, CH_3), 2.26–2.01 (m, 4H), 1.18–1.14 (t, 3H, J 7.32, CH_3), 1.0 (s, 3H, CH_3), 0.87 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.77, 167.52, 156.11, 148.61, 145.32, 143.52, 140.73, 135.92, 132.85, 129.08, 122.31, 121.90, 120.81, 113.98, 111.94, 105.99, 67.73, 59.74, 50.65, 40.75, 35.70, 32.60, 29.39, 27.08, 19.22, 14.19; ν_{max} (KBr)/cm^{-1} 3291, 2958, 2928, 1686, 1608, 1498, 1379, 1219; Anal. Calc. for $C_{30}H_{31}BrN_4O_4$: C 60.92, H 5.28, N 9.47 (*m/z* 590.1523). Found: C 60.99, H 5.29, N 9.50 % (*m/z* 591.1599) ($[M+H]^+$).

*Ethyl 2,7,7-Trimethyl-5-oxo-4-(4-((1-(4-toly)l-1H-1,2,3-triazol-4-yl)methoxy)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1b**)*

Pale-yellow solid, mp 228°C, δ_H (400 MHz, $CDCl_3$) 7.96 (s, 1H, trizolyl-H), 7.57 (d, 2H, J 8.04, ArH), 7.28 (d, 2H, J 8.8, ArH), 7.21 (d, 2H, J 8.8, ArH), 6.82 (d, 2H, J 8.8, ArH), 6.03 (s, 1H, NH), 5.20 and 5.17 (AB system, J 12.48, 2H, $OCH_a.H_b$), 4.97 (s, 1H, CH), 4.05–4.02 (q, 2H, J 6.6, OCH_2), 2.39 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.27–2.05 (m, 4H), 1.18 - 1.15 (t, 3H, J 7.36, CH_3), 1.03 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.49, 167.55, 156.64, 147.74, 145.11, 143.16, 140.35, 138.88, 134.72, 130.22, 129.11, 120.87, 120.53, 114.13, 112.26, 106.16, 62.08, 59.65, 50.79, 41.02, 35.78, 32.70, 29.37, 27.25, 21.07, 19.39, 14.22; ν_{max} (KBr)/cm^{-1} 3338, 2928, 1678, 1617, 1481, 1377, 1218; *m/z* (HRMS ESI) Calc. for $C_{31}H_{34}N_4O_4$: 526.2574. Found: 527.2552 ($[M+H]^+$).

*Ethyl 4-(4-((1-(4-Methoxyphenyl)-1H-1,2,3-triazol-4-yl) methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1c**)*

Pale-yellow solid, mp 230°C, δ_H (400 MHz, $CDCl_3$) 7.93 (s, 1H, trizolyl-H), 7.61 (d, 2H, J 9.62, ArH), 7.25–7.22 (m, 2H, ArH), 7.00 (d, 2H, J 8.72, ArH), 6.84 (d, 2H, J 8.72, ArH), 6.06 (s, 1H, NH), 5.20 and 5.16 (AB system, J 12.36, 2H, $OCH_a.H_b$), 4.99 (s, 1H, CH), 4.06–4.02 (q, 2H, J 7.32, OCH_2), 3.86 (s, 3H, OCH_3), 2.36 (s, 3H, CH_3), 2.29–2.15 (m, 4H), 1.20–1.17 (t, 3H,

J 7.32, CH_3), 1.05 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.68, 167.52, 159.83, 144.90, 156.37, 148.28, 143.90, 140.41, 130.35, 129.08, 122.24, 121.14, 114.72, 114.03, 112.10, 106.04, 61.86, 59.75, 55.59, 50.68, 40.86, 35.67, 32.63, 29.40, 27.15, 19.28, 14.21; ν_{max} (KBr)/cm^{-1} 3341, 2959, 2930, 1682, 1633, 1608, 1518, 1505, 1486, 1379, 1218; Anal. Calc. for $C_{31}H_{34}N_4O_5$: C 68.62, H 6.32, N 10.33 (*m/z* 542.2523). Found: C 68.70, H 6.34, N 10.36 % (*m/z* (HRMS ESI) 543.2610 ($[M+H]^+$)).

*Ethyl 2,7,7-Trimethyl-4-(4-((1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1d**)*

Pale-yellow solid, mp 90°C, δ_H (400 MHz, $CDCl_3$) 8.38 (d, 2H, *J* 9.52, ArH), 8.15 (s, 1H, trizolyl-H), 7.96 (d, 2H, *J* 8.8, ArH), 7.20 (d, 2H, *J* 8.8, ArH), 6.79 (d, 2H, *J* 8.8, ArH), 6.31 (s, 1H, NH), 5.20 and 5.16 (AB system, *J* 13.2, 2H, $OCH_a.H_b$), 4.97 (s, 1H, CH), 4.05–4.0 (q, 2H, *J* 7.32, OCH_2), 2.32 (s, 3H, CH_3), 2.28–2.08 (m, 4H), 1.19–1.15 (t, 3H, *J* 6.6, CH_3), 1.02 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.75, 167.50, 156.16, 148.34, 147.17, 146.18, 143.26, 141.10, 140.57, 129.15, 125.51, 120.79, 120.50, 113.99, 112.02, 106.13, 61.66, 59.80, 50.67, 40.88, 35.77, 32.65, 29.39, 27.13, 19.34, 14.21; ν_{max} (KBr)/cm^{-1} 3293, 2958, 2928, 1690, 1608, 1504, 1379, 1219; *m/z* (HRMS ESI) Calc. for $C_{30}H_{31}N_5O_6$: 557.2268. Found: 558.2252 ($[M+H]^+$).

*Ethyl 4-(4-((1-(4-Fluorophenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1e**)*

Pale-yellow solid, mp 102°C, δ_H (400 MHz, $CDCl_3$) 7.93 (s, 1H, trizolyl-H), 7.65–7.61 (m, 2H, ArH), 7.19–7.12 (m, 4H, ArH), 6.76 (d, 2H, *J* 8.72, ArH), 6.36 (s, 1H, NH), 5.14 and 5.10 (AB system, *J* 12.36, 2H, $OCH_a.H_b$), 4.92 (s, 1H, CH), 4.01–3.95 (q, 2H, *J* 6.88, OCH_2), 2.27 (s, 3H, CH_3), 2.20–1.97 (m, 4H), 1.14–1.11 (t, 3H, *J* 7.32, CH_3), 0.97 (s, 3H, CH_3), 0.84 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.86, 167.63, 156.43, 148.43, 145.42, 143.52, 140.58, 129.23, 122.74, 122.66, 121.27, 116.95, 116.72, 114.14, 112.19, 106.22, 61.91, 59.90, 50.80, 41.00, 35.84, 32.77, 29.52, 27.24, 19.43, 14.34; ν_{max} (KBr)/cm^{-1} 3292, 2959, 1686, 1608, 1517, 1507, 1489, 1380, 1220; Anal. Calc. for $C_{30}H_{31}FN_4O_4$: C 67.91, H 5.89, N 10.56 (*m/z* 530.2323). Found: C 68.02, H 5.88, N 10.59 % (*m/z* (HRMS ESI) 531.2409 ($[M+H]^+$)).

*Ethyl 4-(4-((1-(3-Chloro-4-fluorophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1f**)*

Pale-yellow solid, mp 130°C, δ_H (400 MHz, $CDCl_3$) 8.05 (s, 1H, trizolyl-H), 7.86–7.83 (m, 1H, ArH), 7.63–7.59 (m, 1H, ArH), 7.31–7.20 (m, 3H, ArH), 6.81 (d, 2H, *J* 9.16, ArH), 6.35 (s, 1H, NH), 5.20 and 5.17 (AB system, *J* 13.2, 2H, $OCH_a.H_b$), 4.99 (s, 1H, CH), 4.07–4.02 (q, 2H, *J* 6.6, OCH_2), 2.41 (s, 3H, CH_3), 2.24–2.05 (m, 4H), 1.21–1.17 (t, 3H, *J* 7.36, CH_3), 1.04 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.74, 167.50, 156.24, 148.37, 145.63, 143.30, 140.48, 129.12, 128.97, 123.07, 120.98, 120.33, 120.25, 117.74, 117.52, 114.01, 112.08, 106.14, 61.73, 59.79, 50.66, 40.92, 35.73, 32.66, 29.39, 27.13, 19.33, 14.21; ν_{max} (KBr)/cm^{-1} 3293, 2960, 1686, 1608, 1507, 1380, 1219; Anal. Calc. for $C_{30}H_{30}ClFN_4O_4$: C 63.77, H 5.35, N 9.92 (*m/z* 564.1934). Found: C 63.90, H 5.33, N 9.91 % (*m/z* (HRMS ESI) 565.2015 ($[M+H]^+$)).

*Ethyl 2,7,7-Trimethyl-4-(4-((1-(naphthalen-1-yl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1g**)*

Pale-yellow solid, mp 98°C, δ_H (400 MHz, $CDCl_3$) 7.96–7.92 (m, 3H, ArH), 7.58–7.49 (m, 5H, ArH), 7.23 (d, 2H, *J* 8.8, ArH), 6.85 (d, 2H, *J* 8.8, ArH), 6.57 (s, 1H, NH), 5.28 and 5.24 (AB system, *J* 12.44, 2H, $OCH_a.H_b$), 4.98 (s, 1H, CH), 4.04–3.99 (q, 2H, *J* 7.32, OCH_2), 2.32 (s, 3H, CH_3), 2.27–2.04 (m, 4H), 1.17–1.14 (t, 3H, *J* 6.6, CH_3), 1.00 (s, 3H, CH_3), 0.86 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.70, 167.53, 156.40, 148.32, 144.39, 143.54, 140.48, 134.07, 133.50, 130.46, 129.09, 128.40, 128.24, 127.93, 127.08, 125.44, 124.93, 123.57, 122.21, 114.08, 112.06, 105.99, 61.90, 59.74, 50.65, 40.81, 35.67, 32.60, 29.39, 27.05, 19.24, 14.20 ν_{max} (KBr)/cm^{-1} 3292, 2958, 2928, 1690, 1607, 1505, 1489, 1379, 1219; *m/z* (HRMS ESI) Calc. for $C_{34}H_{34}N_4O_4$: 562.2574.Found: 563.2560 ($[M+H]^+$).

*Ethyl 2,7,7-Trimethyl-5-oxo-4-(4-((1-phenyl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1h**)*

Pale-yellow solid, mp 140°C, δ_H (400 MHz, $CDCl_3$) 8.01 (s, 1H, trizolyl-H), 7.71 (d, 2H, *J* 8.08, ArH), 7.51–7.43 (m, 3H, ArH), 7.25–7.21 (m, 2H, ArH), 6.83 (d, 2H, *J* 8.8, ArH), 6.03 (s, 1H, NH), 5.21 (s, 2H, OCH_2), 4.99 (s, 1H, CH), 4.07–4.02 (q, 2H, *J* 7.32, OCH_2), 2.35 (s, 3H, CH_3), 2.28–2.15 (m, 4H), 1.20–1.16 (t, 3H, *J* 7.32, CH_3), 1.05 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.78, 167.54, 156.32, 148.49, 145.12, 143.54, 140.46, 136.87, 129.73, 129.08, 128.84, 121.00, 120.57, 114.02, 112.02, 106.00, 61.82, 59.75, 50.64, 40.79, 35.68, 32.61, 29.65, 27.08, 19.23, 14.20; ν_{max} (KBr)/cm^{-1} 3293, 2958, 2926, 1600, 1527, 1507, 1379, 1218; *m/z* (HRMS ESI) Calc. for $C_{30}H_{32}N_4O_4$: 512.2418. Found: 513.2499 ($[M+H]^+$).

*Ethyl 4-(4-((1-(3-Chlorophenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1i**)*

Pale-yellow solid, mp 85°C, δ_H (400 MHz, $CDCl_3$) 8.04 (s, 1H, trizolyl-H), 7.77–7.76 (m, 1H, ArH), 7.62–7.60 (m, 1H, ArH), 7.45–7.38 (m, 2H, ArH), 7.21 (d, 2H, *J* 8.24, ArH), 6.81 (d, 2H, *J* 8.72, ArH), 6.70 (s, 1H, NH), 5.18 and 5.15 (AB system, *J* 12.44, 2H, $OCH_a.H_b$), 4.98 (s, 1H, CH), 4.06–4.0 (q, 2H, *J* 6.88, OCH_2), 2.31 (s, 3H, CH_3), 2.06–2.24 (m, 4H), 1.19–1.15 (t, 3H, *J* 7.32, CH_3), 1.02 (s, 3H, CH_3), 0.88 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.85, 167.46, 156.16, 147.71, 143.12, 140.41, 139.79, 135.58, 130.83, 129.44, 129.00, 128.88, 120.83, 118.53, 114.17, 114.08, 112.31, 106.25, 61.88, 59.79, 50.67, 41.10, 35.72. 32.71, 29.38, 27.18, 19.43, 14.21; ν_{max} (KBr)/cm^{-1} 3291, 2929, 1686, 1608, 1507, 1490, 1379, 1218; *m/z* (HRMS ESI) Calc. for $C_{30}H_{31}ClN_4O_4$: 546.2034. Found: 547.2028 $([M+H])^+$.

*Ethyl 2-Methyl-4-(4-((1-(4-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1j**)*

Yellow solid, mp 227°C, δ_H (400 MHz, $CDCl_3$) 8.40 (d, 2H, *J* 8.8, ArH), 8.12 (s, 1H, trizolyl-H), 7.97 (d, 2H, *J* 8.8, ArH), 7.25–7.21 (m, 2H, ArH), 6.82 (d, 2H, *J* 8.8, ArH), 5.80 (s, 1H, NH), 5.26 and 5.22 (AB system, *J* 13.16, 2H, $OCH_a.H_b$), 5.02 (s, 1H, CH), 4.07–4.01 (q, 2H, *J* 7.32, OCH_2), 2.45–2.28 (m, 7H), 2.05–1.89 (m, 2H, CH_2), 1.19–1.16 (t, 3H, *J* 7.32, CH_3); δ_C (100 MHz, $CDCl_3$) 195.81, 167.32, 156.19, 149.18, 146.89,

146.45, 142.85, 141.25, 140.56, 133.30, 129.20, 125.54, 120.53, 114.08, 113.35, 106.27, 61.80, 59.97, 37.05, 35.42, 27.44, 21.03, 19.43. 14.21; ν_{max} (KBr)/cm^{-1} 3280, 2925, 1686, 1600, 1527, 1507, 1483, 1379, 1226; *m/z* (HRMS ESI) Calc. for $C_{28}H_{27}N_5O_6$: 529.1961. Found: 530.1928 ($[M + H]^+$.

*Ethyl 2-Methyl-5-oxo-4-(4-((1-(4-tolyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1k**)*

Pale-yellow solid, mp 217°C, δ_H (400 MHz, $CDCl_3$) 7.99 (s, 1H, trizolyl-H), 7.58 (d, 2H, *J* 8.24, ArH), 7.30 (d, 2H, *J* 8.24, ArH), 7.25–7.21 (m, 2H, ArH), 6.83 (d, 2H, *J* 8.72, ArH), 6.61 (s, 1H, NH), 5.21 and 5.17 (AB system, *J* 13.72, 2H, $OCH_a.H_b$), 5.03 (s, 1H, CH), 4.07–4.01 (q, 2H, *J* 6.88, OCH_2), 2.40 (s, 3H, CH_3), 2.38–2.27 (m, 7H), 1.96–1.84 (m, 2H, CH_2), 1.19–1.15 (t, 3H, *J* 7.36, CH_3); δ_C (100 MHz, $CDCl_3$) 196.03, 165.54, 156.37, 150.03, 144.93, 143.48, 140.55, 139.00, 134.50, 130.22, 129.07, 120.96, 120.48, 114.05, 113.27, 105.94, 61.83, 59.75, 37.00, 35.52, 27.22, 21.07, 20.98, 19.21, 14.19; ν_{max} (KBr)/cm^{-1} 3290, 2926, 1690, 1608, 1505, 1487, 1379, 1226; Anal. Calc. for $C_{29}H_{30}N_4O_4$: C 69.86, H 6.06, N 11.24 (*m/z* 498.2261). Found: C 69.91, H 6.04, N 11.27 % (*m/z* (HRMS ESI) 499.2324 ($[M + H]^+$)).

*Ethyl 4-(4-((1-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1l**)*

Pale-yellow solid, mp 175°C, δ_H (400 MHz, $CDCl_3$) 7.92 (s, 1H, trizolyl-H), 7.59 (d, 2H, *J* 8.8, ArH), 7.20 (d, 2H, *J* 8.8, ArH), 6.98 (d, 2H, *J* 9.52, ArH), 6.81 (d, 2H, *J* 8.08, ArH), 6.38 (s, 1H, NH), 5.19 and 5.16 (AB system, *J* 13.16, 2H, $OCH_a.H_b$), 5.01 (s, 1H, CH), 4.05–4.0 (q, 2H, *J* 6.6, OCH_2), 3.83 (s, 3H, OCH_3), 2.39–2.26 (m, 7H), 1.93–1.87 (m, 2H, CH_2), 1.17–1.14 (t, 3H, *J* 6.6, CH_3); δ_C (100 MHz, $CDCl_3$) 195.70, 167.53, 156.40, 148.32, 144.39, 143.54, 140.48, 134.07, 133.50, 130.46, 129.09, 123.57, 122.21, 114.08, 112.06, 105.99, 61.90, 59.74, 50.65, 40.81, 35.67, 32.60, 27.05, 19.24, 14.20; ν_{max} (KBr)/cm^{-1} 3280, 2937, 1689, 1606, 1508, 1481, 1380, 1256; *m/z* (HRMS ESI) Calc. for $C_{29}H_{30}N_4O_5$: 514.2210. Found: 515.2293 ($[M + H]^+$).

*Ethyl 4-(4-((1-(4-Bromophenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)-2-methyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1m**)*

Pale-yellow solid, mp 203°C, δ_H (400 MHz, $CDCl_3$) 7.99 (s, 1H, trizolyl-H), 7.64–7.58 (m, 4H, ArH), 7.20 (d, 2H, *J* 8.8, ArH), 6.81 (d, 2H, *J* 8.8, ArH), 6.15 (s, 1H, NH), 5.20 and 5.17 (AB system, *J* 13.92, 2H, $OCH_a.H_b$), 5.01 (s, 1H, CH), 4.05–4.0 (q, 2H, *J* 6.6, OCH_2), 2.40–2.26 (m, 7H), 1.98–1.89 (m, 2H, CH_2), 1.17–1.14 (t, 3H, *J* 7.36, CH_3); δ_C (100 MHz, $CDCl_3$) 195.92, 167.38, 156.29, 149.72, 145.50, 143.33, 140.56, 135.96, 132.88, 129.11, 122.68, 121.93, 120.72, 114.06, 113.18, 105.99, 61.81, 59.78, 37.01, 35.56, 27.32, 21.01, 19.30, 14.20; ν_{max} (KBr)/cm^{-1} 3282, 2949, 1694, 1603, 1488, 1377, 1224; *m/z* (HRMS ESI) Calc. for $C_{28}H_{27}BrN_4O_4$: 562.1210. Found: 585.0372 ($[M + Na]^+$).

*Ethyl 4-(3-Methoxy-4-((1-*p*-tolyl-1*H*-1,2,3-triazol-4-yl) methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1n**)*

Pale-yellow solid, mp 230°C, δ_H (400 MHz, [D6]DMSO) 7.97 (s, 1H, trizolyl-H), 7.55 (d, 2H, *J* 8.04, ArH), 7.27 (d, 2H, *J* 8.8, ArH), 6.95 (d, 1H, *J* 1.44, ArH), 6.86 (d, 1H, *J* 8.08, ArH) 6.69–6.72 (m, 1H, ArH), 6.03 (s, 1H, NH), 5.27 and 5.24 (AB system, *J* 13.20, 2H, $OCH_a.H_b$), 4.97 (s, 1H, CH), 4.06–4.01 (q, 2H, *J* 7.32, OCH_2), 3.81 (s, 3H,OCH_3), 2.38 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.22–2.14 (m, 4H), 1.19–1.16 (t, 3H, *J* 6.6, CH_3), 1.03 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); δ_C (100 MHz, DMSO) 194.49, 166.99, 149.65, 148.29, 145.60, 144.70, 143.91, 141.37, 138.42, 134.37, 130.27, 122.85, 120.07, 119.17, 113.37, 111.84, 110.02, 103.65, 61.60, 59.03, 55.19, 50.15, 38.37, 35.14, 32.12, 29.23, 26.45, 20.61, 18.31, 14.28; ν_{max} (KBr)/cm^{-1} 3292, 2958, 1686, 1610, 1508, 1379, 1218; Anal. Calc. for $C_{32}H_{36}N_4O_5$: C 69.05, H 6.52, N 10.06 (*m/z* 556.2680). Found: C 69.11, H 6.53, N 10.09 % (*m/z* (HRMS ESI) 557.2768 ($[M + H]^+$)).

*Ethyl 4-(3-Methoxy-4-((1-(4-methoxyphenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1o**)*

Pale-yellow solid, mp 224°C, δ_H (400 MHz, $CDCl_3$) 7.93 (s, 1H, trizolyl-H), 7.57 (d, 2H, *J* 8.8, ArH), 6.98–6.94 (m, 3H, ArH), 6.86 (d, 1H, *J* 8.08, ArH), 6.72–6.69 (m, 1H, ArH), 6.20 (s, 1H, NH), 5.27 and 5.23(AB system, *J* 12.48, 2H, $OCH_a.H_b$), 4.97 (s, 1H, CH), 4.06–4.01 (q, 2H, *J* 7.32, OCH_2), 3.83 (s, 3H, OCH_3), 3.81 (s, 3H,OCH_3), 2.33 (s, 3H, CH_3), 2.21–2.14 (m, 4H), 1.19–1.16 (t, 3H, *J* 7.32, CH_3), 1.02 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 195.65, 167.49, 159.69, 148.67, 148.09, 145.66, 145.05, 143.37, 141.21, 130.38, 122.23, 121.35, 119.64, 114.71, 113.65, 112.39, 112.06, 105.94, 63.06, 59.76, 55.77, 55.58, 50.67, 40.97, 35.95, 32.63, 29.40, 27.07, 19.34, 14.29; ν_{max} (KBr)/cm^{-1} 3294, 2927, 1615, 1491, 1256; *m/z* (HRMS ESI) Calc. for $C_{32}H_{36}N_4O_6$: 572.2629. Found: 573.2615 ($[M + H]^+$).

*Ethyl 4-(4-((1-(4-Bromophenyl)-1*H*-1,2,3-triazol-4-yl) methoxy)-3-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**1p**)*

Pale-yellow solid, mp 176°C, δ_H (400 MHz, $CDCl_3$) 8.01 (s, 1H, trizolyl-H), 7.64–7.57 (m, 4H, ArH), 6.95 (d, 1H, *J* 2.2, ArH), 6.83 (d, 1H, *J* 8.8, ArH), 6.73–6.70 (m, 1H, ArH), 6.11 (s, 1H, NH), 5.27 and 5.24 (AB system, *J* 13.16, 2H, $OCH_a.H_b$), 4.98 (s, 1H, CH), 4.07–4.02 (q, 2H, *J* 7.32, OCH_2), 3.82 (s, 3H, OCH_3), 2.34 (s, 3H, CH_3), 2.23–2.15 (m, 4H), 1.21–1.17 (t, 3H, *J* 7.32, CH_3), 1.04 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 194.55, 167.18, 149.62, 148.39, 145.56, 144.81, 144.25, 141.31, 135.79, 132.85, 123.03, 122.11, 121.40, 119.18, 113.42, 111.85, 110.02, 103.79, 61.56, 59.02, 55.28, 50.28, 35.22, 32.19, 30.75, 29.25, 26.46, 18.33, 14.29; ν_{max} (KBr)/cm^{-1} 3292, 2958, 1688, 1611, 1497, 1380, 1218; Anal. Calc. for $C_{31}H_{33}BrN_4O_5$: C 59.91, H 5.35, N 9.01 (*m/z* 620.1628). Found: C 59.97, H 5.37, N 8.99 % (*m/z* (HRMS ESI) 621.1713 ($[M + H]^+$)).

Supplementary Material

Tables S1–S6, Figures S1–S7, experimental procedures for antibacterial activity, antifungal activity, antioxidant activity, and copies of ^{1}H NMR and ^{13}C NMR spectra are available on the Journal's website.

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