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# Synthesis and biological evaluation of [1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a] indoles: one-pot reaction under microwave irradiation

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**Abstract:** The synthesis and structural determination of several new fused [1,2,3]triazolo-[4',5':3,4]pyrrolo-[1,2-*a*]indole derivatives (**4a-4p**) utilising $^{1}$HNMR, $^{13}$CNMR, and mass spectrum analysis were discussed. The *in vitro* antibacterial activity of the compounds (**4a-4p**) against three gramme positive bacterial strains such as *B.subtilis*, *S.aureus*, and *S.epidermidis* revealed that the compounds **4h**, **4j**, and **4k** demonstrated greater activity than the remaining compounds. Compounds **4d**, **4i**, and **4l** had comparable activity to the standard. The antioxidant activity screening findings show that compounds **4c**, **4d**, and **4j** have higher activity than conventional Trolox. Compounds **4b**, **4h**, **4k**, and **4l** have high activity, whereas the remaining compounds have moderate to low activity.

**Keywords:** Indole; fused 1,2,3-triazole; MWI; antibacterial activity; antioxidant activity. 

## 1. Introduction

The fact that pathogenic bacteria are growing more resistant to antibiotics is a major source of concern for public health organisations around the world. Bacteria are single-celled bacteria that are normally harmless to humans and, in some cases, beneficial.[1] Some bacteria, on the other hand, are hazardous and can cause significant diseases.[2] As a result, it is critical for public health to develop treatments for microbial infections caused by microbiologically resistant organisms.[3] As a result, there is a critical need for new, stronger antimicrobial medicines with broad inhibitory action, efficacy, and low toxicity. So, a solid method for developing novel antibacterial agents with new modes of action and structural alterations is required to make them more effective and selective for their targets.

Indole derivatives are a promising heterocyclic group with active sites that have the potential to treat a wide range of ailments.[4,5] Many publications have been written regarding indole fragments and their products, which have the potential to fight cancer[6-8] and it will kill bacteria.[9] Over the last few years, fused 1,2,3-triazoles and their hybrids have been the most preferred "lead compounds" in drug discovery. This is due to the fact that they are simple to manufacture and have intriguing pharmacological properties.[10-13] Many antibacterial medicines based on fused 1,2,3-traizole derivatives have also been developed.[14]

As a follow-up to our research on new heterocyclic compounds,[15-19] and in light of what has been stated above, we have decided to continue looking into indole-based 1,2,3-triazoles derivatives,[20]

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with the goal of discovering new compounds with antibacterial and antioxidant properties that could be used to develop new drugs. As illustrated in Figure 1, we created combined [1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole scaffolds by merging the functionalities of the indole group and the 1,2,3-triazole. Every chemical developed was tested to see if it might kill bacteria or fight free radicals.

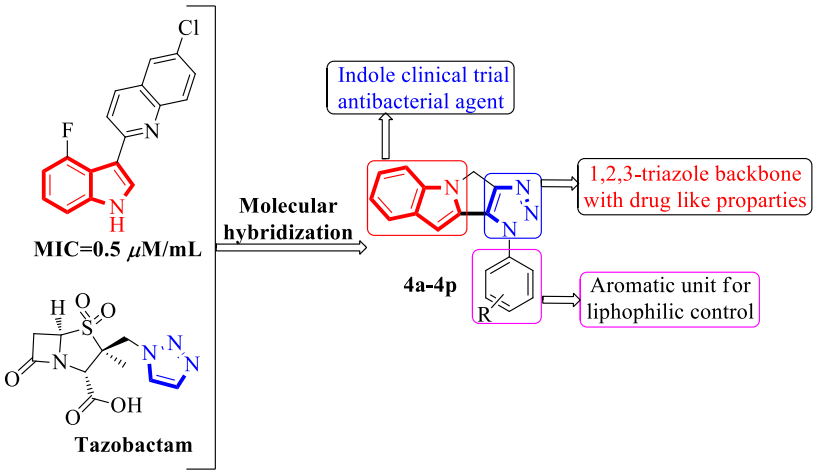



**Figure 1:** Propose plan for new fused [1,2,3] triazolo[4',5':3,4] pyrrolo[1,2-*a*]indole hybrids.

## 2. Experimental

### *2.1. Chemical Material and Apparatus*

All solvents and starting materials were purchased commercially and used without additional purification. The NMR spectra for $^{1}H$ and $^{13}C$ were acquired using a Bruker (400 MHz for $^{1}H$ and 100 MHz for $^{13}C$). Mass spectra were collected using a Jeol JMC-300 spectrometer (ESI, 70 eV). The Carlo Erba 106 and PerkinElmer model 240 analyzers were used to analyse the elements. A Cintex equipment was used to determine uncorrected melting points. TLC was carried out on Merck silica gel 60 F254 precoated plates (0.25 mm), while column chromatography was carried out on silica gel (100-200 mesh). TLC with EtOAc-hexane as an eluent was employed to monitor the progress of the reactions as well as the purity of the compounds.

### *2.2. Synthesis of 2-iodo-1-(prop-2-yn-1-yl)-1H-indole (**2**)*

For 6 hours, a combination of 2-iodo-1*H*-indole (**1**) (5g, 0.02 mol), $K_2CO_3$ (0.06 mol), and propargyl bromide (0.026 mol) in DMF (60 mL) was agitated at 60 °C. After the reaction was completed, the mixture was diluted with water (50 mL) and extracted with ethyl acetate (2 50 mL). The mixed organic layer was washed with brine (2x50 mL), dried with anhydrous $Na_2SO_4$, and then concentrated under vacuum to yield compound **(2)** (72%). $^{1}H$ NMR (400MHz, DMSO-$d_6$; in ppm): δ7.70 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35 - 7.30 (m, 1H), 7.20 (s, 1H), 7.10 - 7.05 (m, 1H), 3.75 (d, *J* = 4.0 Hz, 2H , NC*H*$_2$), 2.21 (t, *J* = 4.0 Hz, 1H, alkyne-H); ESI-MS(m/z): 200 $[M+H]^+$.

### *2.3.3. Synthesis of 1-(aryl)-1,4-dihydro[1,2,3]triazolo-[4',5':3,4]pyrrolo-[1,2-a]indole (**4a-4p**):*

CuI (10 mol%) was added to a solution of 2-iodo-1-(prop-2-yn-1-yl)-1H-indole (2) (1.0 mmol), aryl azide (1.2 mmol), and $^{t}$BuOK (3.0 mmol) in a microwave reactor vessel (10 mL). The mixture was heated at 100 °C for 30-40 minutes. TLC was used to track the course of the reaction. The reaction mixture was carefully emptied into ice-cold water (10 mL) and the product was extracted with ethyl acetate (2x15 mL) after the container was allowed to cool at room temperature. The organic layers were washed in brine and dried over anhydrous $Na_2SO_4$. Following filtration, the solvent was evaporated

under vacuum, and the crude product produced was refined using column chromatography (hexane/ethyl acetate gradient) to yield the pure needed product.

*1-phenyl-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole(**4a**)*: Color: White crystalline solid (74% yield); M.P: 122-124 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.71 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.60 - 7.56 (m, 2H, Ar-H), 7.52 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.43 - 7.39 (m, 3H, Ar-H), 7.33 - 7.28 (m, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.10 - 7.05 (m, 1H, Ar-H), 5.23 (s, 2H, C*H$_2$*); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ 161.24, 139.54, 136.50, 135.33, 129.67(2C), 128.40, 127.34, 124.80, 124.23(2C), 123.49, 122.32, 121.35, 110.76, 107.79, 42.23; ESI-MS(*m/z*): 273 [M+H]. Anal.Cal for $C_{17}H_{12}N_4$; C, 74.98; H, 4.44; N, 20.58; found C, 74.94; H, 4.46; N, 20.60.

*1-(4-methoxyphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4b**)*: Color: White crystalline solid (71% yield); M.P: 130-132 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.78 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.70 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.54 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.35 - 7.31 (m, 1H, Ar-H), 7.19 (s, 1H, Ar-H), 7.10 - 7.06 (m, 1H, Ar-H), 6.99 (d, *J* = 8.0 Hz, 2H, Ar-H), 5.25 (s, 2H, C*H$_2$*), 3.84 (s, 3H, -OCH$_3$); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ 161.66, 159.79, 139.60, 135.09, 131.39, 127.85, 126.37(2C), 124.33, 123.42, 122.52, 121.21, 114.88(2C), 110.45, 108.39, 56.21, 42.36; ESI-MS(*m/z*): 303 [M+H]. Anal.Cal for $C_{18}H_{14}N_4O$; C, 71.51; H, 4.67; N, 18.53; found C, 71.54; H, 4.65; N, 18.51.

*1-(3,5-dimethoxyphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4c**)*: Color: Pale yellow solid (68% yield), M.P: 156-158 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.60 (s, 2H, Ar-H), 7.52 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.30 - 7.26 (m, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 7.11 - 7.06 (m, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 5.23 (s, 2H, C*H$_2$*), 3.83 (s, 6H, 2-OCH$_3$); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ 161.45, 159.24(2C), 139.67, 138.37, 135.35, 127.51, 124.26, 123.35, 122.70, 121.51, 110.72, 107.21, 104.92(2C), 102.96, 56.18(2C), 42.28; ESI-MS(*m/z*): 333 [M+H]. Anal.Cal for $C_{19}H_{16}N_4O_2$; C, 68.66; H, 4.85; N, 16.86; found C, 68.69; H, 4.83; N, 16.84.

*1-(4-chloro-3,5-dimethoxyphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4d**)*: Color: Yellow crystalline solid (78 % yield), M.P: 164-166 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.73 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.51 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.36 - 7.32 (m, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.15 (s, 2H, Ar-H), 7.09 - 7.05 (m, 1H, Ar-H), 5.24 (s, 2H, C*H$_2$*), 3.85 (s, 6H, 2-OCH$_3$); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) 161.53, 156.57(2C), 139.30, 138.09, 135.25, 127.30, 124.19, 123.29, 122.56, 121.08, 118.42, 110.54, 107.72, 104.70(2C), 56.66(2C), 42.27; ESI-MS(*m/z*): 367 [M+H]. Anal.Cal for $C_{19}H_{15}ClN_4O_2$; C, 62.21; H, 4.12; N, 15.27; found C, 62.23; H, 4.14; N, 15.23.

*1-(p-tolyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4e**)*: Color: White solid (70 % yield); M.P: 127-129 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.66 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.51 (d, *J* = 8.0 Hz, 1H, Ar-H), 7. 42 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.35 - 7.30 (m, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 7.10 - 7.06 (m, 1H, Ar-H), 5.25 (s, 2H, C*H$_2$*), 2.31 (s, 3H, -CH$_3$); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ 161.61, 139.38, 138.49, 136.87, 135.18, 130.05 (2C), 127.63, 125.77(2C), 124.08, 123.03, 122.08, 121.09, 110.61, 107.48, 42.37, 21.36; ESI-MS(m/z): 287 [M+H]. Anal.Cal for $C_{18}H_{14}N_4$; C, 75.50; H, 4.93; N, 19.57; found C, 75.55; H, 4.90; N, 19.55.

*1-(3,5-dimethylphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4f**)*: Color: Pale red solid (69 % yield); M.P: 130-132 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-d$_6$; δ in ppm): 7.71 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.52 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.45 (s, 1H, Ar-H), 7.35 - 7.30 (m, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 7. 15 (s, 1H, Ar-H), 7.08 - 7.04 (m, 1H, Ar-H), 5.23 (s, 2H, C*H$_2$*), 2.37 (s, 6H, 2-CH3); $^{13}$C-NMR (100 MHz, DMSO-d$_6$) δ 161.47, 140.24(2C), 139.11, 137.01, 135.14, 128.47, 127.24, 125.37(2C), 124.24, 123.02, 122.07, 121.05, 110.32, 107.65, 42.47, 21.65(2C); ESI-MS(*m/z*): 301 [M+H]. Anal.Cal for $C_{19}H_{16}N_4$; C, 75.98; H, 5.37; N, 18.65; found C, 75.94; H, 5.39; N, 18.67.

*1-(2,3-dimethylphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4g)*** : Color: Pale red solid (66 % yield); M.P: 124-126 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.73 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.51 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.44 - 7.40 (m, 2H, Ar-H), 7.35 - 7.27 (m, 3H, Ar-H), 7.22 (s, 1H, Ar-H), 7.09 - 7.05 (m, 1H, Ar-H), 5.23 (s, 2H, C$H_2$), 2.19 (s, 3H, -$CH_3$), 1.93 (s, 3H, -$CH_3$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.57, 139.38, 138.46, 137.50, 135.43, 131.24, 128.61, 127.46, 125.82, 125.33, 124.80, 123.69, 121.62, 120.56, 110.20, 107.39, 42.41, 19.63, 15.78; ESI-MS(*m/z*): 301 [M+H]. Anal.Cal for $C_{19}H_{16}N_4$; C, 75.98; H, 5.37; N, 18.65; found C, 75.95; H, 5.39; N, 18.66.

*1-(4-chlorophenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4h)***:Color: Pale yellow solid (76 % yield); M.P: 135-137 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.80 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.71 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.53 (d, *J* = 8.0 Hz, 1H, Ar-H), 7. 41 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.34 - 7.30 (m, 1H, Ar-H), 7.19 (s, 1H, Ar-H), 7.09 - 7.05 (m, 1H, Ar-H), 5.24 (s, 2H, C$H_2$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.57, 139.38, 136.41, 135.29, 134.27, 128.62(2C), 127.32, 125.29(2C), 124.41, 123.64, 122.08, 121.36, 110.91, 107.55, 42.47; ESI-MS(*m/z*): 307 [M+H]. Anal.Cal for $C_{17}H_{11}ClN_4$; C, 66.56; H, 3.61; N, 18.26; found C, 66.53; H, 3.63; N, 18.28.

*1-(4-bromophenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4i)*** : Color: White solid (67 % yield); M.P: 143-145 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.73 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.66 - 7.60 (m, 4H, Ar-H), 7.51 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.34 - 7.29 (m, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.10-7.04 (m, 1H, Ar-H), 5.24 (s, 2H, C$H_2$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.30, 139.51, 135.53, 133.88, 131.23(2C), 127.36, 124.80, 124.11(2C), 123.07, 122.42, 121.22, 120.74, 110.64, 107.56, 42.33; ESI-MS(*m/z*): 351 [M+H] & 353[M+3H]. Anal.Cal for $C_{17}H_{11}BrN_4$; C, 58.14; H, 3.16; N, 15.95; found C, 58.17; H, 3.14; N, 15.93.

*1-(3,5-dichlorophenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4j)*** : Color: Pale Yellow solid (77 % yield); M.P: 151-153 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.82 (s, 2H, Ar-H), 7.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.55 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.42 (s, 1H, Ar-H), 7.33 - 7.27 (m, 1H, Ar-H), 7.23 (s, 1H, Ar-H), 7.11-7.06 (m, 1H, Ar-H), 5.26 (s, 2H, C$H_2$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.73, 139.38, 135.44, 134.48, 131.43(2C), 127.42, 124.81, 124.12(2C), 123.33, 122.52, 121.31, 120.22, 110.98, 107.12, 42.22; ESI-MS(*m/z*): 341 [M+H]. Anal.Cal for $C_{17}H_{10}Cl_2N_4$; C, 59.84; H, 2.95; N, 16.42; found C, 59.81; H, 2.94; N, 16.45.

*1-(4-fluorophenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4k)*** : Color: Pale red solid (73 % yield); M.P: 127-129 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 8.10 (d, *J* = 8.0 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.37 - 7.33 (m, 1H), 7.21 (s, 1H), 7.11 - 7.06 (m, 1H), 5.27 (s, 2H, C$H_2$); ESI-MS(*m/z*): 291 [M+H]. Anal.Cal for $C_{17}H_{11}FN_4$; C, 70.34; H, 3.82; N, 19.30; found C, 70.37; H, 3.80; N, 19.32.

*1-(4-(trifluoromethyl)phenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4l)*** : Color: Pale red solid (67 % yield), $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 8.16 (d, *J* = 8.0 Hz, 2H, Ar-H), 8.05 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.75 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.52 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.38 - 7.33 (m, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 7.11 - 7.05 (m, 1H, Ar-H), 5.26 (s, 2H, C$H_2$); ESI-MS(*m/z*): 341 [M+H]. Anal.Cal for $C_{18}H_{11}F_3N_4$; C, 63.53; H, 3.26; N, 16.46; found C, 63.56; H, 3.28; N, 16.42.

*1-(4-nitrophenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4m)*** : Color: Yellow solid (80 % yield); M.P: 150-152 $^{o}$C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 8.41 (d, *J* = 8.0 Hz, 2H), 8.21 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.36 - 7.31 (m, 1H), 7.21 (s, 1H), 7.10 - 7.06 (m, 1H), 5.27 (s, 2H, C$H_2$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.77, 147.65, 140.19, 139.14, 135.03, 127.55, 126.17(2C), 124.07, 123.45(2C), 122.95, 122.08, 121.08, 110.72, 107.12, 42.37; ESI-MS(*m/z*): 318 [M+H]. Anal.Cal for $C_{17}H_{11}N_5O_2$; C, 64.35; H, 3.49; N, 22.07; found C, 64.38; H, 3.47; N, 22.05.

*1-(4-ethylphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4n)*** : Color: White red solid (72 % yield); M.P: 134-136 °C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.70 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.60 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.50 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.38 - 7.34 (m, 1H, Ar-H), 7.28 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.18 (s, 1H, Ar-H), 7.09-7.05 (m, 1H, Ar-H), 5.23 (s, 2H, C$H_2$), 2.28 (q, *J* = 4.0 Hz, 2H. -$CH_2$), 1.68 (t, *J* = 4.0 Hz, 2H. –$CH_3$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.73, 141.27, 139.41, 138.10, 135.21, 129.61(2C), 127.83, 127.23(2C), 124.81, 123.66, 122.53, 121.24, 110.53, 107.28, 42.33, 23.20, 13.78; ESI-MS(*m/z*): 301 [M+H]. Anal.Cal for $C_{19}H_{16}N_4$; C, 75.98; H, 5.37; N, 18.65; found C, 75.94; H, 5.39; N, 18.67.

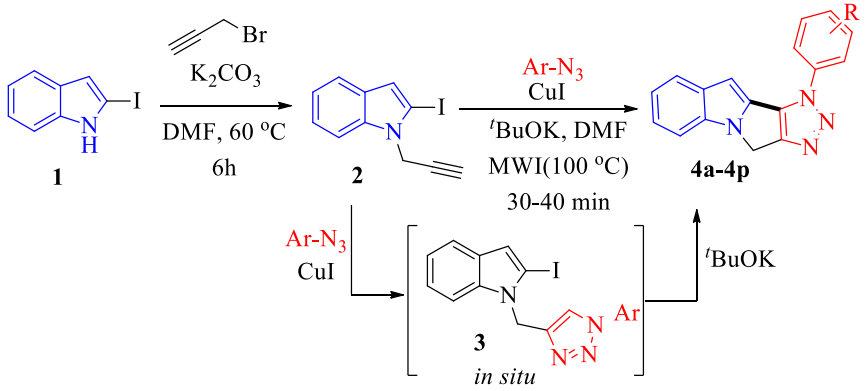
*4-([1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indol-1(4H)-yl)benzonitrile* ***(4o)****:* Color: White solid (72 % yield); M.P: 141-143 °C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.80 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.50 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.41 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.36 - 7.31 (m, 1H, Ar-H), 7.21 (s, 1H, Ar-H), 7.11 - 7.06 (m, 1H, Ar-H), 5.24 (s, 2H, C$H_2$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.48, 139.42, 138.12, 135.38, 127.63, 127.11(2C), 126.10(2C), 124.19, 123.32, 122.42, 121.43, 119.53, 117.54, 110.41, 107.25, 42.22; ESI-MS(*m/z*): 298 [M+H]. Anal.Cal for $C_{18}H_{11}N_5$; C, 72.72; H, 3.73; N, 23.56; found C, 72.76; H, 3.71; N, 23.54.

*1-(4-butylphenyl)-1,4-dihydro-[1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole* ***(4p)*** Color: Pale Yellow solid (66 % yield), M.P: 146-148 °C, $^{1}$H-NMR (400 MHz, DMSO-$d_6$; δ in ppm): 7.72 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.64 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.50 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.35 - 7.30 (m, 1H, Ar-H), 7.24 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.18 (s, 1H, Ar-H), 7.10 - 7.05 (m, 1H, Ar-H), 5.25 (s, 2H, C$H_2$), 2.68 (t, *J* = 4.0 Hz, 2H, -$CH_2$), 1.68 - 1.58 (m, 2H, -$CH_2$), 1.38 - 1.29 (m, 2H, -$CH_2$), 0.94 (t, *J* = 4.0 Hz, 3H, -$CH_3$); $^{13}$C-NMR (100 MHz, DMSO-$d_6$) δ 161.37, 139.33, 138.14(2C), 135.78, 130.01, 129.14(2C), 128.07, 127.03, 124.22, 123.02, 122.38, 121.44, 110.58, 107.53, 42.47, 34.21, 32.89, 21.65, 13.70; ESI-MS(*m/z*): 329 [M+H]. Anal.Cal for $C_{21}H_{20}N_4$; C, 76.80; H, 6.14; N, 17.06; found C, 76.84; H, 6.16; N, 17.00.

## 3. Results and Discussion

### *3.1. Chemistry*

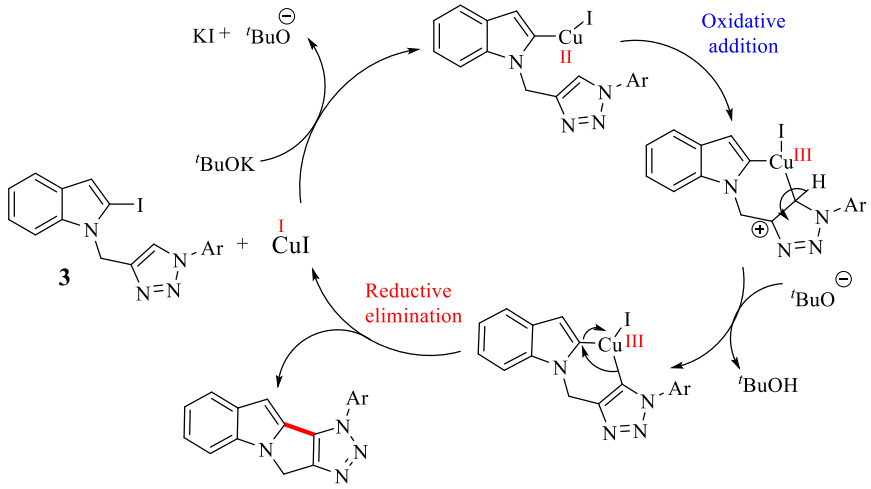
The synthetic procedure utilized to produce the target compounds is depicted in Scheme 1. In dimethylformamide (DMF) with $K_2CO_3$, a 6-hour reaction of 2-iodo-1*H*-indole (**1**) and propargyl bromide yielded 2-iodo-1-(prop-2-yn-1-yl)-1*H*-indole (**2**). The important stage of the synthesis, 1,3-dipolar cyclo addition followed by C-C bond coupling of the terminal alkyne (**2**) with different aryl azides at 100 °C at MWI, produces good to excellent yields of the corresponding fused [1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole (**4a-4p**).




**Scheme 1.** Synthesis of fused [1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-a]indole scaffolds.

Scheme 2.[21] depicts the hypothesised mechanism for the synthesis of [1,2,3]triazolo[4',5':3,4]pyrrolo[1,2-*a*]indole derivatives. The spectral data from the manufactured

compounds all corresponded completely with the predicted structures, and a sample molecule, 4b, was also addressed. In the $^{1}$H-NMR signals are at δ 7.78–6.99 (Aromatic-H), 5.25 (s, 2H, $CH_2$), and 3.84 (s, 3H, -$OCH_3$), and in the $^{13}$C-NMR signals are at 159.79 (C-$OCH_3$), 56.21 (-$OCH_3$), and 42.36 (-$NCH_2$). The [M+H]+ peak at *m/z* 303 in the ESI-mass spectrum confirmed the structure of compound **4b**. The elemental analysis (C, H, and N) data (C, 71.54; H, 4.65; N, 18.51) confirmed the purity of compound **4b**.




**Scheme 2**. The proposed mechanism for the one-pot cycloaddition–fusion reaction.

*3.2. Biological Assay*

*3.2.1. Antibacterial activity*

Using the conventional broth microdilution method, the title compounds (**4a-4p**) were tested for *in vitro* antibacterial activity against gram-positive (G+ve) bacterial strains, with streptomycin serving as a positive control.[22] All derived compounds' minimum inhibitory concentrations (MICs) were indicated in $\mu$g/mL. The results are shown in Table 1. Table 1 demonstrates that **4h**, **4j**, and **4k** demonstrated more efficient bacterial inhibitory action against B. subtilis, with MICs of 3.12, 1.56, and 3.12 $\mu$g/ mL, respectively, whereas typical streptomycin MICs were 6.26 $\mu$g/ mL. Compounds **4d**, **4i**, and **4l** showed equipotent antibacterial action against *B. subtilis*, with MIC values of 6.25 $\mu$g/ mL, whereas the remaining compounds showed moderate to poor activity. Compound **4j** demonstrated more significant activity against *S.aureus*, with a MIC of 1.56 $\mu$g/ mL, and comparable activity against *S.epidermidis*, having a MIC of 6.25 $\mu$g/ mL. With MIC values of 6.25 $\mu$g/mL, compounds **4h** and **4k** similarly demonstrated equipotent activity against *S.aureus*. The remaining drugs were ineffective against the tested strains (Figure 2).

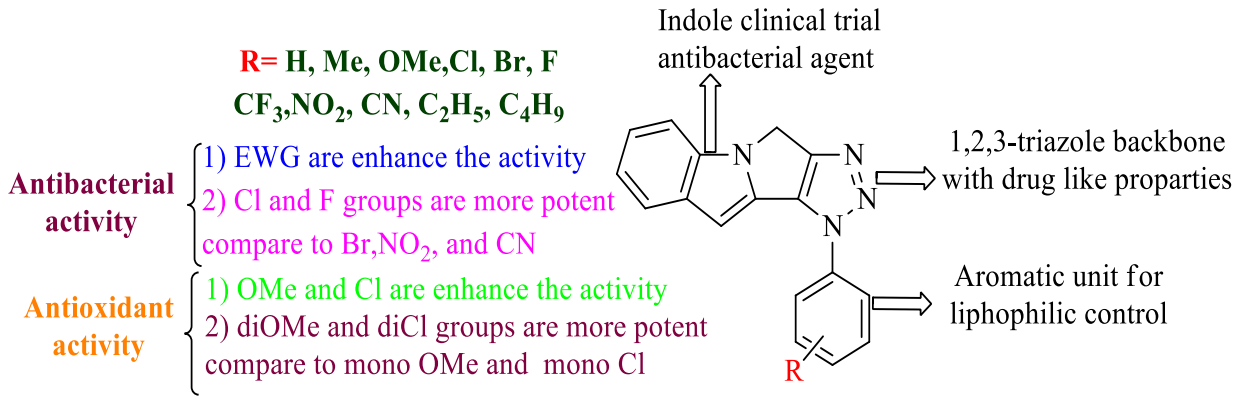


**Figure 2.** SAR of target sulfonyl 1,2,3-triazolyl imidazole derivatives

**Table 1.** *In vitro* antibacterial activity data of compounds **4a-4p**

| Compounds | *R* | *B. subtilis* | *S. aureus* | *S. epidermidis* |
|---|---|---|---|---|
| **4a** | H | 25 | 50 | - |
| **4b** | 4-OMe | 12.5 | 25 | 50 |
| **4c** | 3,5-diOMe | 12.5 | 12.5 | 25 |
| **4d** | 3,5-diOMe, 4-Cl | 6.25 | 12.5 | 6.5 |
| **4e** | 4-Me | 50 | 25 | 50 |
| **4f** | 3,5-diMe | 25 | 25 | 25 |
| **4g** | 2,3-diMe | 50 | - | - |
| **4h** | 4-Cl | **3.12** | 6.25 | 12.5 |
| **4i** | 4-Br | 6.25 | 12.5 | 25 |
| **4j** | 3,5-diCl | **1.56** | **1.56** | **3.12** |
| **4k** | 4-F | **3.12** | 6.25 | 12.5 |
| **4l** | 3-$CF_3$ | 6.25 | 12.5 | 12.5 |
| **4m** | 4-$NO_2$ | 12.5 | 25 | 50 |
| **4n** | 4-$C_2H_5$ | 50 | - | - |
| **4o** | 4-CN | 25 | 25 | - |
| **4p** | 4-$C_4H_9$ | - | - | - |
| **Standard** | **Streptomycin** | **6.25** | **6.25** | **3.12** |

Note: "-" indicates concentration > 50 $\mu$g/mL

*3.2.2. Antioxidant Activity*

By using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) technique, all of the produced compounds **4a-4p** were tested for free radical scavenging activity in terms of hydrogen donating or radical scavenging ability as reported in the literature.[23,24] As a blank, control, and reference, methanol (95%), DPPH solution, and standard chemicals (Trolox and ascorbic acid) were utilized. The findings of the analysis of the free radical scavenging ability of the synthesized compounds **4a-4p** revealed that compounds (**4c**, **4d**, and **4j**) have excellent antioxidant activity with $IC_{50}$ values ranging from 7.26 ± 0.43 to 9.21±1.03 $\mu$M (Table 2). These results on comparison with the standard Trolox with $IC_{50}$ value of 11.05±0.98 $\mu$M found to be active by 1.52 fold for **4d**, 1.31 fold for **4c**, and 1.19 fold for **4j**. The compounds **4b**, **4h**, **4k**, and **4l** have shown good scavenging ability with $IC_{50}$ values 12.12± 0.98 to 13.65± 0.89 $\mu$M, respectively. Remaining compounds have shown moderate to weak scavenging ability/capacity with $IC_{50}$ values ranging from 17.33±1.21 to 31.93±1.93 $\mu$M.

**Table 2.** Antioxidant activity of **4a**–**4p** by DPPH method

| Compound | $IC_{50}$ in µM | Compound | $IC_{50}$ in µM |
|---|---|---|---|
| **4a** | 23.88± 1.66 | **4j** | 9.21±1.03 |
| **4b** | 13.32± 1.12 | **4k** | 12.12± 0.98 |
| **4c** | 8.42± 0.67 | **4l** | 13.65± 0.89 |
| **4d** | 7.26 ± 0.43 | **4m** | 19.42± 1.16 |
| **4e** | 25.35± 1.52 | **4n** | 24.81±1.27 |
| **4f** | 18.79 ± 1.43 | **4o** | 17.33±1.21 |
| **4g** | 28.62 ± 1.81 | **4p** | 31.93±1.93 |
| **4h** | 12.66±1.19 | **Trolox** | **11.05±0.98** |
| **4i** | 23.21± 1.13 | **Ascorbic acid** | **3.34 ± 0.21** |

## 4. Conclusion

Finally, using microwave irradiation and one-pot Cu-catalyzed intramolecular C-H arylation of in situ produced 1,2,3-triazoles, a series of new fused [1,2,3]triazolo [4',5':3,4] pyrrolo[1,2-*a*]indoles (**4a-4p**) were synthesized. *In vitro* antibacterial activity against three different types of gram-positive bacteria was assessed for all of the compounds. The most potent compounds against the bacterial strains tested were **4h**, **4j**, and **4k**. Furthermore, free radical scavenging action in the form of hydrogen donation or radical scavenging ability uses the DPPH method. Compounds **4c**, **4d**, and **4j** were discovered to be more potent antioxidants than normal Trolox. The remaining compounds have moderate to low activity, whereas compounds **4b**, **4h**, **4k**, and **4l** have strong activity. Our next goal is to do time kill tests on human pathogenic organisms utilising **4h**, **4j**, and **4k** chemicals.

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## Supporting Information

Supporting information accompanies this paper on http://www.acgpubs.org/journal/organic-communications

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