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The first ionic liquid-promoted one-pot diastereoselective synthesis of 2,5-diamino-/2-amino-5-mercapto-1,3-thiazin-4-ones using masked amino/mercapto acids

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ABSTRACT

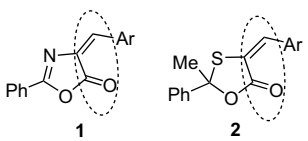
The first expeditious synthesis of 2,5-diamino-/2-amino-5-mercapto-1,3-thiazin-4-ones from masked and activated amino/mercapto acids, viz. 2-phenyl-1,3-oxazol-5-one or 2-methyl-2-phenyl-1,3-oxathiolan-5-one, aromatic aldehydes and thioureas using the ionic liquid [Bmim]Br as an environmentally benign reaction promoter is reported. The synthesis is highly diastereoselective and involves tandem Knoevenagel, Michael and ring transformation reactions in a one-pot procedure. The sequential reaction pathway is supported by the isolation of arylidene derivatives and their Michael adducts with thiourea, and quantitative conversion of the latter into the final products under the same reaction conditions.

1. Introduction

Over the past decade, industrial and academic researches have made powerful one-pot multi-component reaction (MCR) strategies as one of the most efficient and cost-effective tools for combinatorial synthesis in drug discovery processes.[1–7] Furthermore, owing to their green credentials, ionic liquids (ILs) have attracted considerable interest as environmentally benign reaction media[8–11] catalysts,[11–13] and reagents,[14,15] and are easy to recycle.[14,15]

1,3-Thiazines and their derivatives possess remarkable biological activities such as antibacterial, antitumour, insecticidal and fungicidal.[16–18] These are also known as anti-radiation agents and used as radiation-sickness drugs.[19] Furthermore, the antibiotic activity of cephalosporins is due to the presence of 1,3-thiazine nucleus.[20] As regards chemical viewpoint, 1,3-thiazines are important synthetic intermediates in organic syntheses.[21] Transformation of 1,3-thiazines into 6-alkyluracils and dihydropyrimidines has also been reported.[16b,22] Owing to their chemical and biological interest, syntheses of various 1,3-thiazine derivatives have been reported.[16,23] Literature records only few reports on the synthesis of 2-amino-1,3-thiazines starting from α,β-unsaturated carbonyl systems.[16b,17] To date, no effort has been made for the synthesis of 1,3-thiazines incorporating 2,5-diamino or 2-amino-5-mercapto functionalities although they appear as attractive scaffolds to be utilized for exploiting chemical diversity and generating a drug-like library to screen for lead candidates.

Recently, we have reported a convenient synthetic approach for 2-amino-1,3-thiazines from chalcones using a task specific ionic liquid (TSIL).[23o] Keeping the synthetic and pharmacological importance of $-NH_2$ and –SH groups in mind, we turned our attention to utilize such type of α,β-unsaturated carbonyl systems, which can introduce one additional $-NH_2$ and –SH groups into 2-amino-1,3-thiazines, which are the target molecules of the present investigation. For this purpose, we utilized α,β-unsaturated carbonyl building blocks **1** and **2** (Fig. 1) resulting from Knoevenagel condensation of aromatic aldehydes with masked and activated amino and mercapto acids, 2-phenyl-1,3-oxazol-5-one and 2-methyl-2-phenyl-1,3-oxathiolan-5-one, which lead to the desired functionalized 1,3-thiazines and are the cornerstones in the present successful synthetic strategy. The present work is an outcome of



1 2

Figure 1. Designed α,β-unsaturated carbonyl building blocks **1** and **2** for introducing amino and mercapto functionalities.

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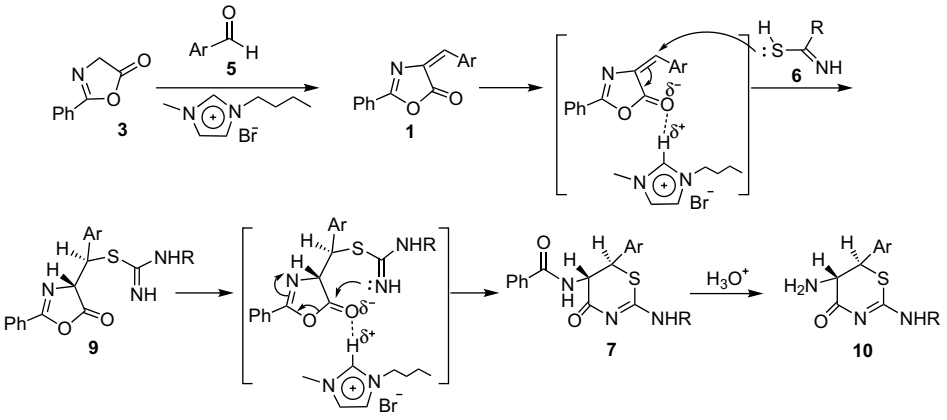


7,9,10	Ar	R	7,9,10	Ar	R
a	Ph	H	**e**	4-$MeOC_6H_4$	H
b	Ph	Ph	**f**	4-$MeOC_6H_4$	Ph
c	4-ClC_6H_4	H	**g**	4-$Me_2NC_6H_4$	H
d	4-ClC_6H_4	Ph	**h**	4-$Me_2NC_6H_4$	Ph

Scheme 1. Tentative mechanism for the formation of 2,5-diamino-1,3-thiazines **7** and **10**.

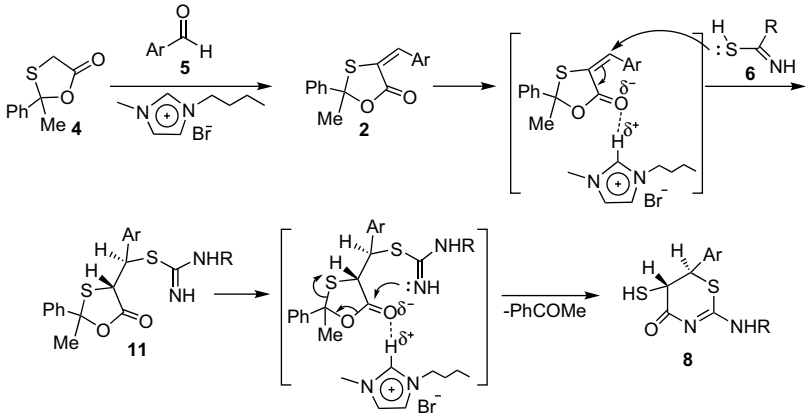
our interest in devising new stereoselective heterocyclization processes.[24]

In order to achieve our goal expeditiously, we relied upon significant advantages of the IL, [Bmim]Br as a green catalyst. Interestingly, the strategy involves the initial treatment of 2-phenyl-1,3-oxazol-5-one **3** or 2-methyl-2-phenyl-1,3-oxathiolan-5-one **4** with aromatic aldehydes **5** followed by reaction of in situ generated arylidenes **1** and **2** with thioureas **6** to afford 2,5-diamino-/2-amino-5-mercapto-1,3-thiazin-4-ones **7** and **8** in excellent yields (81–93%) with 94–99% trans diastereoselectivity (Schemes 1 and 2).

2. Results and discussion

In our initial attempt, 4-benzylidene-2-phenyloxazol-5-one **1** (Ar=Ph; mp 165–166 °C) and 4-benzylidene-2-methyl-2-phenyl-1,3-oxathiolan-5-one **2** (Ar=Ph; mp 187–189 °C) were obtained in 59–64% yield by [Bmim]Br-promoted Knoevenagel condensation of benzaldehyde with masked amino acid **3** and masked mercapto acid **4**, respectively, in acetonitrile at rt. In the next step, the isolated **1** (Ar=Ph) and **2** (Ar=Ph) were treated separately with thiourea **6** (R=H) in the presence of [Bmim]Br under similar reaction conditions to afford the target 1,3-thiazines **7a** and **8a**, respectively, in excellent yields (90% of **7a**, 86% of **8a**) and higher trans diastereoselectivity (96% of **7a**, 97% of **8a**).

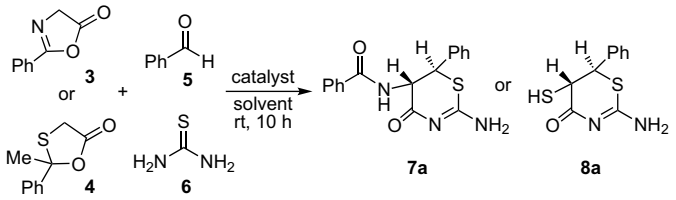
In order to make the synthesis of compounds **7** and **8** more convenient, we turned our attention to perform the above two steps in a one-pot procedure. Thus, we investigated the optimization of reaction conditions in regard with catalyst and solvent both. Herein, benzaldehyde **5** (Ar=Ph) and thiourea **6** (R=H) along with **3** and **4** were chosen as the model substrates for the synthesis of representative compounds **7a** and **8a**, respectively, and the reaction was performed at rt (Table 1). Several imidazolium-based ILs were tested by varying their alkyl substituents as well as the counter anion were tested and [Bmim]Br was found to be the most effective catalyst (Table 1, entry 4) in the present synthetic protocol. On increasing the cation size in the IL no appreciable effect on yields and diastereoselectivities was observed (Table 1, entries 4, 8 and 9). The

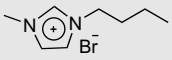
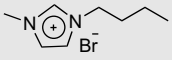
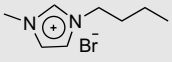
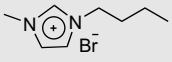
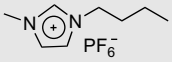
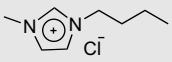
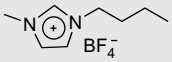
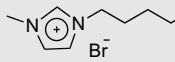
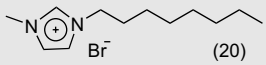
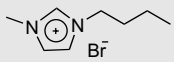
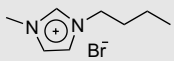


8,11	Ar	R	8,11	Ar	R
a	Ph	H	**e**	4-$MeOC_6H_4$	H
b	Ph	Ph	**f**	4-$MeOC_6H_4$	Ph
c	4-ClC_6H_4	H	**g**	4-$Me_2NC_6H_4$	H
d	4-ClC_6H_4	Ph	**h**	4-$Me_2NC_6H_4$	Ph

Scheme 2. Tentative mechanism for the formation of 2-amino-5-mercapto-1,3-thiazines **8**.

Table 1
Optimization of reaction conditions for the formation of representative compounds **7a** and **8a**[a]



Entry	Cat. (mol %)		Solvent	Yield[b] (%)		cis/trans[c]	
				7a	8a	7a	8a
1		(20)	THF	31	27	23:77	27:73
2		(20)	MeOH	63	59	35:65	38:62
3		(20)	CH_2Cl_2	41	38	45:55	49:51
4		(20)	CH_3CN	90	86	04:96	03:97
5		(20)	CH_3CN	72	78	41:59	43:57
6		(20)	CH_3CN	77	75	21:79	15:85
7		(20)	CH_3CN	65	69	20:80	27:73
8		(20)	CH_3CN	90	86	04:96	03:97
9		(20)	CH_3CN	90	86	04:96	03:97
10		(15)	CH_3CN	73	79	12:88	09:91
11		(25)	CH_3CN	90	86	04:96	03:97
12	—		CH_3CN	00	00	—	—

[a] For the experimental procedure, see Sections 4.3 and 4.6.
[b] Yield of isolated and purified products.
[c] As determined by ^{1}H NMR spectroscopy f the crude products.

optimum catalyst loading for [Bmim]Br was found to be 20 mol %. When the amount of the catalyst decreased to 15 mol % from 20 mol % relative to substrates, the yield and diastereoselectivity of products **7a** and **8a** reduced (Table 1, entry 10), but the use 25 mol % of the catalyst showed the same yield and diastereoselectivity (Table 1, entry 11) as shown in entry 4 of Table 1. However, the reaction did not occur without using the catalyst (Table 1, entry 12). Optimization of the solvents for the synthesis of **7a** and **8a** was also undertaken and it was found that amongst THF, CH_2Cl_2, MeOH and CH_3CN (Table 1, entries 1–4), the best solvent in terms of yield and diastereoselectivity was CH_3CN (Table 1, entry 4). It was noted that a higher reaction temperature, for example, in a refluxing solvent instead of rt, led to decreased diastereoselectivity without any appreciable effect on the yield. Next, in order to investigate the substrate scope of the reaction, a variety of aromatic aldehydes **5** and thioureas **6** were used employing the present optimized reaction conditions and the yields and diastereoselectivities were found to be consistently good (Table 2), the highest yield being 92% of **7** (Table 2, entry 9) and 93% of **8** (Table 2, entry 17) and the best trans diastereoselectivity being 98% of **7** (Table 2, entries 9 and 10) and 99% of **8** (Table 2, entry 17).

The present optimized synthesis is accomplished by stirring a mixture of 2-phenyl-1,3-oxazol-5-one **3** or 2-methyl-2-phenyl-1,3-oxathiolan-5-one **4**, aromatic aldehyde **5** and [Bmim]Br in CH_3CN at rt for 3–5 h followed by addition of thiourea **6** and further stirring of the reaction mixture at rt for 6–9 h. Isolation and purification by recrystallization afforded hitherto unknown 1,3-thiazines **7** and **8** in 81–93% yield with 94–99% diastereoselectivity (Table 2) in favour of the trans isomer as determined by ^{1}H NMR spectroscopy. In trans isomers **7** and **8**, 5-H and 6-H are axial as indicated by their coupling constant ($J_{5,6}$=9.1–9.3 Hz, J_{trans}; the cis coupling constant $J_{5,6}$=3.9 Hz). The absence of any measurable NOE between 5-H and 6-H also supports the trans stereochemistry of compounds **7**–**10**. The diastereomeric ratios in the crude isolates were checked by ^{1}H NMR spectroscopy to note any inadvertent alteration of these ratios during subsequent purification. The crude isolates of **7** and **8** were found to be a diastereomeric mixture containing 92–96% and 93–98% of the trans isomer, respectively. The transition states leading to the formation of Michael adducts **9** and **11** adopt the most stable *anti*-configuration about the ensuing C–C bond. Thus, **9** and **11** are formed with high *anti*-diastereoselectivity, which is also retained in **7** and **8** as the chiral carbons of **9** and **11** incorporated in products **7** and **8** are not involved in any bond breaking/formation (Schemes 1 and 2).

The formation of **7** and **8** may be tentatively rationalized by attack of more nucleophilic sulfur atom of thiourea **6** at the β-carbon of compounds **1** and **2** leading to the formation of adducts **9** and **11,** which undergo intramolecular nucleophilic attack of relatively more nucleophilic unsubstituted nitrogen of thiourea **6** at the carbonyl carbon (C-5) of oxazol-5-one and oxathiolan-5-one nuclei to yield **7** and **8**, respectively (Schemes 1 and 2). Compounds **7** on debenzoylation afforded compounds **10** in 88–94% yields and high diastereoselectivities (Scheme 1). Furthermore, the acetophenone, which was used to activate the mercaptoacetic acid to act as a masked mercapto acid, was removed during the course of reaction without requiring any protection–deprotection step yielding compounds **8** (Scheme 2). These conclusions are based on the observation that the representative intermediate compounds **9a**, **9c**, **9g** and **11a**, **11c**, **11g** could be isolated in 41–52% yields, respectively, and that these could be converted into the corresponding annulated products **7a**, **7c**, **7g** and **8a**, **8c**, **8g** in quantitative yield (Table 2).

3. Conclusion

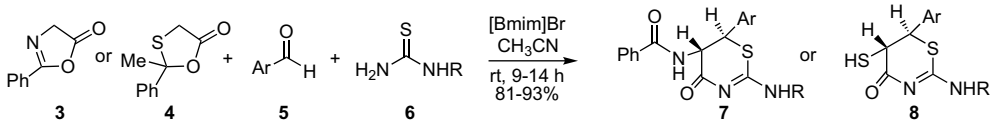
In summary, we have developed an original and practical method for the synthesis of potentially pharmaceutically important 2,5-diamino-/2-amino-5-mercapto-1,3-thiazin-4*H*-ones from readily available simple substrates. This one-pot diastereoselective synthesis is operationally simple, high yielding, and is performed at rt using the ionic liquid [Bmim]Br as an environmentally benign catalyst, and may find application in organic synthesis.

4. Experimental

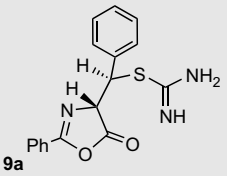
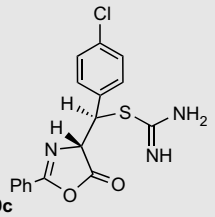
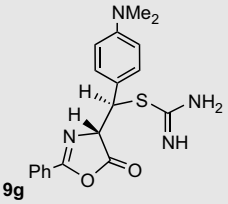
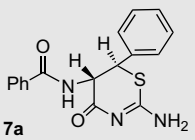
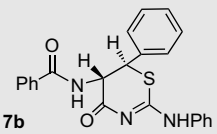
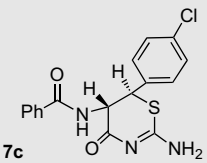
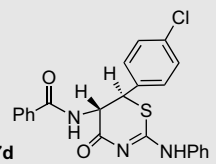
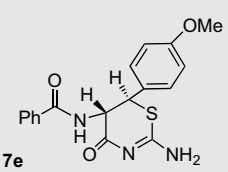
4.1. General

Melting points were determined by open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin–

Table 2
Ionic liquid [Bmim]Br-catalyzed synthesis of products **7**–**11**



3 **4** **5** **6** **7** **8**

Entry	Masked acids **3** and **4**	Products **7**–**11**	Time[a] (h)	Yield[b,c] (%)	cis/trans[d]
1	**3**	 **9a**	5	41	04:96
2	**3**	 **9c**	4	48	05:95
3	**3**	 **9g**	6	52	03:97
4	**3**	 **7a**	10	90	04:96
5	**3**	 **7b**	11	91	03:97
6	**3**	 **7c**	9	88	05:95
7	**3**	 **7d**	11	83	06:94
8	**3**	 **7e**	12	85	05:95

(*continued on next page*)

Table 2 (*continued*)

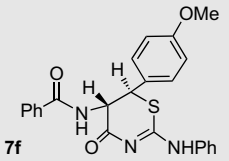
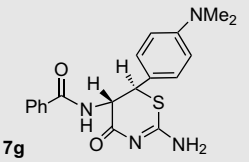
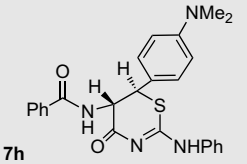
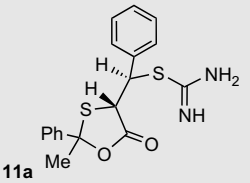
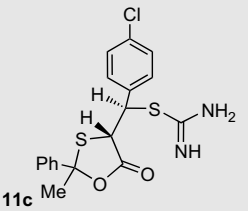
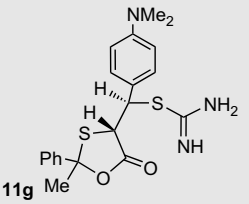
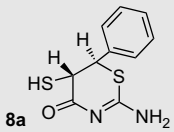
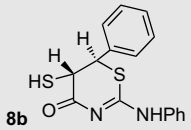
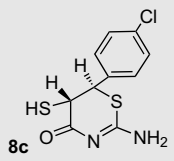
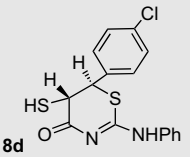
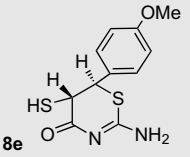
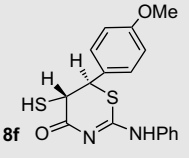
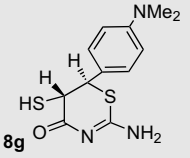
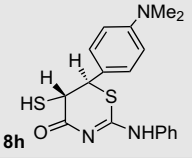
Entry	Masked acids **3** and **4**	Products **7**–**11**	Time[a] (h)	Yield[b,c] (%)	cis/trans[d]
9	**3**	 **7f**	11	92	02:98
10	**3**	 **7g**	11	89	02:98
11	**3**	 **7h**	14	81	06:94
12	**4**	 **11a**	5	44	03:97
13	**4**	 **11c**	4	47	01:99
14	**4**	 **11g**	6	51	02:98
15	**4**	 **8a**	10	86	03:97
16	**4**	 **8b**	12	92	03:97
17	**4**	 **8c**	9	93	01:99

Table 2 (*continued*)

Entry	Masked acids **3** and **4**	Products **7**–**11**	Time[a] (h)	Yield[b,c] (%)	cis/trans[d]
18	**4**	 **8d**	12	88	04:96
19	**4**	 **8e**	13	85	03:97
20	**4**	 **8f**	13	93	02:98
21	**4**	 **8g**	13	91	02:98
22	**4**	 **8h**	14	88	04:96

[a] Stirring time at room temperature.
[b] Yield of isolated and purified products.
[c] All compounds gave C, H and N analyses ±0.37% and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR and EIMS) data.
[d] As determined by ^{1}H NMR spectroscopy of the crude products.

Elmer 993 IR spectrophotometer, ^{1}H NMR spectra were recorded on a Bruker WM-40 C (400 MHz) FT spectrometer in DMSO-d_6+D_2O 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 spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyzer. All chemicals used were reagent grade and were used as received without further purification. Silica gel-G was used for TLC.

4.2. 4-Benzylidene-2-phenyloxazol-5-one 1 (Ar=Ph) and 4-benzylidene-2-methyl-2-phenyl-1,3-oxathiolan-5-one 2 (Ar=Ph): procedure

A mixture of 2-phenyl-1,3-oxazol-5-one **3** (2.0 mmol) or 2-methyl-2-phenyl-1,3-oxathiolan-5-one **4** (2.0 mmol), benzaldehyde (2.0 mmol) and [Bmim]Br (0.4 mmol) in 8 mL of CH_3CN was stirred at rt for 5 h. After completion of the reaction as indicated by TLC, water (10 mL) was added to the reaction mixture and stirred well. The yellowish precipitate thus obtained was washed with water to give the crude product, which was recrystallized from ethanol to afford an analytically pure sample of **1** or **2**, respectively, in 59–64% yield. After isolation of the product, the remaining aqueous layer containing the ionic liquid was washed with ether (2×10 mL) to remove any organic impurity and filtered. The filtrate was extracted with dichloromethane (3×10 mL), dried over $MgSO_4$ and evaporated under reduced pressure to afford [Bmim]Br, which was used in subsequent runs without further purification.

4.2.1. Compound **1** (Ar=Ph)

Yellowish solid (0.30 g, 59%), mp 134–136 °C. IR (KBr) ν_{max} 3011, 1778, 1601, 1579, 1448 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 7.14–7.60 (m, 11H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 110.5, 126.2, 126.8, 127.5, 128.3, 129.0, 130.7, 131.5, 132.2, 133.9, 161.5, 173.5. EIMS (*m*/*z*): 249 (M^+). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 77.41; H, 4.67; N, 5.48.

4.2.2. Compound **2** (Ar=Ph)

Yellowish solid (0.36 g, 64%), mp 112–114 °C. IR (KBr) ν_{max} 1775, 1605, 1585, 1452 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 2.03 (s, 3H, Me), 7.03–7.48 (m, 11H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 17.6, 35.3, 126.4, 127.1, 127.8, 128.4, 129.0, 129.8, 130.5, 131.2, 131.9, 132.6, 173.3. EIMS (*m*/*z*): 282 (M^+). Anal. Calcd for $C_{17}H_{14}O_2S$: C, 72.31; H, 5.00. Found: C, 72.01; H, 5.33.

4.3. 2-Amino-5-benzamido-1,3-thiazin-4H-ones 7: general procedure

A mixture of 2-phenyl-1,3-oxazol-5-one **3** (2.0 mmol), aldehyde **5** (2.0 mmol) and [Bmim]Br (0.4 mmol) in 10 mL of CH_3CN was stirred at rt for 3–5 h. Then, thiourea **6** (2.0 mmol) was added to the mixture and stirring was continued for further 6–9 h at rt. After completion of the reaction as indicated by TLC, 20 mL of water was added, and the product was extracted with EtOAc (3×20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under vacuum to afford the crude product, which was recrystallized from ethanol to afford a diastereomeric mixture

(>93:<07; in the crude products the ratio was >91:<09 as determined by ^{1}H NMR spectroscopy). The product on second recrystallization from ethanol furnished an analytically pure sample of a single diastereomer **7** (Table 2). On the basis of comparison of *J* values with the literature values,[23i,25–30] the trans stereochemistry was assigned to **6**, as the coupling constant ($J_{5,6}$=9.1 Hz) of the major trans isomer was higher than that for the minor cis diastereomer ($J_{5,6}$=3.9 Hz). The ionic liquid [Bmim]Br was recovered by following the same procedure as described in Section 4.2.

4.3.1. Compound **7a**

Yellowish solid (0.59 g, 90%), mp 211–213 °C. IR (KBr) ν_{max} 3343, 3308, 3013, 1745, 1685, 1601, 1582, 1452, 1315 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.06 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.61 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.22–7.81 (m, 10H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.2, 65.7, 127.1, 127.8, 128.5, 129.2, 130.5, 132.0, 132.9, 133.5, 162.8, 172.2, 174.5. EIMS (*m*/*z*): 325 (M$^+$). Anal. Calcd for $C_{17}H_{15}N_3O_2S$: C, 62.75; H, 4.65; N, 12.91. Found: C, 62.38; H, 4.91; N, 12.76.

4.3.2. Compound **7b**

Yellowish solid (0.73 g, 91%), mp 110–112 °C. IR (KBr) ν_{max} 3341, 3307, 3011, 1744, 1687, 1600, 1580, 1455, 1315 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.08 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.60 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.10–7.98 (m, 15H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.3, 65.9, 126.5, 127.1, 127.8, 128.4, 129.0, 129.7, 130.3, 131.0, 131.6, 132.3, 133.0, 133.8, 162.1, 172.4, 173.9. EIMS (*m*/*z*): 401 (M$^+$). Anal. Calcd for $C_{23}H_{19}N_3O_2S$: C, 68.81; H, 4.77; N, 10.47. Found: C, 69.05; H, 4.51; N, 10.72.

4.3.3. Compound **7c**

Yellowish solid (0.63 g, 88%), mp 174–176 °C. IR (KBr) ν_{max} 3348, 3310, 3009, 1747, 1686, 1603, 1583, 1459, 1316 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.09 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.68 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.05–7.51 (m, 7H$_{arom}$), 7.66–7.89 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.4, 65.8, 126.4, 127.7, 128.6, 129.3, 130.4, 131.5, 132.8, 133.4, 162.5, 172.0, 173.5. EIMS (*m*/*z*): 359, 361 (M, M+2). Anal. Calcd for $C_{17}H_{14}ClN_3O_2S$: C, 56.74; H, 3.92; N, 11.68. Found: C, 55.48; H, 4.17; N, 11.91.

4.3.4. Compound **7d**

Yellowish solid (0.72 g, 83%), mp 104–105 °C. IR (KBr) ν_{max} 3338, 3316, 3017, 1748, 1688, 1605, 1586, 1460, 1318 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.07 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.65 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.08–7.49 (m, 12H$_{arom}$), 7.62–7.91 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.7, 66.1, 126.3, 127.0, 127.7, 128.3, 129.1, 129.8, 130.4, 131.0, 131.7, 132.4, 133.0, 133.7, 162.3, 171.9, 173.3. EIMS (*m*/*z*): 435, 437 (M, M+2). Anal. Calcd for $C_{23}H_{18}ClN_3O_2S$: C, 63.37; H, 4.16; N, 9.64. Found: C, 63.69; H, 4.37; N, 9.55.

4.3.5. Compound **7e**

Yellowish solid (0.60 g, 85%), mp 126–128 °C. IR (KBr) ν_{max} 3341, 3310, 3011, 1743, 1682, 1601, 1581, 1455, 1313 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 3.76 (s, 3H, OMe), 5.03 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.60 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.03–7.90 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.6, 56.1, 66.0, 126.7, 127.3, 128.2, 129.0, 129.9, 131.4, 132.4, 133.5, 162.6, 172.2, 174.1. EIMS (*m*/*z*): 355 (M$^+$). Anal. Calcd for $C_{18}H_{17}N_3O_3S$: C, 60.83; H, 4.82; N, 11.82. Found: C, 60.59; H, 4.61; N, 11.91.

4.3.6. Compound **7f**

Yellowish solid (0.80 g, 92%), mp 86–87 °C. IR (KBr) ν_{max} 3343, 3310, 3013, 1744, 1683, 1599, 1582, 1457, 1314 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 3.73 (s, 3H, OMe), 5.09 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.66 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.07–7.88 (m, 14H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.8, 56.4, 65.9, 126.3, 127.0, 127.5, 128.2, 129.2, 129.8, 130.5, 131.2, 131.9, 132.5, 133.1, 133.9, 162.2, 172.5, 173.9. EIMS (*m*/*z*): 431 (M$^+$). Anal. Calcd for $C_{24}H_{21}N_3O_3S$: C, 66.80; H, 4.91; N, 9.74. Found: C, 67.08; H, 4.73; N, 9.92.

4.3.7. Compound **7g**

Yellowish solid (0.66 g, 89%), mp 178–180 °C. IR (KBr) ν_{max} 3341, 3315, 3008, 1743, 1682, 1601, 1581, 1455, 1313 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 2.95 (s, 6H, 2×Me), 5.02 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.61 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 6.98–7.86 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.0, 42.5, 43.4, 65.5, 127.0, 127.7, 128.4, 129.0, 129.7, 131.3, 132.1, 133.2, 162.1, 172.1, 173.5. EIMS (*m*/*z*): 368 (M$^+$). Anal. Calcd for $C_{19}H_{20}N_4O_2S$: C, 61.94; H, 5.47; N, 15.21. Found: C, 61.59; H, 5.62; N, 14.93.

4.3.8. Compound **7h**

Yellowish solid (0.76 g, 86%), mp 141–143 °C. IR (KBr) ν_{max} 3340, 3308, 3011, 1742, 1681, 1604, 1580, 1450, 1312 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 2.97 (s, 6H, 2×Me), 5.01 (d, 1H, $J_{5H,6H}$=9.1 Hz, 6-H), 5.67 (d, 1H, $J_{5H,6H}$=9.1 Hz, 5-H), 7.01–7.91 (m, 14H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.1, 42.7, 43.5, 65.5, 126.6, 127.2, 127.9, 128.6, 129.4, 130.0, 131.7, 131.4, 132.0, 132.7, 133.4, 134.1, 162.0, 172.3, 173.5. EIMS (*m*/*z*): 444 (M$^+$). Anal. Calcd for $C_{25}H_{24}N_4O_2S$: C, 67.54; H, 5.44; N, 12.60. Found: C, 67.88; H, 5.18; N, 12.49.

4.4. Isolation of Michael adducts 9a, 9c and 9g and their conversion into the corresponding annulated products 7a, 7c and 7g

The procedure followed was the same as described above for the synthesis of **7** (Section 4.3) except that the time of stirring in this case after addition of thiourea **6** was 1–2 h instead of 6–9 h for **7**. Adducts **9** were purified by silica gel column chromatography (hexane/EtOAc, 3:1) to obtain an analytically pure sample of **9** in 41–52% yield. The crude product was found to be a diastereomeric mixture containing 92–96% of the *anti* isomer as determined by ^{1}H NMR spectroscopy. Adducts **9** were assigned the *anti* stereochemistry as their ^{1}H NMR spectra exhibited higher values of coupling constant, $J_{NCH,SCH}$=9.3 Hz, than that of *syn* diastereomer, $J_{NCH,SCH}$=4.1 Hz.[23i,25–30] A mixture of the intermediate compound **9a**, **9c** or **9g** (2.0 mmol) and [Bmim]Br (0.4 mmol) in 8 mL of CH_3CN was stirred at rt for 4–7 h to give the corresponding products **7a**, **7c** or **7e** quantitatively. These were isolated and purified in the same way as described above in Section 4.3.

4.4.1. Compound **9a**

Yellowish solid (0.27 g, 41%), mp 189–191 °C. IR (KBr) ν_{max} 3342, 3147, 3050, 1775, 1605, 1583, 1450 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 6.65 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, SCH), 6.78 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, NCH), 7.05–7.79 (m, 10H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 60.3, 63.7, 126.1, 126.8, 127.5, 128.3, 129.0, 129.9, 130.7, 132.5, 159.2, 161.9, 173.2. EIMS (*m*/*z*): 325 (M$^+$). Anal. Calcd for $C_{17}H_{15}N_3O_2S$: C, 62.75; H, 4.65; N, 12.91. Found: C, 62.38; H, 4.81; N, 12.69.

4.4.2. Compound **9c**

Yellowish solid (0.34 g, 48%), mp 155–157 °C. IR (KBr) ν_{max} 3340, 3139, 3039, 1779, 1598, 1585, 1455 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 6.63 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, SCH), 6.80 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, NCH), 7.11–7.59 (m, 7H$_{arom}$), 7.63–7.85 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 60.7, 64.2, 126.3, 127.2, 128.3, 129.2, 130.1, 131.7, 132.8, 133.7, 159.5, 162.4, 172.9. EIMS (*m*/*z*): 359, 361 (M, M+2). Anal. Calcd for $C_{17}H_{14}ClN_3O_2S$: C, 56.74; H, 3.92; N, 11.68. Found: C, 56.49; H, 3.78; N, 11.89.

4.4.3. Compound **9g**

Yellowish solid (0.38 g, 52%), mp 161–163 °C. IR (KBr) ν_{max} 3340, 3143, 3031, 1771, 1608, 1579, 1458 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/

TMS) δ: 2.53 (s, 6H, 2×Me), 6.61 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, SCH), 6.74 (d, 1H, $J_{NCH,SCH}$=9.3 Hz, NCH), 7.19–7.75 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 42.5, 43.8, 60.5, 63.8, 126.2, 127.1, 127.9, 128.3, 129.5, 131.2, 131.9, 132.7, 159.0, 161.8, 173.3. EIMS (*m*/*z*): 368 (M^+). Anal. Calcd for $C_{19}H_{20}N_4O_2S$: C, 61.94; H, 5.47; N, 15.21. Found: C, 62.31; H, 5.59; N, 15.03.

4.5. 2,5-Diamino-1,3-thiazin-4*H*-ones 10: general procedure

Compound **7** (2.0 mmol) was refluxed in H_2SO_4/H_2O (15 mL, 4:3, v/v) for 45 min in an oil bath. The reaction mixture was cooled, the desired product **10** was precipitated by adding concentrated NH_4OH (specific gravity 0.88) under ice cooling and recrystallized from ethanol to obtain an analytically pure sample of **10**.

4.5.1. Compound *10a*

Yellowish solid (0.40 g, 90%), mp 143–145 °C. IR (KBr) ν_{max} 3347, 3311, 3050, 1751, 1605, 1583, 1451, 1310 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 4.91 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.49 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.01–7.51 (m, 5H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.5, 65.8, 126.5, 128.2, 130.5, 132.9, 162.7, 173.5. EIMS (*m*/*z*): 221 (M^+). Anal. Calcd for $C_{10}H_{11}N_3OS$: C, 54.28; H, 5.01; N, 18.99. Found: C, 54.61; H, 5.19; N, 18.83.

4.5.2. Compound *10b*

Yellowish solid (0.52 g, 88%), mp 121–123 °C. IR (KBr) ν_{max} 3341, 3308, 3051, 1745, 1601, 1581, 1456, 1312 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 4.94 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.51 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.11–7.65 (m, 10H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.1, 65.2, 126.2, 127.8, 128.5, 129.7, 130.9, 131.5, 132.2, 133.6, 162.5, 172.8. EIMS (*m*/*z*): 297 (M^+). Anal. Calcd for $C_{16}H_{15}N_3OS$: C, 64.62; H, 5.08; N, 14.13. Found: C, 64.29; H, 5.17; N, 13.99.

4.5.3. Compound *10c*

Yellowish solid (0.47 g, 93%), mp 151–153 °C. IR (KBr) ν_{max} 3338, 3313, 3048, 1750, 1608, 1586, 1449, 1311 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 4.90 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.53 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.01–7.31 (m, 2H$_{arom}$), 7.61–7.75 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.5, 65.5, 126.5, 128.2, 130.8, 132.9, 163.0, 173.1. EIMS (*m*/*z*): 255, 257 (M, M+2). Anal. Calcd for $C_{10}H_{10}ClN_3OS$: C, 46.97; H, 3.94; N, 16.43. Found: C, 46.73; H, 3.65; N, 16.61.

4.5.4. Compound *10d*

Yellowish solid (0.62 g, 89%), mp 88–89 °C. IR (KBr) ν_{max} 3344, 3312, 3055, 1748, 1599, 1581, 1457, 1308 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 4.93 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.48 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.02–7.55 (m, 7H$_{arom}$), 7.62–7.79 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.8, 65.1, 126.0, 127.8, 128.6, 130.9, 131.5, 132.2, 133.0, 133.8, 162.8, 172.6. EIMS (*m*/*z*): 331, 333 (M, M+2). Anal. Calcd for $C_{16}H_{14}ClN_3OS$: C, 57.91; H, 4.25; N, 10.68. Found: C, 58.28; H, 4.07; N, 10.91.

4.5.5. Compound *10e*

Yellowish solid (0.47 g, 94%), mp 103–105 °C. IR (KBr) ν_{max} 3340, 3310, 3045, 1753, 1598, 1579, 1450, 1313 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 3.78 (s, 3H, OMe), 4.88 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.49 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.12–7.65 (m, 4H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.3, 56.3, 66.4, 126.8, 128.9, 131.5, 132.8, 162.7, 173.0. EIMS (*m*/*z*): 251 (M^+). Anal. Calcd for $C_{11}H_{13}N_3O_2S$: C, 52.57; H, 5.21; N, 16.72. Found: C, 52.88; H, 5.47; N, 16.59.

4.5.6. Compound *10f*

Yellowish solid (0.59 g, 90%), mp 95–96 °C. IR (KBr) ν_{max} 3345, 3315, 3047, 1758, 1602, 1580, 1453, 1316 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 3.72 (s, 3H, OMe), 4.89 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.50 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.09–7.83 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.7, 56.1, 66.7, 126.2, 127.1, 127.9, 128.5, 129.4, 130.2, 131.1, 132.8, 163.1, 173.3. EIMS (*m*/*z*): 327 (M^+). Anal. Calcd for $C_{17}H_{17}N_3O_2S$: C, 62.36; H, 5.23; N, 12.83. Found: C, 62.62; H, 5.08; N, 12.71.

4.5.7. Compound *10g*

Yellowish solid (0.49 g, 92%), mp 161–163 °C. IR (KBr) ν_{max} 3339, 3309, 3042, 1752, 1591, 1585, 1452, 1309 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 2.92 (s, 6H, 2×Me), 4.92 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.47 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 7.01–7.63 (m, 4H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.4, 42.1, 43.4, 65.5, 126.3, 128.5, 130.6, 133.2, 162.8, 172.9. EIMS (*m*/*z*): 264 (M^+). Anal. Calcd for $C_{12}H_{16}N_4OS$: C, 54.52; H, 6.10; N, 21.19. Found: C, 54.28; H, 5.89; N, 21.37.

4.5.8. Compound *10h*

Yellowish solid (0.61 g, 88%), mp 117–119 °C. IR (KBr) ν_{max} 3342, 3317, 3049, 1755, 1606, 1576, 1456, 1314 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 2.96 (s, 6H, 2×Me), 4.90 (d, 1H, $J_{5H,6H}$=9.3 Hz, 6-H), 5.54 (d, 1H, $J_{5H,6H}$=9.3 Hz, 5-H), 6.95–7.88 (m, 9H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.1, 42.4, 43.3, 65.1, 126.1, 127.8, 128.5, 129.9, 130.5, 131.3, 132.5, 133.3, 163.2, 173.1. EIMS (*m*/*z*): 340 (M^+). Anal. Calcd for $C_{18}H_{20}N_4OS$: C, 63.50; H, 5.92; N, 16.46. Found: C, 63.27; H, 6.13; N, 16.22.

4.6. 2-Amino-5-mercapto-1,3-thiazin-4*H*-ones 8: general procedure

The procedure followed was the same as described above for the synthesis of **7** except that the starting material in this case was 2-methyl-2-phenyl-1,3-oxathiolan-5-one **4** instead of 2-phenyl-1,3-oxazol-5-one **3**. The crude product **8** obtained was recrystallized from ethanol to afford a diastereomeric mixture (>95:<05; in the crude products the ratio was >92:<08 as determined by ^{1}H NMR spectroscopy). To obtain analytically pure sample of a single diastereomer **8** (Table 2) and to assign the stereochemistry, the same procedure was adopted as described for **7** (Section 4.3). The ionic liquid [Bmim]Br was recovered by following the same procedure as described in Section 4.2.

4.6.1. Compound *8a*

Yellowish solid (0.41 g, 86%), mp 187–189 °C. IR (KBr) ν_{max} 3351, 3052, 1759, 2565, 1598, 1580, 1455, 1315 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.13 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.75 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.41–7.85 (m, 5H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.1, 65.6, 127.2, 129.1, 130.9, 132.1, 163.1, 172.9. EIMS (*m*/*z*): 238 (M^+). Anal. Calcd for $C_{10}H_{10}N_2OS_2$: C, 50.40; H, 4.23; N, 11.75. Found: C, 50.03; H, 4.11; N, 11.99.

4.6.2. Compound *8b*

Yellowish solid (0.58 g, 92%), mp 134–136 °C. IR (KBr) ν_{max} 3348, 3055, 1755, 2559, 1603, 1583, 1449, 1308 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.11 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.72 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.33–7.95 (m, 10H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.7, 66.4, 126.5, 127.2, 128.1, 128.8, 129.8, 130.4, 131.7, 133.2, 162.8, 173.1. EIMS (*m*/*z*): 314 (M^+). Anal. Calcd for $C_{16}H_{14}N_2OS_2$: C, 61.12; H, 4.49; N, 8.91. Found: C, 60.88; H, 4.77; N, 8.72.

4.6.3. Compound *8c*

Yellowish solid (0.51 g, 93%), mp 85–87 °C. IR (KBr) ν_{max} 3355, 3051, 1761, 2561, 1607, 1579, 1452, 1311 cm^{-1}. ^{1}H NMR (DMSO-d_6+D_2O/TMS) δ: 5.18 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.79 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.05–7.39 (m, 2H$_{arom}$), 7.59–7.66 (m, 2H$_{arom}$). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.8, 66.1, 127.5, 128.8, 131.2, 133.3, 162.5, 172.9. EIMS (*m*/*z*): 272, 274 (M, M+2). Anal. Calcd for $C_{10}H_9ClN_2OS_2$: C, 44.03; H, 3.33; N, 10.27. Found: C, 44.27; H, 3.19; N, 10.15.

4.6.4. Compound **8d**

Yellowish solid (0.61 g, 88%), mp 193–195 °C. IR (KBr) ν_{max} 3350, 3051, 1762, 2555, 1599, 1585, 1457, 1317 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 5.12 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.72 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.11–7.58 (m, 7H_{arom}), 7.65–7.85 (m, 2H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.5, 66.2, 126.3, 127.1, 127.8, 128.5, 129.3, 130.1, 130.9, 132.5, 163.2, 173.3. EIMS (*m*/*z*): 348, 350 (M, M+2). Anal. Calcd for $C_{16}H_{13}ClN_2OS_2$: C, 55.08; H, 3.76; N, 8.03. Found: C, 54.73; H, 3.89; N, 8.18.

4.6.5. Compound **8e**

Yellowish solid (0.46 g, 85%), mp 99–101 °C. IR (KBr) ν_{max} 3347, 3048, 1758, 2558, 1601, 1582, 1453, 1310 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 3.75 (s, 3H, OMe), 5.09 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.71 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.08–7.50 (m, 4H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.2, 56.7, 66.8, 127.2, 129.5, 130.9, 133.1, 162.8, 172.8. EIMS (*m*/*z*): 268 (M^+). Anal. Calcd for $C_{11}H_{12}N_2O_2S_2$: C, 49.23; H, 4.51; N, 10.44. Found: C, 49.51; H, 4.33; N, 10.57.

4.6.6. Compound **8f**

Yellowish solid (0.64 g, 93%), mp 123–125 °C. IR (KBr) ν_{max} 3351, 3053, 1752, 2561, 1605, 1577, 1448, 1316 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 3.77 (s, 3H, OMe), 5.15 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.76 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.12–7.91 (m, 9H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 36.1, 56.8, 66.5, 126.5, 127.2, 127.9, 128.8, 129.5, 130.3, 131.5, 132.9, 163.2, 172.6. EIMS (*m*/*z*): 344 (M^+). Anal. Calcd for $C_{17}H_{16}N_2O_2S_2$: C, 59.28; H, 4.68; N, 8.13. Found: C, 59.63; H, 4.79; N, 7.98.

4.6.7. Compound **8g**

Yellowish solid (0.51 g, 91%), mp 111–113 °C. IR (KBr) ν_{max} 3352, 3046, 1753, 2560, 1601, 1581, 1458, 1309 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 3.01 (s, 6H, 2×Me), 5.11 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.73 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.05–7.81 (m, 4H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.9, 42.8, 43.9, 66.5, 127.5, 128.9, 131.5, 133.4, 163.1, 173.3. EIMS (*m*/*z*): 281 (M^+). Anal. Calcd for $C_{12}H_{15}N_3OS_2$: C, 51.22; H, 5.37; N, 14.93. Found: C, 50.91; H, 5.53; N, 15.18.

4.6.8. Compound **8h**

Yellowish solid (0.63 g, 88%), mp 161–163 °C. IR (KBr) ν_{max} 3350, 3049, 1765, 2563, 1606, 1583, 1455, 1312 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 2.99 (s, 6H, 2×Me), 5.14 (d, 1H, $J_{5H,6H}$=9.2 Hz, 6-H), 5.78 (d, 1H, $J_{5H,6H}$=9.2 Hz, 5-H), 7.09–7.93 (m, 9H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 35.6, 42.5, 43.4, 66.2, 126.8, 127.6, 128.5, 129.7, 130.5, 131.3, 132.5, 133.1, 162.9, 172.7. EIMS (*m*/*z*): 357 (M^+). Anal. Calcd for $C_{18}H_{19}N_3OS_2$: C, 60.47; H, 5.36; N, 11.75. Found: C, 60.69; H, 5.21; N, 11.87.

4.7. Isolation of Michael adducts 11a, 11c and 11g and their conversion into the corresponding annulated products 8a, 8c and 8g

Following the same procedure as described above for the isolation of **9** (Section 4.4) analytically pure samples of **11a**, **11c** and **11g** were obtained in 44–51% yield and the stereochemistry was also assigned as *anti*. The crude product in this case was found to be a diastereomeric mixture containing 96–98% of the *anti* isomer as determined by ^1H NMR spectroscopy. Compounds **11a**, **11c** and **11g** were converted into the corresponding annulated products **8a**, **8c** and **8g** quantitatively, in the same way as described above in Section 4.4.

4.7.1. Compound **11a**

Yellowish solid (0.32 g, 44%), mp 108–110 °C. IR (KBr) ν_{max} 3339, 3135, 3038, 1781, 1602, 1587, 1457 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 2.23 (s, 3H, Me), 6.61 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, acyclicSCH), 6.77 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, cyclicSCH), 7.21–7.83 (m, 10H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 17.3, 34.8, 65.1, 68.8, 126.1, 126.7, 127.5, 128.6, 129.7, 130.5, 131.1, 132.9, 162.1, 173.5. EIMS (*m*/*z*): 358 (M^+). Anal. Calcd for $C_{18}H_{18}N_2O_2S_2$: C, 60.31; H, 5.06; N, 7.81. Found: C, 62.57; H, 5.23; N, 7.65.

4.7.2. Compound **11c**

Yellowish solid (0.37 g, 47%), mp 123–125 °C. IR (KBr) ν_{max} 3341, 3133, 3035, 1780, 1606, 1578, 1451 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 2.29 (s, 3H, Me), 6.59 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, acyclicSCH), 6.73 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, cyclicSCH), 7.08–7.49 (m, 7H_{arom}), 7.58–7.71 (m, 2H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 17.5, 34.7, 65.5, 69.5, 126.5, 127.3, 128.0, 128.8, 129.5, 130.2, 131.9, 133.7, 162.8, 172.9. EIMS (*m*/*z*): 392, 394 (M, M+2). Anal. Calcd for $C_{18}H_{17}ClN_2O_2S_2$: C, 55.02; H, 4.36; N, 7.13. Found: C, 55.29; H, 4.17; N, 7.30.

4.7.3. Compound **11g**

Yellowish solid (0.41 g, 51%), mp 140–142 °C. IR (KBr) ν_{max} 3340, 3132, 3031, 1778, 1596, 1575, 1449 cm^{-1}. ^1H NMR (DMSO-d_6+D_2O/TMS) δ: 2.23 (s, 3H, Me), 2.55 (s, 6H, 2×Me), 6.61 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, acyclicSCH), 6.78 (d, 1H, $J_{cyclicSCH,acyclicSCH}$=9.2 Hz, cyclicSCH), 7.21–7.89 (m, 9H_{arom}). ^{13}C NMR (DMSO-d_6/TMS) δ: 17.4, 34.5, 42.1, 43.9, 65.3, 69.6, 126.3, 127.0, 127.8, 128.5, 129.3, 130.1, 131.0, 132.3, 161.9, 172.6. EIMS (*m*/*z*): 401 (M^+). Anal. Calcd for $C_{20}H_{23}N_3O_2S_2$: C, 59.82; H, 5.77; N, 10.46. Found: C, 59.51; H, 5.53; N, 10.21.

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