A new way to quinazolines, perimidines and dibenzo[*d,f*][1,3]diazepines

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A synthesis of quinazolines, perimidines and dibenzo[d,f][1,3]diazepines is described. The method involves rearrangements following cyclisation of 2-anilino-2-methoxy-3-oxo-N-phenylbutanethioamides with aromatic 1,3- and 1,4-diamines.

Keywords: quinazolines, perimidines, fused 1,3-diazepines, rearrangements

Heterocyclic 1,3-diazines are very important and interesting systems as they frequently occur in natural or biologically active substances. Therefore the development of efficient methods for the elaboration of fused 1,3-diazine systems such as quinazolines, perimidines and dibenzodiazepines is an inviting ongoing challenge.

Quinazoline derivatives act as antibacterial and antimycobacterial,[1] anti-inflammatory,[2] and anxiolytic agents.[3] Their main interest emerges from their potent and very selective ability to inhibit the activity of kinases, making them useful or at least promising agents in anticancer therapies.[4]

The perimidine moiety is a strong chromophore; its derivatives find use as dyes with numerous applications. The synthesis and uses of new perimidines are now intensively studied. Novel photochromic materials, prospective for the production of photochromic optical lenses and light-driven molecular devices,[5a] near IR absorbing dyes (NIR dyes) as effective photoreceivers for diode lasers used in optical recording systems, laser printing systems and photodynamic therapies,[5b] and fluorescent indicators used for the sensitive optical detection of low-level water concentrations in various organic solvents,[5c] can be listed. However, most of the recent research in this field is protected by patents. Examples are claiming the syntheses of NIR dyes,[5d,e] and dyes for organic light-emitting devices.[5f] The well known black dye Sudan Black B is still studied.[5g] Perimidines have been also used in the diagnosis and treatment of neurodegenerative and amyloid diseases.[6a] 2-Aminoperimidine shows biological activity of various types such as interaction with cholinesterases[6b] and specific inhibition of bacterial NhaA Na^+/H^+ antiporters.[6c]

Numerous derivatives of 5*H*-dibenzo[*d,f*][1,3]diazepine exhibit antifungal, antibacterial, anticonvulsant and muscle relaxing activity and a variety of psychotropic effects.[7] There are examples of transition metal complexes with chiral 5*H*-dibenzo[*d,f*][1,3]diazepines serving as catalysts in asymmetric syntheses.[8]

In the past years, we have reported syntheses of pyrimidine, 1,3-diazepine, piperazine, pteridine, quinoxaline and pyridopyrazine systems[9] starting from 2-anilino-2-methoxy-3-oxo-*N*-phenylbutanethioamides (**1**). As a part of our ongoing interest in the study of the reactivity of **1** as synthons in obtaining various heterocyclic systems, we now present a new and easy approach to quinazoline, perimidine and dibenzodiazepine systems starting from the thioamides **1**.

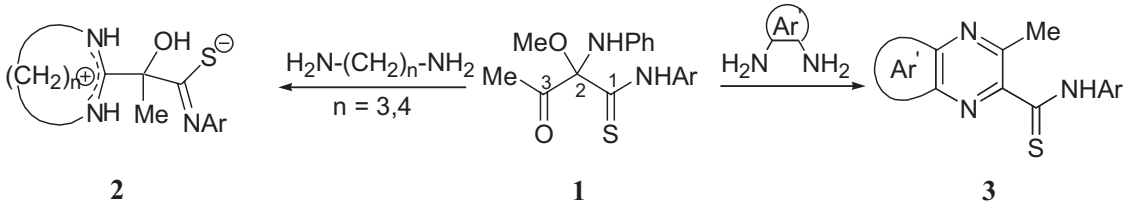
In a previous paper,[9a] we have reported an unusual rearrangement following cyclisation of 2-anilino-2-methoxy-3-oxo-*N*-phenylbutanethioamides (**1**) with aliphatic 1,3- and 1,4-diamines. The processes led to water soluble, very stable pyrimidinylium and 1,3-diazepinylium derivatives **2** (Scheme 1).

In connection with the studies described above we examined aromatic 1,3- and 1,4-diamines as potential reagents providing fused heterocyclic systems. We have recently reported that reactions of **1** with aromatic 1,2-diamines led to cyclocondensation products **3**. In these cases the building-blocks **1** behaved like 1,2-diketo system equivalents and 2,3-binucleophilic attack took place with the formation of aromatic systems **3** instead of rearrangement[9a] (Scheme 1).

Our present work focuses on an investigation of how change in the basicity of amine groups in 1,3- and 1,4-diamines affects the reaction pathway. We have already found that aliphatic 1,3- and 1,4-diamines are basic enough to keep the heterocyclic ring exclusively in the cationic form. We here extend our studies to search for novel routes to non-ionic fused heterocyclic systems

Results and discussion

We first attempted reactions of **1a,b** with 2-(aminomethyl)aniline in boiling methanol. We isolated compounds **4a**,**b** as yellow crystals in good yields (Scheme 2). ^{1}H NMR spectra of **4a**,**b** are in analogy to the spectra of zwitterionic compounds **2** and show a similar broad singlet of two NH protons in the heterocyclic ring. The anionic form of the thioamide moiety in **4a**,**b** is retained as there is no proton signals above 10 ppm, characteristic of a thioamide group. All these facts indicate that zwitterionic forms of **4a,b** are preferred. The structure of the product **4a** (in the form of its hydrochloride) was additionally confirmed by X-ray analysis,[10] which clearly showed the presence of a stabilised cationic centre C6 (Fig. 1). Bonds C6-N15 and C6-N7 are similar in length at 129.1 pm and 132.4 pm respectively.



2 **1** **3**

Scheme 1

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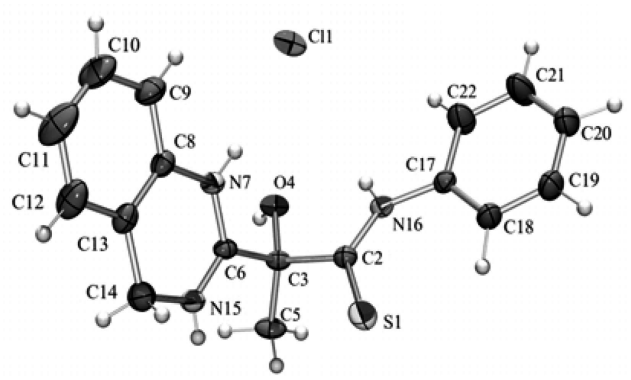


Fig. 1 Crystal structure of **4a** HCl.[10]

As an explanation of the formation of **4a,b** we assume binucleophilic attack on the C2 carbon atom of **1a,b** followed by rearrangement of the 3-oxobutanoic acid derivatives to 2-hydroxypropanoic acid derivatives.

Biphenyl-2,2′-diamine, on reaction with 2-anilino-2-methoxy-3-oxo-*N*-phenylbutanethioamides **1a–c**, gave crystalline products **5a–c** in good to excellent yields (Scheme 2). The NMR spectra suggested a different reaction route than in the case of 1,2-aromatic diamines with **1a–c** (Scheme 1). In the ^{13}C NMR spectra of **5a–c** signals of the sp^3 carbon atoms of the C-OH groups were observed at 78.6–78.4 ppm. The ^{1}H NMR spectra included singlets at 11.71–11.51 ppm, assigned to the thioamide proton. At 8.32–8.20 ppm singlets from only one NH proton of the heterocyclic ring were observed.

In the cases of aliphatic 1,3- and 1,4-diamines, the rearrangements of the 3-oxothiobutanoic acid derivatives **1** leads to 2-hydroxypropanoic acid derivatives **2** as very stable zwitterionic compounds.[9a] The obtained products **5a–c**, however, were not soluble in water, nor did they form easily soluble and well-crystallising hydrochlorides, as in the case of the zwitterionic compounds **2**. This suggested us that the structures of **5a–c** could be different. The structures of **5a–c** were solved with the help of X-ray measurements[12-15] on a sample of **5a**. A perspective view of the molecule of **5a** with the crystallographic atom numbering is shown in Figure 2.

The molecule has one chiral centre (at C4) and the two interconnected rings (C9–C14 and C15–C20) have a chirality axis. The absolute configuration is the same at the chirality centre and on the chirality axis. The structure is

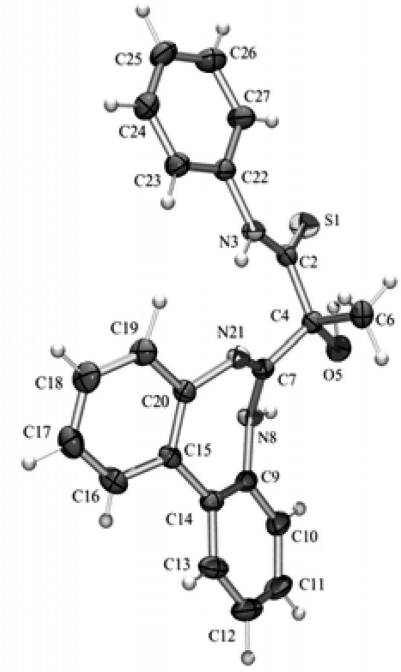
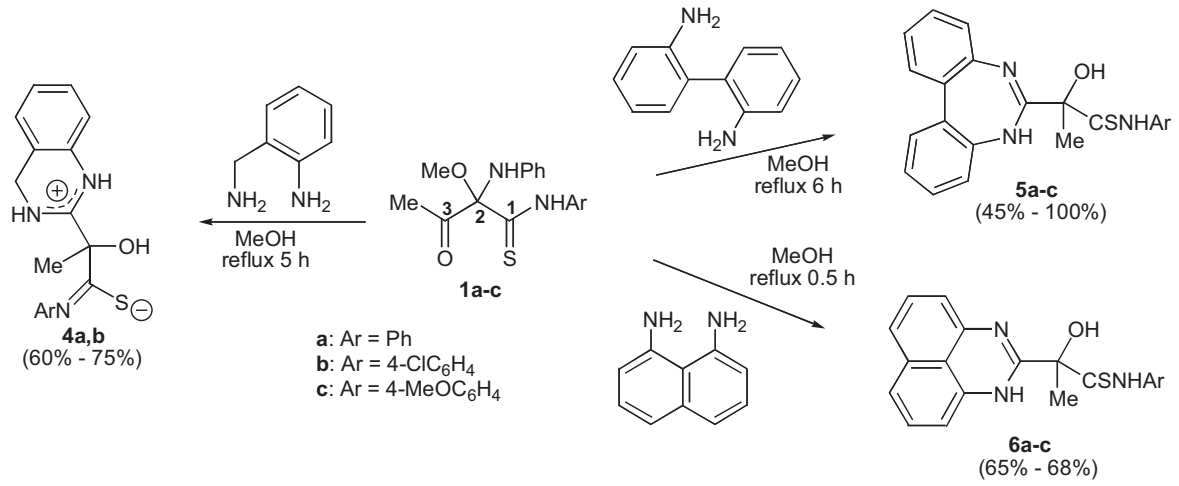


Fig. 2 Crystal structure of **5a**.

centrosymmetric (space group $P2_1/a$); in the unit cell there are two molecules which have (*R,R*) configuration and two with (*S,S*) configuration. The unsaturated seven-membered ring C7–N8–C9–C14–C15–C20–N21 has a boat conformation with N8 as the flap atom. It has two significantly different C–N bonds: one typical double bond (C7–N21, 127.6 pm) and one single bond (C7–N8 137.4 pm). This suggests that there is no carbocationic centre on C7, as in **4a**. In **4a** both C–N bonds (C6–N15 and C6–N7) are of similar length (129.1 pm and 132.4 pm). The C=S double bond is 165.4 pm. The overall conformation of the molecule is stabilised by several intramolecular close contacts (Table 1), of which the strongest is N8-H108...O5. There are no typical intermolecular hydrogen bonds.

As shown by the X-ay diffraction result, only two (one pair of enantiomers) of the four possible diastereoisomers of **5a** are present in the solid state. This observation also applies to the molecule in solution: only one set of signals is present in each of the ^{1}H and ^{13}C NMR spectra of **5a–c**.



Scheme 2

Table 1 Intramolecular hydrogen bonds in **5a**

D–H...A	D–A [pm]	H...A [pm]	D...H [pm]	∠D–H...A [°]
N3–H103..N21	281.4(4)	202(4)	94(4)	141(3)
O5–H105..S1	285.0(3)	191(5)	116(5)	135(4)
N8–H108..O5	258.3(4)	206(3)	85(4)	119(3)
C6–H206..N3	299.0(5)	275(4)	98(4)	95(2)
C6–H206..N21	288.4(5)	261(4)	98(4)	96(2)

The structure revealed by the X-ray experiment supports the idea that the reactions proceed *via* a similar rearrangement as in the case of aliphatic 1,3- and 1,4-diamines. Nevertheless there are important differences: products **5a–c** are non-zwitterionic, with one C=N double bond in the formed 1,3-diazine heterocyclic ring. In **5a–c** one of the NH protons of the zwitterionic heterocyclic rings of **2** or **4a,b** is moved to the nitrogen atom of the thioamide moiety and is observed at 11.71–11.51 ppm in the ^{1}H NMR. Treatment of the compounds **1a–c** with 1,8-naphthalene-diamine furnished the perimidines **6a–c** in good yields after 30 min reflux in methanol (Scheme 2). In the ^{13}C NMR spectra of **6a–c** the sp^3 carbon signals of the C–OH groups were observed at 80.3–75.1 ppm. In the ^{1}H NMR spectra, there were singlets at 12.60–10.57 ppm from the thioamide proton and at 8.92–8.84 ppm singlets from the NH proton of the heterocyclic ring were observed. The NMR spectra clearly showed that an analogous reaction pathway was followed to that leading to the dibenzo[*d,f*][1,3]diazepines **5a–c**.

The MS spectra of the dibenzo[*d,f*][1,3]diazepines (**5a–c**) and perimidines (**6a–c**) are consistent with their assigned structures: in all, significant peaks of the parent ions were observed.

The proposed mechanism of the reactions giving **5a–c** and **6a–c** is shown in Scheme 3 for the example of **5a–c**. The probable pathway the facile attack of the binucleophilic diamine on the electrophilic C2 centre of compounds **1a–c**. The resulting intermediate aminal may form the sterically constrained "pseudospiro" system, disubstituted at C2 by two electron-withdrawing groups. Intramolecular donor-acceptor interaction[13] between the sulfur atom of the thiocarbonyl group and the oxygen atom of the carbonyl group may promote protonation of the oxygen. The key step is then a sigmatropic rearrangement of a 3-oxothiobutanoic acid leading to a C-2 substituted 2-hydroxypropanoic thioanilide. In the process, one of the NH groups loses its proton and the double C=N bond of the 1,3-diazine ring is formed. The aromatic NH groups are not basic enough to prevent the proton shift and compounds **5a–c** and **6a–c** form as the neutral thioanilides.

To explain the difference in reactivity between aromatic 1,3- and 1,4-diamines and aromatic 1,2-diamines we assume that the distances between the amino groups in the 1,3- and 1,4-diamines are large enough to allow simultaneous attack of both amino groups on the C2 carbon atom of **1a–c**.

Our results indicate that the reactions of 2-anilino-2-methoxy-3-oxo-*N*-phenylbutanethioamides (**1a–c**) with aromatic 1,3- and 1,4-diamines lead to non-ionic systems of dibenzo[*d,f*][1,3]diazepines (**5a–c**) and perimidines (**6a–c**). The NH proton present in cationic form in the heterocyclic systems **2** and **4a,b** is shifted to the thioanilide moiety in compounds **5a–c** and **6a–c**, as a result of the lower basicity of the aromatic NH groups in the reacting diamines.

In conclusion: we have demonstrated new, experimentally straightforward and efficient syntheses of three heterocyclic systems: quinazolines (**4a–c**), dibenzo[*d,f*][1,3]diazepines (**5a–c**) and perimidines (**6a,b**), starting from 2-anilino-2-methoxy-3-oxo-*N*-phenylbutanethioamides (**1a–c**). The processes involve sigmatropic rearrangements of 3-oxothiobutanoic acid derivatives to 2-hydroxypropanoic acid derivatives. Easy leaving groups at the C-2 carbon atom of **1a–c** act as a carbonyl group equivalent, allowing various heterocyclic systems to be obtained in reactions with both aliphatic and aromatic diamines.

Experimental

Physical data: m.p.s were determined on an Electrothermal IA9000 digital apparatus. IR spectra were obtained on a Bruker IFS 48 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AMX 500 or 300 NMR spectrometer at room temperature. Chemical shifts are given in ppm. Yields are given for pure products.

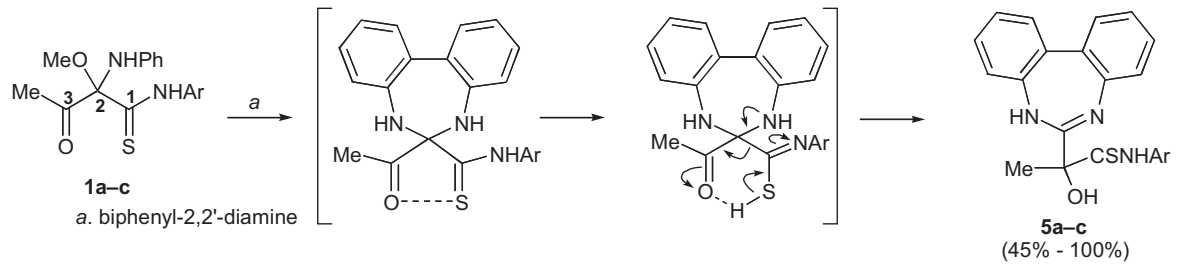
Details of the X-ray crystallographic determination of structure **5a** are summarised.[12] Spectral data for compounds **1a–c** and their preparations are described in our previous work.[16]

2-Hydroxy-2-(1',2',3',4'-tetrahydroquinazolin-2'-ylium-2'-yl)-1-aryliminopropane-1-thiolates (**4a,b**): *general procedure*

The corresponding 2-anilino-2-methoxy-3-oxobutanoic thioanilide (**1a–c**) (2.5 mmol) and 2-(aminomethyl)aniline (0.31 g, 2.5 mmol) were heated to reflux in MeOH (30 ml) for 5 h. The solution was then evaporated to dryness and the mixture was separated by column chromatography (SiO_2; $CHCl_3$). Removal of the solvent gave yellow oils which solidified on standing.

2-Hydroxy-2-(1',2',3',4'-tetrahydroquinazolin-2'-ylium-2'-yl)-1-phenyl-iminopropane-1-thiolate (**4a**): Yellow crystals (0.59 g, 75%), m.p. 94–95°C. IR (KBr): ν_{max} 3397, 2924, 1651 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ = 9.01 (s, 2 H, 2 NH), 7.68 (d, 2 H, J = 7.5 Hz), 7.39 (t, 2 H, J = 7.5 Hz), 7.20 (t, 1H, J = 7.5 Hz), 7.16–6.99 (m, 4 H, quinazoline), 4.61 (s, 2 H, CH_2), 1.75 (s, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ = 198.2 (CS), 160.5 (N–C–N), 141.4, 138.6, 128.5, 127.9, 125.8, 125.5, 124.3, 122.8, 119.3 and 119.3 (C arom), 77.6 (C-2), 43.7 (CH_2), 28.9 (CH_3). EIMS: *m/z* (%) = 175 (100, M$^+$–PhNCS–H), 133 (61, quinazolinylium), 106 (28), 77 (28, Ph$^+$). Anal. Calcd for $C_{17}H_{17}N_3OS$: C, 65.57; H, 5.50; N, 13.49. Found: C, 65.56; H, 5.50; N, 13.42%.

2-Hydroxy-2-(1',2',3',4'-tetrahydroquinazolin-2'-ylium-2'-yl)-1-(4-chlorophenylimino)propane-1-thiolate (**4b**): Yellow crystals (0.48 g, 60%), m.p. 150–151°C. IR (KBr): ν_{max} 3398, 2925, 1650 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 9.09 (s, 2 H, 2 NH), 7.51 (d, 2 H, J = 8.7 Hz, 4-chlorophenyl), 7.37 (d, 2 H, J = 8.7 Hz, 4-chlorophenyl), 7.20–7.00 (m, 4 H, quinazoline), 4.66 (s, 2 H, CH_2), 1.74 (s, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ 194.2 (CS), 162.2 (N-C-N), 144.4, 136.0, 128.1, 127.8, 126.0, 125.0, 124.4, 118.6 and 118.5 (C arom), 77.0 (C-2), 43.1 (CH_2), 28.1 (CH_3). EIMS: *m/z* (%) 175 (100, M$^+$–ClC_6H_4NCS–H), 133 (61, quinazolinylium), 106 (16), 111 (5, $ClC_6H_4^+$). Anal. Calcd



1a–c

a. biphenyl-2,2'-diamine

5a–c

(45% - 100%)

Scheme 3

for $C_{17}H_{16}ClN_3OS$: C, 59.04; H, 4.66; N, 12.15. Found: C, 59.06; H, 4.57; N, 12.11%.

N-Aryl-2-(5H-dibenzo[d,f][1,3]diazepin-6-yl)-2-hydroxypropanethioamides (**5a–c**): *general procedure*

The corresponding 2-anilino-2-methoxy-3-oxobutanoic acid thioanilide **1a–c** (3.0 mmol) and biphenyl-2,2′-diamine (0.55 g, 3.0 mmol) in MeOH (40 ml) was heated under reflux for 6 h. Evaporating of the solvent yielded the crude products quantitatively as dark yellow crystals, which were recrystallised from MeOH. Compound **5a** needed washing with a small amount of cold MeOH only. In the case of **5b,c** purification by column chromatography (SiO_2; $CHCl_3$: MeOH (30:1)) was necessary before crystallisation.

2-(5H-Dibenzo[d,f][1,3]diazepin-6-yl)-2-hydroxy-N-phenylpropanethioamide (**5a**): Yellow prisms (1.12 g, 100%), m.p. 111–112°C. IR (KBr): ν_{max} 3314, 3188, 3121, 1651, 1560, 1478, 1234 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 11.71 (s, 1 H, CSNH), 8.28 (s, 1 H, NH), 7.79 (dd, 2 H, *J* = 8.7, 1.2 Hz), 7.42 (t, 2 H, *J* = 7.8 Hz,), 7.30 (dt, 2 H, *J* = 7.6, 2.0 Hz), 7.28 (s, 1 H, OH), 7.24 (d, 1 H, *J* = 7.2 Hz), 7.17 (t, 2 H, *J* = 7.8 Hz), 7.08 (d, 1 H, *J* = 7.5 Hz), 7.02 (d, 2 H, *J* = 7.8 Hz), 6.73 (d, 1 H, *J* = 7.5 Hz), 1.92 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 199.7 (CS), 164.5 (N-C=N), 146.6, 146.1, 138.1, 133.8, 133.8, 129.9, 129.8, 129.1, 129.0, 128.7, 128.2, 127.0, 126.7, 125.2, 122.9 and 119.9 (C arom), 78.4 (C-2), 30.8 (CH_3). EIMS: *m/z* (%) 237 (100, M^+–PhNCS–H), 195 (95, M^+–PhNCS–CH_3CO), 168 (34, carbazolium), 135 (17, $PhNCS^+$), 77 (18, Ph^+), 43 (15, CH_3CO^+). Anal. Calcd for $C_{22}H_{19}N_3OS$: C, 70.75; H, 5.13; N, 11.25. Found: C, 70.81; H, 5.23; N, 11.42%.

N-(4-Chlorophenyl)-2-(5H-dibenzo[d,f][1,3]diazepin-6-yl)-2-hydroxypropanethioamide (**5b**): Yellow prisms (0.83 g, 68%), m.p. 113–115°C. IR (KBr): ν_{max} 3322, 3172, 1650, 1550, 1478, 1229 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 11.71 (s, 1 H, CSNH), 8.20 (s, 1 H, NH), 7.74 (d, 2 H, *J* = 9.0 Hz), 7.36 (d, 2 H, *J* = 9.0 Hz), 7.28 (dd, 2 H, *J* = 7.5, 1.8 Hz), 7.17–6.71 (m, 7 H), 1.89 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 200.2 (CS), 164.2 (N–C=N), 136.7, 132.2, 129.9, 129.1, 128.8, 128.2, 126.7, 125.3, 124.2 and 119.8 (C arom), 78.6 (C-2), 30.8 (CH_3). EIMS: *m/z* (%) 237 (100, M^+–PhNCS–H), 195 (98, M^+–PhNCS–CH_3CO), 169 (18, ClC_6H_4-NCS), 167 (31, carbazolium–H), 111 (9, $ClC_6H_4^+$), 43 (13, CH_3CO^+). Anal. Calcd for $C_{22}H_{18}ClN_3OS$: C, 64.78; H, 4.45; N, 10.30. Found: C, 64.86; H, 4.45; N, 10.17%.

2-(5H-Dibenzo[d,f][1,3]diazepin-6-yl)-2-hydroxy-N-(4-methoxyphenyl)propanethioamide (**5c**): Yellow prisms (0.54 g, 45%), m.p. 104–105°C. IR (KBr): ν_{max} 3325, 3233, 1660, 1511, 1478, 1249 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 11.51 (s, 1 H, CSNH), 8.32 (s, 1 H, NH), 7.66 (d, 2 H, *J* = 9.0 Hz), 7.28 (dd, 2 H, *J* = 7.5, 1.8 Hz), 7.24–6.98 (m, 6 H), 6.92 (d, 2 H, *J* = 9.0 Hz), 6.74 (s, 1 H, OH), 3.81 (s, 3 H, OCH_3), 1.90 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 199.1 (CS), 158.3 (N–C=N), 131.3, 129.9, 129.0, 128.2, 126.7, 125.4, 124.6, 122.7, 119.9 and 114.1 (C arom), 78.4 (C-2), 55.5 (OCH_3), 30.8 (CH_3). EIMS: *m/z* (%) 238 (87, M^+–$CH_3OC_6H_4$-NCS), 223 (25, M^+–$CH_3OC_6H_4$-NCS–CH_3), 195 (34, M^+–$CH_3OC_6H_4$-NCS–CH_3CO), 167 (57, carbazolium–H), 165 (100, $CH_3OC_6H_4$-NCS^+), 150 (57, C_6H_5O-NCS^+), 122 (72, $CH_3OC_6H_4$-NH^+), 43 (3, CH_3CO^+). Anal. Calcd for $C_{23}H_{21}N_3O_2S$: C, 68.46; H, 5.25; N, 10.41. Found: C, 68.24; H, 5.14; N, 10.45%.

N-Aryl-2-hydroxy-2-(1H-perimidin-2-yl)propanethioamides (**6a-c**): *general procedure*

The corresponding 2-anilino-2-methoxy-3-oxobutanoic acid anilide **1a–c** (3 mmol) and 1,8-naphthalenediamine (0.47 g, 3.0 mmol) in MeOH (50 ml) was heated under reflux for 0.5 h. Cooling the mixture to r.t. yielded green-brown crystals which were separated by suction after 24 h and recrystallised from MeOH.

2-Hydroxy-2-(1H-perimidin-2-yl)-N-phenylpropanethioamide (**6a**): Green-yellow needles (0.68 g (65%), m.p. 138–139°C. IR (KBr): ν_{max} 3387, 3337, 3125, 1635, 1235 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 12.30 (s, 1 H, CSNH), 8.84 (s, 1 H, NH), 7.82 (dd, 2 H, *J* = 8.5, 0.9 Hz), 7.40 (d, 2 H, *J* = 8.5 Hz), 7.27–7.22 (m, 2 H), 7.16–7.10 (m, 3 H), 6.80 (d, 2 H, *J* = 8.5 Hz), 6.26 (s, 1 H, OH), 1.86 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 199.4 (CS), 157.9 (N–C=N), 142.7, 138.5, 136.0, 135.4, 129.0, 128.9, 127.7, 127.0, 122.4, 122.1, 120.8, 119.7, 114.0 and 103.5 (C arom), 75.2 (C-2), 31.9 (CH_3). EIMS: *m/z* (%) 347 (39, M^+), 212 (100, M^+–C_6H_4NCS), 211 (92, M^+–C_6H_4NCS–H), 168 (34, perimidinium), 136 (5, $PhNHCS^+$), 77 (10, Ph^+). Anal. Calcd for $C_{20}H_{17}N_3OS$: C, 69.14; H, 4.93; N, 12.09. Found: C, 69.02; H, 4.96; N, 12.19%.

N-(4-Chlorophenyl)-2-hydroxy-2-(1H-perimidin-2-yl)propanethioamide (**6b**): Green-brown needles (0.78 g, 68%), m.p. 160–161°C. IR (KBr): ν_{max} 3345, 3295, 3111, 1634, 1247 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 10.57 (s, 1 H, CSNH), 7.91 (d, 2 H, *J* = 9.0 Hz), 7.49 (d, 2 H, *J* = 9.0 Hz), 7.11 (d, 2 H), *J* = 8.0 Hz, 7.01 (d, 2 H, *J* = 8.0 Hz), 6.57 (d, 2 H, *J* = 7.5 Hz), 1.83 (s, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ 201.6 (CS), 157.5 (N-C=N), 137.6, 134.9, 130.1, 128.3, 128.2, 125.4, 121.6 and 118.3 (C arom), 80.3 (C-2), 27.3 (CH_3). EIMS: *m/z* (%) 381 (30, M^+), 212 (80, M^+–ClC_6H_4-NCS), 169 (30, ClC_6H_4-$NHCS^+$), 140(14). Anal. Calcd for $C_{20}H_{16}ClN_3OS$: C, 62.90; H, 4.34; N, 11.00. Found: C, 62.90; H, 4.22; N, 10.89%.

2-Hydroxy-N-(4-methoxyphenyl)-2-(1H-perimidin-2-yl)propanethioamide (**6c**): Green-brown needles (0.74 g, 65%), m.p. 170–172°C. IR (KBr): ν_{max} 3381, 3330, 3125, 1635, 1238 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 12.60 (s, 1 H, CSNH), 8.92 (s, 1 H), 7.73 (d, 2 H, *J* = 9.0 Hz), 7.29–7.15 (m, 4 H), 6.95 (d, 2 H, *J* = 9.0 Hz), 6.80 (s, 1 H, NH), 3.83 (s, 3 H, OCH_3), 1.88 (s, 3 H, CH_3). ^{13}C NMR (DMSO-d_6): δ = 198.8 (CS), 158.2 (N–C=N), 135.5, 131.7, 128.9, 127.7, 124.0, 122.1, 120.7, 119.7, 114.1, 114.0, 103.5 and 103.4 (C arom), 75.1 (C-2), 55.5 (OCH_3), 31.9 (CH_3). EIMS: *m/z* (%) 377 (21, M^+), 212 (100, M^+–$CH_3OC_6H_4$-NCS), 166 (35, $CH_3OC_6H_4$-$NHCS^+$), 150 (22), 140(25), 104 (62), 77 (33, Ph^+). Anal. Calcd for $C_{21}H_{19}N_3O_2S$: C, 66.82; H, 5.07; N, 11.13. Found: C, 66.81; H, 4.96; N, 10.98%.

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12 Compound **5a** with formula $C_{22}H_{19}N_3OS$ crystallises in the monoclinic system, space group $P2_1/a$, with unit cell parameters a = 794.48(3), b = 1439.97(5), c = 1639.56(5) pm, β = 93.217(2)º, V = 1872.8(1) 10^6 pm^3, Z = 4. A total of 2774 independent reflections (R(int) = 0.098) were collected on a sample of size 0.35 × 0.20 × 0.15 mm using Kappa CCD diffractometer and MoKα radiation. The structure was solved by direct methods with SHELXS97[13] and refined by the full-matrix least-squares method on F^2 using SHELXL97[14] program. Final discrepancy indices for 1884 reflections with I>2σ(I) were equal R1 = 0.055, wR2 = 0.105 and R1 = 0.094, wR2 = 0.123 for all 2774 data. The final difference Fourier map of electron density was featureless with the largest peak and hole of 0.27 and $–0.23 \cdot 10^{-6}$ $e \cdot pm^{-3}$, respectively. All calculations and molecular graphics were done using the WinGX package.[15] The structural data were deposited at the Cambridge Crystallographic Data Centre. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk) under reference number CCDC 623593.
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