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Synthesis, Characterization and Antimicrobial Activity of Some Novel

1-amino dibenzofuran derivatives

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Abstract: *A series of novel 1-amino dibenzo[b,d]furan derivatives weresynthesised via the 1,3-dinitrophenol with iodophenol compound. The chemical structures of the compound were elucidated by ^{1}H NMR,^{13}C NMR. The mass of the synthesized compounds was estimated by LCMS.The functional groups present in the title compound were revealed from FT-IR and confirmed by elemental analysis. These compounds were also screened for in vitro antibacterial and antifungal activities.*

Keywords*: 1-nitro dibenzofuran;1-amino dibenzofuran;antimicrobial activities.*

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I. Introduction:

The use of metal complexes for biomedical applications is an important one. In this process, the macrocycles were used as chelating agents for metal ions.They play a vital role as fluorescent sensors and neuroimaging agents. One among them is benzofuran which is a fluorescent molecule that has attracted the attention of researchersas it is able to bind to the amyloid plaques formed during Alzheimer's disease. Dibenzofuran bearing compounds, an analog of benzofuran ring, have been reported to exhibit a great variety of biological effects, including thrombosis and anticholinesterase activity[1-2]. Isolation of several Gram-negative or Gram-positive bacteria able to mineralize non-halogenated dibenzofuran was reported earlier[3].Lichen secondary metabolite isolated from*Cladoniasubstellata*, a derivative of dibenzofuran, shows antimycobacterial activity. However, it cannot be used as a drug because of its weak potency. Synthetic analoguederived from dibenzo[b,d]furan possesses good inhibitory activityagainst *M. tuberculosis*[4-6].

In most of the naturally occurring molecules, there is a lack of biological activity and also the isolation is a tedious procedure. Structure activity relationship (SAR) studies showedthe vital role of dibenzo[b,d]furan moiety on their pharmacological properties[7-8]. Therefore itisenvisaged to synthesize a library (series) of small 1-aminoderivatives of dibenzo[b,d]furan byHuisgen's1,3-dipolar cycloaddition reaction and a view to study their anti-mycobacterialand immune modulatory activity[9-10].

II. Experimental:

Materials

The 1,3-dinitrobenzene, 2-iodophenol, potassium tert-butoxide, pyridine and dimethoxyethane were purchased from Sigma-Aldrich, India and used without purification. Methanol, dichloromethane (DCM), ethyl acetate, hexane,Con.HCl,$SnCl_2$ and triethylamine were purchased from Sigma-Aldrich. Dry solvents were supplied bySpectrochem. Reagent and solvent were purchased from commercial sources and used without further purification unless otherwise noted.

Instruments and methods

The melting points were recorded on SRS Optimelt and are uncorrected.^{1}HNMR spectra were recorded on a 400 MHz Varian spectrometer and ^{13}CNMRspectra were recorded on a 100 MHz Bruker spectrometer with tetramethylsilane (TMS) internal standard. Mass spectra were recorded by using Shimadzu mass spectrometer. The FT-IR spectrawere recorded by KBr pellet technique with the help of a Perkin- Elmer spectrum 100series spectrophotometer.

Column chromatography was performed with silica gel 60-120 mesh. All the reactions were monitored by thin layer chromatography (TLC) plates and their spots were visualized by exposingthem to UV lamp,$KMnO_4$or iodine chamber. The elemental analysis has been obtained usinga Varian instrument VARIO EL3 series analyzer.

Scheme 1:

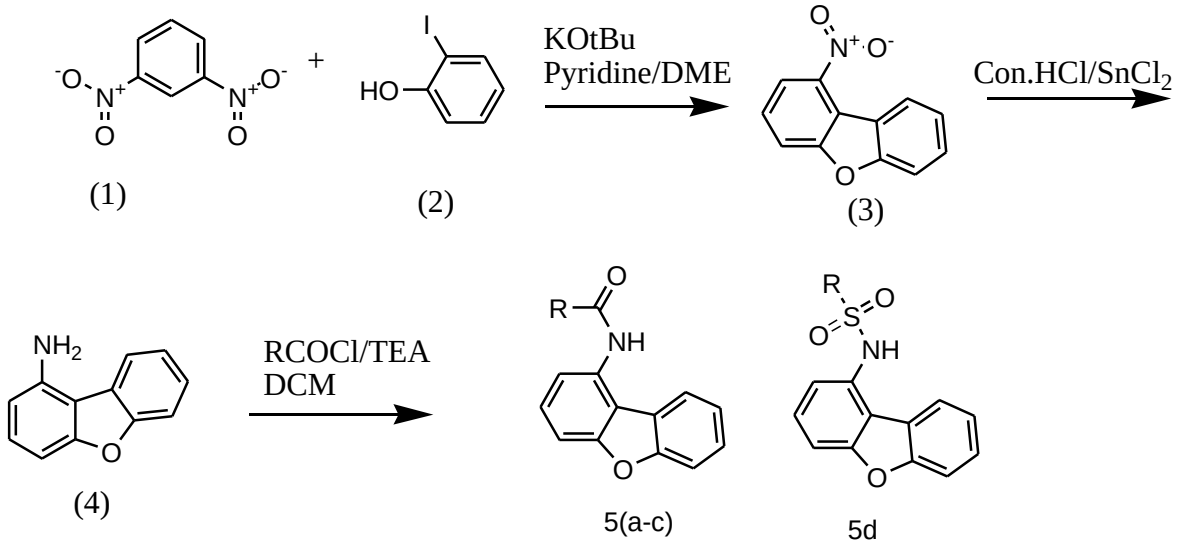
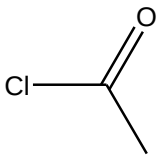
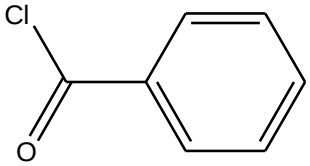
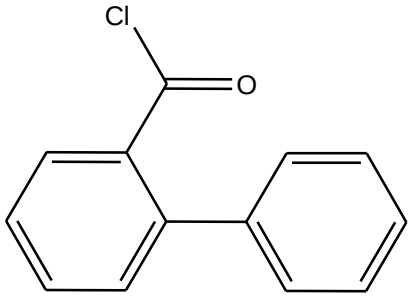
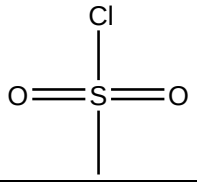


Table 1: Physical constants of 5(a-d)

Compounds	Aryl/Alkyl substituents(-R)	m.p (^{0} C)	R_f
5a		**197-212**	**0.65**
5b		**162-166**	**0.57**
5c		**67-72**	**0.67**
5d		**158-162**	**0.55**

Synthesis and characterization of the compounds

Synthesis of 1-nitro dibenzo[b,d]furan(3)

A solution of 1,3-dinitrobenzene (1)(5g, 29.74mmol, 1eq) and2-iodophenol(2)(6.5g, 29.74mmol, 1eq) was prepared. Now dimethoxyethane (20 mL) and Pyridine (10 mL)were added and stirred again by keeping the temperature at 25°C. The Reaction mixture was stirred for 10 min and then potassium tertiarybutoxide(6.7g, 59.48mmol, 2eq) was added and heated to 100° C for 16 hrs. The progress of the reaction was monitored by TLC. The reaction mixture was cooled to room temperature and quenched with cold water and extracted with

ethyl acetate (2*50 mL), the organic layer was dried (MgSO4) and concentrated. The residue was purified by column chromatography to get 1-nitrodibenzo [b,d]furan (**3**) (3 g, yield 47%, LCMS: 95.5% purity), m.pt.124-135°C. IR (KBr, cm^{-1}): ν_{max} 1518 (N=O), 1690, 1441-1630 (C=C), 973-1150 (C-O, C-N). ^{1}HNMR (400MHz, DMSO-d_6, ppm): δ 8.84 (t, 1H, *J*=8.1Hz, Ar-CH), 8.53 (d, 1H, *J*=7.6Hz, Ar-CH), 8.52-8.25 (m, 3H,Ar-3CH), 7.99-7.58(m, 2H, Ar-2CH). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 112.52,118.16,119.09,120.42,120.57,124.36,125.86,128.20, 129.86,130.62,132.08,143.02. For $C_{12}H_7NO_3$, calculated: 67.61% C, 3.31% H, 6.57% N and 22.51%O. found:67.40% C, 3.39% H, 6.86% N, and 22.18%O. LCMS $[M+1]^+$:m/z 214.19.

Synthesis of 1-amino dibenzo[b,d]furan (4)

Stannous chloride (4 g, 21.12mmol, 1.5eq) was added To a stirred solution compound (3) (3g, 14.08mmol) in Conc.HCl (25 mL) at 0° C, in portionswise. Reaction was stirred for 4hrs at 0° C. The progress of the reaction was monitored by TLC. After the completion, reaction was quenched with ice water. Reaction mixture was extracted with ethyl acetate, dried ($MgSO_4$) and concentrated. Crude residue was purified by column chromatography to get 1-amino dibenzo[b,d]furan(**4**) (2g, yield : 77.8%). LCMS: 95.7% (purity), m.pt.85-117°C. IR (KBr, cm^{-1}): ν_{max} 3368 (NH_2), 1430-1577 (C=C), 1352-1197 (C-O, C-N). ^{1}HNMR (400MHz, DMSO-d_6, ppm): δ 8.27 (t, 1H, *J*=8.4Hz, Ar-CH), 7.61 (d, 1H, *J*=8Hz, Ar-CH), 7.43-7.39 (m, 2H, Ar-2CH), 7.22 (t,1H, *J*=8Hz, Ar-CH), 6.85 (d, 1H, *J*=7.6Hz, Ar-CH), 6.64 (d, 1H, *J*=8Hz,Ar-CH),5.87(s, 2H, NH_2).^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 99.14,108.63,109.52,111.10,122.03,122.99,124.20,125.85, 128.74,144.92,154.81,157.35. For $C_{12}H_9NO$, calculated: 78.67% C, 4.95% H, 7.65% N and 8.73%O. found:78.70% C, 4.79% H, 7.86% Nand 8.58%O. LCMS $[M+1]^+$:m/z 184.21.

Representative procedure to prepare amide derivative*(5 a-d)*

To a solution of 1-amino dibenzo[b,d]furan(4) (100mg, 0.546 mmol) in DCM (2mL), TEA (0.5 mL, 1.09 mmol, 2eq) was added. At 0°C corresponding acid chloride was added dropwise and stirred for 5hrs. The progress of the reaction was monitored by TLC. After the completion, ice water was added then the organic layer was separated, dried ($MgSO_4$) and concentrated. The crude residuewas recrystallized from diethyl ether to give compound (**5a-e**).

Synthesis of N-(dibenzo[b,d]furan-1-yl)acetamide (5a)

Yield: 80 mg, 65%, off-white solid, LCMS: 95.3% (purity), m.pt.197-212°C. IR (KBr, cm^{-1}): ν_{max} 3257 (amide N-H), 1650 (C=O), 1474-1418 (C=C), 1199-1047 (C-O, C-N).^{1}HNMR (400MHz, DMSO-d_6, ppm) : δ10.15 (s,1H, N-H),7.94 (d, 1H, *J*=8.4Hz,Ar-CH), 7.71 (d, 1H, *J*=7.2Hz,Ar-CH), 7.50-7.40 (m, 3H, Ar-3CH), 7.42 (t, 1H, *J*=7.2Hz, Ar-CH), 7.35 (d, 1H, *J*=8Hz, Ar-CH), 2.23 (s,3H,CO-CH_3).^{13}CNMR (100MHz, DMSO-d_6, ppm): δ 39.34, 40.60, 106.11, 107.12, 111.70, 116.22, 123.29, 123.40, 124.60, 127.75, 127.86, 134.12, 145.62, 168.51.For $C_{14}H_{11}NO_2$, calculated: 74.65% C, 4.92% H, 6.22% N and 14.21% O.found: 74.75% C, 4.96% H, 6.27% N and 14.20% O.LCMS $[M+1]^+$:m/z 226.25.

Synthesis of N-(dibenzo[b,d]furan-1-yl)benzamide(5b)

Yield: 85 mg, 51%, white solid, LCMS: 95.4% (purity), m.pt.162-166°C. IR (KBr, cm^{-1}): ν_{max} 3245 (amide N-H), 1690 (C=O), 1521-1425 (C=C), 1268-1125 (C-O, C-N).^{1}HNMR (400MHz, DMSO-d_6, ppm):δ7.86 (d, 1H, *J*=8Hz,Ar-CH), 7.82 (t, 1H, *J*=6.8Hz,Ar-CH), 7.83-7.77 (m, 5H, Ar-5CH),7.71 (d, 1H, *J*=8.4Hz, Ar-CH), 7.56 (t, 1H, *J*=7.2Hz,Ar-CH), 7.50 (d, 1H, *J*=8Hz,Ar-CH),7.44 (t, 1H, *J*=7.6Hz,Ar-CH), 7.42 (t, 1H, *J*=7.8Hz,Ar-CH), 7.34 (d, 1H, *J*=8Hz, Ar-CH).^{13}CNMR (100 MHz,DMSO-d_6,ppm):δ40.60, 112.29,112.62,121.90,124.29, 126.45, 127.65, 128.66,128.89,129.04,129.27,129.33,129.73,132.21, 133.35,134.30,145.08, 156.03, 173.03.For $C_{19}H_{13}NO_2$, calculated: 79.43% C, 4.56% H, 4.88% Nand 11.14%O. found:79.40% C,4.59% H,4.88% Nand 11.18%O.LCMS $[M+1]^+$:m/z 287.32.

Synthesis ofN-(dibenzo[b,d]furan-1-yl)-[1,1'-biphenyl]-4-carboxamide (5c)

Yield: 120mg, 60% white solid, LCMS: 95.3% (purity). m.pt.67-72°C. IR (KBr, cm^{-1}): ν_{max} 3369 (amide N-H), 1651 (C=O), 1594-1306 (C=C), 1264-996 (C-O, C-N).^{1}HNMR (400MHz, DMSO-d_6, ppm) :δ 8.25 (d, 2H, *J*=7.2Hz,Ar-2CH), 7.60 (d, 2H, *J*=8.4Hz,Ar-2CH), 7.42-7.38 (t, 2H, *J*=7Hz,Ar-2CH), 7.35-7.31 (t, 2H, *J*=7.6Hz,Ar-2CH), 7.20-7.16 (t, 2H, *J*=7.8Hz, Ar-CH), 6.83-6.81 (d, 1H, *J*=8Hz, Ar-CH), 6.61-6.59 (d, 2H, *J*=8Hz, Ar-2CH), 5.84(s,4H). ^{13}CNMR (100MHz, DMSO-d_6, ppm): δ 39.97, 40.60, 99.14,108.64,109.52, 111.10, 122.03,122.99,124.21,124.88, 125.85,126.01, 127.34, 127.90, 128.21, 128.74,129.02, 129.40, 129.54, 131.11, 134.34, 136.05, 144.92,157.35, 164.13.For $C_{25}H_{17}NO_2$, calculated: 82.63% C, 4.72% H, 3.85% Nand 8.81%O. found:82.67% C, 4.70% H, 3.87% N and 8.83% O.LCMS $[M+1]^+$:m/z 363.42.

Synthesis of N-(dibenzo[b,d]furan-1-yl)methane sulfonamide (5d)

Yield: 95mg, 67%, 0ff-white solid, LCMS: 95.3% (purity), m.pt.158-162°C. IR (KBr, cm^{-1}): ν_{max} 3019 (amide N-H), 1451 (C=C), 1361-1156 (sulfonamide) 1048-877 (C-O, C-N). ^{1}HNMR (400MHz, DMSO-d_6, ppm): δ 8.22 (d, 1H, *J*=7.2Hz,Ar-CH), 7.93 (d, 1H, *J*=7.6Hz, Ar-CH), 7.80 (d, 1H, *J*=8.4Hz,Ar-CH), 7.67 (d, 1H, *J*=8Hz, Ar-CH), 7.64 (t, 1H, *J*=7.8Hz, Ar-CH), 7.62 (t, 1H, *J*=7.4Hz, Ar-CH), 7.51 (t, 1H, *J*=7.4Hz, Ar-CH), 5.75 (s, 1H, -NH), 2.50 (s, 3H, -CH_3). ^{13}CNMR (100MHz, DMSO-d_6, ppm): δ 39.97,43.70,112.47,114.47,121.88,123.03,124.76,127.30,127.84,128.24,129.07, 139.12, 156.51. For

$C_{13}H_{11}NO_3S$, calculated: 59.76% C, 4.24% H, 5.36% N, 18.37% O and 12.27% S. found:59.66% C, 4.28% H, 5.39% N, 18.39% O and 12.28% S. LCMS $[M+1]^+$:m/z 261.30.

III. Results and discussion:

Chemistry aspect

The synthesis of the N-(dibenzo[b,d]furan-1-yl) substituted amides (5a-e) were carried out as shown in Scheme-I. The starting materials were 1, 3-dinitrobenzene and 2-iodophenol in dimethoxyethane (DME). The obtained intermediate product 1-nitro dibenzo[b,d]furan(3) and 1-amino dibenzo[b,d]furan(4)was then refluxed. Theamine derivatives in dichloromethane (DCM), triethylamine (TEA) with an added acid chloride to get desired compounds (5a-d).

In the IR spectra, the characteristic N–H bands and amide functions were observed at in the range 3245–3369 cm^{-1}. In the NMR spectra, peaks at about 2.22–3.62 ppm, 2.50–2.54 ppm and 10.15–10.17 ppm were seen assigning to CH_3, $CO\text{-}CH_3$, and NH protons respectively. M+1 peaks in mass spectra were agreedwith the calculated molecular weight of the title compounds (5a-d). The weight percentage of C, H and N elements obtained from elemental analysis agree with theoretically calculated values of the compounds.According to LCMS analysis, purity ratio was found greater than 95% for all compounds.

Biological aspect:

Table-1:

Organism	**Zone of inhibition in mm**						
	Bacterial						
	Com3	**Com4**	**5-a**	**5-b**	**5-c**	**5-d**	***Ciprofloxacin***
Salmonella typhi	***13***	***7***	**-**	***8***	***9***	***8***	**20**
Staphylococcus aureus	**-**	***10***	***7***	**-**	***11***	**-**	**15**
Escherichia coli	**-**	***9***	***8***	***8***	***9***	**-**	**12**
Fungi							
Aspergillus niger	***9***	***8***	***8***	***7***	***10***	***9***	***Amphotericin B*** ***10***
Candida albicans	***5***	***9***	***7***	***6***	***11***	***5***	**12**
Candida kefyr	**-**	**8**	**12**	**10**	**10**	**-**	**15**

Collection of microorganisms

The microorganisms such as *Escherichia coli*, *Salmonella typhi*,*Staphylococcus aureus* (*S. aureus*) and fungal development of *Aspergillus niger*, *Candida albicans*, *Candida kefyr* were obtained fromMicro lab, Institute of Research and Technology,Arcot, Vellore,Tamilnadu, India.In the present study,antimicrobial organismswere used for testingmicrobial activities. The bacteria were maintained on nutrient broth (NB) at 37°C and fungus was maintained on potato dextrose agar (PDA) at 28°C.

Antimicrobial activity

The synthesized N-(dibenzo[b,d]furan-1-yl)acetamide (5a), N-(dibenzo[b,d]furan-1-yl)benzamide(5b),N-(dibenzo[b,d]furan-1-yl)-[1,1'-biphenyl]-4-carboxamide(5c),and N-(dibenzo[b,d]furan-1-yl)methanesulfonamide (5d) compounds are subjected to *in-vitro* antibacterial and antifungal activity using agar diffusion.A 20 mL of nutrient agar and PDA medium are used foreach sterile Petri plate (90 mm).It is left for solidification. And then 100 µL of bacterial apprehension was spread on the plates. After 5 minutes, a sterile filter paper disc (6 mm) containing 5 µL of the compound was placed on the surface of each plate. Now the plates were incubated at 37°C for 24 h bacterial development and at 28°C for 48 h for fungal production. The antimicrobial activities of various compounds are examined by measuring the diameter of the inhibition zone (DIZ) in mm.*ciprofloxacin* and *amphotericin B* were served as reference.

IV. Conclusions:

A series of novel 1- amino dibenzo[b,d]furan derivatives were synthesised from the preparation of 1,3-dinitrophenol with 2-iodophenol compound. The functional groups were identified by FT-IR spectral analysis. The ^{1}HNMR and ^{13}CNMR establish the chemical structures of the synthesized compound. Among the series of synthesized compounds, compound 5c shows better antibacterial and antifungal activities. Hence compound 5c can be used for further studies and pharmacological applications.

References:

[1]. Jose Barreto, Tanmaya Joshi, Venkatachalam.T.K, David Reutens.C, Bim Graham andLeoneSpiccia,Journal of coordination chemistry, 2015, 68:2, 335-349.
[2]. LeyleYuttta.S, Usama Abu Mohsen, Ye Sim Ozkan,SimlaCobanoglu, Serkan Levent andZafer Asim Kaplancikli, Journal of enzyme inhib med chem, 2016,31(6), 1177-1183.
[3]. SahadevChirke.S, Jattuboyina Siva Krishna, Balaji Rathod.B, Srinivasa Reddy Bonam,Vijay Khedkar.M, BatchuVenkateswara Rao, HalmuthurMahabalarao Sampath Kumar andPrakasham Reddy Shetty,Journal of medicinal chemistry and drug discovery, 2017, 2,7309-7318.
[4]. Mauro Esposite, Antonella De Roma, Stefania Cavallo, Gianfranco Diletti, Loredana Baldiand`GiampieroScortichini, Toxic, 2017, 5, 33.
[5]. Santhosh Reddy Patpi, Lokesh Pulipati, Perumal Yogeeswari, Dharmarajan Sriram, NishantJain, Balasubramanian Sridhar, Ramalinga Murthy, Anjana Devi.T, Shasi VardhanKalivendi, and Srinivas Kantevari,Journal of medicinal chemistry, 2012, 55, 3911-3922.
[6]. Toshiya Iida, Yuki Mukouzaka, Kaoru Nakamuta, Isamu Yamaguhi and Toshiaki Kudo,Bioscience,Biotechnology and Biochemistry, 2015, 66:7, 1462-1472.
[7]. Venkatachalam.T.K, Jose Barreto, Ute Kreher, David Reutens.C, Leone Spiccia, Journal ofinorganic chemical acta, 2010, 363, 2896-2904.
[8]. MasayoriHagimrdi, Takashi Temma, Shinji Kudo, Kohei Sano, Naoya Kondo, TakahiroMukai,Bioorganic and Medicinal chemistry letters, 2018, 28, 193-195.
[9]. Falko Berndt, Ilya Ioffe, Alexander Granovsky.A, Rainer Mahrwald, Sebastian Tannert,Sergey Kovalenko, Nikolaus Ernsting.P, Journal of photochemistry and photobiology, 2012,234, 164-170.
[10]. Joanne Laub.B, Mark Greenlee.L, Frank Dininno, Joann Huber.L and Jon Sundelof.G,Bioorganic and Medicinal chemistry, 1999, 2973-2979.
[11]. Lanny Liebeskind.S, PavankumarGangireddy and MatthewLindale.G, Journal ofAmerican chemical society, 2016, 138, 6715-6718.
[12]. Anbarasu.S, Kishore Kumar.T, Prem Anad Devarajan, Journal of minerals and materialscharacterization and engineering, 2013, 1, 110-116.
[13]. Ian Armitage, Mingkun Fu, Fredrick Hicks, AdiseshuKattuboina, Jennifer.S.N, AshleyMccarron and Lei Zhu, Journal of heterocyclic, 2015.
[14]. Khoshtariya.T.E, Dzhashi.T.O, Kurkovskaya.L.N, Journal of heterocyclic, 1999, 35, 5.
[15]. Tetsuro Ito, Toshiyuki Tanaka, MunekazuIinuma, Ken IchiNakaya, Yoshikazu Takahashi, Ryuichi Sawa, Hiroshi Naganawa and VeliahChelladurai, Journal of tetrahedron, 2003,59, 1255-1264.

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