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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Design and synthesis of novel triazole linked pyrrole derivatives as potent *Mycobacterium tuberculosis* inhibitors

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Abstract This research is focused on the rational approach to design and synthesis of a novel series of triazole linked pyrrole derivatives through a sequential Paal–Knorr reaction and Click chemistry. These new molecules were screened against *Mycobacterium tuberculosis* H37Rv and found to display promising anti-mycobacterial activity. Among various compounds, **7g** and **7l** were identified as leads with minimum inhibitory concentration value 0.78 (μg/mL), which are more effective than standard drugs such as pyrazinamide, ethambutol, and ciprofloxacin and less active than isoniazid and rifampicin. These molecules (minimum inhibitory concentration values <12.5 μg/mL) were also screened against HEK-293T cancer cell lines. Most of these molecules are less toxic but possess higher selectivity index, which indicates the suitability of these compounds for further evaluation.

Keywords Antitubercular activity · Stetter reaction · Paal–Knorr synthesis · Click chemistry · Trisubstituted pyrrole derivatives

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by pathogenic Gram positive bacteria called *Mycobacterium tuberculosis* (MTB). TB frequently attacks the lungs, but it also affect other parts of the body (Rogoza et al. 2010). The symptoms of pulmonary TB include chronic cough, weight loss, intermittent fever, night sweats, and coughing blood. The World Health Organization (WHO) estimates that one-third of the population is infected with (MTB) annually, there are approximately 8 million new infections and 3 million deaths are attributed to *M. tuberculosis* (Naresh et al. 2010; Marriner et al. 2011). Although TB can be treated and even cured by chemotherapy, the treatment requires 6–9 months of time period that is too long, and is accompanied by a significant toxicity. More than 20 drugs are currently used for the treatment of TB and most of them were developed 50 years ago (Thomas et al. 2014). Therefore, there is an urgent necessity to develop a more powerful and faster acting anti-TB drugs with new mode of action to overcome drug resistance, lengthy treatment duration and toxicity, that enforce the researchers across the globe.

Pyrrole is an important nitrogen containing heterocyclic compound, which is frequently present in a wide range of natural products including pyrrolomycins, pyoluteorin, pyrrolnitrin, chlorophyll, vitamins B12, and bilirubine (Walsh et al. 2006). The biological activity of pyrrole

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derivatives has been evaluated by various research groups (Shrinivas et al. 2014; La Regina et al. 2014). TB activity of substituted pyrrole (BM212) was first reported by Deidda et al. (1998), and its analogs were prepared by Biava et al. (2008). Another pyrrole derivative, LL-3858 was also found to be active against TB, which was reported by Lupin Limited in 2004. Currently it is in phase II clinical trials (Sandeep et al. 2011). The copper-catalyzed a 1,3-dipolar cycloaddition of alkynes and azides to form 1,2,3-triazoles is the most popular reaction in Click chemistry (Krystian et al. 2014). 1,2,3-Triazoles are mainly used as bioisosteres and linkers for the synthesis of bioactive compounds such as anti-tuberculosis (Deepak et al. 2014; Boechat et al. 2011), anti-cancer (Jabeena et al. 2014) and antibacterial (Kavitha et al. 2014) antivirus and antifungal (Ramachandrana et al. 2011). They were considered to be the most useful components for the construction of complex molecules (Antonino et al. 2014) such as pharmaceutical drugs like tazobactam, carboxyamidotriazole, and cefatriazine (Fig. 1). Thus, the Click chemistry has attracted widespread interest from virtually all areas of drug discovery. Inspired by inherent anti-TB activity of pyrrole derivatives (Gholap 2016) (Fig. 2) and potential use of 1,2,3-triazole ring (Rangappa et al. 2015) (Fig. 3) as bioisostere, we were interested in the design and synthesis of triazole linked pyrrole derivatives as new anti-TB agents

Results and discussions

Chemistry

Our synthetic strategy for the triazole linked pyrrole derivatives (**7a–x**) is outlined in Scheme 1. Accordingly, treatment of aldehyde with chalcone (**1a–c**) under Stetter conditions (Reddy et al. 2012; Biava et al. 2005) provided the corresponding 1,4-diketone (**2a–d**). Thus formed 1,4-diketone (**2a–d**) was then treated with 1-(4-aminophenyl) ethanone under Paal-Knorr conditions (Nicolaou and Demopoulos 2003) to afford the corresponding 1-(4-(2,3,5-trisubstituted-1*H*-pyrrol-1-yl)phenyl)ethanone (**3a–d**). These compounds (**3a–d**) were further subjected to reduction using $NaBH_4$ (Kamal et al. 2013) to give the respective alcohols (**4a–d**). Bromination of the alcohols (**4a–d**) followed by the treatment of bromides (**5a–d**) with NaN_3 gave the desired azides (**6a–d**). 1,3-Dipolar cycloaddition (Ackermann and Potukuchi 2010) of azides (**6a–d**) with terminal alkynes afforded the desired 1,2,3-triazole linked pyrrole derivatives (**7a–x**) in good yields.

Biology

Antibacterial activity

All synthesized compounds were evaluated for their anti-tubercular activity against *M. tuberculosis* H37Rv (ATCC27294) by agar dilution method (Franzblau et al. 1998). Isoniazid, rifampicin, ethambutol and ciprofloxacin were used as standard drugs. The minimum inhibitory concentration (MIC) values demonstrated as μg/mL, were determined for each compound against test mycobacteria. Newly synthesized compounds having MIC ≤ 12.5 μg/mL were further scrutinized for cytotoxicity (Gerlier and Thomasset 1986) by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay (MTT) against HEK cell line at 50 μM concentration.

The anti-mycobacterial activity data of all tested compounds were depicted in Table 1. MTB activity of these compounds was shown in MIC values ranging from 0.78 to >25 μg/mL. Among them, triazole linked pyrrole conjugates **7b**, **7c**, **7f**, **7g**, **7j**, **7l**, **7n**, **7q**, **7r**, **7u**, and **7v**, displayed MIC values below 6.25 μg/mL. Remarkably, **7g** and **7l** exhibited potent anti-TB activity (0.78 μg/mL), and in particular, **7j** showed MIC value 1.56 μg/mL and another four compounds **7b**, **7q**, **7u**, and **7v** showed MIC value 3.125 μg/mL. When compared to first-line TB drugs for example ethambutol (MIC 3.13 μg/mL), seven compounds **7b**, **7g**, **7j**, **7l**, **7q**, **7u**, and **7v** were found to be more potent, albeit they were less effective than other TB drugs including isoniazid and rifampicin (Table 1).

The structure–activity relationship of newly synthesized triazole linked pyrrole conjugates has been investigated with respect to standard TB drugs (isoniazid, rifampicin, ethambutol, and ciprofloxacin). Among them, **7a–f** contain R, R^2 = phenyl, R^1 = *p*-chlorophenyl groups, and R^3 = pyridine,

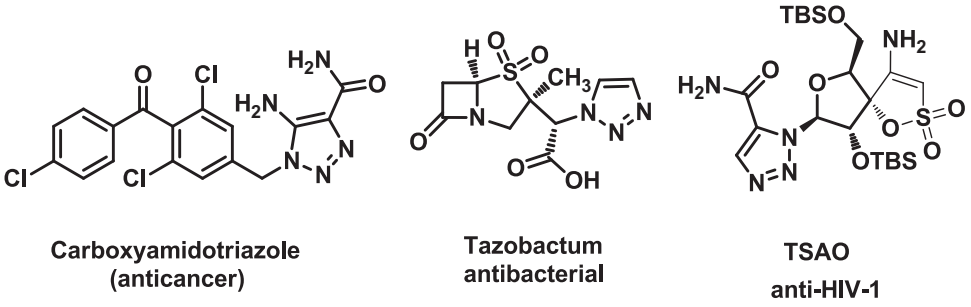


Fig. 1 1,2,3-Triazole containing pharmaceutical agents

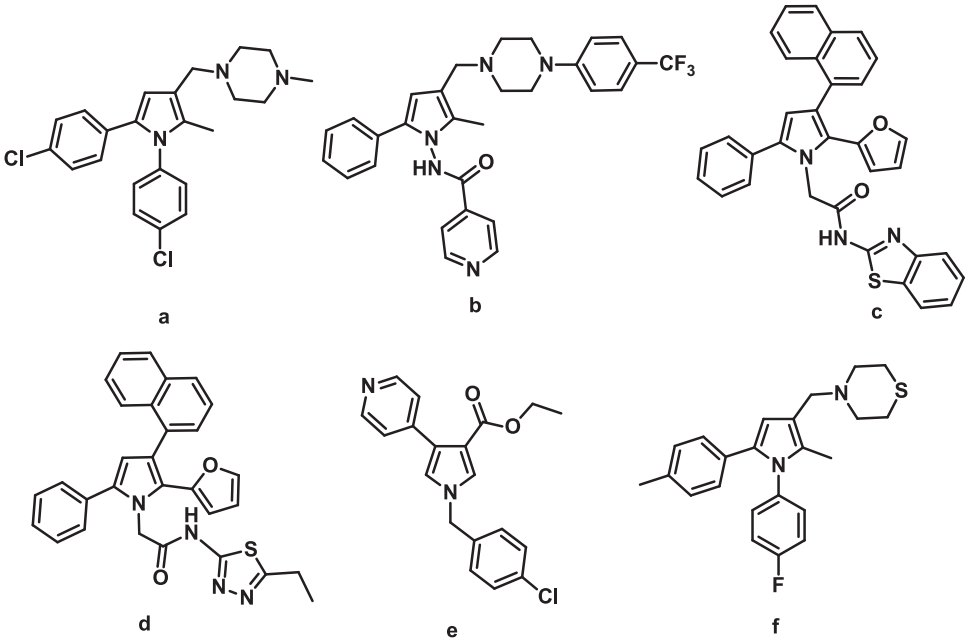


Fig. 2 TB active pyrrole derivatives

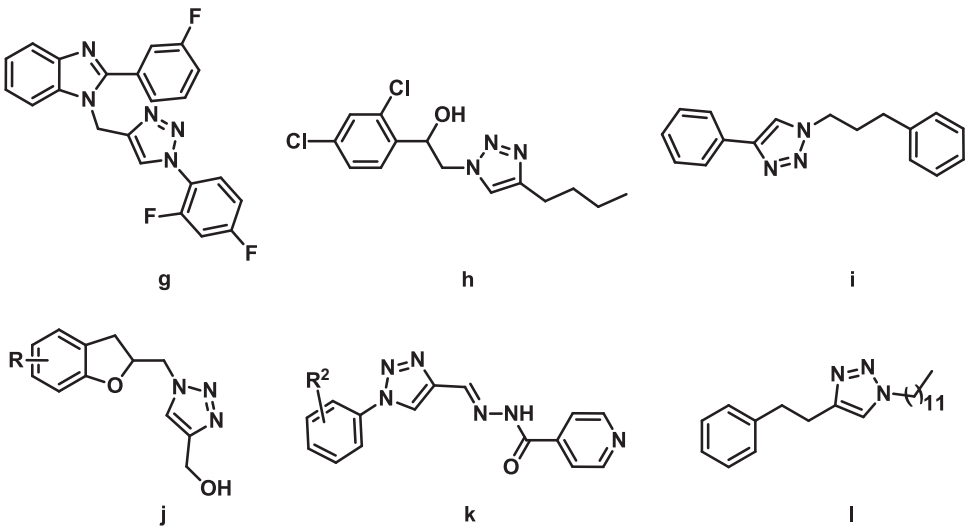
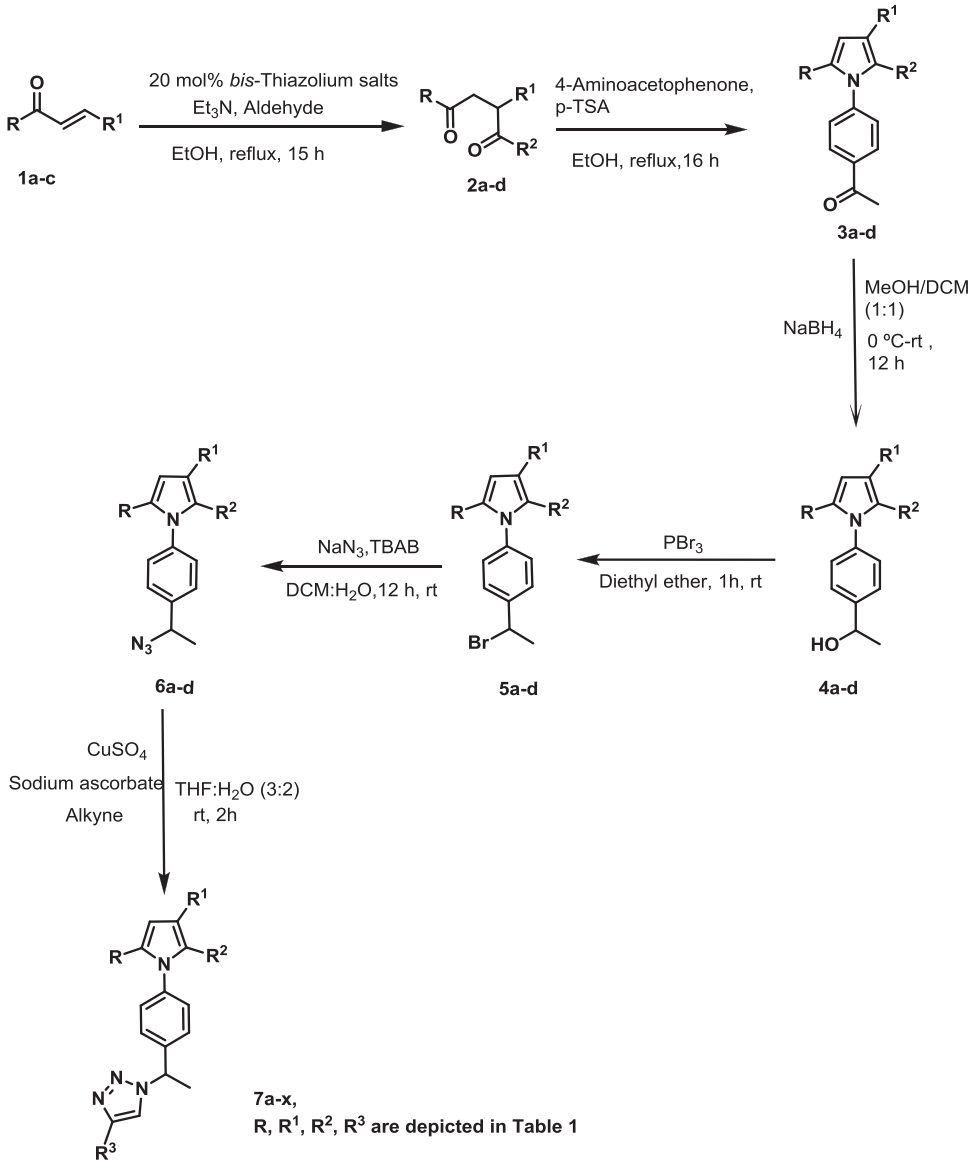


Fig. 3 1,2,3-Triazole containing anti-tubercular agents

7b exhibited good activity (MIC = 3.125 μg/mL). If the pyridine (R^3) is replaced by $-CH_2CH_2CH_2CH_2OH$ (**7a**) or by *p*-tolyl (**7d**), the molecules displayed moderate activity (MIC = 12.5 μg/mL). The presence of CH_2CH_2OH (**7c**) or *n*-pentylbenzene (**7f**), the molecules showed improved activity by two folds (MIC = 6.25 μg/mL). If R^3 is hexyl (**7e**), the molecule displayed lower activity. Compounds **7g–m** contain R^1, R^2 = phenyl, R = *p*-tolyl groups, and R^3 = $-CH_2OH$ (**7g**) or *p*-tolyl (**7l**) exhibited potent activity (MIC = 0.78 μg/mL). If $R^3 = -CH_2CH_2OH$ (**7j**), the molecule displayed excellent activity (MIC = 1.56 μg/mL), if R^3 = $-CH_2CH_2CH_2CH_2OH$ (**7k**), or *n*-pentylbenzene (**7m**), the molecules showed moderate activity (MIC = 12.5 μg/mL), if R^3 = pyridine (**7h**) or phenyl (**7i**) has less effect on the TB activity. Compounds **7n–s** contain R, R2 = *p*-tolyl, R = phenyl groups, and $R^3 = CH_2CH_2OH$, **7q** exhibited the reasonable activity (MIC = 3.125 μg/mL), and R^3 = $-CH_2CH_2CH_2CH_2OH$ (**7n**) or *p*-tolyl (**7r**) displayed moderate activity (MIC = 6.25 μg/mL). If R^3 = pyridine (**7o**), or phenyl (**7p**) or pentylbenzene (**7s**) showed low activity (MIC = 12.5 μg/mL). Compounds **7t–x** contain R, R^1, R^2 = phenyl, and R^3 = phenyl (**7u**) or $-CH_2CH_2CH_2CH_2OH$ (**7v**) exhibited good activity (MIC = 3.125 μg/mL). If R3 = *n*-pentylbenzene (**7x**) showed low activity (MIC = 12.5 μg/mL), and R3 = pyridine (**7t**) or hexyl (**7w**) groups displayed least activity. The above study indicates that the position of the substituent on pyrrole and triazole plays a crucial role in the observed activity and the triazole linked pyrrole derivatives were found to exhibit promising anti-tuberculosis agents.

Scheme 1 Synthesis of triazole linked pyrrole derivatives (**7a–x**)



The active compounds were further subjected to in vitro cytotoxicity studies against HEK-293T cell line at 50 µg/mL concentration (Fig. 4). Selectivity index (SI) ratio between IC_{50} and MIC; if the SI > 25, the compounds were considered as nontoxic. The percentage of growth inhibition, IC_{50} and selectivity index (SI) values presented in Table 2. Compounds **7g**, and **7l** showed 8.954% and 18.956 inhibition respectively at 50 µg/mL with selectivity index of > 64. These results imply the suitability of these compounds in drug development for tuberculosis.

Conclusion

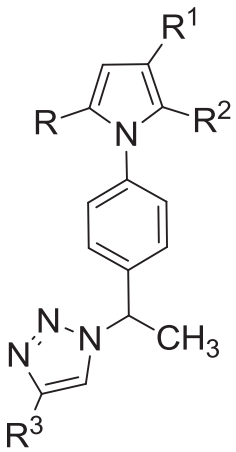
In summary, we have synthesized a novel series of triazole linked pyrrole conjugates employing Paal–Knorr reaction followed by Click chemistry. These molecules were screened for anti-tubercular activity against *M. tuberculosis* H37Rv pathogens. Most of these compounds display moderate to excellent anti-mycobacterial activity (25–0.78 µg/mL). Among them, two compounds (**7g** and **7l**) display potent anti-tubercular activity (0.78 µg/mL) with low cytotoxicity and high selective index. The results reported in this study would be useful in guiding future efforts to discover new compounds with increased tuberculosis activity.

Experimental section

Chemistry protocols

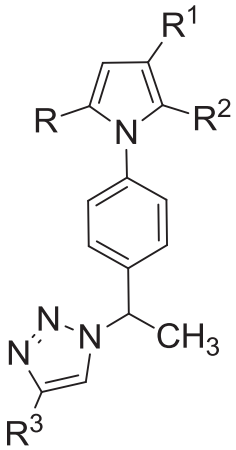
All chemicals (Alfa Aesar and Sigma Aldrich) used possess a purity of >95%. Yield refers to pure products after

Table 1 Synthesis and antimicrobial activity of **7a–x**



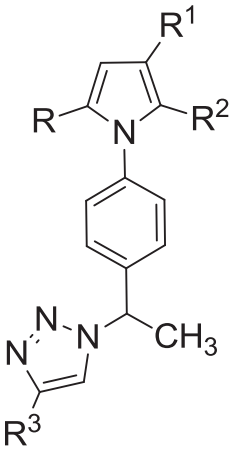
Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv	Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv
7a					12.5	**7m**					12.5
7b					3.125	**7n**					6.25
7c					6.25	**7o**					12.5
7d					12.5	**7p**					12.5

Table 1 continued



Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv	Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv
7e					25	**7q**					3.125
		Cl								HO	
7f					6.25	**7r**					6.25
		Cl									
7g					0.78	**7s**					12.5
				HO							
7h					25	**7t**					25
				N						N	

Table 1 continued



Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv	Entry	R	R^1	R^2	R^3	MIC (μg/mL) MTB H37Rv
7i					25	**7u**					3.125
7j				HO	1.56	**7v**				HO	3.125
7k				HO	12.5	**7w**					25
7l					0.78	**7x**					12.5
Rifampicin					0.24	Rifampicin					0.24
Isoniazid					0.72	Isoniazid					0.72
Ethambutol					7.64	Ethambutol					7.64
Ciprofloxacin					4.71	Ciprofloxacin					4.71

purification and are unoptimized. Melting points were determined in open capillaries on Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Buck Scientific IR M-500 spectrophotometer in KBr pellets, ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra for analytical purpose were recorded in $CDCl_3$, on a Bruker instrument at 300 and 75 MHz, respectively; chemical shifts are expressed in δ-scale downfield from TMS as an internal standard. High-resolution mass spectra were obtained by using ESI-QTOF mass spectrometry. Silica gel 60 (230–400 mesh) was used for the column chromatography. Thin-layer chromatography (TLC) plates (Silica Gel 60 F254) were used for TLC.

General procedure for synthesis of 2a–d

To a stirred solution of the *bis*-thiazolium salts (0.2 mmol) in 3 mL of ethanol were added 0.2 mL of Et_3N (2.0 mmol) and an aldehyde (1.0 mmol). The mixture was allowed to stir for 10 min at room temperature and then chalcone (1 mmol) was added. The resulting mixture was kept under reflux for 15 h at 70 °C.The progress of the reaction was monitored by TLC. The mixture was quenched with water and extracted with ethyl acetate (2×15 mL). Removal of the solvent followed by purification on silica gel column chromatography furnished the pure 1,4-diketone.

2-(4-Chlorophenyl)-1,4-diphenylbutane-1,4-dione ***(2a)***

Colorless oil; yield: 84%; ^{1}H NMR: δ 7.93 (t, 6H, $J = 3.7$ Hz, Ar–H), 7.51 (t, 1H, $J = 7.1$ Hz, Ar–H), 7.41 (t, 2H, $J = 7.5$ Hz, Ar–H), 7.34 (d, 1H, $J = 8.3$ Hz, Ar–H), 7.19–7.31 (m, 4H, Ar–H), 5.20 (dd, 1H, $J = 3.0$, 9.8 Hz, Ar–CH–C = O), 4.15 (dd, 1H, $J = 10.5$, 17.9 Hz, O=C –CH_2–CH–), 3.22 (dd, 1H, $J = 3.0$, 17.9 Hz, O=C –CH_2–CH–); ^{13}C NMR: δ 43.8 (–CH_2–), 48.7 (–CH–), 127.5 (Ar–C), 128.1 (Ar–C), 128.6 (Ar–C), 128.8 (Ar–C), 129.3 (Ar–C), 130.3 (Ar–C), 133.3 (Ar–C), 134.8 (Ar–C), 135.7 (Ar–C), 136.3 (Ar–C), 138.2 (Ar–C), 139.3 (Ar–C), 197.7 (C=O), 198.0 (C=O).

1,2,4-Triphenylbutane-1,4-dione ***(2d)***

Yellow oil; yield: 89%; ^{1}H NMR: δ 7.98 (t, 4H, $J = 7.5$ Hz, Ar–H), 7.14–7.54 (m, 10H, Ar–H), 7.19 (d, 1H, $J = 5.2$ Hz, Ar–H), 5.28 (dd, 1H, $J = 6.7$, 18.2 Hz, Ar–CH–C = O), 4.17 (dd, 1H, $J = 9.8$, 17.9 Hz, O = C –CH_2–CH–), 3.24 (dd, 1H, $J = 3.5$, 17.9 Hz, O = C –CH_2–CH–); ^{13}C NMR: δ 41.8 (–CH_2–), 53.4 (–CH–), 113.6 (Ar–C), 120.7 (Ar–C), 127.4 (Ar–C), 127.4 (Ar–C), 127.8 (Ar–C), 128.0 (Ar–C), 128.1 (Ar–C), 128.7 (Ar–C), 128.8 (Ar–C), 129.4 (Ar–C), 129.7 (Ar–C), 132.9 (Ar–C), 133.2 (Ar–C), 134.4 (Ar–C), 136.0 (Ar–C), 137.5 (Ar–C), 137.8 (Ar–C), 138.8 (Ar–C), 197.7 (C=O), 206.9 (C=O).

General procedure for the preparation of 1,2,3,5-tetrasubstituted pyrrolyl phenyl ethanone 3a–d

Paal-Knorr conditions: To a solution of 1,4-diketone (1 equiv) in EtOH (10 v for 1 g), was added *p*-TSA (1.1 equiv) followed by 4-amino acetophenone (2 equiv). The resulting mixture was stirred at 75 °C for 16 h. The progress of the reaction was monitored by TLC. After completion, the mixture was cooled to room temperature and then concentrated in vacuo to get the crude compound. It was extracted twice with EtOAc and the combined organic layers were washed twice with water and once with brine solution, dried over anhydrous Na_2SO_4, filtered, and the solvent was removed in vacuo. The resulting material was purified by column chromatography to afford the desired product.

*1-(4-(3-(4-Chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl) phenyl)ethanone (****3a****)*

Off white solid; yield: 92%; ^{1}H NMR: δ 7.82 (d, 2H, $J = 8.3$ Hz, Ar–H), 7.34 (d, 3H, $J = 7.3$ Hz, Ar–H), 7.29 (t, 2H, $J = 7.4$ Hz, Ar–H), 7.24–7.11 (m, 10H, Ar–H), 6.71 (s, 1H, pyrrole–CH), 2.56 (s, 3H, O=C–CH_3); ^{13}C NMR: δ 26.5 (–CH_3), 110.8 (pyrrole–CH), 122.0 (Ar–C), 126.2 (Ar–C), 126.9 (Ar–C), 127.4 (Ar–C), 127.6 (Ar–C), 128.1 (Ar–C), 128.2 (Ar–C), 128.2 (Ar–C), 128.3 (Ar–C), 128.5 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 128.9 (Ar–C), 132.1 (Ar–C), 133.0 (Ar–C), 133.2 (Ar–C), 135.1 (Ar–C), 135.5 (Ar–C), 136.0 (Ar–C), 136.3 (Ar–C), 138.2 (Ar–C), 142.5 (Ar–C), 142.9 (Ar–C), 197.1 (C=O).

*1-(4-(2,3-Diphenyl-5-(p-tolyl)-1*H*-pyrrol-1-yl)phenyl) ethanone* ***(3b)***

White solid; yield: 84%; ^{1}H NMR: δ 7.75 (d, 2H, $J = 8.5$ Hz, Ar–H), 7.24–7.07 (m, 10H, Ar–H), 7.03 (d, 2H, $J = 8.6$ Hz, Ar–H), 6.96 (d, 2H, $J = 8.0$ Hz, Ar–H), 6.90 (d, 2H, $J = 8.3$ Hz, Ar–H), 6.71 (s, 1H, pyrrole–CH), 2.54 (s, 3H, O=C–CH_3), 2.28 (s, 3H, Ar–CH_3); ^{13}C NMR: δ 21.2 (Ar–CH_3), 26.5 (O=C–CH_3), 110.7 (pyrrole–CH), 123.8 (Ar–C), 125.5 (Ar–C), 126.5 (Ar–C), 128.1 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 128.8 (Ar–C), 129.0 (Ar–C), 129.1 (Ar–C), 131.1 (Ar–C), 132.0 (Ar–C), 132.5 (Ar–C), 134.5 (Ar–C), 135.1 (Ar–C), 135.8 (Ar–C), 136.9 (Ar–C), 143.0 (Ar–C), 197.2 (C=O).

*1-(4-(3-Phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethanone (**3c**)*

White solid; yield: 84%; ^{1}H NMR: δ 7.75 (d, 2H, $J = 8.5$ Hz, Ar–H), 7.20–7.06 (m, 9H, Ar–H), 7.02 (d, 2H, $J = 8.6$ Hz, Ar–H), 6.95 (d, 2H, $J = 8.0$ Hz, Ar–H), 6.90 (d, 2H, $J = 8.1$ Hz, Ar–H), 6.68 (s, 1H, pyrrole–CH), 2.54 (s, 3H, O=C–CH_3), 2.30 (s, 3H, Ar–CH_3), 2.28 (s, 3H, Ar–CH_3); ^{13}C NMR: δ 21.0 (Ar–CH_3), 21.2 (Ar–CH_3), 26.5 (O=C–CH_3), 110.7 (pyrrole–CH), 123.7 (Ar–C), 126.5 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 128.7 (Ar–C), 128.8 (Ar–C), 129.0 (Ar–C), 129.2 (Ar–C), 131.2 (Ar–C), 131.7 (Ar–C), 132.6 (Ar–C), 132.8 (Ar–C), 133.4 (Ar–C), 135.1 (Ar–C), 136.8 (Ar–C), 143.1 (Ar–C), 197.2 (C=O).

General procedure for the preparation of 1,2,3,5-tetrasubstituted pyrrolyl phenyl ethanol 4a–d

To a solution of 1,2,3,5-tetrasubstituted pyrrolylphenylethanone (1 equiv) in MeOH and DCM (1:1), was added $NaBH_4$ (0.4 equiv) slowly at 0 °C. The resulting reaction mixture was stirred at rt for 12 h. The reaction mixture was quenched with aq. ammonium chloride and concentrated in vacuo. The solvent was removed in vacuo, and the residue was dissolved in EtOAc. The organic phase was washed twice with water and once with brine solution. The organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo and the resulting compound was purified by column chromatography to afford the desired product.

General procedure for the preparation of 1-(4-(1-bromoethyl)phenyl)-2,3,5-trisubstituted-1*H*-pyrrole 5a–d

To a solution of 1,2,3,5-tetrasubstituted pyrrolylphenylethanol (1 equiv) in ether (10 v for 1 g) was added PBr_3 (0.3 equiv) slowly at 0 °C. The resulting mixture was stirred at rt for 1 h. The reaction was quenched with aq. KBr and extracted with ethyl acetate. The organic phase was washed twice with water, once with brine solution. The organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo to get crude, which was directly used in the next step.

General procedure for the preparation of 1-(4-(1-azidoethyl)phenyl)-2,3,5-trisubstituted-1*H*-pyrrole 6a–d

To a solution of 1-(4-(1-bromoethyl)phenyl)-2,3,5-trisubstituted-1*H*-pyrrole (1 equiv) in DCM:water (1:1), was added sodium azide (1.5 equiv) followed by a catalytic amount of TBAB (0.1eq.). The resulting reaction mixture was stirred at rt for 12 h, the residue was dissolved in DCM, the organic phase was washed twice with water, once with brine. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude compound was directly used in next step.

General procedure for the preparation of triazole substituted pyrroles 7a–x

To a solution of 1-(4-(1-azidoethyl)phenyl)-2,3,5-trisubstituted-1*H*-pyrrole (1 equiv) in THF:H_2O (3:2) were added $CuSO_4$ (0.1 equiv), sodium ascorbate (0.05 equiv), and alkyne derivative (1.1 equiv). The reaction mixture was stirred at rt for 2 h. The reaction mixture was diluted with ethyl acetate, the organic phase was washed twice with water, once with brine. The organic phase was dried over anhydrous Na_2SO_4 and filtered. The solvent was removed in vacuo, The crude compound was purified by column chromatography to afford the desired product with good yield.

*4-(1-(1-(4-(3-(4-chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazol-4-yl)butan-1-ol **(7a)***

White solid, mp: 137–138 °C; yield: 83%; ^{1}H NMR: δ 7.27–7.21 (m, 4H, Ar–H), 7.20–7.15 (m, 4H, Ar–H), 7.12–7.04 (m, 7H, Ar–H), 6.99–6.90 (m, 4H, Ar–H), 6.61 (s, 1H, pyrrole-H), 5.77 (qt, 1H, –CH), 3.68 (t, $J = 6.4$ Hz, 2H, –CH_2OH) 2.74 (t, $J = 7.6$ Hz, 2H, –CH_2–), 1.91 (d, $J = 7.0$ Hz, 3H, –CH3), 1.76 (qt, 2H, –CH), 1.65 (qt, 2H, –CH); ^{13}C NMR: δ 21.1 (CH_3–), 25.2 (–CH_2–), 25.4 (–CH_2–), 32.0 (C–CH_2–), 59.2 (–CH_2–OH), 62.2 (–CH–), 110.3 (Pyrrole-CH), 119.1 (Ar–C), 124.1 (Ar–C), 125.7 (Ar–C), 126.6 (Ar–C), 126.7 (Ar–C), 127.9 (Ar–C), 128.1 (Ar–C), 128.5 (Ar–C), 129.4 (Ar–C), 130.4 (Ar–C)), 130.8 (Ar–C), 132.4 (Ar–C), 132.5 (Ar–C),132.9 (Ar–C), 135.1 (Ar–C), 135.5 (Ar–C), 138.6 (Ar–C), 139.0 (Ar–C), 148.0 (Ar–C); IR (KBr): υ 758, 1092, 1211, 1483, 1600, 2934, 3063 cm^{-1}; Electrospray Ionization Mass Spectrometry (ESI-MS): *m/z:* 559 [M + H].

*3-(1-(1-(4-(3-(4-chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazol-4-yl)pyridine **(7b)***

White solid, m.p. 220–222 °C; yield: 89%; ^{1}H NMR: δ 8.60 (d, $J = 4.7$, 1H, Pyridine-H), 8.19 (d, $J = 7.9$ Hz, 1H, pyridine-H), 7.97 (s, 1H, pyridine-H), 7.78 (t, $J = 5.9$ Hz, 1H, pyridine-H), 7.26–7.11 (m, 13H, Ar–H), 7.08–7.05 (m, 2H, Ar–H), 6.99–6.96 (m, 2H, Ar–H), 6.92–6.89 (m, 2 H), 6.69 (s, 1H, pyrrole–H), 5.88 (qt, 1H, –CH–), 1.98 (d, $J = 7.1$, 3H, –CH_3); ^{13}C NMR: δ 21.1 (CH_3–), 59.5 (–CH–), 110.3 (Pyrrole-CH), 118.0 (Ar–C), 124.1 (Ar–C), 125.5 (Ar–C), 125.7 (Ar–C), 126.6 (Ar–C), 126.8 (Ar–C), 127.9 (Ar–C),

128.1 (Ar–C), 128.2 (Ar–C), 128.5 (Ar–C), 128.9 (Ar–C), 129.5 (Ar–C), 130.4 (Ar–C), 130.4 (Ar–C), 130.8 (Ar–C), 132.4 (Ar–C), 132.5 (Ar–C), 133.0 (Ar–C), 135.1 (Ar–C), 135.5 (Ar–C), 138.8 (Ar–C), 147.7(Ar–C); IR (KBr): υ 758, 1091, 1179, 1484, 1601, 2921, 3057 cm^{-1}; ESI-MS: *m/z:* 578 [M + H].

*2-(1-(1-(4-(3-(4-Chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazol-4-yl)ethanol* ***(7c)***

White solid, m.p. 209–211 °C; yield: 87%; ^{1}H NMR: δ7.25–7.20 (m, 4H, Ar–H), 7.19–7.15 (m, 5H, Ar–H), 7.12–7.05 (m, 6H, Ar–H), 6.98 (s, 1H, triazole–H), 6.93 (t, $J = 8.3$ Hz, 3H, Ar–H) 6.67 (s, 1H, pyrrole– H), 5.77 (qt, *J*, 1H, –CH), 3.95 (t, $J = 5.2$ Hz, 2H, $-CH_2OH$), 2.94 (t, $J = 5.2$ Hz, 2H, $-CH_2-$), 1.92 (d, $J = 6.7$ Hz, 3H, $-CH_3$); ^{13}C NMR: δ 21.1 (CH_3-), 28.6 ($-CH_2-$), 59.4 ($-CH_2-OH$), 61.5 (–CH–), 110.3 (pyrrole-CH), 120.0 (Ar–C), 124.1 (Ar–C), 125.8 (Ar–C), 126.6 (Ar–C), 126.7 (Ar–C), 127.9 (Ar–C), 128.1 (Ar–C), 128.1 (Ar–C), 128.2 (Ar–C), 128.5 (Ar–C), 129.5 (Ar–C), 130.4 (Ar–C), 130.9 (Ar–C), 132.4 (Ar–C), 132.5 (Ar–C), 132.9 (Ar–C), 135.1 (Ar–C), 135.5 (Ar–C), 138.7 (Ar–C), 138.8 (Ar–C); IR (KBr): υ 759, 1046, 1207, 1484, 1602, 2929, 3057 cm^{-1}; ESI-MS: *m/z:* 545 [M + H].

*1-(1-(4-(3-(4-Chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl) phenyl)ethyl)-4-p-tolyl-1*H*-1,2,3-triazole* ***(7d)***

White solid, m.p. 185–187 °C; yield: 95%; ^{1}H NMR: δ 7.76–7.52 (m, 4H, Ar–H), 7.51–7.04 (m, 19H, Ar–H), 6.69 (s, 1H, pyrrole–H), 5.87 (qt, 1H, –CH), 2.37 (s 3H, $-CH_3$), 2.02 (d, $J = 7.0$ Hz, 3H, $-CH_3$); ^{13}C NMR: δ 21.2 (CH_3-CH-), 21.3 ($Ar-CH_3$), 59.6 (–CH–), 109.1 (pyrrole-CH), 117.8 (Ar–C), 120.6 (Ar–C), 125.1 (Ar–C), 125.5 (Ar–C), 125.8 (Ar–C), 125.9 (Ar–C), 126.7 (Ar–C), 127.2 (Ar–C), 127.6 (Ar–C), 127.6 (Ar–C), 128.0 (Ar–C), 128.1 (Ar–C), 128.3, (Ar–C), 128.6 (Ar–C), 128.9 (Ar–C), 129.4 (Ar–C), 132.4 (Ar–C), 134.7 (Ar–C), 134.9 (Ar–C), 138.0 (Ar–C), 138.3 (Ar–C), 140.3 (Ar–C), 142.4 (Ar–C), 147.9 (Ar–C); IR (KBr): υ 759, 1074, 1226, 1451, 1603, 2922, 3030 cm^{-1}; ESI-MS: *m/z*: 591 [M + H].

*1-(1-(4-(3-(4-Chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl) phenyl)ethyl)-4-hexyl-1*H*-1,2,3-triazole* ***(7e)***

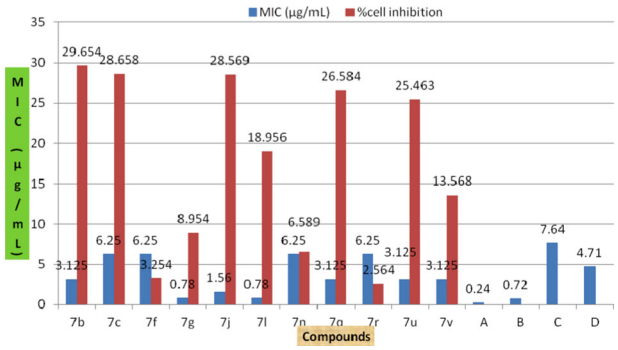
White solid, m.p. 180–181 °C; yield: 90%; ^{1}H NMR: δ 7.29–7.01 (m, 16H, Ar–H, triazole-H), 6.94 (t, $J = 10.7$ Hz, 3H, Ar–H), 6.67 (s, 1H, pyrrole-H), 5.76 (qt, 1H, –CH), 2.70 (t, $J = 6.9$ Hz, 2H, $-CH_2$), 1.91 (d, $J = 6.6$ Hz, 3H, $-CH_3$), 1.72–1.59 (m, 2H, $-CH_2-$), 1.43–1.19 (m, 6H, $-CH_2-$), 0.88 (t, $J = 6.9$ Hz, 3H, $-CH_3$); ^{13}C NMR: δ 14.1 (CH_3-CH_2-), 21.2 (CH_3-CH-), 22.5 ($-CH_2-$), 25.8 ($-CH_2-$), 29.0 ($-CH_2-$), 29.4 ($-CH_2-$), 31.5($-CH_2-$), 59.2 (–CH–), 110.2 (pyrrole-CH), 119.0 (Ar–C), 123.4 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.6 (Ar–C), 127.9 (Ar–C), 128.1 (Ar–C), 128.6 (Ar–C), 128.6 (Ar–C), 129.3 (Ar–C), 129.5 (Ar–C), 131.2 (Ar–C), 132.7 (Ar–C), 134.6 (Ar–C), 136.0 (Ar–C), 136.7 (Ar–C), 138.7(Ar–C), 139.0(Ar–C); IR (KBr): υ 758, 1039, 1207, 1484, 1601, 2925, 3058 cm^{-1}; ESI-MS: *m/z*: 585 $[M + H]^+$; High-resolution mass spectra (HRMS) (ESI) calcd for $C_{38}H_{38}N_4Cl$, 585.27895 $[M + H]^+$, found 585.27900.

*1-(1-(4-(3-(4-Chlorophenyl)-2,5-diphenyl-1*H*-pyrrol-1-yl) phenyl)ethyl)-4-(4-pentylphenyl)-1*H*-1,2,3-triazole* ***(7f)***

White solid, m.p. 196–198 °C; yield: 92%; ^{1}H NMR: δ 7.71 (d, $J = 7.9$ Hz, 2H, Ar–H), 7.48 (s, 1H, triazole-H), 7.28–7.20 (m, 6H, Ar–H), 7.19–7.14 (m, 5H, Ar–H), 7.13–7.06 (m, 5H, Ar–H), 6.90 (d, $J = 8.3$ Hz, 2H, Ar–H), 6.89 (d, $J = 8.3$ Hz, 2H, Ar–H), 6.67 (s, 1H, pyrrole-H), 5.84 (qt, 1H, –CH), 2.63 (t, $J = 7.5$ Hz, 2H, $-CH_2-$), 1.97 (d, $J = 6.9$ Hz, 3H, $-CH_3$), 1.67–1.57 (m, 4H, $-CH_2-$), 1.37–1.28 (m, 2H, –CH), 0.89 (t, $J = 6.6$ Hz, 3H, $-CH_3$); ^{13}C NMR: δ 14.0 (CH_3-CH_2-), 21.1 (CH_3-CH-), 22.5 ($-CH_2-$), 31.0 ($-CH_2-$), 31.4 ($-CH_2-$), 35.6 ($-CH_2-$), 59.4 (–CH–), 110.3 (pyrrole-CH), 117.7 (Ar–C), 124.1 (Ar–C), 125.5 (Ar–C), 125.7 (Ar–C), 126.6 (Ar–C), 126.8 (Ar–C), 127.8 (Ar–C), 128.0 (Ar–C), 128.2 (Ar–C), 128.6 (Ar–C), 128.8 (Ar–C), 129.5 (Ar–C), 130.5 (Ar–C), 130.8 (Ar–C), 132.4 (Ar–C), 132.5 (Ar–C), 133.0(Ar–C), 135.2(Ar–C), 135.5 (Ar–C), 138.7 (Ar–C), 138.9 (Ar–C), 143.1(Ar–C), 147.9 (Ar–C); IR (KBr): υ 758, 1092, 1224, 1483, 1601, 2926, 3026 cm^{-1}; ESI-MS: *m/z:* 647 [M + H].

(1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1H-pyrrol-1-yl)phenyl) ethyl)-1H-1,2,3-triazol-4-yl)methanol ***(7g)***

White solid, m.p. 93–95 °C; yield: 87%; ^{1}H NMR: δ 7.29 (s, 1H, triazole-H), 7.26–7.11 (m, 8H, Ar–H), 7.09–7.04 (m, 4H, Ar–H), 6.98 (d, $J = 8.3$ Hz 2H, Ar–H), 6.94(d, $J = 7.9$ Hz, 2H, Ar–H), 6.88 (d, $J = 8.0$, 2 H), 6.69 (s, 1H, pyrrole-H), 5.78 (qt, 1H, –OH), 4.77 (s, 2H, $-CH_2-$), 2.28 (s, 3H, $-CH_3$), 1.91 (d, $J = 7.1$ Hz, 3H, –CH3); ^{13}C NMR: δ 21.2 (CH_3-CH-), 21.2 (CH_3-Ar), 56.4 ($-CH_2-OH$), 59.6 (–CH–), 110.1 (pyrrole-CH), 120.2 (Ar–C), 123.4 (Ar–C), 125.4 (Ar–C), 126.4 (Ar–C), 126.6 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 129.2 (Ar–C), 129.5 (Ar–C), 131.1 (Ar–C), 132.0 (Ar–C), 132.6 (Ar–C),134.5 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.1 (Ar–C), 139.1 (Ar–C), 147.5 (Ar–C); IR (KBr): υ 759, 1031, 1211, 1486, 1601, 2921, 3030 cm^{-1}; ESI-MS: *m/z*: 510 $[M + H]^+$; HRMS (ESI) calcd for $C_{34}H_{31}ON_4$, 511.24924 $[M + H]^+$, found: 511.24870.



A = rifampicin, B = isoniazid, C = ethambutol, D = ciprofloxacin

Fig. 4 Graphical representation of anti-tubercular activity (MIC < 12.5 µg/mL) and cytotoxicity A = rifampicin, B = isoniazid, C = ethambutol, and D = ciprofloxacin

Table 2 Percentage (%) of cell inhibition and selectivity index (SI) values of triazole linked pyrrole derivatives (**7a–x**) against HEK-293Tcell line

No	MIC (µg/mL)	% inh	IC50 approximation	SI index
7b	3.125	29.654	>50	~ 16
7c	6.25	28.658	>50	~ 8
7f	6.25	3.254	>>50	~ 8
7g	0.78	8.954	>>50	~ 64.1
7j	1.56	28.569	>50	~ 32
7l	0.78	18.956	>50	~ 64.1
7n	6.25	6.589	>>50	~ 8
7q	3.125	26.584	>>50	~ 16
7r	6.25	2.564	>>50	~ 8
7u	3.125	25.463	>50	~ 16
7v	3.125	13.568	13.568	~ 16

% inh: Percentage (%) of cell inhibition

*3-(1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)pyridine* ***(7h)***

White solid, m.p. 176–178 °C; yield: 90%; ^{1}H NMR: δ 8.59 (s, 1H, pyridine-H), 8.19 (d, $J = 2.2$ Hz, 1H, pyridine-H), 7.95 (s, 1H, pyridine-H), 7.79(t, $J = 6.8$ Hz, 1H, pyridine-H), 7.27–7.17 (m, 8H, Ar–H), 7.15–7.07 (m, 5H, Ar–H), 6.99–6.93 (m, 4H, Ar–H), 6.87 (d, $J = 7.7$ Hz, 2 H), 6.69 (s, 1H, pyrrole-H), 5.87 (qt, 1H, –CH–), 2.22 (s, 3H, –CH_3), 1.97(d, $J = 6.7$ Hz, 3 H); ^{13}C NMR: δ 21.1 (CH_3–CH–), 21.2 (CH_3–Ar), 59.5 (–CH–), 110.1 (pyrrole–CH), 117.7 (Ar–C), 123.4 (Ar–C), 125.4 (Ar–C), 126.4 (Ar–C), 126.7 (Ar–C), 127.7 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 129.3 (Ar–C), 129.4 (Ar–C), 129.6 (Ar–C), 131.2 (Ar–C), 132.1(Ar–C), 132.7 (Ar–C), 134.6 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 137.9 (Ar–C), 138.3 (Ar–C), 139.1 (Ar–C), 147.7 (Ar–C); IR (KBr): υ 758, 1078, 1202, 1485, 1599, 2987, 3027 cm^{-1}; ESI-MS: *m/z:* 558 $[M + H]^+$; HRMS (ESI) calcd for $C_{38}H_{32}N_5$, 558.26550 $[M + H]^+$, found: 558.26564.

*1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-4-phenyl-1*H*-1,2,3--triazole* ***(7i)***

White solid, m.p. 150–152 °C; yield: 92%; ^{1}H NMR: δ7.79 (d, 2H, $J = 7.7$ Hz, Ar–H), 7.47 (s, 1H, triazole-H), 7.42 (t, $J = 7.6$ Hz, 2H, Ar–H), 7.33 (t, $J = 7.1$ Hz, 1H, Ar–H), 7.26–7.07 (m, 12H, Ar–H), 7.00 (d, 2H, $J = 8.2$ Hz, Ar–H), 6.90 (qt, 4H, Ar–H), 6.69 (s, 1H, pyrrole-H), 5.82 (qt, $J =$ 1H, –CH), 2.23 (s, 3H, –CH_3) 1.96 (d, $J = 7.0$ Hz, 3H, –CH_3; ^{13}C NMR: δ 21.1 (CH_3–CH–), 21.1 (CH_3–Ar), 59.5 (–CH–), 110.1 (pyrrole-CH), 118.0(Ar–C), 123.3 (Ar–C), 125.4 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.7 (Ar–C), 127.9 (Ar–C), 128.5 (Ar–C), 18.6(Ar–C), 128.7 (Ar–C), 129.3 (Ar–C), 129.6 (Ar–C), 130.5 (Ar–C), 131.1 (Ar–C), 132.1 (Ar–C), 132.7 (Ar–C), 134.5 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.2 (Ar–C), 139.1 (Ar–C), 147.6 (Ar–C); IR (KBr): υ 760, 1077, 1202, 1485, 1600, 2920, 3030 cm^{-1}; ESI-MS: *m/z:* 579 $[M + Na]^+$; HRMS (ESI) calcd for $C_{41}H_{31}N_4$, 579.25256 $[M + H]^+$, found: 557.27041.

*2-(1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)ethanol* ***(7j)***

White solid, m.p. 99–101 °C; yield: 85%; ^{1}H NMR: δ 7.29–7.11 (m, 9H, Ar–H), 7.10–7.01 (m, 3H, Ar–H), 7.00–6.85 (m, 7H, Ar–H), 6.68 (s, 1H, pyrrole-H), 5.75 (qt, 1H, –CH), 4.12–3.77 (m, 2H, –CH_2OH) 2.89 (t, $J = 10.1$ Hz, 2H, –CH_2–), 2.27 (s, 3H, –CH_3), 1.90 (d, $J = 6.7$ Hz, 3H, –CH3); ^{13}C NMR: δ 21.1 (CH_3–CH–), 21.2 (CH_3–Ar), 28.6 (–CH_2–), 59.5 (–CH–), 61.4 (–CH_2–OH), 110.1 (pyrrole-CH), 123.4 (Ar–C), 125.4 (Ar–C), 126.3 (Ar–C), 126.5 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.6 (Ar–C), 129.2 (Ar–C), 129.5 (Ar–C), 131.1 (Ar–C), 132.0 (Ar–C), 132.6 (Ar–C),134.5 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.3 (Ar–C), 139.0 (Ar–C); IR (KBr): υ 759, 1047, 1213, 1485, 1600, 2921, 3348 cm^{-1}; ESI-MS: *m/z:* 525 $[M + H]$; HRMS (ESI) calcd for $C_{34}H_{38}ON_2Cl$, 525.26672 $[M + H]^+$, found: 525.26429.

*4-(1-(1-(4-(2,3-diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)butan-1-ol* ***(7k)***

White solid, m.p. 90–93 °C; Yield: 79%; ^{1}H NMR: δ 7.27–7.11 (m, 8H, Ar–H), 7.10–7.01 (m, 4H, Ar–H), 7.00–6.86 (m, 6H, Ar–H), 6.68 (s, 1H, triazole-H), 5.77 (qt, 1H, –CH), 3.68 (t, $J = 6.1$ Hz, 2H, –CH_2OH), 2.73 (t, $J =$ 7.4 Hz, 2H, –CH_2–), 2.28 (s, 3H, –CH_3), 1.89 (d, $J = 7.0$ Hz, 3H, –CH_3), 1.75 (qt, 2H, –CH_2), 1.63 (qt, 2H, –CH_2); ^{13}C NMR: δ 21.1 (CH_3–CH–), 21.2 (CH_3–Ar), 25.2

(–CH_2–), 25.5 (–CH_2–), 32.1 (–CH_2–), 59.3 (–CH–), 62.2 (–CH_2–OH), 110.1 (pyrrole-CH), 123.4 (Ar–C), 125.4 (Ar–C), 126.3 (Ar–C), 126.5 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.5(Ar–C), 129.3(Ar–C), 129.5 (Ar–C), 131.1 (Ar–C), 132.0 (Ar–C), 132.7 (Ar–C), 134.5 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.6 (Ar–C), 138.9 (Ar–C); IR (KBr): υ 759, 1041, 1212, 1485, 1600, 2935, 3052 cm^{-1}; ESI-MS: *m/z*: 553 $[M + H]^+$; HRMS (ESI) calcd for $C_{37}H_{37}ON_4$, 553.29655 $[M + H]^+$, found: 553.29666.

*1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-4-p-tolyl-1*H*-1,2,3-triazole* ***(7l)***

White solid, m.p. 185–187 °C; yield: 93%; ^{1}H NMR: δ 7.68 (d, $J = 7.5$ Hz, 2H, Ar–H), 7.43 (s, 1H, triazole-H), 7.27–7.20 (m, 6H, Ar–H), 7.19–7.06 (m, 8H, Ar–H), 6.99 (d, $J = 8.3$ Hz, 2H, Ar–H), 6.91 (qt, 4H, Ar–H), 6.69 (s, 1H, pyrrole-H), 5.83 (qt, 1H, –CH), 2.38 (s 3H, –CH_3), 2.24 (s, 3H, –CH_3), 1.96 (d, $J = 6.7$ Hz, 3H, –CH_3), 1.92 (d, $J = 6.7$ Hz, 2H, –CH_3); ^{13}C NMR: δ 21.0 (CH_3–CH–), 21.1 (CH_3–Ar), 21.2 (CH_3–Ar), 59.5 (–CH–), 110.1(pyrrole-CH), 117.7 (Ar–C), 123.3 (Ar–C), 125.4 (Ar–C), 126.3 (Ar–C), 126.7 (Ar–C), 127.9 (Ar–C), 128.5 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.4 (Ar–C), 129.6 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.7 (Ar–C), 132.9 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.6 (Ar–C), 137.9 (Ar–C), 138.2 (Ar–C), 139.2 (Ar–C), 147.7 (Ar–C); IR (KBr): *υ* 757, 1077, 1225, 1485, 1601, 2921, 3028 cm^{-1}; ESI-MS: *m/z:* 593 $[M + Na]^+$; HRMS (ESI) calcd for C42 H33 N4Na, 593.26874 $[M + Na]^+$, found: 593.26866.

*1-(1-(4-(2,3-Diphenyl-5-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-4-(4-pentylphenyl)-1*H*-1,2,3-triazole* ***(7m)***

White solid, mp: 128–131 °C; yield: 90%; ^{1}H NMR: δ 7.69 (d, $J = 8.3$ Hz, 2H, Ar–H), 7.43 (s, 1H, triazole-H) 7.28–7.06 (m, 14H, Ar–H), 6.98 (d, $J = 8.4$ Hz, 2H, Ar–H), 6.95–6.86 (m, 4H, Ar–H), 6.69 (s, 1H, Pyrrole- H), 5.81 (qt, 1H, –CH), 2.63 (t, $J = 7.7$ Hz, 2H, –CH2–), 2.24 (s 3H, –CH_3), 1.96 (d, $J = 6.9$ Hz, 3H, –CH3), 1.69–1.58 (m, 2H, –CH_2–),1.37–1.24 (m, 4H, –CH_2–), 0.89 (t, $J = 6.7$ Hz, 3H, –CH_3); ^{13}C NMR: δ 13.9 (CH_3–CH–), 21.0 (CH_3–CH–), 21.1 (CH_3–Ar), 22.4 (–CH_2–), 31.0 (–CH_2–), 31.3 (–CH_2–), 35.6 (–CH_2–), 59.5 (–CH–), 110.1 (pyrrole-CH), 117.7 (Ar–C), 123.4 (Ar–C), 125.4 (Ar–C), 126.4 (Ar–C), 126.6 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 129.3 (Ar–C), 129.6 (Ar–C), 131.1 (Ar–C), 132.1 (Ar–C), 132.7, (Ar–C), 134.6 (Ar–C), 134.6 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.4 (Ar–C), 139.1 (Ar–C), 143.0 (Ar–C), 147.7 (Ar–C); IR (KBr): *υ* 757, 1074, 1215, 1485, 1600, 2853, 2924 cm^{-1}; ESI-MS: *m/z:* 627 $[M + H]$; HRMS (ESI) calcd for C44 H43 N4, 627.34822 $[M + H]$, found: 627.34851.

*4-(1-(1-(4-(3-phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)butan-1-ol* ***(7n)***

White solid, m.p. 92–94 °C; yield: 88%; ^{1}H NMR: δ 7.23–6.85 (m, 18H, Ar–H), 6.66 (s, 1H, pyrrole- H), 5.74 (qt, 1H, –CH), 3.68 (t, $J = 5.9$ Hz, 2H, –CH_2OH), 2.73 (t, $J = 6.2$ Hz, 2H, –CH_2–), 2.29 (s, 3H, –CH_3), 2.28 (s, 3H, –CH_3) 1.89 (d, $J = 5.7$ Hz, 3H, –CH3), 1.76 (qt, 2H, –CH_2–), 1.64 (qt, 2H, –CH_2); ^{13}C NMR: δ 21.0 (CH_3–CH–), 21.1 (CH_3–Ar–), 21.1 (CH_3–Ar), 25.2 (–CH_2–), 25.4 (–CH_2–), 32.0 (–CH_2–), 59.2 (–CH–), 62.1 (–CH_2–OH–), 110.1 (pyrrole-CH), 119.1 (Ar–C), 123.3 (Ar–C), 126.2 (Ar–C), 126.5 (Ar–C), 127.8 (Ar–C), 128.4 (Ar–C), 128.5 (Ar–C), 128.7 (Ar–C), 129.4 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.7 (Ar–C), 132.9 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.5 (Ar–C), 138.5 (Ar–C), 139.0 (Ar–C), 147.9 (Ar–C); IR (KBr): *υ* 762, 1077, 1263, 1491, 1599, 2919, 3031 cm^{-1}; ESI-MS: *m/z*: 567 $[M + H]^+$.

*3-(1-(1-(4-(3-Phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)pyridine* ***(7o)***

White solid, mp: 179–181 °C; yield: 91%; ^{1}H NMR: δ 8.59 (d, $J = 4.5$ Hz, 1H, Pyridine-H), 8.19 (d, $J = 7.5$ Hz 1H, Pyridine-H), 7.96 (s, 1H, Pyridine-H), 7.79(t, $J = 14.4$ Hz, 1H, Pyridine-H), 7.28–6.84 (m, 18H, Ar–H), 6.67 (s, 1H, Pyrrole-H), 5.87 (qt, 1H, –CH–), 2.30 (s, 3H, –CH_3), 2.22 (s, 3H, –CH_3), 1.96(d, $J = 7.5$, 3 H); ^{13}C NMR: δ 21.0 (CH_3–CH–), 21.1 (CH_3–Ar), 21.1 (CH_3–Ar), 59.6 (–CH–), 110.1 (pyrrole-CH), 120.1 (Ar–C),120.6 (Ar–C), 122.8 (Ar–C), 123.3 (Ar–C), 126.3 (Ar–C), 126.6 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.3 (Ar–C), 129.5 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.6 (Ar–C), 133.0 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.6 (Ar–C), 136.9 (Ar–C), 138.0 (Ar–C), 139.2 (Ar–C), 148.2 (Ar–C), 149.2(Ar–C), 150.1 (Ar–C); IR (KBr): *υ* 760, 1080, 1213, 1491, 1516, 2919, 3050 cm^{-1}; ESI-MS: *m/z:* 572 $[M + H]^+$; HRMS (ESI) calcd for C39 H34 N5, 572.28174 $[M + H]^+$, found: 572.28183.

*4-Phenyl-1-(1-(4-(3-phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl) phenyl)ethyl)-1*H*-1,2,3-triazole* ***(7p)***

White solid, m.p. 180–182 °C; yield: 94%; ^{1}H NMR: δ7.71 (d, $J = 7.3$ Hz, 2H, Ar–H), 7.39 (s, 1H, triazole-H), 7.34 (t, $J = 7.5$ Hz, 1H, Ar–H), 7.26 (d, $J = 7.1$ Hz, 1 H), 7.08–6.98 (m, 10H, Ar–H), 6.92(t, $J = 8.1$ Hz, 4H, Ar–H), 6.85–6.79 (m, 4H, Ar–H), 6.59 (s, 1H, pyrrole- H), 5.74 (qt, 1H, –CH), 2.21 (s, 3H, –CH_3), 2.16 (s, 3H, –CH_3), 1.88 (d, $J =$

6.9 Hz, 3H, –CH_3; ^{13}C NMR: δ 21.1(CH_3–CH–), 21.1 (CH_3–Ar), 59.5 (–CH–), 110.1 (pyrrole-CH), 118.0 (Ar–C), 123.4 (Ar–C), 125.4 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.7 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.1 (Ar–C), 128.5 (Ar–C), 128.6 (Ar–C), 128.7 (Ar–C), 129.3 (Ar–C), 129.6 (Ar–C), 130.5 (Ar–C), 131.1 (Ar–C), 132.1 (Ar–C), 132.7 (Ar–C), 134.5 (Ar–C), 135.9 (Ar–C), 136.7 (Ar–C), 138.2 (Ar–C), 139.1 (Ar–C), 147.6 (Ar–C); IR (KBr): υ 762, 1077, 1273, 1599, 1657, 2986, 3031 cm^{-1}; ESI-MS: *m/z*: 571 [M + H]; HRMS (ESI) calcd for $C_{40}H_{35}N_4$, 571.28623 [M + H], found: 571.28620.

*2-(1-(1-(4-(3-Phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazol-4-yl)ethanol* ***(7q)***

White solid, m.p. 90–92 °C; yield: 83%; ^{1}H NMR: δ 7.62–6.75 (m, 18H, Ar–H), 6.67 (s, 1H, pyrrole- H), 5.76 (qt, 1H, –CH), 4.24–3.72(m, 1H, CH_2OH), 2.91 (t, $J = 3.9$ Hz, 2H, –CH_2) 2.27, (s, 6H, –CH_3), 1.91 (d, $J = 6.2$ Hz, 3H, –CH_3); ^{13}C NMR: δ 21.0 (CH_3–CH–), 21.1 (CH_3–Ar), 21.2 (CH_3–Ar), 29.6 (–CH_2–), 59.7 (–CH–), 61.4 (–CH_2–OH), 110.1 (pyrrole-CH), 123.3 (Ar–C), 126.3 (Ar–C), 126.5 (Ar–C), 127.8 (Ar–C), 128.5 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.3 (Ar–C), 129.5 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.7 (Ar–C), 132.9 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.6 (Ar–C), 138.2 (Ar–C), 139.1 (Ar–C); IR (KBr): υ 760, 1069, 1239, 1484, 1657, 2987, 3048 cm^{-1}; ESI-MS: *m/z:* 538 [M + H]; HRMS (ESI) calcd for $C_{36}H_{35}ON_4$, 539.28054 [M + H], found: 539.28002.

*1-(1-(4-(3-Phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-4-p-tolyl-1*H*-1,2,3-triazole* ***(7r)***

White solid, m.p. 203–205 °C; yield: 92%; ^{1}H NMR: δ 7.60 (d, $J = 8.1$ Hz, 2H, Ar–H), 7.36 (s, 1H, triazole-H) 7.16 (d, $J = 9.0$ Hz, 2H, Ar–H), 7.08–6.98 (m, 10H, Ar–H), 6.97–6.89 (m, 3H, Ar–H), 6.85–6.81 (m, 4H, Ar–H), 6.59 (s, 1H, pyrrole-H), 5.74 (qt, 1H, –CH), 2.30, (s, 3H, –CH_3), 2.22 (s, 3H, –CH_3), 2.17 (s, 3H, –CH_3), 1.88 (d, $J = 6.9$ Hz, 3H, –CH3); ^{13}C NMR: δ 21.0 (CH_3–CH–), 21.1 (CH_3–Ar), 21.1 (CH_3–Ar), 21.2 (CH_3–Ar), 59.5 (–CH–), 110.1 (pyrrole-CH), 117.7 (Ar–C), 123.3 (Ar–C), 125.4 (Ar–C), 126.3 (Ar–C), 126.7 (Ar–C), 127.7 (Ar–C), 127.9 (Ar–C), 128.5 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.4 (Ar–C), 129.6 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.7 (Ar–C), 132.9 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.6 (Ar–C), 137.9 (Ar–C), 138.2 (Ar–C), 139.2 (Ar–C), 147.7 (Ar–C); IR (KBr): υ 695, 1076, 1224, 1491, 1599, 2919, 3023 cm^{-1}; ESI-MS: *m/z:* 585 [M + H]; HRMS (ESI) calcd for C41 H37 N4, 585.30127 [M + H], found: 585.30227.

*4-(4-Pentylphenyl)-1-(1-(4-(3-phenyl-2,5-di-p-tolyl-1*H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazole* ***(7s)***

White solid, mp: 137–139 °C; yield: 89%; ^{1}H NMR: δ 7.70 (d, $J = 8.3$ Hz, 2H, Ar–H), 7.43 (s, 1H, triazole-H), 7.24 (d, $J = 8.3$ Hz, 2H, Ar–H), 7.19–7.06 (m, 10H, Ar–H), 7.05–6.96 (m, 3H, Ar–H), 6.90 (qt, 4H, Ar–H), 6.67 (s, 1H, Pyrrole- H), 5.82 (qt, 1H, –CH), 2.63, (t, 2H, –CH_2), 2.30 (s, 3H, –CH_3), 2.24 (s, 3H, –CH_3), 1.96 (d, $J = 7.5$ Hz, 3H, –CH3), 1.70–1.55 (m, 4H, –CH_2–), 1.41–1.28 (m, 2H, –CH2–), 0.89(s, 3H, –CH_3); ^{13}C NMR: δ 13.9 (CH_3–CH_2–), 21.0 (CH_3–CH–), 21.0 (CH_3–Ar), 21.1 (CH_3–Ar), 22.4 (–CH_2–), 31.0 (–CH_2–), 31.3 (–CH_2–), 35.6 (–CH_2–), 59.4 (CH_3–CH–), 110.1 (pyrrole-CH), 117.7 (Ar–C), 123.3 (Ar–C), 125.4 (Ar–C), 126.3 (Ar–C), 126.6 (Ar–C), 127.9 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.4 (Ar–C), 129.6 (Ar–C), 131.1 (Ar–C), 131.8 (Ar–C), 132.7 (Ar–C), 132.9 (Ar–C), 134.4 (Ar–C), 134.9 (Ar–C), 136.6 (Ar–C), 138.2 (Ar–C), 139.1(Ar–C), 143.0 (Ar–C), 147.7 (Ar–C); IR (KBr): υ 760, 1080, 1213, 1490, 1598, 2919, 3048 cm^{-1}; ESI-MS: *m/z:* 641 [M + H]; HRMS (ESI) calcd for C45 H45 N4, 641.36558 [M + H], found: 641.36568.

*3-(1-(1-(4-(2,3,5-Triphenyl-*1H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazol-4-yl)pyridine* ***(7t)***

White solid, m.p. 130–132 °C; yield: 88%; ^{1}H NMR: δ 8.58 (d, $J = 4.5$ Hz, 1H, pyridine-H), 8.18 (d, $J = 7.1$ Hz, 1H, pyridine-H), 7.95 (s, 1H, pyridine-H), 7.77 (t, 1H, pyridine-H), 7.28–7.05 (m, 17H, Ar–H), 7.04–6.95 (m, 3H, Ar–H), 6.70 (s, 1H, pyrrole- H), 5.86 (qt, 1H, –CH), 1.96 (d, $J = 6.7$ Hz, 3H, –CH_3); ^{13}C NMR: δ 21.1 (CH_3–CH–), 59.6 (–CH–), 110.1 (pyrrole-CH), 120.1 (Ar–C), 120.6 (Ar–C), 122.8 (Ar–C), 123.6 (Ar–C), 125.5 (Ar–C), 126.5 (Ar–C), 126.6 (Ar–C), 127.1 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 129.5 (Ar–C), 131.3 (Ar–C), 132.0 (Ar–C), 132.3 (Ar–C), 132.5 (Ar–C), 134.7(Ar–C), 135.8 (Ar–C), 136.9 (Ar–C), 138.2 (Ar–C), 139.0 (Ar–C), 148.2 (Ar–C), 149.2 (Ar–C), 150.1 (Ar–C); IR (KBr): υ 758, 1078, 1180, 1483, 1600, 2924, 3051 cm^{-1}; ESI-MS: *m/z:* 544 [M + H].

*4-Phenyl-1-(1-(4-(2,3,5-triphenyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazole* ***(7u)***

White solid, m.p. 161–164 °C; yield: 92%; ^{1}H NMR: δ 7.79 (d, $J = 7.1$ Hz,2H, Ar–H), 7.46 (s, 1H, triazole-H) 7.43 (t, $J = 7.7$ Hz, 2H, Ar–H), 7.34 (t, $J = 7.4$ Hz, 1H, Ar–H), 7.26–7.09 (m, 15H, Ar–H), 7.08–6.99 (m, 4H, Ar–H), 6.70 (s, 1H, pyrrole-H), 5.82 (qt, 1H, –CH), 1.97 (d, $J = 7.0$ Hz, 3H, –CH_3); ^{13}C NMR: δ 21.1 (CH_3–CH–), 59.5 (–CH–), 110.1 (pyrrole-CH), 118.1 (Ar–C), 123.6 (Ar–C), 125.5 (Ar–C), 126.5 (Ar–C), 126.7 (Ar–C), 127.1 (Ar–C), 127.8

(Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.1 (Ar–C), 128.5 (Ar–C), 128.7 (Ar–C), 129.6 (Ar–C), 130.5 (Ar–C), 131.4 (Ar–C), 132.0 (Ar–C), 132.4 (Ar–C), 132.6 (Ar–C), 134.7 (Ar–C), 135.8 (Ar–C), 138.4 (Ar–C), 139.1 (Ar–C), 147.6 (Ar–C); IR (KBr): υ 758, 1029, 1207, 1484, 1598, 2936, 3051 cm^{-1}; ESI-MS: *m/z:* 543 [M + H].

*4-(1-(1-(4-(2,3,5-triphenyl-1*H*-pyrrol-1-yl)phenyl)ethyl)-1*H*-1,2,3-triazol-4-yl)butan-1-ol* ***(7v)***

White solid, m.p. 94–96 °C; yield: 82%; ^{1}H NMR: δ 7.29–7.06 (m, 14H, Ar–H), 7.04–6.94 (m, 6H, Ar–H), 6.70 (s, 1H, pyrrole- H), 5.73 (qt, $J = 6.9$ Hz, 1H, –CH), 3.68 (t, $J = 5.9$ Hz, 2H, $–CH_2OH$), 2.73 (t, $J = 7.3$ Hz, 2H, $–CH_2–$), 1.88 (d, $J = 6.7$ Hz, 3H, $–CH_3$), 1.74 (qt, 2H, –CH), 1.64, (qt, 2H,–CH); ^{13}C NMR: δ 21.1 (CH_3–CH–), 25.2 ($–CH_2–$), 25.4 ($–CH_2–$), 32.0 ($–CH_2–$), 59.2 (–CH–), 62.2 ($–CH_2–OH$), 110.1 (pyrrole-CH), 119.1 (Ar–C), 123.0 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.5 (Ar–C), 127.0 (Ar–C), 127.8 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 129.4 (Ar–C), 131.3 (Ar–C), 132.0 (Ar–C), 132.3 (Ar–C), 132.6 (Ar–C), 134.7 (Ar–C), 135.7 (Ar–C), 138.6 (Ar–C), 138.8 (Ar–C), 147.9 (Ar–C); IR (KBr): υ 758, 1040, 1212, 1484, 1600, 2935, 3054 cm^{-1}; ESI-MS: *m/z:* 525 [M + H].

*4-Hexyl-1-(1-(4-(2,3,5-triphenyl-1*H*-pyrrol-1-yl)phenyl) ethyl)-1*H*-1,2,3-triazole* ***(7w)***

White solid, m.p. 115–117 °C; yield: 88%; ^{1}H NMR: δ 7.23 (t, $J = 6.7$ Hz, 2H, Ar–H), 7.19–7.09 (m, 10H, Ar–H), 7.06–6.93 (m, 8H, Ar–H), 6.70 (s, 1H, pyrrole- H), 5.75 (qt, 1H, –CH), 2.68 (t, $J = 7.5$ Hz, 2H, $–CH_2–$), 1.88 (d, $J = 7.5$ Hz, 3H, $–CH_3$), 1.63 (t, $J = 7.5$ Hz, 2H, $–CH_2–$),1.41–1.24 (m, 6H, $–CH_2$), 0.87 (t, $J = 13.4$ Hz, 3H, $–CH_3$); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 14.0 (CH_3–CH_2–), 21.1 (CH_3–CH–), 22.5 ($–CH_2–$), 25.7 ($–CH_2–$), 28.9 ($–CH_2–$), 29.3 ($–CH_2–$), 31.5 ($–CH_2–$), 59.2 (–CH–), 110.1 (pyrrole-CH), 118.9 (Ar–C), 123.6 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.5 (Ar–C), 127.8 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 129.4 (Ar–C), 131.3 (Ar–C), 132.0 (Ar–C), 132.4 (Ar–C), 132.6 (Ar–C), 134.7 (Ar–C), 135.8 (Ar–C), 138.8 (Ar–C), 138.8 (Ar–C), 148.4 (Ar–C); IR (KBr): υ 757, 1068, 1212, 1484, 1599, 2926, 3053 cm^{-1}; ESI-MS: *m/z:* 551 $[M + H]^+$; HRMS (ESI) calcd for $C_{38}H_{39}N_4$, 551.31733 $[M + H]^+$, found: 551.31692.

*4-(4-Pentylphenyl)-1-(1-(4-(2,3,5-triphenyl-1*H*-pyrrol-1-yl) phenyl)ethyl)-1*H*-1,2,3-triazole* ***(7x)***

White solid, m.p. 193–195 °C; yield: 87%; ^{1}H NMR: δ 7.69 (d, $J = 8.0$ Hz, 2H, Ar–H), 7.42 (s, 1H, triazole-H),7.26–7.08 (m, 17H, Ar–H), 7.04–6.98 (m, 4H, Ar–H), 6.70 (s, 1H, pyrrole-H), 5.80 (qt, 1H,–CH), 2.63 (t, $J = 7.6$ Hz, 2H, $–CH_2–$), 1.95 (d, $J = 7.1$ Hz, 3H, $–CH_3$), 1.74–1.59 (m, 2H, $–CH_2–$), 1.37–1.26 (m, 4H, $–CH_2–CH_2–$), 0.89 (t, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR: δ 14.0 (CH_3–CH_2–), 21.1 (CH_3–CH–), 22.4 ($–CH_2–$), 31.0 ($–CH_2–$), 31.4 ($–CH_2–$), 35.6 ($–CH_2–$), 59.4 (–CH–), 110.1 (pyrrole-CH), 117.7 (Ar–C), 123.6 (Ar–C), 125.4 (Ar–C), 125.5 (Ar–C), 126.4 (Ar–C), 126.6 (Ar–C), 127.0 (Ar–C), 127.8 (Ar–C), 127.9 (Ar–C), 128.0 (Ar–C), 128.5 (Ar–C), 128.8 (Ar–C), 129.5 (Ar–C), 131.4(Ar–C), 132.0 (Ar–C), 132.4 (Ar–C), 132.6 (Ar–C), 134.7 (Ar–C), 135.8 (Ar–C), 139.0 (Ar–C), 143.0 (Ar–C), 147.7 (Ar–C); IR (KBr): υ 758, 1076, 1225, 1484, 1599, 2925, 3051 cm^{-1}; ESI-MS: *m/z:* 613 [M + H].

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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