Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c4ob02207f

Catalyst-free synthesis of 2-aryl-1,2-dihydroquinazolin-4(1*H*)-thiones from 2-aminobenzothioamides and aldehydes in water†

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Received 17th October 2014,
Accepted 13th November 2014

DOI: 10.1039/c4ob02207f

www.rsc.org/obc

2-Dihydroquinazolin-4(1*H*)-thiones were prepared in up to excellent yields from 2-aminobenzothioamides and aldehydes. The reaction is carried out in water without the use of any catalyst or promoter. The sulfur-containing substrate can be obtained easily by thiation of the corresponding nitrile by solid sodium hydrosulfide.

Introduction

Quinazolinone alkaloids are an important class of substances with a wide range of biological activities such as thymidylate synthase inhibition[1] or antihypertensive effects.[2] A mentionable example is methaqualone with its hypnotic properties, which is now illicit and withdrawn due to its high addiction potential and widespread abuse.[3] Moreover, quinazolinones are important core structures of a variety of natural alkaloids like sclerotigenin[4] that shows antiinsectan properties (Fig. 1).[5] Various methodologies have been developed to obtain these lactam structures.[6] In contrast to the carbonyl group, thiolactams have different bond lengths, hydrogen bonding abilities and dipole moments.[7] Hence, the exchange of oxygen by sulfur results in different effects on the biological activities.

For example, A. D. Cale *et al.* reported an increased protection against histamine-induced lethality by rocastine compared to the lactam analogue.[8] The group of M. Leost showed that 9-bromo-thiopaullone has a decreased inhibition of GSK3 but an increased CDK1 and CDK5 inhibition.[9] In contrast, E. J. Lien and co-workers observed convulsions and high lethal toxicity (LD_{50} = 23 mg kg^{-1} for azocane-2-thione).[10] In addition, sulfur containing compounds offer a variety of synthetic advantages and are important intermediates to gain more complex structures, for example in the total synthesis of cobalamin.[11]

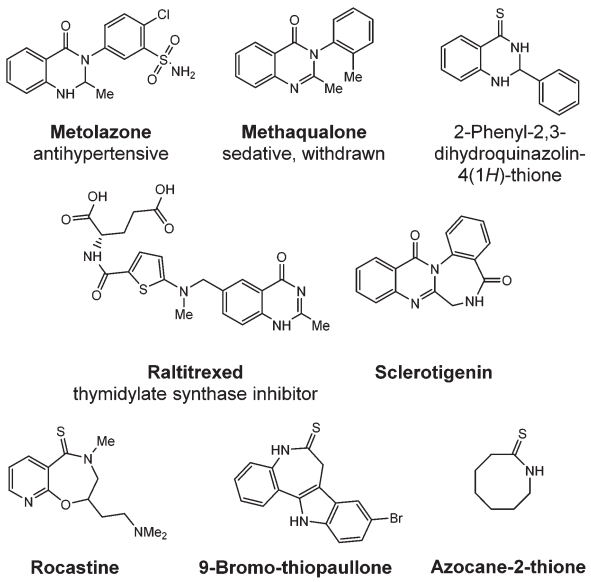

Fig. 1 Selected quinazolinone derivatives and bioactive thiolactams.

Regarding the synthesis, the preparation of thiolactams and thioamides is usually limited to thiation of carbonyl compounds with Lawesson's reagent[12] (LR), gaseous hydrogen sulfide[13] or phosphorus pentasulfide.[14] However, the strong foul smell and high toxicity of these reagents are still problematic. Methods to obtain quinolinthione and quinazolinthione derivatives by thiation with LR of the carbonyl compounds have been reported.[15] However, if more than one carbonyl functionality is present in the molecule, these thiation procedures encounter selectivity problems.[16] Zheng and co-workers reported the synthesis of quinazolindithiones by capturing CS_2 at room temperature.[17] In this work, we have focused on a different pathway to gain access to quinazo-

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†Electronic supplementary information (ESI) available: Analytical data, NMR spectra, and general information. See DOI: 10.1039/c4ob02207f

linthiones starting from thioamides; thus the sulfur is already attached to the substrates.

Results and discussion

Recently, we reported the hydrolysis of anthranilonitrile and the subsequent condensation–cyclization with aldehydes to 2,3-dihydroquinazolinones.[18] Our aim was now to investigate whether the 2-aminobenzothioamide reacts in the same manner as the anthranilamide[19] to yield 2,3-dihydroquinazoline-4(1*H*)-thione. To synthesize the anthranilothioamide, we applied the procedure of A. Manaka and M. Sato for the thiolysis of aromatic nitriles using NaHS as the hydrogen sulfide precursor.[20] Thus, H_2S is generated *in situ* and the use of gaseous sulfur could be avoided. The method could be improved by increasing the reaction time to 72 hours. This can be explained by the electron-withdrawing properties of the amino function in the *ortho* position (Table 1). We observed drastically decreased yields when we increased the temperature.

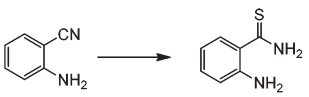
The reaction works well for electron-poor 2-amino-benzonitriles. Nitriles with additional electron donating substituents such as methyl (1i) or methoxy (1j) did not give the desired thioamides (Table 2).

With a range of thioamides in hand, the crucial point was the stability of the *o*-amino-thioamide and the thiolactam in the reaction mixture. Also it was questionable whether the thioamide may undergo the nucleophilic attack on the imine. As per the requirements of green chemistry and sustainable development, water was applied as a green and cheap solvent as our first choice. To our delight, the reaction proceeds very well at 100 °C with excellent yield (88%). Notably, no additional base or Lewis-acid was needed for this transformation. A possible reaction pathway is shown in Scheme 1. The reaction consisted of tandem condensation–cyclization reactions.

Mass analysis and elemental analysis show the presence of sulfur in the compound. 1D- and 2D-NMR spectroscopies were used to prove the successful cyclisation. The thiolactam proton appears to be low-field shifted (9.97 ppm, DMSO-d_6) compared to the corresponding quinazolinone proton (8.29 ppm, DMSO-d_6).[21]

Subsequently, we investigated the limiting effects of substituents on the thioamide as well as on the aldehydes. The substrate scope is shown in Table 3. Fortunately, many different aldehydes give the desired thiolactams in good to excellent

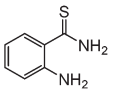
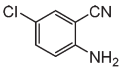
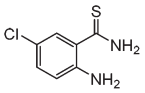
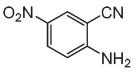
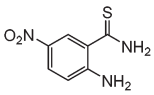
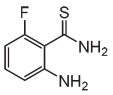
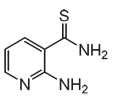
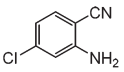
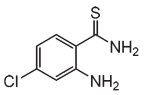
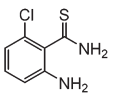
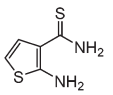
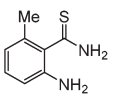
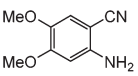
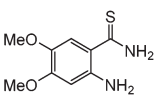
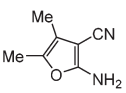
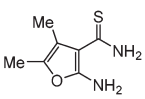
Table 1 Optimization for the synthesis of anthranilothioamide[a]



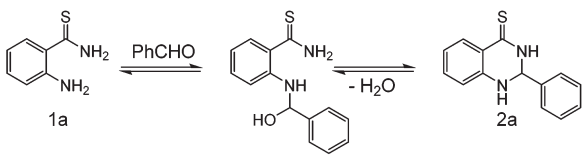
Entry	Time (h)	Temp. (°C)	Yield[b] (%)
1	1.5	20	5
2	48	20	77
3	72	20	88
4	16	130	5
5	20	130	—

[a] Reaction conditions: 0.5 mmol nitrile, 2 eq. NaHS·H_2O, 1 eq. $MgCl_2$, 2 ml DMF. [b] Isolated yields.

Table 2 Synthesis of anthranilothioamides[a]

No.	Nitrile	Thioamide	Yield[b] (%)
1a			88
1b			96
1c			80
1d			97
1e			93
1f			78
1g			62
1h			85
1i			0
1j			0
1k			0

[a] Reaction conditions: 0.5 mmol nitrile, 2 eq. NaHS·H_2O, 1 eq. $MgCl_2$, 2 ml DMF, 20 °C, 72 h. [b] Isolated yields.



Scheme 1 Dihydroquinazolinthione synthesis from 2-amino-benzothioamide.

Table 3 Synthesis of dihydroquinazolinthiones[a]

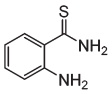
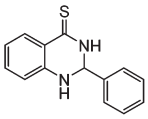
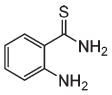
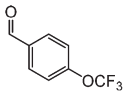
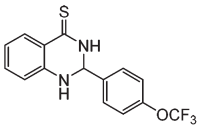
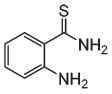
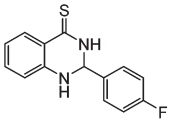
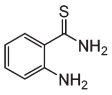
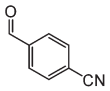
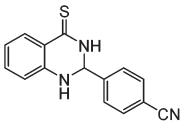
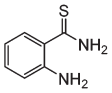
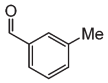
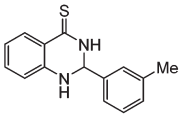
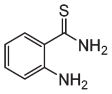
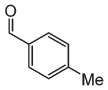
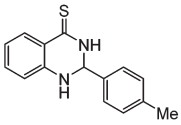
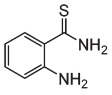
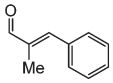
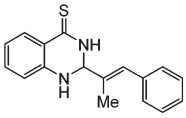
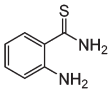
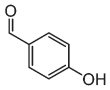
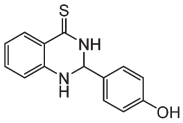
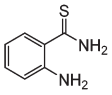
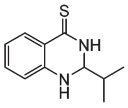
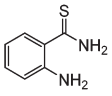
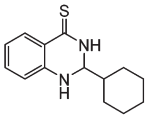
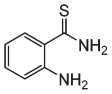
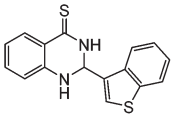
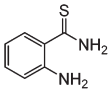
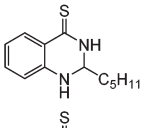
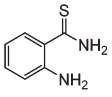
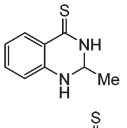
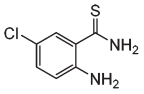
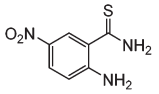
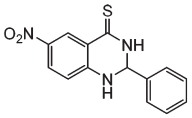
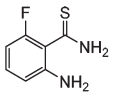
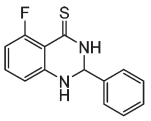
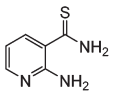
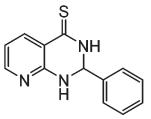
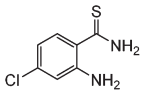
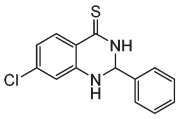
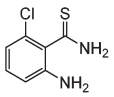
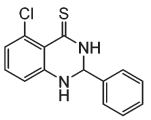
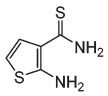
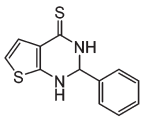
No.	Thioamide	Aldehyde	Product	Yield[b] (%)
2a				84
2b				74
2c				75
2d				80
2e				82
2f				93
2g				71
2h				75
2i				82
2j				84
2k				46
2l				85
2m				57
2n				68

Table 3 *(Contd.)*

No.	Thioamide	Aldehyde	Product	Yield[b] (%)
2o				79
2p				88
2q				73
2r				57
2s				—[c]
2t				—[c]

[a] Reaction conditions: 0.5 mmol thioamide, 1 eq. aldehyde, 1 mL H_2O, 100 °C, 24 h. [b] Isolated yields. [c] The compound decomposes during purification.

yields. The reaction proceeds very well with aromatic and aliphatic aldehydes. Besides, electron-withdrawing substituents on the benzothioamide-ring decrease the yield whereas the strongest effect can be observed with chlorine attached in the *para* position to the thioamide (**2s**). Additionally, the reaction works fine for more complex aldehydes such as 2-methyl-cinnamyl-aldehyde (**2g**) or benzo[*b*]-thiophene-2-carboxaldehyde (**2k**). To our delight, the reaction proceeds well also with acetaldehyde to give 2-methylquinazolinthione (**2m**). This structural element can also be found in *e.g.* methaqualone and metolazone. The significant NH-signals of the isolated compounds appear in the same pattern in ^{1}H-NMR spectroscopy compared to the model substance. Therefore we conclude the successful cyclisation for all the presented thiolactams. Pure compounds were obtained by recrystallization from ethyl acetate/hexane. Compounds (**2s**) and (**2t**) could be found on GC/MS analysis of the crude reaction mixture but decomposed during the purification process.

Conclusions

In summary, we have described a convenient and facile procedure for the synthesis of dihydroquinazolinthiones from 2-aminobenzothioamide with aldehydes. The reactions took place in water without the need for a Lewis-acid or other catalysts and represent a convenient alternative to the thiation of lactams with Lawesson's reagent or P_4S_{10}. Various different aldehydes and thioamides were shown to be suitable for this tandem condensation–cyclisation reaction. The desired substances were easily purified by recrystallization. Besides, the thioamide substrates can be obtained by the thiolysis of 2-aminobenzonitriles with NaHS in DMF.

Experimental section

General

Distilled water was used as the solvent. All commercially available chemicals were used without further purification. NMR-data were recorded on Bruker AVANCE 300 III, Bruker AVANCE 250 III, Bruker ARX 300 and Bruker ARX 400 spectrometers. ^{1}H- and ^{13}C-spectra were referenced to the residue solvent signals in the deuterated solvent. The signals were characterized as broad (br), singlet (s), doublet (d), doublet of doublet (dd), triplet (t), triplet of triplet (tt), quartet (q) and multiplet (m). Gas-chromatography-mass analysis was carried out using an Agilent HP-5890 with an Agilent HP-5973 Mass Selective Detector (EI) and an HP-5-capillary column using helium as the carrier gas. An elemental analysis was performed on a Flash EA 112, and IR-spectra were recorded on a Nicolet 380 FT-IR spectrometer. IR-bands were classified as strong (s),

medium (m) and weak (w). Column-chromatography was performed using Merck silica-gel 60 (0.043–0.06 mm) and distilled solvents were used.

Representative procedure for the synthesis of 2-aminobenzothioamides (1a). 27 mmol 2-aminobenzonitrile (3.18 g), 27 mmol $MgCl_2$ (2.57 g) and 54 mmol $NaHS{\cdot}H_2O$ (3.99 g) and 70 ml dry DMF are placed in a round-bottom flask which is subsequently sealed by a needle-pierced septum. The reaction mixture is stirred at 20 °C for 72 hours. The conversion is monitored by TLC. After complete conversion, the reaction is quenched with distilled water and the solution is extracted three times with ethyl acetate. The aqueous phase is acidified with 10 ml of 10% HCl and again extracted with ethyl acetate. The combined organic phases are washed with saturated NaCl-solution and dried over Na_2SO_4. The crude product was purified by column chromatography (hexane–ethyl acetate 8 : 2) yielding 3.58 g (88%) 2-aminobenzothioamide as a yellow solid. M.P.: 121–122 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 9.63 (1H, br *s*, $CSNH_2$), 9.29 (1H, br *s*, $CSNH_2$), 7.16 (1H, *dd*, ^3J = 7.8 Hz, ^4J = 1.5 Hz, CH(6)), 7.09 (1H, *ddd*, ^3J = 8.6 Hz, ^3J = 7.2 Hz, ^4J = 1.6 Hz, CH(4)), 6.71 (1H, *dd*, ^3J = 8.2, ^4J = 1.0 Hz, CH(3)), 6.52 (1H, *ddd*, ^3J = 7.8 Hz, ^3J = 7.2 Hz, ^4J = 1.2 Hz, CH(5)), 6.17 (2H, br *s*, NH_2) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 200.1 (C═S), 147.0 (C_{quart}(2)), 130.6 (CH(4)), 126.9 (CH(6)), 123.6 (C_{quart}(1)), 116.4 (CH(5)), 115.0 (CH(3)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 152 ([M]$^+$, 79), 119 (100), 118 (18), 92 (27), 65 (21); IR: (ATR) $\tilde{\nu}$ = 3407 (w), 3282 (w), 3054 (w), 1603 (m), 1454 (m), 1408 (m), 1404 (m), 1284 (m), 906 (s), 751 (s), 737 (s) cm^{-1}; Elemental analysis: Calcd for: $C_7H_8N_2S$: C, 55.24; H, 5.30; N, 18.40; S, 21.06. Found: C, 54.81; H, 5.30; N, 18.32; S, 21.16.

2-Amino-5-chlorobenzothioamide (1b). MP.: 143–144 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 9.78 (1H, br *s*, $CSNH_2$), 9.44 (1H, br *s*, $CSNH_2$), 7.16 (1H, *d*, ^3J = 2,5 Hz, CH(6)), 7.12 (1H, *dd*, ^3J = 8,6 Hz, ^4J = 2,5 Hz, CH(4)), 6.73 (1H, *d*, ^3J = 8.7 Hz, CH (3)), 6.22 (2H, br *s*, NH_2) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 198.7 (C═S), 145.8 (C_{quart}(2)), 130.2 (CH(4)), 126.3 (CH(6)), 124.6 (C_{quart}(5)), 118.4 (C_{quart}(1)), 118.0 (C_{quart}(3)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 188 ([M]$^+$, ^{37}Cl, 30), 186 ([M]$^+$, ^{35}Cl, 56), 155 (23), 154 (39), 153 (100), 152 (80), 125 (24), 118 (23), 90 (23), 63 (21), 61 (20), 52 (18); IR: (ATR) $\tilde{\nu}$ = 3411 (w), 3404 (w), 3220 (w), 3021 (w), 1618 (w), 1477 (m), 1431 (m), 1155 (m), 930 (m), 820 (s), 738 (s), 658 (s), 557 (m), 485 (m) cm^{-1}.

2-Amino-5-nitrobenzothioamide (1c). MP.: 146–147 °C; ^{1}H-NMR (500 MHz, DMSO-d_6) δ = 9.97 (1H, br *s*, $CSNH_2$), 9.68 (1H, br *s*, $CSNH_2$), 8.07 (1H, *d*, ^4J = 2.7 Hz, CH(6)), 7.98 (1H, *dd*, ^3J = 9.2 Hz, ^4J = 2.7 Hz, CH(4)), 7.39 (2H, br *s*, NH_2), 6.81 (1H, *d*, ^3J = 9.2, CH(3)) ppm; ^{13}C-NMR (126 MHz, DMSO-d_6) δ = 197.7 (C═S), 152.6 (C_{quart}(5)), 135.1 (C_{quart}(2)), 126.3 (CH(6)), 124.1 (CH(4)), 122.0 (C_{quart}(1)), 115.6 (CH(3)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 197 ([M]$^+$, 90), 164 (100), 133 (19), 118 (51), 90 (28), 63 (20), 32 (16); IR: (ATR) $\tilde{\nu}$ = 3403 (w), 3282 (m), 3159 (m), 2229 (w), 1927 (w), 1646 (m), 1631 (m), 1592 (m), 1568 (m), 1481 (m), 1436 (m), 1300 (s), 1258 (s), 746 (s), 677 (s), 648 (s) cm^{-1}.

2-Amino-6-fluorobenzothioamide (1d). MP.: 114–115 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.12 (1H, br *s*, $CSNH_2$), 9.64 (1H, br *s*, $CSNH_2$), 7.02 (1H, *ddd*, ^3J = 8.2 Hz, ^3J = 8.2 Hz, ^4J = 6.5 Hz, CH(4)), 6.52 (1H, *dd*, ^3J = 8.2 Hz, ^4J = 0.8 Hz, CH(3)), 6.35 (1H, *ddd*, ^3J = 10.0 Hz, ^3J = 8.2 Hz, ^4J = 1.0 Hz, CH(5)), 5.54 (2H, br *s*, NH2) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 195.2 (*d*, ^3J = 0.9 Hz, C═S), 157.4 (*d*, ^1J = 242.7 Hz, C_{quart}(6)), 146.9 (*d*, ^3J = 5.8 Hz, C_{quart}(2)), 129.6 (*d*, ^3J = 10.9 Hz, CH(4)), 115.4 (*d*, ^2J = 19.0 Hz, C_{quart}(1)), 111.3 (*d*, ^4J = 2.4 Hz, CH(3)), 102.1 (*d*, ^2J = 22.4 Hz, CH(5)) ppm; ^{19}F-NMR (282 MHz, DMSO-d_6): δ = −116.87 ppm. GC/MS: (EI, 70 eV) *m*/*z* (%) = 170 ([M]$^+$, 100), 137 (96), 136 (17), 117 (29), 109 (16), 90 (26), 83 (18); IR: (ATR) $\tilde{\nu}$ = 3422 (w), 3331 (w), 3257 (w), 3134 (w), 1611 (m), 1462 (m), 1396 (m), 899 (m), 781 (m), 628 (m), 540 (s), 494 (s) cm^{-1}.

2-Aminopyridine-3-carbothioamide (1e). MP.: 128–129 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 9.81 (1H, br *s*, $CSNH_2$), 9.49 (1H, br s, $CSNH_2$), 8.02 (1H, *dd*, ^3J = 4.7 Hz, ^4J = 1.7 Hz, CH(4)), 7.52 (1H, *dd*, ^3J = 7.6 Hz, ^4J = 1.6 Hz, CH(6)), 6.83 (2H, br *s*, NH_2), 6.59 (1H, *dd*, ^3J = 7.6 Hz, ^3J = 4.8 Hz, CH(5)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 198.9 (C═S), 156.8 (C_{quart}(1)), 149.9 (CH(Ar)), 134.8 (CH(Ar)), 118.5 (C_{quart}(2)), 111.7 (CH(Ar)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 153 ([M]$^+$, 69), 120 (100), 103 (25), 93 (15), 92 (12), 66 (13), 60 (11), 52 (11), 39 (15); IR: (ATR) $\tilde{\nu}$ = 3391 (w), 3265 (w), 3104 (m), 2770 (w), 1614 (m), 1598 (m), 1565 (m), 1465 (m), 1450 (m), 1239 (m), 907 (m), 850 (m), 529 (s), 427 (s) cm^{-1}.

2-Amino-4-chlorobenzothioamide (1f). MP.: 142–143 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 9.71 (1H, br, *s*, $CSNH_2$), 9.36 (1H, br *s*, $CSNH_2$), 7.17 (1H, *dd*, ^3J = 8.4 Hz, ^4J = 1.3 Hz, CH(6)), 6.77 (1H, *dd*, ^4J = 2.2 Hz, ^5J = 1.3 Hz, (CH(3)), 6.53 (1H, *ddd*, ^3J = 8.4 Hz, ^4J = 2.2 Hz, ^5J = 1.2 Hz, (CH(5)), 6.42 (2H, br *s*, NH_2) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 199.0 (C═S), 148.4 (C_{quart}(2)), 135.0 (C_{quart}(4)), 128.8 (CH(6)), 122.3 (C_{quart}(1)), 115.1 (CH(5)), 114.6 (CH(3)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 188 ([M]$^+$, ^{37}Cl, 24), 186 ([M]$^+$, ^{35}Cl, 65), 155 (32), 154 (21), 153 (100), 152 (45), 125 (13), 118 (23), 117 (12), 90 (21), 63 (23), 62 (12), 60 (11), 52 (16); IR: (ATR) $\tilde{\nu}$ = 3436 (w), 3419 (w), 3266 (w), 3141 (w), 1621 (m), 1593 (m), 1557 (m), 1435 (m), 1297 (m), 1246 (m), 919 (s), 835 (m), 799 (s), 607 (s), 487 (s), 422 (s) cm^{-1}.

2-Amino-6-chlorobenzothioamide (1g). MP.: 111–112 °C, ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.15 (1H, br *s*, $CSNH_2$), 9.68 (1H, br *s*, $CSNH_2$), 6.98 (1H, *dd*, ^3J = 8.0 Hz, ^3J = 8.0 Hz, CH(4)), 6.68–6.54 (2H, *m*, CH(3 + 5)), 5.18 (2H, br *s*, NH_2) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 198.3 (C═S), 145.3 (C_{quart}(2)), 129.0 (CH(4)), 128.2 (C_{quart}(6)), 126.9 (C_{quart}(1)), 116.2 (CH(3)), 13.8 (CH(5)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 188 ([M]$^+$, ^{37}Cl, 31), 186 ([M]$^+$, ^{35}Cl, 79), 155 (30), 154 (20), 153 (100), 152 (37), 151 (111), 125 (13), 118 (17), 117 (57), 90 (54), 75 (10), 65 (14), 64 (12), 63 (31), 62 (15), 61 (11), 60 (17), 52 (15), 39 (12); IR: (ATR) $\tilde{\nu}$ = 3427 (w), 3393 (w), 3313 (w), 3085 (w), 1637 (w), 1620 (w), 1595 (m), 1570 (m), 1472 (w), 1447 (m), 1402 (m), 1295 (m), 1202 (w), 1155 (w), 1106 (w), 1047 (w), 964 (w), 88 (m), 878 (m), 775 (s), 746 (m), 719 (m), 654 (m), 608 (s), 580 (s), 540 (s), 502 (s), 453 (s), 430 (s) cm^{-1}.

2-Aminothiophene-3-carbothioamide (1h). MP.: 118–119 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 8.60 (2H, br *s*, NH_2), 8.49 (1H, br *s*, $CSNH_2$), 8.43 (1H, br *s*, $CSNH_2$), 7.12 (1H, *dd*, ^3J = 6.3

Hz, ^4J = 2.0 Hz, CH(4)), 6.24 (1H, *dd*, ^3J = 6.0 Hz, ^4J = 2.1 Hz, CH(5)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 189.2 ($CSNH_2$), 167.8 (C_{quart}(2), 123.4 (C_{quart}(3), 111.2 (CH(4)), 104.7 (CH(5)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 159 (11), 158 ([M]$^+$, 100), 141 (27), 125 (94), 124 (27), 98 (19), 97 (19), 81 (11), 71 (12), 70 (15), 69 (17), 60 (22), 54 (21), 52 (27), 45 (32), 38 (11), 37 (10); IR: (ATR) $\tilde{\nu}$ = 3267 (w), 3165 (w), 1622 (w), 1598 (w), 1559 (m), 1516 (w), 1412 (m), 1386 (m), 1286 (w), 1264 (w), 1082 (w), 911 (w), 869 (w), 830 (s), 776 (m), 724 (w), 643 (s), 588 (s), 554 (s), 483 (s), 446 (s) cm^{-1}

General procedure for the synthesis of 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-thione (2a). A 25 ml glass pressure tube is charged with 1 mmol **1a** (152 mg), 1 mmol benzaldehyde (122 µl) and 2 ml H_2O and the tube is subsequently sealed. The mixture is heated under stirring to 100 °C for 24 h whilst a yellow solid is precipitating. The crude product is filtered off and washed with water. The solid is dissolved in a minimum amount of boiling ethyl acetate and recrystallized by the addition of hexane, giving 201 mg (84%) 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-thione as a yellow solid. M.P.: 174–175 °C; ^{1}H-NMR (250 MHz, DMSO-d_6): δ = 10.68–10.45 (1H, *m*, NH(3)), 8.05 (1H, *d*, ^3J = 8.0 Hz, CH(5)), 7.56 (1H, *d*, ^3J = 2.0 Hz, NH(1)), 7.48–7.31 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 7.26 (1H, *ddd*, ^3J = 8.4 Hz, ^3J = 7.1 Hz, ^4J = 1.6 Hz, CH(7), 6.78–6.73 (1H, *m*, CH(8)), 6.66 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.1 Hz, ^4J = 1.1 Hz, CH(6)), 5.77–5.74 (1H, *m*, (CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.2 (C═S(4)), 143.4 (C_{quart}(8a)), 141.0 (C_{quart}(9)), 134.1 (CH(7)), 131.5 (CH(5)), 128.4 (CH(12)), 128.4 (CH(11 + 13)), 126.5 (CH(10 + 14)), 119.5 (C_{quart}(4a)), 117.3 (CH(6)), 114.8 (CH(8)), 65.6 (CH(2)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 240 ([M]$^+$, 55), 208 (18), 207 (100), 206 (17), 163 (34), 136 (16), 129 (21), 104 (17), 102 (15), 77 (21); IR: (ATR) $\tilde{\nu}$ = 3260 (w), 3139 (w), 3029 (w), 2973 (w), 1609 (m), 1524 (m), 1211 (m), 1197 (m), 1149 (m), 1124 (m), 1009 (m), 999 (m), 861 (w), 842 (w), 757 (s), 694 (s), 591 (m) cm^{-1}; Elemental analysis: Calcd for $C_{14}H_{12}N_2S$: C, 69.97; H, 5.03; N, 11.66; S, 13.34. Found: C, 70.28; H, 5.01; N, 11.22; S, 12.67.

2-(4-Trifluoromethoxy)phenyl-2,3-dihydroquinazoline-4(1*H*)-thione (2b). MP.: 161–162 °C; 1H-NMR (250 MHz, DMSO-d_6): δ = 10.65–10.55 (1H, *m*, NH(3)), 8.06 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.4 Hz, CH(5)), 7.63–7.57 (2H, *m*, (CH(11 + 13)), 7.57–7.54 (1H, *m*, NH(1)), 7.45–7.36 (2H, *m*, CH(10 + 14)), 7.28 (1H, *ddd*, ^3J = 8.5 Hz, ^3J = 7.2 Hz, ^4J = 1.6 Hz, CH(7)), 6.82–6.73 (1H, *m*, CH(8)), 6.68 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.2 Hz, ^4J = 1.1 Hz, CH(6)), 5.96–5.61 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.3 (C═S(4)), 148.3 (C_{quart}(12)), 143.2 (C_{quart}(8a)), 140.2 (C_{quart}(9), 134.2 (CH(7)), 131.5 (CH(5)), 128.7 (CH(11 + 13)), 121.1 (CH(10 + 14), 120.0 (*q*, ^1J = 256.4 Hz, (OCF_3)), 119.5 (C_{quart}(4a)), 117.6 (CH(6)), 114.9 (CH(8)), 64.9 (CH(2)) ppm; ^{19}F-NMR (282 MHz, DMSO-d_6): δ = −56.43 ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 324 ([M]$^+$, 56), 292 (22), 291 (100), 289 (18), 163 (25), 136 (16), 69 (27); IR: (ATR) $\tilde{\nu}$ = 3253 (w), 3136 (w), 2974 (w), 2146 (w), 2075 (w), 2019 (w), 1611 (m), 1526 (m), 1505 (m), 1378 (w), 1253 (m), 1210 (s), 1130 (s), 1014 (m), 764 (s), 522 (m), 493 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{15}H_{11}O_1N_2F_3S_1$, 324.05387, found mass: 324.05320.

2-(4-Fluorophenyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2c). MP.: 176–177 °C; ^{1}H-NMR (250 MHz, DMSO-d_6): δ = 10.54 (1H, *d*, ^3J = 2.2 Hz, NH(3)), 8.06 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.4 Hz, CH(5)), 7.54 (1H, br *s*, NH(1)), 7.53–7.43 (2H, *m*, CH(11 + 13)), 7.35–7.16 (3H, *m*, CH(7 + 10 + 14), 6.76 (1H, *dd*, ^3J = 8.3 Hz, ^4J = 1.1 Hz, CH(8)), 6.67 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.1 Hz, ^4J = 1.1 Hz, CH(6)), 5.79–5.76 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.3 (C═S(4)), 162.1 (*d*, ^1J = 244.5 Hz, (C_{quart}(12)), 143.3 (C_{quart}(8a)), 137.1 (*d*, ^4J = 3.0 Hz (C_{quart}(9)), 134.2 (CH(7)), 131.5 (CH(5)), 128.8 (*d*, ^3J = 8.5 Hz (CH(10 + 14)), 119.5 (C_{quart}(4a)), 117.5 (CH(6)), 115.2 (*d*, ^2J = 21.6 Hz, (CH(11 + 13)), 114.9 (CH(8)), 65.1 (CH(2)) ppm; ^{19}F-NMR (282 MHz, DMSO-d_6): δ = −113.08 to −113.47 (*m*) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 258 ([M]$^+$, 48), 226 (19), 225 (100), 224 (19), 163 (19), 129 (17), 102 (15); IR: (ATR) $\tilde{\nu}$ = 3255 (w), 3148 (w), 3026 (w), 2968 (w), 2842 (w), 1607 (m), 1508 (s), 1210 (m), 1199 (m), 1150 (s), 1009 (m), 995 (m), 833 (m), 764 (s), 588 (m), 500 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{14}H_{11}N_2F_1S_1$, 258.06215, found mass: 258.06171.

2-(4-Cyanophenyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2d). MP.: 230–231 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.68 (1H, *d*, ^3J = 2.6 Hz, NH(3)), 8.04 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.5 Hz, CH(5)), 7.90–7.85 (2H, *m*, CH(10 + 14)), 7.71 (1H, *s*, NH(1)), 7.64–7.57 (2H, *m*, CH(11 + 13)), 7.28 (1H, *ddd*, ^3J = 8.5 Hz, ^3J = 7.2 Hz, ^4J = 1.6 Hz, CH(7)), 6.78 (1H, *d*, ^3J = 7.4 Hz, CH(8)), 6.71–6.65 (1H, *m*, CH(8)), 5.89–5.85 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.3 (C═S(4)), 146.4 (C_{quart}(8a)), 142.8 (C_{quart}(9)), 134.4 (CH(7)), 132.5 (CH(11 + 13)), 131.5 (CH(5)), 127.4 (CH(10 + 14)), 119.5 (C_{quart}(4a)), 118.6 (C(CN)), 117.7 (CH(6)), 114.8 (CH(8)), 111.2 (C_{quart}(12)), 64.6 (CH(2)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 265 ([M]$^+$, 40), 233 (15), 332 (100), 231 (18), 230 (25), 163 (15); IR: (ATR) $\tilde{\nu}$ = 3319 (w), 3043 (w), 2833 (w), 2226 (w), 1609 (m), 1582 (m), 1524 (m), 1485 (m), 1208 (s), 1199 (s), 1150 (m), 1132 (m), 1019 (m), 833 (m), 757 (s), 590 (m), 526 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{15}H_{11}N_3S_1$, 265.06682, found mass: 265.06625.

2-(3-Methylphenyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2e). MP.: 191–192 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.49 (1H, *s*, NH(3)), 8.05 (1H, *d*, ^3J = 7.8 Hz, CH(5)), 7.52 (1H, *s*, NH(1)), 7.31–7.11 (5H, *m*, CH(7 + 10 + 12 + 13 + 14)), 6.75 (1H, *d*, ^3J = 8.1 Hz, CH(8)), 6.66 (1H, *m*, CH(6)), 5.71 (1H, *s*, CH(2)), 2.29 (3H, *s*, CH_3(15)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.2 (C═S(4)), 143.5 (C_{quart}(8a)), 140.9 (C_{quart}(9)), 137.5 (C_{quart}(11)), 134.1 (CH(7)), 131.5 (CH(5)), 129.1 (CH(12)), 128.3 (CH(13)), 127.2 (CH(14)), 123.7 (CH(10)), 119.5 (C_{quart}(4a)), 117.3 (CH(6)), 114.8 (CH(8)), 65.7 (CH(2)), 21.1 (CH3(15)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 254 ([M]$^+$, 63), 253 (20), 222 (24), 221 (100), 219 (29), 206 (24), 163 (51), 136 (19), 129 (27), 118 (16), 102 (19), 91 (20), 77 (17), 65 (15); IR: (ATR) $\tilde{\nu}$ = 3262 (w), 3130 (w), 3019 (w), 2968 (w), 2917 (w), 1608 (m), 1583 (m), 1523 (m), 1482 (m), 1205 (s), 1146 (m), 1121 (m), 1033 (m), 998 (m), 762 (s), 697 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{15}H_{14}N_2S_1$, 254.08722, found mass: 254.08700.

2-(4-Methylphenyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2f). MP.: 234–235 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.50 (1H, *d*, ^3J = 2.3 Hz, NH(3)), 8.04 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.4 Hz,

CH(5)), 7.51 (1H, *s*, NH(1)), 7.31 (2H, *d*, ^3J = 8.1 Hz, CH(10 + 14)), 7.25 (1H, *ddd*, ^3J = 8.4 Hz, ^3J = 7.2 Hz, ^4J = 1.6 Hz, CH(7)), 7.17 (2H, *d*, ^3J = 8.0 Hz, CH(11 + 13)), 6.74 (1H, *dd*, ^3J = 8.2 Hz, ^4J = 0.7 Hz, CH(8)), 6.65 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.2 Hz, ^4J = 1.1 Hz, CH(6)), 5.74–5.67 (1H, *m*, CH(2)), 2.27 (3H, *s*, CH3(15)) ppm; ^{13}C-NMR (126 MHz, DMSO-d_6): δ = 189.1 (C═S(4)), 143.4 (C_{quart}(8a)), 138.0 (C_{quart}(9)), 137.7 (C_{quart}(12)), 134.0 (CH(7)), 131.4 (CH(5)), 128.9 (CH(11 + 13)), 126.4 (CH(10 + 14)), 119.5 (C_{quart}(4a)), 117.3 (CH(6)), 114.8 (CH(8)), 65.4 (CH(2)), 20.7 (CH3(15)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 254 ([M]$^+$, 63), 253 (19), 221 (100), 219 (38), 206 (17), 163 (28), 136 (30), 129 (24), 102 (17), 77 (17), 44 (17), 32 (22); IR: (ATR) $\tilde{\nu}$ = 3270 (m), 3144 (m), 3029 (w), 2974 (w), 2911 (w), 2842 (w), 16.12 (m), 1529 (s), 1209 (s), 1198 (s), 1147 (s), 1007 (m), 817 (s), 586 (s); 493 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{15}H_{14}N_2S_1$, 254.08722, found mass: 254.08698.

(*E*)-2-(1-Phenylprop-1-en-2-yl)-2,3-dihydroquinazoline-4(1*H*)-thione (2g). MP.: 198–199 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.27 (1H, *s*, NH(3)), 8.07 (1H, *d*, ^3J = 6.9 Hz, CH(5)), 7.42–7.21 (7H, *m*, NH(1), CH(7 + 12 + 13 + 14 + 15 + 16)), 6.75 (1H, *d*, ^3J = 8.1 Hz, CH(8)), 6.69–6.62 (1H, *m*, CH(6)), 6.59 (1H, *s*, CH(10)), 5.27 (1H, *s*, CH(2)), 1.91 (3H, *s*, CH3(17)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.7 (C═S(4)), 144.1 (C_{quart}(8a)), 136.3 (C_{quart}(11)), 135.6 (C_{quart}(9)), 134.0 (CH(7)), 131.5 (CH(5)), 128.9 (CH(13 + 15)), 128.5 (CH(14)), 128.3 (CH(12 + 16)), 127.1 (CH(10)), 119.0 (C_{quart}(4a)), 117.1 (CH(6)), 114.5 (CH(8)), 70.8 (CH(2)), 13.5 (CH3(17)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 280 ([M]$^+$, 55), 279 (53), 278 (23), 277 (33), 263 (23), 247 (100), 246 (33), 245 (86), 232 (26), 231 (28), 163 (92), 129 (23), 115 (23); IR: (ATR) $\tilde{\nu}$ = 3317 (w), 3130 (w), 2977 (w), 1608 (m), 1573 (m), 1518 (m), 1208 (s), 1155 (m), 1126 (m), 993 (m), 756 (s), 699 (s), 516 (s), 443 (s), 427 (m) cm^{-1}; HRMS (ESI-TOF; M + H)$^+$ *m*/*z*: Calcd for $C_{17}H_{16}N_2S_1$, 281.11070, found mass: 281.11077.

2-(4-Hydroxyphenyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2h). M.P.: 214–216 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.36 (1H, *d*, ^3J = 2.9 Hz, NH(3)), 9.52 (1H, *s*, OH), 8.05 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.6 Hz, CH(5)), 7.41–7.36 (1H, *m*, NH(2)), 7.30–7.20 (3H, *m*, CH(7 + 10 + 14), 6.75–6.69 (3H, *m*, CH(8 + 11 + 13), 6.65 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.1 Hz, ^4J = 1.1 Hz, CH(6)), 5.63 (1H, *dd*, ^3J = 3.3 Hz, ^3J = 1.7 Hz, CH(2)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 189.1 (C═S(4)), 157.7 (C_{quart}(10)), 143.7 (C_{quart}(8)), 134.0 (CH(7)), 131.5 (CH(5)), 131.0 (C_{quart}(9)), 128.0 (CH(11 + 13)), 119.4 (C_{quart}(4a)), 117.2 (CH(6)), 115.0 (CH (10 + 14)), 114.7 (CH(8)), 65.8 (CH(2)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 256 ([M]$^+$, 37), 255 (10), 254 (16), 224 (15), 223 (81), 222 (100), 221 (50), 195 (17), 129 (10), 119 (13); IR: (ATR) $\tilde{\nu}$ = 3149 (br, m), 1608 (m), 1575 (w), 1530 (m), 1511 (s), 1480 (m), 1365 (m), 1297 (w), 1242 (m), 1196 (s), 1168 (s), 1154 (s), 1125 (s), 1015 (m), 999 (s), 829 (s), 760 (s). 750 (s), 706 (s), 526 (s), 501 (s), 466 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{14}H_{12}O_1N_2S_1$, 256.06649, found mass: 256.06662.

2-(Isopropyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2i). MP.: 185–186 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.09 (1H, *s*, NH(3)), 8.03 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.6 Hz, CH(5)), 7.24 (1H, *ddd*, ^3J = 8.4 Hz, ^3J = 7.1 Hz, ^4J = 1.6 Hz, CH(7)), 6.92 (1H, *s*, NH (1)), 6.75 (1H, *dd*, ^3J = 8.2 Hz, ^4J = 1.1 Hz, CH(8)), 6.62 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.1 Hz, ^4J = 1.2 Hz, CH(6)), 4.41–4.37 (1H, *m*, CH(2)), 2.03–1.90 (1H, *m*, CH(9)), 0.93 (3H, *d*, ^3J = 6.9 Hz, CH_3), 0.89 (3H, *d*, ^3J = 6.8 Hz, CH_3) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.3 (C═S(4)), 4.2 (C_{quart}(8a)), 133.9 (CH(7)), 131.5 (CH(5)), 119.5 (C_{quart}(4a)), 116.8 (CH(6)), 114.5 (CH(8)), 69.2 (CH(2)), 32.17 (CH(9)), 17.08 (CH_3(Me)), 16.66 (CH_3(Me)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 206 ([M]$^+$, 6), 164 (10), 163 (100), 136 (6), 129 (12), 108 (5), 41 (6); IR: (ATR) $\tilde{\nu}$ = 3279 (m), 3139 (m), 3057 (w), 2997 (w), 2955 (m), 2909 (w), 2865 (w), 1612 (m), 1535 (m), 1474 (m), 1279 (m), 1216 (s), 1146 (s), 981 (m), 766 (s), 749 (s), 689 (m), 435 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{11}H_{14}N_2S_1$, 206.08722, found mass: 206.08683.

2-(Cyclohexyl)-2,3-dihydroquinazoline-4(1*H*)-thione (2j). MP.: 182–183 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.11 (1H, *s*, NH(3)), 8.02 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.3 Hz, CH(5)), 7.23 (1H, *ddd*, ^3J = 8.4 Hz, ^3J = 7.1 Hz, ^4J = 1.5 Hz, CH(7)), 6.97 (1H, *s*, NH(1)), 6.74 (1H, *dd*, ^3J = 8.2 Hz, ^3J = 0.8 Hz, CH(8)), 6.61 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 5.8 Hz, ^4J = 1.1 Hz, CH(6)), 4.36 (1H, *s*, CH(2)), 1.79–0.99 (11H, *m*, CH_2(Cy)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 189.0 (C═S(4)), 144.0 (C_{quart}(8a)), 133.9 (CH(7)), 131.5 (CH(5)), 119.5 (C_{quart}(4a)), 116.7 (CH(6)), 114.5 (CH(8)), 68.38 (CH(2)), 42.0 (CH2(Cy)), 27.0 (CH2(Cy)), 26.8 (CH2(Cy)), 25.8 CH2(Cy)), 25.4 (CH2(Cy)), 25.3 (CH(Cy)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 246 ([M]$^+$, 16), 189 (10), 164 (19), 163 (100), 129 (10); IR: (ATR) $\tilde{\nu}$ = 3338 (w), 3150 (w), 3041 (w), 2992 (w), 2927 (m), 2848 (w), 1610 (m), 1576 27 (m), 1536 (s), 1213 (s), 1148 (m), 1162 (m), 1003 (m), 989 (m), 956 (m), 761 (s), 743 (s), 530 (s), 524 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{14}H_{18}N_2S_1$, 246.11852, found mass: 246.11846.

2-(Benzo[*b*]thiophen-2-yl)-2,3-dihydroquinazoline-4(1*H*)-thione (2k). M.P.: 253–255 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.57 (1H, br s, (NH(3)), 8.20–8.14 (1H, *m*, CH(12)), 8.11 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.4 Hz, CH(15)), 8.04–7.99 (1H, *m*, CH(5)), 7.66 (1H, *s*, CH(10)), 7.55 (1H, *s*, NH(1)), 7.49–7.37 (2H, *m*, CH(13 + 14)), 7.29 (1H, *m*, CH(7)), 6.80–6.66 (1H, *m*, (CH(6 + 8)), 6.18 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 189.7 (C═S(4)), 143.7 (C_{quart}(8a)), 140.3 (C_{quart}(9), 136.6 (C_{quart}(11a)), 134.5 (C_{quart}(15a)), 134.1 (CH(7)), 131.6 (CH(5)), 126.9 (CH(13)), 124.7 (CH(14)), 124.2 (CH(15)), 123.1 (CH(10)), 123.1 (CH(12)), 119.7 (C_{quart}(4a)), 117.6 (CH(6)), 114.9 (CH(8)), 62.0 (CH(2)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 297 (10), 296 ([M]$^+$, 54), 264 (21), 263 (100), 262 (36), 261 (28), 178 (10), 129 (11), 44 (11); IR: (ATR) $\tilde{\nu}$ = 3274 (w), 3105 (w), 2960 (w), 1607 (w), 1579 (m), 1521 (m), 1460 (m), 1425 (m), 1343 (m), 1240 (m), 1208 (s), 1146 (m), 1125 (m), 1002 (S), 936 (m), 848 (m), 754 (s), 733 (S), 600 (s), 522 (s), 453 (S), 424 (s) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{16}H_{12}N_2S_2$, 296.04364, found mass: 296.04315.

2-Pentyl-2,3-dihydroquinazoline-4(1*H*)-thione (2l). M.P.: 138–139 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.12 (1H, *d*, ^3J = 2.5 Hz, NH(3)), 8.03 (1H, *dd*, ^3J = 8.0 Hz, ^4J = 1.6 Hz, CH(5)), 7.25 (1H, *ddd*, ^3J = 8.5 Hz, ^3J = 7.1 Hz, ^4J = 1.6 Hz, CH (7)), 6.90 (1H, s, NH(1)), 6.73 (1H, *dd*, ^3J = 8.3 Hz, ^4J = 1.1 Hz, CH(8)), 6.66 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.1 Hz, ^4J = 1.1 Hz, CH(6)), 4.62 (1H, *tdd*, ^3J = 5.4 Hz, ^3J = 2.5 Hz, ^3J = 1.2 Hz,

CH(9)), 1.68 (2H, td, ^3J = 8.2 Hz, ^4J = 5.0 Hz, CH(10)), 1.49–1.20 (6H, *m*, CH_2(11 + 12 + 13), 0.87 (3H, *m*, CH_3(14)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 189.4 (C═S(4)), 144.4 (C_{quart}(8a)), 133.8 (CH(7)), 131.5 (CH(5)), 119.7 (C_{quart}(4a)), 117.1 (CH(6)), 114.7 (CH(8)), 64.4 (CH(2)), 33.6 (CH_2(10)), 31.0 (CH_2(11)), 22.9 (CH_2(12)), 22.0 (CH_2(13)), 13.9 (CH_3(14)) ppm. GC/MS: (EI, 70 eV) *m*/*z* (%) = 235 (20), 234 ([M]$^+$, 84), 233 (15), 232 (12), 201 (10), 189 (16), 177 (14), 176 (54), 165 (48), 164 (83), 163 (100), 162 (16), 146 (12), 145 (34), 144 (13), 136 (40), 132 (19), 131 (10), 129 (49), 118 (11), 109 (12), 108 (10), 104 (17), 102 (17), 77 (15); IR: (ATR) $\tilde{\nu}$ = 3288 (w), 3172 (m), 2923 (m), 2854 (w), 1615 (s), 1579 (s), 1526 (s), 1478 (s), 1446 (m), 1378 (m), 1350 (w), 1310 (w), 1238 (w), 1207 (s), 1148 (s), 1139 (s), 1114 (w), 1026 (w), 994 (S), 856 (w), 769 (s), 747 (s), 647 (w), 525 (m), 514 (m), 452 (m), 418 (m) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{13}H_{18}N_2S_1$, 234.11852, found mass: 234.11812.

2-Methyl-2,3-dihydroquinazoline-4(1*H*)-thione (2m). M.P:: 150–152 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.19–10.01 (1H, *m*, NH(3)), 8.04 (1H, *dd*, ^3J = 8.3 Hz, ^4J = 1.6 Hz, CH(5)), 7.26 (1H, *ddd*, ^3J = 8.1 Hz, ^3J = 7.2 Hz, ^4J = 1.6 Hz, CH(7)), 6.92 (1H, *s*, NH(1)), 6.75–6.62 (2H, *m*, CH(6 + 8)), 4.81–4.67 (1H, *m*, CH(2)), 1.37 (3H, *d*, ^3J = 5.8 Hz, CH_3) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 189.8 (C═S(4)), 144.8 (C_{quart}(8a), 133.8 (CH(7)), 131.5 (CH5)), 120.0 (C_{quart}(4a)), 117.5 (CH(6)), 114.7 (CH(8)), 61.1 (CH(2)), 20.2 (CH_3) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 178 ([m]$^+$, 74), 177 (10), 164 (10), 163 (100), 146 (13), 145 (56), 136 (21), 135 (12), 129 (16), 118 (12), 109 (12), 108 (18), 104 (20), 77 (16); IR: (ATR) $\tilde{\nu}$ = 3162 (w), 2974 (w), 1609 (m), 1578 (m), 1531 (s), 1471 (m), 1383 (m), 1346 (m), 1248 (w), 1213 (S), 1140 (m), 1102 (m), 1067 (m), 994 (s), 850 (w), 753 (s), 718 (m), 692 (m), 584 (m), 521 (s), 454 (s), 436 (s) cm^{-1}.

6-Chloro-2-phenyl-2,3-dihydroquinazoline-4(1*H*)-thione (2n). MP.: 174–175 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.74 (1H, *d*, ^3J = 2.1 Hz, NH(3)), 8.01 (1H, *d*, ^4J = 2.5 Hz, CH(5)), 7.77 (1H, *s*, NH(1)), 7.46–7.33 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 7.30 (1H, *dd*, ^3J = 8.7 Hz, ^4J = 2.6 Hz, CH(7)), 6.80 (1H, *d*, ^3J = 8.7 Hz, CH(8)), 5.82–5.78 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 187.8 (C═S(4)), 142.1 (C_{quart}(8a)), 140.6 (C_{quart}(9)), 133.7 (CH(7)), 130.1 (CH(5)), 128.6 (CH(12)), 128.5 (CH(11 + 13)), 126.5 (CH(10 + 14)), 120.8 (C_{quart}(4a)), 120.3 (C_{quart}(6)), 117.0 (CH(8)), 65.6 (CH(2)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 276 ([M]$^+$, 37Cl, 17), 274 ([M]$^+$, 35Cl, 58), 243 (35), 242 (23), 241 (100), 206 (20), 197 (42), 163 (21), 77 (33), 51 (20); IR: (ATR) $\tilde{\nu}$ = 3339 (w), 3311 (w), 3132 (w), 2945 (w), 1658 (w), 1611 (m), 1575 (m), 1523 (s), 1363 (m), 1188 (s), 1012 (m), 817 (m), 764 (m), 699 (s), 576 (m) cm^{-1}, HRMS (ESI-TOF; M + H)$^+$ *m*/*z*: Calcd for $C_{14}H_{11}N_2Cl_1S_1$, 275.04042, found mass: 275.04017.

6-Nitro-2-phenyl-2,3-dihydroquinazoline-4(1*H*)-thione (2o). MP.: 230–231 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.97 (1H, *d*, ^3J = 1.7 Hz, NH(3)), 8.97 (1H, *d*, ^4J = 2.7 Hz, CH(5)), 8.89 (1H, *s*, NH(1)), 8.11 (1H, *dd*, ^3J = 9.1 Hz, ^4J = 2.7 Hz, CH(7)), 7.46–7.36 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 6.87 (1H, *d*, ^3J = 9.1, CH(8)), 6.05–6.01 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 187.2 (C═S(4)), 147.8 (C_{quart}(8a)), 140.5 (C_{quart}(9)), 137.5 (C_{quart}(6)), 129.1 (CH(5)), 129.0 (CH(7)), 128.8 (CH(11 + 13)), 128.2 (CH(12)), 126.3 (CH(10 + 14)), 116.8 (C_{quart}(4a)), 115.1 (CH(8)), 65.8 (CH(2)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 285 ([M]$^+$, 36), 253 (100), 252 (80), 220 (87), 206 (26), 57 (20), 44 (39); IR: (ATR) $\tilde{\nu}$ = 3372 (w), 3294 (w), 3146 (w), 3086 (w), 2973 (w), 1615 (m), 1589 (m), 1537 (m), 1453 (m), 1317 (s), 1193 (m), 1094 (s), 825 (m), 745 (m), 698 (s), 440 (m) cm^{-1}, HRMS (ESI-TOF; M + H)$^+$ *m*/*z*: Calcd for $C_{14}H_{11}N_3O_2S_1$, 286.06447, found mass: 286.06441.

5-Fluoro-2-phenyl-2,3-dihydroquinazoline-4(1*H*)-thione (2p). MP.: 178–179 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.49 (1H, *d*, ^3J = 3.6 Hz, NH(3)), 7.91 (1H, *s*, NH(1)), 7.44–7.30 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 7.27–7.18 (1H, *m*, CH(Ar)), 6.66 (1H, *d*, ^3J = 8.3 Hz, CH(Ar)), 6.42 (1H, *ddd*, ^3J = 11.8 Hz, ^3J = 8.1 Hz, ^4J = 0.9 Hz, CH(Ar)), 5.67–5.62 (1H, *m*, CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 184.4 (*d*, ^3J = 4.5 Hz, C═S(4)), 162.7 (*d*, ^1J = 258.9 Hz, C_{quart}(5)), 146.1 (*d*, ^3J = 2.1 Hz, C_{quart}(8a)), 139.9 (C_{quart}(9)), 134.2 (*d*, ^3J = 11.8 Hz, CH(7)), 128.5 (CH(12)), 128.4 (CH(11 + 13)), 126.6 (CH(10 + 14)), 111.1 (*d*, ^4J = 3.7 Hz, CH(8)), 110.4 (*d*, ^2J = 7.1 Hz, C_{quart}(4a)), 105.4 (*d*, ^2J = 22.5 Hz, CH(6)), 64.8 (CH(2)) ppm; ^{19}F-NMR (282 MHz, DMSO-d_6): δ = −107.37 ppm. MS: (EI, 70 eV) *m*/*z* (%) = 258 ([M]$^+$, 31), 226 (23), 225 (100), 224 (59), 223 (50), 181 (16), 147 (19), 122 (20), 104 (19), 77 (42), 51 (16); IR: (ATR) $\tilde{\nu}$ = 3263 (w), 3127 (w), 3033 (w), 2979 (w), 2929 (w), 1618 (m), 1523 (s), 1192 (s), 1056 (m), 987 (m), 794 (m), 747 (m), 696 (s), 595 (m), 453 (s) cm^{-1}, HRMS (ESI-TOF; M + H)$^+$ *m*/*z*: Calcd for $C_{14}H_{11}N_2F_1S_1$, 259.06997, found mass: 259.07012.

2-Phenyl-2,3-dihydropyrido[2,3-*d*]pyrimidine-4(1*H*)-thione (2q). MP.: 249–250 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.79 (1H, *s*, NH(3)), 8.36 (1H, *s*, NH(1)), 8.30 (1H, *d*, ^3J = 7.2 Hz, CH(5)), 8.19 (1H, *d*, ^3J = 2.7 Hz, CH(7)), 7.45–7.25 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 6.75–6.68 (1H, *m*, CH(6)), 5.87 (1H, *s*, CH(2)) ppm; ^{13}C-NMR (63 MHz, DMSO-d_6): δ = 188.7 (C═S(4)), 154.0 (CH(7)), 153.0 (C_{quart}(8a)), 141.3 (C_{quart}(9)), 139.6 (CH(5)), 128.6 (CH(10 + 12)), 128.5 (CH(11)), 126.0 (CH(11 + 13)), 114.2 (CH(6)), 113.7 (C_{quart}(4a)), 65.6 (CH(2)) ppm; MS: (EI, 70 eV) *m*/*z* (%) = 241 ([M]$^+$, 100), 242 (13), 208 (37), 164 (53), 137 (13), 105 (11), 103 (14); IR: (ATR) $\tilde{\nu}$ = 3141 (w), 2963 (w), 2845 (w), 1606 (m), 1532 (m), 1440 (w), 1365 (w), 1247 (m), 1218 (m), 1114 (m), 1001 (m), 765 (s), 699 (s), 496 (s), 428 (m) cm^{-1}; HRMS (ESI-TOF) *m*/*z*: Calcd for $C_{13}H_{11}N_3S_1$, 241.06682, found mass: 241.06630.

7-Chloro-2-phenyl-2,3-dihydroquinazoline-4(1*H*)-thione (2r). MP.: 94–96 °C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ = 10.71–10.65 (1H, m, NH(3)), 8.05 (1H, *d*, ^3J = 8.6 Hz, (CH(5)), 7.47–7.30 (5H, *m*, CH(10 + 11 + 12 + 13 + 14)), 6.81 (1H, *d*, ^4J = 2.1 Hz, CH(8)), 6.69 (1H, *dd*, ^3J = 8.6 Hz, ^4J = 2.1 Hz, CH(6)), 5.82 (1H, *dd*, ^3J = 3.6 Hz, ^3J = 1.7 Hz, CH(2)) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δ = 188.2 (C═S(4)), 144.2 (C_{quart}(8a)), 140.7 (C_{quart}(9)), 138.8 (C_{quart}(7)), 133.5 (CH(5)), 128.7 (CH(12)), 128.5 (CH(11 + 13)), 126.5 (CH(10 + 14)), 118.1 (C_{quart}(4a)), 117.4 (CH(6)), 113.8 (CH(8)), 65.6 (CH(2)) ppm; GC/MS: (EI, 70 eV) *m*/*z* (%) = 276 ([M]$^+$ ^{37}Cl, 20), 275 (14), 274 ([M]$^+$ ^{35}Cl, 78), 273 (16), 256 (13), 243 (31), 242 (28), 241 (100), 240 (25), 239 (57), 206 (19), 197 (28), 170 (10), 163 (11), 153 (16), 138 (10), 104 (10), 77 (17); IR: (ATR) $\tilde{\nu}$ = 3134 (w), 1669 (w), 1601 (s), 1568 (m), 1506 (m),

1339 (w), 1289 (w), 1194 (s), 1129 (m), 1080 (s), 1000 (m), 899 (m), 806 (m), 761 (m), 693 (s), 456 (m), 418 (m) cm^{-1}.

Acknowledgements

The authors thank the state of Mecklenburg-Vorpommern and the Bundesministerium für Bildung und Forschung (BMBF) for financial support. We also thank Drs W. Baumann, C. Fischer, D. Michalik, Ms S. Schareina and Ms S. Buchholz (LIKAT) for analytical support.

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