Chemistry & Biology Interface, 2019, 9, 4, 208-215

RESEARCH PAPER ISSN: 2249 –4820

CHEMISTRY & BIOLOGY INTERFACE

An official Journal of ISCB, Journal homepage; www.cbijournal.com

Synthesis and spectroscopic analysis of some novel Benzo[1,3]oxazine-2,4-dione by different methods

N. R. SHARMA and J. M. PARMAR*

Department of Chemistry, Maharaja Shree Mahendra Sinhji Science College, Morbi-363642, (Gujarat), India.
E-mail: sharmanitish48@gmail.com
Received 14 June 2019, Accepted 20 August 2019

Abstract: Now a days the chemistry of Benzo[1,3]oxazine-2,4-dione moiety enhanced important due to their marvelous activities in medicinal field. Hence, some novel benzo[1,3]oxazine-2,4-dione derivatives were synthesized by various methods including eco-friendly methods like microwave irradiation and mortar pastel. These methods are then compared with conventional method. Comparatively study of % yield and reaction time in different method and solvents is described. The structure characterization of synthesized compound was carried out by ^{1}H NMR, IR and mass spectrometry. From the result, it is observed that the microwave irradiation method is superior than the other two method to the synthesis of Benzo[1,3] oxazine-2,4-dione derivatives.

Keywords: conventional method, microwave irradiation, mortar pestle, Benzo[1,3]oxazine-2,4-dione derivatives

Introduction

Benzo[1,3]oxazine is composed of an oxazine ring, a heterocyclic aromatic six-member ring with oxygen and nitrogen located at 1st and 3rd position in the ring, attached to a benzene ring. A literature survey has revealed that the compound possess benzo[1,3]oxazine moiety show various pharmaceutical and biological activities [1,2]. Hence, now day such molecule gets much attention of various chemists. Benzo[1,3]oxazine showed various biological activity including cyclo oxygenase inhibitors [3], analgesic and anti-inflammatory [4], antimalarial [5].

Literature survey shows that the benzoxazine derivatives exhibited wide range of biological and pharmaceutical activities such as anticancer [6], progesterone receptor modulators [7], antimalarial [8], analgesic and anti-inflammatory [9], antimycobacterial [10], antibacterial and antiviral [11].

Juan *et al*. [12] reported the synthesis of 1H-benzoxazine-2,4-diones from phthallic

anhydride and trimethylsylilazide (TMSA). These synthesized compounds showed good to moderate toxicity, antimicrobial activities and antioxidant activities. New derivatives of 6-chloro-2,4-diphenyl 3,4-dihydro-2H-1,3-benzoxazin were synthesized from substituted aldehyde and phenol in presence of ammonia. The synthesized compounds are subjected for anti microbial activity [13].

In the present work, the synthesis of some new benzo[1,3]oxazine derivatives have been reported by different methods in four selected solvents likes *N,N*-dimethyl formamide, dimethyl sulphoxide, tetrahydrofuran and ethyl acetate. The conformation of the synthesized compounds was done by using various spectroscopic data.

Material and Method

Chemicals

All research chemicals and solvents were purchased from Spectrochem Pvt. Ltd and LOBA chem Pvt. Ltd and were used as received. Reaction monitored by thin layer chromatography (TLC) on precoated silica gel by using appropriate solvent system.
Melting points were determined in open capillaries and are uncorrected.

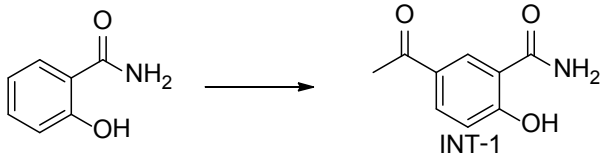
Instrument

Infrared (IR) spectra were recorded on a Shimadzu IR affinity-1S spectrophotometer over frequencies ranging from 4000-400 cm^{-1}. The proton nuclear magnetic resonance (1H NMR) spectra recorded Bruker Advance Spectrospin 400 MHz spectrophotometer using DMSO-d_6, as solvent and TMS as internal standard. Mass spectra recorded on Shimadzu GC-MS QP-2010 spectrometer.

Experimental

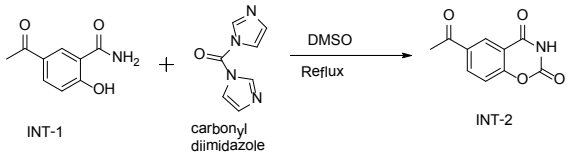
Synthesis of 5-acetyl-2-hydroxybenzamide [14]:

Salicylamide (0.01 mmol) was added into round bottom flask with three-necked. The reaction was carried out under nitrogen atmosphere. Given amounts of [BMIM]Cl-nAlCl3 ionic liquid and acetyl chloride were added into the reaction mixture drop wise. Reflux the content for appropriate time. Reaction progress was checked by thin layer chromatography using 7:3 v/v- hexane: ethyl acetate mobile phase. After completion of reaction, the reaction mass was poured in to crushed ice and acidified with 50 ml 10 % HCl solution. The obtained solid was filtered and dried under vacuum.



Synthesis of 3-acetyl-2H-chromen-2-one (Int-2):

The solution of INT-1 (0.01 mmol) was prepared in to 10 ml dimethyl sulphoxide. To solution, carbonyldiimidazole (0.011 mmol) was added and refluxed the resultant solution for 4 to 6 hours at 120º C temperatures with constant stirring. The progress of reaction was checked by prepared thin layer chromatography using 5:5 v/v- Hexane: Ethyl acetate mobile phase. After completion of reaction cool the reaction mass and filter obtained solid. The product dried under vacuum. The obtained solid was then triturated in mixture of n-hexane and ethyl acetate (7:3) to remove non-reacted impurities.



Synthesis of Schiff bases:

Benzo[1,3]oxazine derivatives were synthesized by two ways:

[1] Conventional method
[2] Microwave irradiation method
[3] Mortar pestle method

[1] Conventional method:

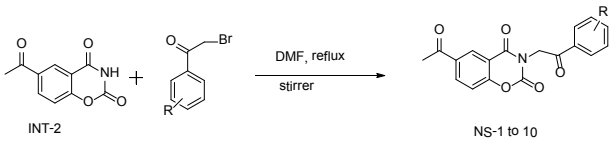
Equimolar mixture of 6-acetyl-2H-benzo[e][1,3] oxazine-2,4(3H)-dione (INT-2) and different phenacyl bromide was done in appropriate selected solvent and was refluxed for 2 to 4 hours with constant stirring in the presence of triethylamine (TEA) used as catalyst. Reaction monitored by thin layer chromatography (TLC) on precoated silica gel by using appropriate solvent system. After completion of reaction, cool the reaction mixture into ice bath. The obtained solid was filtered, washed with cold diethyl ether and was dried under vacuum.

[2] Microwave irradiation method:

A mixture of 6-acetyl-2H-benzo[e][1,3] oxazine-2,4(3H)-dione (INT-2) (0.01 mmol) and different substituted phenacyl bromide (0.01 mmol) was prepared in appropriate solvent and was subjected to microwave irradiation for 14-20 minutes at 450 Watt. The reaction status was checked by TLC precoated with silica gel using mixture of chloroform: methanol (7:3) as a mobile phase. After completion of reaction, the content was poured in to water and was allowed to stirrer for 10-12 hours. The obtained solid was filtered and dried under vacuum.

[3] Mortar Pastel method:

Prepared slurry of 6-acetyl-2H-benzo[e][1,3] oxazine-2,4(3H)-dione (INT-2) (0.01 mmol) and different substituted phenacyl bromide (0.01 mmol) in DMF. The paste then was grinding in a mortar with pastel in presence of catalytic amount of TEA. The progress of reaction was checked through TLC precoated with silica gel using mixture of chloroform: methanol (7:3) as a mobile phase. After completion of reaction the reaction mixture was poured into cold water and was stirred for 2-3 hours to remove undesired salt product. The obtained solid was then filtered and dried under vacuum.



For the purified of the synthesized compound, the compound was triturated with hexane to remove non polar impurities. The crystallization of these synthesized compounds was carried out in mixture of hexane: ethyl acetate (5:5).

Results and Discussion

Table 1: The physical data of synthesized Benzo[1,3]oxazine-2,4-dione derivatives

Compound Code	*Substitution R*	*Molecular formula*	*Molecular weight (g/mol)*	*Melting points (°C)*	R_f^* *value*
SN-1	H	$C_{18}H_{13}O_5N$	323.30	311-314	0.59
SN-2	2-OCH_3	$C_{19}H_{15}O_6N$	353.09	280-284	0.52
SN-3	4-Br	$C_{18}H_{12}O_5NBr$	400.99	328-332	0.68
SN-4	3-Cl-4-F	$C_{18}H_{11}O_5NClF$	375.03	318-321	0.66
SN-5	2-F	$C_{18}H_{12}O_5NF$	341.07	325-329	0.54
SN-6	4-CH_3	$C_{19}H_{15}O_5N$	337.10	278-282	0.58
SN-7	4-OCH_3	$C_{19}H_{15}O_6N$	353.09	256-260	0.69
SN-8	4-Cl	$C_{18}H_{12}O_5NCl$	357.04	299-304	0.73
SN-9	2-CH_3	$C_{19}H_{15}O_5N$	337.10	267-271	0.53
SN-10	2,4-Cl	$C_{18}H_{11}O_5NCl_2$	392.00	305-309	0.72

*7:3v/v- chloroform: methanol

Table 1 shows the physical parameters such as molecular weight, meting points; R_f etc for synthesized compounds are reported along with substitution. Table 2 shows the reaction time for the synthesis of benzo[1,3]oxazine derivatives by different methods; conventional, microwave irradiation and mortar pastel.

Table 2: The reaction time required for the synthesis by microwave irradiation, conventional and mortar pastel methods

Compound Code	*Reaction Time*		
	Microwave Irradiation (minutes)	*Conventional (hours)*	*Mortar pastel (hours)*
SN-1	15	2	4
SN-2	20	4	4
SN-3	15	3	4
SN-4	17	3	4
SN-5	14	3	4
SN-6	20	4	4
SN-7	20	4	4
SN-8	15	3	4
SN-9	20	3	4
SN-10	15	2	4

From the Table 2, it is observed that the reaction time decreases dramatically from conventional and mortar pastel method to microwave irradiation method. In conventional and mortar pastel method reaction time was in hours which are reduced into minutes in microwave irradiation method. Table 3 shows some physical parameters likes' dielectric constant, dipole moment of solvents used in synthesis. The % yield obtained in different solvents by different methods is reported in Table 4.

The IR spectrum of SN-1 compounds was given as Figure 1. The ^{1}H NMR and mass spectrum of SN-1 compound was shown as Figure 2 and 3 respectively.

Table 3: physical properties of selected solvents for synthesis

Solvent	Dipole moment	Dielectric constant
N,N-dimethyl formamide (DMF)	3.82	38.3
dimethyl sulphoxide (DMSO)	3.96	47.2
Tetrahydrofuran (THF)	1.63	7.52
Ethyl acetate	1.78	6.02

Table 4: % yield of the synthesized compounds in different methods

Compound code	Microwave irradiation method				Conventional method				Mortar pestle method			
	DMF	DMSO	THF	EA	DMF	DMSO	THF	EA	DMF	DMSO	THF	EA
SN-1	74	70	66	54	56	52	47	41	16	14	15	14
SN-2	68	65	62	52	52	50	45	35	18	17	15	13
SN-3	69	64	58	49	52	49	43	32	23	21	18	16
SN-4	67	60	56	51	48	45	44	35	21	19	17	15
SN-5	69	62	58	46	58	54	47	38	19	17	18	16
SN-6	73	67	56	43	60	60	52	41	16	16	17	18
SN-7	68	61	53	42	58	57	47	39	12	13	12	14
SN-8	68	63	54	44	53	54	46	34	18	17	15	14
SN-9	74	69	58	49	55	52	44	32	28	25	19	17
SN-10	77	72	61	51	49	52	49	38	15	14	12	11

Figure 1: IR spectrum of SN-1

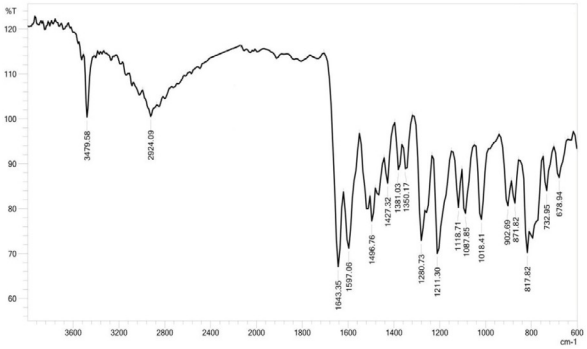


Figure 2: ^{1}H NMR spectrum of SN-1

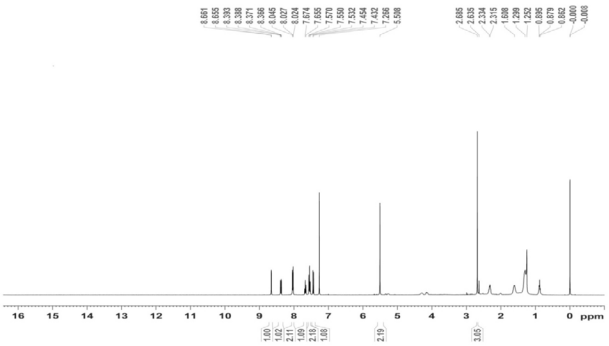
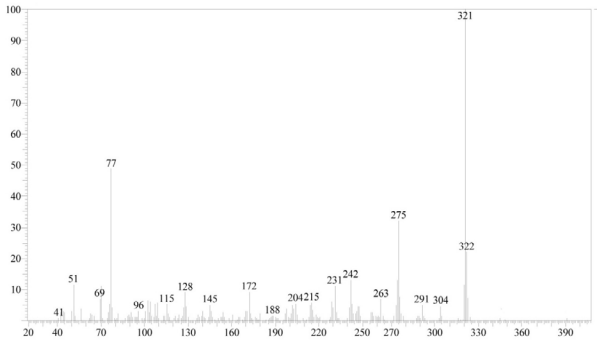


Figure 3: Mass spectrum of SN-1



Spectral data

SN-1

M.P.: 311-314, ***IR (ν, cm^{-1})***: 3479.58 (-OH stretching), 2924.09 (C-H stretching, alkane), 1643.35 (C=C stretching, alkene), 1597.06 (C-C stretching in ring, aromatic), 1381.03, 1350.17 (C-H rock alkane), 1280.75 (C-O stretching), 1211.30 (C-N stretching), 1118.71, 1087.45 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d$_6$) (δ ppm)***: 2.635 (s, 3H, -CH_3), 5.508 (s, 2H, -CH_2-), 7.266 (s, 1H, Ar-H), 7.432-7.454 (doublet, 2H, Ar-H, J= 8.8), 7.532-7.570 (multiplet, 1H, aromatic), 8.024-8.045 (multiplet, 2H, aromatic), 8.360-8.392 (quartet, 1H, aromatic, J= 12.8), 8.655-8.661 (doublet, 1H, aromatic, J= 2.4). ***MS (EI) m/z***: calculated for $C_{18}H_{13}O_5N$ [M+]:323.30; found 322.

SN-2

M.P.: 280-284, ***IR (ν, cm^{-1})***: 3471.48 (-OH stretching), 2921.12 (C-H stretching, alkane), 1640.21 (C=C stretching, alkene), 1591.45 (C-C stretching in ring, aromatic), 1383.43, 1355.56 (C-H rock alkane), 1285.74 (C-O stretching), 1217.56 (C-N stretching), 1119.32, 1090.43 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d$_6$) (δ ppm)***: 2.639 (s, 3H, -CH_3), 3.210 (s, 3H, -OCH_3), 5.501 (s, 2H, -CH_2-), 7.272 (s, 1H, aromatic), 7.439-7.464 (doublet, 2H, aromatic, = 10), 7.539-7.578 (multiplet, 1H, aromatic), 8.123-8.142 (multiplet, 1H, aromatic), 8.378-8.399 (quartet, 1H, aromatic, J= 8.4), 8.659-8.665 (doublet, 1H, aromatic, J= 2.4). ***MS (EI) m/z***: calculated for $C_{19}H_{15}O_6N$ [M+]:353.09; found 352.

SN-3

M.P.: 328-332. ***IR (ν, cm^{-1})***: 3474.55 (-OH stretching), 2925.02 (C-H stretching, alkane), 1635.09 (C=C stretching, alkene), 1598.73 (C-C stretching in ring, aromatic), 1384.76, 1359.23 (C-H rock alkane), 1289.82 (C-O stretching), 1221.37 (C-N stretching), 1120.83, 1085.67 (C-N stretching, aliphatic) 580.56, 551.47 (C-Br stretching). ***^{1}H NMR (400 MHz, DMSO-d$_6$) (δ ppm)***: 2.631 (s, 3H, -CH_3), 5.503 (s, 2H, -CH_2-), 7.269 (s, 1H, aromatic), 7.536-7.545 (doublet, 2H, aromatic, J= 3.6), 8.124-8.145 (doublet, 2H, aromatic, J= 8.4), 8.585-8.599 (doublet, 2H, aromatic, J= 5.6). ***MS (EI) m/z***: calculated for $C_{18}H_{12}O_5NBr$ [M+]: 400.99; found 400.

SN-4

M.P.: 318-321. ***IR (ν, cm^{-1})***: 3472.78 (-OH stretching), 2926.34 (C-H stretching, alkane), 1638.24 (C=C stretching, alkene), 1594.78 (C-C stretching in ring, aromatic), 1386.23, 1361.34 (C-H rock alkane), 1286.67 (C-O stretching), 1219.11 (C-N stretching), 1121.56, 1082.65 (C-N stretching, aliphatic) 640.98, 678.35 (C-Cl stretching). ***^{1}H NMR (400 MHz, DMSO-d$_6$) (δ ppm)***: 2.641 (s, 3H, -CH_3), 5.497 (s, 2H, -CH_2-), 7.269 (s, 1H, aromatic), 7.378-7.391 (doublet, 2H, aromatic, J= 5.2), 8.461-8.478 (doublet, 2H, aromatic, J= 6.8), 8.484-8.495 (doublet, 2H, aromatic, J= 4.4). ***MS (EI) m/z***: calculated for $C_{18}H_{11}O_5NClF$ [M+]: 375.01; found 374.

SN-5

M.P.: 325-329. ***IR (ν, cm^{-1})***: 3478.34 (-OH stretching), 2923.23 (C-H stretching, alkane),

1641.78 (C=C stretching, alkene), 1589.23 (C-C stretching in ring, aromatic), 1387.34, 1366.23 (C-H rock alkane), 1284.34 (C-O stretching), 1222.56 (C-N stretching), 1122.76, 1083.78 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm)****:* 2.634 (s, 3H, -CH_3), 5.511 (s, 2H, -CH_2-), 7.271 (s, 1H, aromatic), 7.458-7.469 (doublet, 2H, aromatic, J= 4.4), 7.829-7.247 (multiplet, 1H, aromatic), 8.132-8.143 (doublet, 1H, aromatic, J= 4.4), 8.368-8.379 (multiplet, 1H, aromatic), 8.689-8.703 (doublet, 1H, aromatic). ***MS (EI) m/z****:* calculated for $C_{18}H_{12}O_5NF$ [M+]: 341.07; found 340.

SN-6

M.P.: 278-282. *IR (v, cm^{-1}):* 3472.31 (-OH stretching), 2920.79 (C-H stretching, alkane), 1638.69 (C=C stretching, alkene), 1588.24 (C-C stretching in ring, aromatic), 1391.75 (C-H rock alkane), 1283.34 (C-O stretching), 1224.23 (C-N stretching), 1119.49, 1079.39 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm)****:* 2.619 (s, 3H, -CH_3), 2.782 (s, 3H, -CH_3), 5.519 (s, 2H, -CH_2-), 7.255 (s, 1H, aromatic), 7.511-7.523 (doublet, 2H, aromatic, J= 8.4), 8.008-8.022 (doublet, 2H, aromatic, J= 5.6), 8.101-8.116 (doublet, 2H, aromatic, J= 6). ***MS (EI) m/z****:* calculated for $C_{19}H_{15}O_5N$ [M+]: 337.10; found 336.

SN-7

M.P.: 256-260. ***IR (v, cm^{-1})****:* 3476.24 (-OH stretching), 2915.56 (C-H stretching, alkane), 1641.36 (C=C stretching, alkene), 1585.28 (C-C stretching in ring, aromatic), 1392.28, 1355.27 (C-H rock alkane), 1281.73 (C-O stretching), 1219.29 (C-N stretching), 1117.72, 1084.19 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm)****:* 2.627 (s, 3H, -CH_3), 3.424 (s, 3H, -OCH_3), 5.521 (s, 2H, -CH_2-), 7.251 (s, 1H, aromatic), 7.518-7.529 (doublet, 2H, aromatic, J= 4.4), 7.718-7.731 (doublet, 2H, aromatic, J= 5.2), 7.768-7.782 (doublet, 2H, aromatic, J= 5.6). ***MS (EI) m/z****:* calculated for $C_{19}H_{15}O_6N$ [M+]:353.09; found 352.

SN-8

M.P.: 299-304. ***IR (v, cm^{-1})****:* 3476.84 (-OH stretching), 2921.46 (C-H stretching, alkane), 1648.76 (C=C stretching, alkene), 1598.27 (C-C stretching in ring, aromatic), 1385.28, 1354.78 (C-H rock alkane), 1283.01 (C-O stretching), 1218.58 (C-N stretching), 1117.08 (C-N stretching, aliphatic), 667.91, 690.34 (C-Cl stretching). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm):*** 2.647 (s, 3H, -CH_3), 5.531 (s, 2H, -CH_2-), 7.273 (s, 1H, aromatic), 7.551-7.562 (doublet, 2H, aromatic, J= 4.4), 8.157-8.171 (doublet, 2H, aromatic, J= 5.6), 8.589-8.603 (doublet, 2H, aromatic, J= 5.6). ***MS (EI) m/z****:* calculated for $C_{18}H_{12}O_5NCl$ [M+]:357.04; found 356.

SN-9

M.P.: 267-271. ***IR (v, cm^{-1})****:* 3481.23 (-OH stretching), 2922.01 (C-H stretching, alkane), 1649.34 (C=C stretching, alkene), 1597.04 (C-C stretching in ring, aromatic), 1384.45, 1351.38 (C-H rock alkane), 1279.34 (C-O stretching), 1208.34 (C-N stretching), 1119.34, 1085.79 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm):*** 2.636 (s, 3H, -CH_3), 5.516 (s, 2H, -CH_2-), 7.278 (s, 1H, aromatic), 7.437-7.449 (doublet, 2H, aromatic, J= 4.8), 7.326-7.345 (multiplet, 1H, aromatic), 7.545-7.559 (doublet, 1H, aromatic, J= 5.6), 8.062-8.074 (multiplet, 1H, aromatic), 8.603-8.617 (doublet, 1H, aromatic, J= 5.6). ***MS (EI) m/z****:* calculated for $C_{19}H_{15}O_5N$ [M+]: 337.10; found 336.

SN-10

M.P.: 305-309. ***IR (v, cm^{-1})****:* 3484.23 (-OH stretching), 2929.28 (C-H stretching, alkane), 1646.32 (C=C stretching, alkene), 1592.59 (C-C stretching in ring, aromatic), 1389.24, 1359.10 (C-H rock alkane), 1284.37 (C-O

stretching), 1215.39 (C-N stretching), 1116.29 (C-N stretching, aliphatic). ***^{1}H NMR (400 MHz, DMSO-d_6) (δ ppm)***: 2.672 (s, 3H, -CH_3), 5.545 (s, 2H, -CH_2-), 7.266 (s, 1H, aromatic), 7.478-7.492 (doublet, 2H, aromatic, J= 5.6), 8.231-8.249 (doublet, 2H, aromatic, J= 8.2), 8.689-8.703 (singlet, 1H, aromatic). ***MS (EI) m/z***: calculated for $C_{18}H_{11}O_5NCl_2$ [M+]: 392.00; found 391.

Spectroscopic study

IR spectra

The IR spectrum of SN-1 given as Figure 1, shows peak around 3500-3200 cm^{-1} is due to presence of hydroxyl group in the molecule. The –C-H- stretching and rocking IR frequency observed in the region of 3100-3000 cm^{-1} and 1370-1350 cm^{-1} respectively. The peak observed near to 1750 cm^{-1} is due to carbonyl group. The Ar-C=C stretching is observed around 1549-1695 cm^{-1} whereas alkane C-H bending is observed around 1369-1390 cm^{-1}. The peaks around 1300-1330 cm^{-1} and 1025-1082 cm^{-1} are of C-O stretching of ester and C-O stretching of ether respectively.

^{1}H NMR spectra

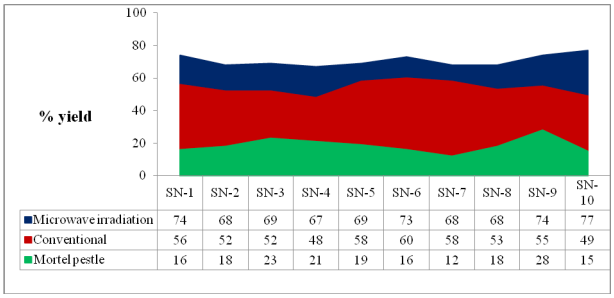
The 1H NMR peak of methyl group, present in compound, observed at 2.635 δ ppm as singlet. The proton peak of methylene group observed at 5.508 δ ppm as singlet. The aromatic protons of two phenyl rings are shown between 7.266 to 8.661 δ ppm with their appropriate multiplicity.

All the ^{1}H NMR splitting of peak suggests that compounds are synthesized successfully.

Mass spectra

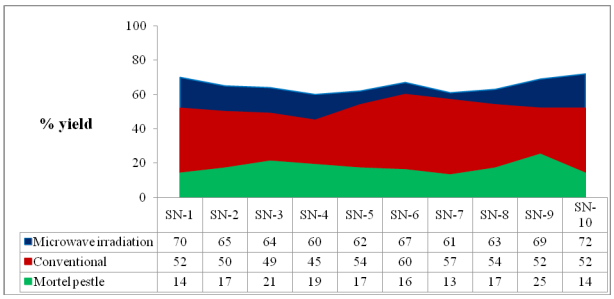
Figure 3 shows the mass spectrum of compound SN-1. From mass fragmentations, the synthesized compounds are confirmed.

Figure 4: % yield of benzo[1,3]oxazine-2,4-dione derivatives by different method in N,N-dimethyl formamide



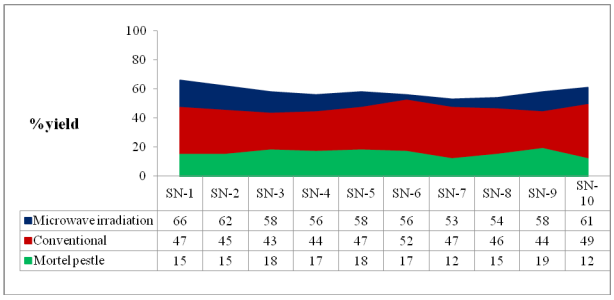
	SN-1	SN-2	SN-3	SN-4	SN-5	SN-6	SN-7	SN-8	SN-9	SN-10
Microwave irradiation	74	68	69	67	69	73	68	68	74	77
Conventional	56	52	52	48	58	60	58	53	55	49
Mortel pestle	16	18	23	21	19	16	12	18	28	15

Figure 5: % yield of benzo[1,3]oxazine-2,4-dione derivatives by different method in dimethyl sulphoxide



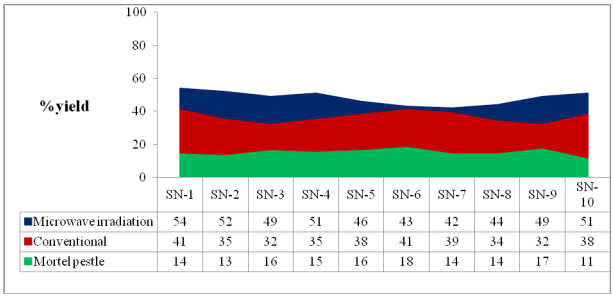
	SN-1	SN-2	SN-3	SN-4	SN-5	SN-6	SN-7	SN-8	SN-9	SN-10
Microwave irradiation	70	65	64	60	62	67	61	63	69	72
Conventional	52	50	49	45	54	60	57	54	52	52
Mortel pestle	14	17	21	19	17	16	13	17	25	14

Figure 6: % yield of benzo[1,3]oxazine-2,4-dione derivatives by different method in tetrahydro furan



	SN-1	SN-2	SN-3	SN-4	SN-5	SN-6	SN-7	SN-8	SN-9	SN-10
Microwave irradiation	66	62	58	56	58	56	53	54	58	61
Conventional	47	45	43	44	47	52	47	46	44	49
Mortel pestle	15	15	18	17	18	17	12	15	19	12

Figure 7: % yield of benzo[1,3]oxazine-2,4-dione derivatives by different method in ethyl acetate



	SN-1	SN-2	SN-3	SN-4	SN-5	SN-6	SN-7	SN-8	SN-9	SN-10
Microwave irradiation	54	52	49	51	46	43	42	44	49	51
Conventional	41	35	32	35	38	41	39	34	32	38
Mortel pestle	14	13	16	15	16	18	14	14	17	11

It is evident from Figures 4 to 7 that % yields of benzo[1,3]oxazine derivatives increased significantly using microwave irradiation method. The lowest % yield is observed in mortar pastel method in all solvent. In conventional method % yield increase rapidly than the mortar pastel method but lower than microwave irradiation method. In different solvents, % yield also occur different for same method of synthesis. This indicates that the solvent also play an important role in synthesis of benzo[1,3]oxazine derivatives. The higher % yield is observed in *N,N*-dimethyl formamide (DMF) solvent where as lowest % yield is observed in ethyl acetate solvent. From the table 3, it is clearly observed that the as dielectric constant and dipole moment of solvent decreases, % yield also decreases except DMF. In case of DMF, higher % yield is observed than the DMSO solvent having higher dipole moment and dielectric constant. Due to presence of nitrogen in DMF, may responsible for increases in % yield for all methods [15, 16]. Further, it is also observed that the compound containing halide side chains have higher % yield than other alkane substituted containing compounds.

The Schiff bases containing nitro aryl side chains have higher % yield than other halide containing bases. In conventional method, reaction time is in hours whereas in microwave irradiation method, it is reduced into minutes. Hence it is concluded that the microwave irradiation method is more favorable for the synthesis of such kind of molecules.

References

1. H Goossens, Chemotherapy 51, 2005, 177.
2. B P Mathew, M Nath, Chem Med Chem., 4, 2009, 310.
3. T Zebardast, A Zarghi, B Daraie, M Hedayati, O G Dadrass, Bioorg Med Chem., 19, 2009, 3162.
4. B. Tozkoparan, G. Aktay, E. Yesilada, Farmaco., 57, 2002, 145.
5. A Barazarte, J Camacho, J Dominguez, O G Lob, N Gamboa, J Roderigues, M N Capparelli, J. Bioorg. Med Chem., 16, 2008, 3661.
6. R Kalirajan, V Kulshrestha, S Sankar, Eur. J. Med. Chem., 56, 2012, 217.
7. A Fensome, R Bender, R Chopra, J Cohen, M K Collins, V Hudak, K Malakian, S Lochead, J. Med. Chem., 48, 2005, 5092.
8. K Takasu, T Shimogama, C Satoh, M Kaiser, R Brun, M Ihara, Med. Chem. Res., 20, 2011, 1147.
9. M Akhter, S Habibullah, S M Hasan, M M Alam, N Akhter, M Shaquiquzzaman, Med. Chem. Res., 20, 2011, 1147.
10. A V Velikorodov, N G Urlyapova, A D Daudova, Pharm. Chem. J., 40, 2006, 32.
11. S I Wael, E Abou, A I Hashem, Med. Chem. Res., 22, 2013, 2005.
12. J I Sylvia, P Díaz-Camacho, F García-Páez, P Bastidas-Bastidas, Quim. Nova, 37, 2014, 1297.
13. S S Didwagh, P B Piste, J. Chem. Pharm. Res., 5, 2013, 271.
14. W Chen, H Yin, Y Zhang, Z Lu, A Wang, Y Shen, T Jiang, L Yu, J Ind. Eng. Chem., 16, 2010, 800.
15. S Baluja, R Talaviya, Inter. J. Pharma. Chem. Bio. Sci., 5, 2015, 960.
16. S Baluja, R Talaviya, J. Chem. Engg. Data, 61, 2016, 1431.