The Pharmaceutical and Chemical Journal, 2020, 7(6):118-122

Available online www.tpcj.org

Research Article

ISSN: 2349-7092
CODEN(USA): PCJHBA

Green approach for the synthesis of new 1,3-oxazines

Ghufran T. Sadeek[1], Mohammad S. Al-Ajely [2], Neim H. Saleem[1]

[1]Chemistry Dept. College of Education of Pure Science, Mosu University, Iraq
[2]Chemistry Dept. College of Education for Girls, Mosul University Mosul, Iraq
Corresponding Author E-Mail id: mohamadalajelee@ yahoo.com

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

1. 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 methylamino salicylate reaction with amino acids[2]. From phenol, aniline and 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 methanolicammonia, 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 anti-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-4*H*-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-2*H*-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-2*H*-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 naphtho[1,2-*e*][1,3]oxazines bearing an arylsulfonamide moiety a is the work of Seyed Gholamhossein *et al* work [14].

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.

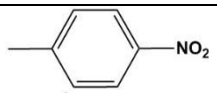
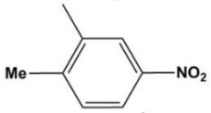
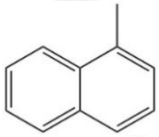
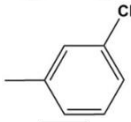
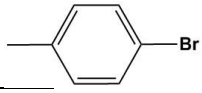
Experimental

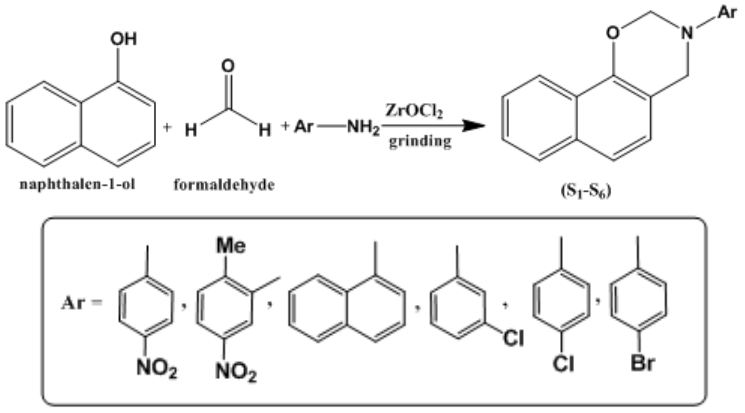
Melting points were uncorrected using thermal SMP30 UK melting point apparatus. IR spectra were recorded using Alpha (ATR) instrument.[1] HNMR spectra were recorded using Varian Agilent 499.53MHZ instrument, DMSO as internal solvent. All chemical were supplied by sigma –Aldrich, BHD and Fluka companies.

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.

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

Comp. No.	Ar.	Molecular Formula	M.Wt gm/mol	M.P. (^{0}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



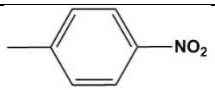
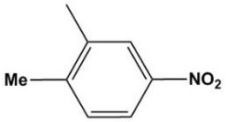
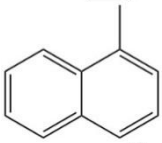
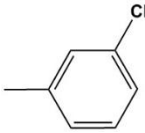
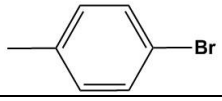
Scheme 1: Reaction route for the synthesis of compounds (S_{1-6})

Results and Discussion

N-Aryl 2,4*H*[1,2-*e*](1,3)naphthaoxazine compounds (s_{1-6})

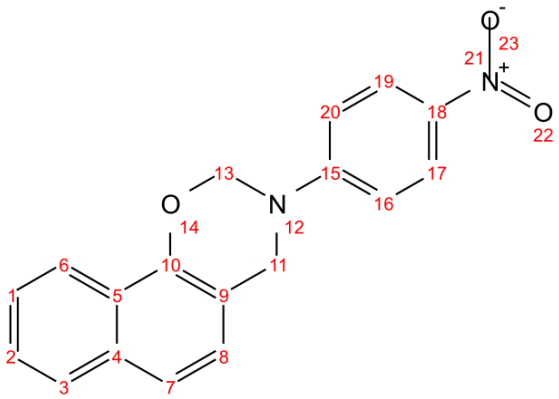
The titled compounds were prepared following similar procedure [20] and were characterized by IR which showed the following main absorption bands (3043-3061)for C-H, sharp bands at (1450-1616) for C=C aromatic while C-N appeared at (1208-1364),C-O-C (1042-1149), and other band were listed in Table 2.

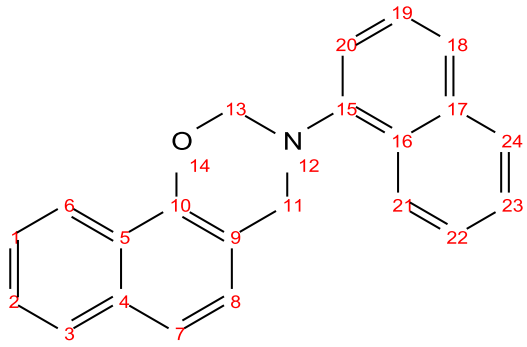
Table 2: IR spectal details

Comp. No.	Ar.	IR ν (cm^{-1})				
		C-H Ar.	C=C Ar.	C-N	C-O-C	Others
S_1		3061	1456,1577	1310	1108,1127	N-O sym / 1315 Assy / 1550
S_2		3052	1450,1617	1346	1042,1149	N-O sym / 1278 Assy / 1522
S_3		3062	1519,1595	1208	1065,1127	.....
S_4		3052	1483,1589	1312	1071,1120	C-Cl / 541
S_5		3043	1456,1604	1323	1047,1125	C-Cl / 552
S_6		3051	1483,1589	1312	1071,1120	C-Br / 542

^{1}HNMR for two representative Compounds were shown in Table 3.

Table 3: ^{1}HNMR spectra for compounds S_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

Proton chemical shift are assigned according to carbon number of the aromatic rings as they are shown in the 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.

Acknowledgments

Authors would like to thank the Iraqi Ministry of Higher Education and Research for providing Ghufran Seedek Thanoon a Scholarship to do this work which is part of her thesis. Thanks also to the Chemistry Dept. of Education College for Girls for providing all the facilities to do this project.

References

[1]. Taati M.R,. Mamaghani M, Mahmoodi N.O. and Ghmanifar A. (2009). A Simple Access to the Synthesis of 5,6-Dihydro-4*H*-1,3-Oxazines Under Solvent-Free Conditions and Microwave Irradiation, Transactions C.Chemistry and Chemical Engineering, vol.16, No. 1, 17-21.

[2]. Al-Ajely mohammad Salman (2013). Synthesis and Antiplatelet of 2-(ethyl amino acid esters, Amino pyridyl 1,3-oxzine, J.of Advances in chemistry, 2, (2)91-96.

[3]. Cheng-Xi Zhang, Yu-Yuan Deng, Yi-Yang Zhang, Po Yang, Yi Gu (2015). Study on products and reaction paths for synthesis of 3,4-dihydro-2H-3-phenyl-1,3-benzoxazine from phenol, aniline And formaldehyde Chinese Chemical Letters 26, 348–352.

[4]. El-Mekabaty Ahmed, (2013). Chemistry of 4*H*-3,1-Benzoxazin-4-ones, International Journal of Modern Organic Chemistry, 2(2): 81-121.

[5]. Sayaji S. Didwagh, B. Pravina. Piste (2013). Novel one - pot Synthesis and Antimicrobial Activity of 6-chloro-2,4-diphenyl-3,4-dihydro-2*H*-1,3-benzoxazine derivatives, International Journal of Chem Tech. Research, Vol. 5, No. 5, 2199-2203.

[6]. Chaitra G. and Rohini RM (2018). Synthesis of 1,3-Oxazine derivative from Chalcone and Screening for their Anti-Oxidant and Anti-Inflammatory activity, International Research Journal of Pharmaceutical and Biosciences, 4.19-27.

[7]. Thirunarayanan G., Sundararajan R. and Arulkumaran R. (2013). Aryl Chalcones as Efficient Precursors for Deriving Oxazine: Solvent-free Synthesis and Antimicrobial Activities of some Oxazine-2-amines, International Letters of Chemistry, Physics and Astronomy. 23, 82-97.

[8]. Sayaji S. Didwagh and B. Pravina Piste (2013). Green synthesis of thiazine and oxazine derivatives - a short review, International Journal of Pharmaceutical Sciences and Research Vol. 4, Issue 6, 2045-61.

[9]. Chaitra G. and Rohini R.M. (2018) Synthesis of 1,3-Oxazine derivative from Chalcone and Screening for their Anti-Oxidant and Anti-Inflammatory activity, International Research Journal of Pharmaceutical and Biosciences, 4 No. 19-27.

[10]. V. Sharma, K. Pradeep. Jaiswal, Mukeshsaran, Dharmendra Kumar Yadav, Saloni, Manas Mathur, Ajit K. Swami, Sanjeev (2018). Discovery of C-3 Tethered 2-oxo-benzo[1,4]oxazines as Potent Antioxidants: Bio-Inspired Based Design, Synthesis, Biological Evaluation, Cytotoxic, and in Silico Molecular Docking Studies. Frontiers in Chemistry, doi: 10.3389/fchem.2018.00056

[11]. Dadmohammad Balouchzehi and Alireza Hassanabadi (2019). Synthesis of 2-Aryl-4-Thioxo-4*H*-Naphtho[2,3-e] [1,3]-oxazine-5,10-dione under Solvent-Free Conditions at Ambient Temperature, The Journal of the International Society for Polycyclic Aromatic Compounds, https://doi.org/10.1080.

[12]. Egemen Foto, Çigdem Özen, Fatma Zilifd, Betül, Tekiner-Gülbaş İlkay Yıldı, Esin Akı-Yalçın, Nuran DirilİIsmail Yalçın (2020). Benzoxazines as new human topoisomerase I inhibitors and potential poisons, DARU Journal of Pharmaceutical Sciences, 2865-73.

[13]. Abd el-Salam Nabaweya Sharafel-din (2019). 3,4-Dihydro-2*H*-1,3-benzoxazines and their oxo-derivatives chemistry and bioactivities, J. Serb. Chem. Soc. 83 (0) 1-36.

[14]. Seyed Gholamhossein Mansouri, Hassan Zali-Boei (2020). Synthesis of novel naphtho[1,2-e][1,3]oxazines bearing an arylsulfonamide moiety and their anticancer and antifungal activity evaluations, Arabian Journal of Chemistry, 13,1273-82.

[15]. Al Ajely M. S and Noori A M (2019). Synthesis of New Oxazin Compounds Derived from Furfural, Chalcons and Schiff Bases, J of Pharmacology and clinical research, Volume 1 - Issue 3,66-71.

[16]. Al-Ajelly M.S and Al-Norri A., (2020). An Efficient and Solvent Free Synthesis of N-aryl-2,3-dihydro-4*H* naphtho-[2,1-*e*]-1,3-oxazines, Bio medical journal of scientific and technical research, 29, Issue 3, 22510-16.

[17]. Sadeek T. Ghufran, Al-Ajely M. S and Saleem Neim H (2020). New Approach for the Synthesis of Aryloxy 1,3-Oxazines, Journal of Material Sciences & Manufacturing Research, Volume 1(2)1-5.

[18]. Sadeek T., Ghufran, Al-Ajely M. S and Saleem Neam H (2020). Synthesis of Some Oxazine Compounds Derived from TDI and Schiff Bases, Acta Scientific medical sciences, Volume 4 Issue 9, 120-128.

[19]. Sadeek T. Ghufran, Al Ajely M. S, Saleem Neam H. (2020). Synthesis of some oxazine compounds derived from phenols & 8-hydroxy quinolone, Solid State Technology, Volume: 63 Issue: 5, 3179-90.

[20]. Kategaonkar A., Sonar S.S., Pokalwar R., Shingate, B.B, Kategaonkar, A.H., (2010). An Efficient Synthesis of 3,4-Dihydro-3-substituted-2*H*-naphtho[2,1-*e*][1,3]oxazine Derivatives Catalyzed by Zirconyl(IV) Chloride and Evaluation of Its Biological Activities, Bulletin of the Korean Chemical Society, (31):1657-1660.