$Cu(OTf)_2$-catalysed synthesis of structurally novel bicyclic 1,3-oxazines via condensation-dehydrazinative ring transformation cascades

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The $Cu(OTf)_2$-catalysed expeditious synthesis of 1,3-oxazin-2-ones(thiones) from unprotected D-glucose and D-xylose in excellent yields is reported. $Cu(OTf)_2$ plays a dual role of a Lewis acid and an oxidant for dehydrazination, which is the cornerstone in the present investigation. The 1,3-oxazin-2-ones(thiones) serve as synthons for diversity oriented synthesis of structurally distinct bicyclic 1,3-oxazin-2-ones(thiones), when subjected to Malaprade reaction, followed by $Cu(OTf)_2$-catalysed cyclisation with an appropriate traditional reagent such as phenylhydrazine, amidines, hydroxylamine, or semi(thiosemi)carbazide.

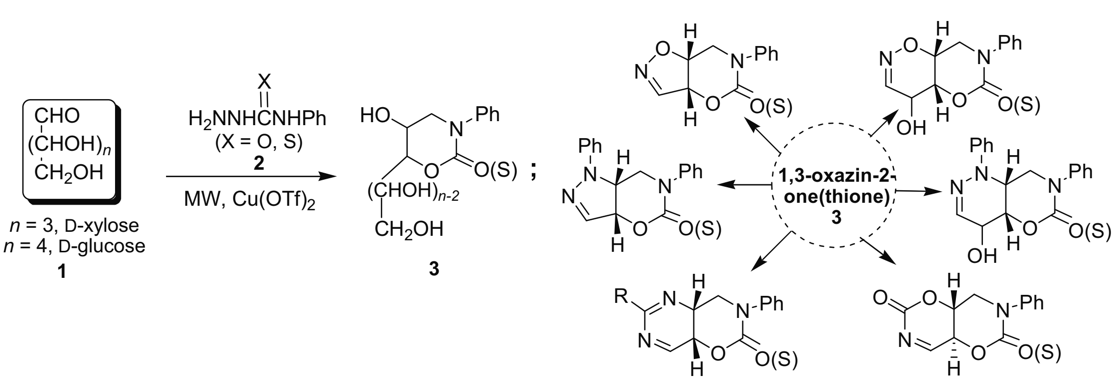
Keywords: carbohydrates, copper(II) triflate, diversity oriented synthesis, 1,3-oxazines, solvent-free, microwaves

The use of biorenewable resources in organic synthesis is a promising approach as it is in accord with sustainable development. Carbohydrates are major raw materials for organic chemicals with tailor-made industrial applications, because they are inexpensive, accessible on a ton-scale and have diverse chemical possibilities.[1] Lewis acid catalysts have been advantageously used in organic syntheses. Amongst these, $Cu(OTf)_2$ is an inexpensive, air and moisture stable catalyst, which has been found useful for several catalytic stereoselective transformations.[2,3]

The 1,3-oxazine nucleus features prominently in many biologically important molecules.[4-6] The most outstanding of these, Sustiva (Efavirenz), a fused ring 1,3-oxazin-2-one derivative, is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that has been approved by the FDA and is presently in clinical use for the treatment of AIDS. 1,3-Oxazin-2-one derivatives have also been recognised as chiral auxiliaries in asymmetric synthesis.[7] Furthermore, five- and six-membered heterocycles containing a C=N bond are important structural units in both natural products and synthetic pharmaceutical targets. Half of the small molecule drugs receiving FDA approval in 2005–06 contain at least one azole (five-membered) or azine (six-membered) ring.[8] Recently, $Cu(OTf)_2$-catalysed Biginelli type condensation has been reported for the synthesis of 1,3-oxazin-2-ones.[9]

In continuation of our quest for developing new solvent-free microwave (MW)-assisted cyclisation processes,[10-12] especially using carbohydrates as raw material,[13,14] we planned the synthesis and annulation of 1,3-oxazine ring with five- and six-membered heterocycles containing a C=N bond. Although many routes are well documented for the synthesis of 1,3-oxazines fused with a benzene ring,[15-22] this work presents a new report on $Cu(OTf)_2$-promted efficient synthesis of various C=N bond-containing structurally novel five- and six-membered bioactive heterocycles fused with biologically potential 1,3-oxazine nucleus starting from unprotected D-glucose/D-xylose **1** and *N*-phenylsemi(thiosemi)carbazide **2** (Scheme 1), which are attractive scaffolds to be utilised for exploiting chemical diversity and generating a drug-like library to screen for potential new leads.

To realise our idea, first we optimised the synthesis of 1,3-oxazin-2-ones(thiones) **3**, which are synthons for the present diversity oriented synthesis (DOS). We tested several mineral catalysts for the synthesis of compounds **3** and the best result was obtained with montmorillonite K-10 clay affording **3** in 81–88% yields. Other mineral catalysts, namely, $CeCl_3.7H_2O$/NaI, $CeCl_3.7H_2O$ and acidic, neutral, or basic alumina were far less effective resulting in either no reaction (in the case of basic alumina) or relatively moderate yields (39–52%, in case of $CeCl_3.7H_2O$ $CeCl_3.7H_2O$/NaI), or too low yields (12–23%, in case of silica gel, neutral and acidic alumina) of compounds **4'**. Compounds **4'** on further treatment with copper(II) sulfate on alumina support afforded the target 1,3-oxazines **3** in 59–66% yields. Then, we turned our attention to improve the yield and synthesise **3** in a one-pot procedure, and we were successful in this effort by using $Cu(OTf)_2$ as catalyst. Thus, the present optimised one-step synthesis is accomplished by microwave (MW) irradiation of an intimate solvent-free mixture of D-glucose/D-xylose **1**, *N*-phenylsemi(thiosemi)carbazide **2** and $Cu(OTf)_2$ (30 mol%) in an open vessel under air. The reaction proceeds via domino cycloisomerisation of *in situ* formed *N*-phenylsemi(thiosemi)carbazones **4** to 4-hydrazino-1,3- oxazin-2-ones(thiones) **4'** and dehydrazination of compounds **4'** to target oxazines **3** in 81–88% yields (Scheme 2). Here, $Cu(OTf)_2$ plays a dual role of a Lewis acid catalyst and an oxidant. Only 0.3 equivalent



Scheme 1 Synthesis of bicyclic scaffolds from D-glucose and D-xylose.

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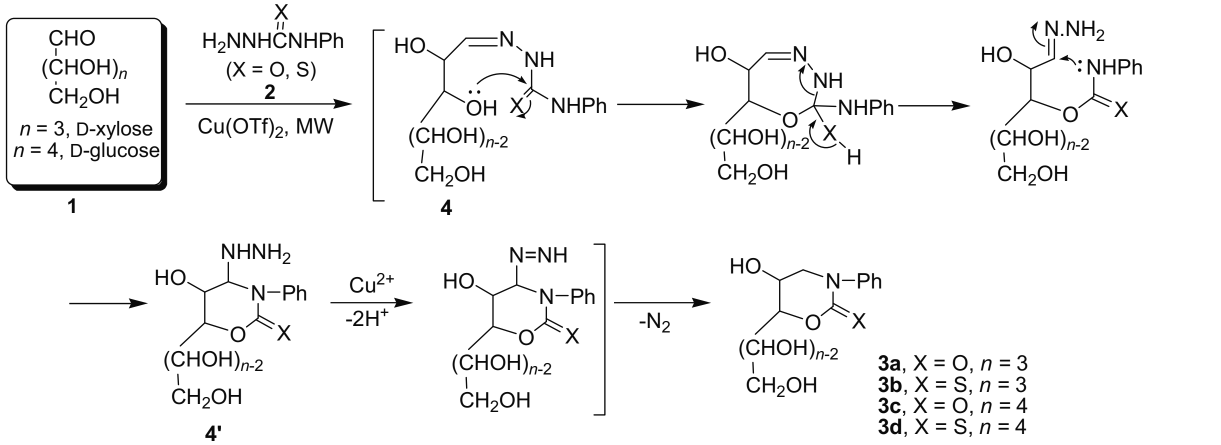


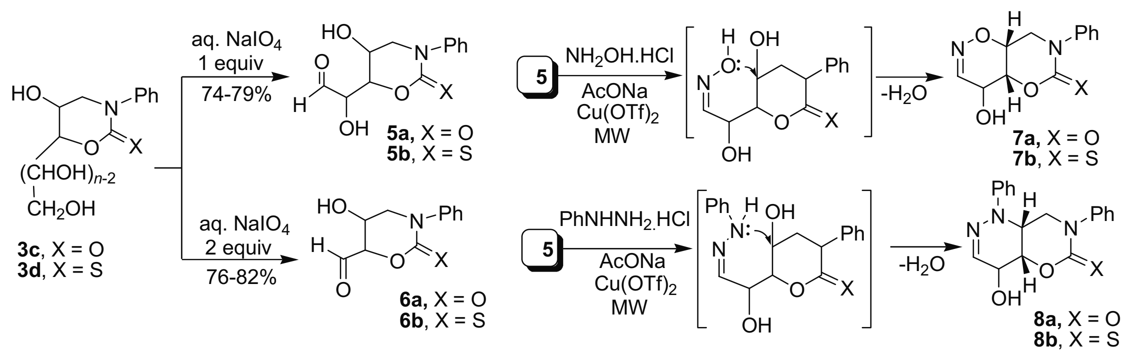
Scheme 2 Plausible mechanism for the formation of 1,3-oxazin-2-ones(thiones) **3** from D-glucose/D-xylose **1**.

of $Cu(OTf)_2$ is sufficient to complete the reaction because Cu(I) formed is oxidised to Cu(II) by air under the reaction conditions. Along with dehydrazinative reactions using Cu(II) reported in the literature, we report here its novel application to dehydrazinative ring-transformation reactions leading to 1,3-oxazin-2-ones(thiones) **3**.[23-26]

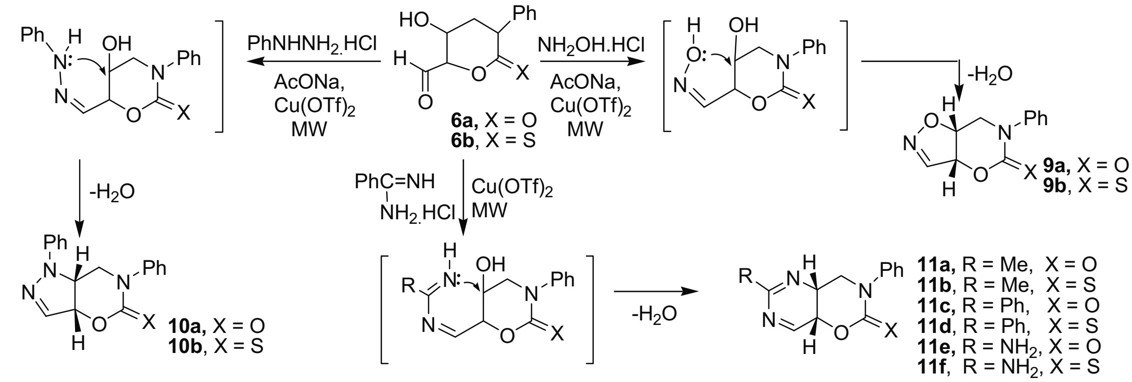
The 1,3-oxazin-2-ones(thiones) **3** were subjected to Malaprade reaction[27] (Scheme 3) to afford aldehydes **5** and **6**, which were converted into the target compounds **7**–**11** and **13** by judicious use of the reagents (Schemes 3–5). The strategy for the envisaged solvent-free green synthesis of 1,3-oxazin-2-one(thione)-fused isoxazoles **9**, pyrazoles **10** and pyrimidines **11** consisted of microwave irradiation of an intimate solvent-free mixture of compound **5**, $Cu(OTf)_2$ and sodium acetate with hydroxylamine hydrochloride, phenylhydrazine hydrochloride and amidines hydrochlorides respectively, at 85 °C for 7–12 min (Scheme 4). Isolation and purification by recrystallisation from ethanol afforded **9**, **10** and **11** in 77–94% yields (Table 1). Similarly, compounds **7** and **8** were synthesised in 82–92% yields (Table 1) by MW irradiation of an intimate solvent-free mixture of $Cu(OTf)_2$ and sodium acetate with hydroxylamine hydrochloride and phenylhydrazine hydrochloride respectively, at 90 °C for 8–10 min (Scheme 3). The formation of compounds **7**–**11** may be tentatively explained by acid-catalysed condensation of hydroxylamine, phenylhydrazine or amidines with aldehydic >C=O group of **5** and **6** followed by cyclodehydration of the resulting condensation product (Schemes 3 and 4). Furthermore, MW irradiation of a thoroughly mixed *N*-phenylsemi(thiosemi)carbazones **12** and $Cu(OTf)_2$ at 90 °C for 8-10 min afforded compounds **13** in 90–93% yields (Table 1) via cycloisomerisation-dehydrazination of **12** (Scheme 5). The mechanism shown in Scheme 5 is supported by the formation of hydrazine during the reaction as detected by the *p*-dimethylaminobenzaldehyde method.[28]

All the chiral carbons in **3**–**6** have the same absolute configuration as that of the corresponding carbons in their precursor carbohydrates because they are not involved in any bond breaking/formation. This fact is supported by the observation that there was no change in the absolute configuration of any chiral carbon of D-xylose or D-glucose when an intimate solvent-free mixture of D-xylose or D-glucose (1 mmol) and $Cu(OTf)_2$ (0.3 mmol) was subjected to MW irradiation at 90 °C for 12 min, *i.e.* under the present reaction conditions. The structures of all the synthesised compounds were established on the basis of their IR, ^1H NMR, ^{13}C NMR and EIMS data. The stereochemistry of compounds **7**–**11** and **13** was established by ^1H NMR spectroscopic analysis and the coupling constant of 3.1 to 3.7 Hz for the ring junction protons in **7**–**11** evidences that the rings are *cis*-fused, whereas in compound **13**, the coupling constant of 7.6–7.8 Hz for the ring junction protons shows that the rings are *trans*-fused. For sake of convenience, the relative stereochemistry at the ring junction in each of the bicyclic 1,3-oxazines has been depicted in Schemes 4 and 5.

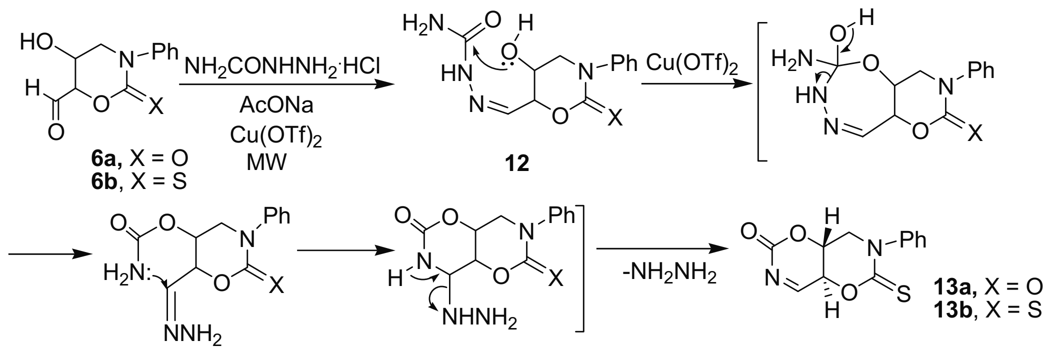
The structure and relative stereochemistry was further confirmed by NOE interaction experiments of all the synthesised compounds. For example, 13.2% and 12.8% NOEs were observed between 4a-H and 7a-H in compounds **9a** and **10a**, respectively, whereas 13.7%, 12.8% and 11.5% NOEs were observed between 4a-H and 8a-H protons in products **7a, 8a** and **11a** respectively. On the other hand, there was no any measurable NOE present between 4a-H and 8a-H in compound **13**. These results reveal that 4a-H and 7a-H in compounds **9** and **10**; 4a-H and 8a-H in compounds **7, 8** and **11** are located on the same face of the molecule, that is, *cis*



Scheme 3 Malaprade reaction to afford aldehydes **5** and **6** and formation of compounds **7** and **8** from **5**.



Scheme 4 Routes for the formation of compounds **9–11** from compounds **6**.



Scheme 5 Routes for the formation of compounds **13** via **12** from compounds **6**.

Table 1 MW-assisted solvent-free synthesis of compounds **7–11** and **13** from aldehydes **5** and **6**

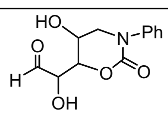
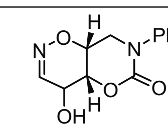
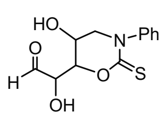
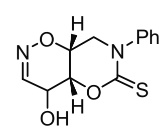
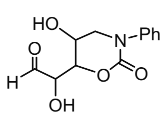
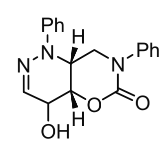
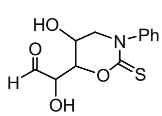
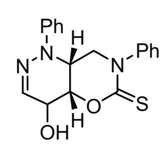
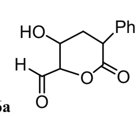
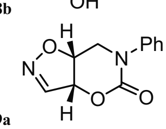
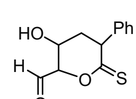
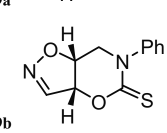
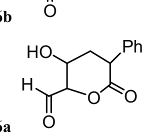
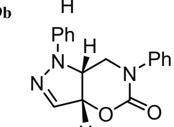
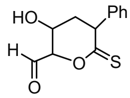
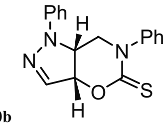
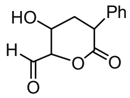
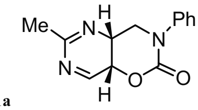
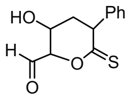
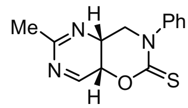
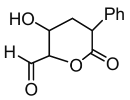
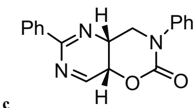
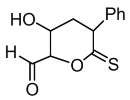
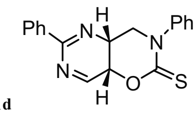
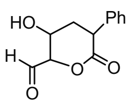
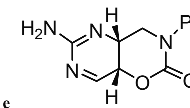
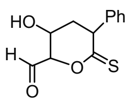
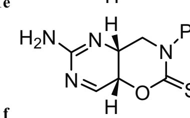
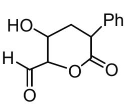
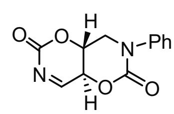
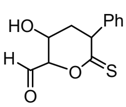
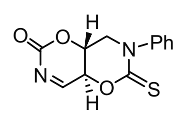
Entry	Aldehydes **5** and **6**	Time/min[a]	Compounds **7–11** and **13**	Yield/%[b,c]
1	 5a	8	 7a	82
2	 5b	8	 7b	88
3	 5a	9	 8a	91
4	 5b	10	 8b	92
5	 6a	7	 9a	77
6	 6b	7	 9b	80
7	 6a	12	 10a	94

Table 1 *Continued*

Entry	Aldehydes **5** and **6**	Time/min[a]	Compounds **7–11** and **13**	Yield/%[b,c]
8	 **6b**	10	 **10b**	90
9	 **6a**	8	 **11a**	83
10	 **6b**	9	 **11b**	85
11	 **6a**	9	 **11c**	80
12	 **6b**	10	 **11d**	89
13	 **6a**	7	 **11e**	82
14	 **6b**	8	 **11f**	81
15	 **6a**	8	 **13a**	93
16	 **6b**	10	 **13b**	90

[a]Microwave irradiation time for the formation of products. [b]Yield of isolated and purified products. [c]All compounds gave C, H and N analyses within ± 0.34% and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR and EIMS) data.

to each other and thus confirming their *cis* stereochemistry. Furthermore, the absence of any measurable NOE between 4a-H and 8a-H along with their coupling constants (7.6–7.8 Hz) indicates that these are *trans* to each other, which confirms the *trans* stereochemistry of the compound **13**.

In summary, we have developed a general, straightforward diversity oriented green synthetic approach for stereoselective synthesis of various 1,3-oxazin-2-one(thione)-fused heterocycles containing C=N bond using D-glucose and D-xylose as biorenewable resources under solvent-free microwave irradiation conditions.

Experimental

Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 993 IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker WM-40 C (400 MHz) FT spectrometer in DMSO-d_6 using TMS as internal reference. ^{13}C NMR spectra were recorded on the same instrument at 100 MHz in DMSO-d_6 and TMS was used as internal reference. Mass (EI) spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyser. A chemical laboratory microwave oven (Model; BP-310/50, 230 volt, 50 Hz power input) was used for all experiments. All chemicals used were reagent grade and were used as received without further purification. Silica gel-G was used for TLC.

General procedure for the preparation of 1,3-oxazin-2-ones(thiones) **3a–d**

Thoroughly mixed D-xylose/D-glucose (1 mmol) **1**, *N*-phenyl semicarbazide/thiosemicarbazide (1 mmol) **2** and $Cu(OTf)_2$ (0.3 mmol) were taken in a 20 mL open vial and subjected to MW irradiation for 2–4 min at 90 °C under air. After completion of the reaction as indicated by TLC, water (10 mL) was added to give the crude product which was recrystallised from ethanol to obtain an analytically pure sample of **3**. The physical and spectra data of the compounds **3a–d** are as follows.

5-Hydroxy-6-(1,2-dihydroxyethyl)-3-phenyl-1,3-oxazin-2-one (**3a**): Colourless solid; m.p. 154–156 °C, yield 88%. $[\alpha]_D^{20}$ + 79.1 (c 0.75, EtOH). IR (KBr): 3399, 3010, 1698, 1605, 1581, 1456 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.91 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,5H}$=7.6 Hz, 1 H, 4-H_b), 3.37 (dd, $J_{4Ha,4Hb}$=12.3 Hz, $J_{4Ha,5H}$=2.8 Hz, 1 H, 4-H_a), 3.65 (dd, $J_{2'Ha,\ 2'Hb}$ = 10.8 Hz, $J_{1'H,2'Ha,}$ = 4.8 Hz, 1 H, 2'Ha), 3.89 (dd, $J_{2'Ha,2'Hb}$ = 10.8 Hz, $J_{1'H,2'Hb}$ = 2.7 Hz, 1 H, 2'Hb), 4.01 (ddd, $J_{1'H,6H}$ = 6.1 Hz, $J_{1'H,2'Ha,}$ = 4.8 Hz, $J_{1'H,2'Hb}$ = 2.7 Hz, 1 H, 1'H), 4.23 (dd, $J_{1'H,6H}$ = 6.1 Hz, $J_{5H,6H}$ = 9.3 Hz, 1 H, 6H), 4.45 (ddd, $J_{4Ha,5H}$ = 2.8 Hz, $J_{4Hb,5H}$ = 7.6 Hz, $J_{5H,6H}$ = 9.3 Hz, 1 H, 5H), 7.05–7.72 (m, 5 H_{arom}). ^{13}C NMR (DMSO-d_6/TMS): δ = 63.1, 65.9, 69.3, 71.9, 75.3, 121.5, 128.7, 131.7, 133.4, 172.5. MS (FAB): m/z = 254 [MH^+]. Anal. Calcd for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53. Found: C, 56.73; H, 5.85; N, 5.79%.

5-Hydroxy-6-(1,2-dihydroxyethyl)-3-phenyl-1,3-oxazine-2-thione (**3b**): Colourless solid; m.p. 159–161 °C, yield 85%. $[\alpha]_D^{20}$ + 80.3 (*c* 0.75, EtOH). IR (KBr): 3392, 3009, 1599, 1579, 1458, 1052 cm^{-1}.

^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.95 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,5H}$ = 7.6 Hz, 1 H, 4-H_b), 3.36 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,5H}$ = 2.7 Hz, 1 H, 4-H_a), 3.61 (dd, $J_{2'Ha,2'Hb}$ = 10.8 Hz, $J_{1'H,2'Ha}$ = 4.8 Hz, 1 H, 2'Ha), 3.91 (dd, $J_{2'Ha,2'Hb}$ = 10.8 Hz, $J_{1'H,2'Hb}$ = 2.7 Hz, 1 H, 2'Ha), 4.05 (ddd, $J_{1'H,6H}$ = 6.1 Hz, $J_{1'H,2'Ha}$ = 4.8 Hz, $J_{1'H,2'Hb}$ = 2.7 Hz, 1 H, 1'H), 4.21 (dd, $J_{1'H,6H}$ = 6.1 Hz, $J_{5H,6H}$ = 9.2 Hz, 1 H, 6H), 4.48 (ddd, $J_{4Ha,5H}$ = 2.7 Hz, $J_{4Hb,5H}$ = 7.6 Hz, $J_{5H,6H}$ = 9.2 Hz, 1 H, 5H), 7.03–7.78 (m, 5 H_{arom}). ^{13}C NMR (DMSO-d_6/TMS): δ = 63.5, 66.1, 69.2, 72.6, 75.5, 122.5, 127.8, 130.9, 131.9, 192.5. MS (FAB): *m/z* = 270 [MH^+]. Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20. Found: C, 53.86; H, 5.39; N, 5.85%.

5-Hydroxy-6-(1,2,3-trihydroxypropyl)-3-phenyl-1,3-oxazin-2-one (**3c**): Colourless solid; m.p. 140–141 °C, yield 86%. $[\alpha]_D^{20}$ + 85.1 (*c* 0.75, EtOH). IR (KBr): 3395, 3007, 1692, 1601, 1583, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.93 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Hb,5H}$ = 7.8 Hz, 1 H, 4-H_b), 3.39 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Ha,5H}$ = 2.8 Hz, 1 H, 4-H_a), 3.43 (ddd, $J_{2'H,3'Ha}$ = 4.5 Hz, $J_{1'H,2'H}$ = 5.9 Hz, $J_{2'H,3'Hb}$ = 2.8 Hz, 1 H, 2'H), 3.67 (dd, $J_{3'Ha,3'Hb}$ = 10.3 Hz, $J_{2'H,3'Ha}$ = 4.5 Hz, 1 H, 3'H_a), 3.92 (dd, $J_{3'Ha,3'Hb}$ = 10.3 Hz, $J_{2'H,3'Hb}$ = 2.8 Hz, 1 H, 3'H_b), 3.99 (dd, $J_{1'H,6H}$ = 9.1 Hz, $J_{1'H,2'H}$ = 5.9 Hz, 1 H, 1'H), 4.19 (dd, $J_{1'H,6H}$ = 9.1 Hz, $J_{5H,6H}$ = 9.4 Hz, 1 H, 6H), 4.51 (ddd, $J_{4Ha,5H}$ = 2.8 Hz, $J_{4Hb,5H}$ = 7.8 Hz, $J_{5H,6H}$ = 9.4 Hz, 1 H, 5H), 7.11–7.81 (m, 5 H_{arom}). ^{13}C NMR (DMSO-d_6/TMS): δ = 63.5, 66.3, 69.1, 71.7, 72.5, 75.6, 121.7, 124.5, 129.5, 131.8, 172.5. MS (FAB): *m/z* = 284 [MH^+]. Anal. Cald for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94. Found: C, 55.41; H, 6.26; N, 4.85%.

5-Hydroxy-6-(1,2,3-trihydroxypropyl)-3-phenyl-1,3-oxazine-2-thione(**3d**): Colourless solid; m.p. 156–158 °C, yield 81%. $[\alpha]_D^{20}$+72.9 (*c* 0.50, EtOH). IR (KBr): 3395, 3008, 1607, 1581, 1453, 1055 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.92 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Hb,5H}$ = 7.5 Hz, 1 H, 4-H_b), 3.33 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Ha,5H}$ = 2.7 Hz, 1 H, 4-H_a), 3.41 (ddd, $J_{2'H,3'Ha}$ = 4.5 Hz, $J_{1'H,2'H}$ = 5.9 Hz, $J_{2'H,3'Hb}$ = 2.7 Hz, 1 H, 2'H), 3.66 (dd, $J_{3'Ha,3'Hb}$ = 10.5 Hz, $J_{2'H,3'Ha}$ = 4.5 Hz, 1 H, 3'H_a), 3.89 (dd, $J_{3'Ha,3'Hb}$ = 10.5 Hz, $J_{2'H,3'Hb}$ = 2.7 Hz, 1 H, 3'H_b), 3.97 (dd, $J_{1'H,6H}$ = 9.1 Hz, $J_{1'H,2'H}$ = 5.9 Hz, 1 H, 1'H), 4.18 (dd, $J_{1'H,6H}$ = 9.1 Hz, $J_{5H,6H}$ = 9.3 Hz, 1 H, 6H), 4.49 (ddd, $J_{4Hb,5H}$ = 7.5 Hz, $J_{5H,6H}$ = 9.3 Hz, $J_{4Ha,5H}$ = 2.7 Hz, 1 H, 5H), 7.09–7.83 (m, 5 H_{arom}). ^{13}C NMR (DMSO-d_6/TMS): δ = 63.1, 65.7, 69.5, 71.5, 72.7, 75.4, 123.5, 126.3, 130.8, 133.2, 192.8. MS (FAB): *m/z* = 300 [MH^+]. Anal. Calcd for $C_{13}H_{17}NO_5S$: C, 52.16; H, 5.72; N, 4.68. Found: C, 51.93; H, 5.85; N, 4.47%.

General procedure for Malaprade reaction to afford aldehydes **5**, **6**

A solution of sodium periodate (1 mmol) in water (8 mL) was added dropwise with stirring to a well stirred ice-cold solution of 1,3-oxazin-2-one(thione) **3** (1 mmol) in ethanol (15 mL). The reaction mixture was further stirred for 2–3 h at room temperature. After completion of reaction, as indicated by TLC, solvent was evaporated under reduced pressure to get solid residue which was extracted with ethyl acetate (3 × 10 mL). The extract was filtered and filtrate was the concentrated under the reduced pressure to leave the crude product, which on recrystallisation from ethanol afforded pure compounds **5** as white solid. The procedure followed for **6** was exactly the same, except that in this case 2 mmol of sodium periodate was used instead of 1 mmol of sodium periodate for **5**. The physical and spectra data of the compounds **5a,b** and **6a,b** are as follows.

2-Hydroxy-2-(5-hydroxy-2-oxo-3-phenyl-1,3-oxazin-6-yl) acetaldehyde (**5a**): Colourless solid; m.p. 101–102 °C, yield 79%. $[\alpha]_D^{20}$ + 69.3 (*c* 0.60, EtOH). IR (KBr): 3393, 3008, 1717, 1695, 1602, 1583, 1451 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.91 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,5H}$ = 7.5 Hz, 1 H, 4-H_b), 3.43 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Ha,5H}$ = 2.6 Hz, 1 H, 4-H_a), 4.41 (dd, $J_{1'H,6H}$ = 5.9 Hz, $J_{5H,6H}$ = 9.5 Hz, 1 H, 6H), 4.52 (ddd, $J_{4Hb,5H}$ = 7.5 Hz, $J_{5H,6H}$ = 9.5 Hz, $J_{4Ha,5H}$ = 2.6 Hz, 1 H, 5H), 4.85 (d, $J_{1'H,6H}$ = 5.9 Hz, 1 H, 1'H), 7.11–7.69 (m, 5 H_{arom}), 9.83 (s, 1 H, CHO). ^{13}C NMR (DMSO-d_6/TMS): δ = 66.1, 69.0, 77.5, 85.9, 121.7, 122.9, 129.9, 132.5, 171.1, 173.7. MS (FAB): *m/z* = 252 [MH^+]. Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.13; H, 5.41; N, 5.62%.

2-Hydroxy-2-(5-hydroxy-3-phenyl-2-thioxo-1,3-oxazin-6-yl)acetaldehyde (**5b**): Colourless solid; m.p. 119–121 °C, yield 74%. $[\alpha]_D^{20}$ + 78.2 (*c* 0.60, EtOH). IR (KBr): 3390, 3009, 1720, 1602, 1579, 1457, 1055 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.95 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,5H}$ = 7.5 Hz, 1 H, 4-H_b), 3.40 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Ha,5H}$ = 2.7 Hz, 1 H, 4-H_a), 4.39 (dd, $J_{1'H,6H}$ = 5.5 Hz, $J_{5H,6H}$ = 9.3 Hz, 1 H, 6H), 4.55 (ddd, $J_{4Hb,5H}$ = 7.5 Hz, $J_{5H,6H}$ = 9.3 Hz, $J_{4Ha,5H}$ = 2.7 Hz, 1 H, 5H), 4.82 (d, $J_{1'H,6H}$ = 5.5 Hz, 1 H, 1'H), 7.08–7.64 (m, 5 H_{arom}), 9.82 (s, 1 H, CHO). ^{13}C NMR (DMSO-d_6/TMS): δ = 66.3, 69.1, 77.2, 85.8, 122.2, 123.4, 128.9, 130.7, 171.5, 193.4. MS (FAB): *m/z* = 268 [MH^+]. Anal. Calcd for $C_{12}H_{13}NO_4S$: C, 53.92; H, 4.90; N, 5.24. Found: C, 54.17; H, 4.79; N, 5.51%.

5-Hydroxy-2-oxo-3-phenyl-1,3-oxazine-6-carbaldehyde (**6a**): Colourless solid; m.p. 129–130 °C, yield 82%. $[\alpha]_D^{20}$ + 73.7 (*c* 1.00, EtOH). IR (KBr): 3391, 3006, 1718, 1693, 1605, 1585, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.92 (dd, $J_{4Ha,4Hb}$ = 12.1 Hz, $J_{4Hb,5H}$ = 7.7 Hz, 1 H, 4-H_b), 3.42 (dd, $J_{4Ha,4Hb}$ = 12.1 Hz, $J_{4Ha,5H}$ = 2.8 Hz, 1 H, 4-H_a), 4.39 (ddd, $J_{4Hb,5H}$ = 7.7 Hz, $J_{5H,6H}$ = 9.3 Hz, $J_{4Ha,5H}$ = 2.8 Hz, 1 H, 5H), 5.13 (d, $J_{5H,6H}$ = 9.3 Hz, 1 H, 6H), 7.01–7.59 (m, 5 H_{arom}), 9.81 (s, 1 H, CHO). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.6, 69.1, 101.3, 122.7, 123.5, 129.1, 132.8, 171.4, 173.8. MS (FAB): *m/z* = 222 [MH^+]. Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.55; H, 5.13; N, 6.01%.

5-Hydroxy-3-phenyl-2-thioxo-1,3-oxazine-6-carbaldehyde (**6b**): Colourless solid; m.p. 135–137 °C, yield 76%. $[\alpha]_D^{20}$ + 60.9 (*c* 1.30, EtOH). IR (KBr): 3392, 3017, 1715, 1601, 1587, 1449, 1052 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.89 (dd, $J_{4Ha,4Hb}$ = 12.1 Hz, $J_{4Hb,5H}$ = 7.8 Hz, 1 H, 4-H_b), 3.39 (dd, $J_{4Ha,4Hb}$ = 12.1 Hz, $J_{4Ha,5H}$ = 2.8 Hz, 1 H, 4-H_a), 4.38 (ddd, $J_{4Hb,5H}$ = 7.7 Hz, $J_{5H,6H}$ = 9.2 Hz, $J_{4Ha,5H}$ = 2.8 Hz, 1 H, 5H), 5.12 (d, $J_{5H,6H}$ = 9.2 Hz, 1 H, 6H), 7.11–7.65 (m, 5 H_{arom}), 9.80 (s, 1 H, CHO). ^{13}C NMR (DMSO-d_6/TMS) δ = 65.8, 69.1, 101.5, 122.7, 123.5, 129.1, 132.8, 171.5, 173.8. MS (FAB): *m/z* = 238 [MH^+]. Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90. Found: C,55.34; H, 4.73; N, 5.69%.

General procedure for the preparation of 4-hydroxy-1,2-oxazino-, pyridazino-1,3-oxazin-6-ones(thiones) **7**, **8**

An intimate solvent-free mixture of 5 (1 mmol), sodium acetate (1 mmol), and hydroxylamine hydrochloride (1 mmol), or phenylhydrazine hydrochloride (1 mmol) in the presence of $Cu(OTf)_2$ (0.3 mmol) was taken in a 20 mL vial and subjected to MW irradiation at 80 °C for 7–12 min to get the crude product which was extracted with dichloromethane (3 × 10 mL). The extract was filtered, the filtrate was evaporated under reduced pressure and the residue thus obtained was recrystallised from ethanol to obtain an analytically pure sample of compounds **7** and **8** as a white solid. The physical and spectra data of the compounds **7** and **8** are as follows.

4,4a,8,8a-Tetrahydro-4-hydroxy-7-phenyl-[1,2]oxazino[6,5-e][1,3]oxazin-6(7H)-one (**7a**): Colourless solid; m.p. 141–143 °C. $[\alpha]_D^{20}$ + 33.5 (*c* 1.20, EtOH). IR (KBr): 3395, 3007, 1694, 1637, 1599, 1585, 1457 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.93 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,4aH}$ = 7.6 Hz, 1 H, 4-H_b), 3.53 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4-H_a), 3.75 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{7H,8H}$ = 6.5 Hz, 1 H, 8H), 4.01 (ddd, $J_{4Hb,4aH}$ = 7.6 Hz, $J_{4aH,8aH}$ = 3.1 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4aH), 4.31 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{4aH,8aH}$ = 3.1 Hz, 1 H, 8aH), 7.12–7.61 (m, 5 H_{arom}), 7.56 (d, $J_{7H,8H}$ = 6.5 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.3, 68.5, 70.2, 76.5, 121.8, 123.9, 128.8, 130.5, 162.2, 172.8. MS (FAB): *m/z* = 249 [MH^+]. Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 57.83; H, 4.55; N, 11.09.

4,4a,8,8a-Tetrahydro-4-hydroxy-7-phenyl-[1,2]oxazino[6,5-e][1,3]oxazine-6(7H)-thione (**7b**): Colourless solid; m.p. 128–130 °C. $[\alpha]_D^{20}$ + 38.9 (*c* 1.00, EtKH). IR (OBr): 3391, 3013, 1634, 1602, 1581, 1456, 1057 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.92 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,4aH}$ = 7.6 Hz, 1 H, 4-H_b), 3.51 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H_a), 3.81 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{7H,8H}$ = 6.6 Hz, 1 H, 8H), 3.98 (ddd, $J_{4Hb,4aH}$ = 7.6 Hz, $J_{4aH,8aH}$ = 3.1 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 4.35 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{4aH,8aH}$ = 3.1 Hz, 1 H, 8aH), 7.08–7.79 (m, 5 H_{arom}), 7.61 (d, $J_{7H,8H}$ = 6.6 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.5, 68.9, 71.2, 76.3, 123.5, 128.2, 130.1, 131.8, 162.5, 193.5. MS (FAB): *m/z* = 265 [MH^+]. Anal. Calcd for $C_{12}H_{12}N_2O_3S$: C, 54.53; H, 4.58; N, 10.60. Found: C, 54.84; H, 4.75; N, 10.49%.

4,4a,8,8a-Tetrahydro-4-hydroxy-1,7-diphenyl-1H-pyridazino[3,4-e][1,3]oxazin-6(7H)-one (**8a**): Colourless solid; m.p. 167–169 °C. $[\alpha]_D^{20}$ + 48.5 (c 1.00, EtOH). IR (KBr): 3395, 3011, 1698, 1631, 1604, 1587, 1451 cm^{-1}. 1H NMR (DMSO-d6/TMS + D2O): δ = 2.98 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,4aH}$ = 7.8 Hz, 1 H, 4-Hb), 3.53 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-Ha), 3.95 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{7H,8H}$ = 6.3 Hz, 1 H, 8H), 4.23 (ddd, $J_{4Hb,4aH}$ = 7.8 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 4.59 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.08–7.79 (m, 10 Harom), 7.62 (d, $J_{7H,8H}$ = 6.3 Hz, 1 H, 7H). 13C NMR (DMSO-d6/TMS): δ = 62.1, 66.0, 70.8, 77.3, 121.2, 123.8, 125.3, 126.8, 128.8, 129.7, 131.2, 133.5, 161.8, 172.3. MS (FAB): *m/z* = 324 [MH +]. Anal. Calcd for $C_{18}H_{17}N_3O_3$: C, 66.86; H, 5.30; N, 13.00. Found: C, 66.61; H, 5.18; N, 12.89%.

4,4a,8,8a-Tetrahydro-4-hydroxy-1,7-diphenyl-1H-pyridazino[3,4-e][1,3]oxazine-6(7H)-thione (**8b**): White solid; m.p. 181–183 °C. $[\alpha]_D^{20}$ + 53.2 (*c* 0.75, EtOH). IR (KBr): 3388, 3008, 1634, 1599, 1581, 1455, 1049 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.99 (dd, $J_{4Ha,4Hb}$ = 12.4 Hz, $J_{4Hb,4aH}$ = 7.8 Hz, 1 H, 4-H$_b$), 3.57 (dd, $J_{4Ha,4Hb}$ = 12.4 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4-H$_a$), 3.93 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{7H,8H}$ = 6.3 Hz, 1 H, 8H), 4.18 (ddd, $J_{4Hb,4aH}$ = 7.8 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4aH), 4.61 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.11–7.87 (m, 10 H$_{arom}$), 7.61 (d, $J_{7H,8H}$ = 6.3 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 62.5, 65.4, 71.2, 76.9, 122.8, 123.9, 125.4, 127.9, 128.8, 130.2, 131.5, 132.8, 162.2, 192.8. MS (FAB): *m/z* = 340 [MH$^+$]. Anal. Calcd for $C_{18}H_{17}N_3O_2S$: C, 63.70; H, 5.05; N, 12.38. Found: C, 63.42; H, 5.29; N, 12.58%.

General procedure for preparation of isoxazolo-, pyrazolo-, pyrimido-1,3-oxazin-2-ones(thiones) **9–11**

An intimate solvent-free mixture of **6** (1 mmol), sodium acetate (1 mmol), and hydroxylamine hydrochloride (1 mmol), or phenylhydrazine hydrochloride (1 mmol), or acetamidine/-benzamidine/guanidine hydrochloride (1 mmol) in the presence of Cu(OTf)$_2$ (0.3 mmol) was taken in a 20 mL vial and subjected to MW irradiation at 80 °C for 7–12 min to get the crude product which was extracted with dichloromethane (3 × 10 mL). The extract was filtered, the filtrate was evaporated under reduced pressure and the residue thus obtained was recrystallised from ethanol to obtain an analytically pure sample of compounds **9**, **10**, or **11** as a white solid. The physical and spectra data of the compounds **9–11** are as follows.

7,7a-Dihydro-6-phenyl-3aH-isoxazolo[5,4-e][1,3]oxazin-5(6H)-one (**9a**): Colourless solid; m.p. 182–184 °C. $[\alpha]_D^{20}$ + 29.5 (*c* 0.75, EtOH). IR (KBr): 3011, 1692, 1635, 1605, 1581, 1451 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 3.01 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,4aH}$ = 7.6 Hz, 1 H, 4-H$_b$), 3.57 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H$_a$), 3.81 (ddd, $J_{4Hb,4aH}$ = 7.6 Hz, $J_{4aH,7aH}$ = 3.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 5.09 (dd, $J_{7aH,7H}$ = 8.9 Hz, $J_{4aH,7aH}$ = 3.3 Hz, 1 H, 7aH), 7.08–7.69 (m, 5 H$_{arom}$), 7.63 (d, $J_{7aH,7H}$ = 8.9 Hz, 1 H, 7-H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.3, 67.9, 75.1, 122.5, 124.5, 126.8, 130.5, 161.8, 172.5. MS (FAB): *m/z* = 219 [MH$^+$]. Anal. Calcd for $C_{11}H_{10}NO_3$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.79; H, 4.51; N, 12.50%.

7,7a-Dihydro-6-phenyl-3aH-isoxazolo[5,4-e][1,3]oxazine-5(6H)-thione (**9b**): Colourless solid; m.p. 168–170 °C. $[\alpha]_D^{20}$ + 38.3 (*c* 0.70, EtOH). IR (KBr): 3013, 1638, 1602, 1587, 1455, 1057 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 3.05 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,4aH}$ = 7.7 Hz, 1 H, 4-H$_b$), 3.56 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H$_a$), 3.83 (ddd, $J_{4Hb,4aH}$ = 7.7 Hz, $J_{4aH,7aH}$ = 3.3 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 5.10 (dd, $J_{7aH,7H}$ = 8.8 Hz, $J_{4aH,7aH}$ = 3.3 Hz, 1 H, 7aH), 7.03–7.71 (m, 5 H$_{arom}$), 7.66 (d, $J_{7aH,7H}$ = 8.8 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.5, 68.5, 74.9, 123.1, 125.8, 127.9, 131.3, 162.3, 192.5. MS (FAB): *m/z* = 235 [MH$^+$]. Anal. Calcd for $C_{11}H_{10}N_2O_2S$: C, 56.39; H, 4.30; N, 11.96. Found: C, 56.65; H, 4.19; N, 12.11%.

7,7a-Dihydro-1,6-diphenylpyrazolo[3,4-e][1,3]oxazin-5(1H,3aH,6H)-one (**10a**): Colourless solid; m.p. 140–142 °C. $[\alpha]_D^{20}$ + 61.9 (*c* 1.00, EtOH). IR (KBr): 3009, 1695, 1631, 1608, 1577, 1449 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.98 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Hb,4aH}$ = 7.7 Hz, 1 H, 4-H$_b$), 3.51 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4-H$_a$), 3.80 (ddd, $J_{4Hb,4aH}$ = 7.7 Hz, $J_{4aH,7aH}$ = 3.1 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4aH), 4.99 (dd, $J_{7aH,7H}$ = 9.1 Hz, $J_{4aH,7aH}$ = 3.1 Hz, 1 H, 7aH), 7.11–7.83 (m, 10 H$_{arom}$), 7.61 (d, $J_{7aH,7H}$ = 9.1 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.1, 66.9, 75.3, 121.8, 122.5, 124.5, 126.9, 128.4, 129.3, 131.5, 132.3, 161.9, 173.2. MS (FAB): *m/z* = 294 [MH$^+$]. Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.47; H, 5.31; N, 14.18%.

7,7a-Dihydro-1,6-diphenylpyrazolo[3,4-e][1,3]oxazine-5(1H,3aH,6H)-thione (**10b**): Colourless solid; m.p. 188–190 °C. $[\alpha]_D^{20}$ + 65.8 (*c* 1.20, EtOH). IR (KBr): 3342, 1633, 1596, 1582, 1451, 1053 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.99 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,4aH}$ = 7.7 Hz, 1 H, 4-H$_b$), 3.55 (dd, $J_{4Ha,4Hb}$ = 12.2 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4-H$_a$), 3.79 (ddd, $J_{4Hb,4aH}$ = 7.7 Hz, $J_{4aH,7aH}$ = 3.5 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4aH), 5.02 (dd, $J_{7aH,7H}$ = 9.1 Hz, $J_{4aH,7aH}$ = 3.5 Hz, 1 H, 7aH), 7.18–7.89 (m, 10 H$_{arom}$), 7.66 (d, $J_{7aH,7H}$ = 9.1 Hz, 1 H, 7H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.1, 66.2, 75.3, 121.5, 122.7, 123.9, 125.2, 127.3, 128.9, 130.0, 131.5, 161.5, 193.1. MS (FAB): *m/z* = 310 [MH$^+$]. Anal. Calcd for $C_{17}H_{15}N_3OS$: C, 66.00; H, 4.89; N, 13.58. Found: C, 66.26; H, 4.97; N, 13.45%.

4,4a-Dihydro-6-methyl-3-phenyl-3H-pyrimido[4,5-e][1,3]oxazin-2(8aH)-one (**11a**): Colourless solid; m.p. 124–126 °C. $[\alpha]_D^{20}$ + 55.7 (*c* 0.75, EtOH). IR (KBr): 3012, 1695, 1633, 1607, 1583, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 1.58 (s, 3 H, Me), 2.95 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Hb,4aH}$ = 7.5 Hz, 1 H, 4-H$_b$), 3.51 (dd, $J_{4Ha,4Hb}$ = 12.3 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4-H$_a$), 3.76 (ddd, $J_{4Hb,4aH}$ = 7.7 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4aH), 4.55 (dd, $J_{8H,8aH}$ = 8.5 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.11–7.83 (m, 5 H$_{arom}$), 7.62 (d, $J_{8H,8aH}$ = 8.5 Hz, 1 H, 8-H). ^{13}C NMR (DMSO-d_6/TMS): δ = 50.9, 55.3, 71.8, 79.5, 121.5, 123.1, 129.5, 132.8, 161.8, 162.5, 172.2. MS (FAB): *m/z* = 244 [MH$^+$]. Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27. Found: C, 64.01; H, 5.53; N, 17.41%.

4,4a-Dihydro-6-methyl-3-phenyl-3H-pyrimido[4,5-e][1,3]oxazine-2(8aH)-thione (**11b**): Colourless solid; m.p. 112–114 °C. $[\alpha]_D^{20}$ + 59.3 (*c* 1.10, EtOH). IR (KBr): 3015, 1637, 1601, 1585, 1458, 1055 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 1.61 (s, 3 H, Me), 2.99 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,4aH}$ = 7.8 Hz, 1 H, 4-H$_b$), 3.58 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4-H$_a$), 3.80 (ddd, $J_{4Hb,4aH}$ = 7.8 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.7 Hz, 1 H, 4aH), 4.56 (dd, $J_{8H,8aH}$ = 8.5 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.09–7.71 (m, 5 H$_{arom}$), 7.61 (d, $J_{8H,8aH}$ = 8.5 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 51.1, 55.7, 65.7, 72.1, 122.5, 123.8, 128.9, 130.1, 161.5, 162.2, 192.5. MS (FAB): *m/z* = 260 [MH$^+$]. Anal. Calcd for $C_{13}H_{13}N_3OS$: C, 60.21; H, 5.05; N, 16.20. Found: C, 59.98; H, 5.29; N, 16.03%.

4,4a-*Dihydro-3,6-diphenyl-3H-pyrimido[4,5-e][1,3]oxazin-2(8aH)-one* (**11c**): Colourless solid; m.p. 138–140 °C. $[\alpha]_D^{20}$ + 61.7 (*c* 0.90, EtOH). IR (KBr): 3009, 1692, 1634, 1605, 1579, 1459 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 3.01 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Hb,4aH}$ = 7.8 Hz, 1 H, 4-H$_b$), 3.50 (dd, $J_{4Ha,4Hb}$ = 12.5 Hz, $J_{4Ha,4aH}$ = 2.4 Hz, 1 H, 4-H$_a$), 3.75 (ddd, $J_{4Hb,4aH}$ = 7.8 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.4 Hz, 1 H, 4aH), 4.51 (dd, $J_{8H,8aH}$ = 8.9 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.19–7.85 (m, 10 H$_{arom}$), 7.63 (d, $J_{8H,8aH}$ = 8.9 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 55.1, 65.9, 71.5, 121.5, 123.5, 125.5, 127.8, 128.9, 129.5, 130.2, 131.8, 161.9, 163.1, 172.5. MS (FAB): *m/z* = 306 [MH$^+$]. Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.47; H, 4.79; N, 13.83%.

4,4a-Dihydro-3,6-diphenyl-3H-pyrimido[4,5-e][1,3]oxazine-2(8aH)-thione (**11d**): Colourless solid; m.p. 115–117 °C. $[\alpha]_D^{20}$ + 69.1 (*c* 0.75, EtOH). IR (KBr): 3008, 1631, 1601, 1579, 1459, 1051 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.95 (dd, $J_{4Ha,4Hb}$ = 12.4 Hz, $J_{4Hb,4aH}$ = 7.5 Hz, 1 H, 4-H$_b$), 3.52 (dd, $J_{4Ha,4Hb}$ = 12.4 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H$_a$), 3.78 (ddd, $J_{4Hb,4aH}$ = 7.5 Hz, $J_{4aH,8aH}$ = 3.7 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 4.55 (dd, $J_{8H,8aH}$ = 9.1 Hz, $J_{4aH,8aH}$ = 3.7 Hz, 1 H, 8aH), 7.21–7.83 (m, 10 H$_{arom}$), 7.65 (d, $J_{8H,8aH}$ = 9.1 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 55.7, 65.6, 71.8, 122.2, 123.8, 124.9, 126.5, 127.4, 128.5, 130.1, 132.5, 161.3, 162.6, 193.1. MS (FAB): *m/z* = 322 [MH$^+$]. Anal. Calcd for $C_{18}H_{15}N_3OS$: C, 67.27; H, 4.70; N, 13.07. Found: C, 67.51; H, 4.59; N, 13.23%.

6-Amino-4,4a-dihydro-3-phenyl-3H-pyrimido[4,5-e][1,3]oxazin-2(8aH)-one (**11e**): Colourless solid; m.p. 184–186 °C. $[\alpha]_D^{20}$ + 59.5 (*c* 0.75, EtOH). IR (KBr): 3010, 1692, 1633, 1601, 1583, 1450 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.96 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Hb,4aH}$ = 7.5 Hz, 1 H, 4-H$_b$), 3.53 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H$_a$), 3.81 (ddd, $J_{4Hb,4aH}$ = 7.5 Hz, $J_{4aH,8aH}$ = 3.4 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4aH), 4.52 (dd, $J_{8H,8aH}$ = 8.8 Hz, $J_{4aH,8aH}$ = 3.4 Hz, 1 H, 8aH), 7.04–7.69 (m, 5 H$_{arom}$), 7.62 (d, $J_{8H,8aH}$ = 8.8 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 55.1, 65.8, 72.0, 122.8, 123.9, 128.5, 131.9, 162.1, 162.9, 172.8. MS (FAB): *m/z* = 245 [MH$^+$]. Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.28; H, 5.03; N, 22.71%.

6-Amino-4,4a-dihydro-3-phenyl-3H-pyrimido[4,5-e][1,3]oxazine-2(8aH)-thione (**11f**): Colourless solid; m.p. 203–205 °C. $[\alpha]_D^{20}$ + 65.0 (*c* 0.60, EtOH). IR (KBr): 3009, 1637, 1597, 1579, 1451, 1055 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 2.98 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Hb,4aH}$ = 7.6 Hz, 1 H, 4-H$_b$), 3.49 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4-H$_a$), 3.79 (ddd, $J_{4Hb,4aH}$ = 7.6 Hz, $J_{4aH,8aH}$ = 3.4 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4aH), 4.49 (dd, $J_{8H,8aH}$ = 8.5 Hz, $J_{4aH,8aH}$ = 3.4 Hz, 1 H, 8aH), 7.11–7.75 (m, 5 H$_{arom}$), 7.61 (d, $J_{8H,8aH}$ = 8.5 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 55.7, 66.2, 71.9, 123.2, 125.9, 128.9, 130.8, 161.7, 163.3, 192.6. MS (FAB): *m/z* = 261 [MH$^+$]. Anal. Calcd for $C_{12}H_{12}N_4OS$: C, 55.37; H, 4.65; N, 21.52. Found: C, 55.59; H, 4.39; N, 21.42%.

General Procedure forpreparation of 1,3-oxazino[6,5-e][1,3] *oxazine-2,6-dione(6-thioxo-2-one)* **13**

Thoroughly mixed aldehyde **6** (2 mmol), semicarbazide hydrochloride (2 mmol), sodium acetate (2 mmol), and Cu(OTf)$_2$ (0.6 mmol) were taken in a 20 mL vial and subjected to microwave irradiation at 90 °C for 8–10 min to afford crude product which was extracted with dichloromethane (3 × 20 mL). The extract was filtered and the filtrate was evaporated under reduced pressure to leave the product which was recrystallised from ethanol to obtain analytically pure sample of **13**. The physical and spectra data of the compounds **13a,b** are as follows.

4,4a-Dihydro-3-phenyl-[1,3]oxazino[6,5-e][1,3]oxazine-2,6 (3H,8aH)-dione (**13a**): Colourless solid; m.p. 179–181 °C. $[\alpha]_D^{20}$ + 49.3 (*c* 0.85, EtOH). IR (KBr): 3391, 3011, 1692, 1601, 1581, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 3.05 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Hb,4aH}$ = 7.3 Hz, 1 H, 4-H_b), 3.70 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4-H_a), 4.62 (ddd, $J_{4Hb,4aH}$ = 7.3 Hz, $J_{4aH,8aH}$ = 7.8 Hz, $J_{4Ha,4aH}$ = 2.8 Hz, 1 H, 4aH), 4.81 (dd, $J_{8H,8aH}$ = 6.8 Hz, $J_{4aH,8aH}$ = 7.8 Hz, 1 H, 8aH), 7.05–7.71 (m, 5 H_{arom}), 7.56 (d, $J_{8H,8aH}$ = 6.8 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.9, 66.5, 77.5, 122.9, 124.6, 128.1, 130.5, 161.7, 172.1, 173.2. MS (FAB): *m/z* = 247 [MH^+]. Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C,58.79; H, 4.18; N, 11.55%.

6,7,8,8a-Tetrahydro-7-phenyl-6-thioxo-[1,3]oxazino[6,5-e][1,3] oxazin-2(4aH)-one (**13b**): Colourless solid; m.p. 166–168 °C. $[\alpha]_D^{20}$ + 53.8 (*c* 1.20, EtOH). IR (KBr): 3392, 3009, 1693, 1605, 1585, 1449, 1055 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS + D_2O): δ = 3.01 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Hb,4aH}$ = 7.3 Hz, 1 H, 4-H_b), 3.73 (dd, $J_{4Ha,4Hb}$ = 12.7 Hz, $J_{4Ha,4aH}$ = 2.5 Hz, 1 H, 4-H_a), 4.58 (ddd, $J_{4Hb,4aH}$ = 7.3 Hz, $J_{4aH,8aH}$ = 7.6 Hz, $J_{4Ha,4aH}$ = 7.6 Hz, 1 H, 4aH), 4.79 (dd, $J_{8H,8aH}$ = 6.8 Hz, $J_{4aH,8aH}$ = 7.6 Hz, 1 H, 8aH), 7.02–7.75 (m, 5 H_{arom}), 7.59 (d, $J_{8H,8aH}$ = 6.8 Hz, 1 H, 8H). ^{13}C NMR (DMSO-d_6/TMS): δ = 65.7, 66.3, 77.3, 122.7, 125.9, 130.2, 132.5, 162.3, 172.3, 192.7. MS (FAB): *m/z* = 263 [MH^+]. Anal. Calcd for $C_{12}H_{10}N_2O_3S$: C, 54.95; H, 3.84; N, 10.68. Found: C, 54.61; H, 3.97; N, 10.42%.

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