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Research Article

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Bis [2-(4`-aryl-1`, 2`, 4`-triazol-5`-yl)-3-methoxy-5-nitrobenzofuran] sulphides and disulphides: Synthesis and their antimicrobial potency

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ABSTRACT

The title compounds were synthesized respectively by treating 3-methyl-5-nitro-2(4`-aryl-3`-mercapto-1`,2`,4`-triazol-5`-yl)benzofurans (1a-c) with thionyl chloride and ethanolic bromine at room temperature for 2½ hours in good yields (2a-c) (3a-c). The structural assignment of these title compounds was done on the basis of our earlier observations, analytical and spectral data. The newly synthesized compounds were subjected to antimicrobial screening using gram positive and gram negative bacteria and fungi. The results are summarized in the preceding table.

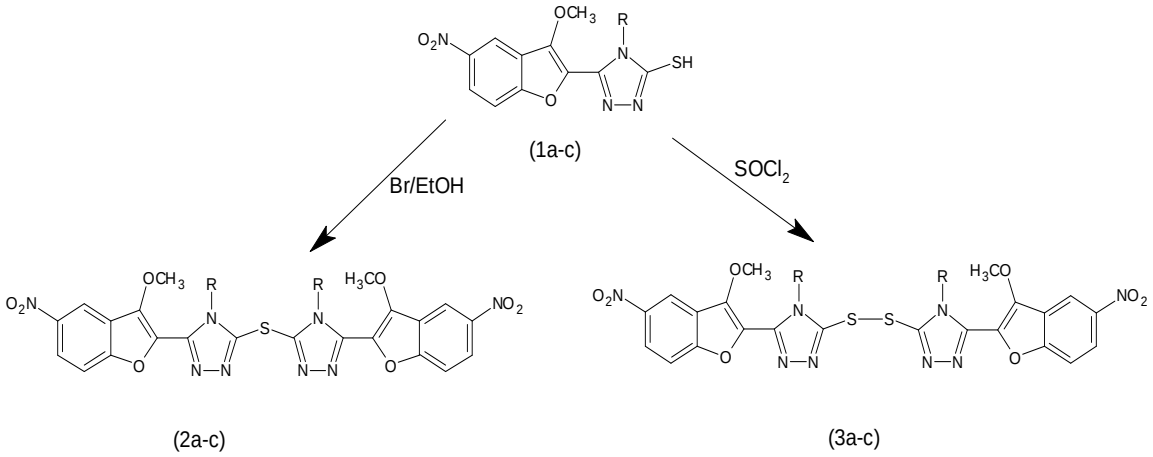
Keywords: Benzofuran, Triazole, antibacterial, antifungal, sulphides and disulphide

INTRODUCTION

Several 1, 2, 4-triazlyl sulphides[1-2], disulphides[3-5] and Sulphones are known to possess broad biocidal spectrum. We reported the synthesis and biological evaluation of 3-methyl-5-nitro-2(4`-aryl-3`-mercapto-1`, 2`, 4`-triazol-5`-yl)benzofurans (1a-c) in our earlier research publication[6]. Our laboratory had also reported the synthesis and biological activity of similar sulphides and disulphides of simple benzofurans[7]. Long before in the year 1979 sing and coworkers have reported the herbicidal and fungicidal properties of such sulphied and disulphides[8]. All these compounds incorporate >N-C-S moiety, the toxophoric importance of it has been well established[9-10]. In view of these facts and In continuation of our search for biologically active benzofuran derivatives we now tried to synthesize bis heterocycles of 3-methyl-5-nitro-2(4`-aryl-3`-mercapto-1`,2`,4`-triazol-5`-yl)benzofurans (1a-c). The antimicrobial potency of precursor compound and its analogs have encouraged us to screen these title compounds for their antimicrobial activity.

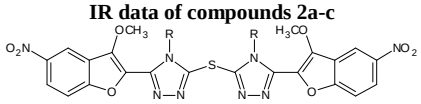
Theory:
A convenient rout for converting 3-mercapto-1, 2, 4-triazoles into sulphides and disulphides was reported from our laboratory[7]. The treatment of 3-methyl-5-nitro-2(4`-aryl-3`-mercapto-1`,2`,4`-triazol-5`-yl)benzofurans (1a-c) with thionyl chloride at room temperature for 2½ an hour produced bis[2-(4`-aryl-1`,2`,4`-triazol-5`-yl)-3-methoxy-5-nitrobenzofuran]sulphides (2a-c) and with ethanolic bromine at room temperature gave bis[2-(4`-aryl-1`,2`,4`-triazol-5`-yl)-3-methoxy-5-nitrobenzofuran] disulphides (3a-c). The structure of these compounds was established based on our earlier observations, analytical and spectral data. The IR spectra of sulphide and disulphides showed the absence of characteristic absorption band due to C=S and NH that were present in their precursors.

Reaction Scheme-1



	R
a	C6H5
b	C6H4.CH3(4)
c	C6H4.CH3(4)

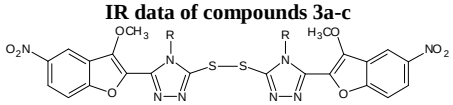
Table-1
IR data of compounds 2a-c



(2a-c)

Sl. No	Compound	Substituent (R)	IR data in cm^{-1}
01	2a	C6H5	1620 (C=N)
02	2b	C6H4.CH3(4)	1640 (C=N)
03	2c	C6H4.CH3(4)	1650 (C=N)

Table-2
IR data of compounds 3a-c



(3a-c)

Sl. No	Compound	Substituent (R)	IR data in cm^{-1}
01	3a	C6H5	1620 (C=N)
02	3b	C6H4.CH3(4)	1600 (C=N)
03	3c	C6H4.CH3(4)	1640 (C=N)

EXPERIMENTAL SECTION

Bis [2-(4`-aryl-1`,2`,4`-triazol-5`-yl)-3-methoxy-5-nitrobenzofuran] sulphides (2a-c):
A mixture of 3-methoxy-5-nitro-2-(4`aryl-3`-mercapto-1`,2`,4-triazol-5`-yl)benzofurans (1a-e) (0.001mol) and thionyl chloride was stirred at room temperature for 2 ½ hour. The excess of thionyl chloride was distilled off. The residual solid was treated with cold water. The solid compound was filtered at pump and purified by recrystallization using suitable solvent. The physical constant, solvent for crystallization, percentage of yield and analytical data are given in the table No.3

Bis [2-(4`-aryl-1`,2`,4`-triazol-5`-yl)-3-methoxy-5-nitrobenzofuran] disulphides (3a-c):
3-Methoxy-5-nitro-2-(4`aryl-3`-mercapto-1`,2`,4-triazol-5`-yl)benzofurans (1a-e) (0.001 mol) was stirred in a solution of bromine (0.001 mol) in ethanol (1.5 ml) for 2½ hours. The reaction mixture was evaporated to dryness under reduced pressure. The residual solid was washed with water and purified by recrystallization using suitable

solvent. The physical constant, solvent for crystallization, percentage of yield and analytical data are given in the table No.3

Table-3

Comp	Substituent R	M. P in ^oC	Yield in %	Solvent
2a	C_6H_5	267	60	Methanol
2b	$C_6H_4.CH_3(4)$	221	65	Methanol
2c	$C_6H_4.CH_3(4)$	243	62	Ethanol
3a	C_6H_5	179	68	Methanol
3b	$C_6H_4.CH_3(4)$	212	72	1,4-Dioxane
3c	$C_6H_4.CH_3(4)$	280	63	Ethanol

Antimicrobial Activity:

A] Antibacterial Activity: The antibacterial activity of newly synthesized compounds was studied in comparison with standard drugs viz… Gentamycin and Ciprofloxacin by cup-plate method using two gram positive and two gram negative organisms[11]. Test samples were used at a concentration of 100 µg/0.1 ml and the standard sample at 10 µg/0.1 ml. The bacteria selected for the study are *S.aureus, b subtilis, E coli and P aeruginosa*. DMF was used as solvent control. The results are summarized in the table No-4.

B] Antifungal Activity: The antifungal activity of test compounds is performed in comparison with standard drugs like Griseofulvin and Flucanazole by Cup-plate method[11]. The fungi used are *Asperagillus niger* and *Candida albicans.* Concentration of test compounds used for the present investigation is 100mg/0.1 ml in DMF. The standard drug is prepared in distilled water. Both the solvents are tested for their antifungal activity along with test compounds as solvent control. Zone of inhibition recorded is the average of six measurements for each sample. Results are presented in the table No-5.

RESULTS AND DISCUSSION

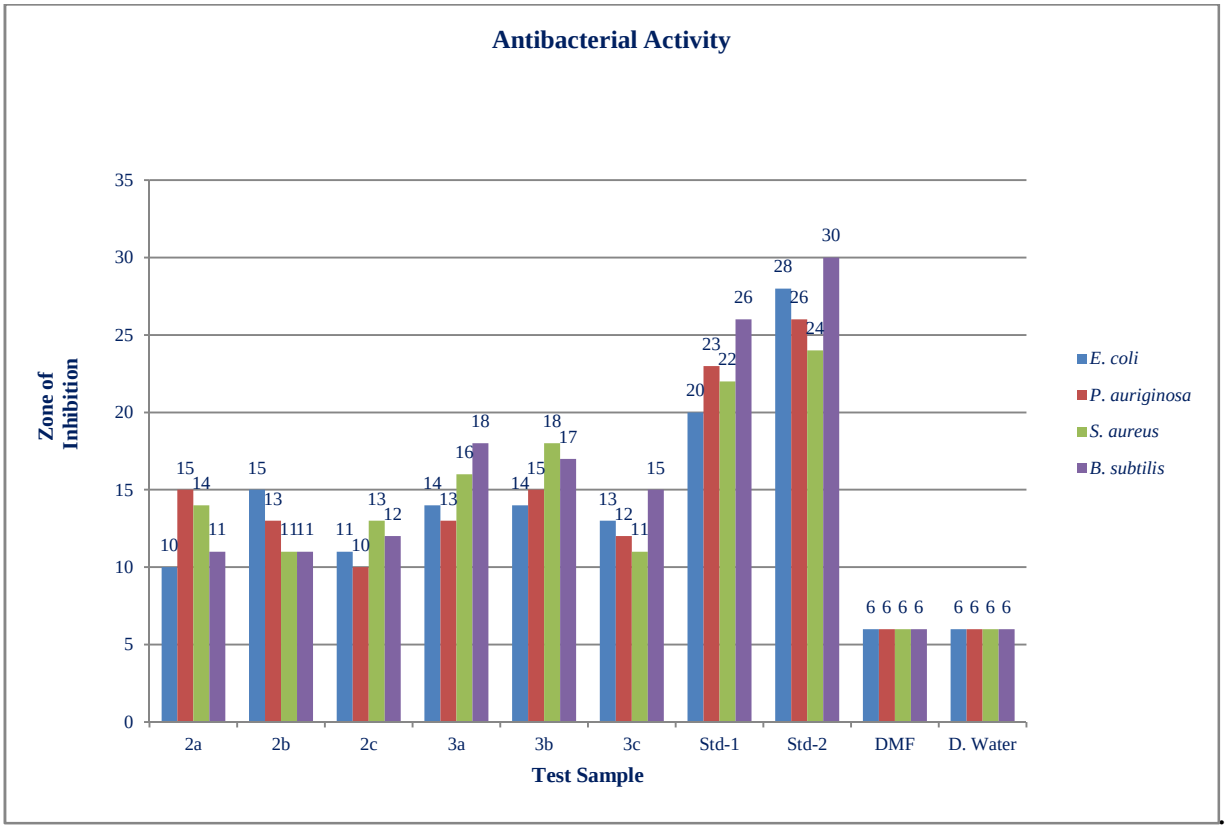
A] Antibacterial Activity: The comparative antibacterial screening of test compounds have shown varied results. The results are summarized in the preceding table No-4.

Among the compounds 2a-c, compound 2a has exhibited good activity against bacteria *P.aeruginosa* and *S.aureus,* whereas it is moderately active against *E.coli* and *B.subtilis*. Compound 2b has shown good activity against *E.coli* and *P.aeruginosa* and it is moderately active against remaining two bacteria used for testing. Compound 2c is moderately active against all the bacteria used.

Out of 3 analogous compounds of 3a-e, compound 3a and 3b have shown challenging activity against *S.aureus* and *B. subtilis* whereas against *E.coli* and *P.aeruginosa* they are good. The compound 3c has exhibited moderate to good activity against all bacteria used.

Table-4 Antibacterial activity results

Comp	'R'	Zone of Inhibition after 24 hours of incubation (in mm)			
		E. coli	*P. aeruginosa*	*S. aureus*	*B. subtilis*
2a	C6H5	**10**	**15**	**14**	**11**
2b	C6H4.CH3(4)	**15**	**13**	**11**	**11**
2c	C6H4.CH3(4)	**11**	**10**	**13**	**12**
3a	C6H5	**14**	**13**	**16**	**18**
3b	C6H4.CH3(4)	**14**	**15**	**18**	**17**
3c	C6H4.CH3(4)	**13**	**12**	**11**	**15**
Std-1	Gentamycin	**20**	**23**	**22**	**26**
Std-2	Ciprofloxacin	**28**	**26**	**24**	**30**
Control	DMF	**6**	**6**	**6**	**6**
Control	D. Water	**6**	**6**	**6**	**6**



Test compound concentration: 100µg/0.1ml
Standard drug Concentration: 10 µg/0.1ml
Cup diameter: 6mm

B] Antifungal Activity:

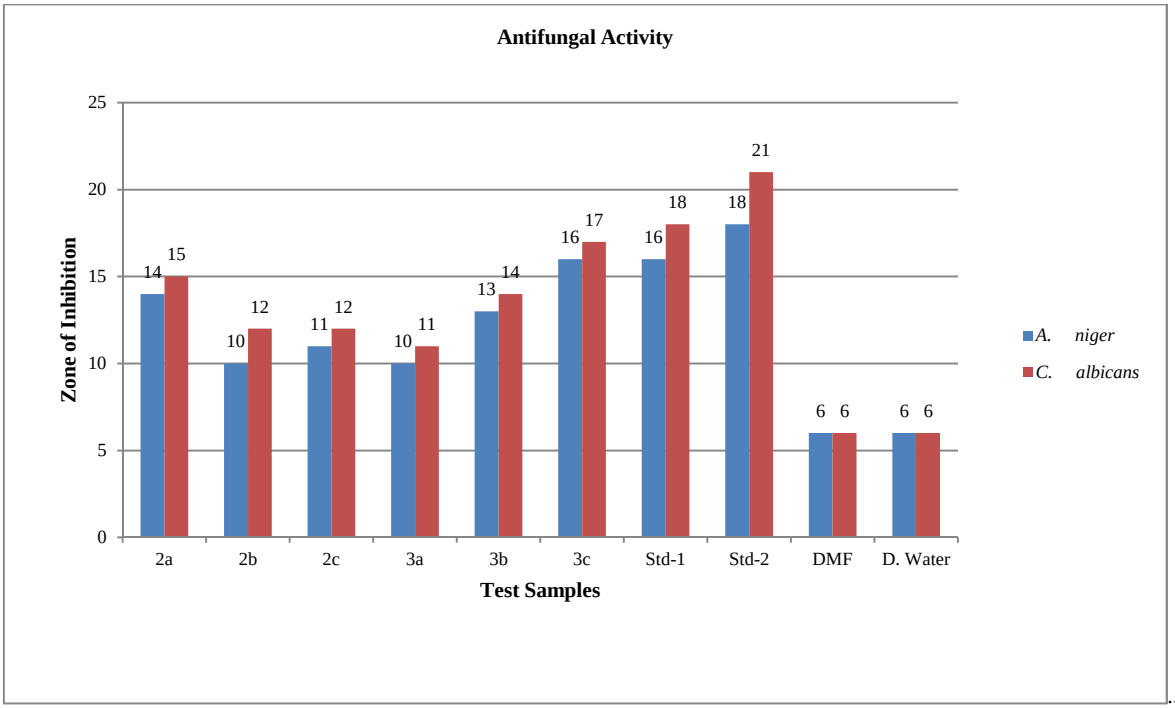
The antifungal activity of title compounds is done in comparison with standard drug. The results are given in the following table No-5.

Among the compounds tested 2a-c, compound 2a is good at inhibiting the growth of fungi *A.niger* and *C.albicans*, the remaining two compounds viz… 2b and 2c are moderately active against both the fungi used.

Among compounds 3a-c, compound 3c has shown good activity against both the fungi used, whereas 3a and 3b are moderately active.

Table-5 Antifungal activity results

Comp	'R'	Zone of inhibition (in mm)	
		A. niger	***B. albicans***
2a	C6H5	14	15
2b	C6H4.CH3(4)	10	12
2c	C6H4.CH3(4)	11	12
3a	C6H5	10	11
3b	C6H4.CH3(4)	13	14
3c	C6H4.CH3(4)	16	17
Std-1	Griseofulvin	16	18
Std-2	Flucanazole	18	21
Control	DMF	6	6
Control	D. water	6	6



Test compound concentration: 100 g/0.1ml
Standard drug Concentration: 10 g/0.1ml
Cup diameter: 6mm

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