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Synthesis and biological evaluation of a series of novel benzofuran-2-carboxylate 1,2,3-triazoles

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A facile and efficient synthetic route has been developed to substituted benzofuran-2-carboxylate 1,2,3-triazoles for the first time by reacting prop-2-yn-1-yl benzofuran-2-carboxylate with a variety of substituted aryl/benzyl azides in DMF/H_2O system employing standard click reaction. This new method has the lead of good yields, inexpensive reagents, easily available, easy work-up, mild reaction conditions, and environmentally friendly reaction conditions. All these compounds have been characterized by modern spectral techniques such as IR, ^{1}H NMR, and mass spectroscopy, *etc*. Evaluation of synthesized compounds for antimicrobial activity against specific bacterial strains like *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa* along with antifungal activity against *Aspergillus niger* and *Sclerotium rolfsii* have been carried out.

Keywords: 1,2,3-Triazoles, benzofuran-2-carboxylate, green chemistry, antimicrobial activity

Infections caused by the microorganisms are a severe challenge to the therapeutic area and show up the importance and urgent need for new, more effective and selective antimicrobial agents. In this regard, heterocyclic ring systems have emerged as powerful scaffolds for many biological evaluations[1]. Heterocyclic compounds take up a central position in organic chemistry and these are an essential part of the chemical and life sciences[2-4]. These compounds play an important role in the design and discovery of new pharmacologically active molecules[5]. These are of particular interest and significant importance in the search for new bioactive molecules in both the agrochemical and pharmaceutical industries.

In this context, oxygen containing heterocyclic derivatives exhibit diverse biological and pharmacological activities[6]. Benzofuran is a heterocyclic compound consisting of fused benzene and furan ring. Benzofurans occur in a great number of natural products. Many of the natural benzofurans have physiological, pharmacological and toxic properties. Benzofurans nucleus presents in various synthetic as well as natural compounds and have diverse biological and potential applications[7].

Benzofuran and its derivatives are central pharmacophores and privileged structures in medicinal chemistry. Benzofuran scaffolds have drawn considerable attention due to their intense chemotherapeutic properties as well as their prevalent occurrence in nature[8]. Benzofuran derivatives are versatile agents that can be used to design and develop new biologically active agents[9]. Benzofuran derivatives display potent biological properties including antimicrobial[10], antihyperglycemic[11], analgesic[12], antiparasitic[13], antitumor and kinase inhibitor[14,15] activities. Recently, benzofurans derivatives exhibited potent cytotoxic activities against human breast cancer cells and ovarian cancer cells[16,17]. The most prominent benzofuran compounds are amiodarone, angelicin, xanthotoxin, bergapten, nodekenetin and usnic acid. Thus, benzofuran core structure can be taken as lead compounds for the synthesis of new derivatives with a range of biological activities.

Hence we plan to couple the benzofuran nucleus with 1,2,3- triazole moiety and screen for their antimicrobial activities. 1,2,3-Triazole substituted derivatives have received considerable attention during last few decades as they are endowed with variety of biological activities and have wide range of therapeutic properties. When one biologically active derivative is connected to another active moiety, the resultant molecule generally has increased potency. Hence in the present study the two pharmacophores,

i.e. benzofuran 1,2,3- triazole moieties are connected to obtain potentially more effective, specific and less toxic antimicrobial agents.

Results and Discussion

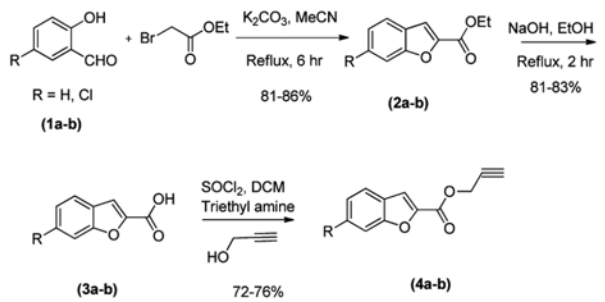
Chemistry

Initially the intermediate, prop-2-yn-1-yl benzofuran-2-carboxylate **(4a- b)** was synthesized by a three step procedure, Further the intermediate was converted to 1,2,3-triazoles employing substituted aryl azides and benzyl azides as substrates. For the preparation of intermediate **(4a- b)** salicylaldehydes (**1a-b**) on reaction with ethyl bromoacetate in the presence of base in acetonitrile as solvent at reflux temperature obtained ethyl benzofuran-2-carboxylate (**2a-b**) in 86% yield[18].

It was treated with sodium hydroxide in ethanol under heating conditions to obtain the corresponding acid (**3a-b**) in 82% yield[19]. This benzofuran-2-carboxylic acid subjected to thionylchloride reaction followed by propargylation in presence of base in dichloromethane as a solvent at 0°C to obtain key intermediate prop-2-yn-1-yl benzofuran-2-carboxylate **(4a-b)** in 75% yield[20] (Scheme I).

This intermediate compound **(4a-b)** converted to corresponding 1,2,3-triazoles employing standard click reaction conditions *i.e*. substituted Aryl azides and benzyl azides in presence of catalytic system $CuSO_4 \cdot 5H_2O$–sodium ascorbate and DMF–H_2O (1 : 1) as a solvent at RT provided (1-phenyl-1H-1,2,3-triazol-4-yl)methyl benzofuran-2-carboxylates (**5a-d** and **6a-i**) in 75-80% yields (Scheme II).

The structures of **5a-b** and **6a-i** were proved by the spectral analysis. In the ^{1}H NMR spectrum of compound **5b** a characteristic signal at δ 8.14, singlet (1H, triazole-H) and 2.42, singlet (3H, $–CH_3$) were observed. The ^{13}C NMR spectrum of **5b** showed signals at δ 144.88, 21.08 ppm which were in the agreement with the proposed structure; the mass spectrum of **5b** contained a main peak at *m/z* $[M + H]^+$ 334.



Scheme I — Synthesis of key intermediate prop-2-yn-1-yl benzofuran-2-carboxylate **4a-b**

Biology Results

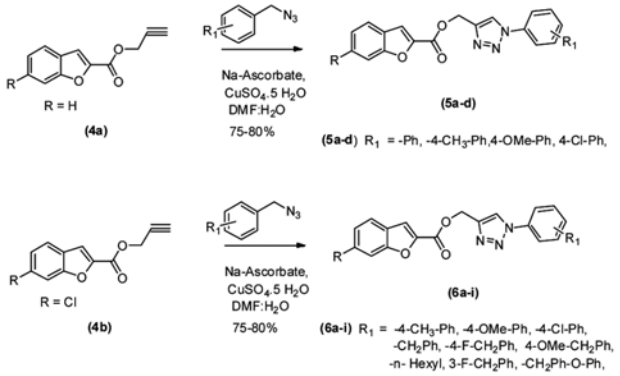
Antibacterial Activity by Paper Disc Method

In this study, we determined *in vitro* antibacterial activity against two gram positive bacteria *Staphylococcus aureus*(MTCC-96), *Bacillus subtilis* and two gram negative bacteria

Escherichia coli (MTCC-443), *Pseudomonas aeruginosa* (MTCC-424), *Klebsiella pneumonia* by the cup-plate agar diffusion method 1 at different concentrations (1 mg /mL). (Table I, Figure 1) displays the inhibition zone diameters for the tested bacteria and Norfloxacin and Ofloxacin served as control[21].

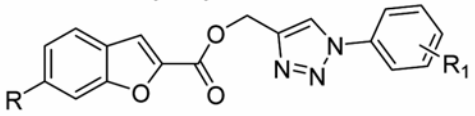
The investigation of the antimicrobial screening data along with the statistical analysis shown in **Table I** revealed that the synthesized compounds showed promising results against the microorganisms. Compounds **6g, 6h** and **6i** expressed the best antibacterial activity compared with other synthesized derivatives, with inhibition zone diameters 8, 9 and 10 mm against the tested bacteria except *Pseudomonas aeruginosa* (MTCC-424). As shown in Table I, for gram negative bacteria *Escherichia coli* (MTCC-443), compound **6i** acts as the most effective one and is mostly comparable to the effectiveness of the control with zone of inhibition 10 mm.

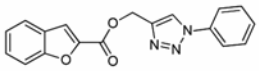
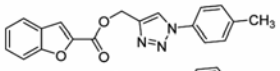
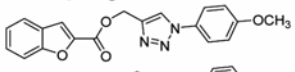
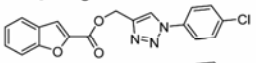
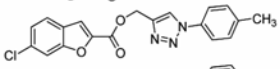
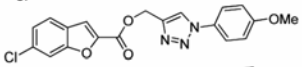
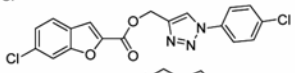
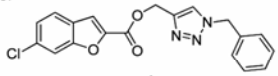
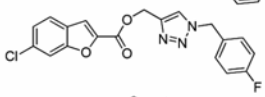
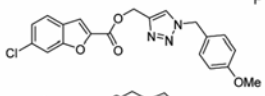
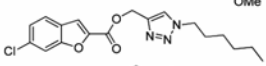
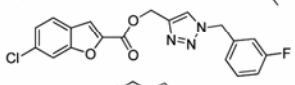
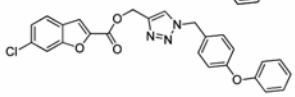
According to the inhibition zone diameter results and compound structures in Table I, the antimicrobial activity against tested bacteria depended on chemical structure. Different structure of compounds exhibited varied bioactivity. Overall, the compounds with chloro substituent on benzofuran and benzene ring exhibited significant bioactivity. The compounds that exhibited



Scheme II — Synthesis of novel (1-phenyl-1*H*-1,2,3-triazol-4-yl)methyl benzofuran-2-carboxylates (**5a-b** and **6a-i**).

Table I — Evaluation of anti-bacterial activity of synthesized novel benzofuran-2-carboxylate 1,2,3-triazoles



S. No.	Structure	Compd	Zone of inhibition in (mm)			
			Pseudomonas aeruginosa (− ve)	*Escherichia coli* (− ve)	*Staphylococcus aureus* (+ ve)	*Bacillus subtilis* (+ ve)
1		**5a**	2	6	2	7
2		**5b**	2	5	2	4
3		**5c**	2	6	7	7
4		**5d**	2	8	7	7
5		**6a**	2	3	4	3
6		**6b**	2	5	5	8
7		**6c**	2	3	4	2
8		**6d**	2	6	6	7
9		**6e**	2	6	6	4
10		**6f**	2	4	6	5
11		**6g**	2	8	9	8
12		**6h**	2	9	7	7
13		**6i**	2	10	9	9
	Norfloxacin (1 mg/mL)		9	–	11	–
	Ofloxacin(1 mg/mL)		–	10	–	10

the most bioactivity were those with chloro substituent on benzofuran ring. The electron-withdrawing group (-Cl) contributed remarkably to the bioactivity. These findings suggest that the new benzofuran-2-carboxylate 1,2,3-triazole compounds exhibit a broad spectrum of antimicrobial activity.

Antifungal activity

The antifungal activity of substituted benzofuran-2-carboxylate 1,2,3-triazoles derivatives (Table II, Figure 2) have been evaluated against *Aspergillus niger* and *Sclerotium rolfsii* by employing Ketoconazole as the standard drug concentration of 1.0 mg/mL[22,23]. The antifungal activity of compounds **5b, 6a, 6c, 6d and 6e** revealed good zone of inhibition, with inhibition zone diameters 4, 4, 4, 4 and 3 mm against the tested against *Sclerotium rolfsii*. The electron donating groups such as methyl, methoxy, chloro, aryl and benzyl substituted groups showed better antifungal activity also electronegative

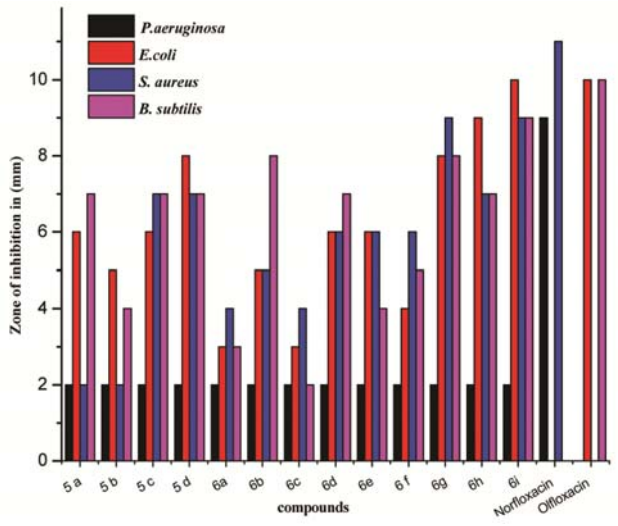


Figure 1 — Antibacterial activity of compounds **5a-d** and **6a-6i** against *Pseudomonas aeruginosa*, *Echerichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*.Micro organisms were screened using potato dextrose agar with *Pseudomonas aeruginosa*, *Echerichia coli*, *Staphylococcus aureus* and *Bacillus subtilis* are showing zone of inhibition (mm) with different concentration of compound.

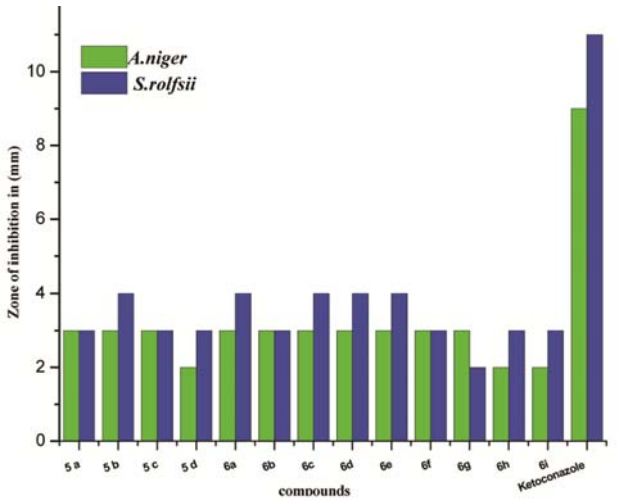


Figure 2 — Antifungal activity of compounds **5a-d** and **6a-i** against *Aspergillusniger and Sclerotium rolfsii*

fluorine containing analogues showed good activity. Whereas the other compounds were showing moderate activity against the fungal strains. The most compounds exhibited bioactivity when compounds with chloro substituent on benzofuran ring. These findings suggest that the new benzofuran-2-carboxylate 1,2,3-triazole compounds exhibit a broad spectrum of anti-fungal activity.

Experimental Section

All the chemicals used in this study were purchased from different commercial sources from Indian vendors with more than 99% purity and were used without any further purification. Reactions were monitored on TLC with UV detection. Final purification was carried out using silica gel 60-120 mesh. The ^{1}H and ^{13}C NMR spectra were recorded on 500, 400, 125 and 100 MHz, respectively, and TMS was used as an internal standard. Chemical shifts relative to TMS as internal standards were reported as δ values in ppm. Mass spectra were recorded using electron spray ionization on Waters e2695 Separators module (Waters, Milford, MA, USA) mass spectrometer. IR spectra were recorded on a Fourier transform (FT-IR), USA (Perkin-Elmer model 337) instrument. The melting points were determined on a Barnstead Electro Thermal 9200 Instrument.

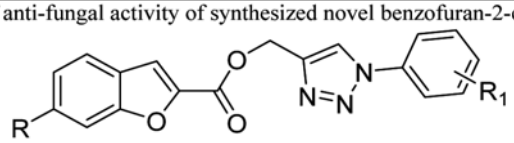
General procedure for the synthesis of ethyl benzofuran-2-carboxylate, 2a-b

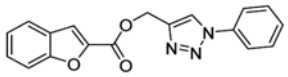
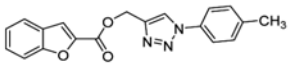
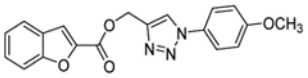
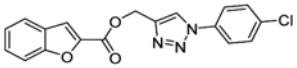
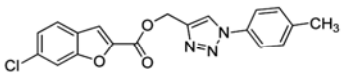
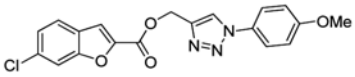
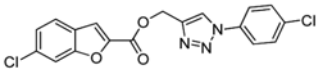
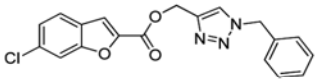
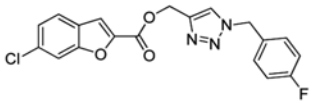
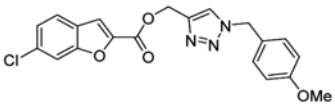
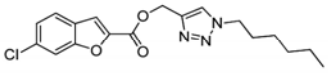
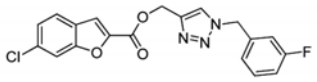
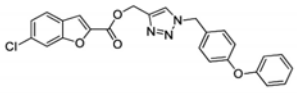
To a solution of salicylaldehyde **1a** (1mmol) in acetonitrile (100 mL), K_2CO_3 (3.0mmol) and the α-bromo ester (1.2mmol) was added slowly to reaction mixture at ambient temperature. The reaction mixture refluxed for 24 hours. After completion of the reaction (monitored by TLC), the solvent was removed under reduced pressure. The resultant crude product was dissolved in ethyl acetate (200 mL) and the resultant solution was washed with 5% dil. HCl. The organic layer was washed with water (50 mL), brine solution (50 mL) and dried over anhydrous sodium sulphate. The crude product was purified by column chromatography over 60-120 mesh silica gel and eluted with ethyl acetate: hexane 1:10 to give title compound **2a** as off white solid 86%yield.

General procedure for the synthesis of benzofuran-2-carboxylic acid, 3a-b

Ethyl benzofuran-2-carboxylate **2a** was dissolved in 80 mL of ethanol and the reaction mixture was cooled to 10°C. To this cooled mixture, a solution of KOH (2.0 mmol) was added drop-wise. After completion of the addition, the resulting mixture was refluxed for 2-3 hours. Excess ethanol was removed under reduced pressure. A light off white solid was obtained to which aqueous HCl was (30 mL) was added. The solid precipitate was collected by filtration and washed with water (50 mL), followed by column chromatography over 60-120 mesh silica gel and

Table II — Evaluation of anti-fungal activity of synthesized novel benzofuran-2-carboxylate 1,2,3-triazoles



S. No	Structure	Compd	Zone of inhibition in (mm) *Aspergillus niger* (mm)	Zone of inhibition in (mm) *Sclerotium rolfsii* (mm)
1.		**5a**	3	3
2.		**5b**	3	4
3.		**5c**	3	3
4.		**5d**	2	3
5.		**6a**	3	4
6.		**6b**	3	3
7.		**6c**	3	4
8.		**6d**	3	4
9.		**6e**	3	4
10.		**6f**	3	3
11.		**6g**	3	2
12.		**6h**	2	3
13.		**6i**	2	3
	Ketoconazole (1 mg/1 mL)		9	11

eluted with ethyl acetate : hexane 3:7 to give title compound **3a** as off white solid in 82%yield.

General procedure for the synthesis of prop-2-yn-1-yl benzofuran-2-carboxylate, 4a-b

A solution of benzofuran-2-carboxylic acid **3a** (1.0mmol) in $SOCl_2$ (1.0 mmol) was stirred at 90°C for 1 hour. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to 0°C, diluted with CH_2Cl_2, and triethyl amine (1.5 mmol) and propargyl alcohol (1.1 mmol) were added. The resulting solution was stirred for 2 hours at ambient temperature. After completion of the reaction, CH_2Cl_2 was removed under vacuum; the

residue obtained was diluted with chilled water and extracted with Ethyl acetate (2 × 50 mL). The combined organic layers were dried over anhydrous sodium sulphate, the solvent was removed under reduced pressure. The crude product was purified by column chromatography using silica gel (60–120 mesh) eluting with ethyl acetate and petroleum ether (2:8) to afford compound **4a** as off white solid in 77% yield.

4a: IR (neat): 3265, 2126, 1725, 1564, 1291, 1172, 1090, 746 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 7.69 (d, 1H, *J* = 7.742 Hz), 7.59 (d, 2 H, *J* = 6.232 Hz), 7.47 (dt, 1 H, *J* = 7.365,1.13 Hz), 7.32 (t, 1 H, *J* = 7.365 Hz), 4.98 (d, 2 H, *J* = 2.266 Hz), 2.57 (t, 1 H, *J* = 2.266 Hz); ^{13}C NMR (100MHz, $CDCl_3$):δ 158.614, 155.835, 144.579,127.921, 126,762, 123.877, 122.906, 114.834, 112.380, 75.605, 52.709; ESI-MS: *m/z* $[M + 1]^+$ 200.94.

4b: IR (neat): 3260, 2132, 1727, 1558, 1275, 1170 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 7.67 (d, 1H, *J* = 2.28 Hz), 7.52 (d, 2 H, *J* = 9.003 Hz), 7.42 (dd, 1 H, *J* = 8.697,1.984 Hz), 4.98 (d, 2 H, *J* = 2.441 Hz), 2.58 (t, 1 H, *J* = 2.441 Hz); ^{13}C NMR (125MHz, $CDCl_3$):δ 158.198, 154.080, 145.842, 129.572, 128.278, 127.967, 122.270, 114.003, 113.453, 76.820, 75.781, 52,889; ESI-MS: *m/z* $[M + 2]^+$236.6.

General procedure for the synthesis of (1-phenyl-1H-1,2,3-triazol-4-yl)methyl benzofuran-2-carboxylate5a-d and 6a-i

Prop-2-yn-1-yl benzofuran-2-carboxylate **4a** (1mmol) and the corresponding aryl or alkyl azides (1.1 mmol) were dissolved in 4 mL of a mixture DMF–H_2O (3 : 1). The reaction mixture was stirred at RT for 10 min, then $CuSO_4 \cdot 5H_2O$ (0.1 mmol) and sodium ascorbate (0.2 mmol) were added. The reaction mixture was stirred at ambient temperature for 6-8 hours. After completion of the reaction (monitored by TLC) add 5 mL of water filtered off the crude solid followed by column chromatography using silica gel (60–120 mesh) eluting with ethyl acetate and petroleum ether (3:7) to afford compound **5a** as off white to brown solid in 78% yield.

5a: IR (neat):3147, 1720, 1502, 1292, 1171, 748 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 8.19 (s, 1 H), 7.75 (d, 2 H, *J* = 7.934 Hz), 7.68 (d, 1 H, *J* = 7.782 Hz), 7.61-7.56 (m, 2 H), 7.53 (t, 2 H, *J* = 7.782 Hz), 7.45 (t, 2 H, *J* = 7.782 Hz), 7.31 (t, 1 H, *J* = 7.477 Hz), 5.61(s, 2 H); ^{13}C NMR (100MHz, $CDCl_3$):δ 159.476, 155.832, 144.852, 143.040, 136.827, 129.772, 128.970, 127.871, 126.799, 123.874, 122.927, 122.600, 120.645, 114.678, 112.344, 58.324; ESI-MS: *m/z* $[M + 1]^+$ 320.29.

5b: IR (neat): 3143,1726, 1520, 1294, 1175, 1094, 750 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$): δ 8.14 (s, 1 H), 7.68 (d, 1 H, *J* = 7.742 Hz), 7.63-7.55 (m, 4 H), 7.45 (t, 1 H, *J* = 7.176 Hz), 7.35-7.27 (m, 3 H), 5.61(s, 2 H), 2.42 (s, 3 H); ^{13}C NMR (100MHz, $CDCl_3$):δ 159.482, 155.824, 144.884, 139.123, 134.548, 130.253, 127.849, 126.807, 123.862, 122.922, 122.587, 120.535, 114.647, 112.346, 58.363, 21.086; ESI-MS: *m/z* $[M + 1]^+$ 334.08.

5c: IR (neat): 3145, 1724, 1518, 1255, 1175, 751cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 8.09 (s, 1 H), 7.68 (d, 1 H, *J* = 7.782 Hz), 7.63 (d, 2 H, *J* = 8.850 Hz), 7.61-7.56 (m, 2 H), 7.45 (t, 1 H, *J* = 7.782 Hz), 7.31 (t, 1 H, *J* = 7.477 Hz), 7.02 (d, 2 H, *J* = 8.850 Hz), 5.60 (s, 2 H), 3.87 (s, 3 H); ^{13}C NMR (100MHz, DMSO-d_6):δ 159.248, 158.261, 155.013, 144.465, 142.270, 129.790, 127.990, 126.480, 123.955, 123.182, 121.738, 114.743, 114.668, 112.042, 57.954, 55.429; ESI-MS: *m/z* $[M + 1]^+$ 350.31.

5d: IR (neat): 3122, 3080, 1730, 1502, 1296, 1175, 1091, 746 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$): δ 8.21 (s, 1 H), 7.72-7.66 (m, 3 H), 7.60-7.56 (m, 2 H), 7.53-7.49 (m, 2 H), 7.46 (dt, 1 H, *J* = 7.354, 0.916 Hz), 7.31 (t, 1 H, *J* = 7.324 Hz), 5.61(s, 2 H); ^{13}C NMR (100MHz, $CDCl_3$):δ 159.476, 155.847, 144.789, 135.348, 134.817, 129.986, 127.927, 126.784, 123.913, 122.943, 121.785, 114.750, 112.353, 58.299; ESI-MS: *m/z* $[M + 2]^+$ 355.96.

6a: IR (neat): 3440, 2977, 2251, 2125, 1658, 1219, 1051, 1023, 821, 752 cm^{-1}; ^1H NMR (500MHz, DMSO-d_6): δ8.93 (bs, 1 H), 7.96 -7.70 (m, 5 H), 7.62 -7.34 (m, 3 H), 5.55 (s, 2 H), 2.38 (s, 3 H); ^{13}C NMR (100MHz, DMSO-d_6):δ; ESI-MS: *m/z* $[M +2]^+$ 370.

6b:IR (neat): 3440, 2977, 2251, 1659, 1220, 1052, 1024, 821, 757 cm^{-1}; ^1H NMR (400MHz, DMSO-d_6): δ 8.80 (s, 1 H), 7.95 -7.70 (m, 5 H), 7.56 (bs, 1 H), 7.14 (bs, 2 H), 5.54 (s, 2 H), 3.84 (s, 3 H); ^{13}C NMR (100MHz, DMSO-d_6):δ 159.265, 157.909, 153.461, 145.814, 142.127, 129.765, 128.306, 127.995, 123.242, 122.453, 121.776, 114.771, 114.095, 113.846, 58.115, 55.462; ESI-MS: *m/z* $[M + 2]^+$ 386.

6c: IR (neat): 3439, 2251, 1661, 1051, 1023, 1002, 821, 759cm^{-1}; ^1H NMR (400MHz, DMSO-d_6): δ 9.01 (s, 1 H), 7.98 (d, 2 H, *J* = 8.925 Hz), 7.90 (d, 1 H, *J* = 2.201 Hz), 7.80 (d, 2 H, J = 8.558 Hz),7.70 (d, 2 H, *J* = 8.803 Hz), 7.57 (dd, 1 H, *J* = 8.925, 2.078 Hz), 5.56

(s, 2 H); ^{13}C NMR (100MHz, DMSO-d_6):δ157.951, 153.526, 145.844, 142.614, 135.209, 133.112, 129.847, 128.388, 128.008, 123.431, 122.569, 121.901, 114.225, 113.912, 58.063; ESI-MS: *m/z* $[M + 2]^+$ 389.99.

6d: IR (neat): 3441, 2251, 1659, 1052, 1024, 821, 758cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): δ 8.34 (s, 1 H), 7.93 -7.67 (m, 3 H), 7.62 -7.21 (m, 6 H), 5.63 (s, 2 H), 5.44 (s, 2 H); ^{13}C NMR (100MHz, DMSO-d_6):δ 157.953, 153.456, 145.837, 141.429, 135.779, 128.693, 128.316, 128.124, 127.979, 125.211, 122.475, 114.043, 113.875, 58.215, 52.793; ESI-MS: *m/z* $[M + 2]^+$ 370.03.

6e: IR (neat):3456, 2979, 2251, 1658, 1220, 1052, 1024, 821, 748 cm^{-1}; ^{1}H NMR (500MHz, DMSO-d_6): δ 8.34 (s, 1 H), 7.85 (d, 1 H, *J* = 1.678 Hz), 7.78 -7.71 (m, 2 H), 7.54 (dd, 1 H, *J* = 8.850, 1.984 Hz), 7.45-7.39 (m, 2 H), 7.21 (t, 2 H, *J* = 8.850 Hz), 5.60 (s, 2 H), 5.44 (s, 2 H); ^{13}C NMR (125MHz, DMSO-d_6):δ 162.782, 160.841, 157.936, 153.431, 145.811, 132.013, 130.358, 130.286, 128.308, 127.977, 125.209, 122.459, 115.605, 115.438, 114.029, 113.827, 58.189, 51.993; ESI-MS: *m/z* $[M + 2]^+$ 388.03.

6f: IR (neat): 3289, 3147, 3094, 2960, 1733, 1572, 1449, 1304, 1175cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): δ 8.35 (bs, 1 H), 8.0-7.69 (m, 4 H), 7.58 (bs, 1 H), 7.30 (bs, 1 H), 6.92(bs, 2 H), 5.59(s, 2 H), 5.45(s, 2 H), 3.74(s, 3 H); ^{13}C NMR(100 MHz, DMSO-d_6):δ159.402, 157.999, 153.514, 141.470, 137.258, 130.026, 128.372, 128.084, 125.306, 122.658, 120.100, 114.234, 113.817, 113.498, 58.275, 54.116, 52.758 ; ESI-MS: *m/z* $[M + NH_3]^+$ 420.

6g: IR (neat): 3132, 2927, 2861, 1716, 1570, 1451, 1292, 1177, 821 cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): δ 8.29 (bs, 1 H), 7.97-7.66 (m, 3 H), 7.56(bs, 1 H), 5.45(s, 2 H), 4.38(s, 2 H), 1.80(s, 2 H), 1.25(bs, 6 H), 0.83(s, 3 H); ^{13}C NMR (100MHz, DMSO-d_6):δ158.167, 153.612, 146.021, 128.506, 128.194, 125.174, 122.690, 114.216, 113.990, 58.400, 49.528, 30.585, 29.672, 25.510, 21.954, 13.850; ESI-MS: *m/z* $[M + NH_3]^+$ 384.

6h: IR (neat): 3148, 3024, 2344, 2119, 1731, 1574, 1306, 1176, 767 cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): δ8.41 (bs, 1 H), 7.96 -7.69 (m, 5 H), 7.64 -7.50 (m, 2 H), 7.48-7.31 (m, 1 H), 5.66 (s, 2 H), 5.46 (s, 2 H); ^{13}C NMR (100MHz, DMSO-d_6):δ163.238, 160.803, 157.950, 153.441, 145.831, 138.456, 130.838, 128.319, 128.001, 125.397, 124.092, 122.762, 115.109, 114.893, 114.031, 113.856, 58.197, 52.089; ESI-MS: *m/z* $[M +1]^+$ 386.

6i: IR (neat): 3275, 2925, 2858, 1730, 1579, 1488, 1260, 1173, 768 cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6): δ 8.36 (bs, 1 H), 7.96-7.67 (m, 3 H), 7.63-7.28 (m, 4 H), 7.24-6.85 (m, 6 H), 5.63(s, 2 H), 5.45(s, 2 H); ^{13}C NMR (100MHz, DMSO-d_6):δ 157.972, 156.885, 156.068, 153.472, 145.854, 141.467, 137.956, 130.428, 130.032, 128.341, 128.022, 125.365, 123.666, 122.831, 122.489, 118.764, 117.946, 114.062, 113.900, 58.219, 52.369; ESI-MS: *m/z* $[M + 2]^+$ 462.

Conclusion

In summary, we have developed a new and efficient method for the synthesis of substituted novel benzofuran-2-carboxylate 1,2,3-triazoles derivatives which are of interest in several fields for their biological properties and synthetic utility in excellent yields using standard Click chemistry method at ambient temperature conditions in DMF/H_2O media. Compared to other methods, this new method has the lead of good yields, inexpensive reagents, easily available, easy work-up, mild reaction conditions, and environmentally friendly reaction conditions. The *in vitro* antibacterial, antifungal evaluation showed that most of the synthesized substituted benzofuran-2-carboxylate 1,2,3-triazoles derivatives exhibited moderate to good zone of inhibition. From the results of antibacterial and antifungal activity of compounds it is interesting to note that substituents like methoxy, methyl and fluoro show better antibacterial and moderate antifungal activity compared to other substituted compounds. Noticeably, compound **6g, 6h** and **6i** were most potent compounds *in vitro* against bacterial and fungal strains.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

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