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Catalyst-free synthesis of 2-aryl-1,2-dihydro-quinazolin-4(1*H*)-thiones from 2-aminobenzothio-amides and aldehydes in water

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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.

Inroduction

Quinazolinone alkaloids are an important substance class with a wide range of biological activities such as thymidylate synthase inhibition[1] or antihypertensive effect.[2] Mentionable is methaqualone with its hypnotic properties, which is now illicit and withdrawn due to its high addiction potential and the widespread abuse.[3] Moreover, quinazolinones are important core structures of a variety of natural alkaloids like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 moment.[7] Hence, the exchange of oxygen by sulfur results in different effects on the biological activities.

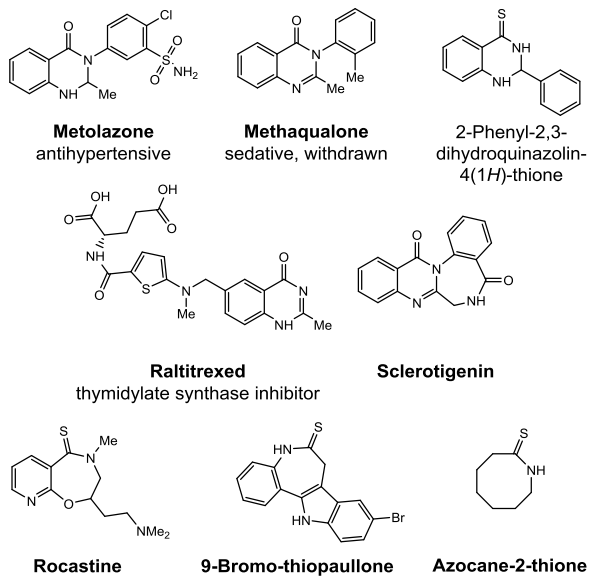


Fig. 1: Selected quinazolinone derivatives and bioactive thiolactams.

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 decreased inhibition of GSK3 but increased CDK1 and CDK5 inhibition.[9] In contrast, E. J. Lien and co-workers observed convulsions and high lethal toxicity (LD50 = 23 mg/kg for azocane-2-thione).[10] In addition, sulfur containing compounds provide a variety of synthetic advantages and are important intermediates to gain more complex structures, for example in the total synthesis of cobalamin.[11]

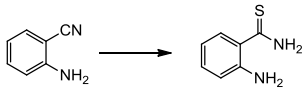
Regarding the synthesis, the preparation of thiolactams and thioamides is usually limited to thiation of carbonyl compounds with Lawesson's reagent[12] (LR), gaseous hydrogen sulfide[13] or phosphorus pentasulfide.[14] However, the strong foul smell and high toxicity of these reagents are still problematic. Methods to obtain quinolinthione and quionazolinthione 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 face selectivity problems.[16] Zheng and co-workers reported the synthesis of quinazolindithiones by capturing CS_2 at room temperature.[17] In this work, we focused on a different pathway to gain access to quinazolinthiones starting from thioamides, thus the sulfur is already attached to the substrates.

Results and Discussion

Recently, we reported the hydrolysis of anthranilonitrile and 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 obtain 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 with NaHS as hydrogen sulfide precursor.[20] Thus, H_2S is generated in situ and the use of gaseous sulfur could be avoided. The method was suitable with

increased reaction time to 72 hours. This can be explained by the electronwithdrawing properties of the aminofunction in ortho position (Table 1). We observed drastically decreased yields when we increased the temperature.

Table 1: Optimization for the synthesis of anthranilothioamide[a]

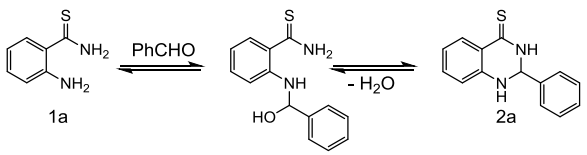


entry	time (hrs)	temp. (°C)	yield (%)[b]
1	1.5	20	5
2	48	20	77
3	72	20	88
4	16	130	5
5	20	130	-

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

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).

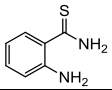
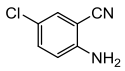
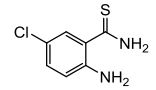
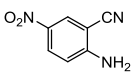
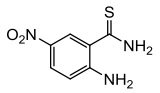
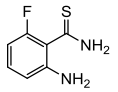
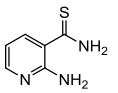
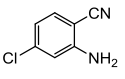
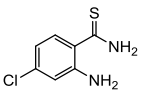
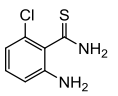
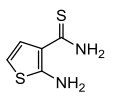
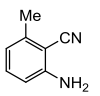
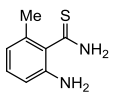
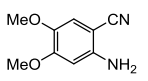
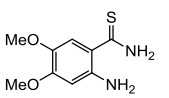
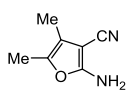
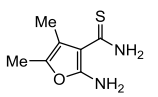
With a range of thioamides in hand, the crucial points were the stability of the o-amino-thioamide and the thiolactam in the reaction mixture. Also it was questionable if the thioamide may undergo the nucleophilic attack on the imine. As the requests of green chemistry and sustainable development, water was applied as a green and cheap solvent in 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. The reaction can be understood analogically to the tandem condensation-cyclisation-reaction of anthranilamide with aldehyde (Scheme 1).



Scheme 1: Dihydroquinazolinthion-synthesis from 2-aminobenzothioamide

Mass analysis and elemental analysis show the presence of the sulfur in the compound. 1D- and 2D-NMR-spectroscopy were used to prove the successful cyclisation. The thiolactam proton appears low-field shifted (9.97 ppm, DMSO-*d*6) compared to the corresponding quinazolinone proton (8.29 ppm, DMSO-*d*6).[21]

Table 2: Synthesis of anthranilothioamides[a]

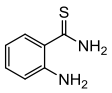
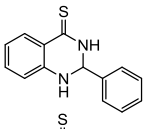
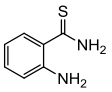
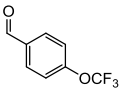
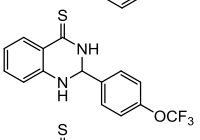
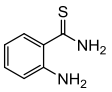
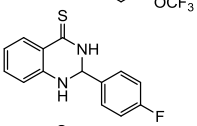
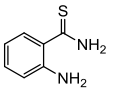
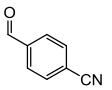
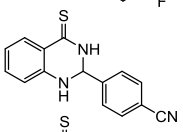
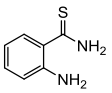
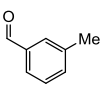
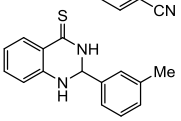
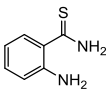
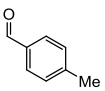
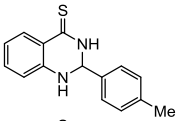
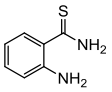
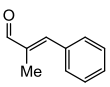
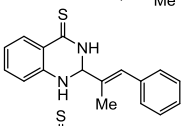
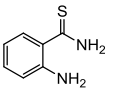
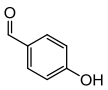
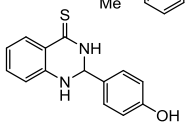
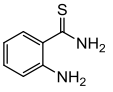
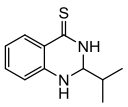
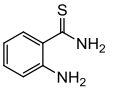
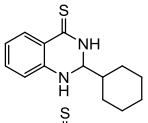
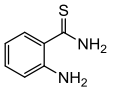
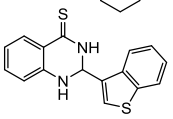
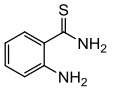
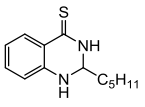
No.	nitrile	thioamide	yield (%)[b]
1a			88
1b			96
1c			80
1d			97
1e			93
1f			78
1g			62
1h			85
1i			0
1j			0
1k			0

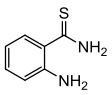
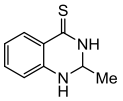
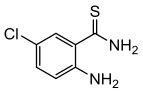
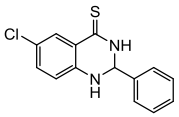
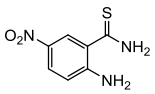
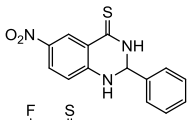
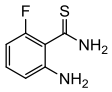
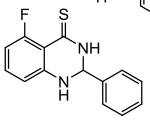
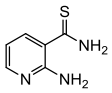
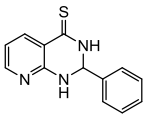
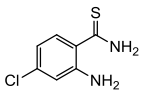
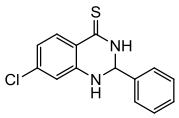
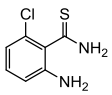
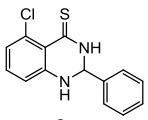
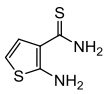
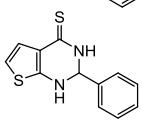
[a]. Reaction conditions: 0.5 mmol nitrile, 2 eq. $NaHS \cdot H_2O$, 1 eq. $MgCl_2$, 2 ml DMF, 20 °C, 72 hrs. [b]. Isolated yields

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 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 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 also well with acetaldehyde to obtain the 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 presented thiolactams. Pure compounds were obtained by recrystallization from ethyl acetetate / hexane. Compounds (2s) and (2t) could

be found in GC/MS analysis of the crude reaction mixture but decomposed during the purification process.

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
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 hrs. [b]. Isolated yields. [c]. Compound decomposes during purification

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 of Lewis-acid or other catalyst and represent a convenient alternative to the thiation of lactams with Lawesson's reagent or P_4S_{10}. Various different aldehydes and thioamides showed 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 solvent. All commercial available chemicals were used without further purification. NMR-Data were recorded on a Bruker AVANCE 300 III, Bruker AVANCE 250 III, Bruker ARX 300 and Bruker ARX 400 spectrometer. ^{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 Agilent HP-5973 Mass Selective Detector (EI) and an HP-5-capillary column using helium as carrier gas. Elemental analysis was performed on a Flash EA 112 and IR-spectra were recorded on a Nicolet 380 FT-IR spectrometer. IR-bands are 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 roundbottom 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 *via* column chromatography (hexane: ethyl acetate 8:2) yielding 3.58 g (88%) 2-aminobenzothioamide as yellow solid. MP.: 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 1mmol **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 hrs. whilst a yellow solid is precipitating. The crude product is filtered off and washed with water. The solid is dissolved in the 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. MP.: 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-d6): δ = 10.65 - 10.55 (1H, *m*, NH(3)), 8.06 (1H, *dd*, ^{3}J = 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-d6): 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 − -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*, ^{3}J = 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(1H)-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, ^{4}J = 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*, ^{4}J = 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}.

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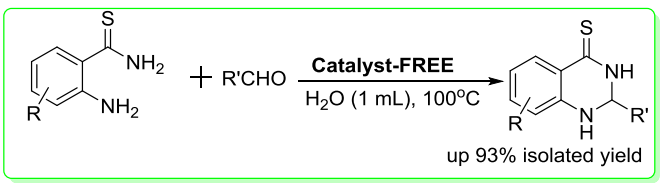

A convenient and facile procedure for the synthesis of dihydroquinazolinthiones from 2-aminobenzothioamide with aldehydes has been developed. The reactions took place in water and without need of any additive.