One Pot Synthesis of [1,3]-Oxazine and [1,3]-Thiazine Derivatives Under Thermal and Microwave Conditions

S. Tumtin,[a] I. T. Phucho,[a] A. Nongpiur,[a] R. Nongrum,[a] J. N. Vishwakarma,[b] B. Myrboh,[a] and R. L. Nongkhlaw[a]*

[a]Department of Chemistry, North-Eastern Hill University, Shillong, Meghalaya 793022, India
[b]Organic Chemistry Research Laboratory, Department of Chemistry, St Anthony's College, Shillong, Meghalaya 793001, India
*E-mail: rlnongkhlaw@nehu.ac.in

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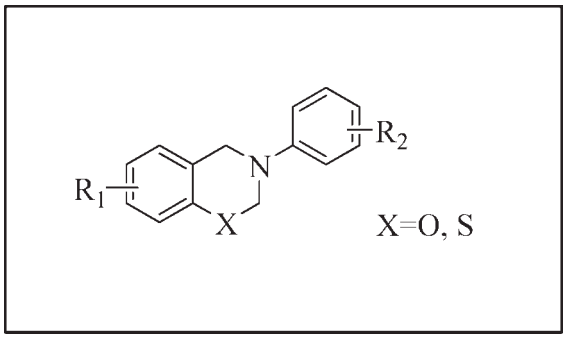

A simple and efficient synthesis of substituted benzo [1,3] oxazine and benzo [1,3] thiazine derivatives under conventional heating, as well as microwave irradiation is reported. The compounds were obtained by the reaction of electron rich phenols, formaldehyde, and aromatic amines in methanol. Reactions which take 12–16 hr under conventional heating were successfully completed within a few minutes under microwave irradiation (solventless) with moderate to excellent yields.

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INTRODUCTION

Development of novel synthetic methods for the construction of new analogs of bioactive heterocyclic compounds represents a major challenge in synthetic organic and medicinal chemistry. The importance of [1,3]-oxazines and [1,3]-thiazines in biological systems has attracted great interest because of their medicinal and pharmacological characteristics [1]. Many compounds containing [1,3]-oxazine moiety have found wide biological activities such as being anticancer [2], analgesic [3], antifungal [3], antitubercular [4], antihypertensive [5], antithromobotic [6], antiulcer [7], anticonvulsant, and antibacterial [8]. Moreover, certain kinds of [1,3]-oxazines are of interest as photochromic compounds [9].

It is well known that the presence of a thiol function in many enzymes ('–SH enzymes') is essential for their enzyme activity. Likewise, incorporation of a thiol function in heterocycles, nucleosides or nucleotides has led to a number of analogues possessing interesting biological and therapeutic properties [10–17]. The [1,3]-thiazine nucleus is the active core of cephalosporins, which are among the most widely used β-lactam antibiotics. Owing to their chemical and biological interest, synthesis of various unsubstituted and substituted 1,3-oxazine and 1,3-thiazine derivatives is reported as they appear to be attractive scaffolds for exploiting chemical diversity. Previously, napth-1, 3-oxazine derivatives have been reported using 2-napthol and various substituted aryl and heteroaryl aldehydes in the presence of dry methanolic ammonia [18–20]. In view of the importance of substituted [1,3]-oxazines and [1,3]-thiazines, we have initiated a programme for the development of simpler and more convenient methods for preparing heterocyclic systems with high efficacy.

RESULTS AND DISCUSSION

Our present study mainly focuses on the synthesis of various substituted [1,3]-oxazines and [1,3]-thiazines (Scheme 1) and their relative comparison with microwave assisted synthesis. ^{1}H and ^{13}C NMR spectra show that the products were obtained in good purity. The substituents on benzyl ring did not have significant influence on the reaction time and yields. All reactions which take many hours under conventional heating were completed in 3–8 min under microwave irradiation with enhanced yields. The results are presented in Table 1.

For these one-pot reactions of phenol, formaldehyde, and aromatic amines, it is noteworthy that simultaneous mixing resulted in poor yields [21]; however good

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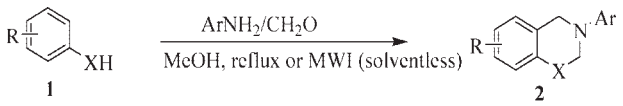
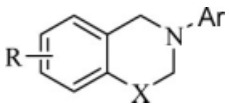
Scheme 1



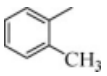
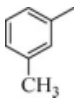
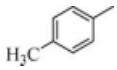
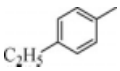
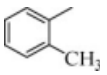
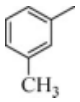
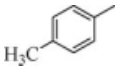
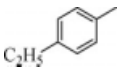
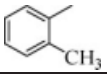
yields were obtained by the pretreatment of formaldehyde with the aromatic amines to form Schiff bases, which upon treatment with phenol yielded the required 1,3-oxazines. Also it has been found that this reaction worked well with formaldehyde but failed with other aldehydes. Here we presume that steric hindrance stops

Table 1

Comparison between microwave irradiation (MWI) and conventional heating in the synthesis of compounds 2 (**a**–**y**).

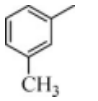
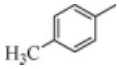
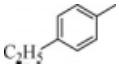
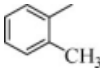
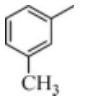
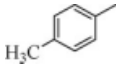
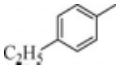
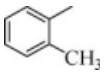
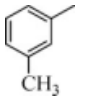
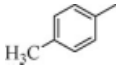
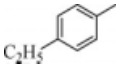


2 (a-y)

					Thermal		MWI			
Products	R	Ar	X	Mp (°C)	Time (hr)	Yield (%)	Press. (bar)	Power (watt)	Time (sec)	Yield (%)
2a	H		O	48	14	62	5	80	180	71
2b	H		O	52	14	66	5	80	200	72
2c	H		O	55	16	57	6	85	180	68
2d	H		O	66	15	63	6	90	180	70
2e	H		O	69	15	59	8	80	210	68
2f	2-CH_3		O	42	15	62	6	90	180	70
2g	2-CH_3		O	54	16	64	5	100	180	73
2h	2-CH_3		O	57	16	63	7	90	225	70
2i	2-CH_3		O	68	15	65	7	110	185	71
2j	2-CH_3		O	67	14	66	8	110	180	72
2k	3-CH_3		O	54	15	65	6	90	220	73
2l	3-CH_3		O	63	16	60	7	90	200	68

(*Continued*)

Table 1
(*Continued*)

					Thermal		MWI			
Products	R	Ar	X	Mp (°C)	Time (hr)	Yield (%)	Press. (bar)	Power (watt)	Time (sec)	Yield (%)
2m	3-CH_3		O	75	15	66	7	120	180	72
2n	3-CH_3		O	78	16	65	8	120	185	71
2o	3-CH_3		O	72	15	62	9	90	250	69
2p	4-CH_3		O	40	16	62	7	90	190	70
2q	4-CH_3		O	62	15	63	6	80	195	71
2r	4-CH_3		O	68	16	64	7	90	190	72
2s	4-CH_3		O	65	16	64	8	100	200	72
2t	4-CH_3		O	66	16	60	10	120	210	68
2u	H		S	38	15	58	8	100	180	67
2v	H		S	43	16	59	8	110	200	68
2w	H		S	45	16	61	9	100	210	68
2x	H		S	56	16	63	9	110	215	71
2y	H		S	58	16	58	10	120	240	67

the reaction at the open-chain Schiff bases without proceeding further to the cyclocondensation products. Reactions with other aromatic aldehydes gave same results [18,22]. Mcdonagh and Smith [23] reported the ring-chain tautomerism of the condensation products of o-hydroxybenzylamine with a number of aldehydes where aliphatic aldehydes tend to give predominantly or exclusively 1, 3-oxazines whereas aromatic aldehydes tend to give predominantly open chain structures (Schiff bases). Hence, it suggests that the Schiff bases formed are quite stable and do not react further even with increasing reaction time as well as temperature. In course of our study, it has been found that electron donating substituents on the alcohol, as well as the aromatic primary amines favour the reactions to give the desired products. All the observations in both conventional as well as microwave synthesis are similar except in the reaction time and yield. This clearly indicates the advantages of microwave chemistry which is fast developing as a convenient and ecofriendly mode of synthesis.

In summary, the aforementioned protocol reports the conventional and microwave synthesis of 1, 3-oxazines, as well as a few numbers of 1, 3-thiazines from simple and easily available starting materials in which microwave synthesis is preferred as an alternative mode of reactions. This microwave induced procedure offers several advantages including operational simplicity, high yields, simple work up and reactions are completed within short time.

EXPERIMENTAL SECTION

Microwave reactions were carried out in a CEM Discover Benchmate microwave digester. Melting points were determined in open capillary tubes with a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a BOMEM DA-8 FTIR instrument and the frequencies are expressed in cm^{-1}. ^1H and ^{13}C NMR (400 MHz) spectra were recorded on a Bruker Avance II-400 spectrometer using $CDCl_3$ as the solvent. Chemical shifts are reported in ppm downfield from internal tetramethylsilane and are given on the δ scale. Mass spectral data were obtained with a JEOL D-300 (EI) mass spectrometer. Elemental analyses were carried out on a Heraeus CHN-O-Rapid analyzer. All compounds give satisfactory elemental analyses within ± 0.4% of the theoretical values. All reactions were monitored by TLC using precoated aluminum sheets (silica gel 60 F 254 0.2 mm thickness) and developed in an iodine chamber or under UVGL-15 mineral light 254 lamp. Column chromatographic separations were carried out using ACME silica gel (60–120 mesh).

General procedure for conventional synthesis. To a well stirred solution of the amine (1 mmol) in 5 mL of methanol, formaldehyde (2 mmol) was added dropwise upon which a thick white precipitate was formed. After stirring at room temperature for about 15–20 min, phenol (1 mmol) dissolved in methanol was added dropwise. The reaction mixture was then refluxed at 70°C for 14–16 hr. After the reaction was completed (monitored by TLC), the solvent was evaporated under reduced pressure and the resultant mixture was purified by column chromatography to afford the pure compound.

General procedure for microwave assisted synthesis. A mixture of the amine (1 mmol), formaldehyde (2 mmol) and phenol (1 mmol) was irradiated in a microwave digester at 5–10 bar, 80–120 W, 180–250 seconds without the use of solvent. After the reaction was completed (monitored by TLC) the resultant mixture was purified by column chromatography to afford the pure compound.

The physical and spectral data of the products are as follows:

3,4-Dihydro-3-phenyl-2*H*-benzo[e][1,3]oxazine (2a). mp 48°C, IR (KBr): 3036 (Ar—C—H), 1597 (C=C), 1227 (Ar—C—O), 1087 (—CH_2—O), 1370 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.61 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.77–7.02 (m, 9H, ArH). ^{13}C NMR ($CDCl_3$): δ 49.9, 79.0, 115.4, 116.1, 117.9, 120.3, 125.4, 127.4, 128.8, 128.9, 128.9, 129.4, 147.9, 153.9. MS: m/z =211 (M^+). *Anal. Calcd*. For $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63%. Found: C, 79.63; H, 6.18; N, 6.67%.

3,4-Dihydro-3-o-tolyl-2*H*-benzo[e][1,3]oxazine (2b). mp 52°C, IR (KBr): 3037 (Ar—C—H), 1596 (C=C), 1227 (Ar—C—O), 1084 (—CH_2—O), 1372 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.24 (s, 3H, CH_3), 4.55 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.65–7.11 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 18.7, 58.3, 79.6, 115.1, 115.9, 118.5, 121.3, 122.7, 127.4, 127.9, 128.6, 129.8, 130.6, 148.0, 157.6. MS: m/z =225 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 79.99; H, 6.75; N, 6.18%.

3,4-Dihydro-3-m-tolyl-2*H*-benzo[e][1,3]oxazine (2c). mp 55°C, IR (KBr): 3035 (Ar—C—H), 1597 (C=C), 1226 (Ar—C—O), 1079 (—CH_2—O), 1373 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 3H, CH_3), 4.60 (s, 2H, CH_2), 5.41 (s, 2H, CH_2), 6.39–7.02 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 18.4, 55.1, 78.9, 110.7, 115.2, 115.8, 118.4, 120.7, 123.0, 127.8, 129.8, 130.2, 138.8, 147.9, 157.4. MS: m/z =225 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 79.98; H, 6.74; N, 6.19%.

3,4-Dihydro-3-p-tolyl-2*H*-benzo[e][1,3]oxazine (2d). mp 66°C, IR (KBr): 3037 (Ar—C—H), 1597 (C=C), 1228 (Ar—C—O), 1088 (—CH_2—O), 1371 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 4.55 (s, 2H, CH_2), 5.40 (s, 2H, CH_2), 6.47–7.10 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 23.2, 55.7, 79.2, 113.7, 114.6, 114.8, 120.4, 123.7, 126.0, 128.4, 129.6, 130.7, 132.8, 145.9, 155.4. MS: m/z =225 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 80.01; H, 6.67; N, 6.26%.

3-(4-ethylphenyl)-3,4-dihydro-2*H*-benzo[e][1,3]oxazine (2e). mp 69°C, IR (KBr): 3036 (Ar—C—H), 1596 (C=C), 1225 (Ar—C—O), 1087 (—CH_2—O), 1368 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.26 (s, 3H, CH_3), 2.63 (q, 2H, CH_2), 4.60 (s, 2H, CH_2), 5.42 (s, 2H, CH_2), 6.54–7.02 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 16.1, 35.2, 54.3, 88.9, 113.8, 114.2, 114.6, 120.5, 123.3, 127.1, 127.9, 128.7, 129.2, 129.7, 147.4, 156.8. MS: m/z =239 (M^+). *Anal. Calcd*. For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.14; N, 5.88%.

3,4-Dihydro-8-methyl-3-phenyl-2*H*-benzo[e][1,3]oxazine (2f). mp 42°C, IR (KBr): 3024 (Ar—C—H), 1609 (C=C), 1223 (Ar—C—O), 1085 (—CH_2—O), 1336 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.33 (s, 3H, CH_3), 4.58 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.56–7.13 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 15.3, 56.3, 79.9, 114.2, 114.6, 118.5, 121.3, 122.1, 124.9, 126.7, 128.2, 129.1, 129.7, 148.4, 157.6. MS: m/z =225 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 80.00; H, 6.68; N, 6.24%.

3,4-Dihydro-8-methyl-3-o-tolyl-2*H*-benzo[e][1,3]oxazine (2g). mp 54°C, IR (KBr): 3025 (Ar—C—H), 1583 (C=C), 1227 (Ar—C—O), 1085 (—CH_2—O), 1367 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.62 (s, 2H, CH_2), 5.35 (s, 2H, CH_2), 6.47–7.02 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 15.3, 16.4, 58.3, 79.7, 114.7, 118.5, 120.5, 124.5, 126.3, 126.5, 127.4, 128.9, 126.7, 128.2, 146.6, 156.6. MS: m/z =239 (M^+). *Anal. Calcd*. For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.33; H, 7.13; N, 5.81%.

3,4-Dihydro-8-methyl-3-m-tolyl-2*H*-benzo[e][1,3]oxazine (2h). mp 57°C, IR (KBr): 3027 (Ar—C—H), 1590 (C=C), 1223 (Ar—C—O), 1087 (—CH_2—O), 1375 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.36 (s, 6H, CH_3), 4.62 (s, 2H, CH_2), 5.41 (s, 2H, CH_2), 6.39–7.11 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 15.7, 23.7, 58.3, 79.3, 111.4, 114.4, 118.7, 120.2, 121.4, 123.5, 126.6, 128.3, 129.4, 138.9, 148.6, 156.8. MS: m/

z = 239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.12; N, 5.82%.

3,4-Dihydro-8-methyl-3-p-tolyl-2*H*-benzo[e][1,3]oxazine (2i). mp 68°C, IR (KBr): 3027 (Ar—C—H), 1581 (C=C), 1220 (Ar—C—O), 1085 (—CH_2—O), 1360 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.32 (s, 6H, CH_3), 4.58 (s, 2H, CH_2), 5.40 (s, 2H, CH_2), 6.47–7.10 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.7, 25.7, 58.2, 78.9, 115.4, 115.4, 120.6, 122.4, 124.5, 126.7, 127.7, 128.6, 129.4, 130.8, 147.6, 155.8. MS: m/z = 239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.13; N, 5.87%.

3-(4-ethylphenyl-3,4-dihydro-8-methyl-2*H*-benzo[e][1,3] oxazine (2j). mp 67°C, IR (KBr): 3024 (Ar—C—H), 1582 (C=C), 1266 (Ar—C—O), 1087 (—CH_2—O), 1362 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.26 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.60 (q, 2H, CH_2), 4.60 (s, 2H, CH_2), 5.37 (s, 2H, CH_2), 6.74–7.18 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.1, 15.2, 33.7, 56.9, 78.6, 114.5, 114.6, 120.5, 123.3, 126.1, 127.9, 129.7, 129.7, 130.1, 132.9, 147.4, 157.8. MS: m/z =253 (M^+). *Anal. Calcd.* For $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.64; H, 7.57; N, 5.51%.

3,4-Dihydro-7-methyl-3-phenyl-2*H*-benzo[e][1,3]oxazine (2k). mp 54°C, IR (KBr): 3027 (Ar—C—H), 1601 (C=C), 1227 (Ar—C—O), 1084 (—CH_2—O), 1327 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.64 (s, 3H, CH_3), 4.59 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.62–7.09 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 21.1, 50.2, 79.4, 114.6, 117.2, 117.7, 118.1, 118.2, 121.3, 126.0, 129.2, 129.2, 137.8, 148.4, 154.1. MS: m/z =225 (M^+). *Anal. Calcd.* For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 79.99; H, 6.75; N, 6.18%.

3,4-Dihydro-7-methyl-3-o-tolyl-2*H*-benzo[e][1,3]oxazine (2l). mp 63°C, IR (KBr): 3026 (Ar—C—H), 1589 (C=C), 1223 (Ar—C—O), 1087 (—CH_2—O), 1351 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.35 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.77–7.01 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 15.6, 25.1, 56.2, 79.4, 112.6, 114.2, 117.7, 119.1, 126.2, 127.3, 128.5, 129.2, 136.2, 137.8, 148.4, 154.1. MS: m/z =239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.33; H, 7.13; N, 5.82%.

3,4-Dihydro-7-methyl-3-m-tolyl-2*H*-benzo[e][1,3]oxazine (2m). mp 75°C, IR (KBr): 3023 (Ar—C—H), 1576 (C=C), 1225 (Ar—C—O), 1084 (—CH_2—O), 1327 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.45 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.65–7.00 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.6, 25.1, 56.2, 79.2, 111.6, 112.2, 114.7, 119.1, 119.2, 121.3, 128.5, 129.2, 136.9, 139.8, 148.5, 156.1. MS: m/z =239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.14; N, 5.81%.

3,4-Dihydro-7-methyl-3-p-tolyl-2*H*-benzo[e][1,3]oxazine (2n). mp 78°C, IR (KBr): 3036 (Ar—C—H), 1597 (C=C), 1229 (Ar—C—O), 1082 (—CH_2—O), 1370 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.52 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.67–7.10 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.6, 24.1, 56.2, 79.2, 112.2, 113.6, 114.7, 119.3, 121.2, 127.3, 128.5, 129.2, 130.2, 137.8, 146.4, 157.2. MS: m/z =239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.32; H, 7.15; N, 5.81%.

3-(4-ethylphenyl)-3,4-dihydro-7-methyl-2*H*-benzo[e][1,3] oxazine (2o). mp 72°C, IR (KBr): 3041 (Ar—C—H), 1604 (C=C), 1231 (Ar—C—O), 1085 (—CH_2—O), 1365 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.25 (s, 3H, CH_3), 2.60 (q, 2H, CH_2), 4.62 (s, 2H, CH_2), 5.38 (s, 2H, CH_2), 6.54–7.02 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.1, 25.2, 32.6, 53.3, 78.9, 113.8, 114.2, 114.7, 120.5, 121.3, 127.1, 128.5, 128.7, 129.1, 137.7, 147.4, 156.8. MS: m/z =253 (M^+). *Anal. Calcd.* For $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.64; H, 7.52; N, 5.55%.

3,4-Dihydro-6-methyl-3-phenyl-2*H*-benzo[e][1,3]oxazine (2p). mp 40°C, IR (KBr): 3110 (Ar—C—H), 1585 (C=C), 1230 (Ar—C—O), 1085 (—CH_2—O), 1366 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 3H, CH_3), 4.59 (s, 2H, CH_2), 5.34 (s, 2H, CH_2), 6.62–7.11 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.1, 53.2, 79.7, 114.6, 114.2, 115.7, 118.1, 122.2, 128.3, 129.0, 129.2, 129.8, 130.2, 148.5, 154.2. MS: m/z =225 (M^+). *Anal. Calcd.* For $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%. Found: C, 79.99; H, 6.75; N, 6.18%.

3,4-Dihydro-6-methyl-3-o-tolyl-2*H*-benzo[e][1,3]oxazine (2q). mp 62°C, IR (KBr): 3037 (Ar—C—H), 1598 (C=C), 1228 (Ar—C—O), 1087 (—CH_2—O), 1370 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.41 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.71–7.10 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 15.6, 24.1, 56.2, 79.2, 114.7, 114.9, 118.7, 122.4, 126.6, 127.3, 128.0, 129.2, 130.9, 130.8, 146.5, 155.1. *Anal.* MS: m/z =239 (M^+). *Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.13; N, 5.81%.

3,4-Dihydro-6-methyl-3-m-tolyl-2*H*-benzo[e][1,3]oxazine (2r). mp 68°C, IR (KBr): 3041 (Ar—C—H), 1600 (C=C), 1237 (Ar—C—O), 1081 (—CH_2—O), 1372 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.34 (s, 6H, CH_3), 4.51 (s, 2H, CH_2), 5.33 (s, 2H, CH_2), 6.68–7.10 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.1, 24.1, 56.2, 79.6, 111.7, 114.7, 114.9, 118.4, 122.6, 128.5, 129.5, 130.3, 130.8, 139.0, 148.4, 155.1. MS: m/z =239 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.33; H, 7.14; N, 5.82%.

3,4-Dihydro-6-methyl-3-p-tolyl-2*H*-benzo[e][1,3]oxazine (2s). mp 65°C, IR (KBr): 3126 (Ar—C—H), 1580 (C=C), 1227 (Ar—C—O), 1087 (—CH_2—O), 1380 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.23 (s, 6H, CH_3), 4.55 (s, 2H, CH_2), 5.29 (s, 2H, CH_2), 6.61–7.02 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 20.5, 21.1, 50.7, 116.8, 117.3, 117.7, 118.6, 119.0, 121.4, 126.5, 127.0, 128.4, 129.7, 129.9, 146.8, 152.8. MS: m/z =238 (M^+). *Anal. Calcd.* For $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85%. Found: C, 80.34; H, 7.14; N, 5.81%.

3-(4-ethylphenyl)-3,4-dihydro-6-methyl-2*H*-benzo[e][1,3] oxazine (2t). mp 66°C, IR (KBr): 3036 (Ar—C—H), 1599 (C=C), 1227 (Ar—C—O), 1082 (—CH_2—O), 1373 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.25 (s, 3H, CH_3), 2.60 (q, 2H, CH_2), 4.62 (s, 2H, CH_2), 5.32 (s, 2H, CH_2), 6.54–7.01 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.8, 25.2, 32.5, 53.7, 78.0, 113.9, 114.2, 114.6, 122.5, 128.3, 128.6, 128.8, 129.7, 130.2, 130.7, 147.4, 156.8. MS: m/z =253 (M^+). *Anal. Calcd.* For $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.64; H, 7.52; N, 5.55%.

3,4-Dihydro-3-phenyl-2*H*-benzo[e][1,3]thiazine (2u). mp 38°C, IR (KBr): 3036 (Ar—C—H), 1596 (C=C), 756 (C-S), 1367 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.63 (s, 2H, CH_2), 4.88 (s, 2H, CH_2), 6.81–7.03 (m, 9H, ArH). ^{13}C NMR ($CDCl_3$): δ 49.5, 61.7, 115.8, 116.1, 117.7, 120.3, 125.4, 127.4, 128.8, 128.9, 128.9, 129.4, 147.9, 153.9. MS: m/z =227 (M^+). *Anal. Calcd.* For $C_{14}H_{13}NS$: C, 73.97; H, 5.76; N, 6.16%. Found: C, 74.01; H, 5.72; N, 6.18%.

3,4-Dihydro-3-o-tolyl-2*H*-benzo[e][1,3]thiazine (2v). mp 43°C, IR (KBr): 3035 (Ar—C—H), 1597 (C=C), 745 (C—S), 1391 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.36 (s, 3H,

CH_3), 4.50 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 6.67–7.06 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.9, 56.3, 62.7, 114.90 118.1, 125.0, 126.6, 126.9, 127.0, 127.8, 128.9, 130.1, 130.2, 147.3, 148.3. MS: m/z =241 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NS$: C, 74.65; H, 6.26; N, 5.80%. Found: C, 74.68; H, 6.24; N, 5.78%.

3,4-Dihydro-3-m-tolyl-2*H*-benzo[e][1,3]thiazine (2w). mp 45°C, IR (KBr): 3041 (Ar—C—H), 1596 (C=C), 756 (C—S), 1365 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.32 (s, 3H, CH_3), 4.57 (s, 2H, CH_2), 4.81 (s, 2H, CH_2), 6.49–7.06 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 24.9, 57.3, 63.0, 111.9, 114.1, 118.0, 125.6, 126.9, 127.0, 128.1, 129.6, 130.1, 131.2, 139.3, 148.3. MS: m/z =241 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NS$: C, 74.65; H, 6.26; N, 5.80%. Found: C, 74.68; H, 6.23; N, 5.76%.

3,4-Dihydro-3-p-tolyl-2*H*-benzo[e][1,3]thiazine (2x). mp 56°C, IR (KBr): 3037 (Ar—C—H), 1597 (C=C), 750 (C—S), 1385 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 4.59 (s, 2H, CH_2), 4.86 (s, 2H, CH_2), 6.81–7.03 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 22.1, 56.3, 67.7, 116.9, 120.1, 121.6, 124.9, 125.0, 126.8, 127.6, 128.6, 129.1, 132.2, 147.3, 150.3. MS: m/z =241 (M^+). *Anal. Calcd*. For $C_{15}H_{15}NS$: C, 74.65; H, 6.26; N, 5.80%. Found: C, 74.69; H, 6.23; N, 5.77%.

3-(4-ethylphenyl)-3,4-dihydro-2*H*-benzo[e][1,3]thiazine (2y). mp 58°C, IR (KBr): 3035 (Ar—C—H), 1597 (C=C), 748 (C—S), 1367 (Ar—C—N) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.26 (t, 3H, CH_3), 2.56 (q, 2H, CH_2), 4.59 (s, 2H, CH_2), 4.82 (s, 2H, CH_2), 6.51–7.03 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$): δ 14.6, 32.1, 57.3, 66.7, 114.9, 115.1, 125.6, 126.9, 127.0, 128.2, 128.6, 128.9, 129.2, 130.3, 131.3, 146.7. MS: m/z =255 (M^+). *Anal. Calcd*. For $C_{16}H_{17}NS$: C, 75.25; H, 6.71; N, 5.48%. Found: C, 75.29; H, 6.68; N, 5.49%.

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