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ORIGINAL PAPER

# Synthesis, antimalarial and antioxidant activity of coumarin appended 1,4-disubstituted 1,2,3-triazoles

**C. P. Kaushik**[1] · **Manisha Chahal**[1]

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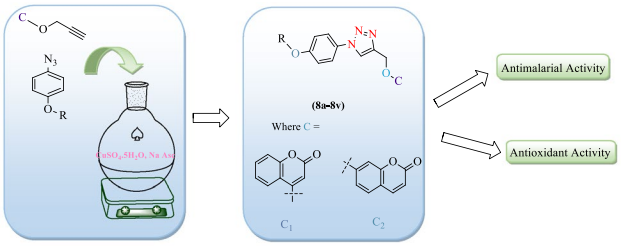
## Abstract

A series of coumarin appended triazole hybrids of biotic interest was synthesized through click chemistry approach from the coumarin based terminal alkynes and aromatic azides. All the synthesized triazoles were characterized by FT-IR, $^{1}$H NMR, $^{13}$C NMR, and HRMS and assessed for antimalarial activities against *plasmodium falciparum* strain. Results revealed that most of the synthesized coumarin–triazole hybrid compounds possess moderate to good activity. Further, the synthesized coumarin triazole hybrids were employed for antioxidant activities and were found to be potent antioxidant when compared with standard drug.

### Graphic abstract




**Keywords** Coumarin · 1,4-Disubstituted 1,2,3-triazoles · Click chemistry · Antimalarial activity · Antioxidant activity

## Introduction

Malaria, a devastating tropical parasitic disease, remains the main cause of high morbidity and mortality among communicable diseases [1]. The protozoa *Plasmodium falciparum* and *Plasmodium vivax* that are transmitted by *Anopheles* mosquitoes is among the most prevalent species infecting humans and result in large number of deaths annually, especially in young children and pregnant women [2]. Historically, plants have proved to be an important source of antimalarial drugs, like quinine and artemisinin. Quinine, the most abundant Cinchona alkaloid, was the only known antimalarial drug for a long time. Since the discovery of quinine, many compounds with a quinoline scaffold have displayed good antimalarial activity, such as chloroquine, amodiaquine, piperaquine, and mefloquine. Despite the progress in reduction of malaria cases, parasite resurgence and developing resistance of plasmodium to clinically used chemotherapeutic agent such as chloroquine, artemisinin, and its derivatives are provocating the researchers to explore new, effective, safe, and inexpensive antimalarial chemotypes to curb malaria effectively.

Among the oxygen heterocycles, coumarins are privileged structural motifs that have attracted much interest in recent years because of their diverse pharmacological properties.

Coumarin derivatives are versatile compounds as they exhibit enormous biological activities such as, acetylcholinesterase inhibitor [3], anticancer [4–11], antimalarial [12], antioxidant [13–15], antimicrobial [16–21], antitubercular

✉ C. P. Kaushik
kaushikcp@gmail.com

[1] Department of Chemistry, Guru Jambheshwar University of Science and Technology, Hisar, Haryana 125001, India

[22, 23], LSD1 inhibitory [24], anti-inflammatory [25–27], antidiabetic [28], etc. reflecting the prime reason for their inclusion in the hybrid framework. In addition, hydroxycoumarins are recognized as prevailing chain-breaking antioxidants which can avert free radical injury by scavenging reactive oxygen species with application in parasitic diseases. The action of reactive oxygen species (ROS) results in alterations and function modulations of key biomolecules. Antioxidants play a vital role in the body defense mechanism by regulating the elimination of reactive oxygen species (ROS) such as hydroxyl radicals, superoxide radicals, singlet oxygen, and hydrogen peroxide radicals generated from excessive oxidative stress and normal metabolic activities.

Triazoles represent a key motif in heterocyclic chemistry and occupy a prime place in medicinal chemistry due to their competence to exhibit a wide spectrum of biological activities [29–73].

In the context of attempting promising biological activity, it may be an attractive strategy to combine both pharmacophoric units, i.e., coumarin and 1,2,3-triazole in a single framework to explore biological activities. Here, we synthesized a series of coumarin appended 1,4-disubstituted 1,2,3-triazole hybrids and explore their antimalarial and antioxidant activities.

## Results and discussion

### Chemistry

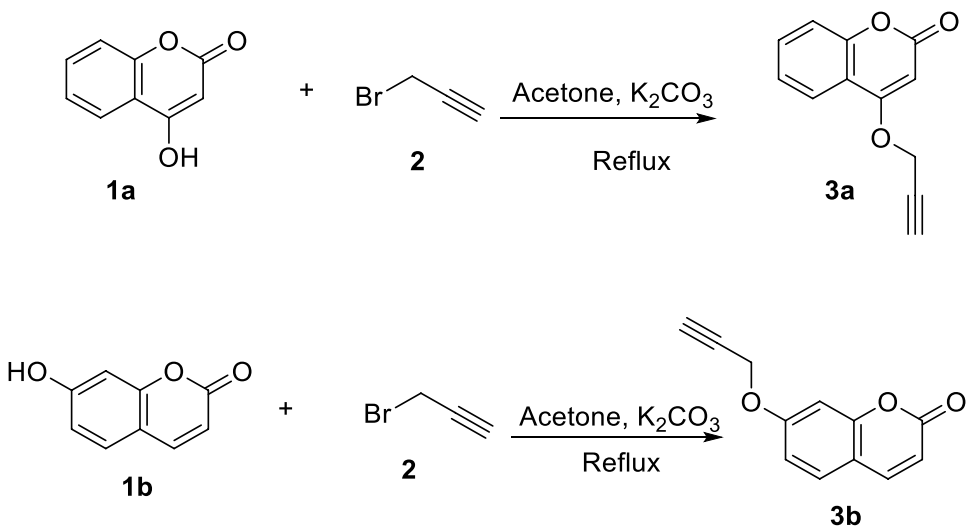
The synthetic strategy for the synthesis of compounds **8a**–**8v** is outlined in Scheme 1. Terminal alkynes, 4-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (**3a**)/7-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (**3b**) were obtained from the propargylation of 7-hydroxy-2*H*-chromen-2-one (**1a**)/4-hydroxy-2*H*-chromen-2-one (**1b**) in acetone using potassium carbonate as a base (Scheme 1).

For the synthesis of 1-azido-4-benzylbenzene derivatives **7a**–**7j**, firstly, 4-aminophenol converted into 4-azidophenol (**5**) using 6N hydrochloric acid, sodium nitrite, and aqueous solution of sodium azide. Then, reaction of 4-azidophenol (**5**) was performed with benzyl bromide derivatives **6a**–**6j** in the presence of potassium carbonate as base**,** to get substituted azides **7a**–**7j** (Scheme 2).

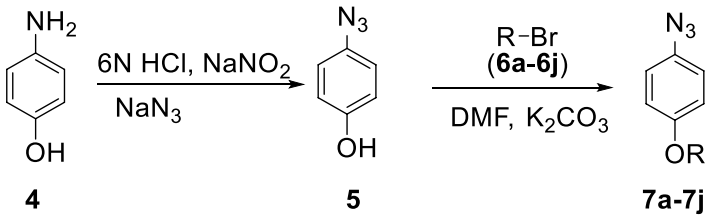
Finally targeted 4-[[1-[4-(benzyloxy)phenyl]-1*H*-1,2,3-triazol-4-yl]methoxy]-2*H*-chromen-2-one/7-[[1-[4-(benzyloxy)phenyl]-1*H*-1,2,3-triazol-4-yl]methoxy]-2*H*-chromen-2-one derivatives **8a**–**8v** were synthesized by click reaction of aromatic azides **5** and **7a**–**7j** and 4-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (**3a**)/7-(prop-2-yn-1-yloxy)-2*H*-chromen-2-one (**3b**) in DMF:$H_2O$ using copper sulphate pentahydrate and sodium ascorbate (Scheme 3).

The propargylation of the 7-hydroxy-2*H*-chromen-2-one (**1a**)/4-hydroxy-2*H*-chromen-2-one (**1b**) was confirmed by the presence of a signal in a range of $\delta = 5.12–5.26$ ppm (s, 2H, $CH_2$) in the $^1$H NMR spectra. The formation of ether linkage was confirmed by the presence of singlet in a range of 5.30–5.51 ppm. The formation of 1,2,3-triazoles was confirmed by the resonance of the triazolyl proton as singlet in a range of 7.97–8.98 ppm for different derivatives. The structural assignment was also supported by the $^{13}$C NMR spectral data, which showed the C-atom signals corresponding to triazole derivatives. The final confirmation was made by the HRMS analysis which showed the presence of $[M]^+$ or $[M+1]^+$ ion peaks.

**Scheme 1**



**Scheme 2**




| Compound | R | Compound | R |
|---|---|---|---|
| **6a**, **7a** | $C_6H_5CH_2$ | **6f**, **7f** | 3-$NO_2C_6H_4CH_2$ |
| **6b**, **7b** | 2-$CH_3C_6H_4CH_2$ | **6g**, **7g** | 4-$NO_2C_6H_4CH_2$ |
| **6c**, **7c** | 3-$CH_3C_6H_4CH_2$ | **6h**, **7h** | 4-$FC_6H_4CH_2$ |
| **6d**, **7d** | 4-$CH_3C_6H_4CH_2$ | **6i**, **7i** | 4-$ClC_6H_4CH_2$ |
| **6e**, **7e** | 2-$NO_2C_6H_4CH_2$ | **6j**, **7j** | 4-$BrC_6H_4CH_2$ |

## In vitro antimalarial activities

Antimalarial potential of synthesized compounds was measured and results are reported in Table 1. Among the synthesized coumarin–triazole hybrids, compounds **8c**, **8p**, **8t**, and **8v** ($IC_{50}$ value of 0.53, 0.38, 0.49 and 0.54 μg/cm$^3$, respectively) expressed better antimalarial potential. Of these, **8p** (having methyl group attached at *para* position of benzyl ring) showed significant antimalarial potential exhibiting $IC_{50}$ values of 0.38 μg/cm$^3$ against *P. falciparum* strains.

Following structure–activity relationship has been drawn from above data:

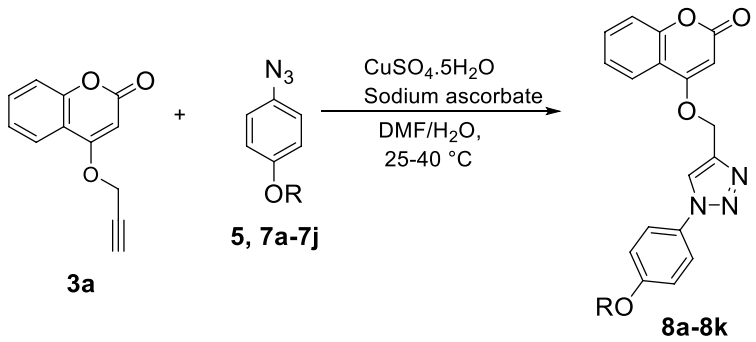
1. Remarkably, the substitution of benzyl hydrogen with methyl group at any position expressed better activity compared to substitution with nitro group at any position.
2. In case of 1,2,3-triazoles containing 7-chromen-2-one ring, substitution with methyl group at *para* position in benzyl ring provided the better antimalarial activity, as compared to *ortho*/*meta* substituted counterparts while triazole derivatives having 4-chromen-2-one ring containing derivatives, methyl substituent at *ortho* position of benzyl ring exhibited better activity than *meta*/*para* substituent.
3. In most of the cases, the nitro substituted analogues exhibited weak antiplasmodial activities than unsubstituted benzyl ring.
4. Interestingly, introduction of fluoro functionality at *para* position of benzyl nucleus (**8i** and **8t**) improved antimalarial activity as compared to chloro and bromo counterparts.
5. In most of the cases, the presence of benzyloxy group showed a clear drift towards rise in antimalarial activity compared to free hydroxyl group in synthesized triazoles.
6. 7-Chromen-2-one containing ring derivatives showed improved antimalarial activity compared to 4-chromen-2-one containing ring derivatives.
7. Incorporation of triazole ring improved antiplasmodial activities compared to its alkyne counterparts.

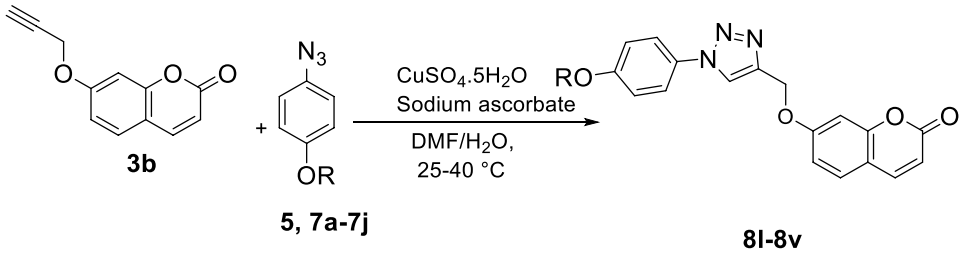
## In vitro antioxidant activity

Free radical scavenging potential of synthesized compounds was measured spectrophotometrically using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay with ascorbic acid as standard by following the procedure reported by Kaushik et al.

Table 2 summarizes the radical scavenging activities of all compounds, compared to the synthetic antioxidant

**Scheme 3**




**5**: R = H
**7a**: R = $C_6H_4CH_2$
**7b**: R = 2-$CH_3C_6H_4CH_2$
**7c**: R = 3-$CH_3C_6H_4CH_2$
**7d**: R = 4-$CH_3C_6H_4CH_2$
**7e**: R = 2-$NO_2C_6H_4CH_2$
**7f**: R = 3-$NO_2C_6H_4CH_2$
**7g**: R = 4-$NO_2C_6H_4CH_2$
**7h**: R = 4-$FC_6H_4CH_2$
**7i**: R = 4-$ClC_6H_4CH_2$
**7j**: R = 4-$BrC_6H_4CH_2$

| Compound | R | Compound | R |
|---|---|---|---|
| **8a** | H | **8l** | H |
| **8b** | $C_6H_5CH_2$ | **8m** | $C_6H_5CH_2$ |
| **8c** | 2-$CH_3C_6H_4CH_2$ | **8n** | 2-$CH_3C_6H_4CH_2$ |
| **8d** | 3-$CH_3C_6H_4CH_2$ | **8o** | 3-$CH_3C_6H_4CH_2$ |
| **8e** | 4-$CH_3C_6H_4CH_2$ | **8p** | 4-$CH_3C_6H_4CH_2$ |
| **8f** | 2-$NO_2C_6H_4CH_2$ | **8q** | 2-$NO_2C_6H_4CH_2$ |
| **8g** | 3-$NO_2C_6H_4CH_2$ | **8r** | 3-$NO_2C_6H_4CH_2$ |
| **8h** | 4-$NO_2C_6H_4CH_2$ | **8s** | 4-$NO_2C_6H_4CH_2$ |
| **8i** | 4-$FC_6H_4CH_2$ | **8t** | 4-$FC_6H_4CH_2$ |
| **8j** | 4-$ClC_6H_4CH_2$ | **8u** | 4-$ClC_6H_4CH_2$ |
| **8k** | 4-$BrC_6H_4CH_2$ | **8v** | 4-$BrC_6H_4CH_2$ |

**Table 1** Antimalarial activity of coumarin appended 1,4-disubstituted 1,2,3-triazoles **8a**–**8v**

| Compound | $IC_{50}$/μg $cm^{-3}$ | Compound | $IC_{50}$/μg $cm^{-3}$ |
|---|---|---|---|
| **8a** | 1.52 | **8l** | 2.20 |
| **8b** | 0.84 | **8m** | 0.73 |
| **8c** | 0.53 | **8n** | 0.93 |
| **8d** | 1.05 | **8o** | 0.78 |
| **8e** | 2.18 | **8p** | 0.38 |
| **8f** | 0.98 | **8q** | 1.20 |
| **8g** | 0.60 | **8r** | 1.32 |
| **8h** | 1.22 | **8s** | 1.20 |
| **8i** | 0.70 | **8t** | 0.49 |
| **8j** | 1.72 | **8u** | 0.86 |
| **8k** | 1.25 | **8v** | 0.54 |
| Quinine | 0.268 | Quinine | 0.268 |

**Table 2** In vitro antioxidant activity of coumarin appended 1,4-disubstituted 1,2,3-triazoles **8a**–**8v**

| Compound | $IC_{50}$/μg $cm^{-3}$ | Compound | $IC_{50}$/μg $cm^{-3}$ |
|---|---|---|---|
| **8a** | 6.68 | **8l** | 5.82 |
| **8b** | 8.75 | **8m** | 3.86 |
| **8c** | 4.63 | **8n** | 7.01 |
| **8d** | 3.33 | **8o** | 4.81 |
| **8e** | 4.42 | **8p** | 5.82 |
| **8f** | 9.74 | **8q** | 7.26 |
| **8g** | 6.27 | **8r** | 5.24 |
| **8h** | 8.65 | **8s** | 6.36 |
| **8i** | 6.25 | **8t** | 5.11 |
| **8j** | 6.39 | **8u** | 5.69 |
| **8k** | 6.41 | **8v** | 6.21 |
| Ascorbic acid | 1.23 | | |

ascorbic acid. Several compounds showed excellent free radical scavenging activity.

1. The presence of electron donating group on benzyl ring of synthesized triazoles increases antioxidant potential compared to electron withdrawing group. Remarkably, the substitution of benzylic hydrogen with methyl group at any position showed better activity compared to substitution with nitro group.
2. 7-Chromen-2-one ring containing triazoles favored antioxidant activity compared to 4-chromen-2-one derivatives.
3. Methyl substituted 1,2,3-triazoles have better radical scavenging activity as compared to nitro substituted triazoles.
4. In case of scaffolds carrying $–CH_3$ groups, those with methyl substituent at *meta* position of benzyl ring are more active than *ortho* and *para* congeners.
5. Triazoles with $–NO_2$ groups at *meta* position of benzyl ring were found to show diligent activity than *ortho* and *para* congeners.
6. The presence of fluoro group on benzyl ring imparted better antioxidant activity than chloro and bromo counterparts.
7. Among the synthesized coumarin–triazole hybrids, compounds **8d** and **8m** showed better antioxidant potential in the series.

## Conclusion

In nut shell, synthesis of coumarin appended 1,4-disubstituted 1,2,3-triazole hybrids using click chemistry has been described. All the synthesized compounds were screened for in vitro antimalarial and antioxidant activities. Some of the coumarin–triazole hybrids exhibited promising antimalarial (**8c**, **8p**, **8t**, and **8v**) and antioxidant (**8d** and **8m**) activities. The compound **8p** showed encouraging antimalarial potential when compared to standard drug quinine at same dosage.

## Experimental

All chemicals were purchased from Alfa Aesar, Hi-Media, and Sigma–Aldrich and used without further purification. Compounds and reaction progress were routinely analyzed on the silica gel plates (SIL G/UV254, ALUGRAM) visualized under UV at wavelength 254 nm. Melting points of compounds were determined in open capillary tubes. High resolution mass spectrometry (HRMS) was carried out on Bruker micro TOF Q-II spectrometer. Nuclear magnetic resonance (NMR) spectra were determined on BRUKER AVANCE II spectrometer operating at 400 MHz ($^1$H) and 100 MHz ($^{13}$C), in DMSO-$d_6$ and $CDCl_3$ as solvent. Chemical shifts ($\delta$) are given in parts per million downfield from tetramethylsilane (TMS). $^1$H NMR spectra are reported in order: multiplicity, coupling constant (*J* value) in hertz (Hz), and number of protons; signals were characterized as s (singlet), d (doublet), t (triplet), m (multiplet), and Ar (aryl). The IR spectra were recorded using SHIMAZDU IR AFFINITY-I FTIR spectrometer using potassium bromide (KBr) powder and values are given in $cm^{-1}$. All the synthesized compounds were screened for antimalarial activity in the Microcare Laboratory & TRC, Surat, Gujarat.

## General procedure for the synthesis of terminal alkynes 3a, 3b

7-Hydroxy-2*H*-chromen-2-one (**1a**)/4-hydroxy-2*H*-chromen-2-one (**1b**) (1.0 mmol) was taken in 20 $cm^3$ acetone in a round-bottomed flask. To this, anhydrous potassium carbonate (1.5 mmol) was added and the resulting suspension was refluxed for 30 min. Propargyl bromide (1.5 mmol) was added slowly to the reaction mixture and the reaction mixture was further refluxed for 7–8 h. Progress of the reaction was monitored by TLC. After the completion of reaction, reaction content was poured into crushed ice, the separated solid was filtered and recrystallized using ethyl acetate to get the desired alkynes **3a**, **3b** [74].

## General procedure for the synthesis of aromatic azides 5, 7a–7j

To the stirred cold solution of aminophenol **4** in dichloromethane, 6N hydrochloric acid (15–20 $cm^3$) was added followed by addition of saturated solution of sodium nitrite. After 30 min, aqueous solution of sodium azide (3.0 mmol) was added dropwise to the reaction mixture at 0–5 ºC and stirred the content for 2–3 h. After completion of reaction, as indicated by TLC, the product was extracted with dichloromethane. The solvent was dried with anhydrous sodium sulphate and evaporated under reduced pressure to get aromatic azide **5**. Further, the synthesis of substituted aromatic azides [75] **7a**–**7j** was carried out by the reaction of aromatic azide **5** with aralkyl bromides **6a**–**6j** in dimethylformamide in the presence of potassium carbonate as a base with continuous stirring of 4–5 h. The progress of reaction was judged by TLC. On completion of reaction, cold water was poured into the reaction mixture when precipitates of final compounds **7a**–**7j** appeared, which were filtered, washed with cold water, and dried.

## General procedure for coumarin appended 1,4-disubstituted 1,2,3-triazoles 8a–8v

To a solution of aromatic azides **5**, **7a–7j** and coumarin based alkynes **3a**, **3b** in *N*,*N*-dimethylformamide, catalytic amount of copper sulphate pentahydrate ($CuSO_4 \cdot 5H_2O$), dissolved in water and sodium ascorbate were added. The resulting mixture was stirred for 6–12 h at ambient temperature until the starting material was consumed as reflected from TLC. After the completion of reaction, reaction mixture was quenched with ice-cold water and ammonia solution, when precipitates of the final triazole appeared. The precipitates were filtered and recrystallized from ethyl acetate to yield the pure 1,4-disubstituted 1,2,3-triazoles **8a**–**8v**.

**4-[[1-(4-Hydroxyphenyl)-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8a, $C_{18}H_{13}N_3O_4$)** Brown solid; yield: 79%; m.p.: 158–160 °C; FT-IR (KBr): $\overline{V}$ = 3398 (O–H str.), 3182 (C–H str. triazole), 3078 (C–H str. aromatic ring), 2928 (C–H str., aliphatic), 1719 (C=O str. lactone), 1617, 1512 (C=C str., aromatic ring), 1328 (C–N), 1132 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.97 (s, 1H, C–H triazole), 7.95 (s, 1H), 7.63 (s, 1H), 7.61 (s, 1H), 7.015 (d, $J$ = 4.0 Hz, 2H), 6.965 (d, $J$ = 4.0 Hz, 1H), 6.945 (d, $J$ = 4.0 Hz, 1H), 6.29 (s, 1H), 6.27 (s, 1H), 4.90 (3H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 160.71, 155.64, 144.78, 130.06, 113.49, 113.42, 102.28, 79.46, 79.04, 56.60 ppm; HRMS: *m/z* calculated for $C_{18}H_{13}N_3O_4$ ($[M+H]^+$) 336.0906, found 336.0904.

**4-[[1-[4-(Benzyloxy)phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8b, $C_{25}H_{19}N_3O_4$)** Brown solid; yield: 79%; m.p.: 168–170 °C; FT-IR (KBr): $\overline{V}$ = 3447 (O–H str.), 3179 (C–H str. triazole), 3086 (C–H str. aromatic ring), 2937 (C–H str., aliphatic), 1718 (C=O str. lactone), 1618, 1510 (C=C str., aromatic ring), 1335 (C–N), 1142 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.09 (s, 1H, C–H triazole), 7.84 (d, $J$ = 8.0 Hz, 1H), 7.68 (d, $J$ = 8.0 Hz, 2H), 7.59–7.54 (m, 1H), 7.47–7.36 (m, 6H), 7.26 (d, $J$ = 8.0 Hz, 1H), 7.14 (d, $J$ = 8.0 Hz, 2H), 5.93 (s, 1H), 5.44 (s, 2H), 5.16 (s, 2H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 165.00, 162.62, 159.29, 153.39, 136.20, 132.61, 130.33, 128.74, 128.30, 127.49, 123.96, 123.18, 122.40, 121.81, 116.82, 115.89, 115.69, 115.47, 91.26, 70.44, 62.66 ppm; HRMS: *m/z* calculated for $C_{25}H_{19}N_3O_4$ ($[M+H]^+$) 426.1409, found 426.1413.

**4-[[1-[4-[(2-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8c, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 212–214 °C; FT-IR (KBr): $\overline{V}$ = 3412 (O–H str.), 3167 (C–H str. triazole), 3071 (C–H str. aromatic ring), 2923 (C–H str., aliphatic), 1719 (C=O str. lactone), 1623, 1517 (C=C str., aromatic ring), 1348 (C–N), 1121 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.09 (s, 1H, C–H triazole), 7.85 (d, $J$ = 8.0 Hz, 1H), 7.69 (d, $J$ = 8.0 Hz, 2H), 7.58 (t, $J$ = 8.0 Hz, 1H), 7.435 (d, $J$ = 4.0 Hz, 1H), 7.35 (d, $J$ = 8.0 Hz, 1H), 7.31–7.26 (m, 5H), 7.16 (d, $J$ = 8.0 Hz, 1H), 6.99 (s, 1H), 5.94 (s, 1H), 5.45 (s, 2H), 5.14 (s, 2H), 2.42 (s, 3H, –$CH_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 164.98, 162.55, 159.39, 153.42, 138.14, 133.17, 132.58, 130.27, 129.40, 129.30, 127.61, 123.93, 123.17, 122.37, 121.79, 119.99, 116.81, 116.23, 115.91, 115.49, 91.28, 70.42, 62.68, 21.20 ppm; HRMS: *m/z* calculated for $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1566, found 440.1601.

**4-[[1-[4-[(3-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8d, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 172–174 °C; FT-IR (KBr): $\overline{V}$ = 3435 (O–H

str.), 3151 (C–H str. triazole), 3079 (C–H str. aromatic ring), 2925 (C–H str., aliphatic), 1718 (C=O str. lactone), 1618, 1517 (C=C str., aromatic ring), 1345 (C–N), 1138 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 8.09$ (s, 1H, C–H triazole), 7.85 (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.58 (t, $J = 8.0$ Hz, 1H), 7.435 (d, $J = 4.0$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 1H), 7.31–7.26 (m, 5H), 7.16 (d, $J = 8.0$ Hz, 1H), 6.99 (s, 1H), 5.94 (s, 1H), 5.45 (s, 2H), 5.14 (s, 2H), 2.42 (s, 3H, $-CH_3$) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 164.94$, 162.13, 153.42, 138.46, 136.11, 132.57, 129.03, 128.61, 128.18, 124.55, 123.93, 123.16, 122.46, 115.96, 91.34, 70.55, 63.35, 21.39 ppm; HRMS: *m/z* calculated $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1566, found 440.1575.

**4-[[1-[4-[(4-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8e, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 188–190 °C; FT-IR (KBr): $\overline{V} = 3396$ (O–H str.), 3131 (C–H str. triazole), 3074 (C–H str. aromatic ring), 2921 (C–H str., aliphatic), 1728 (C=O str. lactone), 1624, 1519 (C=C str., aromatic ring), 1327 (C–N), 1138 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (s, 1H, C–H triazole), 7.84 (d, $J = 8.0$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.59–7.55 (m, 1H), 7.36 (d, $J = 8.0$ Hz, 3H), 7.24 (d, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 8.0$ Hz, 2H), 6.97 (s, 1H), 5.93 (s, 1H), 5.44 (s, 2H), 5.12 (s, 2H), 2.40 (s, 3H, $-CH_3$) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 164.98$, 162.55, 159.39, 153.42, 138.14, 133.17, 132.58, 130.27, 129.40, 129.30, 127.61, 123.93, 123.17, 122.37, 121.79, 119.99, 116.81, 116.23, 115.91, 115.49, 91.28, 70.42, 62.68, 21.20 ppm; HRMS: *m/z* calculated $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1566, found 440.1582.

**4-[[1-[4-[(2-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8f, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 176–178 °C; FT-IR (KBr): $\overline{V} = 3427$ (O–H str.), 3239 (C–H str. triazole), 3077 (C–H str. aromatic ring), 2918 (C–H str., aliphatic), 1718 (C=O str. lactone), 1610, 1517 (C=C str., aromatic ring), 1341 (C–N), 1128 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J = 8.0$ Hz, 2H), 8.10 (s, 1H, C–H triazole), 7.85–7.83 (m, 1H), 7.73–7.70 (m, 2H), 7.66 (d, $J = 8.0$ Hz, 2H), 7.60–7.56 (m, 2H), 7.37–7.34 (m, 2H), 7.16–7.13 (m, 2H), 5.93 (s, 1H), 5.45 (s, 2H), 5.27 (s, 2H) ppm; $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta = 164.18$, 161.88, 153.26, 134.59, 133.47, 129.81, 125.45, 124.91, 123.27, 122.61, 117.06, 116.35, 115.40, 92.18, 80.71, 77.68, 57.89 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1243.

**4-[[1-[4-[(3-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8g, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 186–188 °C; FT-IR (KBr): $\overline{V} = 3421$ (O–H str.), 3145 (C–H str. triazole), 3088 (C–H str. aromatic ring), 2922 (C–H str., aliphatic), 1720 (C=O str. lactone), 1622, 1518 (C=C str., aromatic ring), 1350 (C–N), 1139 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J = 8.0$ Hz, 2H), 8.10 (s, 1H, C–H triazole), 7.85–7.83 (m, 1H), 7.715 (d, $J = 12.0$ Hz, 2H), 7.66 (d, $J = 8.0$ Hz, 2H), 7.60–7.56 (m, 2H), 7.37–7.34 (m, 2H), 7.16–7.13 (m, 2H), 5.93 (s, 1H), 5.45 (s, 2H), 5.27 (s, 2H) ppm; $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta = 164.18$, 161.88, 153.26, 134.59, 133.47, 129.81, 125.45, 124.91, 123.27, 122.61, 117.06, 116.35, 115.40, 92.18, 80.71, 77.68, 57.89 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1225.

**4-[[1-[4-[(4-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8h, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 174–176 °C; FT-IR (KBr): $\overline{V} = 3422$ (O–H str.), 3238 (C–H str. triazole), 3076 (C–H str. aromatic ring), 2918 (C–H str., aliphatic), 1718 (C=O str. lactone), 1623, 1518 (C=C str., aromatic ring), 1346 (C–N), 1141 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J = 8.0$ Hz, 2H), 8.10 (s, 1H, C–H triazole), 7.85–7.83 (m, 1H), 7.73–7.70 (m, 2H), 7.66 (d, $J = 8.0$ Hz, 2H), 7.60–7.56 (m, 2H), 7.355 (d, $J = 12.0$ Hz, 2H), 7.145 (d, $J = 12.0$ Hz, 2H), 5.93 (s, 1H), 5.45 (s, 2H), 5.27 (s, 2H) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta = 164.95$, 162.59, 158.58, 154.24, 153.39, 142.07, 132.63, 127.66, 123.97, 123.13, 122.53, 116.84, 115.85, 115.44, 91.29, 69.05, 62.61 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1211.

**4-[[1-[4-[(4-Fluorobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8i, $C_{25}H_{18}FN_3O_4$)** Brown solid; yield: 79%; m.p.: 210–212 °C; FT-IR (KBr): $\overline{V} = 3409$ (O–H str.), 3155 (C–H str. triazole), 3077 (C–H str. aromatic ring), 2918 (C–H str., aliphatic), 1720 (C=O str. lactone), 1623, 1510 (C=C str., aromatic ring), 1330 (C–N), 1144 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta = 8.95$ (s, 1H, C–H triazole), 7.83–7.78 (m, 3H), 7.65–7.62 (m, 1H), 7.53–7.48 (m, 2H), 7.39 (d, $J = 8.0$ Hz, 1H), 7.33–7.29 (m, 1H), 7.21 (t, $J = 8.0$ Hz, 4H), 6.17 (s, 1H), 5.47 (s, 2H), 5.15 (s, 2H) ppm; $^{13}C$ NMR (100 MHz, DMSO-$d_6$): $\delta = 164.82$, 162.305 (d, $J = 243$ Hz, 1C), 162.00, 158.84, 153.25, 142.49, 133.345 (d, $J = 5$ Hz, 1C), 130.555 (d, $J = 9$ Hz, 1C), 124.68, 123.82, 123.50, 122.42, 116.93, 116.28, 115.785 (d, $J = 21$ Hz, 1C), 115.68, 115.53, 91.92, 69.37, 63.33 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}FN_3O_4$ ($[M+H]^+$) 444.1315, found 444.1346.

**4-[[1-[4-[(4-Chlorobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8j, $C_{25}H_{18}ClN_3O_4$)** Brown solid; yield: 79%; m.p.: 188–190 °C; FT-IR (KBr): $\overline{V} = 3380$ (O–H str.), 3145 (C–H str. triazole), 3073 (C–H str. aromatic ring), 2928 (C–H str., aliphatic), 1720 (C=O str. lactone), 1610, 1517 (C=C str., aromatic ring), 1329 (C–N), 1124 (C–O) $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta = 8.98$ (s,

1H, C–H triazole), 7.84 (t, $J = 8.0$ Hz, 3H), 7.72–7.63 (m, 2H), 7.50 (dd, $J = 16.0$, 8.0 Hz, 5H), 7.35 (t, $J = 8.0$ Hz, 1H), 7.24 (d, $J = 8.0$ Hz, 1H), 6.21 (s, 1H), 5.51 (s, 2H), 5.21 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 164.83$, 161.99, 158.76, 153.25, 142.50, 136.20, 133.31, 133.02, 130.62, 130.04, 128.96, 124.68, 123.82, 123.50, 122.45, 116.91, 116.32, 115.54, 91.91, 69.25, 63.32 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}ClN_3O_4$ ($[M+H]^+$) 460.0986, ($[M+3]^+$) 462.0956, found ($[M+H]^+$) 460.0982, ($[M+3]^+$) 462.0960.

**4-[[1-[4-[(4-Bromobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8k, $C_{25}H_{18}BrN_3O_4$)** Brown solid; yield: 79%; m.p.: 216–218 °C; FT-IR (KBr): $\overline{V} = 3394$ (O–H str.), 3147 (C–H str. triazole), 3071 (C–H str. aromatic ring), 2918 (C–H str., aliphatic), 1719 (C=O str. lactone), 1621, 1517 (C=C str., aromatic ring), 1348 (C–N), 1142 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.95$ (s, 1H, C–H triazole), 7.84–7.77 (m, 3H), 7.65–7.60 (m, 1H), 7.57 (d, $J = 8.0$ Hz, 2H), 7.42–7.36 (m, 3H), 7.33–7.28 (m, 1H), 7.19 (d, $J = 8.0$ Hz, 2H), 6.17 (s, 1H), 5.47 (s, 2H), 5.15 (m, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 164.88$, 162.09, 158.77, 153.30, 142.56, 136.67, 133.39, 131.96, 130.66, 130.43, 124.76, 123.89, 123.57, 122.49, 121.63, 117.00, 116.35, 115.57, 91.98, 69.28, 63.39 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}BrN_3O_4$ ($[M+H]^+$) 504.0481, ($[M+3]^+$) 506.0460, found ($[M+H]^+$) 504.0546, ($[M+3]^+$) 506.0486.

**7-[[1-(4-Hydroxyphenyl)-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8l, $C_{18}H_{13}N_3O_4$)** Brown solid; yield: 79%; m.p.: 174–176 °C; FT-IR (KBr): $\overline{V} = 3398$ (O–H str.), 3274 (C–H str. triazole), 3081 (C–H str. aromatic ring), 2917 (C–H str., aliphatic), 1718 (C=O str. lactone), 1611, 1505 (C=C str., aromatic ring), 1343 (C–N), 1130 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.97$ (s, 1H, C–H triazole), 7.95 (s, 1H), 7.63 (s, 1H), 7.61 (s, 1H), 7.015 (d, $J = 4.0$ Hz, 2H), 6.965 (d, $J = 4.0$ Hz, 1H), 6.945 (d, $J = 4.0$ Hz, 1H), 6.29 (s, 1H), 6.27 (s, 1H), 4.90 (3H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 160.71$, 155.64, 144.78, 130.06, 113.49, 113.42, 102.28, 79.46, 79.04, 56.60 ppm; HRMS: *m/z* calculated for $C_{18}H_{13}N_3O_4$ ($[M+H]^+$) 336.0906, found 336.0901.

**7-[[1-[4-(Benzyloxy)phenyl)-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8m, $C_{25}H_{19}N_3O_4$)** Brown solid; yield: 79%; m.p.: 206–208 °C; FT-IR (KBr): $\overline{V} = 3392$ (O–H str.), 3145 (C–H str. triazole), 3089 (C–H str. aromatic ring), 2918 (C–H str., aliphatic), 1716 (C=O str. lactone), 1618, 1516 (C=C str., aromatic ring), 1346 (C–N), 1128 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.85$ (s, 1H, C–H triazole), 7.97 (d, $J = 8.0$ Hz, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.62 (d, $J = 8.0$ Hz, 1H), 7.44 (d, $J = 6.4$ Hz, 2H), 7.37 (t, $J = 8.0$ Hz, 2H), 7.315 (d, $J = 4.0$ Hz, 1H), 7.20–7.15 (m, 3H), 7.015 (d, $J = 4.0$ Hz, 1H), 6.275 (d, $J = 4.0$ Hz, 1H), 5.30 (s, 2H), 5.15 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 161.58$, 160.83, 158.94, 155.83, 144.85, 143.42, 137.17, 130.57, 130.11, 129.03, 128.52, 128.33, 123.72, 122.42, 116.31, 113.45, 113.28, 102.11, 70.10, 62.13 ppm; HRMS: *m/z* calculated for $C_{25}H_{19}N_3O_4$ ($[M+H]^+$) 426.1409, found 426.1443.

**7-[[1-[4-[(2-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8n, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 170–172 °C; FT-IR (KBr): $\overline{V} = 3387$ (O–H str.), 3143 (C–H str. triazole), 3073 (C–H str. aromatic ring), 2928 (C–H str., aliphatic), 1717 (C=O str. lactone), 1619, 1518 (C=C str., aromatic ring), 1329 (C–N), 1140 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.10$ (s, 1H, C–H triazole), 7.84 (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.59–7.54 (m, 1H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.34 (d, $J = 8.0$ Hz, 1H), 7.31–7.23 (m, 4H), 7.15 (d, $J = 8.0$ Hz, 2H), 5.93 (s, 1H), 5.44 (s, 2H), 5.13 (s, 2H), 2.42 (s, 3H, –$CH_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 160.97$, 159.26, 155.80, 143.21, 138.10, 133.22, 129.39, 128.96, 127.60, 116.07, 113.62, 113.14, 112.75, 102.33, 70.42, 21.18 ppm; HRMS: *m/z* calculated for $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1532, found 440.1595.

**7-[[1-[4-[(3-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8o, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 180–182 °C; FT-IR (KBr): $\overline{V} = 3436$ (O–H str.), 3145 (C–H str. triazole), 3085 (C–H str. aromatic ring), 2914 (C–H str., aliphatic), 1727 (C=O str. lactone), 1610, 1515 (C=C str., aromatic ring), 1348 (C–N), 1128 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.02$ (s, 1H, C–H triazole), 7.67–7.644 (m, 3H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.34–7.24 (m, 3H), 7.185 (d, $J = 4.0$ Hz, 1H), 7.12 (d, $J = 8.0$ Hz, 2H), 7.02–6.96 (m, 2H), 6.29 (d, $J = 8.0$ Hz, 1H), 5.36 (s, 2H), 5.11 (s, 2H), 2.40 (s, 3H, -$CH_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 161.29$, 160.95, 159.29, 155.79, 143.22, 138.46, 136.17, 129.02, 128.97, 128.61, 128.20, 124.56, 122.46, 115.96, 113.61, 113.13, 112.74, 102.31, 70.54, 21.39 ppm; HRMS: *m/z* calculated for $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1532, found 440.1601.

**7-[[1-[4-[(4-Methylbenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8p, $C_{26}H_{21}N_3O_4$)** Brown solid; yield: 79%; m.p.: 208–210 °C; FT-IR (KBr): $\overline{V} = 3396$ (O–H str.), 3153 (C–H str. triazole), 3082 (C–H str. aromatic ring), 2926 (C–H str., aliphatic), 1722 (C=O str. lactone), 1618, 1510 (C=C str., aromatic ring), 1346 (C–N), 1124 (C–O) cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.02$ (s, 1H, C–H triazole), 7.68–7.63 (m, 3H), 7.44–7.41 (m, 1H), 7.35 (d, $J = 8.0$ Hz, 2H), 7.23 (d, $J = 7.8$ Hz, 2H), 7.11 (d, $J = 8.0$ Hz, 2H), 7.01–6.97 (m, 2H), 6.295 (d, $J = 8.0$ Hz,

1H), 5.36 (s, 2H), 5.11 (s, 2H), 2.39 (s, 3H, $-CH_3$) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 160.97$, 159.26, 155.80, 143.21, 138.10, 133.22, 129.39, 128.96, 127.60, 116.07, 113.62, 113.14, 112.75, 102.33, 70.42, 21.18 ppm; HRMS: *m/z* calculated for $C_{26}H_{21}N_3O_4$ ($[M+H]^+$) 440.1532, found 440.1599.

**7-[[1-[4-[(2-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8q, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 206–208 °C; FT-IR (KBr): $\overline{V} = 3396$ (O–H str.), 3159 (C–H str. triazole), 3095 (C–H str. aromatic ring), 2928 (C–H str., aliphatic), 1722 (C=O str. lactone), 1622, 1517 (C=C str., aromatic ring), 1352 (C–N), 1145 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.37$ (s, 1H, C–H triazole), 8.24 (d, $J = 8.0$ Hz, 1H), 8.04 (s, 1H), 7.81 (d, $J = 8.0$ Hz, 1H), 7.72–7.64 (m, 4H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.14 (d, $J = 8.0$ Hz, 2H), 7.01–6.98 (m, 2H), 6.30 (d, $J = 8.0$ Hz, 1H), 5.37 (s, 2H), 5.25 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 164.18$, 161.88, 153.26, 134.59, 133.47, 129.81, 125.45, 124.91, 123.27, 122.61, 117.06, 116.35, 115.40, 92.18, 80.71, 77.68, 57.89 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1293.

**7-[[1-[4-[(3-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8r, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 210–212 °C; FT-IR (KBr): $\overline{V} = 3396$ (O–H str.), 3149 (C–H str. triazole), 3064 (C–H str. aromatic ring), 2932 (C–H str., aliphatic), 1720 (C=O str. lactone), 1624, 1512 (C=C str., aromatic ring), 1350 (C–N), 1143 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J = 8.0$ Hz, 2H), 8.04 (s, 1H, C–H triazole), 7.71–7.63 (m, 4H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 2H), 6.31 (s, 1H), 5.37 (s, 2H), 5.26 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 164.18$, 161.88, 153.26, 134.59, 133.47, 129.81, 125.45, 124.91, 123.27, 122.61, 117.06, 116.35, 115.40, 92.18, 80.71, 77.68, 57.89 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1215.

**7-[[1-[4-[(4-Nitrobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8s, $C_{25}H_{18}N_4O_6$)** Brown solid; yield: 79%; m.p.: 210–212 °C; FT-IR (KBr): $\overline{V} = 3398$ (O–H str.), 3151 (C–H str. triazole), 3086 (C–H str. aromatic ring), 2945 (C–H str., aliphatic), 1716 (C=O str. lactone), 1614, 1516 (C=C str., aromatic ring), 1348 (C–N), 1124 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.30$ (d, $J = 8.0$ Hz, 2H), 8.04 (s, 1H, C–H triazole), 7.71–7.63 (m, 4H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 2H), 6.31 (s, 1H), 5.37 (s, 2H), 5.26 (s, 2H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 164.95$, 162.59, 158.58, 154.24, 153.39, 142.07, 132.63, 127.66, 123.97, 123.13, 122.53, 116.84, 115.85, 115.44, 91.29, 69.05, 62.61 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}N_4O_6$ ($[M+H]^+$) 471.1226, found 471.1301.

**7-[[1-[4-[(4-Fluorobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8t, $C_{25}H_{18}FN_3O_4$)** Brown solid; yield: 79%; m.p.: 244–246 °C; FT-IR (KBr): $\overline{V} = 3389$ (O–H str.), 3143 (C–H str. triazole), 3087 (C–H str. aromatic ring), 2937 (C–H str., aliphatic), 1718 (C=O str. lactone), 1610, 1514 (C=C str., aromatic ring), 1344 (C–N), 1116 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.86$ (s, 1H, C–H triazole), 7.97 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 2H), 7.63 (d, $J = 8.0$ Hz, 1H), 7.52–7.47 (m, 2H), 7.23–7.17 (m, 5H), 7.04–7.01 (m, 1H), 6.28 (d, $J = 8.0$ Hz, 1H), 5.31 (s, 2H), 5.14 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 164.82$, 162.305 (d, $J = 243$ Hz, 1C), 162.00, 158.84, 153.25, 142.49, 133.345 (d, $J = 5$ Hz, 1C), 130.555 (d, $J = 9$ Hz, 1C), 124.68, 123.82, 123.50, 122.42, 116.93, 116.28, 115.785 (d, $J = 21$ Hz, 1C), 115.68, 115.53, 91.92, 69.37, 63.33 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}FN_3O_4$ ($[M+H]^+$) 444.1218, found 444.1350.

**7-[[1-[4-[(4-Chlorobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8u, $C_{25}H_{18}ClN_3O_4$)** Brown solid; yield: 79%; m.p.: 206–208 °C; FT-IR (KBr): $\overline{V} = 3396$ (O–H str.), 3142 (C–H str. triazole), 3076 (C–H str. aromatic ring), 2927 (C–H str., aliphatic), 1719 (C=O str. lactone), 1610, 1513 (C=C str., aromatic ring), 1341 (C–N), 1122 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta = 8.08$ (s, 1H, C–H triazole), 7.84 (d, $J = 8.0$ Hz, 1H), 7.685 (d, $J = 12.0$ Hz, 2H), 7.58 (t, 1H), 7.44–7.34 (m, 6H), 7.12 (d, $J = 8.0$ Hz, 2H), 5.93 (s, 1H), 5.44 (s, 2H), 5.13 (s, 2H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta = 160.90$, 143.50, 134.71, 132.58, 128.93, 128.77, 123.92, 123.15, 122.43, 121.69, 116.82, 115.91, 115.49, 91.31, 69.69, 62.66 ppm; HRMS: *m/z* calculated for $C_{25}H_{18}ClN_3O_4$ ($[M+H]^+$) 460.0986, ($[M+3]^+$) 462.0956, found ($[M+H]^+$) 460.0975, ($[M+3]^+$) 462.0947.

**7-[[1-[4-[(4-Bromobenzyl)oxy]phenyl]-1*H*-1,2,3-triazol-4-yl]-methoxy]-2*H*-chromen-2-one (8v, $C_{25}H_{18}BrN_3O_4$)** Brown solid; yield: 79%; m.p.: 210–212 °C; FT-IR (KBr): $\overline{V} = 3395$ (O–H str.), 3136 (C–H str. triazole), 3088 (C–H str. aromatic ring), 2938 (C–H str., aliphatic), 1712 (C=O str. lactone), 1606, 1514 (C=C str., aromatic ring), 1344 (C–N), 1120 (C–O) $cm^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.86$ (s, 1H, C–H triazole), 7.97 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 8.0$ Hz, 2H), 7.625 (d, $J = 4.0$ Hz, 1H), 7.575 (d, $J = 4.0$ Hz, 2H), 7.405 (d, $J = 4.0$ Hz, 2H), 7.20–7.16 (m, 3H), 7.03–7.01 (m, 1H), 6.28 (d, $J = 8.0$ Hz, 1H), 5.31 (s, 2H), 5.15 (s, 2H) ppm; $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 161.58$, 160.80, 155.84, 144.84, 143.42, 136.68, 131.96, 130.43, 130.10, 123.73, 122.44, 121.63, 116.35, 113.45, 113.29, 102.13, 69.27, 62.15 ppm; HRMS: *m/z* calculated for

$C_{25}H_{18}BrN_3O_4$ ($[M+H]^+$) 504.0481, ($[M+3]^+$) 506.0460, found ($[M+H]^+$) 504.0550, ($[M+3]^+$) 506.0530.

### General procedure for in vitro antimalarial activities

The in vitro antimalarial assay was carried out in 96-well microtitre plates according to the micro assay protocol of Rieckmann and co-workers [76–81] with minor modifications. The cultures of *P. falciparum* strain were maintained in medium RPMI-1640 supplemented with 25 mM HEPES, 1% D-glucose, 0.23% sodium bicarbonate, and 10% heat inactivated human serum. The asynchronous parasites of *P. falciparum* were synchronized after 5% D-sorbitol treatment to obtain only the ring stage parasitized cells. For carrying out the assay, the initial ring stage parasitaemia of 0.8 to1.5% at 3% haematocrit in a total volume of 200 $mm^3$ of medium RPMI-1640 was determined by Jaswant Singh Bhattacharya (JSB) staining to assess the percent parasitaemia (rings) and uniformally maintained with 50% RBC ($O^+$). A stock solution of 5 mg/$cm^3$ of each of the test samples was prepared in DMSO and subsequent dilutions were prepared with culture medium. The diluted samples in 20 $mm^3$ volume were added to the test wells so as to obtain final concentrations (at fivefold dilutions) ranging from 0.4 to 100 µg/$cm^3$ in duplicate well containing parasitized cell preparation. The culture plates were incubated at 37 ºC in a candle jar. After 36–40 h incubations, thin blood smears from each well were prepared and stained with JSB stain. The slides were microscopically observed to record maturation of ring stage parasites into trophozoites and schizonts in the presence of different concentrations of test agents. The test concentration which inhibited the complete maturation into schizonts was recorded as the minimum inhibitory concentrations (MIC). Quinine was used as the reference drug.

### Observations of the in vitro antimalarial screening

The mean number of rings, trophozoites, and schizonts recorded per 100 parasites from duplicate wells after incubation for 38 h and percent maturation inhibition with respect to control group.

### General procedure for antioxidant activity

In the present study, in vitro antioxidant activity [82] or radical scavenging ability of synthesized coumarin–triazole hybrid has been assessed by rapid and convenient technique using 1,1-diphenyl-2-picryl-hydrazyl (DPPH) assay and the hydrogen atom or electron donation ability of the compounds was measured from the bleaching of the purple-colored methanol solution of 1,1-diphenyl-1-picrylhydrazyl (DPPH). The spectrophotometric assay uses the stable radical DPPH as a reagent. Ascorbic acid was used as standard drug in methanol and the results of these findings are presented in Table 2. Methanol, DPPH solution (0.004 g DPPH in 100 $cm^3$ methanol) and standard drugs (20–100 µg/$cm^3$) were used as blank, control and reference, respectively. Stock solution of the organic compounds was diluted to different concentrations in the range of 20–100 µg/$cm^3$ in methanol. 2 $cm^3$ of various concentrations of the test compounds (20–100 µg/$cm^3$) in methanol was added to 1 $cm^3$ of 0.004% (w/v) (0.004 g DPPH in 100 $cm^3$ methanol) freshly prepared DPPH solution. After a 30 min incubation period at room temperature, the absorbance was measured against blank at 517 nm (at an absorption maximum of DPPH) with UV–Visible spectrophotometer and the percentage of scavenging activity was calculated. The percentage inhibition ($I\%$) of the tested compounds was calculated according to the following equation:

$$I\% = \left(A_0 - A_1\right)/A_0 \times 100,$$

where $A_0$ is the absorbance of the control reaction and $A_1$ is the absorbance of the test sample. All tests and analyses were performed in triplicate and the average absorbance was noted for each concentration. $IC_{50}$ values were calculated from the plot of percentage inhibition against concentration (µg/$cm^3$).

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