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Research Article

Green Approach for the Synthesis of New 1,3-Oxazines -

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ABSTRACT

Oxazine compounds was found to have versatile application in pharmacology and medicine now a days .Their utility and application as drug and co-drug have drew attention of chemist to find different ways for the synthesis of this important type of heterocyclic compounds. They are important not as pharm chemical compounds but also as synthetic intermediates for other chemical and medical compounds .Accordingly we tried to find green and friendly procedure for the synthesis of new oxazine compounds(S_{1-6}) using grinding technique .The synthesized compounds were studied by spectral methods and are discussed.

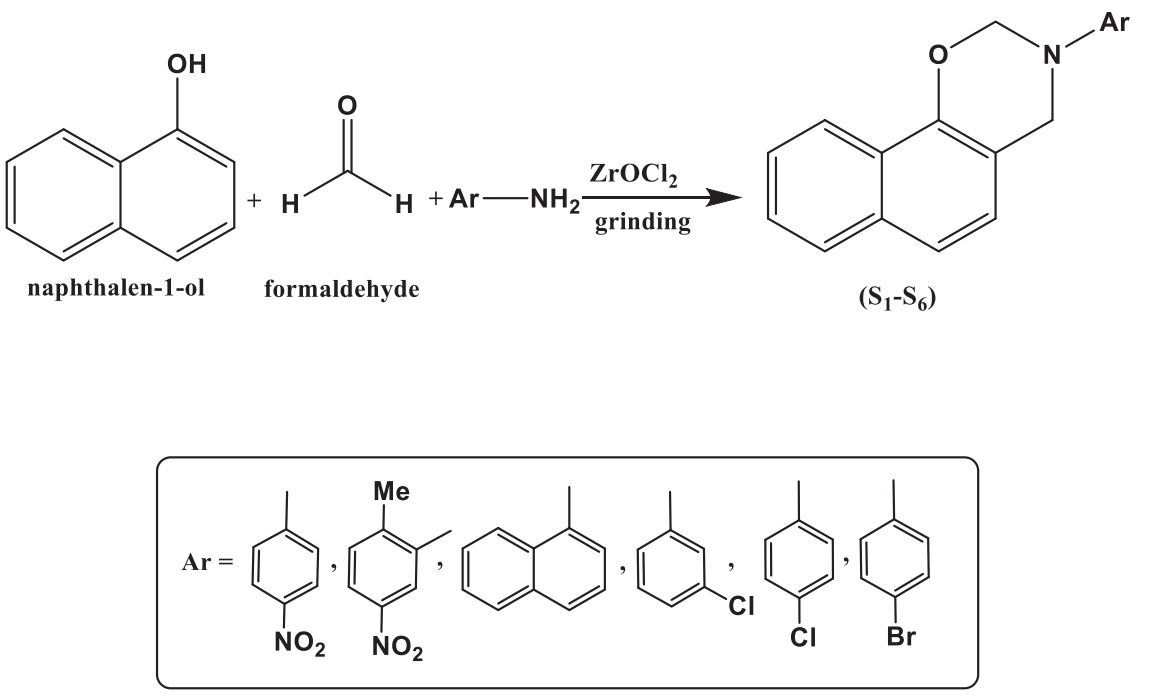
Keywords: Green; Approach; Synthesis; New; Oxazines

INTRODUCTION

There are many strategies were found in the literature for the synthesis of 1,3- oxazine compounds some of them the condensation of 3-amino propanol with carboxylic acid derivatives using solvent free condition [1], from methyl amino salicylate reaction with amino acids [2]. From phenol, anilineand and formaldehyde [3]. Antharanilic acid or its derivatives as precursor. These reactions were reviewed by Ahmed El-Mekabaty [4]. Other routes were from phenols and aromatic aldehydes in methanolic ammonia,These compounds were studied by Sayaji and Pravina B. They screened the synthesized compounds against two types of gram positive and gram negative bacteria [5].

Other researchers have prepared the 1,3-oxazine compounds from the cyclization of chalcone compounds using fly ash and have studied their Anti-Oxidant and Anti-Inflammatory activity [6] Thirunarayanan et-al have investigate the synthesis of 1.3-oxazine compounds from chalcones using solvent free protocol and studied their antimicrobial activities [7]. Sayaji et-al have reviewed miscellaneous methods for the green synthesis and the biological effects of 1,3- oxazines [8].

Chaitra G. and Rohini RM have studied the preparation of some 1,3- oxazne compounds from chalcone derivatives of pyridine and investigate these compounds as nti-Oxidant and Anti-Inflammatory agents [9] Vashundhra Sharma and his coworkers have synthesized some oxazine compounds and investigate their anti-cancer activity [10]. Dadmohammad et-al have synthesized 2-Aryl-4-Thioxo-4H-Naphtho[2,3-e] [1,3] Oxazine-5,10-Dione from the reaction of ammonium thiocyanate and aroyl chlorides with 2-hydroxy-1,4-naphthoquinone in the presence of catalytic amounts of N-methylimidazole under solvent-free condition and at Ambient temperature [11] in 2019 researchers have tested previously synthesized 3,4-dihydro-2H-1,4-benzoxazin-3-one derivatives to reveal their human DNA topoisomerase I inhibitory activities. The result of this study is the significant action and might serve novel constructs for future anticancer agent deigns [12]. Nabaweya et-al have reviewed one ,two and third steps of 3,4-Dihydro-2H-1,3-benzoxazines through the one-pot Mannich reaction and studied their diverse biological activities [13] Resent study on the preparation and anticancer , antifungal activity evaluations of naphtha [1,2-e] [1,3] oxazines bearing an arylsulfonamide moiety a is the work of Seyed Gholamhossein et-al work [14].



Scheme 1: Reaction route for the synthesis of compounds (S_{1-6})

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According to the above pharmacological importance of oxazine compounds and in continuing our efforts for our drug discovery program [15-19] we have synthesized new series of oxazine compounds using eco and friendly protocol.

Experimental

Melting points were uncorrected using thermal SMP30 UK melting point apparatus. IR spectra were recorded using Alpha (ATR) instrument [1]. HNMR spectra were recorded using Varian Agilent 499.53MHZ instrument, DMSO as internal solvent. All chemical were supplied by sigma –Aldrich, BHD and Fluka companies.

General procedure for the synthesis of naphthaoxazine compounds ($_{S1-6}$)

Formaldehyde (0.2 mol), zirconyl chloride ($ZrOCl_2.8H_2O$) (O.2 mol.), 1-naphthol, (0.1 mol) and aromatic amine (0.1mol).this mixture was grinded by porcelain mortar and pistel for 30 min.,after that dichloromethane (CH_2CL_2) was then added .The organic layer was then separated and washed twice with brine then with water .The organic layer was separated evaporation of the solvent by rotary evaporator afforded a crude product which was recrystallized from minimum amount of methanol physical properties were shone in the following Table (1)

RESULTS AND DISCUSSION

N-Aryl 2,4H(1,2E)(1,3) naphthaoxazine compounds (s_{1-6})

The titled compounds were prepared following similar procedure [20] and were characterized by IR which showed the following main absorption bands (3043-3061)for C-H ,sharp bands at (1450-1616) for C=C aromatic while C-N appeared at (1208-1364),C-O-C (1042-1149), and other band were listed in Table (2)

Proton chemical shift are assigned according to carbon number of the aromatic rings as they are shown in the second column of the above Table 3.

It is worth to note here that these compounds will studied for their biological activities against certain organisms during our drug discovery program which showed significant results for other series of this project and will be published when completed.

Table 1: Physical properties of compounds (S_{1-6})

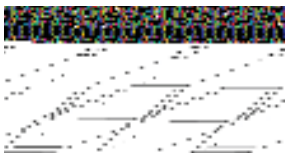
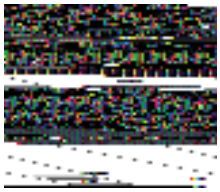
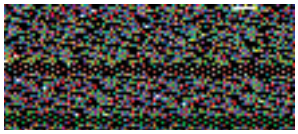
Comp. No.	Ar.	Molecular Formula	M.Wt gm/mol	M.P. (°C)	Yield %	Color
S_1		$C_{18}H_{14}N_2O_3$	306	66-67	87	dark yellow
S_2		$C_{19}H_{16}N_2O_3$	320	159-160 dec	80	Light yellow
S_3		$C_{22}H_{17}NO$	311	79-80	77	purple
S_4		$C_{18}H_{14}ClNO$	295	98-100	63	yellow
S_5		$C_{18}H_{14}ClNO$	295	112-115	58	Light brown
S_6		$C_{18}H_{14}BrNO$	340	56-58	65	White

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Table2: HNMR for two representative Compounds were shown

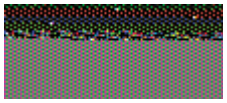
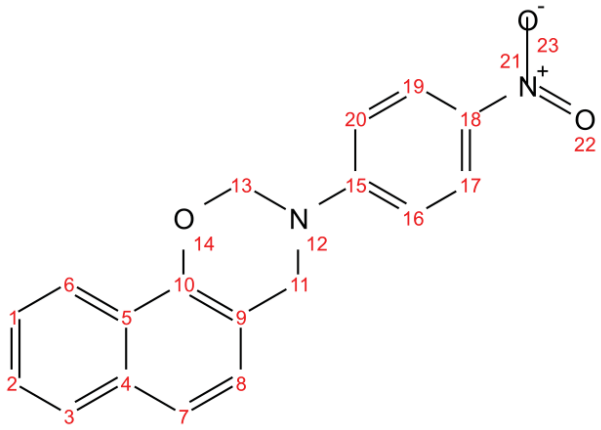
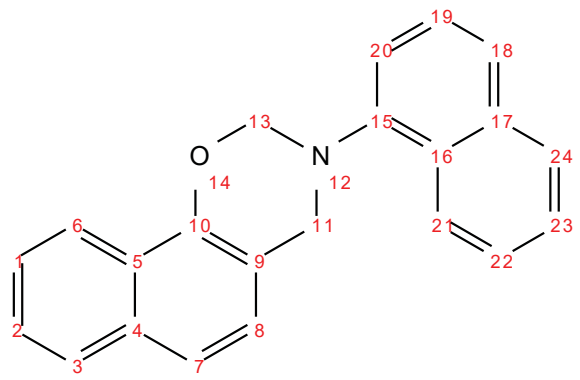
Comp. No.	Ar.	IR v cm^{-1}				
		C-H Ar.	C=C Ar.	C-N	C-O-C	Others
S_1		3061	14,561,577	1310	11,081,127	N-O sym / 1315 Assy / 1550
S_2		3052	14,501,617	1346	10,421,149	N-O sym / 1278 Assy / 1522
S_3		3062	15,191,595	1208	10,651,127	.....
S_4		3052	14,831,589	1312	10,711,120	C-Cl / 541
S_5		3043	14,561,604	1323	10,471,125	C-Cl / 552
S_6		3051	14,831,589	1312	10,711,120	C-Br / 542

Table 3: HNMR spectra for compoundsS_1 and S_3

Comp.no.	Structure compounds	H^1NMR (PPM) DMSO-d6
S1		5.37 (2H,S,C_{11}-H)4.66(2H,S,C13-H))6.9,7.01,8.07,8.09,8.1) (AB)(q) (4H, P-nitro phenyl), ;(6.98-7.01) (2H,d.C_1,C_{10}-H);(7.35-7.46) (2H,,m,2H,C_7,C_8-H) (7.53-7.93) (2H,m,C_5,C_6-H) ;(8.07-8.10) (2H,d,C_1,C_2-H)
S3		4.69 (2H,S,C_{11}-H) ;5.43(2H,S,C_{13}-H); (6.94-6.96) (1H,S,C20-H);(7.73-7.75) (2H,m,C_8, C_{19}-H)(7.4-7.5) (2H ,d,c_1,c_{22}-H) (7.5-7.69) (2H,m,C_2,C_{23}-H)7.80 (5H ,m,C_3,C_7,C_{18},C_{21},C_{24},-H) (7.91-7.93) (1H,d,C_6-H

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