



Simple and Selective Synthesis of 1,3-Benzoxazine Derivatives

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ABSTRACT

A simple and selective synthesis of 1,3-benzoxazine-2,4-dione and 4-methylene-1,3-benzoxazine-2-one derivatives is reported from the reaction of Schiff bases and triphosgene. The selective synthesis of those 1,3-benzoxazine derivatives were found to be dependent on the type of substituents present on the Schiff base.

Key words: 1,3-benzoxazine, triphosgene, Schiff bases, 1,3-benzoxazine-2,4-dione.

INTRODUCTION

Triphosgene [bis(trichloromethyl)-carbonate] a white crystalline compound, has emerged as a diversified reagent for the synthesis of varieties of heterocyclic ring systems¹. It has several advantages such as safe in handling, less hazardous, and high reactivity over its gaseous congener, phosgene and is being frequently used in many organic synthesis as a substitute for the hazardous gaseous phosgene. Recently, triphosgene has been effectively used in the preparation of ureas², Bischler-Napieralski reaction,³ carbamoyl azides,⁴ and β -lactams⁵. On the other hand, Schiff bases (Imines) are considered as an important class of compounds and due to their diverse reactivity, they are widely

used in industrial synthetic processes⁶ as well as in many laboratory organic synthesis⁷. They are particularly more useful in the preparation of heterocyclic ring systems⁸ and non natural β -aminoacids⁹. Consequently, several synthetic protocols have been developed for their synthesis¹⁰.

Benzoxazine, on the other hand, are very important class of heterocyclic compounds and play an important and central role in pharmacologically and therapeutically active substances¹¹ as well as in natural products¹². They possesses broad spectrum of biological activities¹³ behaving as antirheumatic,^{13a} neuroprotective antioxidants,^{13b} anticancer,^{13c} antihypertensive,^{13d} and other activities^{13e-g}. *Efavirenz* a 3,1-benzoxazine

derivative also famous with its brand name *Sustiva* and *Stocrin*, is a non-nucleoside reverse transcriptase inhibitor (NNRTI) and is being effectively used as part of highly active antiretroviral therapy (HAART) for the treatment of the human immunodeficiency virus (HIV) since its approval by the FDA in 1998¹⁴. Various analogs of *Efavirenz* have also been reported to possess promising anti-HIV activity¹⁵. Similarly, 1,3-benzoxazine and its derivatives have also been reported to exhibit a wide range of biological activities¹⁶ including antimicrobial,^{16d-e} CNS agents,^{16f} antagonism to progesterone receptor,^{16g} antitumour,^{16h-i} antiviral,^{16j-k} antithrombotic,^{16l} anti-inflammatory,^{16m} antidiabetic and hypolipidaemic¹⁶ⁿ effects, inhibitors of human leucocyte elastase,^{16o} serotonin reuptake,^{16p} K⁺ channel opener,^{16q} anti-HIV,^{16r-s}. In addition, 1,3-benzoxazines have been reported to transform into their 3,1-benzoxazine isomer¹⁷. Recently, 1,3-benzoxazine-2,4-dione and related derivatives have been reported as a potential useful agent for treating infections caused by *Mycobacterium* species¹⁸. Although 1,3-benzoxazines have been reported to play a significant role in the field of medicinal and pharmaceutical chemistry, perusal of literature revealed that comparing to other series of benzoxazines, only few methods are available for the synthesis of 1,3-benzoxazine-2,4-diones¹⁹.

In continuation of our interest in the synthesis of heterocyclic compounds,²⁰ we report herein the synthesis of Schiff bases and their cyclization into 1,3-benzoxazine-2,4-diones. It is worth mentioning here that synthetic protocols for the preparation of 1,3-benzoxazine-2,4-diones are very scanty^{19a} and to the best of our knowledge, synthesis of 1,3-benzoxazine-2,4-diones have never been reported earlier from the reaction of Schiff bases and triphosgene.

MATERIALS AND METHODS

All the chemicals and reagents used were purchased from Sigma-Aldrich. Melting points were determined on a Gallen Kamp melting point apparatus and are uncorrected. ¹H and ¹³C-NMR spectra were recorded with a JEOL ECP-400 spectrophotometer. The NMR samples were prepared in CDCl₃ with tetramethylsilane (TMS) as an internal standard. The chemical shifts and

coupling constants (J) were expressed in d and Hz, respectively. MS spectra were recorded on Shimadzu QP5050A GC/MS system. The thin layer chromatography (TLC) was carried out on pre-coated Silica gel 60 F254 (0.2 mm, Merck) plates. The developed TLC plates were visualized under UV light at 254 and 365 nm.

Preparation of the Schiff bases

The Schiff bases **2a-u** were prepared using the procedure previously described^{20d}.

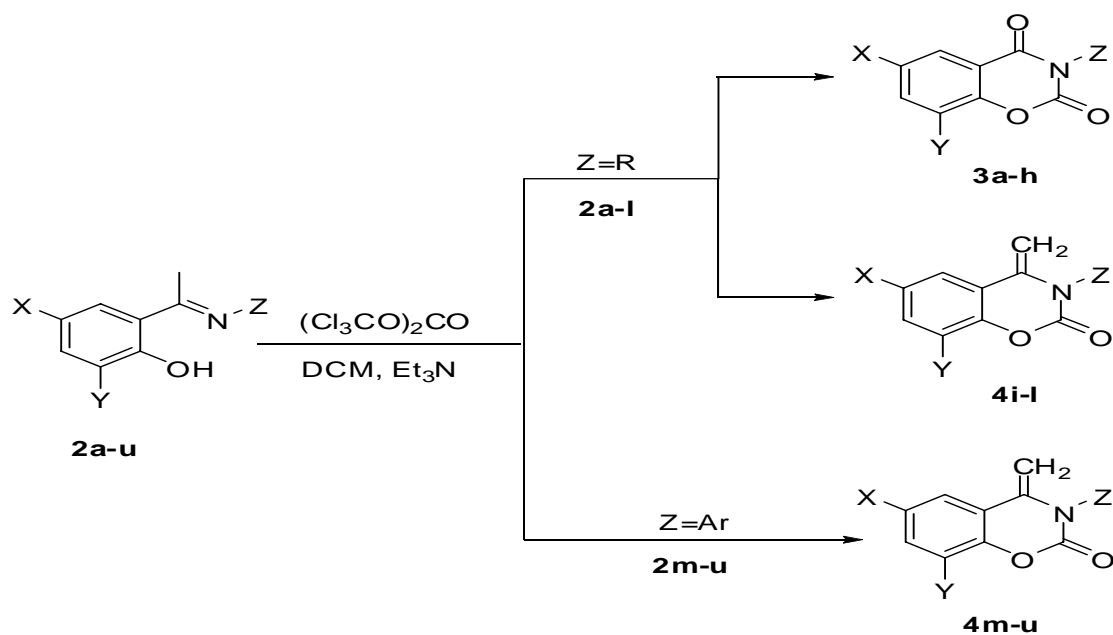
Preparation of 1,3-benzoxazine derivatives

A 250 ml three neck round bottom flask containing the appropriate Schiff base (7.26 mmol) was equipped with reflux condenser, dropping funnel and an adapter to allow the passage of N₂ gas. Dichloromethane (30 ml) and Et₃N (1 ml) were added to dissolve the Schiff base followed by a drop wise addition under N₂ atmosphere of a solution of 0.7 equivalent of triphosgene in 15 ml of dichloromethane. The mixture was then stirred at room temperature for one hour followed by reflux for 2 hours. The mixture was washed with distilled water, dried over magnesium sulphate and evaporated to dryness and crystallized from a mixture of hexane and ethanol to give pure 1,3-benzoxazine derivatives.

RESULTS AND DISCUSSION

In a previous study,^{20d} we reported the synthesis of various 4-methylene-1,3-benzoxazine derivatives involving the reaction of triphosgene and Schiff bases substituted with electron withdrawing groups. However, when the same reaction was carried out using triphosgene and Schiff bases substituted with electron donating groups under optimal conditions, the desired 4-methylene-1,3-benzoxazine was not produced. Instead, an unidentified product was obtained in high yield. Herein, we report on further detail study of this reaction, which led to the development of a facile, convenient and selective synthesis of either 1,3-benzoxazine-2,4-diones or 4-methylene-1,3-benzoxazine in single step.

The Schiff bases **2a-2u** (Table 1) prepared according to the previously described method,^{20d} were dissolved in a mixture of DCM and Et₃N (20:2)



Scheme 1

Table 1. Schiff bases, 2a-u

X	Y	Z	Product ^a	Yield ^b (%)
H	H	n-propyl	2a	99
H	H	n-butyl	2b	96
H	H	Isobutyl	2c	72
H	H	n-hexyl	2d	85
OMe	H	n-propyl	2e	99
OMe	H	n-butyl	2f	92
OMe	H	Isobutyl	2g	87
OMe	H	n-hexyl	2h	85
Cl	Cl	n-propyl	2i	98
Cl	Cl	Isopropyl	2j	78
Cl	Cl	Isobutyl	2k	80
Cl	Cl	n-hexyl	2l	92
H	H	Phenyl	2m	62
H	H	2'-Methylphenyl	2n	60
H	H	3'-Chlorophenyl	2o	60
Cl	Cl	Phenyl	2p	70
Cl	Cl	2'-Methylphenyl	2q	78
Cl	Cl	3'-Chlorophenyl	2r	68
OMe	H	Phenyl	2s	68
OMe	H	2'-Methylphenyl	2t	72
OMe	H	3'-Chlorophenyl	2u	77

^a Identified by ^1H , ^{13}C , EI-MS and by comparison of their spectral data with those of related compounds.^b Isolated Yield

and treated with triphosgene. Two different products were obtained using the same reaction conditions (**Scheme 1**). The first one is 1,3-benzoxazine-2,4-dione **3a-3h** obtained when Z=R and X, Y=H, OMe. The second one is 4-methylene-1,3-benzoxazine-2-one **4i-4u**, obtained when; (i) Z=R and X, Y=Cl (ii) Z=Ar and X, Y=H, OMe, Cl (**Table 2**). Careful observation of the results indicate that substituents of the Schiff bases, **2a-2l** (derived from aliphatic amines) played a key role in the selective synthesis of either 1,3-benzoxazine-2,4-dione **3a-3h** or 4-methylene-1,3-benzoxazine-2-one **4i-4u**. 1,3-benzoxazine-2,4-dione **3a-3h** were obtained when Schiff bases were substituted with electron donating groups (Z=R and X, Y=H, OMe). Whereas 4-methylene-1,3-benzoxazine-2-one **4i-4l** were formed when Schiff bases were substituted with electron withdrawing groups (Z=R and X, Y=Cl). On

the other hand, substituents of the Schiff bases **2m-2u** (derived from aromatic amines) have no effects on the formation of final products. They synthesized only 4-methylene-1,3-benzoxazine-2-one, **4m-4u** as sole products when reacted with triphosgene under optimal conditions.

Derivatives of 1,3-benzoxazine-2,4-diones **3a-h** showed two clear downfield signals at 152.7 and 160.7 ppm in the ^{13}C NMR spectrum confirming the presence of two carbonyl carbons (C-2 and C-4 respectively). Moreover, in contrast to the 4-methylene-1,3-benzoxazine-2-ones **4i-u**, the exocyclic double bond signal appears at 4.95 and 135 ppm in their ^1H and ^{13}C NMR spectra, these signals were not present in the spectra of **3a-h** confirming the absence of the exocyclic methylene group at C-4. Finally, the MS spectra of 1,3-benzoxazine-2,4-diones **3a-h** showed clear and distinct molecular ion peaks for each compound agreeing with the expected molecular weight.

Derivatives of 4-methylene-1,3-benzoxazine **4i-u** exhibited similar spectroscopic data to their analogous compounds previously reported^{20d}.

CONCLUSION

In conclusion, we have developed a very simple and selective synthesis of either 1,3-benzoxazine-2,4-diones or 4-methylene-1,3-benzoxazine-2-ones from the reaction of Schiff bases and triphosgene in single step. Comparing to other series of benzoxazines, synthesis of 1,3-benzoxazine-2,4-diones are very rare and to the best of our knowledge they are being prepared for the first time from the reaction of Schiff bases and triphosgene.

3-Propyl-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (**3a**)

M.p. 73°C; ^1H NMR: 0.95 (t, J=7.32 Hz, 3H), 1.70 (m, 2H), 3.96 (t, J=7.32 Hz, 2H), 7.27 (d, J=8.06 Hz, 1H), 7.35 (t, J=8.06 Hz, 1H), 7.66 (t, J=8.06 Hz, 1H), 8.07 (d, J=8.06 Hz, 1H); ^{13}C NMR: 11.3, 20.9, 44.2, 114.3, 116.5, 125.4, 128.2, 136.1, 148.2, 152.7, 160.7; EI-MS: m/z 205 (M^+), 164, 120, 92, 63.

3-Butyl-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (**3b**)

Table 2. 1,3-benzoxazine-2,4-diones, **3a-h** and 4-methylene-1,3-benzoxazine-2-one, **4i-u**

X	Y	Product ^a	Yield ^b (%) of 3 & 4
H	H	3a	84
H	H	3b	79
H	H	3c	72
H	H	3d	75
OMe	H	3e	85
OMe	H	3f	82
OMe	H	3g	87
OMe	H	3h	85
Cl	Cl	4i	92
Cl	Cl	4j	78
Cl	Cl	4k	74
Cl	Cl	4l	73
H	H	4m	86
H	H	4n	69
H	H	4o	60
Cl	Cl	4p	65
Cl	Cl	4q	58
Cl	Cl	4r	62
OMe	H	4s	51
OMe	H	4t	63
OMe	H	4u	77

^a Identified by ^1H , ^{13}C , EI-MS and by comparison of their spectral data with those of related compounds.

^b Isolated Yield

M.p. 70°C; ¹H NMR: 0.93 (t, J=7.32 Hz, 3H), 1.66 (m, 2H), 1.83 (m, 2H), 4.00 (t, J=7.32 Hz, 2H), 7.27 (m, 1H), 7.35 (m, 1H), 7.65 (m, 1H), 8.05 (m, 1H); ¹³C NMR: 13.8, 20.1, 29.7, 42.6, 114.3, 116.4, 125.4, 128.1, 136.1, 148.2, 152.7, 160.7; EI-MS: m/z 219 (M⁺), 164, 120, 92, 63.

3-Isobutyl-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3c)

M.p. 87°C; ¹H NMR: 0.92 (d, J=6.6 Hz, 6H), 2.18 (m, 1H), 3.87 (d, J=7.32 Hz, 2H), 7.26 (d, J=8.06 Hz, 1H), 7.35 (t, J=8.06 Hz, 1H), 7.68 (t, J=8.06 Hz, 1H), 8.06 (d, J=8.06 Hz, 1H); ¹³C NMR: 20.1, 27.1, 49.4, 114.2, 116.5, 125.43, 128.3, 136.1, 148.5, 152.7, 160.9; EI-MS: m/z 219 (M⁺), 164, 120, 92, 64, 56.

3-Hexyl-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3d)

M.p. 61°C; ¹H NMR: 0.87 (t, J=7.32 Hz, 3H), 1.29 (m, 6H), 1.65 (m, 2H), 3.99 (t, J=7.32 Hz, 2H), 7.27 (m, 1H), 7.35 (m, 1H), 7.67 (m, 1H), 8.06 (m, 1H); ¹³C NMR: 14.1, 22.6, 26.52, 27.6, 31.5, 42.8, 114.3, 116.5, 125.4, 128.2, 136.0, 148.2, 152.7, 160.6; EI-MS: m/z 247 (M⁺), 205, 177, 164, 120, 92, 64, 56.

6-Methoxy-3-propyl-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3e)

M.p. 81°C; ¹H NMR: 0.96 (t, J=7.32 Hz, 3H), 1.70 (m, 2H), 3.86 (s, 3H), 3.97 (t, J=7.32 Hz, 2H), 7.20 (d, J=8.80 Hz, 1H), 7.23 (dd, J=8.80 & 2.93 Hz, 1H), 7.45 (d, J=2.93 Hz, 1H); ¹³C NMR: 11.3, 20.9, 44.3, 56.1, 108.6, 114.6, 117.8, 124.8, 147.0, 148.3, 156.9, 160.8; EI-MS: m/z 235 (M⁺), 150, 107, 79, 65, 51.

3-butyl-6-methoxy-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3f)

M.p. 86°C; ¹H NMR: 0.92 (t, J=7.32 Hz, 3H), 1.37 (m, 2H), 1.67 (m, 2H), 3.85 (s, 3H), 3.99 (t, J=7.32 Hz, 2H), 7.18 (d, J=8.80 Hz, 1H), 7.22 (dd, J=8.80 & 2.93 Hz, 1H), 7.43 (d, J=2.93 Hz, 1H); ¹³C NMR: 13.8, 20.1, 29.7, 42.6, 56.1, 108.6, 114.6, 117.8, 124.8, 147.0, 148.3, 156.9, 160.8; EI-MS: m/z 249 (M⁺), 150, 107, 79, 65, 53.

3-Isobutyl-6-methoxy-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3g)

M.p. 100°C; ¹H NMR: 0.94 (d, J=6.59 Hz,

6H), 2.19 (m, 1H), 3.86 (s, 3H), 3.88 (d, J=7.32 Hz, 2H), 7.20 (d, J=8.80 Hz, 1H), 7.23 (dd, J=8.80 & 2.93 Hz, 1H), 7.44 (d, J=2.93 Hz, 1H); ¹³C NMR: 20.1, 27.1, 49.5, 56.1, 108.73, 114.5, 117.8, 124.8, 147.0, 148.5, 156.9, 161.1; EI-MS: m/z 249 (M⁺), 150, 107, 79, 65, 53.

3-Hexyl-6-methoxy-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione (3h)

M.p. 80°C; ¹H NMR: 0.85 (t, J=7.32 Hz, 3H), 1.29 (m, 6H), 1.64 (m, 2H), 3.85 (s, 3H), 3.98 (t, J=7.32 Hz, 2H), 7.18 (d, J=9.52 Hz, 1H), 7.21 (dd, J=9.52 & 2.93 Hz, 1H), 7.44 (d, J=2.93 Hz, 1H); ¹³C NMR: 14.1, 22.6, 26.5, 27.6, 31.5, 42.9, 56.1, 108.6, 114.6, 117.8, 124.7, 147.0, 148.3, 156.9, 160.7; EI-MS: m/z 277 (M⁺), 150, 107, 79, 65, 53.

6,8-Dichloro-4-methylene-3-propyl-3,4-dihydro-2H-1,3-benzoxazine-2-one (4i)

M.p. 87°C; ¹H NMR: 0.94 (t, J=7.32 Hz, 3H), 1.70 (m, 2H), 3.75 (t, J=7.32 Hz, 2H), 4.54 (d, J=2.93 Hz, 1H), 4.94 (d, J=2.93 Hz, 1H), 7.35 (d, J=2.19 Hz, 1H), 7.39 (d, J=2.19 Hz, 1H); ¹³C NMR: 11.2, 18.9, 47.5, 89.8, 119.3, 121.9, 122.8, 129.8, 130.8, 136.1, 143.5, 146.4; EI-MS: m/z 275 (M⁺+4), 273 (M⁺+2), 271 (M⁺), 256, 229, 186, 123, 87, 63.

6,8-Dichloro-3-isopropyl-4-methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4j)

M.p. 92°C; ¹H NMR: 1.51 (m, 6H), 4.26 (m, 1H), 4.74 (d, J=2.93 Hz, 1H), 4.96 (d, J=2.93 Hz, 1H), 7.35 (d, J=2.19 Hz, 1H), 7.34 (d, J=2.19 Hz, 1H); ¹³C NMR: 19.1, 52.0, 92.8, 121.3, 122.0, 122.4, 129.7, 130.5, 137.6, 143.6, 145.6; EI-MS: m/z 275 (M⁺+4), 273 (M⁺+2), 271 (M⁺), 256, 229, 188, 123, 97, 87, 70, 60.

6,8-Dichloro-3-isobutyl-4-methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4k)

M.p. 107-109°C; ¹H NMR: 0.95 (d, J=6.59 Hz, 6H), 2.17 (m, 1H), 3.72 (d, J=7.32 Hz, 2H), 4.56 (d, J=2.93 Hz, 1H), 4.98 (d, J=2.93 Hz, 1H), 7.39 (d, J=2.19 Hz, 1H), 7.41 (d, J=2.19 Hz, 1H); ¹³C NMR: 20.1, 25.3, 52.3, 90.4, 119.3, 122.0, 122.8, 129.8, 130.9, 136.3, 143.6, 146.9; EI-MS: m/z 289 (M⁺+4), 287 (M⁺+2), 285 (M⁺), 230, 186, 123, 56.

6,8-Dichloro-3-hexyl-4-methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4l)

M.p. 52°C; ¹H NMR: 0.85 (t, J=7.32 Hz, 3H),

1.29 (m, 6H), 1.68 (m, 2H), 3.78 (t, $J=8.06$ Hz, 2H), 4.54 (d, $J=2.93$ Hz, 1H), 4.94 (d, $J=2.93$ Hz, 1H), 7.39 (d, $J=2.19$ Hz, 1H), 7.36 (d, $J=2.19$ Hz, 1H); ^{13}C NMR: 14.1, 22.6, 25.5, 26.5, 31.5, 46.0, 89.7, 119.3, 121.9, 122.8, 129.8, 130.8, 136.1, 143.5, 146.3; EI-MS: m/z 317 ($\text{M}^+ + 4$), 315 ($\text{M}^+ + 2$), 313 (M^+), 298, 230, 186, 123, 55.

4-Methylene-3-phenyl-3,4-dihydro-2H-1,3-benzoxazine-2-one (4m)

M.p. 155°C ; ^1H NMR: 3.85 (s, 1H), 4.88 (s, 1H), 7.13 (d, $J=7.32$ Hz, 1H), 7.17 (t, $J=7.32$ Hz, 1H), 7.31 (d, $J=8.80$ Hz, 2H), 7.39 (t, $J=8.80$ Hz, 1H), 7.45 (t, $J=7.32$ Hz, 1H), 7.51 (t, $J=8.80$ Hz, 2H), 7.57 (d, $J=7.32$ Hz, 1H); ^{13}C NMR: 90.2, 116.6, 117.0, 123.8, 125.0, 128.6, 129.0, 130.2, 131.1, 137.8, 140.5, 147.4, 148.7; EI-MS: m/z 237 (M^+), 219, 165, 118, 90, 77, 51.

4-Methylene-3-(2'-methylphenyl)-3,4-dihydro-2H-1,3-benzoxazine-2-one (4n)

M.p. 91°C ; ^1H NMR: 2.23 (s, 3H), 3.78 (s, 1H), 4.85 (s, 1H), 7.14 (d, $J=8.06$ Hz, 1H), 7.20 (t, $J=8.06$ Hz, 1H), 7.22 (m, 1H), 7.34-7.38 (m, 3H), 7.40 (t, $J=8.06$ Hz, 1H), 7.58 (d, $J=8.06$ Hz, 1H); ^{13}C NMR: 17.2, 89.3, 116.3, 117.0, 123.8, 125.0, 127.9, 128.5, 131.2, 129.4, 131.7, 136.2, 136.3, 139.2, 146.9, 148.8; EI-MS: m/z 251 (M^+), 236, 192, 102, 89, 63.

3-(3'-chlorophenyl)-4-Methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4o)

M.p. 130°C ; ^1H NMR: 3.87 (d, $J=2.93$ Hz, 1H), 4.90 (d, $J=2.93$ Hz, 1H), 7.13 (m, 1H), 7.20 (m, 1H), 7.34-7.38 (m, 2H), 7.43-7.49 (m, 3H), 7.56 (m, 1H); ^{13}C NMR: 90.5, 116.3, 117.0, 123.8, 125.1, 127.1, 129.1, 129.4, 131.2, 131.3, 135.6, 138.8, 140.2, 147.2, 148.6; EI-MS: m/z 273 ($\text{M}^+ + 2$), 271 (M^+), 235, 191, 165, 118, 95, 89, 75, 63.

6,8-dichloro-4-Methylene-3-phenyl-3,4-dihydro-2H-1,3-benzoxazine-2-one (4p)

White needles. M.p. 145°C ; ^1H NMR: 3.96 (d, $J=2.93$ Hz, 1H), 4.87 (d, $J=2.93$ Hz, 1H), 7.30 (d, $J=7.32$ Hz, 2H), 7.44 (d, $J=2.19$ Hz, 1H), 7.46 (d, $J=2.19$ Hz, 1H), 7.48 (t, $J=7.32$ Hz, 1H), 7.54 (t, $J=7.32$ Hz, 2H); ^{13}C NMR: 92.7, 119.2, 122.0, 123.2, 128.4, 129.3, 130.1, 130.4, 131.1, 137.3, 139.1, 143.7, 145.9; EI-MS: m/z 309 ($\text{M}^+ + 4$), 307 ($\text{M}^+ + 2$), 305 (M^+), 287, 186, 123, 95, 77, 51.

6,8-dichloro-4-Methylene-3-(2'-methylphenyl)-3,4-dihydro-2H-1,3-benzoxazine-2-one (4q)

M.p. 162°C ; ^1H NMR: 2.21 (s, 3H), 3.89 (d, $J=2.93$ Hz, 1H), 4.85 (d, $J=2.93$ Hz, 1H), 7.18 (m, 1H), 7.32-7.38 (m, 3H), 7.45 (m, 2H); ^{13}C NMR: 17.1, 91.2, 118.9, 122.1, 123.2, 128.0, 128.3, 129.6, 130.1, 131.2, 131.9, 135.8, 136.0, 137.9, 143.8, 145.3; EI-MS: m/z 323 ($\text{M}^+ + 4$), 321 ($\text{M}^+ + 2$), 319 (M^+), 304, 269, 186, 159, 123, 102, 63.

6,8-dichloro-3-(3'-chlorophenyl)-4-Methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4r)

M.p. 175°C ; ^1H NMR: 3.99 (d, $J=2.93$ Hz, 1H), 4.91 (d, $J=2.93$ Hz, 1H), 7.31 (d, $J=2.19$ Hz, 1H), 7.43 (dd, $J=7.32$ & 2.19 Hz, 1H), 7.44 (t, $J=7.32$ Hz, 1H), 7.46 (d, $J=2.19$ Hz, 1H), 7.60 (d, $J=2.19$ Hz, 1H), 7.66 (d, $J=2.19$ Hz, 1H); ^{13}C NMR: 93.0, 119.0, 122.0, 123.2, 126.9, 129.0, 129.8, 130.3, 131.3, 135.8, 138.2, 138.8, 143.5, 145.7; EI-MS: m/z 345 ($\text{M}^+ + 6$), 343 ($\text{M}^+ + 4$), 341 ($\text{M}^+ + 2$), 339 (M^+), 304, 269, 186, 123, 113, 75, 63.

6-Methoxy -4-Methylene-3-phenyl-3,4-dihydro-2H-1,3-benzoxazine-2-one (4s)

M.p. 128°C ; ^1H NMR: 3.82 (s, 3H), 3.84 (s, 1H), 4.82 (s, 1H), 6.94 (dd, $J=8.80$ & 2.19 Hz, 1H), 7.00 (d, $J=2.19$ Hz, 1H), 7.06 (d, $J=8.80$ Hz, 1H), 7.31 (d, $J=7.32$ Hz, 2H), 7.44 (t, $J=7.32$ Hz, 1H), 7.53 (t, $J=7.32$ Hz, 2H); ^{13}C NMR: 55.9, 90.2, 117.0, 107.3, 117.8, 118.0, 128.6, 129.0, 130.2, 137.9, 140.6, 142.9, 147.6, 156.5; EI-MS: m/z 267 (M^+), 252, 148, 133, 105, 77, 51.

6-Methoxy -4-Methylene-3-(2'-methylphenyl)-3,4-dihydro-2H-1,3-benzoxazine-2-one (4t)

M.p. 128°C ; ^1H NMR: 2.22 (s, 3H), 3.83 (s, 3H), 3.87 (s, 1H), 4.79 (s, 1H), 6.95 (dd, $J=8.80$ & 2.93 Hz, 1H), 7.02 (d, $J=2.93$ Hz, 1H), 7.07 (d, $J=8.80$ Hz, 1H), 7.20 (m, 1H), 7.33-7.36 (m, 3H); ^{13}C NMR: 17.2, 55.9, 89.2, 107.3, 127.9, 128.5, 129.3, 131.7, 136.2, 139.3, 143.0, 116.7, 117.8, 118.0, 136.5, 147.1, 156.6; EI-MS: m/z 281 (M^+), 266, 133, 105, 91, 77, 51.

3-(3'-chlorophenyl)-6-Methoxy-4-Methylene-3,4-dihydro-2H-1,3-benzoxazine-2-one (4u)

Light brown powder. M.p. 165°C ; ^1H NMR: 3.83 (s, 3H), 3.99 (d, $J=2.93$ Hz, 1H), 4.91 (d, $J=2.93$ Hz, 1H), 6.95 (dd, $J=8.80$ & 2.93 Hz, 1H), 7.00 (d, $J=2.93$ Hz, 1H), 7.06 (d, $J=8.80$ Hz, 1H), 7.22 (d,

J=1.47 Hz, 1H), 7.33 (d, J=1.47 Hz, 1H), 7.44 (dd, J=8.06 & 1.47 Hz, 1H), 7.47 (t, J=8.06 Hz, 1H); ¹³C NMR: 55.9, 90.5, 107.3, 116.8, 117.9, 118.0, 127.1, 129.2, 129.4, 131.2, 135.6, 138.9, 140.3, 142.7, 147.3 156.6; EI-MS: m/z 303 (M⁺+2), 301, 265, 148, 133, 105, 89, 77, 51.

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