Environmentally benign and convenient synthesis of solid state fluorinated 1, 8-naphthyridinyl phthalazine -1, 4-dithiones

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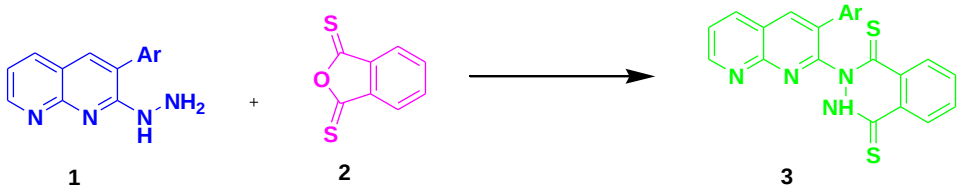
ABSTRACT

A new series of fluorinated 1, 8-naphthyridine -1,4-dithiones **3(a-f)** were obtained by the treatment of 3-aryl-2-hydrazino-1,8-naphthyridnes **1(a-f)** with isobenzo furan-1,3-dithione **2** in the presence of *p*-toluenesulphonic acid (PTSA) in the solid state at room temperature as one pot. All the products are monitored by TLC and isolated by GC and furthermore confirmed by spectral analysis.

Keywords— 1, 8-naphthyridine, *p*-TSA, one-pot synthesis.



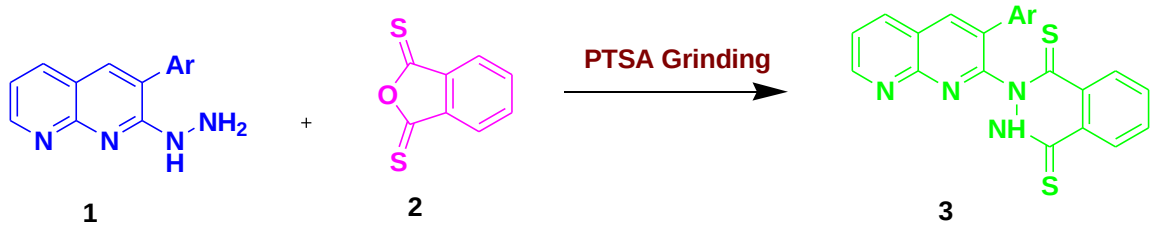
Graphical Abstract

INTRODUCTION

1,8-Naphthyridines constitute one of the most active class of compounds possessing diverse pharmacological and microbiological activity[1]. Phthalazines represent a heterocyclic system of remarkable biological efficiency[2-5].Fluorine containing organic compounds constitute an area of rapidly growing interest because of their unique physical and biological properties[6-8].

Solid state organic synthesis is an active area of research. So, the grinding method has increasingly been used in organic synthesis in recent years. Compared to traditional methods, many organic reactions occur more efficiently in the solid state than in solution and in some cases even more selectively. Furthermore, the solid state reaction has many advantages: reduction pollution, low costs and simplicity in process and handling [9-11].

In view of this, we report herein a convenient and efficient method for the synthesis of fluorinated 2-(3-aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4-dithiones **3** using *p*-toluenesulphonic acid (PTSA) in the solid state at RT.(Scheme I)



1 2 3

Ar		Ar	
a:	2-F C_6H_4	**d**:	2-CF_3 C_6H_4
b:	3-F C_6H_4	**e**:	3-CF_3 C_6H_4
c:	4-F C_6H_4	**f**:	4-CF_3 C_6H_4

Scheme I

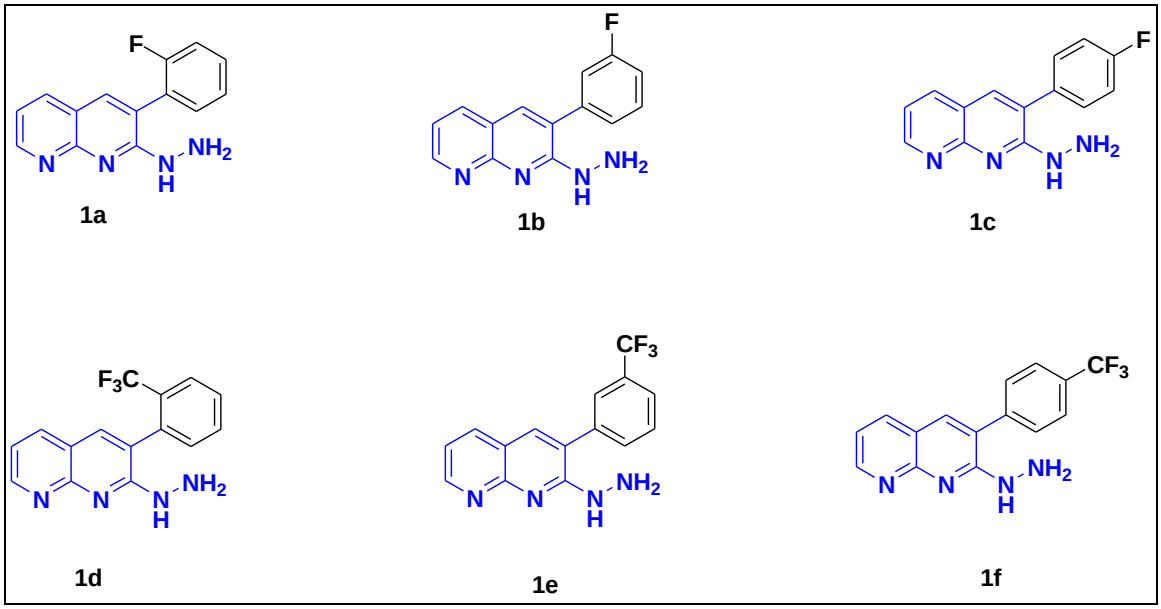


Fig: 1 2-hydrazino-1,8-naphthyridnes 1(a-f)

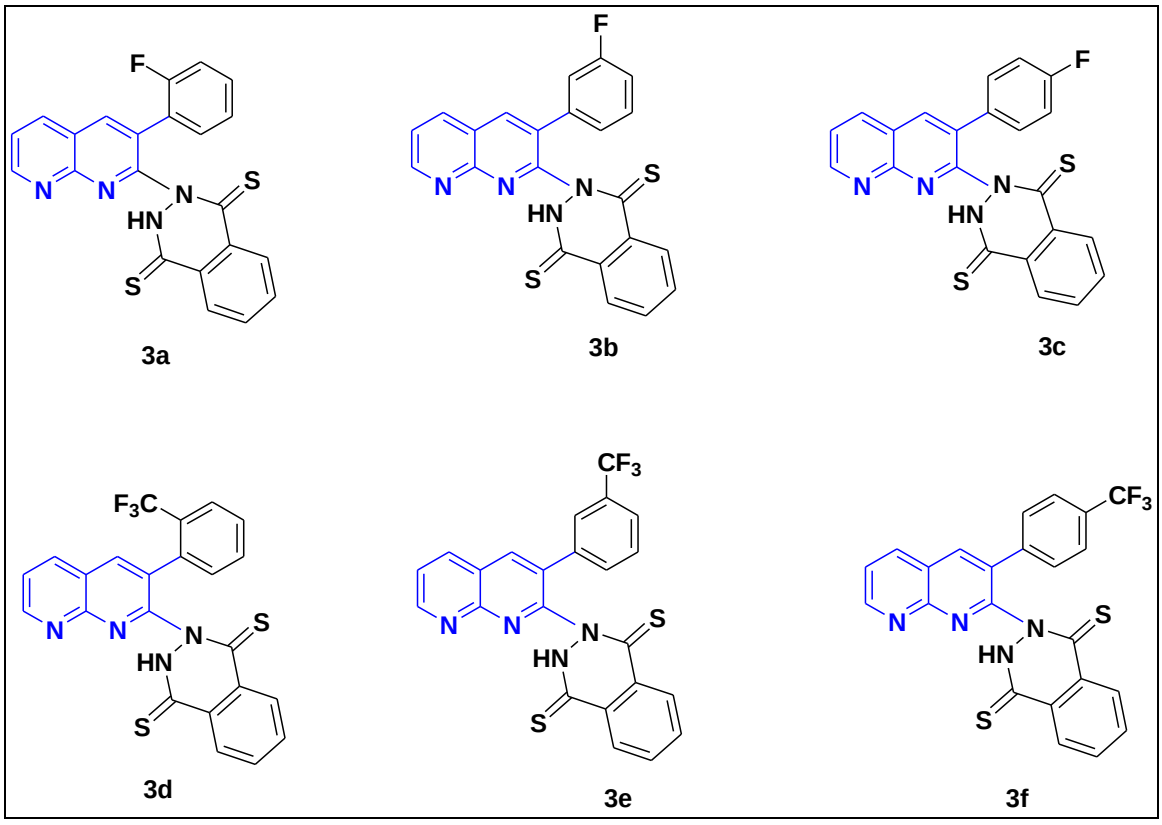


Fig: 2 fluorinated 1, 8-naphthyridine -1, 4-dithiones (3a-f)

MATERIAL AND METHODS

The ^{1}H NMR spectra were recorded in $CDCl_3$ solvent on JEOL Eclipse (400 MHZ) instrument respectively with TMS as internal standard and values are given in ppm (δ). Mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer. Thin layer chromatography (TLC) plates were coated with silica gel G and exposed to iodine vapors to check the homogeneity as well as the progress of reaction. Petroleum ether refers to a fraction of boiling point 60-80^{O}C. Sodium sulphate (anhydrous) was used as a drying agent.

EXPERIMENTAL SECTION

Treatment of 3-aryl-2-hydrazino-1,8-naphthyridnes **1(a-f)** with isobenzo furan-1,3-dithione **2** in the presence of *p*-toluenesulphonic acid (PTSA) in the solid state at room temperature resulted in the formation of the corresponding 2-(3-aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4-dithiones **3(a-f)** (**Scheme I**).

In a typical case, an equimolar mixture of 3-(2-flourophenyl)-2-hydrazino-1,8-naphthyridine **1a** with isobenzo furan- 1,3-dithione **2** and PTSA was ground in mortar by pestle at room temperature for 5.0 min. After usual work-up of the reaction mixture afforded 2-[3-(2-fluorophenyl)-1,8-naphthyrdin-2yl]-1,2,3,4-tetrahydrophthalazine-1,4-dithione **3 (Ar= 2-F C_6H_4)** in 90% yield.

The reaction is of general applicability and the various 2-(3-aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4- dithione **3 (** Ar= 2-F C_6H_4, 3-F C_6H_4, 4-F C_6H_4, 2-CF_3 C_6H_4, 3-CF_3 C_6H_4, 4-CF_3 C_6H_4)synthesized are given in **Table III**.

The structures of the compounds **3** were determined by spectral (^{1}HNMR and MS) and analytical data.

RESULTS AND DISCUSSION

^{1}H NMR spectra

The ^{1}H NMR (400 MHz) spectra of 2-(3-aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4-dithiones **3** were recorded in $CDCl_3$ and the data are summarized in **Table I**.

Table I ^{1}H NMR spectral data of 2-(3-Aryl-1,8-naphthyridin-2-yl)-1,2,3,4-Tetrahydro-5,6,7,8-tetrachlorophthalazine-1,4-dithiones 3.

Entry	Ar	^{1}H NMR (400 MHz, $CDCl_3$) (, ppm)
3a	2- F C_6H_4	7.65 (m, 1H, C_6-H), 7.75 (m, 2H, C_4-H, C_5-H), 8.32 (m, 1H, C_7-H), 7.00-7.50 (m, 8H, Ar-H), 10.10 (s, 1H, NH).
3b	3- F C_6H_4	7.68 (m, 1H, C_6-H), 7.80 (m, 2H, C_4-H, C_5-H), 8.34 (m, 1H, C_7-H), 6.98-7.59 (m, 8H, Ar-H), 10.22 (s, 1H, NH).
3c	4- F C_6H_4	7.80 (m, 1H, C_6-H), 8.10 (m, 2H, C_4-H, C_5-H), 8.30 (m, 1H, C_7-H), 7.00-7.67 (m, 8H, Ar-H), 10.25 (s, 1H, NH).
3d	2- CF_3 C_6H_4	7.80 (m, 1H, C_6-H), 8.15 (m, 2H, C_4-H,C_5-H), 8.35 (m, 1H, C_7-H), 6.98-7.70 (m, 8H, Ar-H), 10.23 (s, 1H, NH).
3e	3- CF_3 C_6H_4	7.68 (m, 1H, C_6-H), 7.95 (m, 2H, C_4-H,C_5-H), 8.30 (m, 1H, C_7-H), 7.00-7.62 (m, 8H, Ar-H), 10.15 (s, 1H, NH).
3f	4- CF_3 C_6H_4	7.65 (m, 1H, C_6-H), 7.80 (m, 2H, C_4-H,C_5-H), 8.28 (m, 1H, C_7-H), 6.90-7.61 (m, 8H, Ar-H), 10.22 (s, 1H, NH).

Table II Mass spectral data of 2-(3-Aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4-dithiones **3**

Entry	Ar	ESI MS $(M^+ + H)m/z$
3a	2- F C_6H_4	431
3b	3- F C_6H_4	431
3c	4- F C_6H_4	431
3d	2- CF_3 C_6H_4	481
3e	3- CF_3 C_6H_4	481
3f	4- CF_3 C_6H_4	481

Table III Characterization data of 2-(3-Aryl-1,8-naphthyridin-2-yl)-1,2,3,4-tetrahydro-5,6,7,8-tetrachlorophthalazine-1,4-dithiones **3**

Entry	Ar	Reaction time (min)	m.p. °C	Yield (%)	Mol. Formula	Found % (Calcd)		
						C	H	N
3a	2- F C_6H_4	5.0	272	90	$C_{23}H_{16}FN_4S_2$	64.03 (64.01	4.40 4.38	12.90 12.87)
3b	3- F C_6H_4	4.5	260	89	$C_{23}H_{16}FN_4S_2$	64.03 (64.01	4.40 4.38	12.88 12.86)
3c	4- F C_6H_4	4.0	264	92	$C_{23}H_{16}FN_4S_2$	64.03 (64.01	3.40 4.37	12.88 12.86)
3d	2- CF_3 C_6H_4	5.5	258	92	$C_{24}H_{16}F_3N_4S_2$	59.86 (59.84	3.35 3.33	11. 64 11.62)
3e	3- CF_3 C_6H_4	5.0	266	90	$C_{24}H_{16}F_3N_4S_2$	59.86 (59.82	3.35 3.32	11.64 11.62)
3f	4- CF_3 C_6H_4	5.5	270	94	$C_{24}H_{16}F_3N_4S_2$	59.86 (59.83	3.37 3.34	11.64 11.60)

CONCLUSION

2-(3-aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine-1,4-dithiones are displayed. Reactions are not consuming and the yields of the products are very good. The products were obtained with a high degree of purity by this procedure. The process is environmentally benign. The experimental procedure is very simple. The significant advantages of this procedure are operation simplicity, mild reaction conditions, economic viability, high yields and excellent purities of the products and inexpensive and non-toxic catalyst.

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