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Design, Synthesis, and Structure–Activity Correlations of Novel Dibenzo[*b,d*]furan, Dibenzo[*b,d*]thiophene, and *N*-Methylcarbazole Clubbed 1,2,3-Triazoles as Potent Inhibitors of *Mycobacterium tuberculosis*

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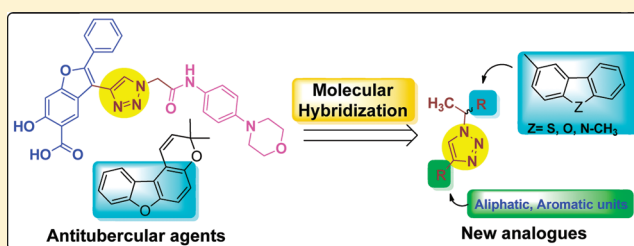
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Supporting Information

ABSTRACT: A molecular hybridization approach is an emerging structural modification tool to design new molecules with improved pharmacophoric properties. In this study, 1,2,3-triazole-based *Mycobacterium tuberculosis* inhibitors and synthetic and natural product-based tricyclic (carbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene) antimycobacterial agents were integrated in one molecular platform to prepare various novel clubbed 1,2,3-triazole hybrids using click chemistry. Structure–activity correlations and in vitro activity against *M. tuberculosis* strain H37Rv of new analogues revealed the order: dibenzo[*b,d*]thiophene > dibenzo[*b,d*]furan > 9-methyl-9*H*-carbazole series. Two of the most potent *M. tuberculosis* inhibitors **13h** and **13q** with MIC = 0.78 µg/mL (~1.9 µM) displayed a low cytotoxicity and high selectivity index (50–255) against four different human cancer cell lines. These results together provided the potential importance of molecular hybridization and the development of triazole clubbed dibenzo[*b,d*]thiophene-based lead candidates to treat mycobacterial infections.



■ INTRODUCTION

Tuberculosis (TB) is an ancient, contagious disease caused by infection with *Mycobacterium tuberculosis* and characterized by tubercle lesions in the lungs.¹ It may also affect the skin, lymph nodes, brain, and almost every other organ. According to the latest WHO report,² TB has become a more prevalent chronic disease in the world today with millions of new cases of infected individuals and millions of deaths being notified each year globally. It is anticipated that by 2020, one billion people will be newly infected, over 125 million people will get sick, and over 30 million will die of TB if control is not further strengthened.^{2,3} TB is also declared to be a global health emergency because of the increase in secondary infections and/or coinfection in immunocompromised patients [such as those infected with human immunodeficiency virus (HIV)] and the emergence of resistant strains of *M. tuberculosis* [multidrug-resistant (MDR) and extensively drug resistant (XDR) TB strains].⁴ The long and complex TB regimen and lack of appropriate treatments are also increasing the burden of TB.⁵ Therefore, the current situation necessitates the re-engineering and repositioning of old drug families for developing new

antimycobacterial entities with novel mechanisms of action to achieve effective TB control even against the resistant forms of TB.^{4–6}

The natural products are essential sources for new antimicrobial agents.⁷ They are generally derived from plants or microbes. They offer promising and amazing chemical diversity, thereby inspiring the development of structurally diverse new molecules to play a major role in drug discovery.⁸ The promising natural antimycobacterials include carbazole alkaloids,⁹ such as Clausine (**1**) and Micromeline (**2**), isolated independently from several sources, and dibenzofuran based on the secondary metabolite of lichen usnic acid (**3**) (Figure 1), isolated from *Cladonia substellata*,¹⁰ and were shown to have moderate antitubercular activity. Modified natural products like synthetic analogues **4**, **5a**, and **5b** of dibenzofuran and carbazole exhibited significantly improved in vitro as well as in vivo antitubercular activity against *M. tuberculosis* H37Rv.¹¹ Structure–activity relationship (SAR) studies direct that the

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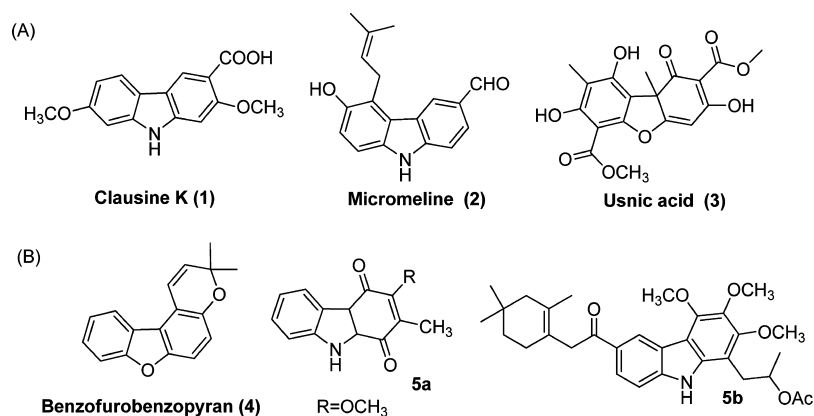


Figure 1. Antitubercular dibenzofuran and carbazole analogues of (A) natural and (B) synthetic origin.

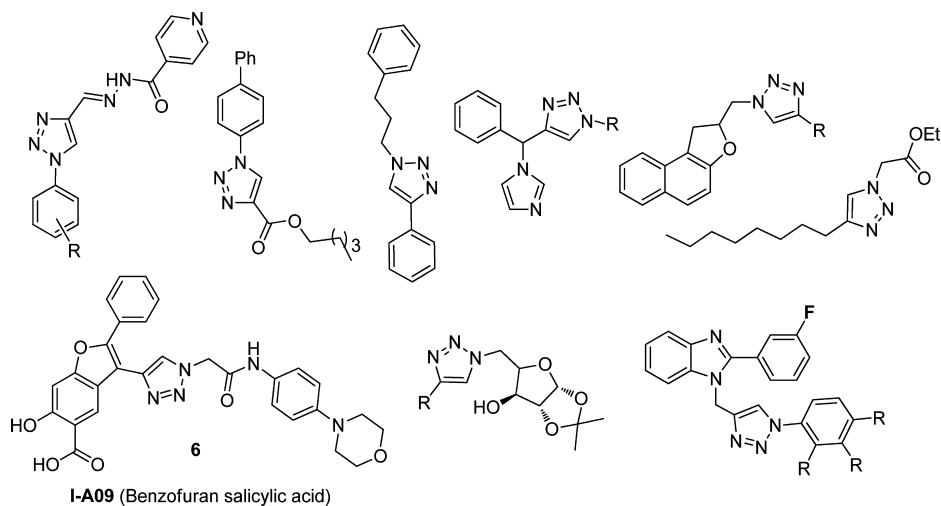


Figure 2. Heterocyclic hybrids of [1,2,3]triazole with antitubercular activity.

presence of dibenzo[*b,d*]furan or a carbazole moiety plays a vital role on their pharmacological properties.^{10,11} On the other hand, 1,2,3-triazoles conjugated with a wide range of heterocyclic moieties were reported¹² to exhibit potent antitubercular activity (Figure 2). Among them, benzofuran salicylic acid derivative **6** (I-A09, Figure 2) is a lead antitubercular agent currently in clinical evaluation.¹³

Our continued interest in developing new antimycobacterial agents¹⁴ led to molecular hybridization¹⁵ of dibenzo[*b,d*]furan or 9-methyl-9*H*-carbazole and 1,2,3-triazole to integrate them in one molecular platform to generate a new scaffold for biological evaluation. Considering the fact that 1,2,3-triazoles were efficiently made through Cu(I)-catalyzed click chemistry,¹⁶ we present here an efficient synthesis of novel 9-methyl-9*H*-carbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene conjugated 1,2,3-triazole hybrids **11a–h**, **12a–h**, and **13a–t**. The inclusion of dibenzo[*b,d*]thiophene in this series is due to structural similarity with dibenzo[*b,d*]furan and recent findings of potential pharmacophoric properties (NU7441 as DNA-dependent protein kinase inhibitor).¹⁷ All of the hybrid heterocycles **11a–h**, **12a–h**, and **13a–t** were evaluated for their in vitro antimycobacterial activity against *M. tuberculosis* H37Rv (ATCC 27294 strain). Structure–antitubercular activity relationship of all of the new compounds were correlated with respect to dibenzo[*b,d*]furan, dibenzo[*b,d*]thiophene, and 9-methyl-9*H*-carbazole skeleton. The most promising antituber-

cular compounds were also evaluated for their in vitro cytotoxicity.

RESULTS AND DISCUSSION

Chemistry. The design strategy adopted here is based on the most recent molecular hybridization approach.¹⁵ Molecular hybridization is a strategy of rational design of new ligands or prototypes based on the recognition of pharmacophoric subunits in the molecular structure of two or more known bioactive derivatives.¹⁸ The adequate fusion of these subunits leads to the design of a new hybrid architecture that maintains preselected characteristics of the original template. Here, a triazole ligand of **6**¹³ and a core structure of natural alkaloids **1–3**^{9,10} were hybridized in one molecular platform for optimized affinity and better pharmacological properties associated with the target diseases, TB. The designed scaffold (Figure 3) has three parts: 1,2,3-triazole as a central backbone, attachment of dibenzo[*b,d*]furan or dibenzothiophene or 9-methyl-9*H*-carbazole to a triazole unit to enhance desired pharmacophoric behavior with druglike properties, and aliphatic or aromatic groups to the other side of the triazole core for lipophilicity. The method adopted for the synthesis of 1,2,3-triazole conjugates was based on a Huisgen 1,3-dipolar cycloaddition reaction (click reaction) of alkynes and azides. The azide precursors **9a**, **9b**, and **9c** required for the preparation of triazole conjugates were synthesized starting

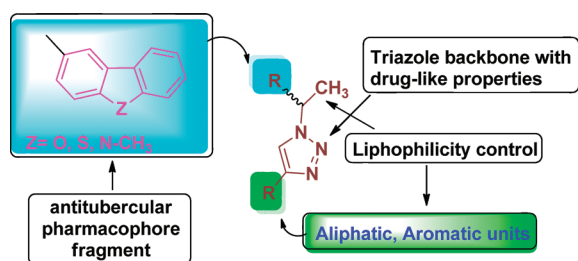
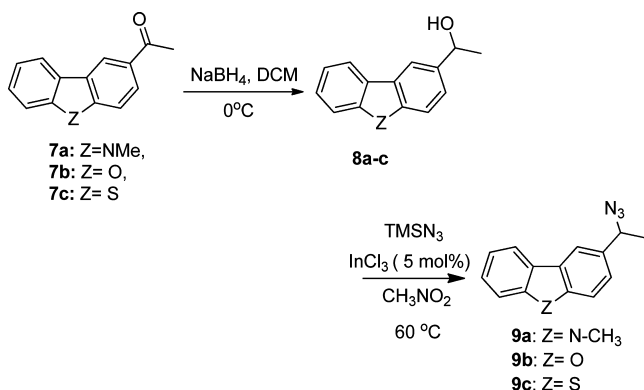


Figure 3. Illustration of the design strategy for library generation.

from 9-methylcarbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene, respectively (Scheme 1). Compounds **7a**, **7b**, and

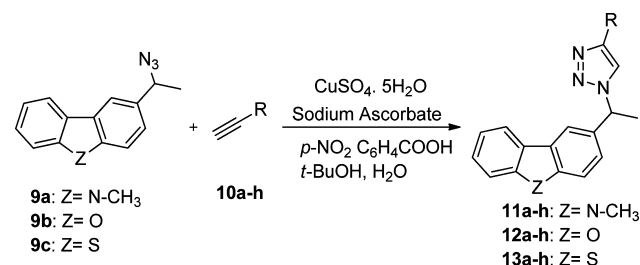
Scheme 1. Synthesis of Azides **9a–c**



7c, prepared by acylation of 9-methylcarbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene, respectively, were reduced to alcohol derivatives **8a–c** using NaBH_4 . The azide building blocks **9a–c** were accomplished in excellent yields (96–98%) from alcohols **8a–c** at 60 °C by a direct InCl_3 -catalyzed protocol using trimethylsilyl azide (TMSN_3).

Initially, to assess the structure–activity correlations with respect to *M. tuberculosis* inhibitory activity, a uniform series of 9-methyl-9*H*-carbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene clubbed 1,2,3-triazoles **11a–h**, **12a–h**, and **13a–h** were synthesized through 1,3-dipolar cycloaddition reaction (Scheme 2) between azides **9a–c** and alkynes **10a–h** (Figure

Scheme 2. Synthesis of 1,2,3-Triazole Hybrid Heterocycles through Click Reaction



4) using copper sulfate and sodium ascorbate at RT in aqueous *tert*-butanol (Table 1) with the addition of 0.5 mol % 4-nitrobenzoic acid.¹⁹ Furthermore, to expand the series, dibenzo[*b,d*]thiophene conjugated triazole analogues **13i–t** were prepared by a cycloaddition reaction between azide building block **9c** and alkynes **10i–t** (Table 2) as described in the Experimental Section. All of the reactions proceeded well in

0.5–6.0 h to give products in excellent yields. All of the compounds were purified through silica gel column chromatography (HPLC purity >95%) and were fully characterized by IR, ^1H nuclear magnetic resonance (NMR), ^{13}C NMR, electrospray ionization (ESI), and high-resolution mass spectral (HRMS) analysis (Supporting Information). The single-crystal X-ray diffraction studies of **13h** unambiguously confirmed the structure (Figure 5).

Biological Evaluation and Structure–Activity Correlations

A total of 36 new 1,2,3-triazole hybrids **11a–h**, **12a–h**, and **13a–t** were screened for *in vitro* activity against *M. tuberculosis* H37Rv (ATCC 27294 strain) using the agar dilution method. The MIC (minimum inhibitory concentration) is defined as the minimum concentration of the compound required to completely inhibit bacterial growth. The MIC values ($\mu\text{g/mL}$ and μM) of all of the synthesized compounds and three standard antitubercular drugs determined in triplicate at pH 7.40 are presented in Tables 1 and 2. Several derivatives displayed MIC values below 6.25 $\mu\text{g/mL}$, a value postulated by the global program for the discovery of new antituberculosis drugs as an upper threshold for the evaluation of new *M. tuberculosis* therapies.^{12d} Twenty-seven compounds from all three series **11a–h**, **12a–h**, and **13a–t** have MIC values in the micromolar range, varying from 1.89 to 41.0 μM . In series **11a–h** containing 9-methyl-9*H*-carbazole unit, two compounds **11g** and **11h**; in series **12a–h** containing dibenzo[*b,d*]furan unit, six compounds **12a–d,g,h**; and in series **13a–h** containing dibenzo[*b,d*]thiophene unit, almost all of the compounds except **13n** are more active than the first-line antitubercular drug pyrazinamide (MIC = 50.8 μM). Ten compounds, **13a**, **13c,d**, **13g,h**, **13k**, and **13p–s**, are more active, and one compound **13f** is equipotent to another first-line antitubercular drug ethambutol (MIC = 7.6 μM). Incidentally, almost all of the compounds from dibenzo[*b,d*]thiophene series are more active than ethambutol. Out of all of the library of compounds tested, two compounds **13h** and **13q** possess the maximum *M. tuberculosis* inhibitory activity with MIC = 1.9 μM (0.78 $\mu\text{g/mL}$) and are 26 times more active than pyrazinamide and four times more active than ethambutol. However, all of the compounds were less active than isoniazid (INH), the most active first-line anti-TB drug. Figure 6 allows a visual comparison of the structure–activity correlations for an uniform series of 9-methyl-9*H*-carbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene clubbed 1,2,3-triazoles **11a–h**, **12a–h**, and **13a–h** with respect to their *M. tuberculosis* inhibitory activity and to that of three standard drugs. From the point of view of the establishment of structure–*M. tuberculosis* inhibitory activity relationships, the data in Table 1 and 2 and Figure 6 disclose that (i) in general, compounds of series **13a–h** have higher activity by several fold than those in series **12a–h**, which, in turn, are more potent than the corresponding compounds in series **11a–h**; that is, structure–activity correlation of uniform series of compounds is in the order series **13** > series **12** > series **11**. (ii) In the series **13a–h**, most of the compounds have low MIC values and are very useful for further evaluation as potential candidates; (iii) in the extended series **13i–t**, introduction of more variations in the lipophilic handle attached to 1,2,3-triazole unit did not show any significant changes in *M. tuberculosis* inhibitory activity as compared to **13a–h**, except in one case, that is, **13n**. The higher *M. tuberculosis* inhibitory activity for dibenzothiophene series suggests a blend of electronic factors underlying the activity due to the presence of sulfur atom. These observations

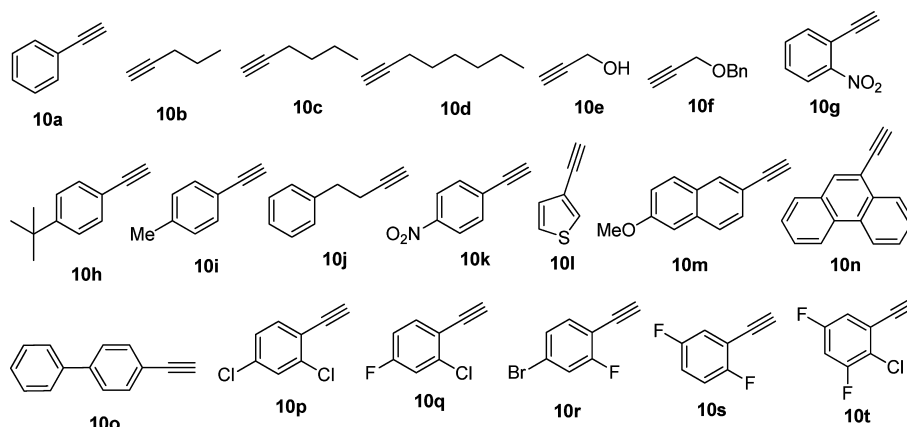


Figure 4. Alkynes 10a–t used in the present study.

Table 1. Synthesis and in Vitro Activity Evaluation (against *M. tuberculosis* H37Rv) of 11a–h, 12a–h, and 13a–h Using Copper-Catalyzed Click Chemistry

entry	azide	alkyne	reaction time (h)	product	yield (%) ^a	CLog P ^b	MIC (μg/mL)	MIC (μM)
1	9a	10a	0.5	11a	96	5.48	25	71
2	9a	10b	1.0	11b	90	4.71	25	78
3	9a	10c	1.5	11c	98	5.24	25	75.3
4	9a	10d	1.5	11d	93	6.30	25	70
5	9a	10e	1.0	11e	87	2.34	25	81.7
6	9a	10f	1.5	11f	82	4.54	25	63.1
7	9a	10g	0.5	11g	94	5.30	12.5	31.5
8	9a	10h	1.0	11h	92	7.31	12.5	30.6
9	9b	10a	1.0	12a	91	5.59	6.25	18.4
10	9b	10b	2.0	12b	84	4.81	12.5	41
11	9b	10c	3.0	12c	93	5.34	12.5	39.2
12	9b	10d	5.0	12d	88	6.40	6.25	18.0
13	9b	10e	2.0	12e	90	2.45	25	85.3
14	9b	10f	2.5	12f	93	4.64	25	65.2
15	9b	10g	4.0	12g	88	5.41	6.25	16.3
16	9b	10h	2.5	12h	94	7.41	6.25	15.8
17	9c	10a	1.0	13a	85	6.05	1.56	4.4
18	9c	10b	3.0	13b	84	5.51	3.13	9.75
19	9c	10c	4.5	13c	88	6.04	1.56	4.66
20	9c	10d	6.0	13d	78	7.10	1.56	4.3
21	9c	10e	3.0	13e	95	2.92	6.25	20.2
22	9c	10f	3.0	13f	97	5.11	3.13	7.84
23	9c	10g	4.5	13g	89	5.88	1.56	3.9
24	9c	10h	6.0	13h	85	7.88	0.78	1.89
25	INH						0.05	0.37
26	ethambutol						1.56	7.6
27	pyrazinamide						6.25	50.08

^aIsolated yield. ^bCLog P calculated using Chemdraw Ultra 12.0 software by Cambridge Soft.

have close relevance to previously reported sulfur-containing nitrofuranyl amides as antituberculosis agents.²⁰

Cytotoxicity Evaluation. The cytotoxicity of 14 most potent antitubercular dibenzo[*b,d*]thiophene-1,2,3-triazole hybrids 13a–c, 13f–k, and 13p–t with MIC ≤ 3.13 μg/mL was assessed by (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay (MTT) assay against A549 (human lung carcinoma epithelial), SK-N-SH (human neuroblastoma), HeLa (human epithelial cervical cancer), and DU145 (human prostate cancer) cell lines. The inhibitory activities (IC₅₀) in μM are summarized in Table 3. The ratios between cytotoxicity (IC₅₀ in μM) and antimycobacterial activity (MIC in μM) in vitro enabled the determination of selectivity index (SI).

Compounds that exhibited SI values greater than 10 in all four cell lines were considered nontoxic.²¹ When comparing the toxicity exhibited by the potent antitubercular dibenzo[*b,d*]thiophene-1,2,3-triazole hybrids 13a–c, 13f–k, and 13p–t using the four cell lines, five compounds 13b, 13i,j, 13s,t exhibited lower SI values (<10) in one or more examined cell lines. The remaining compounds showed low toxicity, that is, higher SI values (Figure 7). The results demonstrated that the compounds 13h and 13q with high inhibitory activity against *M. tuberculosis* also exhibited lowest toxicity, that is, high SI (55–255) against all four cell lines examined.

Table 2. Synthesis and in Vitro Activity Evaluation (MICs) of 13i–t against *M. tuberculosis* H37Rv (ATCC 27294 Strain)

entry	azide	alkyne	reaction time (h)	product	yield (%) ^a	CLog P ^b	MIC (μg/mL)	MIC (μM)
1	9c	10i	2.5	13i	82	6.55	3.13	8.48
2	9c	10j	3.0	13j	93	6.40	3.13	8.17
3	9c	10k	4.0	13k	89	5.88	1.56	3.9
4	9c	10l	5.0	13l	89	5.75	12.5	34.6
5	9c	10m	3.5	13m	94	7.15	12.5	28.7
6	9c	10n	3.5	13n	96	8.40	25	54.9
7	9c	10o	3.0	13o	92	7.94	6.25	14.5
8	9c	10p	6.0	13p	83	7.27	1.56	3.68
9	9c	10q	6.0	13q	85	6.70	0.78	1.91
10	9c	10r	6.0	13r	85	7.10	1.56	3.45
11	9c	10s	6.0	13s	87	6.38	1.56	3.98
12	9c	10t	6.0	13t	84	6.85	3.13	12.5

^aIsolated yield. ^bCLog P calculated using Chemdraw Ultra 12.0 software by Cambridge Soft.

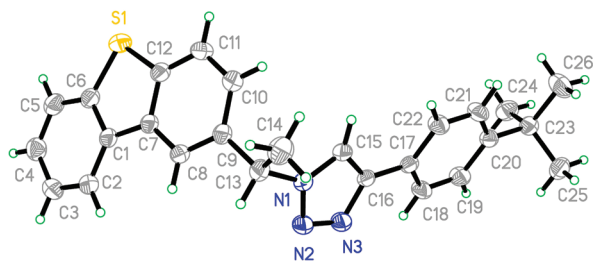


Figure 5. ORTEP representation of compound 13h with thermal displacement ellipsoids drawn at the 30% probability.

CONCLUSIONS

In summary, the new 1,2,3-triazole derivatives 11a–h, 12a–h, and 13a–t, successfully designed through molecular hybridization approach, exhibited potent in vitro antimycobacterial activity against *M. tuberculosis* H37Rv (ATCC 27294 strain) with low toxicity. The synthesis of the 9-methyl-9H-carbazole, dibenzo[*b,d*]furan, and dibenzo[*b,d*]thiophene clubbed 1,2,3-triazoles 11a–h, 12a–h, and 13a–t took advantage of azide and alkyne reactivity in the Huisgen cycloaddition (click

Table 3. Cytotoxicity (IC₅₀ in μM) of Triazole Hybrids 13a–c, 13f–k, and 13p–t against HeLa, A549, DU145, and SK-N-SH Cell Lines^a

T	compd	HeLa	A549	DU145	SK-N-SH
1	13a	329 ± 5.1	444 ± 5.2	90 ± 3.5	291 ± 5.9
2	13b	87 ± 3.9	68 ± 1.8	96 ± 3.6	93 ± 4.5
3	13c	62 ± 3.3	80 ± 2.2	107 ± 3.9	101 ± 4.9
4	13f	438 ± 4.3	189 ± 3.8	225 ± 4.8	103 ± 5.2
5	13g	136 ± 3.8	190 ± 4.2	126 ± 4.5	386 ± 6.8
6	13h	191 ± 4	482 ± 6.6	105 ± 3.7	260 ± 5.5
7	13i	164 ± 3.9	108 ± 4.2	174 ± 5.1	32 ± 2.9
8	13j	79 ± 2.5	78 ± 3.5	100 ± 4.2	ND
9	13k	210 ± 4.2	852 ± 7.2	138 ± 5.2	30 ± 2.8
10	13p	162 ± 3.8	400 ± 5.5	150 ± 5.5	477 ± 6.3
11	13q	155 ± 3.7	249 ± 5.2	147 ± 6.1	342 ± 5.9
12	13r	457 ± 4.6	219 ± 3.8	222 ± 6.5	76 ± 3.2
13	13s	96 ± 4.4	272 ± 4.7	767 ± 7.2	21 ± 1.9
14	13t	116 ± 4.1	507 ± 6.5	120 ± 4.5	46 ± 2.2

^aND, not determined; IC₅₀ values are indicated as means ± SD of three independent experiments.

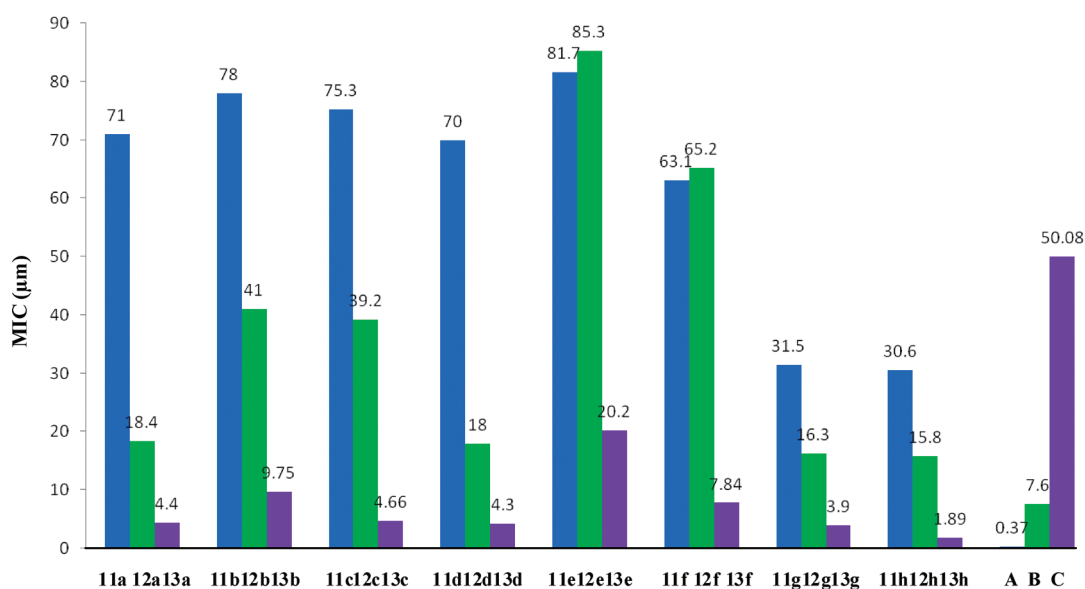


Figure 6. Comparative analysis of triazole analogues 11a–h, 12a–h, and 13a–h with respect to their in vitro activity against *M. tuberculosis* H37Rv (ATCC 27294 strain) expressed by MIC in μM (controls: A, INH; B, ethambutol; and C, pyrazinamide).

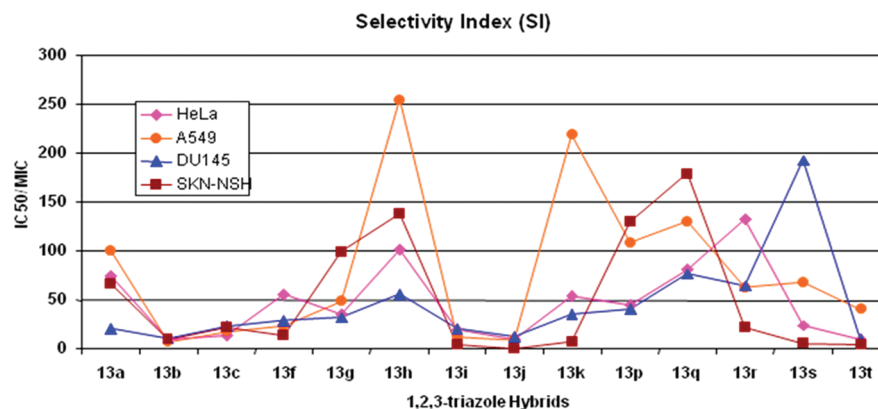


Figure 7. SI for triazole hybrids **13a–c**, **13f–k**, and **13p–t** against HeLa, A549, DU145, and SK-N-SH cell lines. SI is the ratio of cytotoxicity (IC_{50} in μM) to in vitro activity against *M. tuberculosis* H37Rv (ATCC 27294 strain) expressed as MIC in μM .

chemistry) using $CuSO_4$ and sodium ascorbate with the addition of a small amount (0.5 mol %) of 4-nitrobenzoic acid. Several derivatives displayed MIC values below $6.25 \mu g/mL$, a value postulated by the global program for the discovery of new antituberculosis drugs as an upper threshold for the evaluation of new *M. tuberculosis* therapies. From the point of view of the establishment of SAR, the order of the *M. tuberculosis* inhibitory activity of the compounds is dibenzo-[*b,d*]thiophene series **13** > dibenzo[*b,d*]furan series **12** > 9-methyl-9*H*-carbazole series **11**. Out of the library of all compounds tested, two compounds, **13h** and **13q**, possess the maximum *M. tuberculosis* inhibitory activity with MIC = $1.9 \mu M$ ($0.78 \mu g/mL$) and is 26 times more active than pyrazinamide and four times more active than ethambutol and has low toxicity profile (SI in the range of 55–255 for four different cell lines). We believe that the observed results should be useful in guiding future global efforts to discover new compounds with improved antitubercular activity.

EXPERIMENTAL SECTION

Chemistry. Reagents and all solvents were analytically pure and were used without further purification. All reactions were carried out in oven-dried flasks with magnetic stirring. All of the experiments were monitored by analytical thin-layer chromatography (TLC) performed on silica gel GF254 precoated plates. After elution, the plate was visualized under UV illumination at 254 nm for UV active materials. Staining with PMA and charring on a hot plate achieved further visualization. Solvents were removed in vacuo and heated on a water bath at $35^\circ C$. Silica gel finer than 200 mesh was used for column chromatography. Columns were packed as a slurry of silica gel in hexane and equilibrated with the appropriate solvent/solvent mixture prior to use. The compounds were loaded neat or as a concentrated solution using the appropriate solvent system. Applying pressure with an air pump assisted the elution. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. Appropriate names for all of the new compounds were given with the help of ChemBioOffice 2010. Melting points were measured with a Fischer–Johns melting point apparatus and are uncorrected. The purities of all of the compounds (>95%) used for biological screening were determined by analytical HPLC (SPD-M20A, make: Shimadzu) using an ODS column eluted with a gradient mixture of acetonitrile–water. IR spectra were recorded as neat liquids or KBr pellets, and absorptions are reported in cm^{-1} . NMR spectra were recorded on 300 (Bruker) and 500 MHz (Varian) spectrometers in appropriate solvents using tetramethylsilane (TMS) as an internal standard or the solvent signals as secondary standards, and the chemical shifts are shown in δ scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for

unresolved lines), etc. ^{13}C NMR spectra were recorded on 75 MHz spectrometer. HRMS were obtained by using ESI-QTOF mass spectrometry.

General Procedure for the Preparation of 7a–c. Anhydrous $AlCl_3$ (13.09 mmol) in chloroform (10 mL) was added to acetyl chloride (13.09 mmol) and then dibenzo[*b,d*]furan (11.9 mmol) in chloroform (20 mL) slowly and left at RT for 0.75 h. After the reaction (TLC) was completed, the reaction mixture was quenched with 1 N HCl and extracted with chloroform (2×25 mL). The combined organic extracts were washed with H_2O , dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuum. The crude product obtained was purified over silica gel column chromatography using hexane/ethyl acetate (94:6) to obtain the pure product **7b** as a white solid.

1-(9-Methyl-9*H*-carbazol-3-yl)ethanone (7a). Yield = 64%, mp = $90–92^\circ C$. IR ν_{max} (cm^{-1}): 2924, 1657, 1593, 1475, 1364, 1252, 1132, 1018, 817, 748. 1H NMR (300 MHz, $CDCl_3$): δ 8.65 (s, 1H), 8.13–8.03 (m, 2H), 7.52–7.41 (m, 1H), 7.40–7.21 (m, 3H), 3.86 (s, 3H), 2.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.9, 143.4, 141.5, 128.7, 126.3, 123.0, 122.4, 121.6, 120.4, 119.9, 108.8, 107.8, 29.1, 26.5. MS (ESI) m/z 224 $[M + H]^+$. HR-MS (ESI) calcd for $C_{15}H_{14}NO$ $[M + H]^+$, 224.1075; found, 224.1085.

1-(Dibenzo[*b,d*]furan-2-yl)ethanone (7b). Yield = 95%, mp = $58–60^\circ C$. IR ν_{max} (cm^{-1}): 2989, 1673, 1582, 1252, 1198, 1020, 819, 749. 1H NMR (300 MHz, $CDCl_3$): δ 8.58 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.01 (d, $J = 7.6$ Hz, 1H), 7.66–7.56 (m, 2H), 7.50 (t, $J = 7.6$ Hz, 1H), 7.39 (t, $J = 7.6$ Hz, 1H), 2.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.2, 158.8, 156.8, 132.4, 128.5, 127.9, 124.5, 123.3, 121.5, 120.8, 120.3, 111.8, 111.5, 26.7. MS (ESI) m/z 211 $[M + H]^+$. HR-MS (ESI) calcd for $C_{14}H_{11}O_2$ $[M + H]^+$, 211.0759; found, 211.0769.

1-(Dibenzo[*b,d*]thiophen-2-yl)ethanone (7c). Yield = 70%, mp = $110–112^\circ C$. IR ν_{max} (cm^{-1}): 3049, 2921, 1675, 1585, 1415, 1354, 1236, 1019, 808, 761, 736. 1H NMR (300 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.26–8.11 (m, 1H), 8.07–7.96 (m, 1H), 7.95–7.80 (m, 2H), 7.52–7.43 (m, 2H), 2.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.5, 144.4, 139.5, 133.5, 127.3, 126.1, 124.8, 122.8, 122.5, 121.7, 121.5, 26.7. MS (ESI) m/z 227 $[M + H]^+$. HR-MS (ESI) calcd for $C_{14}H_{11}OS$ $[M + H]^+$, 227.0530; found, 227.0527.

General Procedure for the Preparation of 8a–c. To the solution of 1-(dibenzo[*b,d*]furan-2-yl)ethanone **7b** (9.5 mmol) in dichloromethane/methanol (1:1, 20 mL), sodium borohydride (9.5 mmol) was added at $0^\circ C$ and stirred at RT for 1 h. The crude reaction mixture was evaporated under vacuum, water (15 mL) and dichloromethane (2×25 mL) were added, and the organic layer was separated, washed with H_2O , dried over anhydrous Na_2SO_4 , and filtered. The residue thus obtained after rotary evaporation was chromatographed over silica gel column and eluted with hexane/ethyl acetate (90:10) to give **8b**.

1-(9-Methyl-9*H*-carbazol-3-yl)ethanol (8a). Syrup, yield = 94%. IR ν_{max} (cm^{-1}): 3325, 2967, 2922, 1598, 1482, 1330, 1246, 1070, 806, 737. 1H NMR (300 MHz, $CDCl_3$): δ 8.07–7.93 (m, 2H), 7.39 (d, $J = 6.9$ Hz, 2H), 7.33–7.10 (m, 3H), 5.00 (q, $J = 6.4$ Hz, 1H), 3.78 (s,

3H), 1.56 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 141.2, 140.5, 134.7, 125.6, 125.3, 124.2, 122.8, 120.3, 118.8, 118.6, 118.4, 108.3, 75.5, 44.7, 25.3. MS (ESI) m/z 226 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{15}\text{H}_{15}\text{NONa}$ $[\text{M} + \text{Na}]^+$, 248.1051; found, 248.1063.

1-(Dibenzo[*b,d*]furan-2-yl)ethanol (8b). Yield = 96%, mp = 62–64 °C. IR ν_{max} (cm^{-1}): 3366, 2971, 2923, 1449, 1197, 1073, 748. ^1H NMR (300 MHz, CDCl_3): δ 8.04–7.76 (m, 2H), 7.61–7.36 (m, 4H), 7.35–7.26 (m, 1H), 5.04 (q, $J = 6.4$ Hz, 1H), 1.57 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 156.5, 140.5, 127.1, 124.7, 124.2, 124.1, 122.6, 120.6, 120.1, 117.4, 111.6, 111.4, 70.4, 25.6. MS (ESI) m/z 235 $[\text{M} + \text{Na}]^+$. HR-MS (ESI) calcd for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{Na}$ $[\text{M} + \text{Na}]^+$, 235.0734; found, 235.0730.

1-(Dibenzo[*b,d*]thiophen-2-yl)ethanol (8c). Yield = 95%, mp = 61–62 °C. IR ν_{max} (cm^{-1}): 3280, 2956, 1490, 1229, 1085, 760. ^1H NMR (300 MHz, CDCl_3): δ 8.18–8.06 (m, 2H), 7.87–7.73 (m, 2H), 7.48–7.36 (m, 3H), 5.05 (q, $J = 6.4$ Hz, 1H), 1.57 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 142.3, 139.7, 138.4, 126.7, 124.3, 122.8, 122.7, 121.5, 118.2, 70.4, 25.5. MS (ESI) m/z 211 $[\text{M} - \text{OH}]^+$. HR-MS (ESI) calcd for $\text{C}_{14}\text{H}_{11}\text{S}$ $[\text{M} - \text{OH}]^+$, 211.0581; found, 211.0578.

General Procedure for the Preparation of 9a–c. To the mixture of 1-(dibenzo[*b,d*]furan-2-yl) ethanol **8b** (9.4 mmol) and trimethylsilyl azide (9.4 mmol) in nitromethane (12 mL), indium chloride (5 mol %) was added and heated at 60 °C for 0.5 h. After completion of the reaction, solvent was evaporated, and the crude residue was purified over silica gel column using hexane/ethylacetate (97:3) to give a pale yellow syrup **8c**.

3-(1-Azidoethyl)-9-methyl-9H-carbazole (9a). Syrup, yield = 96%. IR ν_{max} (cm^{-1}): 2924, 2857, 2097, 1602, 1483, 1246, 741. ^1H NMR (300 MHz, CDCl_3): δ 8.05 (d, $J = 7.7$ Hz, 1H), 7.99 (s, 1H), 7.47–7.29 (m, 4H), 7.23–7.18 (m, 1H), 4.78 (q, $J = 6.7$ Hz, 1H), 3.85 (s, 3H), 1.62 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 141.4, 140.7, 131.2, 126.0, 124.3, 122.8, 122.5, 120.3, 119.0, 118.3, 108.7, 108.6, 61.8, 29.1, 22.0. MS (ESI) m/z 208 $[\text{M} - \text{N}_3]^+$. HR-MS (ESI) calcd for $\text{C}_{15}\text{H}_{14}\text{N}$ $[\text{M} - \text{N}_3]^+$, 208.1126; found, 208.1118.

2-(1-Azidoethyl)dibenzo[*b,d*]furan (9b). Syrup, yield = 98%. IR ν_{max} (cm^{-1}): 2978, 2102, 1479, 1449, 1198, 748. ^1H NMR (300 MHz, CDCl_3): δ 7.99–7.82 (m, 2H), 7.60–7.48 (m, 2H), 7.47–7.19 (m, 3H), 4.75 (q, $J = 6.7$ Hz, 1H), 1.61 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 156.7, 155.9, 135.6, 127.4, 125.5, 124.7, 124.0, 122.8, 120.7, 118.5, 111.9, 111.8, 61.2, 22.4. MS (ESI) m/z 195 $[\text{M} - \text{N}_3]^+$. HR-MS (ESI) calcd for $\text{C}_{14}\text{H}_{11}\text{O}$ $[\text{M} - \text{N}_3]^+$, 195.0804; found, 195.0795.

2-(1-Azidoethyl)dibenzo[*b,d*]thiophene (9c). Syrup, yield = 98%. IR ν_{max} (cm^{-1}): 3280, 2956, 1490, 1229, 1085, 760. ^1H NMR (300 MHz, CDCl_3): δ 8.21–8.03 (m, 2H), 7.88–7.77 (m, 2H), 7.49–7.34 (m, 3H), 4.78 (q, $J = 6.7$ Hz, 1H), 1.63 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 140.0, 139.3, 137.5, 135.9, 135.3, 126.9, 125.0, 124.4, 123.1, 122.9, 121.7, 119.3, 61.2, 22.3. MS (ESI) m/z 211 $[\text{M} - \text{N}_3]^+$. HR-MS (ESI) calcd for $\text{C}_{14}\text{H}_{11}\text{S}$ $[\text{M} - \text{N}_3]^+$, 211.0581; found, 211.0578.

General Procedure for the Preparation of 11a–h, 12a–h, and 13a–t. A mixture of 2-(1-azidoethyl) dibenzo[*b,d*]thiophene (0.39 mmol), phenyl acetylene (0.39 mmol), CuSO_4 pentahydrate (1.0 mol %), and sodium ascorbate (2.0 mol %), 4-nitrobenzoic acid (0.5 mol %) in *tert*-butanol (1 mL), and H_2O (1 mL) was stirred at RT for an appropriate time, monitored by TLC, and subsequently extracted with chloroform (3 \times 5 mL). The combined organic extracts were washed with H_2O , dried over anhydrous Na_2SO_4 , filtered, and concentrated in vacuo. The crude residue was purified over silica gel column using hexane/ethyl acetate to obtain the pure product.

9-Methyl-3-(1-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl)-9H-carbazole (11a). mp = 187–189 °C. IR ν_{max} (cm^{-1}): 3122, 2923, 1599, 1477, 1332, 1249, 1152, 1034, 763. ^1H NMR (400 MHz, CDCl_3): δ 8.12–8.00 (m, 2H), 7.76–7.68 (dd, $J = 1.1$ and 8.2 Hz, 2H), 7.51–7.28 (m, 7H), 7.24–7.17 (m, 2H), 6.02 (q, $J = 7.0$ Hz, 1H), 3.88 (s, 3H), 2.17 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 147.5, 141.4, 140.8, 130.7, 130.0, 128.6, 127.9, 126.1, 125.5, 124.5, 122.9, 122.5, 120.3, 119.2, 118.5, 118.4, 108.9, 108.6, 60.6, 29.1, 21.6. MS

(ESI) m/z 353 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{23}\text{H}_{21}\text{N}_4$ $[\text{M} + \text{H}]^+$, 353.1766; found, 353.1760.

9-Methyl-3-(1-(4-propyl-1H-1,2,3-triazol-1-yl)ethyl)-9H-carbazole (11b). mp = 120–122 °C. IR ν_{max} (cm^{-1}): 3113, 3060, 2958, 2926, 1598, 1489, 1330, 1249, 1126, 1043, 742. ^1H NMR (300 MHz, CDCl_3): δ 8.07–7.97 (m, 2H), 7.50–7.39 (m, 1H), 7.40–7.28 (m, 3H), 7.24–7.15 (m, 1H), 7.03 (s, 1H), 5.91 (q, $J = 7.5$ Hz, 1H), 3.85 (s, 3H), 2.60 (t, $J = 7.5$ Hz, 2H), 2.09 (d, $J = 7.5$ Hz, 3H), 1.63 (sex, $J = 7.5$ Hz, 2H), 0.92 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 148.0, 141.3, 140.6, 130.4, 126.1, 124.4, 122.8, 122.3, 120.2, 119.3, 119.1, 118.4, 108.8, 108.6, 60.3, 29.1, 27.7, 22.6, 21.6, 13.7. MS (ESI) m/z 319 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{20}\text{H}_{23}\text{N}_4$ $[\text{M} + \text{H}]^+$, 319.1922; found, 319.1924.

3-(1-(4-Butyl-1H-1,2,3-triazol-1-yl)ethyl)-9-methyl-9H-carbazole (11c). mp = 139–141 °C. IR ν_{max} (cm^{-1}): 3118, 3060, 2951, 2927, 2861, 1599, 1489, 1332, 1250, 1126, 1042, 743. ^1H NMR (300 MHz, CDCl_3): δ 8.08–7.97 (m, 2H), 7.50–7.40 (m, 1H), 7.39–7.29 (m, 3H), 7.24–7.16 (m, 1H), 7.02 (s, 1H), 5.92 (q, $J = 6.9$ Hz, 1H), 3.87 (s, 3H), 2.63 (t, $J = 7.5$ Hz, 2H), 2.09 (d, $J = 6.9$ Hz, 3H), 1.59 (qt, $J = 7.5$ Hz, 2H), 1.33 (sex, $J = 7.5$ Hz, 2H), 0.89 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 148.3, 141.3, 140.7, 130.7, 126.1, 124.5, 122.3, 120.3, 119.1, 118.4, 108.8, 108.6, 60.3, 31.5, 29.1, 25.4, 22.3, 21.6, 13.7. MS (ESI) m/z 355 $[\text{M} + \text{Na}]^+$. HR-MS (ESI) calcd for $\text{C}_{21}\text{H}_{25}\text{N}_4$ $[\text{M} + \text{H}]^+$, 333.2079; found, 333.2086.

3-(1-(4-Hexyl-1H-1,2,3-triazol-1-yl)ethyl)-9-methyl-9H-carbazole (11d). mp = 130–132 °C. IR ν_{max} (cm^{-1}): 3115, 3060, 2925, 2855, 1599, 1489, 1332, 1250, 1126, 1044, 743. ^1H NMR (400 MHz, CDCl_3): δ 8.07–7.97 (m, 2H), 7.49–7.41 (m, 1H), 7.40–7.30 (m, 3H), 7.20 (t, $J = 7.8$ Hz, 1H), 7.03 (s, 1H), 5.92 (q, $J = 6.8$ Hz, 1H), 3.86 (s, 3H), 2.62 (t, $J = 7.4$ Hz, 2H), 2.09 (d, $J = 6.8$ Hz, 3H), 1.59 (qt, $J = 7.4$ Hz, 2H), 1.35–1.23 (m, 6H), 0.84 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 141.3, 140.7, 130.4, 126.1, 124.4, 122.8, 122.3, 120.3, 119.1, 118.4, 108.7, 108.6, 60.3, 31.4, 29.3, 29.1, 28.9, 25.7, 22.4, 21.6, 13.9. MS (ESI) m/z 383 $[\text{M} + \text{Na}]^+$. HR-MS (ESI) calcd for $\text{C}_{23}\text{H}_{29}\text{N}_4$ $[\text{M} + \text{H}]^+$, 361.2392; found, 361.2387.

1-(1-(9-Methyl-9H-carbazol-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)-methanol (11e). mp = 109–111 °C. IR ν_{max} (cm^{-1}): 3282, 3123, 2919, 1599, 1490, 1331, 1246, 1143, 1015, 741, 712. ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ 8.13 (s, 1H), 8.07 (d, $J = 7.7$ Hz, 1H), 7.83 (s, 1H), 7.52–7.41 (m, 4H), 7.18 (t, $J = 6.7$ Hz, 1H), 6.01 (q, $J = 7.1$ Hz, 1H), 4.52 (s, 2H), 3.85 (s, 3H), 2.05 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$): δ 148.0, 140.9, 140.2, 131.2, 125.9, 124.5, 121.8, 121.7, 121.1, 120.2, 118.8, 118.4, 109.2, 59.5, 55.0, 28.9, 21.3. MS (ESI) m/z 307 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{18}\text{H}_{19}\text{N}_4\text{O}$ $[\text{M} + \text{H}]^+$, 307.1558; found, 307.1548.

3-(1-(4-(Benzyloxymethyl)-1H-1,2,3-triazol-1-yl)ethyl)-9-methyl-9H-carbazole (11f). mp = 117–119 °C. IR ν_{max} (cm^{-1}): 3127, 3063, 2922, 2854, 1598, 1490, 1251, 1121, 740. ^1H NMR (300 MHz, CDCl_3): δ 8.08–7.97 (m, 2H), 7.51–7.29 (m, 5H), 7.28–7.14 (m, 6H), 5.95 (q, $J = 7.1$ Hz, 1H), 4.58 (s, 2H), 4.51 (s, 2H), 3.85 (s, 3H), 2.10 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 144.9, 141.3, 140.7, 137.7, 129.9, 128.3, 127.8, 127.6, 126.1, 124.5, 122.8, 122.3, 121.2, 120.3, 119.1, 118.5, 108.8, 108.6, 72.4, 63.7, 60.6, 29.1, 21.6. MS (ESI) m/z 397 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{25}\text{H}_{25}\text{N}_4\text{O}$ $[\text{M} + \text{H}]^+$, 397.2028; found, 397.2045.

9-Methyl-3-(1-(4-(2-nitrophenyl)-1H-1,2,3-triazol-1-yl)ethyl)-9H-carbazole (11g). mp = 126–128 °C. IR ν_{max} (cm^{-1}): 3137, 3078, 2926, 1604, 1524, 1352, 1248, 1154, 1035, 747. ^1H NMR (300 MHz, CDCl_3): δ 8.11 (dd, $J = 1.2$ and 7.8 Hz, 1H), 8.07–8.02 (m, 2H), 7.72 (dd, $J = 0.9$ and 8.0 Hz, 1H), 7.63 (s, 1H), 7.62–7.55 (m, 1H), 7.46–7.38 (m, 3H), 7.37–7.32 (m, 2H), 7.22–7.16 (m, 1H), 6.01 (q, $J = 7.1$ Hz, 1H), 3.86 (s, 3H), 2.16 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 148.0, 141.8, 141.3, 140.7, 132.3, 131.0, 129.8, 128.6, 126.1, 124.8, 124.2, 123.8, 122.9, 121.7, 120.3, 119.1, 118.4, 108.9, 108.6, 61.0, 29.0, 21.7.

3-(1-(4-(4-*tert*-Butylphenyl)-1H-1,2,3-triazol-1-yl)ethyl)-9-methyl-9H-carbazole (11h). mp = 164–166 °C. IR ν_{max} (cm^{-1}): 3121, 2960, 2868, 1601, 1490, 1334, 1251, 1221, 1035, 828, 747. ^1H NMR (300 MHz, CDCl_3): δ 8.11–8.00 (m, 2H), 7.69–7.59 (m, 2H), 7.51–7.27 (m, 7H), 7.24–7.17 (m, 1H), 6.00 (q, $J = 6.9$ Hz, 1H), 3.87 (s, 3H), 2.15 (d, $J = 6.9$ Hz, 3H), 1.30 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3): δ

152.3, 150.9, 140.7, 130.1, 127.9, 126.1, 125.5, 125.3, 124.5, 122.3, 120.3, 119.2, 118.5, 108.9, 108.6, 60.6, 34.5, 31.2, 29.1, 21.7. MS (ESI) m/z 409 $[M + H]^+$. HR-MS (ESI) calcd for $C_{27}H_{29}N_4$ $[M + H]^+$, 409.2392; found, 409.2380.

1-(1-(Dibenzo[b,d]furan-2-yl)ethyl)-4-phenyl-1H-1,2,3-triazole (12a). mp = 169–170 °C. IR ν_{\max} (cm^{-1}): 3079, 2988, 2927, 1591, 1443, 1198, 1075, 1030, 758. 1H NMR (300 MHz, $CDCl_3$): δ 7.98–7.84 (m, 2H), 7.75 (d, J = 7.1 Hz, 2H), 7.61–7.50 (m, 2H), 7.50–7.19 (m, 7H), 5.98 (q, J = 6.9 Hz, 1H), 2.15 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 155.9, 147.7, 134.4, 130.5, 128.7, 128.0, 127.6, 125.7, 125.6, 124.8, 123.6, 122.9, 120.7, 118.8, 118.3, 112.1, 11.7, 60.3, 21.6. MS (ESI) m/z 340 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{18}N_3O$ $[M + H]^+$, 340.1449; found, 340.1464.

1-(1-(Dibenzo[b,d]furan-2-yl)ethyl)-4-propyl-1H-1,2,3-triazole (12b). mp = 67–69 °C. IR ν_{\max} (cm^{-1}): 3115, 3064, 2956, 2926, 1550, 1445, 1201, 1045, 817, 747. 1H NMR (300 MHz, $CDCl_3$): δ 7.97–7.80 (m, 2H), 7.58–7.27 (m, 5H), 7.09 (s, 1H), 5.89 (q, J = 6.9 Hz, 1H), 2.64 (t, J = 7.3 Hz, 2H), 2.08 (d, J = 6.9 Hz, 3H), 1.66 (sex, J = 7.3 Hz, 2H), 0.94 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 148.2, 134.8, 127.5, 125.5, 122.8, 121.2, 120.9, 120.6, 119.3, 118.7, 111.9, 111.6, 109.6, 59.8, 27.6, 22.5, 21.6, 13.7. MS (ESI) m/z 306 $[M + H]^+$. HR-MS (ESI) calcd for $C_{19}H_{20}N_3O$ $[M + H]^+$, 306.1606; found, 306.1618.

4-Butyl-1-(1-(dibenzo[b,d]furan-2-yl)ethyl)-1H-1,2,3-triazole (12c). mp = 84–86 °C. IR ν_{\max} (cm^{-1}): 3115, 3067, 2922, 2858, 1591, 1440, 1202, 1038, 743. 1H NMR (300 MHz, $CDCl_3$): δ 7.96–7.79 (m, 2H), 7.60–7.19 (m, 6H), 5.88 (q, J = 6.9 Hz, 1H), 2.65 (t, J = 7.3 Hz, 2H), 2.07 (d, J = 6.9 Hz, 3H), 1.61 (qt, J = 7.3 Hz, 2H), 1.36 (sex, J = 7.3 Hz, 2H), 0.91 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 155.8, 148.5, 134.8, 127.6, 125.6, 122.9, 120.7, 119.2, 118.77, 112.0, 111.7, 59.9, 31.4, 25.4, 22.3, 21.6, 13.7. MS (ESI) m/z 320 $[M + H]^+$. HR-MS (ESI) calcd for $C_{20}H_{22}N_3O$ $[M + H]^+$, 320.1762; found, 320.1750.

1-(1-(Dibenzo[b,d]furan-2-yl)ethyl)-4-hexyl-1H-1,2,3-triazole (12d). mp = 91–93 °C. IR ν_{\max} (cm^{-1}): 3117, 3070, 2923, 2851, 1585, 1445, 1202, 1047, 818, 747. 1H NMR (300 MHz, $CDCl_3$): δ 7.95–7.79 (m, 2H), 7.59–7.49 (m, 2H), 7.48–7.39 (m, 1H), 7.38–7.21 (m, 2H), 7.09 (s, 1H), 5.89 (q, J = 6.9 Hz, 1H), 2.65 (t, J = 7.5 Hz, 2H), 2.07 (d, J = 6.9 Hz, 3H), 1.62 (sex, J = 7.5 Hz, 2H), 1.34–1.20 (m, 6H), 0.85 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.8, 148.5, 134.8, 127.5, 125.6, 124.6, 123.6, 122.9, 120.7, 119.2, 118.7, 111.9, 111.7, 109.6, 59.9, 31.4, 29.3, 28.8, 25.7, 22.4, 21.6, 13.9. MS (ESI) m/z 348 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{26}N_3O$ $[M + H]^+$, 348.2075; found, 348.2085.

1-(1-(Dibenzo[b,d]furan-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)-methanol (12e). mp = 117–119 °C. IR ν_{\max} (cm^{-1}): 3278, 3116, 3072, 2925, 1589, 1196, 1141, 1030, 750. 1H NMR (300 MHz, $DMSO-d_6$): δ 8.07–7.88 (m, 2H), 7.78–7.65 (m, 1H), 7.62–7.38 (m, 4H), 7.32 (t, J = 7.5 Hz, 1H), 5.98 (q, J = 6.9 Hz, 1H), 4.86 (s, br, 1H), 4.59 (s, 2H), 2.07 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $DMSO$): δ 155.9, 148.1, 136.1, 128.0, 126.4, 123.8, 123.4, 121.5, 121.3, 111.9, 111.8, 109.8, 59.2, 55.1, 21.3. MS (ESI) m/z 294 $[M + H]^+$. HR-MS (ESI) calcd for $C_{17}H_{16}N_3O_2$ $[M + H]^+$, 294.1242; found, 294.1248.

4-(Benzyloxymethyl)-1-(1-(dibenzo[b,d]furan-2-yl)ethyl)-1H-1,2,3-triazole (12f). mp = 82–83 °C. IR ν_{\max} (cm^{-1}): 3137, 3061, 2926, 2858, 1451, 1199, 1094, 1043, 749. 1H NMR (300 MHz, $CDCl_3$): δ 7.95–7.83 (m, 2H), 7.59–7.19 (m, 11H), 5.93 (q, J = 7.1 Hz, 1H), 4.61 (s, 2H), 4.55 (s, 2H), 2.10 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 145.2, 137.6, 134.3, 128.3, 127.9, 127.7, 127.6, 125.7, 124.7, 123.6, 122.6, 122.9, 121.2, 120.7, 118.9, 112.0, 111.7, 109.8, 72.6, 63.7, 60.2, 21.6. MS (ESI) m/z 384 $[M + H]^+$. HR-MS (ESI) calcd for $C_{24}H_{22}N_3O_2$ $[M + H]^+$, 384.1712; found, 384.1719.

1-(1-(Dibenzo[b,d]furan-2-yl)ethyl)-4-(2-nitrophenyl)-1H-1,2,3-triazole (12g). mp = 64–66 °C. IR ν_{\max} (cm^{-1}): 3065, 2924, 2856, 1611, 1526, 1439, 1350, 1192, 1026, 743. 1H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, J = 7.5 Hz, 1H), 7.90–7.79 (m, 2H), 7.75 (s, 1H), 7.69 (d, J = 7.3 Hz, 1H), 7.60–7.44 (m, 3H), 7.43–7.31 (m, 3H), 7.26 (t, J = 7.3 Hz, 1H), 5.94 (q, J = 6.9 Hz, 1H), 2.08 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 155.9, 148.1, 142.0, 134.3, 132.4, 131.0, 128.8, 127.6, 125.6, 124.7, 123.9, 123.6, 122.9, 121.8, 121.2, 120.8, 118.8, 112.2, 111.7, 60.6, 21.8. MS (ESI) m/z 385 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{16}N_4O_3$ $Na[M + Na]^+$, 407.1114; found, 407.1105.

4-(4-tert-Butylphenyl)-1-(1-(dibenzo[b,d]furan-2-yl)ethyl)-1H-1,2,3-triazole (12h). mp = 134–136 °C. IR ν_{\max} (cm^{-1}): 3133, 2964, 1594, 1450, 1358, 1206, 1033, 828, 747. 1H NMR (300 MHz, $CDCl_3$): δ 7.95–7.83 (m, 2H), 7.66 (d, J = 8.1 Hz, 2H), 7.61–7.21 (m, 8H), 5.95 (q, J = 6.9 Hz, 1H), 2.12 (d, J = 6.9 Hz, 3H), 1.31 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.8, 151.1, 147.7, 134.6, 127.6, 125.68, 125.63, 125.3, 122.9, 121.3, 121.1, 120.7, 118.8, 118.1, 112.0, 111.7, 60.2, 34.5, 31.2, 21.6. MS (ESI) m/z 396 $[M + H]^+$. HR-MS (ESI) calcd for $C_{26}H_{26}N_3O$ $[M + H]^+$, 396.2075; found, 396.2077.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-phenyl-1H-1,2,3-triazole (13a). mp = 149–151 °C. IR ν_{\max} (cm^{-1}): 3122, 2923, 2853, 1462, 1424, 1227, 1073, 1024, 764, 731. 1H NMR (300 MHz, $CDCl_3$): δ 8.17–8.07 (m, 2H), 7.88–7.79 (m, 2H), 7.78–7.72 (m, 2H), 7.59 (s, 1H), 7.48–7.20 (m, 6H), 6.00 (q, J = 7.55 Hz, 1H), 2.16 (d, J = 7.55 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.3, 136.2, 136.0, 134.9, 130.5, 128.7, 128.0, 127.1, 127.0, 125.6, 125.1, 124.5, 123.4, 122.8, 121.7, 120.6, 120.0, 119.6, 118.4, 60.3, 21.5. MS (ESI) m/z 356 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{17}N_3SNa$ $[M + Na]^+$, 378.1040; found, 378.1050.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-propyl-1H-1,2,3-triazole (13b). mp = 67–69 °C. IR ν_{\max} (cm^{-1}): 3112, 3062, 2925, 2853, 1463, 1426, 1128, 1023, 817, 761, 730. 1H NMR (300 MHz, $CDCl_3$): δ 8.15–8.06 (m, 1H), 8.02 (s, 1H), 7.86–7.78 (m, 2H), 7.47–7.40 (m, 2H), 7.38–7.32 (dd, J = 1.9 and 9.8 Hz, 1H), 7.11 (s, 1H), 5.90 (q, J = 6.8 Hz, 1H), 2.64 (t, J = 7.8 Hz, 2H), 2.09 (d, J = 6.8 Hz, 3H), 1.67 (sex, J = 7.8 Hz, 2H), 0.94 (t, J = 7.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.3, 139.8, 139.4, 136.6, 135.9, 134.9, 127.0, 125.0, 124.5, 123.3, 122.8, 121.6, 119.5, 60.0, 27.6, 22.6, 21.4, 13.7. MS (ESI) m/z 322 $[M + H]^+$. HR-MS (ESI) calcd for $C_{19}H_{20}N_3S$ $[M + H]^+$, 322.1377; found, 322.1372.

4-Butyl-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13c). mp = 84–86 °C. IR ν_{\max} (cm^{-1}): 3111, 3061, 2926, 2859, 1546, 1458, 1425, 1220, 1131, 1034, 730. 1H NMR (300 MHz, $CDCl_3$): δ 8.15–8.05 (m, 1H), 8.01 (d, J = 8.3 Hz, 1H), 7.86–7.77 (m, 2H), 7.49–7.39 (m, 2H), 7.38–7.30 (dd, J = 1.5 and 8.3 Hz, 1H), 7.11 (s, 1H), 5.90 (q, J = 6.9 Hz, 1H), 2.66 (t, J = 7.5 Hz, 2H), 2.09 (d, J = 6.9 Hz, 3H), 1.62 (q, J = 7.3 Hz, 2H), 1.36 (sex, J = 7.3 Hz, 2H), 0.91 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.8, 136.6, 135.9, 134.9, 127.0, 125.0, 124.4, 123.2, 122.8, 121.9, 121.6, 121.4, 120.5, 119.4, 119.3, 59.9, 31.4, 25.4, 22.2, 13.7. MS (ESI) m/z 336 $[M + H]^+$. HR-MS (ESI) calcd for $C_{20}H_{22}N_3S$ $[M + H]^+$, 336.1534; found, 336.1543.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-hexyl-1H-1,2,3-triazole (13d). mp = 71–73 °C. IR ν_{\max} (cm^{-1}): 3112, 3061, 2924, 2854, 1461, 1425, 1222, 1130, 1026, 729. 1H NMR (300 MHz, $CDCl_3$): δ 8.15–8.05 (m, 1H), 8.01 (s, 1H), 7.88–7.86 (m, 2H), 7.49–7.39 (m, 2H), 7.38–7.29 (m, 1H), 7.11 (s, 1H), 5.90 (q, J = 6.9 Hz, 1H), 2.65 (t, J = 7.5 Hz, 2H), 2.08 (d, J = 6.9 Hz, 3H), 1.62 (q, J = 7.5 Hz, 2H), 1.34–1.22 (m, 6H), 0.85 (t, J = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.6, 139.8, 139.4, 136.6, 135.8, 134.9, 127.0, 125.0, 124.4, 123.2, 122.8, 121.9, 121.6, 120.5, 119.4, 59.9, 31.4, 29.3, 28.8, 25.7, 22.4, 21.4, 13.9. MS (ESI) m/z 364 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{26}N_3S$ $[M + H]^+$, 364.1847; found, 364.1850.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazol-4-yl)-methanol (13e). mp = 155–157 °C. IR ν_{\max} (cm^{-1}): 3293, 3116, 3072, 2923, 2854, 1462, 1419, 1343, 1140, 1026, 732. 1H NMR (300 MHz, $CDCl_3$): δ 8.14–8.09 (m, 1H), 8.05 (s, 1H), 7.87–7.79 (m, 2H), 7.48–7.42 (m, 2H), 7.41–7.32 (m, 2H), 5.94 (q, J = 7.1 Hz, 1H), 4.71 (s, 2H), 2.11 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7, 139.8, 139.6, 136.0, 134.8, 127.1, 125.0, 124.5, 123.3, 122.8, 121.6, 120.5, 119.6, 60.3, 56.3, 21.4. MS (ESI) m/z 310 $[M + H]^+$. HR-MS (ESI) calcd for $C_{17}H_{15}N_3ONa$ $[M + Na]^+$, 332.0833; found, 332.0833.

4-(Benzyloxymethyl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13f). Syrup. IR ν_{\max} (cm^{-1}): 3139, 3060, 2925, 2857,

1452, 1322, 1226, 1077, 1042, 764. ^1H NMR (300 MHz, CDCl_3): δ 8.15–8.07 (m, 1H), 8.04 (s, 1H), 7.89–7.77 (m, 2H), 7.49–7.33 (m, 4H), 7.30–7.18 (m, 5H), 5.94 (q, J = 6.9 Hz, 1H), 4.61 (s, 2H), 4.55 (s, 2H), 2.11 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 145.2, 139.8, 139.6, 137.6, 136.1, 135.9, 134.9, 128.3, 127.9, 127.7, 127.1, 125.1, 124.5, 123.3, 122.8, 121.6, 121.2, 119.6, 72.6, 63.7, 60.2, 21.4. MS (ESI) m/z 400 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{24}\text{H}_{21}\text{N}_3\text{ONaS}$ $[\text{M} + \text{Na}]^+$, 422.1303; found, 422.1299.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(2-nitrophenyl)-1H-1,2,3-triazole (13g). mp = 144–146 °C. IR ν_{max} (cm^{-1}): 3123, 2924, 2852, 1532, 1355, 1228, 764, 732. ^1H NMR (300 MHz, CDCl_3): δ 8.18–8.08 (m, 2H), 8.05 (s, 1H), 7.89–7.72 (m, 4H), 7.63 (t, J = 7.5 Hz, 1H), 7.51–7.36 (m, 4H), 6.00 (q, J = 6.9 Hz, 1H), 2.16 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 148.0, 139.7, 139.6, 136.1, 135.9, 134.8, 132.4, 131.0, 128.8, 127.0, 124.8, 124.6, 124.4, 123.9, 123.3, 122.7, 121.9, 121.7, 119.4, 60.6, 21.6. MS (ESI) m/z 401 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}_2\text{NaS}$ $[\text{M} + \text{Na}]^+$, 423.0891; found, 423.0895.

4-(4-tert-Butylphenyl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13h). mp = 131–133 °C. IR ν_{max} (cm^{-1}): 3091, 2959, 2925, 2861, 1452, 1421, 1269, 1225, 1080, 1028, 727. ^1H NMR (300 MHz, CDCl_3): δ 8.17–8.08 (m, 1H), 8.06 (s, 1H), 7.87–7.77 (m, 2H), 7.67 (t, J = 8.3 Hz, 2H), 7.56 (s, 1H), 7.49–7.32 (m, 5H), 5.99 (q, J = 6.9 Hz, 1H), 2.15 (d, J = 6.9 Hz, 3H), 1.32 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3): δ 151.1, 147.8, 139.8, 139.6, 136.4, 135.9, 134.9, 127.7, 127.1, 125.6, 125.3, 125.0, 124.5, 123.3, 122.8, 121.7, 119.5, 118.1, 60.2, 34.5, 31.2, 21.5. MS (ESI) m/z 412 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{26}\text{H}_{25}\text{N}_3\text{NaS}$ $[\text{M} + \text{Na}]^+$, 434.1666; found, 434.1679.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-p-tolyl-1H-1,2,3-triazole (13i). mp = 163–165 °C. IR ν_{max} (cm^{-1}): 3103, 2920, 1888, 1589, 1495, 1420, 1225, 1152, 1040, 761, 731. ^1H NMR (300 MHz, CDCl_3): δ 8.16–8.03 (m, 2H), 7.88–7.75 (m, 2H), 7.63 (d, J = 7.9 Hz, 2H), 7.55 (s, 1H), 7.50–7.32 (m, 3H), 7.13 (d, J = 7.9 Hz, 2H), 5.97 (q, J = 7.1 Hz, 1H), 2.34 (s, 3H), 2.14 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 147.8, 139.8, 137.8, 136.3, 134.9, 129.3, 127.7, 127.1, 125.5, 125.0, 124.5, 123.3, 122.8, 122.0, 121.6, 120.6, 119.5, 118.0, 60.2, 21.5, 21.2. MS (ESI) m/z 370 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{23}\text{H}_{20}\text{N}_3\text{S}$ $[\text{M} + \text{H}]^+$, 370.1377; found, 370.1362.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-phenethyl-1H-1,2,3-triazole (13j). mp = 94–96 °C. IR ν_{max} (cm^{-1}): 3109, 3024, 2924, 1544, 1469, 1451, 1422, 1212, 1024, 818, 761, 695. ^1H NMR (300 MHz, CDCl_3): δ 8.19–8.04 (m, 1H), 7.97 (s, 1H), 7.89–7.75 (m, 2H), 7.52–7.39 (m, 2H), 7.28 (d, J = 7.5 Hz, 1H), 7.21–6.93 (m, 6H), 5.88 (q, J = 6.6 Hz, 1H), 2.97 (s, br, 4H), 2.06 (d, J = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 140.9, 139.8, 139.4, 136.5, 135.9, 134.9, 128.3, 128.1, 127.0, 125.8, 124.9, 124.3, 123.1, 122.7, 121.7, 119.4, 60.2, 35.3, 27.5, 21.5. MS (ESI) m/z 384 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{24}\text{H}_{22}\text{N}_3\text{S}$ $[\text{M} + \text{H}]^+$, 384.1534; found, 384.1537.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(4-nitrophenyl)-1H-1,2,3-triazole (13k). mp = 185–187 °C. IR ν_{max} (cm^{-1}): 3097, 2924, 1606, 1509, 1384, 1341, 1235, 1108, 850, 758. ^1H NMR (300 MHz, CDCl_3): δ 8.97 (s, 1H), 8.42 (s, 1H), 8.38–8.23 (m, 3H), 8.12 (d, J = 8.6 Hz, 2H), 8.01–7.88 (m, 2H), 7.60–7.44 (m, 3H), 6.20 (q, J = 6.9 Hz, 1H), 2.11 (d, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 146.2, 144.3, 138.8, 138.3, 137.0, 136.8, 135.1, 134.5, 126.8, 125.6, 125.1, 124.2, 123.7, 122.9, 122.5, 121.8, 121.7, 119.7, 59.5, 21.0. MS (ESI) m/z 401 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{17}\text{N}_4\text{O}_2\text{S}$ $[\text{M} + \text{H}]^+$, 401.1072; found, 401.1065.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(thiophen-3-yl)-1H-1,2,3-triazole (13l). mp = 124–126 °C. IR ν_{max} (cm^{-1}): 3124, 2924, 1604, 1421, 1232, 1070, 853, 780, 732, 619. ^1H NMR (300 MHz, CDCl_3): δ 8.15–8.05 (m, 2H), 7.88–7.74 (m, 2H), 7.65–7.58 (m, 1H), 7.52 (s, 1H), 7.48–7.33 (m, 4H), 7.32–7.26 (m, 1H), 5.98 (q, J = 7.1 Hz, 1H), 2.13 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 143.8, 139.6, 136.0, 132.7, 131.4, 127.1, 126.2, 125.7, 125.0, 124.5, 123.4, 122.8, 121.6, 121.2, 119.5, 118.3, 115.3, 115.6, 60.4, 21.4. MS (ESI) m/z 362 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{20}\text{H}_{16}\text{N}_3\text{S}_2$ $[\text{M} + \text{H}]^+$, 362.0785; found, 362.0770.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(6-methoxynaphthalen-2-yl)-1H-1,2,3-triazole (13m). mp = 195–197 °C. IR ν_{max} (cm^{-1}): 3122, 2924, 1614, 1480, 1346, 1265, 1208, 1025, 854, 731. ^1H NMR

(300 MHz, CDCl_3): δ 8.75–8.54 (m, 1H), 8.48–8.10 (m, 3H), 8.07–7.87 (m, 3H), 7.85–7.72 (m, 2H), 7.61–7.39 (m, 3H), 7.27–7.05 (m, 2H), 6.16 (q, J = 7.1 Hz, 1H), 3.89 (s, 3H), 2.13 (d, J = 7.1 Hz, 3H). MS (ESI) m/z 436 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{27}\text{H}_{22}\text{N}_3\text{OS}$ $[\text{M} + \text{H}]^+$, 436.1483; found, 436.1476.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(phenanthren-9-yl)-1H-1,2,3-triazole (13n). mp = 149–151 °C. IR ν_{max} (cm^{-1}): 3074, 2982, 1430, 1231, 1051, 896, 763, 728. ^1H NMR (300 MHz, CDCl_3): δ 8.72 (d, J = 8.1 Hz, 1H), 8.66 (d, J = 8.1 Hz, 1H), 8.48 (d, J = 7.9 Hz, 1H), 8.40–8.09 (m, 3H), 7.95 (s, 1H), 7.91–7.75 (m, 3H), 7.71–7.50 (m, 5H), 7.50–7.35 (m, 2H), 6.16 (q, J = 7.1 Hz, 1H), 2.21 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 145.6, 138.9, 138.3, 137.0, 135.1, 134.5, 130.6, 129.2, 129.4, 129.3, 128.2, 127.4, 126.7, 126.5, 126.4, 126.3, 126.1, 125.2, 124.2, 122.8, 122.6, 122.5, 122.4, 122.2, 121.6, 119.8, 59.5, 21.1. MS (ESI) m/z 456 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{30}\text{H}_{22}\text{N}_3\text{S}$ $[\text{M} + \text{H}]^+$, 456.1534; found, 456.1525.

4-(Biphenyl-4-yl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13o). mp = 193–195 °C. IR ν_{max} (cm^{-1}): 3099, 2923, 1595, 1482, 1232, 1024, 841, 818, 730, 693. ^1H NMR (300 MHz, CDCl_3): δ 8.18–8.08 (m, 2H), 7.91–7.78 (m, 5H), 7.62 (s, 1H), 7.60–7.53 (m, 4H), 7.49–7.27 (m, 5H), 6.00 (q, J = 7.1 Hz, 1H), 2.17 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 146.0, 139.4, 139.3, 138.9, 138.2, 137.5, 135.1, 134.6, 129.7, 128.8, 127.4, 127.2, 127.0, 126.4, 125.6, 125.4, 124.7, 123.3, 123.0, 122.0, 120.1, 120.0, 59.4, 21.1. MS (ESI) m/z 432 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{28}\text{H}_{22}\text{N}_3\text{S}$ $[\text{M} + \text{H}]^+$, 432.1534; found, 432.1528.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(2,4-dichlorophenyl)-1H-1,2,3-triazole (13p). mp = 124–126 °C. IR ν_{max} (cm^{-1}): 2924, 1549, 1465, 1342, 1229, 1103, 1051, 861, 821, 762, 731. ^1H NMR (300 MHz, CDCl_3): δ 8.26 (d, J = 8.4 Hz, 1H), 8.16–8.05 (m, 3H), 7.89–7.76 (m, 2H), 7.49–7.37 (m, 4H), 7.33 (dd, J = 2.0 and 8.4 Hz, 1H), 6.01 (q, J = 7.1 Hz, 1H), 2.17 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 143.1, 139.8, 139.6, 136.1, 135.9, 134.8, 133.9, 131.4, 130.4, 129.7, 127.8, 127.4, 127.0, 124.8, 124.4, 123.3, 122.8, 122.0, 121.6, 119.4, 60.5, 21.6. MS (ESI) m/z 424 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{SCl}_2$ $[\text{M} + \text{H}]^+$, 424.0441; found, 424.0440.

4-(2-Chloro-4-fluorophenyl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13q). mp = 147–149 °C. IR ν_{max} (cm^{-1}): 3127, 2926, 1604, 1478, 1260, 1226, 1045, 895, 814, 731. ^1H NMR (300 MHz, CDCl_3): δ 8.51–8.32 (m, 1H), 8.31–8.09 (m, 3H), 7.95–7.77 (m, 2H), 7.56–7.39 (m, 3H), 7.33–7.01 (m, 2H), 6.13 (q, J = 7.1 Hz, 1H), 2.15 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 162.6, 138.9, 138.3, 136.8, 135.1, 134.5, 130.7, 130.5, 126.6, 124.9, 124.1, 122.7, 122.4, 122.1, 121.5, 119.5, 116.8, 116.4, 114.3, 114.0, 59.4, 21.0. MS (ESI) m/z 408 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{FSCl}$ $[\text{M} + \text{H}]^+$, 408.0737; found, 408.0730.

4-(4-Bromo-2-fluorophenyl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13r). mp = 115–117 °C. IR ν_{max} (cm^{-1}): 3075, 2924, 1614, 1570, 1549, 1472, 1339, 1224, 1153, 1062, 730. ^1H NMR (300 MHz, CDCl_3): δ 8.21 (t, J = 8.1 Hz, 1H), 8.16–8.01 (m, 2H), 7.89–7.72 (m, 3H), 7.53–7.32 (m, 4H), 7.30–7.18 (m, 1H), 6.00 (q, J = 7.1 Hz, 1H), 2.16 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 160.4, 157.0, 139.9, 136.2, 136.1, 134.9, 128.8, 128.0, 127.1, 124.9, 124.5, 123.4, 122.8, 122.1, 121.1, 120.6, 119.5, 119.3, 119.0, 60.5, 21.7. MS (ESI) m/z 452 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{FSBr}$ $[\text{M} + \text{H}]^+$, 452.0232; found, 452.0230.

1-(1-(Dibenzo[b,d]thiophen-2-yl)ethyl)-4-(2,5-difluorophenyl)-1H-1,2,3-triazole (13s). mp = 133–135 °C. IR ν_{max} (cm^{-1}): 3136, 2937, 1591, 1496, 1232, 1066, 885, 817, 762, 731. ^1H NMR (300 MHz, CDCl_3): δ 8.25–8.10 (m, 2H), 8.05 (d, J = 3.5 Hz, 1H), 8.02–7.90 (m, 1H), 7.89–7.78 (m, 2H), 7.52–7.38 (m, 3H), 7.17–6.86 (m, 2H), 6.08 (q, J = 7.1 Hz, 1H), 2.16 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.8, 156.7, 152.8, 138.9, 138.2, 137.3, 135.1, 134.5, 127.2, 125.5, 124.6, 123.3, 123.0, 122.0, 120.0, 117.7, 117.4, 115.7, 113.2, 112.8, 59.6, 20.8. MS (ESI) m/z 392 $[\text{M} + \text{H}]^+$. HR-MS (ESI) calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{F}_2\text{S}$ $[\text{M} + \text{H}]^+$, 392.1033; found, 392.1030.

4-(2-Chloro-3,5-difluorophenyl)-1-(1-(dibenzo[b,d]thiophen-2-yl)ethyl)-1H-1,2,3-triazole (13t). mp = 185–187 °C. IR ν_{max} (cm^{-1}): 3087, 2924, 1469, 1430, 1235, 924, 836, 814, 732. ^1H NMR (300 MHz, CDCl_3): δ 8.54 (s, 1H), 8.43–8.22 (m, 2H), 8.07–7.84 (m, 2H), 7.63–7.37 (m, 4H), 7.36–7.20 (m, 1H), 6.23 (q, J = 7.1 Hz,

1H), 2.13 (d, $J = 7.1$ Hz, 3H). MS (ESI) m/z 426 $[M + H]^+$. HR-MS (ESI) calcd for $C_{22}H_{15}N_3$ F_2SCl $[M + H]^+$, 426.0643; found, 426.0666.

Mycobacterial Growth Assay. Two-fold serial dilutions of each test compound/drug were prepared and incorporated into Middlebrook 7H11 agar medium with oleic acid, albumin, dextrose, and catalase (OADC) growth supplement to get final concentrations of 25, 12.5, 6.25, 3.13, 1.56, and 0.78 $\mu\text{g/mL}$. Inoculum of *M. tuberculosis* H37Rv ATCC 27294 was prepared from fresh Middlebrook 7H11 agar slants with OADC (Difco) growth supplement adjusted to 1 mg/mL (wet weight) in Tween 80 (0.05%) saline diluted to 10^{-2} to give a concentration of $\sim 10^7$ cfu/mL. Five microliters of this bacterial suspension was spotted onto 7H11 agar tubes containing different concentrations of the drug as discussed above. The tubes were incubated at 37 °C, and final readings (as MIC in $\mu\text{g/mL}$) were determined after 28 days. The MIC is defined as the minimum concentration of compound required to give complete inhibition of bacterial growth. This method is similar to that recommended by the National Committee for Clinical Laboratory Standards for the determination of MIC in triplicate.

Cell Cultures, Maintenance, and Cytotoxicity Evaluation. All cell lines used in this study were purchased from the American Type Culture Collection (ATCC, United States). A549, SK-N-SH, and HeLa were grown in Dulbecco's modified Eagle's medium (containing 10% FBS in a humidified atmosphere of 5% CO_2 at 37 °C). DU145 cells were cultured in Eagle's minimal essential medium (MEM) containing nonessential amino acids, 1 mM sodium pyruvate, 10 mg/mL bovine insulin, and 10% FBS. Cells were trypsinized when subconfluent from T25 flasks/60 mm dishes and seeded in 96-well plates. The synthesized 1,2,3-triazole hybrids 13a–c, 13f–k, and 13p–t were evaluated for their *in vitro* cytotoxicity in four different human cancer cell lines. A protocol of 48 h continuous drug exposure was used, and a MTT cell proliferation assay was used to estimate cell viability or growth. The cell lines were grown in their respective media containing 10% fetal bovine serum and were inoculated into 96-well microtiter plates in 200 μL aliquots at plating densities depending on the doubling time of individual cell lines. The microtiter plates were incubated at 37 °C, 5% CO_2 , 95% air, and 100% relative humidity for 24 h prior to addition of experimental drugs. Aliquots of 2 μL of the test compounds were added to the wells already containing 198 μL of cells, resulting in the required final drug concentrations. For each compound, four concentrations (1, 10, 100, and 1000 μM) were evaluated, and each was done in triplicate wells. Plates were incubated further for 48 h, and the assay was terminated by the addition of 10 μL of 5% MTT and incubated for 60 min at 37 °C. Later, the plates were air-dried. Bound stain was subsequently eluted with 100 μL of DMSO, and the absorbance was read on an ELISA plate reader at a wavelength of 560 nm. Percent growth was calculated on a plate by plate basis for test wells relative to control wells. The above determinations were repeated thrice. The growth inhibitory effects of the compounds were analyzed by generating dose–response curves as a plot of the percentage surviving cells versus compound concentration. The sensitivity of the cancer cells to the test compound was expressed in terms of IC_{50} , a value defined as the concentration of compound that produced 50% reduction as compared to the control absorbance. IC_{50} values are indicated as means \pm SD of three independent experiments.

X-ray Data. X-ray data for the compounds were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å) with the ω -scan method.²² Preliminary lattice parameters and orientation matrices were obtained from four sets of frames. Integration and scaling of intensity data were accomplished using SAINT program [1]. The structure was solved by direct methods using SHELXS97, and refinement was carried out by full-matrix least-squares technique using SHELXL97.²² Anisotropic displacement parameters were included for all nonhydrogen atoms. All H atoms attached to C and N were located in different Fourier maps and subsequently geometrically optimized and allowed for riding atoms, with C–H = 0.93–0.97 Å, N–H = 0.86 Å, with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H or $1.2U_{\text{eq}}(\text{C}, \text{N})$. The methyl groups were allowed to rotate but not to tip. Crystal data for 4-

(4-*tert*-butylphenyl)-1-(1-(dibenzo[*b,d*]thiophen-2-yl)ethyl)-1H-1,2,3-triazole 13 h: $C_{26}H_{25}N_3S$, $M = 411.55$, monoclinic, space group $P2_1/c$, $a = 7.9466(5)$ Å, $b = 26.2967(16)$ Å, $c = 10.7696(7)$ Å, $\beta = 102.466(1)^\circ$, $V = 2197.5(2)$ Å³, $Z = 4$, $D_{\text{calcd}} = 1.244$ mg m^{-3} , $T = 294(2)$ K, $\mu = 0.165$ mm⁻¹, $F(000) = 872$, $\lambda = 0.71073$ Å. Data collection yielded 21020 reflections resulting in 3875 unique, averaged reflections, 3353 with $I > 2\sigma(I)$. Full-matrix least-squares refinement led to a final $R = 0.0571$, $wR = 0.1336$, and GOF = 1.142.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ¹H, ¹³C NMR, and mass (HRMS) of all of the compounds, 7a–c, 8a–c, 9a–c, 11a–h, 12a–h, and 13a–t; single-crystal X-ray diffraction data (cif file) for 13h. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Author Contributions

S.K., S.R.P., and L.P. conceived, performed the experiments, and characterized the compounds with spectral data. B.S. performed single-crystal X-ray analysis. P.Y. and D.S. evaluated compounds for antitubercular activity. R.M., N.J., and S.V.K. performed cytotoxicity evaluations. S.K., T.A.D., and S.R.P. analyzed the data and cowrote the manuscript and Supporting Information.

Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS USED

TB, tuberculosis; HIV, human immunodeficiency virus; MDR-TB, multiple drug-resistant *M. tuberculosis*; XDR-TB, extremely drug-resistant *M. tuberculosis*; INH, isoniazid; MIC, minimum inhibitory concentration; NMR, nuclear magnetic resonance; FTIR, infrared spectroscopy; HRMS, high-resolution mass spectrometry; OADC, oleic acid, albumin, dextrose, and catalase; MTT, (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay; SI, selectivity index; TLC, thin-layer chromatography; TMS, tetramethylsilane; IC_{50} , minimum inhibitory concentration for 50% of the cells; A549, human lung carcinoma epithelial; SK-N-SH, human neuroblastoma; HeLa, human epithelial cervical cancer; DU145, human prostate cancer

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