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Mineral supported syntheses of benzoxazine-2-thiones under microwave irradiation

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Abstract—An original montmorillonite K-10 clay catalysed cycloisomerisation of salicylaldehyde 4-arylthiosemicarbazones yields 3,4-dihydro-4-hydrazino-2*H*-benz[*e*]-1,3-oxazine-2-thiones, which on reductive dehydrazination on alumina-supported copper(II) sulfate readily furnish 3,4-dihydro-2*H*-benz[*e*]-1,3-oxazine-2-thiones under solvent-free microwave irradiation. Under the same conditions salicylaldehyde thiosemicarbazones undergo cyclodehydrazination to yield 2*H*-benz[*e*]-1,3-oxazine-2-thiones.

Recently, benzoxazinone derivatisation has attained considerable significance in potential antiviral target compounds.[1–6] The prime driving force in this area is the fight against HIV by developing more efficacious drugs than Efavirenz (Sustiva), a benzoxazinone derivative, which is presently in clinical use for the treatment of AIDS. The hydrazine function is synthetically readily manipulable, thus the present cycloisomerisation expeditiously yielding 4-hydrazinobenzoxazine-2-thiones **6** offers an attractive scaffold to be utilized for exploiting chemical diversity and generating a drug-like library to screen for lead candidates.

Heterogeneous organic reactions have proven useful to chemists both in academia and in industry. Clay-catalysed organic transformations have generated considerable interest because of their inexpensive nature and special catalytic attributes under heterogeneous reaction conditions.[7–9] The application of microwave (MW) irradiation as a non-conventional energy source for activation of reactions, in general and on inorganic solid supports in particular, have gained popularity over the usual homogeneous and heterogeneous reactions, as they can be performed rapidly to give pure products in high yields under solvent-free conditions with several eco-friendly advantages in the context of green chemistry.[10–14]

Considering the above reports and in pursuing our work on new cyclisation methods,[15–17] we contemplated an original montmorillonite K-10 clay catalysed MW activated cycloisomerisation of 4-arylthiosemicarbazones **1** to 4-hydrazinobenzoxazine-2-thiones **6** (Scheme 1). Interestingly, this is the first example of the synthesis of 4-hydrazinobenzoxazine-2-thiones **6**, and their reductive dehydrazination to the corresponding benzoxazine-2-thiones **8**. The key element in our approach is the novel utilization of salicylaldehyde as a bifunctional building block whose application to the construction of various benzo-fused oxygen heterocycles of chemical and biological interest is well documented.[18–23]

1. Results and discussion

After some preliminary experimentation, it was found that the cycloisomerisation envisaged (**1**→**6**) can be effected using montmorillonite K-10 clay with intermittent irradiation for 2 min in an unmodified domestic MW oven at 560 W followed by thorough mixing for 2 min outside the oven. This intermittent irradiation-mixing cycle was repeated for the total irradiation time specified in Table 1 to afford benzoxazine-2-thiones **6** in 76–87% yield (Table 1). However, the use of other mineral supports, viz. silica gel, neutral or basic alumina, was far less effective resulting in either no reaction (in the case of basic alumina) or relatively very low yields (14–32%) of **6** (in the cases of silica gel and neutral alumina). Hydrazines **6** readily formed hydrazones with benzaldehyde, further confirmation of their identity. 4-Hydrazinobenzoxazine-2-thiones **6** underwent MW-assisted reductive dehydrazination on alumina-supported copper(II) sulfate under solvent-free conditions to furnish the corresponding benzoxazine-2-thiones **8** (Table 1). When salicylaldehyde thiosemicarbazones **1**, R^3=H, were subjected to MW irradiation under the same conditions as for the synthesis of **6** from **1**, R^3=aryl (Ar), cyclodehydrazination occurred to furnish **7** in 84–92% yield (Table 1).

Keywords: Mineral supported; Microwaves; Solvent free; Benzoxazine-2-thiones; Salicylaldehyde thiosemicarbazones.
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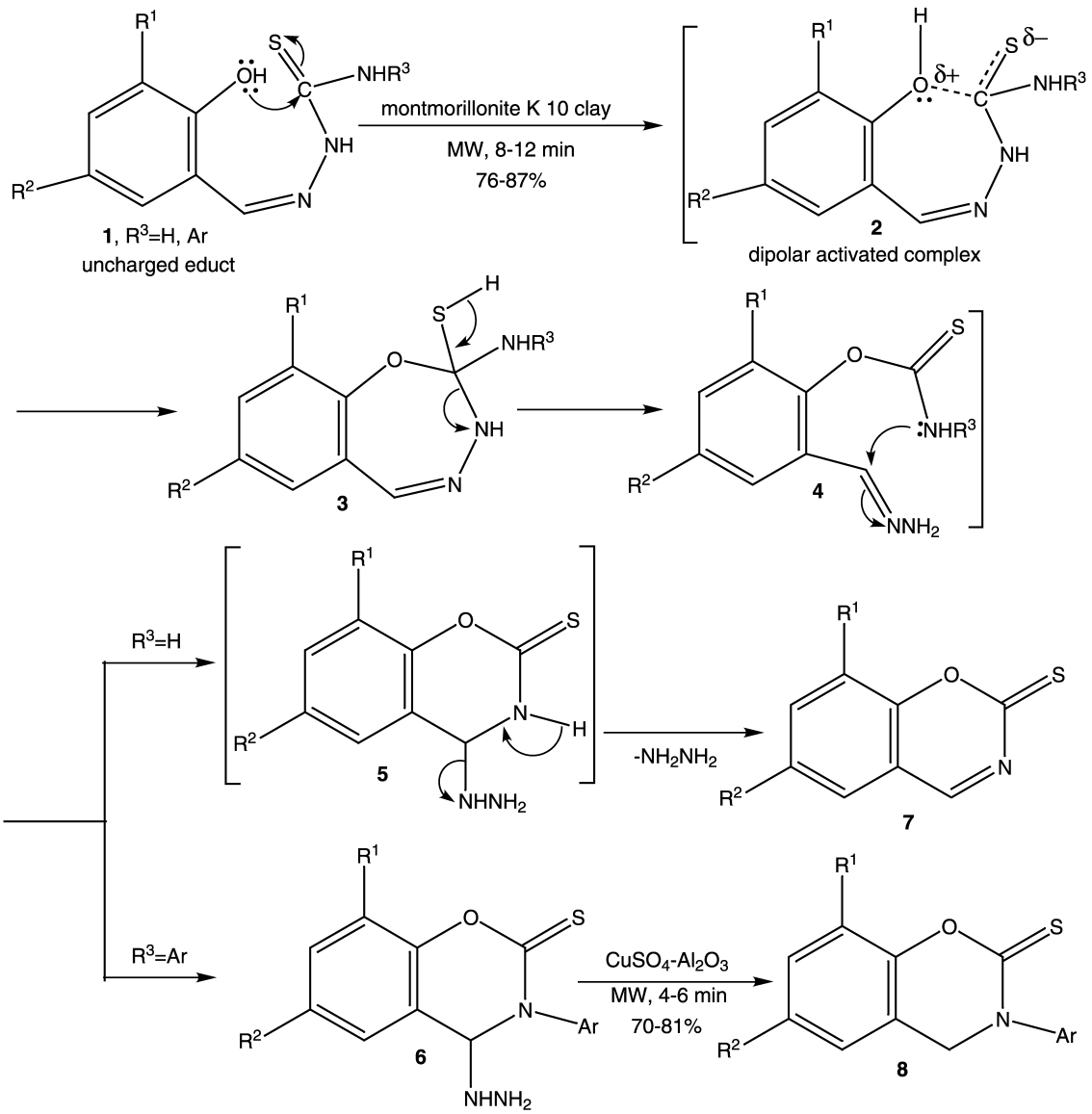

1-8	R^1	R^2	1 Ar	-8	R^1	R^2	Ar
a	H	H	Ph	**f**	H	H	4-MeC_6H_4
b	H	Br	Ph	**g**	H	Br	4-MeC_6H_4
c	Br	Br	Ph	**h**	Br	Br	4-MeC_6H_4
d	H	Cl	Ph	**i**	H	Cl	4-MeC_6H_4
e	Cl	Cl	Ph	**j**	Cl	Cl	4-MeC_6H_4

Scheme 1.

For comparison purposes, the final temperature was measured by immersing a glass thermometer into the reaction mixture immediately after MW irradiations and was found to be <90 °C. The cycloisomerisations (**1→6**, R^3=Ar) and cyclodehydrazinations (**1→7**, R^3=H) were also carried out using a thermostated oil bath under the same conditions of time (Table 1) and temperature (90 °C) as for the MW activated method. It was found that significantly lower yields (14–32%) were obtained using oil-bath heating rather than the MW activated method (Table 1). Similar results were obtained in the case of reductive dehydrazination of **6** to **8** (Table 1). These observations may be rationalised on the basis of the formation of a dipolar activated complex from an uncharged educt in these cycloisomerisations (Scheme 1 shows an activated complex **2** as an example) and the greater stabilisation of the more polar activated complex by dipole–dipole interactions with the electromagnetic field of MWs as compared to the less polar educt which may reduce the activation energy ($\Delta G^{\neq}$) resulting in the rate enhancement.[14]

Table 1. Products **6**–**8** prepared on mineral support under solvent-free microwave irradiation

Product	Time[a] (min)	Yield[b] (%)	Product	Time[a] (min)	Yield[b] (%)
6a	10 (10)	82 (22)	**7d**	10 (10)	92 (31)
6b	10 (10)	84 (23)	**7e**	8 (8)	90 (28)
6c	8 (8)	86 (21)	**8a**	5 (5)	76 (14)
6d	10 (10)	87 (25)	**8b**	5 (5)	77 (16)
6e	8 (8)	87 (29)	**8c**	4 (4)	79 (17)
6f	12 (12)	76 (18)	**8d**	5 (5)	75 (15)
6g	12 (12)	78 (19)	**8e**	4 (4)	81 (19)
6h	12 (12)	81 (20)	**8f**	6 (6)	70 (11)
6i	10 (10)	83 (26)	**8g**	6 (6)	71 (13)
6j	8 (8)	85 (27)	**8h**	6 (6)	73 (15)
7a	10 (10)	91 (23)	**8i**	5 (5)	72 (16)
7b	10 (10)	84 (29)	**8j**	4 (4)	78 (15)
7c	8 (8)	87 (26)			

[a] Microwave irradiation time (power=560 W). Parentheses show the time for oil-bath heating at 90 °C.
[b] Yield of isolated and purified product. Parentheses show yield obtained using oil-bath heating.

2. Conclusion

In summary, we have developed original, mineral supported syntheses of various potentially pharmaceutically useful benzoxazine-2-thiones from readily and widely available salicylaldehyde thiosemicarbazones under solvent-free MW irradiation. The present high yielding, expeditious and eco-friendly conversions lead to synthetically readily manipulable products, which may find application in the synthesis of compounds of this class.

3. Experimental

3.1. General

An unmodified domestic MW oven (Kenstar, Model MWO 9808, operating at 2450 MHz) was used at an output of 560 W for all the experiments. 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 using the same solvent and internal reference. Mass spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyser. All chemicals used were reagent grade. Silica gel-G was used for TLC.

3.2. 3,4-Dihydro-4-hydrazino-2*H*-benz[*e*]-1,3-oxazine-2-thiones 6. General procedure

To a solution of salicylaldehyde 4-arylthiosemicarbazone **1** (5.0 mmol) in a small amount of dichloromethane (10 mL) was added montmorillonite K-10 clay (7.5 g), mixed thoroughly and dried under reduced pressure. The contents were taken in a 100 mL conical flask and subjected to MW irradiation at 560 W for 2 min. The reaction mixture was then thoroughly mixed outside the MW oven for 2 min and again irradiated for another 2 min. This intermittent irradiation-mixing cycle was repeated for the total irradiation time (Table 1). After completion of the reaction as indicated by TLC (hexane–AcOEt, 8:2, v/v), the product was extracted with dichloromethane (3×50 mL), the extract was filtered and the filtrate was evaporated under reduced pressure to leave the crude product which was recrystallised from ethanol to obtain an analytically pure sample of **6**.

3.2.1. Compound 6a. Yellowish needles (1.11 g, 82%), mp 171–172 °C; ν_{max} (KBr) 3362, 3005, 1595, 1578, 1450 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS, 400 MHz) δ: 3.05 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.74 (d, 1H, J=8 Hz, 4-H), 7.18–7.87 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS, 100 MHz) δ: 78.6, 113.1, 114.2, 118.4, 120.3, 122.5, 129.0, 129.6, 130.2,150.0, 166.2, 191.9. MS (*m*/*z*): 271 (M^+). Analysis found: C, 61.68; H, 4.67; N, 15.72%. Calcd for $C_{14}H_{13}N_3OS$: C, 61.97; H, 4.83; N, 15.49%.

3.2.2. Compound 6b. Yellowish needles (1.47 g, 84%), mp 185–187 °C; ν_{max} (KBr) 3365, 3018, 1596, 1580, 1453 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 3.07 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.75 (d, 1H, J=8.0 Hz, 4-H), 7.29 (d, 1H, J=9.0 Hz, 8-H), 7.90 (dd, 1H, J=9.0, 2.4 Hz, 7-H), 8.22 (d, 1H, J=2.4 Hz, 5-H), 7.16–7.84 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 78.7, 113.1, 114.3, 118.6, 120.1, 122.5, 129.2, 129.8, 130.6, 150.1, 166.3, 192.0. Mass (*m*/*z*): 349 (M^+). Analysis found: C, 47.76; H, 3.32; N, 11.79%. Calcd for $C_{14}H_{12}BrN_3OS$: C, 48.01; H, 3.45; N, 12.00%.

3.2.3. Compound 6c. Yellowish needles (1.84 g, 86%), mp 195–198 °C; ν_{max} (KBr) 3370, 3025, 1598, 1583, 1460 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 3.09 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.78 (d, 1H, J=8.0 Hz, 4-H), 7.88 (d, 1H, J=2.5 Hz, 7-H), 8.17 (d, 1H, J=2.5 Hz, 5-H), 7.18–7.86 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 78.9, 113.2, 114.5, 118.6, 120.3, 122.6, 129.4, 130.1, 130.9, 150.2, 166.5, 192.1. Mass (*m*/*z*): 427 (M^+). Analysis found: C, 38.91; H, 2.69; N, 9.98%. Calcd for $C_{14}H_{11}Br_2N_3OS$: C, 39.18; H, 2.58; N, 9.79%.

3.2.4. Compound 6d. Yellowish needles (1.33 g, 87%), mp 178–179 °C; ν_{max} (KBr) 3368, 3028, 1600, 1582, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 3.08 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.77 (d, 1H, J=8.1 Hz, 4-H), 7.31 (d, 1H, J=9.2 Hz, 8-H), 7.91 (dd, 1H, J=9.2, 2.5 Hz, 7-H), 8.23 (d, 1H, J=2.5 Hz, 5-H), 7.15–7.86 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 78.8, 113.2, 114.2, 118.7, 120.3, 122.5, 129.1, 129.9, 130.8, 150.3, 166.5, 192.1. Mass (*m*/*z*): 305 (M^+). Analysis found: C, 55.19; H, 3.79; N, 13.89%. Calcd for $C_{14}H_{12}ClN_3OS$: C, 54.99; H, 3.96; N, 13.74%.

3.2.5. Compound 6e. Yellowish needles (1.48 g, 87%), mp 189–191 °C; ν_{max} (KBr) 3375, 3030, 1605, 1586, 1462 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 3.11 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.80 (d, 1H, J=8.1 Hz, 4-H), 7.91 (d, 1H, J=2.6 Hz, 7-H), 8.20 (d, 1H, J=2.6 Hz, 5-H), 7.20–7.88 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 79.1, 113.3, 114.7, 118.7, 120.5, 122.7, 129.6, 130.5 131.3, 150.4, 166.7, 192.2. Mass (*m*/*z*): 339 (M^+). Analysis found: C, 49.16; H, 3.10; N, 12.57%. Calcd for $C_{14}H_{11}Cl_2N_3OS$: C, 49.42; H, 3.26; N, 12.35%.

3.2.6. Compound 6f. Yellowish needles (1.08 g, 76%), mp 175–176 °C; ν_{max} (KBr) 3360, 3010, 1592, 1575, 1452 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.31 (s, 3H, Me), 3.03 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.70 (d, 1H, J=7.9 Hz, 4-H), 7.14–7.85 (m, $8H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.2, 78.5, 113.0, 114.0, 118.3, 120.2, 122.3, 128.8, 129.5, 130.2, 150.0, 166.1, 191.7. Mass (*m/z*): 285 (M^+). Analysis found: C, 62.88; H, 5.18; N, 14.95%. Calcd for $C_{15}H_{15}N_3OS$: C, 63.13; H, 5.30; N, 14.73%.

3.2.7. Compound 6g. Yellowish needles (1.42 g, 78%), mp 187–189 °C; ν_{max} (KBr) 3362, 3015, 1595, 1578, 1450 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.32 (s, 3H, Me), 3.06 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.72 (d, 1H, J=8.0 Hz, 4-H), 7.27 (d, 1H, J=9.0 Hz, 8-H), 7.88 (dd, 1H, J=9.0, 2.4 Hz, 7-H), 8.21 (d, 1H, J=2.4 Hz, 5-H), 7.14–7.80 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.3, 78.6, 113.0, 114.1, 118.4, 120.0, 122.3, 129.0, 129.8, 130.5, 150.0, 166.2, 191.8. Mass (*m/z*): 363 (M^+). Analysis found: C, 49.66; H, 3.89; N, 11.36%. Calcd for $C_{15}H_{14}BrN_3OS$: C, 49.46; H, 3.87; N, 11.54%.

3.2.8. Compound 6h. Yellowish needles (1.79 g, 81%), mp 198–201 °C; ν_{max} (KBr) 3363, 3028, 1595, 1580, 1458 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.33 (s, 3H, Me), 3.07 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.75 (d, 1H, J=8.0 Hz, 4-H), 7.86 (d, 1H, J=2.5 Hz, 7-H), 8.16 (d, 1H, J=2.5 Hz, 5-H), 7.16–7.83 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.4, 78.7, 113.0, 114.4, 118.5, 120.1, 122.3, 129.2, 130.0, 131.1, 150.0, 166.3, 192.0. Mass (*m/z*): 441 (M^+). Analysis found: C, 40.35; H, 2.79; N, 9.69%. Calcd for $C_{15}H_{13}Br_2N_3OS$: C, 40.65; H, 2.96; N, 9.48%.

3.2.9. Compound 6i. Yellowish needles (1.32 g, 83%), mp 170–171 °C; ν_{max} (KBr) 3365, 3025, 1602, 1579, 1460 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.34 (s, 3H, Me), 3.06 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.74 (d, 1H, J=8.1 Hz, 4-H), 7.30 (d, 1H, J=9.2 Hz, 8-H), 7.90 (dd, 1H, J=9.2, 2.5 Hz, 7-H), 8.21 (d, 1H, J=2.5 Hz, 5-H), 7.16–7.81 (m, 4H, 4-$MeOC_6H_4$). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.3, 78.6, 113.1, 114.0, 118.5, 120.1, 122.4, 129.0, 129.7, 130.6, 150.1, 166.3, 192.0. Mass (*m/z*): 319 (M^+). Analysis found: C, 56.05; H, 4.22; N, 13.28%. Calcd for $C_{15}H_{14}ClN_3OS$: C, 56.33; H, 4.41; N, 13.14%.

3.2.10. Compound 6j. Yellowish needles (1.50 g, 85%), mp 183–185 °C; ν_{max} (KBr) 3371, 3032, 1600, 1585, 1464 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 2.36, (s, 3H, Me), 3.08 (br s, 3H, $NHNH_2$, exchanges with D_2O), 6.77 (d, 1H, J=8.1 Hz, 4-H), 7.90 (d, 1H, J=2.6 Hz, 7-H), 8.18 (d, 1H, J=2.6 Hz, 5-H), 7.16–7.84 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.4, 78.8, 113.1, 114.6, 118.5, 120.4, 122.5, 129.4, 130.6, 131.1, 150.2, 166.6, 192.1. Mass (*m/z*): 353 (M^+). Analysis found: C, 50.98; H, 3.79; N, 11.99%. Calcd for $C_{15}H_{13}Cl_2N_3OS$: C, 50.86; H, 3.70; N, 11.86%.

3.3. 2*H*-Benz[*e*]-1,3-oxazine-2-thiones 7. General procedure

The procedure followed was the same as described above for the synthesis of **6** except that the starting material in this case was **1**, R^3=H, instead of **1**, R^3=aryl (Ar), for **6** (Table 1). Compounds **7a**, **7c**, **7f**, **7g**, **7h**, **7i**, and **7j** are known and their characterisation data agreed well with those reported in the literature.[23]

3.3.1. Compound 7b. Yellow needles (1.01 g, 84%), mp 163–165 °C; ν_{max} (KBr) 3015, 1595, 1579, 1450 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 7.31 (d, 1H, J=9.5 Hz, 8-H), 7.95 (dd, 1H, J=9.5, 2.6 Hz, 7-H), 8.23 (d, 1H, J=2.6 Hz, 5-H), 8.50 (s, 1H, 4-H). ^{13}C NMR (DMSO-d_6/TMS) δ: 114.3, 123.2, 125.4, 127.3, 138.1, 150.2, 166.3, 192.2. Mass (*m/z*): 241 (M^+). Analysis found: C, 39.41; H, 1.59; N, 5.90%. Calcd for C_8H_4BrNOS: C, 39.69; H, 1.67; N, 5.79%.

3.3.2. Compound 7d. Yellow needles (0.91 g, 92%), mp 158–159 °C; ν_{max} (KBr): 3032, 1602, 1584, 1458 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 7.33 (d, 1H, J=9.5 Hz, 8-H), 7.98 (dd, 1H, J=9.5, 2.6 Hz, 7-H), 8.27 (d, 1H, J=2.6 Hz, 5-H), 8.51 (s, 1H, 4-H). ^{13}C NMR (DMSO-d_6/TMS) δ: 114.9, 125.2, 127.5, 135.1, 138.5, 150.4, 166.4, 192.2. Mass (*m/z*): 197 (M^+). Analysis found: C, 48.86; H, 2.00; N, 7.21%. Calcd for C_8H_4ClNOS: C, 48.62; H, 2.04; N, 7.09%.

3.3.3. Compound 7e. Yellow needles (1.04 g, 90%), mp 170–172 °C; ν_{max} (KBr) 3028, 1603, 1582, 1460 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 7.93 (d, 1H, J=2.6 Hz, 7-H), 8.21 (d, 1H, J=2.6 Hz, 5-H), 8.53 (s, 1H, 4-H). ^{13}C NMR (DMSO-d_6/TMS) δ: 115.1, 125.3, 134.6, 135.3, 138.6, 150.6, 166.6, 192.3. Mass (*m/z*): 231 (M^+). Analysis found: C, 41.11; H, 1.21; N, 6.20%. Calcd for $C_8H_3Cl_2NOS$: C, 41.40; H, 1.30; N, 6.04%.

3.4. 3,4-Dihydro-2*H*-benz[*e*]-1,3-oxazine-2-thiones 8. General procedure

An intimate mixture of **6** (2.5 mmol) and $CuSO_4$–Al_2O_3 (4.4 g, 2.5 mmol of $CuSO_4{\cdot}5H_2O$) was taken in a 100 mL conical flask and subjected to MW irradiation at 560 W for 1 min. The reaction mixture was then thoroughly mixed outside the MW oven for 2 min and again irradiated for another 1 min. This intermittent irradiation-mixing cycle was repeated for the total irradiation time (Table 1). After completion of the reaction as indicated by TLC (hexane–AcOEt, 9:1, v/v), the product was extracted with dichloromethane (3×25 mL) and the extract was evaporated under reduced pressure to leave the crude product which was recrystallised from ethanol to obtain an analytically pure sample of **8**.

3.4.1. Compound 8a. Yellow needles (0.46 g, 76%), mp 162–163 °C; ν_{max} (KBr) 3012, 1598, 1579, 1455 cm^{-1}. ^1H NMR (DMSO-d_6/TMS, 400 MHz) δ: 6.59 (d, 1H, J=13 Hz, axial H of CH_2), 6.64 (d, 1H, J=13 Hz, equatorial H of CH_2), 7.14–7.80 (m, $9H_{arom}$). ^{13}C NMR (DMSO-d_6/TMS, 100 MHz) δ: 64.3, 112.9, 114.0, 118.3, 120.2, 122.3, 128.9, 129.7, 130.1, 149.9, 166.0, 191.8. Mass (*m/z*): 241 (M^+). Analysis found: C, 69.40; H, 4.42; N, 5.98%. Calcd for $C_{14}H_{11}NOS$: C, 69.68; H, 4.59; N, 5.80%.

3.4.2. Compound 8b. Yellowish needles (0.61 g, 77%), mp 173–174 °C; ν_{max} (KBr) 3025, 1600, 1584, 1460 cm^{-1}. ^1H NMR (DMSO-d_6/TMS) δ: 6.60 (d, 1H, J=13.0 Hz, one of CH_2), 6.65 (d, 1H, J=13.0 Hz, one of CH_2), 7.28 (d, 1H, J=9.0 Hz, 8-H), 7.90 (dd, 1H, J=9.0, 2.4 Hz, 7-H), 8.19 (d,

1H, J=2.4 Hz, 5-H), 7.15–7.81 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 64.4, 113.0, 114.2, 118.5, 120.3, 122.5, 128.8, 129.4, 130.1, 150.0, 166.1, 191.9. Mass (m/z): 319 (M^+). Analysis found: C, 52.36; H, 3.00; N, 4.56%. Calcd for $C_{14}H_{10}BrNOS$: C, 52.51; H, 3.15; N, 4.37%.

3.4.3. Compound 8c. Yellowish needles (0.79 g, 79%), mp 182–184 °C; ν_{max} (KBr) 3032, 1602, 1586, 1465 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 6.61 (d, 1H, J=13.0 Hz, one of CH_2), 6.65 (d, 1H, J=13.0 Hz, one of CH_2), 7.86 (d, 1H, J=2.5 Hz, 7-H), 8.16 (d, 1H, J=2.5 Hz, 5-H), 7.16–7.83 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 64.5, 113.1, 114.2, 118.6, 120.5, 122.6, 128.9, 129.9, 130.6, 150.1, 166.2, 192.1. Mass (m/z): 399 (M^+). Analysis found: C, 42.00; H, 2.09; N, 3.26%. Calcd for $C_{14}H_9Br_2NOS$: C, 42.13; H, 2.27; N, 3.51%.

3.4.4. Compound 8d. Yellowish needles (0.52 g, 75%), mp 168–169 °C; ν_{max} (KBr) 3035, 1604, 1585, 1462 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 6.61 (d, 1H, J=13.0 Hz, one of CH_2), 6.67 (d, 1H, J=13.0 Hz, one of CH_2), 7.28 (d, 1H, J=9.0 Hz, 8-H), 7.92 (dd, 1H, J=9.0, 2.4 Hz, 7-H), 8.21 (d, 1H, J=2.4 Hz, 5-H), 7.16–7.83 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 64.5, 113.2, 114.3, 118.5, 120.4, 122.7, 128.9, 130.0, 135.2, 151.2, 166.2, 192.0. Mass (m/z): 275 (M^+). Analysis found: C, 61.18; H, 3.49; N, 5.29%. Calcd for $C_{14}H_{10}ClNOS$: C, 60.98; H, 3.66; N, 5.08%.

3.4.5. Compound 8e. Yellowish needles (0.63 g, 81%), mp 177–179 °C; ν_{max} (KBr) 3033, 1603, 1582, 1460 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 6.62 (d, 1H, J=13.0 Hz, one of CH_2), 6.67 (d, 1H, J=13.0 Hz, one of CH_2), 7.88 (d, 1H, J=2.5 Hz, 7-H), 8.18 (d, 1H, J=2.5 Hz, 5-H), 7.18–7.86 (m, 5H, Ph). ^{13}C NMR (DMSO-d_6/TMS) δ: 64.6, 113.2, 114.4, 118.6, 120.6, 122.8, 129.0, 130.2, 135.4, 151.3, 166.3, 192.1. Mass (m/z): 309 (M^+). Analysis found: C, 53.98; H, 2.79; N, 4.36%. Calcd for $C_{14}H_9Cl_2NOS$: C, 54.21; H, 2.92; N, 4.52%.

3.4.6. Compound 8f. Yellow needles (0.45 g, 70%), mp 150–151 °C; ν_{max} (KBr) 3018, 1595, 1576, 1460 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.30 (s, 3H, Me), 6.57 (d, 1H, J=13.0 Hz, one of CH_2), 6.62 (d, 1H, J=13.0 Hz, one of CH_2), 7.16–7.83 (m, 8H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.2, 64.2, 113.1, 114.2, 118.3, 120.4, 122.3, 128.7, 129.4, 130.0, 150.0, 166.0, 191.7. Mass (m/z): 255 (M^+). Analysis found: C, 70.28; H, 4.98; N, 5.28%. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49%.

3.4.7. Compound 8g. Yellow needles (0.59 g, 71%), mp 166–167 °C; ν_{max} (KBr) 3022, 1603, 1580, 1456 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.31 (s, 3H, Me), 6.58 (d, 1H, J=13.0 Hz, one of CH_2), 6.63 (d, 1H, J=13.0 Hz, one of CH_2), 7.27 (d, 1H, J=9.0 Hz, 8-H), 7.88 (dd, 1H, J=9.0, 2.4 Hz, 7-H), 8.18 (d, 1H, J=2.4 Hz, 5-H) 7.15–7.81 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.3, 64.2, 113.2, 114.3, 118.4, 120.6, 122.5, 128.9, 129.7, 130.4, 150.2, 166.2, 191.8. Mass (m/z): 333 (M^+). Analysis found: C, 54.14; H, 3.49; N, 4.35%. Calcd for $C_{15}H_{12}BrNOS$: C, 53.90; H, 3.62; N, 4.19%.

3.4.8. Compound 8h. Yellow needles (0.75 g, 73%), mp 181–183 °C; ν_{max} (KBr) 3035, 1598, 1583, 1465 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.32 (s, 3H, Me), 6.59 (d, 1H, J=13.0 Hz, one of CH_2), 6.63 (d, 1H, J=13.0 Hz, one of CH_2), 7.85 (d, 1H, J=2.5 Hz, 7-H), 8.15 (d, 1H, J=2.5 Hz, 5-H) 7.17–7.84 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.3, 64.3, 113.2, 114.2, 118.5, 120.7, 122.7, 128.8, 129.6, 130.5, 150.3, 166.3, 191.9. Mass (m/z): 411 (M^+). Analysis found: C, 43.78; H, 2.50; N, 3.55%. Calcd for $C_{15}H_{11}Br_2NOS$: C, 43.61; H, 2.68; N, 3.39%.

3.4.9. Compound 8i. Yellow needles (0.52 g, 72%), mp 161–162 °C; ν_{max} (KBr) 3038, 1603, 1585, 1470 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.33 (s, 3H, Me), 6.59 (d, 1H, J=13.0 Hz, one of CH_2), 6.65 (d, 1H, J=13.0 Hz, one of CH_2), 7.28 (d, 1H, J=9.0 Hz, 8-H), 7.90 (dd, 1H, J=9.0, 2.4 Hz, 7-H) 8.20 (d, 1H, J=2.4 Hz, 5-H), 7.17–7.83 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.4, 64.3, 113.2, 114.5, 118.5, 120.8, 122.6, 128.9, 130.2, 135.3, 150.3, 166.4, 191.9. Mass (m/z): 289 (M^+). Analysis found: C, 62.01; H, 4.09; N, 5.00%. Calcd for $C_{15}H_{12}ClNOS$: C, 62.17; H, 4.17; N, 4.83%.

3.4.10. Compound 8j. Yellow needles (0.63 g, 78%), mp 174–176 °C; ν_{max} (KBr) 3040, 1605, 1588, 1475 cm^{-1}. ^{1}H NMR (DMSO-d_6/TMS) δ: 2.34 (s, 3H, Me), 6.61 (d, 1H, J=13.0 Hz, one of CH_2), 6.65 (d, 1H, J=13.0 Hz, one of CH_2), 7.86 (d, 1H, J=2.5 Hz, 7-H) 8.17 (d, 1H, J=2.5 Hz, 5-H) 7.19–7.87 (m, 4H, 4-MeC_6H_4). ^{13}C NMR (DMSO-d_6/TMS) δ: 21.4, 64.4, 113.3, 114.4, 118.5, 120.9, 122.8, 129.1, 130.3, 135.4, 150.4, 166.5, 192.0. Mass (m/z): 323 (M^+). Analysis found: C, 55.28; H, 3.28; N, 4.49%. Calcd for $C_{15}H_{11}Cl_2NOS$: C, 55.57; H, 3.42; N, 4.32%.

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