Asian Journal of Chemistry Vol. 6, No. 4 (1994), 945–949

Synthesis and Antibacterial Activity of Some 2-Amino-4-[2′- (2″, 6″-dinitro-4″-trifluoromethylphenoxy)-5′-methyl-phen-1′-yl]-6-substituted Phenyl Pyrimidines

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2-Amino-4-[2′-(2″,6″-dinitro-4-trifluoromethyl-phenoxy)-5′-methylphen-1′-yl]-6-substituted phenyl pyrimidines have been synthesised by the condensation of 1-[2′-(2″,6″-dinitro-4″-trifluoromethylphenoxy)-5-′-methylphen-1′-yl]-3-substituted phenyl -2- propen-1-one with guanidine nitrate. These compounds were screened for antibacterial activity against *S. aureus* and *E. coli*.

INTRODUCTION

2-Aminopyrimidines are known for their physiological importance.[1-4] Ahluwalia and coworkers[5] have synthesised some new 2-aminopyrimidines which were evaluated as antibacterial agents. The present communication deals with the reaction of 1-(2′-hydroxy-5′-methylphen-1′-yl)-3-phenyl-2-propen-1-one[6] with 4-chloro-3,5-dinitrobenzotrifluoride[7] in presence of aqueous potassium hydroxide which gave 1a. Condensation of 1a with guanidine nitrate furnished a number of new 2-amino-pyrimidines 2a (Scheme 1).

Antibacterial activity

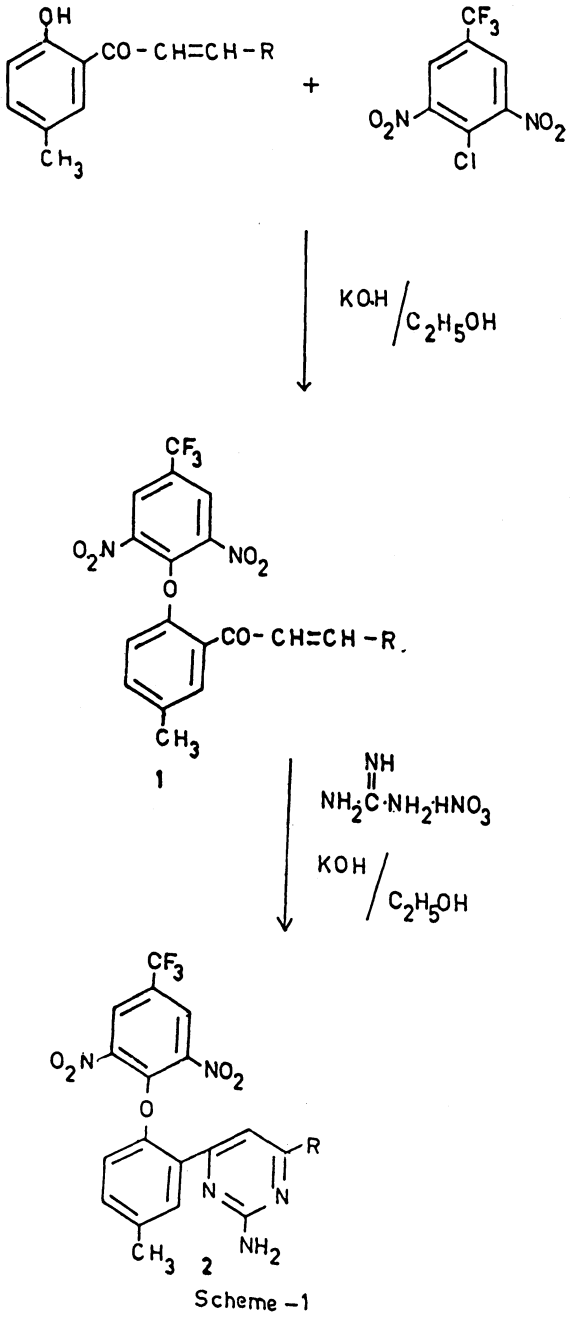
Compounds 2a–o were screened for antibacterial activity using cup-plate agar diffusion method.[8] The testing was carried out at concentration of 50 μg using gram-positive bacteria *Staphylococcus aureus* and gram-negative bacteria *Escherichia coli*. The results of antibacterial activity are given in Table 3.

EXPERIMENTAL

Melting points are uncorrected. The IR spectra (KBr) were taken on the Perkin-Elmer-377 model spectrophotometer and elemental analyses were carried out by Carlo Erba 1108 analyser.

1-[2′-(2″,6″-dinitro-4″-trifluoromethylphenoxy)-5′-methylphen-1′-yl]-3-phenyl-2-propen -1-one (General Procedure) 1a

A mixture of 1-(2′-hydroxy-5′-methylphen-1′-yl)-3-phenyl-2-propen-1-one (4.72 g, 0.01 mol), aqueous potassium hydroxide (20%, 5 ml), 4-chloro-3,5-dinitrobenzotrifluoride (2.70 g, 0.01 mol) and absolute alcohol (25 mL) was



Scheme –1

refluxed for 2 h. The content was then poured into crushed ice, and took about 8 h, when the product separated. It was filtered and crystallised from ethanol.

Yield; 56%, m.p. 92°C; found: C, 58.32; H, 3.12; N, 6.04; F, 12.16%. $C_{23}H_{15}O_6N_2F_3$ requires: C, 58.47; H, 3.17; N, 5.93; F, 12.07%; ν_{max}(KBr) 535 (C–CF_3), 1535, 1355 (NO_2), 1255, 1020 (C—O—C), 1635 (C=O) and 1590 cm^{-1} (C=C).

The other compounds were prepared by the aformentioned method (Table 1).

TABLE 1
PHYSICAL DATA OF 1-[2′-(2″,6″-DINITRO-4″-TRIFLUOROMETHYL PHENOXY)-5′-METHYLPHEN-1′-YL]-3-SUBSTITUTED PHENYL-2-PROPEN-1-ONE (1a–o)*

Compd. No.	R	m. p. (°C)	Colour†	Yield (%)	Mol. formula
1 a	H	92	Y	56	$C_{23}H_{15}O_6N_2F_3$
1 b	Cl(2)	73	LY	54	$C_{23}H_{14}O_6F_3ClN_2$
1 c	Cl(4)	169	LY	50	$C_{23}H_{14}O_6F_3ClN_2$
1 d	Cl(2), Cl(4)	78	Y	49	$C_{23}H_{13}O_6F_3Cl_2N_2$
1 e	Cl(2), Cl(6)	144	Y	47	$C_{23}H_{13}O_6F_3Cl_2N_2$
1 f	NO_2(2)	158	BY	42	$C_{23}H_{14}O_8F_3N_3$
1 g	NO_2(3)	120	BY	47	$C_{23}H_{14}O_8F_3N_3$
1 h	NO_2(4)	154	BY	48	$C_{23}H_{14}O_8F_3N_3$
1 i	CH_3(4)	131	Y	46	$C_{24}H_{17}O_6F_3N_2$
1 j	C_2H_5(4)	137	DY	44	$C_{25}H_{19}O_6F_3N_2$
1 k	C_3H_7(4)	146	DY	44	$C_{26}H_{21}O_6F_3N_2$
1 l	OCH_3(2)	89	Y	47	$C_{24}H_{17}O_7F_3N_2$
1 m	OCH_3(3), OCH_3(4)	94	Y	45	$C_{25}H_{19}O_8F_3N_2$
1 n	$N(CH_3)_2$(4)	87	OR	48	$C_{25}H_{20}O_6F_3N_3$
1 o	OCH_3(3), OH(4)	119	OR	45	$C_{24}H_{17}O_8F_3N_2$

*All compounds gave satisfactory elemental analysis.
†Y = Yellow, LY = light yellow, DY = dark yellow, BY = brown yellow, OR = orange red

2-Amino-4-[2′-(2″,6″-dinitro-4″-trifluoromethylphenoxy)-5′-methylphen-1′-yl]-6-phenyl pyrimidines (General Procedure) 2a

A mixture of 1-[2′-(2″,6″-dinitro-4″-trifluoromethyl phenoxy)-5′-methylphen-1′-yl]-3-phenyl-2-propen-1-one (5.11 g, 0.01 mol), guanidine nitrate (1.12 g, 0.01 mol) and absolute alcohol (50 ml) was refluxed on water bath. Then aqueous solution of potassium hydroxide (40%, 5 ml) was added to it portion wise for 3 h. The reflux was continued further for 6 h. The contents were cooled, when the product separated. It was filtered and crystallised from DMF.

Yield 71%; m.p. 166°C; Found: C, 56.31; H, 3.08; N, 13.78; F, 11.27%. $C_{24}H_{16}O_5N_5F_3$ requires: C, 56.36; H, 3.13; N, 13.69; F, 11.15%. ν_{max} (KBr) 490 (C—CF_3), 1540, 1360 (NO_2), 1250, 1030 (C—O—C), 1590 (C=N) and 3430 cm^{-1} (NH).

The other 2-aminopyrimidines were prepared by the aformentioned method. (Table 2).

TABLE 2
PHYSICAL DATA OF 2-AMINO-4-[2'-(2'',6''-DINITRO-4''-TRIFLUOROMETHYL PHENOXY)- 5'-METHYLPHEN-1'-YL]-6-SUBSTITUTED PHENYL PYRIMIDINES (2a–o)*

Compd. No.	R	m.p. (°C)	Colour†	Yield (%)	Mol. Formula
2 a	H	166	Y	71	$C_{24}H_{16}O_5F_3N_5$
2 b	Cl(2)	178	PY	74	$C_{24}H_{15}O_5F_3ClN_5$
2 c	Cl(4)	235	Y	73	$C_{24}H_{15}O_5F_3ClN_5$
2 d	Cl(2), Cl(4)	187	Y	73	$C_{24}H_{14}O_5F_3Cl_2N_5$
2 e	Cl(2), Cl(6)	205	BY	78	$C_{24}H_{14}O_5F_3Cl_2N_5$
2 f	NO_2(2)	216	Y	76	$C_{24}H_{15}O_7F_3N_6$
2 g	NO_2(3)	179	Y	75	$C_{24}H_{15}O_7F_3N_6$
2 h	NO_2(4)	184	BY	76	$C_{24}H_{15}O_7F_3N_6$
2 i	CH_3(4)	177	Y	74	$C_{25}H_{18}O_5F_3N_5$
2 j	C_2H_5(4)	240	Y	78	$C_{26}H_{20}O_5F_3N_5$
2 k	C_3H_7(4)	266	Y	76	$C_{27}H_{22}O_5F_3N_5$
2 l	OCH_3(2)	217	Y	74	$C_{25}H_{18}O_6F_3N_5$
2 m	OCH_3(3), OCH_3(4)	181	PY	75	$C_{26}H_{20}O_7F_3N_5$
2 n	$N(CH_3)_2$(4)	195	Y	79	$C_{26}H_{21}O_5F_3N_6$
2 o	OCH_3(3), OH(4)	173	PY	80	$C_{25}H_{18}O_7F_3N_5$

* All compounds gave satisfactory elemental analysis.
† Y = yellow, PY = pale yellow, BY = brown yellow.

RESULTS AND DISCUSSION

The zone of inhibition in mm for the compounds 2a–o tested for antibacterial activity. Activities of standard drugs are also given for comparison.

Evaluation of bacterial activity reveals that the compound 2b having chlorine group in 2-position of substituted phenyl ring showed activity upto 3.0 mm against both bacteria. It is nearly 60–50% as active as ampicillin and tetracyclin. It was also observed that the compound possessing group of *ortho*-position showed better activity than the compound possessing a group at *para* position.

ACKNOWLEDGEMENT

Authors are thankful to Bio-Science Department, South Gujarat University, Surat for the biological screening of compounds.

TABLE 3
ANTIBACTERIAL ACTIVITY OF THE COMPOUNDS 2a–o AND STANDARD DRUGS

Compd. No.	Zone of inhibition in mm, after 24 h. Disc potency 50 μg	
	S. Aureus	*E. Coli*
2 a	—	2.0
2 b	3.0	3.0
2 c	1.5	1.0
2 d	2.0	2.5
2 e	2.0	2.5
2 f	2.5	2.5
2 g	2.0	2.0
2 h	2.0	2.5
2 i	2.0	2.5
2 j	2.0	3.0
2 k	2.0	3.0
2 l	3.0	2.5
2 m	1.5	1.0
2 n	1.0	1.5
2 o	2.0	1.5
Standard drugs:		
Ampicillin	5.0	—
Tetracycline	—	6.0

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(*Received*: 24 September 1993; *Accepted*: 29 January 1994) AJC-775