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# Diversity oriented synthesis of fused-ring 1,3-oxazines from carbohydrates as biorenewable feedstocks

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## Abstract

Microwave enhanced diversity oriented synthesis (MEDOS) of various *N*- and *O*-heterocyclic systems fused with 1,3-oxazine ring is reported. The synthesis represents a new montmorillonite K-10 clay-catalyzed green protocol, which utilizes D-glucose/D-xylose as biorenewable feedstocks. D-Glucose/D-xylose-derived 1,3-oxazin-2-ones(thiones) either directly undergo K-10 clay-catalyzed cyclization to yield pyrano-/furo-1,3-oxazine systems under solvent-free microwave irradiation conditions or afford azolo-/azino-1,3-oxazines when subjected to Malaprade reaction followed by cyclization with appropriate reagents, viz. phenylhydrazine, hydroxylamine, acetamidine, phenylurea and semi(thiosemi)-carbazide.

*Keywords:* Diversity oriented synthesis; 1,3-Oxazines; Solvent-free; Microwaves; Montmorillonite K-10; Carbohydrates

## 1. Introduction

Diversity oriented synthesis (DOS) has emerged as a valuable approach to generate libraries of various classes of compounds.[1–5] Efforts in DOS have produced powerful new biological probes and also served as a new driving force for synthetic organic chemistry. Although the earlier combinatorial chemical libraries of drug-like small molecules were reported over a decade ago,[6] DOS remains relatively less extensively studied.

Carbohydrates are the major raw materials for organic chemicals with tailor-made industrial applications. This is because they are inexpensive, accessible in ton-scale and have better worked out ensuing chemistry. Advantages of the application of microwave (MW) irradiation in conjunction with mineral supported reagents under solvent-free conditions have now been well established.

The 1,3-oxazine nucleus features prominently in many biologically important natural products[7] and other bioactive molecules.[8–10] The most outstanding of these is Sustiva (Efavirenz), a non-nucleoside reverse transcriptase inhibitor that has been approved by the FDA in 1998 and is presently in clinical use for the treatment of AIDS.[10b] This has been the prime driving force for the synthesis of various compounds incorporating the 1,3-oxazine moiety. 1,3-Oxazin-2-one derivatives have been used as the key intermediates in the synthesis of several natural products, and have also been recognized as chiral auxiliaries in asymmetric synthesis.[11]

Along with the synthetic strategies reported in the literature for oxazines,[12–19] we have also reported the synthesis of 1,3-oxazin-2-ones(thiones) fused with benzene ring[20–23] and their *C*- and *N*-nucleoside analogues using salicylaldehyde as a bifunctional building block.[24–26] To the best of our knowledge, there has been no report on the synthesis of 1,3-oxazin-2-one-(thione) fused with various pharmaceutically and agrochemically important *N*- and *O*-heterocycles, starting from D-glucose and D-xylose, although they appear to be attractive scaffolds to be utilized for exploiting chemical diversity and generating a drug-like library to screen for potential new leads.

Considering the above valid points and our ongoing efforts to develop new cyclization processes,[20–28] we describe herein the microwave enhanced diversity oriented synthetic (MEDOS) approach for the unprecedented synthesis of pharmaceutically

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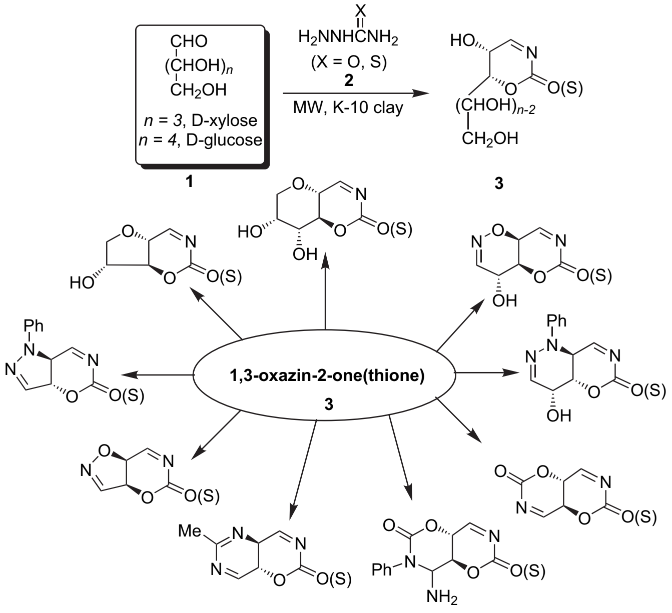
and agrochemically important furo-, isoxazolo-, oxazino-, pyrazolo-, pyrano-, pyrimidino-, pyrazinoxazin-2-ones(thiones) and oxazinoxazin-2,6-ones(thiones) using D-glucose and D-xylose under solvent-free mineral supported reaction conditions (Scheme 1).

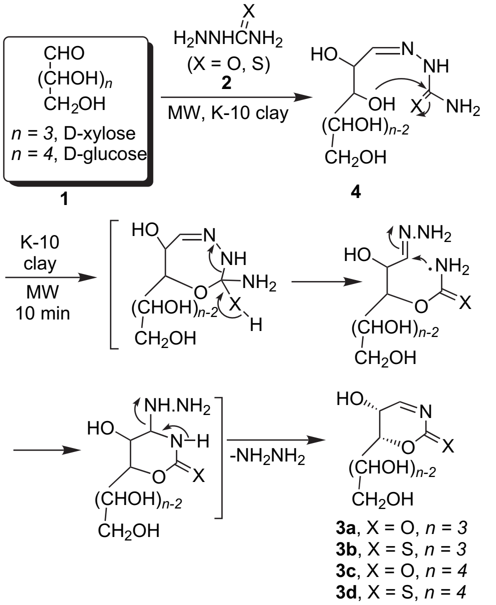


Scheme 1. MEDOS of fused-ring 1,3-oxazin-2-ones(thiones) from D-glucose and D-xylose.

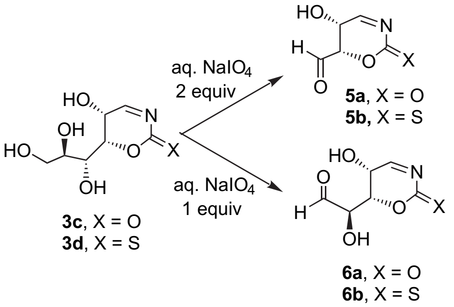
## 2. Results and discussion

The hitherto unreported 1,3-oxazin-2-ones(thiones) **3** were obtained via montmorillonite K-10 clay-catalyzed domino cycloisomerization, dehydrazination and dehydration of D-glucose/D-xylose semi(thiosemi)carbazones **4** under solvent-free MW irradiation conditions in a one-pot procedure (Scheme 2). The mechanism shown in Scheme 2 is supported by the formation of hydrazine during the reaction. It was noted that other mineral catalysts, viz. silica gel, neutral or basic alumina, were far less effective resulting in either no reaction (in the case of basic alumina) or relatively very low yields (15–28%) of **3** (in the cases of silica gel and neutral alumina).

1,3-Oxazin-2-ones(thiones) **3** were synthesized in 79–85% yields by solvent-free MW irradiation of D-glucose/D-xylose **1**, semi(thiosemi)carbazide **2** and montmorillonite K-10 clay (Scheme 2). 1,3-Oxazin-2-ones(thiones) **3** were subjected to Malaprade reaction (Scheme 3) to afford aldehydes **5** and **6**, which were converted into the target compounds **7–11**; compounds **14** and **16** by judicious use of catalysts and reagents (Schemes 4, 5, 7 and 8). The MEDOS strategy for the envisaged solvent-free synthesis of 1,3-oxazin-2-one(thione)-fused isoxazoles **7**, pyrazoles **8** and pyrimidines **9** consisted in microwave (MW) irradiation of an intimate solvent-free mixture of compound **5**, montmorillonite K-10 clay and sodium acetate with hydroxylamine hydrochloride, phenylhydrazine hydrochloride and acetamidine hydrochloride, respectively, at 80 °C for 5–12 min (Scheme 4). Isolation and purification by recrystallization from ethanol afforded **7–9** in 80–93% yields. Similarly, compounds **10** and **11** were synthesized in 81–92% yields by MW irradiation of an intimate solvent-free mixture of compound **6**, montmorillonite K-10 clay and sodium acetate with hydroxylamine hydrochloride and phenylhydrazine hydrochloride, respectively, at 90 °C for 5–11 min (Scheme 5).



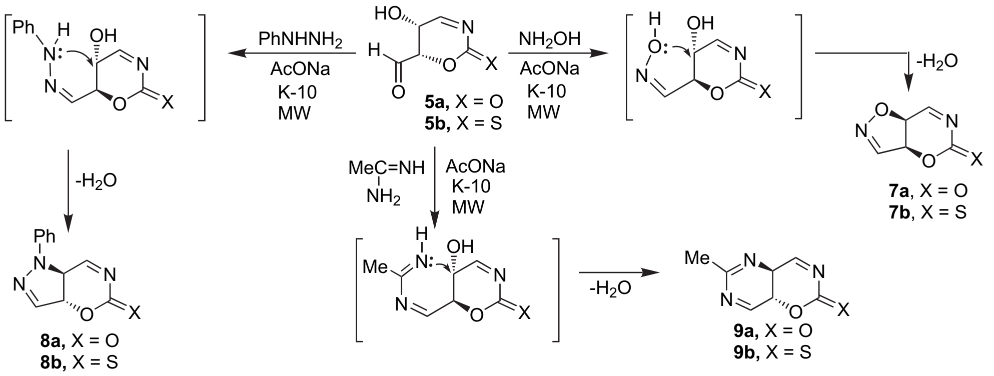
Scheme 2. Plausible mechanism for the formation of 1,3-oxazin-2-ones(thiones) **3** from D-glucose/D-xylose semi(thiosemi)carbazones **4**.



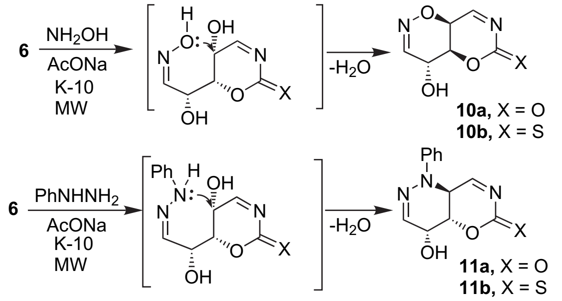
Scheme 3. Malaprade reaction to afford aldehydes **5** and **6**.

The formation of compounds **7–11** may be tentatively explained by acid-catalyzed condensation of hydroxylamine, phenylhydrazine or acetamidine with aldehydic $>C=O$ group of **5** and **6** followed by cyclodehydration of the resulting condensation product (Schemes 4 and 5). Montmorillonite K-10 clay-catalyzed cyclodehydration of 1,3-oxazin-2-ones(thiones) **3** (Scheme 6) under solvent-free MW irradiation afforded furo-1,3-oxazin-2-ones(thiones) **12** (83–85% yields) and pyrano-1,3-oxazin-2-ones(thiones) **13** in 87–90% yields (Table 1). The use of other mineral catalysts, viz. silica gel, neutral or basic alumina, resulted in relatively very low yields of **7–9** (19–35%) and 21–29% of **12** and **13**.

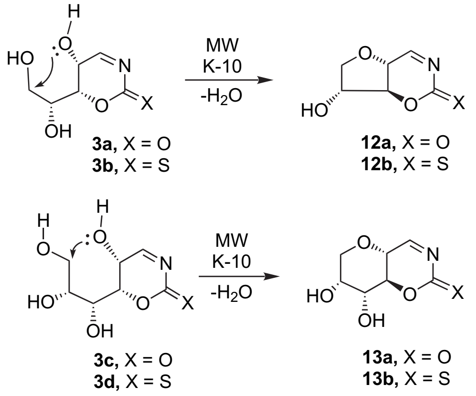
The MEDOS strategy for compounds **14** was successful when an intimate mixture of phenylurea, ammonium acetate,



Scheme 4. Routes for the formation of compounds **7–9** from compounds **5**.



Scheme 5. Formation of compounds **10** and **11** from **6**.



Scheme 6. Formation of compounds **12** and **13** from **3**.

K-10 clay and **5** was subjected to MW irradiation for 9–10 min at 90 °C (Scheme 7). Isolation and purification by recrystallization from ethanol afforded 4-amino oxazine-2,6-diones(6-one-2-thiones) **14** in 89–93% yields (Table 1). That the first step in the present three component coupling strategy involves the conversion of phenylurea into phenyl isocyanate intermediate was supported by its trapping as *p*-tolylurea derivatives. Phenylurea with ammonium acetate and **5** yielded an aldimine intermediate **14′**, which upon cycloisomerization afforded compounds **14** (Scheme 7). Furthermore, MW irradiation of thoroughly mixed semicarbazones **15** and Montmorillonite K-10 clay at 90 °C for 8–11 min afforded compounds **16** in 90–91% yields (Table 1) via domino cycloisomerization and dehydrazination reactions of **15** (Scheme 8).

Table 1

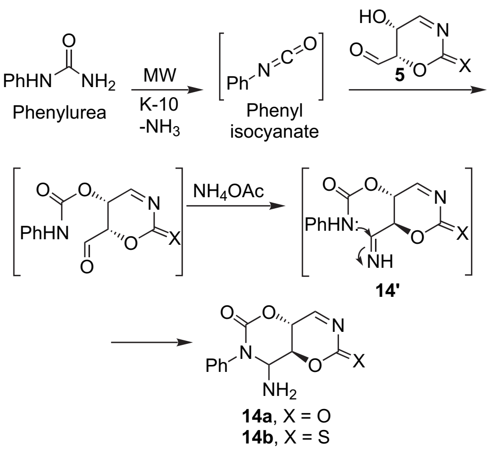
Microwave enhanced synthesis of compounds **3**, **4** and **7–16** under solvent-free conditions

| Compound | Time[a] (min) | Yield[b,c] (%) | Compound | Time[a] (min) | Yield[b,c] (%) |
|---|---|---|---|---|---|
| **3a** | 3 | 83 | **10b** | 7 | 88 |
| **3b** | 2 | 79 | **11a** | 9 | 92 |
| **3c** | 2 | 81 | **11b** | 11 | 91 |
| **3d** | 4 | 85 | **12a** | 8 | 85 |
| **7a** | 5 | 80 | **12b** | 8 | 83 |
| **7b** | 5 | 83 | **13a** | 7 | 90 |
| **8a** | 12 | 91 | **13b** | 8 | 87 |
| **8b** | 11 | 93 | **14a** | 10 | 89 |
| **9a** | 7 | 85 | **14b** | 9 | 93 |
| **9b** | 9 | 82 | **16a** | 11 | 91 |
| **10a** | 5 | 81 | **16b** | 8 | 90 |

[a] Microwave irradiation time.

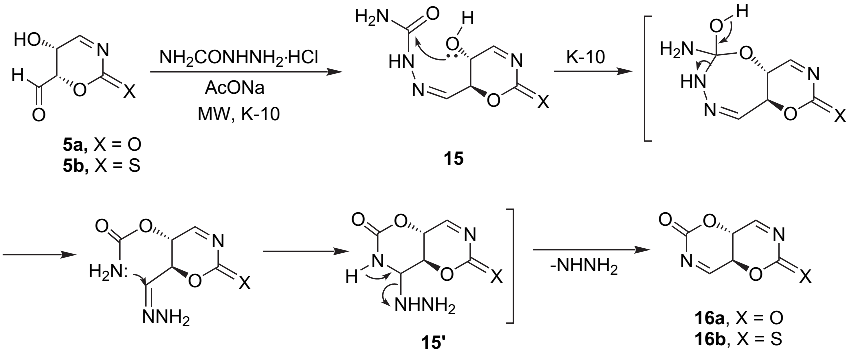
[b] Yield of isolated and purified products.

[c] All compounds gave C, H and N analyses within ±0.36%, and satisfactory spectral (IR, $^1$H NMR, $^{13}$C NMR and EIMS) data.



Scheme 7. Plausible mechanism for the formation of compounds **14** from phenylurea.

The mechanism shown in Scheme 8 is supported by the formation of hydrazine during the reaction. The relatively poor yields (11–19%) of **16** were obtained by using other mineral catalysts, viz. silica gel, neutral or basic alumina.



Scheme 8. Plausible mechanism for the formation of **15** from **16**.

## 3. Conclusion

In summary, we have developed a general, straightforward diversity oriented synthetic approach for the synthesis of various 1,3-oxazin-2-one(thione)-fused *N*- and *O*-heterocyclic systems using D-glucose and D-xylose as biorenewable resources under solvent-free microwave irradiation conditions. The present protocol is an excellent illustration for the utilization of carbohydrate feedstocks in organic synthesis.

## 4. Experimental

### 4.1. General

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 an 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 analyzer. A Chemical Laboratory Microwave Oven (Model: BP-310/50, 230 volt, 50 Hz power input) was used for all the experiments. All chemicals used were of reagent grade and were used as-received without further purification. Silica gel-G was used for TLC.

### 4.2. 1,3-Oxazin-2-ones(thiones) 3: general procedure

Thoroughly mixed D-xylose/D-glucose (1 mmol) **1**, semicarbazide hydrochloride/thiosemicarbazide (1 mmol) **2**, sodium acetate (1 mmol) and montmorillonite K-10 clay (0.10 g) were taken in a 20 mL vial and subjected to microwave irradiation for 2–4 min at 90 °C. After completion of the reaction as indicated by TLC, water (10 mL) was added to give the crude product and recrystallized from ethanol to obtain analytically pure sample of **3**.

#### 4.2.1. Compound 3a

White solid (83%), mp 147–149 °C. IR (KBr) $\nu_{max}$ 3392–3385, 3011, 1692, 1635 cm$^{-1}$. $^{1}H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.85 (dd, 1H, $J_{4H,5H}$=8.1 Hz, $J_{5H,6H}$=3.4 Hz, 5-H), 4.11 (dd, 1H, $J_{2'Ha,2'Hb}$=10.1 Hz, $J_{1'H,2'Ha}$=5.4 Hz, $2'H_a$), 4.23 (dd, 1H, $J_{6H,1'H}$=6.1 Hz, $J_{5H,6H}$=3.4 Hz, 6-H), 4.30 (ddd, 1H, $J_{6H,1'H}$=6.1 Hz, $J_{1'H,2'Ha}$=5.4 Hz, $J_{1'H,2'Hb}$=2.9 Hz, 1′H), 4.63 (dd, 1H, $J_{2'Ha,2'Hb}$=10.1 Hz, $J_{1'H,2'Hb}$=2.9 Hz, $2'H_b$), 4.93–5.24 (br s, 3H, 3×OH, exchangeable with $D_2O$), 7.65 (d, 1H, $J_{4H,5H}$=8.1 Hz, 4-H). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 64.5, 65.3, 73.7, 86.2, 163.1, 172.5. MS (FAB) *m/z* 176 (MH$^{+}$). Anal. Calcd for $C_6H_9NO_5$: C, 41.15; H, 5.18; N, 8.00%. Found: C, 41.43; H, 5.09; N, 7.82%.

#### 4.2.2. Compound 3b

White solid (79%), mp 156–158 °C. IR (KBr) $\nu_{max}$ 3391–3385, 3015, 1695, 1636 cm$^{-1}$. $^{1}H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.87 (dd, 1H, $J_{4H,5H}$=8.1 Hz, $J_{5H,6H}$=3.4 Hz, 5-H), 4.10 (dd, 1H, $J_{2'Ha,2'Hb}$=10.2 Hz, $J_{1'H,2'Ha}$=5.4 Hz, $2'H_a$), 4.19 (dd, 1H, $J_{6H,1'H}$=6.1 Hz, $J_{5H,6H}$=3.4 Hz, 5-H), 4.33 (ddd, 1H, $J_{6H,1'H}$=6.1 Hz, $J_{1'H,2'Ha}$=5.4 Hz, $J_{1'H,2'Hb}$=2.9 Hz, 1′H), 4.59 (dd, 1H, $J_{2'Ha,2'Hb}$=10.2 Hz, $J_{1'H,2'Hb}$=2.9 Hz, $2'H_b$), 4.93–5.27 (br s, 3H, 3×OH, exchangeable with $D_2O$), 7.69 (d, 1H, $J_{4H,5H}$=8.1 Hz, 4-H). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 64.4, 65.7, 71.9, 85.7, 104.8, 163.0, 192.3. MS (FAB) *m/z* 192 (MH$^{+}$). Anal. Calcd for $C_6H_9NO_4S$: C, 37.69; H, 4.74; N, 7.33%. Found: C, 37.95; H, 4.91; N, 7.23%.

#### 4.2.3. Compound 3c

White solid (81%), mp 161–164 °C. IR (KBr) $\nu_{max}$ 3398–3382, 3008, 1690, 1635 cm$^{-1}$. $^{1}H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.88 (ddd, 1H, $J_{2'H,3'Ha}$=5.4 Hz, $J_{1'H,2'H}$=4.6 Hz, $J_{2'H,3'Hb}$=2.7 Hz, 2′H), 3.91 (dd, 1H, $J_{4H,5H}$=8.1 Hz, $J_{5H,6H}$=3.1 Hz, 5-H), 4.03 (dd, 1H, $J_{3'Ha,3'Hb}$=10.5 Hz, $J_{2'H,3'Ha}$=5.4 Hz, $3'H_a$), 4.27 (dd, 1H, $J_{6H,1'H}$=6.7 Hz, $J_{5H,6H}$=3.1 Hz, 6-H), 4.37 (dd, 1H, $J_{6H,1'H}$=6.7 Hz, $J_{1'H,2'H}$=4.6 Hz, 1′H), 4.59 (dd, 1H, $J_{3'Ha,3'Hb}$=10.5 Hz, $J_{2'H,3'Hb}$=2.7 Hz, $3'H_b$), 5.01–5.37 (br s, 4H, 4×OH, exchangeable with $D_2O$), 7.63 (d, 1H, $J_{4H,5H}$=8.1 Hz, 4-H). $^{13}C$ NMR (DMSO-$d_6$/TMS): $\delta$ 55.7, 64.3, 65.9, 71.7, 73.5, 81.5, 163.2, 174.8. MS (FAB) *m/z* 206 (MH$^{+}$). Anal. Calcd for $C_7H_{11}NO_6$: C, 40.98; H, 5.40; N, 6.83%. Found: C, 40.73; H, 5.57; N, 6.71%.

#### 4.2.4. Compound 3d

White solid (85%), mp 142–144 °C. IR (KBr) $\nu_{max}$ 3399–3384, 3012, 1693, 1638 cm$^{-1}$. $^{1}H$ NMR (DMSO-$d_6$/TMS) $\delta$:

3.81 (ddd, 1H, $J_{2'H,3'Ha}$=5.4 Hz, $J_{1'H,2'H}$=4.6 Hz, $J_{2'H,3'Hb}$=2.7 Hz, 2′H), 3.90 (dd, 1H, $J_{4H,5H}$=8.1 Hz, $J_{5H,6H}$=3.1 Hz, 5-H), 4.04 (dd, 1H, $J_{3'Ha,3'Hb}$=10.5 Hz, $J_{2'H,3'Ha}$=5.4 Hz, 3′$H_a$), 4.23 (dd, 1H, $J_{6H,1'H}$=6.7 Hz, $J_{5H,6H}$=3.1 Hz, 6-H), 4.41 (dd, 1H, $J_{6H,1'H}$=6.7 Hz, $J_{1'H,2'H}$=4.6 Hz, 1′H), 4.57 (dd, 1H, $J_{3'Ha,3'Hb}$=10.5 Hz, $J_{2'H,3'Hb}$=2.7 Hz, 3′$H_b$), 5.03–5.33 (br s, 4H, 4×OH, exchangeable with $D_2O$), 7.66 (d, 1H, $J_{4H,5H}$=8.1 Hz, 4-H). $^{13}C$ NMR (DMSO-$d_6$/TMS): $\delta$ 55.6, 64.8, 65.6, 71.6, 73.8, 81.3, 163.1, 192.9. MS (FAB) *m/z* 222 ($MH^+$). Anal. Calcd for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.33%. Found: C, 38.32; H, 5.16; N, 6.29%.

### *4.3. Malaprade reaction to afford aldehydes **5** and **6**: general procedure*

To a well stirred ice-cold solution of 1,3-oxazin-2-ones-(thiones) **3** (1 mmol) in 15 mL ethanol was added dropwise with stirring a solution of sodium periodate (2 mmol) in 8 mL of water. The reaction mixture was further stirred for 2–3 h at rt. 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 concentrated under vacuum to leave the crude product, which on recrystallization from ethanol afforded pure compounds **5** as white solid. The procedure followed for **6** was exactly the same, except that in this case 1 mmol of sodium periodate was used instead of 2 mmol of sodium periodate for **5**.

#### *4.3.1. Compound **5a***

White solid (74%), mp 120–122 °C. IR (KBr) $\nu_{max}$ 3391, 3009, 1715, 1695, 1632 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.98 (dd, 1H, $J_{4H,5H}$=7.8 Hz, $J_{5H,6H}$=3.2 Hz, 5-H), 4.95 (br s, 1H, OH, exchangeable with $D_2O$), 5.57 (d, 1H, $J_{5H,6H}$=3.2 Hz, 6-H), 7.53 (d, 1H, $J_{4H,5H}$=7.8 Hz, 4-H), 9.85 (s, 1H, CHO). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 61.9, 92.5, 163.1, 172.5, 176.5. MS (FAB) *m/z* 144 ($MH^+$). Anal. Calcd for $C_5H_5NO_4$: C, 41.97; H, 3.52; N, 9.79%. Found: C, 41.73; H, 3.47; N, 9.92%.

#### *4.3.2. Compound **5b***

White solid (79%), mp 132–134 °C. IR (KBr) $\nu_{max}$ 3390, 3011, 1718, 1635, 1055 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.95 (dd, 1H, $J_{4H,5H}$=7.9 Hz, $J_{5H,6H}$=3.2 Hz, 5-H), 4.98 (br s, 1H, OH, exchangeable with $D_2O$), 5.53 (d, 1H, $J_{5H,6H}$=3.2 Hz, 6-H), 7.55 (d, 1H, $J_{4H,5H}$=7.9 Hz, 4-H), 9.87 (s, 1H, CHO). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 62.3, 92.1, 163.3, 172.1, 192.5. MS (FAB) *m/z* 160 ($MH^+$). Anal. Calcd for $C_5H_5NO_3S$: C, 37.73; H, 3.17; N, 8.80%. Found: C, 37.95; H, 3.56; N, 8.89%.

#### *4.3.3. Compound **6a***

White solid (81%), mp 112–113 °C. IR (KBr) $\nu_{max}$ 3393, 3385, 3012, 1713, 1697, 1634 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.71 (d, 1H, $J_{1'H,6H}$=5.9 Hz, 1′H), 4.01 (dd, 1H, $J_{4H,5H}$=7.8 Hz, $J_{5H,6H}$=3.5 Hz, 5-H), 4.97–5.19 (br s, 2H, 2×OH, exchangeable with $D_2O$), 5.58 (dd, 1H, $J_{1'H,6H}$=5.9 Hz, $J_{5H,6H}$=3.5 Hz, 6-H), 7.61 (d, 1H, $J_{4H,5H}$=7.8 Hz, 4-H), 9.91 (s, 1H, CHO). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 62.5, 78.1, 91.8, 163.7, 172.1, 176.8. MS (FAB) *m/z* 174 ($MH^+$). Anal. Calcd for $C_6H_7NO_5$: C, 41.63; H, 4.08; N, 8.09%. Found: C, 41.43; H, 4.29; N, 8.23%.

#### *4.3.4. Compound **6b***

White solid (78%), mp 105–107 °C. IR (KBr) $\nu_{max}$ 3395, 3385, 3015, 1716, 1637, 1058 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.73 (d, 1H, $J_{1'H,6H}$=5.9 Hz, 1′H), 4.05 (dd, 1H, $J_{4H,5H}$=8.1 Hz, $J_{5H,6H}$=3.5 Hz, 5-H), 5.03–5.27 (br s, 2H, 2×OH, exchangeable with $D_2O$), 5.61 (dd, 1H, $J_{1'H,6H}$=5.9 Hz, $J_{5H,6H}$=3.5 Hz, 6-H), 7.57 (d, 1H, $J_{4H,5H}$=8.1 Hz, 4-H), 9.90 (s, 1H, CHO). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 62.1, 78.3, 92.7, 162.9, 176.1, 192.2. MS (FAB) *m/z* 190 ($MH^+$). Anal. Calcd for $C_6H_7NO_4S$: C, 38.09; H, 3.73; N, 7.40%. Found: C, 38.39; H, 3.49; N, 7.76%.

### *4.4. Isoxazolo-, pyrazolo- and pyrimidinoxazin-2-ones(thiones) **7**–**9**: general procedure*

An intimate solvent-free mixture of **5** (0.143 g for **5a**, 1 mmol), sodium acetate (0.082 g, 1 mmol) and hydroxylamine hydrochloride (0.069 g, 1 mmol) or phenylhydrazine hydrochloride (0.145 g, 1 mmol) or acetamidine hydrochloride (0.095 g, 1 mmol) in the presence of montmorillonite K-10 clay (0.10 g) was taken in a 20 mL vial and subjected to MW irradiation at 80 °C for 5–12 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 recrystallized from ethanol to obtain as analytically pure sample of compound **7**, **8** or **9** as a yellowish solid.

#### *4.4.1. Compound **7a***

Yellowish solid (80%), mp 164–166 °C. IR (KBr) $\nu_{max}$ 3010, 1691, 1639 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.91 (dd, 1H, $J_{4aH,4H}$=8.7 Hz, $J_{4aH,7aH}$=3.5 Hz, 4a-H), 5.17 (dd, 1H, $J_{7aH,7H}$=9.1 Hz, $J_{4aH,7aH}$=3.5 Hz, 7a-H), 7.56 (d, 1H, $J_{4aH,4H}$=8.7 Hz, 4-H), 7.64 (d, 1H, $J_{7aH,7H}$=9.1 Hz, 7-H). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 65.5, 72.3, 159.2, 161.5, 173.4. MS (FAB) *m/z* 141 ($MH^+$). Anal. Calcd for $C_5H_4N_2O_3$: C, 42.87; H, 2.88; N, 20.00%. Found: C, 43.18; H, 2.53; N, 19.89%.

#### *4.4.2. Compound **7b***

Yellowish solid (83%), mp 159–161 °C. IR (KBr) $\nu_{max}$ 3008, 1632, 1052 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 4.07 (dd, 1H, $J_{4aH,4H}$=8.7 Hz, $J_{4aH,7aH}$=3.9 Hz, 4a-H), 5.13 (dd, 1H, $J_{7aH,7H}$=9.1 Hz, $J_{4aH,7aH}$=3.9 Hz, 7a-H), 7.59 (d, 1H, $J_{4aH,4H}$=8.7 Hz, 4-H), 7.67 (d, 1H, $J_{7aH,7H}$=9.1 Hz, 7-H). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 65.2, 71.9, 158.7, 161.2, 193.2. MS (FAB) *m/z* 157 ($MH^+$). Anal. Calcd for $C_5H_4N_2O_2S$: C, 38.46; H, 2.58; N, 17.94%. Found: C, 38.69; H, 2.69; N, 17.76%.

#### *4.4.3. Compound **8a***

Yellowish solid (91%), mp 152–154 °C. IR (KBr) $\nu_{max}$ 3012, 1696, 1634, 1605, 1581, 1455 $cm^{-1}$. $^1H$ NMR

(DMSO-$d_6$/TMS) $\delta$: 4.23 (dd, 1H, $J_{4aH,4H}$=8.2 Hz, $J_{4aH,7aH}$=3.7 Hz, 4a-H), 5.71 (dd, 1H, $J_{7aH,7H}$=7.6 Hz, $J_{4aH,7aH}$=3.7 Hz, 7a-H), 7.12–7.57 (m, 5$H_{arom}$), 7.56 (d, 1H, $J_{7aH,7H}$=7.6 Hz, 7-H), 7.69 (d, 1H, $J_{4aH,4H}$=8.2 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 56.2, 78.3, 121.2, 125.7, 127.7, 130.2, 156.2, 161.3, 172.5. MS (FAB) *m/z* 216 (MH$^+$). Anal. Calcd for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53%. Found: C, 61.03; H, 4.43; N, 19.37%.

### 4.4.4. Compound **8b**

Yellowish solid (93%), mp 168–171 °C. IR (KBr) $\nu_{max}$ 3009, 1631, 1601, 1579, 1449, 1321, 1312, 1057 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 4.19 (dd, 1H, $J_{4aH,4H}$=8.2 Hz, $J_{4aH,7aH}$=3.3 Hz, 4a-H), 5.75 (dd, 1H, $J_{7aH,7H}$=7.6 Hz, $J_{4aH,7aH}$=3.3 Hz, 7a-H), 7.18–7.61 (m, 5$H_{arom}$), 7.59 (d, 1H, $J_{7aH,7H}$=7.6 Hz, 7-H), 7.72 (d, 1H, $J_{4aH,4H}$=8.2 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 55.9, 81.2, 122.5, 125.9, 127.5, 130.5, 156.5, 161.2, 192.7. MS (FAB) *m/z* 232 (MH$^+$). Anal. Calcd for $C_{11}H_9N_3OS$: C, 57.13; H, 3.92; N, 18.17%. Found: C, 57.38; H, 3.77; N, 17.95%.

### 4.4.5. Compound **9a**

Yellowish solid (85%), mp 185–187 °C. IR (KBr) $\nu_{max}$ 2998, 1692, 1635 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 1.67 (s, 3H, Me), 3.12 (dd, 1H, $J_{4aH,4H}$=8.5 Hz, $J_{4aH,8aH}$=3.9 Hz, 4a-H), 4.57 (dd, 1H, $J_{8aH,8H}$=7.9 Hz, $J_{4aH,8aH}$=3.9 Hz, 8a-H), 7.53 (d, 1H, $J_{8aH,8H}$=7.9 Hz, 8-H), 7.61 (d, 1H, $J_{4aH,4H}$=8.5 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 51.3, 75.2, 159.2, 161.5, 162.7, 163.8, 173.5. MS (FAB) *m/z* 166 (MH$^+$). Anal. Calcd for $C_7H_7N_3O_2$: C, 50.91; H, 4.27; N, 25.44%. Found: C, 50.67; H, 4.49; N, 25.32%.

### 4.4.6. Compound **9b**

Yellowish solid (82%), mp 159–161 °C. IR (KBr) $\nu_{max}$ 3005, 1631, 1055 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 1.72 (s, 3H, Me), 3.15 (dd, 1H, $J_{4aH,4H}$=8.5 Hz, $J_{4aH,8aH}$=3.6 Hz, 4a-H), 4.63 (dd, 1H, $J_{8aH,8H}$=7.9 Hz, $J_{4aH,8aH}$=3.6 Hz, 8a-H), 7.49 (d, 1H, $J_{8aH,8H}$=7.9 Hz, 8-H), 7.60 (d, 1H, $J_{4aH,4H}$=8.5 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 51.5, 74.8, 157.9, 160.8, 162.5, 163.2, 192.3. MS (FAB) *m/z* 182 (MH$^+$). Anal. Calcd for $C_7H_7N_3OS$: C, 46.40; H, 3.89; N, 23.19%. Found: C, 46.27; H, 3.95; N, 23.55%.

## 4.5. 1,2-Oxazino- and pyrazino-1,3-oxazin-2-ones(thiones) **10** and **11**: general procedure

These were prepared by following the similar procedure as described above for **7**–**9**, except that in this case **6** (1 mmol) was used in place of **5** to yield **10** and **11**. To obtain analytically pure sample of compounds **10** and **11**, the same procedure was adopted as described for **7**–**9**.

### 4.5.1. Compound **10a**

Yellowish solid (81%), mp 173–175 °C. IR (KBr) $\nu_{max}$ 3393, 3008, 1694, 1638 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 3.85 (dd, 1H, $J_{8aH,8H}$=9.3 Hz, $J_{7H,8H}$=6.8 Hz, 8-H), 4.03 (dd, 1H, $J_{4aH,4H}$=8.9 Hz, $J_{4aH,8aH}$=3.3 Hz, 4a-H), 4.78 (dd, 1H, $J_{8aH,8H}$=9.3 Hz, $J_{4aH,8aH}$=3.3 Hz, 8a-H), 5.01 (br s, 1H, OH, exchangeable with $D_2O$), 7.47 (d, 1H, $J_{4aH,4H}$=8.9 Hz, 4-H), 7.55 (d, 1H, $J_{7H,8H}$=6.8 Hz, 7-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 55.9, 70.9, 81.5, 159.5, 161.5, 173.4. MS (FAB) *m/z* 171 (MH$^+$). Anal. Calcd for $C_6H_6N_2O_4$: C, 42.36; H, 3.55; N, 16.47%. Found: C, 42.64; H, 3.38; N, 16.11%.

### 4.5.2. Compound **10b**

Yellowish solid (88%), mp 181–183 °C. IR (KBr) $\nu_{max}$ 3395, 3006, 1639, 1051 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 3.87 (dd, 1H, $J_{8aH,8H}$=9.2 Hz, $J_{7H,8H}$=6.8 Hz, 8-H), 3.99 (dd, 1H, $J_{4aH,4H}$=8.9 Hz, $J_{4aH,8aH}$=3.3 Hz, 4a-H), 4.81 (dd, 1H, $J_{8aH,8H}$=9.2 Hz, $J_{4aH,8aH}$=3.3 Hz, 8a-H), 4.99 (br s, 1H, OH, exchangeable with $D_2O$), 7.44 (d, 1H, $J_{4aH,4H}$=8.9 Hz, 4-H), 7.53 (d, 1H, $J_{7H,8H}$=6.8 Hz, 7-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 56.2, 71.2, 80.9, 160.2, 161.7, 193.4. MS (FAB) *m/z* 187 (MH$^+$). Anal. Calcd for $C_6H_6N_2O_3S$: C, 38.70; H, 3.25; N, 15.05%. Found: C, 38.51; H, 3.36; N, 15.26%.

### 4.5.3. Compound **11a**

Yellowish solid (92%), mp 133–135 °C. IR (KBr) $\nu_{max}$ 3392, 3003, 1692, 1635 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 3.81 (dd, 1H, $J_{4aH,4H}$=8.5 Hz, $J_{4aH,8aH}$=3.7 Hz, 4a-H), 3.92 (dd, 1H, $J_{8aH,8H}$=9.3 Hz, $J_{7H,8H}$=6.5 Hz, 8-H), 4.81 (dd, 1H, $J_{8aH,8H}$=9.3 Hz, $J_{4aH,8aH}$=3.7 Hz, 8a-H), 4.95 (br s, 1H, OH, exchangeable with $D_2O$), 7.05–7.61 (m, 5$H_{arom}$), 7.45 (d, 1H, $J_{4aH,4H}$=8.5 Hz, 4-H), 7.55 (d, 1H, $J_{7H,8H}$=6.5 Hz, 7-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 62.3, 70.7, 81.9, 123.4, 127.9, 129.7, 130.6, 160.2, 161.1, 172.9. MS (FAB) *m/z* 246 (MH$^+$). Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.52; N, 17.13%. Found: C, 58.49; H, 4.37; N, 17.29%.

### 4.5.4. Compound **11b**

Yellowish solid (91%), mp 143–145 °C. IR (KBr) $\nu_{max}$ 3390, 3007, 1631, 1057 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$/TMS) $\delta$: 3.80 (dd, 1H, $J_{4aH,4H}$=8.5 Hz, $J_{4aH,8aH}$=3.3 Hz, 4a-H), 3.91 (dd, 1H, $J_{8aH,8H}$=9.1 Hz, $J_{7H,8H}$=6.5 Hz, 8-H), 4.83 (dd, 1H, $J_{8aH,8H}$=1.3 Hz, $J_{4aH,8aH}$=3.3 Hz, 8a-H), 4.98 (br s, 1H, OH, exchangeable with $D_2O$), 7.09–7.58 (m, 5$H_{arom}$), 7.48 (d, 1H, $J_{4aH,4H}$=8.5 Hz, 4-H), 7.56 (d, 1H, $J_{7H,8H}$=6.5 Hz, 7-H). $^{13}$C NMR (DMSO-$d_6$/TMS) $\delta$: 62.7, 71.5, 82.7, 122.5, 123.7, 127.8, 130.1, 159.8, 161.5, 192.8. MS (FAB) *m/z* 262 (MH$^+$). Anal. Calcd for $C_{12}H_{11}N_3O_2S$: C, 55.16; H, 4.24; N, 16.08%. Found: C, 55.31; H, 4.13; N, 16.37%.

## 4.6. Furo- and pyrano-1,3-oxazin-2-ones(thiones) **12** and **13**: general procedure

An intimate solvent-free mixture of 1,3-oxazin-2-ones(thiones) (2 mmol) **3** and montmorillonite K-10 clay (0.20 g) was taken in a 20 mL vial and subjected to MW irradiation at 95 °C for 5–8 min to get the crude product, which was extracted with ethyl acetate (3×20 mL). The extract was filtered, the filtrate was evaporated under reduced pressure and the residue thus obtained was recrystallized from ethanol to afford analytically pure sample of **12** or **13**.

### 4.6.1. Compound **12a**

Yellowish solid (85%), mp 113–114 °C. IR (KBr) $\nu_{max}$ 3392, 3015, 1698, 1633 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 3.56 (dd, 1H, $J_{6Ha,Hb}$=11.8 Hz, $J_{6Ha,7H}$=4.4 Hz, 6-Ha), 3.81 (dd, 1H, $J_{6Ha,Hb}$=11.8 Hz, $J_{6Hb,7H}$=2.6 Hz, 6-Hb), 3.94 (ddd, 1H, $J_{7H,7Ha}$=8.8 Hz, $J_{6Ha,7H}$=4.4 Hz, $J_{6Hb,7H}$=2.6 Hz, 7-H), 4.19 (dd, 1H, $J_{4aH,4H}$=8.1 Hz, $J_{4aH,7aH}$=4.2 Hz, 4a-H), 4.92 (dd, 1H, $J_{7H,7Ha}$=8.8 Hz, $J_{4aH,7aH}$=4.2 Hz, 7a-H), 5.02 (br s, 1H, OH, exchangeable with $D_2O$), 7.45 (d, 1H, $J_{4aH,4H}$= 8.1 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 56.5, 71.3, 81.6, 82.7, 162.6, 172.8. MS (FAB) *m/z* 158 (MH$^{+}$). Anal. Calcd for $C_6H_7NO_4$: C, 45.86; H, 4.49; N, 8.91%. Found: C, 45.95; H, 4.57; N, 8.73%.

### 4.6.2. Compound **12b**

Yellowish solid (83%), mp 139–141 °C. IR (KBr) $\nu_{max}$ 3395, 3009, 1635, 1053 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 3.55 (dd, 1H, $J_{6Ha,Hb}$=12.1 Hz, $J_{6Ha,7H}$=4.1 Hz, 6-Ha), 3.76 (dd, 1H, $J_{6Ha,Hb}$=12.1 Hz, $J_{6Hb,7H}$=2.6 Hz, 6-Hb), 3.88 (ddd, 1H, $J_{7H,7Ha}$=8.9 Hz, $J_{6Ha,7H}$=4.1 Hz, $J_{6Hb,7H}$=2.6 Hz, 7-H), 4.21 (dd, 1H, $J_{4aH,4H}$=8.2 Hz, $J_{4aH,7aH}$=4.2 Hz, 4a-H), 4.89 (dd, 1H, $J_{7H,7Ha}$=8.9 Hz, $J_{4aH,7aH}$=4.2 Hz, 7a-H), 4.97 (br s, 1H, OH, exchangeable with $D_2O$), 7.48 (d, 1H, $J_{4aH,4H}$=8.2 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 58.2, 70.9, 79.8, 81.8, 163.2, 192.5. MS (FAB) *m/z* 174 (MH$^{+}$). Anal. Calcd for $C_6H_7NO_3S$: C, 41.61; H, 4.07; N, 8.09%. Found: C, 41.39; H, 4.21; N, 7.88%.

### 4.6.3. Compound **13a**

Yellowish solid (90%), mp 150–152 °C. IR (KBr) $\nu_{max}$ 3391, 3383, 3013, 1692, 1638 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 3.39 (ddd, 1H, $J_{6Ha,7H}$=9.5 Hz, $J_{7H,8H}$=9.3 Hz, $J_{6Hb,7H}$=3.8 Hz, 7-H), 3.57 (dd, 1H, $J_{6Ha,Hb}$=12.7 Hz, $J_{6Ha,7H}$= 9.5 Hz, 6-Ha), 3.91 (dd, 1H, $J_{6Ha,Hb}$=12.7 Hz, $J_{6Hb,7H}$= 3.8 Hz, 6-Hb), 4.05 (dd, 1H, $J_{7H,8H}$=9.3 Hz, $J_{8H,8aH}$=8.8 Hz, 8-H), 4.18 (dd, 1H, $J_{4aH,4H}$=8.1 Hz, $J_{4aH,8aH}$=3.2 Hz, 4a-H), 4.25 (dd, 1H, $J_{8H,8Ha}$=8.8 Hz, $J_{4aH,8aH}$=3.2 Hz, 8a-H), 4.95–5.18 (br s, 2H, 2×OH, exchangeable with $D_2O$), 7.47 (d, 1H, $J_{4aH,4H}$=8.1 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 65.5, 71.2, 76.3, 81.5, 82.9, 163.0, 172.5. MS (FAB) *m/z* 188 (MH$^{+}$). Anal. Calcd for $C_7H_9NO_5$: C, 44.92; H, 4.85; N, 7.48%. Found: C, 45.21; H, 4.68; N, 7.24%.

### 4.6.4. Compound **13b**

Yellowish solid (87%), mp 173–175 °C. IR (KBr) $\nu_{max}$ 3393, 3382, 3009, 1633, 1058 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 3.43 (ddd, 1H, $J_{6Ha,7H}$=9.3 Hz, $J_{7H,8H}$=9.0 Hz, $J_{6Hb,7H}$=3.8 Hz, 7-H), 3.61 (dd, 1H, $J_{6Ha,Hb}$=12.4 Hz, $J_{6Ha,7H}$= 9.3 Hz, 6-Ha), 3.89 (dd, 1H, $J_{6Ha,Hb}$=12.4 Hz, $J_{6Hb,7H}$= 3.8 Hz, 6-Hb), 4.06 (dd, 1H, $J_{7H,8H}$=9.0 Hz, $J_{8H,8Ha}$=8.8 Hz, 8-H), 4.14 (dd, 1H, $J_{4aH,4H}$=8.1 Hz, $J_{4aH,8aH}$=3.2 Hz, 4a-H), 4.24 (dd, 1H, $J_{8H,8aH}$=8.8 Hz, $J_{4aH,8aH}$=3.2 Hz, 8a-H), 4.93–5.19 (br s, 2H, 2×OH, exchangeable with $D_2O$), 7.51 (d, 1H, $J_{4aH,4H}$=8.2 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 65.2, 71.3, 76.5, 81.4, 83.1, 162.8, 193.2. MS (FAB) *m/z* 204 (MH$^{+}$). Anal. Calcd for $C_7H_9NO_4S$: C, 41.37; H, 4.46; N, 6.89%. Found: C, 41.55; H, 4.29; N, 6.63%.

## 4.7. 4-Amino oxazine-2,6-diones(6-one-2-thiones) **14**: general procedure

Thoroughly mixed phenylurea (0.272 g, 2 mmol), aldehyde **5** (0.286 g for **5a**, 2 mmol), ammonium acetate (0.154 g, 2 mmol) and montmorillonite K-10 clay (0.20 g) were taken in a 20 mL vial subjected to microwave irradiation at 90 °C for 9–10 min. After completion of the reaction as indicated by TLC (hexane/AcOEt, 8:2, v/v), the product was extracted with dichloromethane (3×20 mL), the extract was filtered and the filtrate was evaporated under reduced pressure to leave the crude product, which was recrystallized from ethanol to obtain an analytically pure sample of **14** as yellowish needles.

### 4.7.1. Compound **14a**

Yellowish solid (89%), mp 181–182 °C. IR (KBr) $\nu_{max}$ 3342, 3007, 1691, 1638 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 2.98–3.12 (br s, 2H, NH, exchangeable with $D_2O$), 4.32 (dd, 1H, $J_{4aH,4H}$=8.5 Hz, $J_{4aH,8aH}$=2.9 Hz, 4a-H), 4.97 (dd, 1H, $J_{8aH,8H}$=7.3 Hz, $J_{4aH,8aH}$=2.9 Hz, 8a-H), 5.78 (m, 1H, 8-H), 7.03–7.51 (m, 5$H_{arom}$), 7.58 (d, 1H, $J_{4aH,4H}$=8.5 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 55.8, 76.5, 81.3, 125.1, 128.2, 129.4, 130.7, 161.5, 172.1, 173.4. MS (FAB) *m/z* 262 (MH$^{+}$). Anal. Calcd for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09%. Found: C, 55.39; H, 4.11; N, 16.31%.

### 4.7.2. Compound **14b**

Yellowish solid (93%), mp 168–171 °C. IR (KBr) $\nu_{max}$ 3347, 3011, 1699, 1631, 1057 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 2.94–3.10 (br s, 2H, NH, exchangeable with $D_2O$), 4.27 (dd, 1H, $J_{4aH,4H}$=8.0 Hz, $J_{4aH,8aH}$=2.9 Hz, 4a-H), 5.01 (dd, 1H, $J_{8aH,8H}$=7.3 Hz, $J_{4aH,8aH}$=2.9 Hz, 8a-H), 5.83 (m, 1H, 8-H), 7.12–7.65 (m, 5$H_{arom}$), 7.53 (d, 1H, $J_{4aH,4H}$= 8.0 Hz, 4-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 55.2, 75.9, 82.5, 126.2, 127.9, 128.8, 130.1, 162.7, 172.7, 193.2. MS (FAB) *m/z* 278 (MH$^{+}$). Anal. Calcd for $C_{12}H_{11}N_3O_3S$: C, 51.98; H, 4.00; N, 15.15%. Found: C, 51.67; H, 4.29; N, 15.21%.

## 4.8. Oxazine-2,6-diones(6-one-2-thiones) **16**

Thoroughly mixed aldehyde **5** (0.286 g for **5a**, 2 mmol), semicarbazide hydrochloride (0.223 g, 2 mmol), sodium acetate (0.164 g, 2 mmol) and montmorillonite K-10 clay (0.10 g) were taken in a 20 mL vial and subjected to microwave irradiation at 90 °C for 8–11 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 recrystallized from ethanol to obtain analytically pure sample of **16**.

### 4.8.1. Compound **16a**

Yellowish solid (91%), mp 163–165 °C. IR (KBr) $\nu_{max}$ 2995, 1695, 1638 cm$^{-1}$. $^{1}$H NMR (DMSO-$d_6$/TMS) δ: 4.32 (d, 2H, $J_{4,4aH}$($J_{8,8aH}$)=8.2 Hz, 4a-H, 8a-H), 7.56 (d, 2H, $J_{4,4aH}$($J_{8,8aH}$)=8.2 Hz, 4-H, 8-H). $^{13}$C NMR (DMSO-$d_6$/TMS) δ: 71.5, 162.3, 172.5. MS (FAB) *m/z* 169 (MH$^{+}$).

Anal. Calcd for $C_6H_4N_2O_4$: C, 42.87; H, 2.40; N, 16.66%. Found: C, 42.61; H, 2.61; N, 16.49%.

### 4.8.2. Compound **16b**

Yellowish solid (90%), mp 175–177 °C. IR (KBr) $\nu_{max}$ 3002, 1693, 1633, 1053 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$/TMS) $\delta$: 3.98 (dd, 1H, $J_{4H,4aH}$=7.9 Hz, $J_{4aH,8aH}$=5.5 Hz, 4a-H), 4.05 (d, 1H, $J_{8H,8aH}$=6.3 Hz, 8-H), 4.19 (dd, 1H, $J_{8H,8aH}$=6.3 Hz, $J_{4aH,8aH}$=3.1 Hz, 8a-H), 7.51 (d, 1H, $J_{4,4aH}$=7.9 Hz, 4-H). $^{13}C$ NMR (DMSO-$d_6$/TMS) $\delta$: 65.5, 71.9, 161.9, 172.5, 193.1. MS (FAB) *m/z* 185 ($MH^+$). Anal. Calcd for $C_6H_4N_2O_3S$: C, 39.13; H, 2.19; N, 15.21%. Found: C, 39.38; H, 2.12; N, 15.43%.

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## References and notes

1. Fitzmaurice, R. J.; Etheridge, Z. C.; Jumel, E.; Woolfson, D. N.; Caddick, S. *Chem. Commun.* **2006**, 4814–4816.
2. Tan, D. S. *Nature Chem. Biol.* **2005**, *1*, 74–84.
3. Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46–58.
4. Spring, D. R. *Org. Biomol. Chem.* **2003**, *1*, 3867–3870.
5. Schreiber, S. L. *Science* **2000**, *287*, 1964–1969.
6. Bunin, B. A.; Plunkett, M.; Ellman, J. A. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *81*, 4708–4712.
7. Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; John Wiley and Sons: New York, NY, 1989; 423.
8. Kobayashi, M.; Kitazawa, M.; Sotio, T.; Yamamoto, R.; Harada, H. *Yakugaku Zasshi* **1984**, *104*, 659–679; *Chem. Abstr.* **1985**, *102*, 6344m.
9. Testa, E.; Fontanella, L.; Cristiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1928–1936.
10. (a) Raynaud, G.; Sergant, M.; Douzon, C.; Fauran, C. U.S. 3,821,215, 1974; *Chem. Abstr.* **1975**, *82*, 49951r; (b) Vrouenraets, S. M.; Wit, W. F.; van Tongeren, J.; Lange, J. M. *Expert Opin. Pharmacother.* **2007**, *8*, 851–871.
11. Abbas, T. R.; Cadogan, J. I. G.; Doyle, A. A.; Gosney, I.; Hodgson, P. K. G.; Howells, G. E.; Hulme, A. N.; Parsons, S.; Sadler, I. H. *Tetrahedron Lett.* **1997**, *38*, 4917–4920 and references cited therein.
12. Klash, A.; Koristek, K.; Polis, J.; Kosmrlj, J. *Tetrahedron* **2000**, *56*, 1551–1560.
13. Mindl, J.; Hrabik, O.; Sterba, V.; Kavalek, J. *Collect. Czech. Chem. Commun.* **2000**, *65*, 1262–1272.
14. Waxman, L.; Darke, P. L. *Antiviral Chem. Chemother.* **2000**, *11*, 1–6.
15. Girgis, A. S. *Pharmazie* **2000**, 426–430.
16. Patel, M.; Ko, S. S.; Mc Hugh, R. J., Jr.; Markwalder, J. A.; Srivastava, A. S.; Cordova, B. C.; Klabe, R. M.; Erickson-Viitanen, S.; Trainor, G. L.; Seitz, S. P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2805–2810.
17. Patel, M.; Mc Hugh, R. J., Jr.; Cordova, B. C.; Klabe, R. M.; Erickson-Viitanen, S.; Trainor, G. L.; Koo, S. S. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3221–3226.
18. Thomas, K. *Tetrahedron* **2005**, *61*, 3091–3096.
19. Dijkstra, H. P.; Gaulon, C.; Niculescu-Duvaz, D.; Springer, C. J. *Synlett* **2006**, 1519–1522.
20. Yadav, L. D. S.; Singh, S.; Singh, A. *Tetrahedron Lett.* **2002**, *43*, 8551–8553.
21. Yadav, L. D. S.; Yadav, B. S.; Dubey, S. *Tetrahedron* **2004**, *60*, 131–136.
22. Yadav, L. D. S.; Kapoor, R. *J. Org. Chem.* **2004**, *69*, 8118–8120.
23. Yadav, L. D. S.; Kapoor, R. *Synlett* **2005**, 3055–3058.
24. Yadav, L. D. S.; Yadav, B. S.; Rai, V. K. *Tetrahedron Lett.* **2004**, *45*, 5351–5353.
25. Yadav, L. D. S.; Rai, V. K. *Tetrahedron Lett.* **2006**, *47*, 395–397.
26. Yadav, L. D. S.; Rai, V. K. *Synlett* **2007**, 1227–1230.
27. Yadav, L. D. S.; Awasthi, C.; Rai, V. K.; Rai, A. *Tetrahedron Lett.* **2007**, *48*, 4899–4902.
28. Yadav, L. D. S.; Rai, A.; Rai, V. K.; Awasthi, C. *Synlett* **2007**, 1905–1908.