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Facile synthesis of novel 7-aminofuro- and 7-aminothieno[2,3-*d*] pyridazin-4(5*H*)-one and 4-aminophthalazin-1(2*H*)-ones

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ABSTRACT

We hereby report the synthesis of a novel class of compounds, 7-aminofuro- and 7-aminothieno[2,3-*d*] pyridazin-4(5*H*)-one and 4-aminophthalazin-1(2*H*)-ones starting from methyl 2-(2-methoxy-2-oxoethyl)furan- and thiophene-3-carboxylate and methyl 2-(2-methoxy-2-oxoethyl)benzoate. The ester functionalities connected directly to the aromatic ring were regiospecifically converted to the acid, whereas methylene groups were oxidized to the corresponding ketoesters. Reaction of the ketoesters with hydrazine provided the hydrazone derivatives. An intramolecular cyclization in the presence of thionyl chloride formed a fused pyridazinone skeleton. Hydrolysis of the remaining ester groups and transformation of the acid functionalities to the acyl azides followed by Curtius rearrangement gave the isocyanates. Reaction of the isocyanates with methanol and water produced urethane and aminopyridazinone derivatives, respectively.

1. Introduction

Pyridazinone (1) and phthalazinone (2) derivatives are an important class of biologically active compounds and they have attracted the attention of several research groups.[1] Pyridazinone (1) derivatives are well known for their use in the treatment in cardiovascular and heart diseases.[2] 4,5-Dihydropyridazin-3(2*H*)-ones show a wide range of pharmacological properties.

Selected examples are platelet aggregation inhibitors,[3] inhibitors of cyclooxygenase-2 (COX-2),[4] inhibitors of adenosine 3′,5′-cyclic phosphate phosphodiesterase III (CAMP PDE III),[5] p38 mitogen-activated protein (MAP) kinase inhibitors,[6] and in compounds with antihypertensive, antithrombotic, antiinflammatory, and antiulcer activities.[7,8]

4-Aminophthalazin-1(2*H*)-ones (**3**)[9] have shown potential as anticancer agents[10] and in the treatment of autoimmune and inflammatory diseases (Fig. 1).[11] Recently, 2-phenyl-4-aminophthalazinone **4** and derivatives have been reported as the core skeleton for the design of potent and selective human A_3 adenosine receptor antagonists.[12] Furthermore, they have been identified as poly(ADP-ribose) polymerase (PARP) inhibitors.[13]

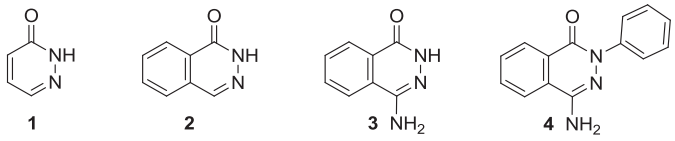

Fig. 1. Representative pyridazinone and phthalazinone derivatives.

Heteroaromatic fused pyridazinone derivatives are not widely distributed. 4,5-Fused thienopyridazinone derivatives, such as **5** (Fig. 2), were synthesized as histamine H3 receptor antagonists.[14] Yamaguchi et al.[15] synthesized some thieno- and furopyridazinone derivatives (**6**) and showed that thienopyridazinone derivatives are antiasthmatic agents with dual activities of thromboxane A2 synthetase inhibition and bronchodilation. Furthermore, they demonstrated that a thiophene ring is able to replace the benzene ring of a phthalazinone without loss of biological activities.[16] Functionalized pyridazinone systems are an important class of nitrogen-containing heterocycles possessing a broad spectrum of biological activities.[17,18] Efforts in our laboratory have been devoted to developing efficient protocols for the preparation of diverse fused heterocyclic scaffolds (Fig. 3).

In this paper we report the synthesis of various substituted aminopyridazinone derivatives fused to thiophene, furan, and

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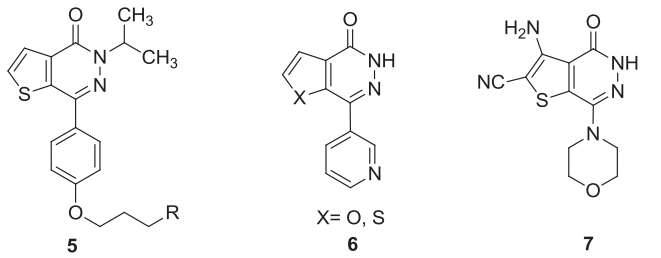


Fig. 2. Representative fused pyridazinone derivatives.

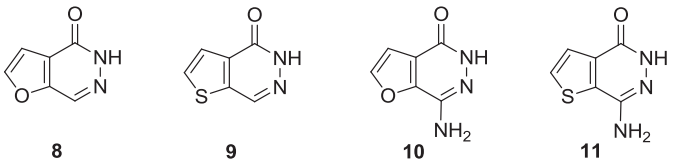
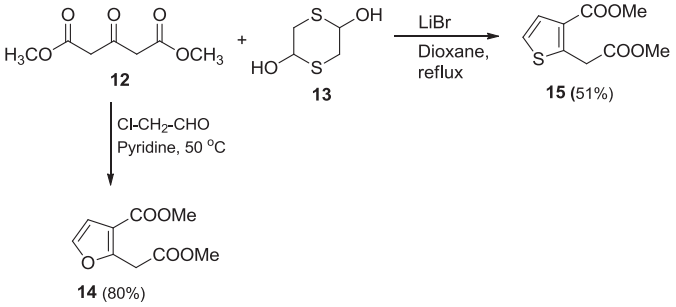


Fig. 3. Representative fused pyridazinone and aminopyridazinone derivatives.

benzene. In the literature, only a single compound **7** having a thienopyridazinone skeleton is described.[19]

2. Results and discussion

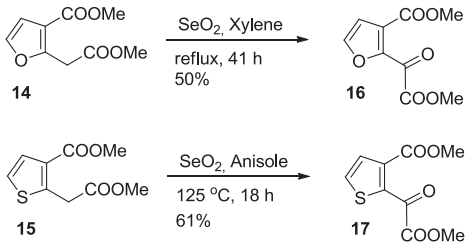
The synthesis of the starting materials **14** and **15** used in the synthesis of furo- and thienofused pyridazinones began with the readily available dimethyl acetonedicarboxylate **12**. Treatment of **12** with chloroacetaldehyde in the presence of pyridine yielded the diester **14** in 80% yield.[20] Reaction of **12** with 2,5-dihydroxy-1,4-dithiane in the presence of lithium bromide in dioxane gave the diester **15** in 51% yield (Scheme 1).[21]



Scheme 1. The synthesis of furan and thiophene diesters **14** and **15**.

The next step was the oxidation of methylene functionality to a carbonyl group. Selenium dioxide is a useful reagent for allylic oxidation of alkenes. The allylic alcohols that are initially formed can be further oxidized to carbonyl groups. Moreover, selenium dioxide can also oxidize the α-position of carbonyl groups to 1,2-dicarbonyl compounds.[22] Heating of the diesters **14** and **15** in xylene or anisole in the presence of selenium dioxide yielded the oxidized products **16** and **17** (Scheme 2).

First, the ester functional groups in **16** and **17** were hydrolyzed to the corresponding carboxylic acids **18** and **19** with KOH at 50 °C (Scheme 3). Recently, we reported that reactivity of the ester groups connected to benzene or furan rings is different than the reactivity of ester groups connected to an alkyl group.[23] Similarly, carboxylic acid functionality adjacent to a methylene group or a carbonyl group as in **18** and **19** is more reactive than the other. Therefore, it was possible to convert one of the acid functionalities in **18** and **19** regiospecifically to the corresponding monoesters **20**



Scheme 2. Synthesis of ketoesters **16** and **17**.

and **21** by treatment of diacids with concentrated HCl in methanol in reasonable yields.

Thus, reaction of acids with various substituted hydrazines in different solvents furnished the hydrazone derivatives **22** and **23**, which were not isolated and used for cyclization reactions (Scheme 3). To increase the reactivity of the acid carbonyl group, the acid functionalities were converted into acyl chlorides **24** and **25**. The acids **22** and **23** were treated with $SOCl_2$ in THF and the resulting mixture was heated at 60–80 °C for 16 h. The in situ formed acyl chlorides were cyclized to the desired pyridazinone derivatives **26** and **27**. The structures of all compounds were deduced from their NMR spectra.

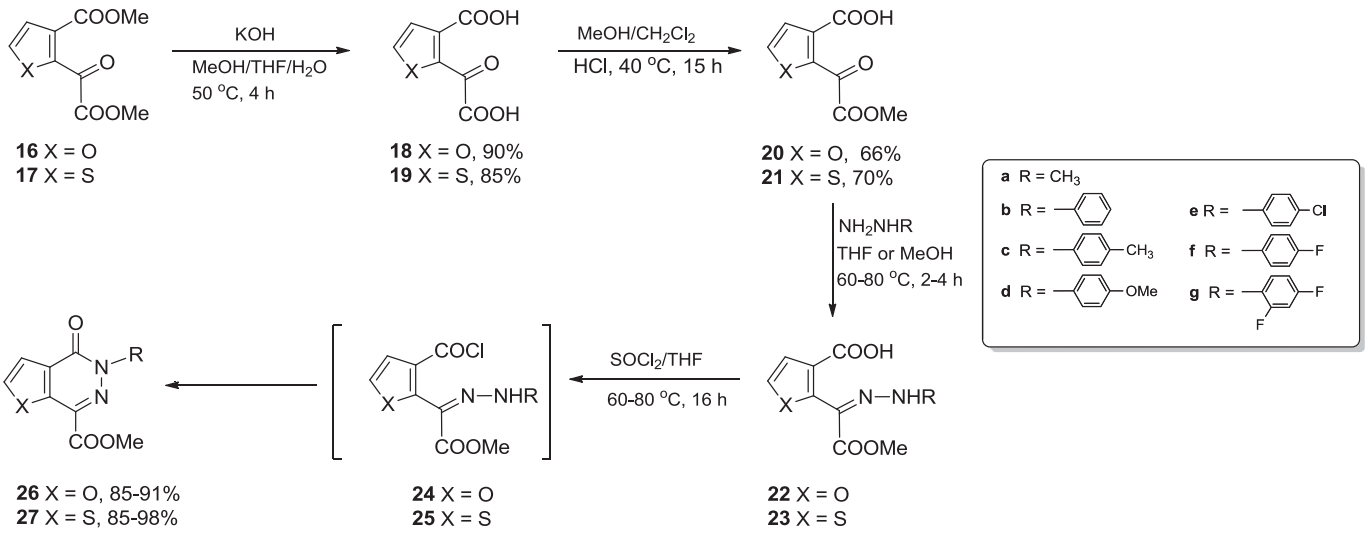
Conversion of the pyridazinone esters **26** and **27** to the corresponding aminopyridazinone derivatives was achieved through Curtius rearrangement. First, the esters **26** and **27** were treated with KOH at 50 °C to give the corresponding acids **28** and **29** (Scheme 4). The most general and versatile synthesis of acyl azides involves the reaction of acyl chlorides with NaN_3 in an aqueous medium. The acids **28** and **29** were treated with thionyl chloride or oxalyl chloride in appropriate solvents followed by reaction of the formed acyl chloride with NaN_3 to give the acyl azides **30** and **31**. Finally, heating of the acyl azide **30** and **31** in benzene provided the expected isocyanates cleanly.

Treatment of isocyanates in benzene with MeOH gave the urethane derivatives **32** and **33** in 43–83% yields. The hydrolysis of isocyanate with 8 M HCl provided the desired aminopyridazinone derivatives **34** and **35**. The ^1H and ^{13}C NMR spectra allowed the assignment of the structures **32**–**35**. Finally, X-ray diffraction analysis of a representative sample **32a** was carried out. The results of this study confirmed unambiguously the proposed structure (Fig. 4).

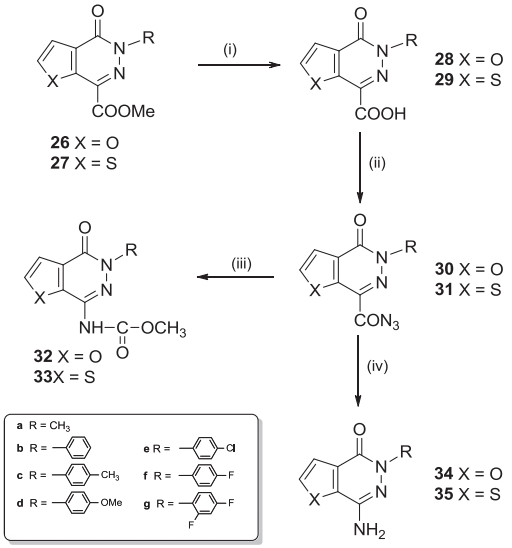
Homophthalic acid **36** was first reacted with thionyl chloride to give an anhydride that was then treated with methanol to produce the monoester **37**.[24] Treatment of **37** with SeO_2 in anisole afforded the ketoester **38**[25] in 51% yield (Scheme 5). Under conditions similar to those as reported in Scheme 4 the ketoesters were reacted with various substituted hydrazine derivatives to give hydrazone derivatives, which were directly cyclized with thionyl chloride to phthalazinone derivatives **39**. Conversion of phthalazinone esters to amino and urethane derivatives **43** and **42** was achieved through the acyl azides **41**. Hydrolysis of **39** with KOH in THF/MeOH afforded the corresponding acids **40**, which were directly used for generation of acyl azides **41** by treatment with oxalyl chloride followed by reaction of the formed acyl chlorides with NaN_3. Finally, heating of the acyl azide **41** in benzene provided isocyanate intermediates, which were converted to urethane and amino derivatives **42** and **43** upon treatment with HCl and MeOH, respectively (Scheme 5).

3. Conclusion

We have developed a new, facile, and efficient methodology for the synthesis of aminophthalazinone and thiophene and furan condensed pyridazinone derivatives. The strategies and experimental protocols described here can be applied to the synthesis of benzene and heteroaromatic ring substituted phthalazinone and pyridazinone



Scheme 3. Synthesis of furo- and thienocondensed pyridazinone derivatives.



Scheme 4. Synthesis of furo- and thieno-condensed aminopyridazinone derivatives. (i) KOH, $CHCl_3$/THF/MeOH/H_2O, 50 °C (57–78%); (ii) a: $SOCl_2$, $CHCl_3$/MeCN reflux or $(COCl)_2$, DMF, CH_2Cl_2, b: NaN_3, acetone (62–95%); (iii) a: benzene, reflux b: MeOH (43–83%); (iv) a: benzene, reflux b: 8 M HCl *c*: 2 M NaOH (42–68%).

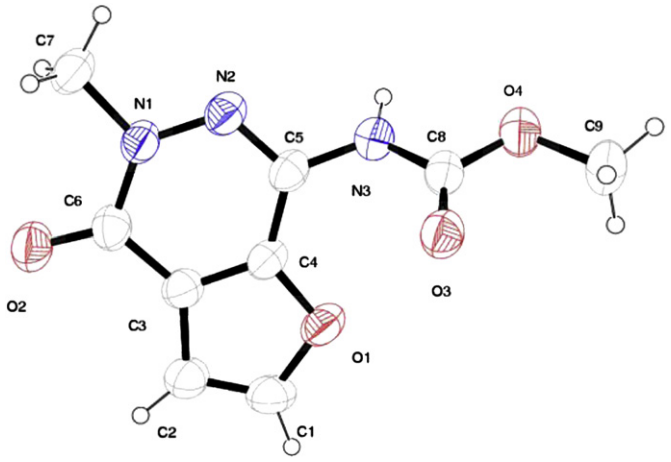


Fig. 4. ORTEP drawing of the molecule **32a**. Thermal ellipsoids are shown at 50% probability level.

derivatives. Furthermore, amide functionality as well as the amino group can be further functionalized.

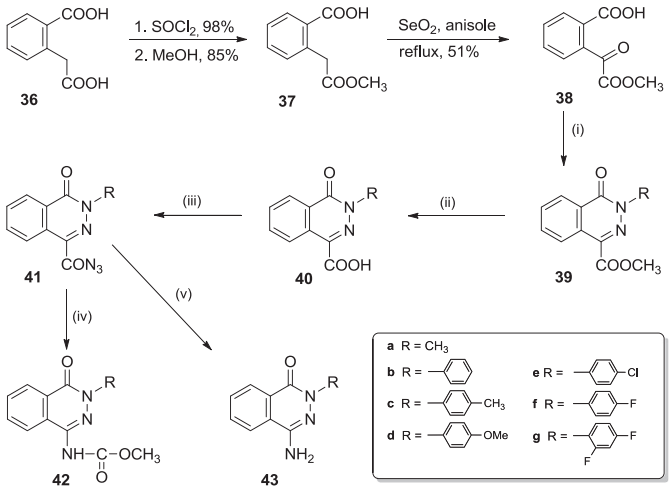
4. Experimental section

4.1. General

Melting points were determined on a Thomas-Hoover capillary melting point apparatus. IR spectra were recorded on a Perkin Elmer 980 spectrometer. NMR spectra were recorded on a Bruker instrument at 400 MHz for ^1H and 100.6 MHz for ^{13}C NMR. Apparent splitting is given in all cases. Elemental analysis was determined on an Leco CHNS-932 instrument (Ataturk University). Column chromatography was performed on silica gel (60-mesh, Merck), TLC was carried out on Merck 0.2 mm silica gel 60 F_{254}analytical aluminum plates.

*4.1.1. Methyl 2-(2-methoxy-2-oxoacetyl)furan-3-carboxylate (**16**).* SeO_2 (3.36 g, 30.30 mmol) was added to a stirred solution of diester **14** (3.0 g, 15.15 mmol) in xylene (60 mL) and heated at reflux for 18 h. The reaction was monitored on TLC and further SeO_2 (2.5 g, 22.71 mmol) was added and stirred for 7 h. TLC showed starting compound and further SeO_2 (1.68 g, 15.15 mmol) was added and stirred for a further 16 h. After the completion of the reaction, the mixture was cooled, filtered, and washed with ethyl acetate (100 mL). The filtrate was extracted with ethyl acetate (100 mL) and water (100 mL) and the water layer re-extracted with ethyl acetate (100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography (silica gel) eluting with hexane/ethyl acetate (3:1, 2:1) to give oxidized diester **16** as a white solid (1.59 g, 50%), mp 49–50 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J=1.7 Hz, 1H, H-5), 6.82 (d, J=1.7 Hz, 1H, H-4), 3.89 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 174.9, 162.6, 161.9, 148.6, 147.5, 126.0, 113.2, 53.1, 52.5; ν_{max} (ATR) 3128, 2956, 1732, 1669, 1574, 1470, 1480, 1438, 1301, 1232, 1206, 1174, 1076, 1050 cm^{-1}; [found: C, 51.03; H, 4.18. $C_9H_8O_6$ requires C, 50.95; H, 3.80%].

*4.1.2. Methyl 2-(2-methoxy-2-oxoacetyl)thiophene-3-carboxylate (**17**).* SeO_2 (2.6 g, 23.30 mmol) was added to a stirred solution of diester **15** (2.0 g, 9.3 mmol) in anisole (50 mL) and heated at 125 °C for 18 h. The reaction was monitored on TLC. After the completion of the reaction, the mixture was cooled, filtered, and washed with



Scheme 5. Synthesis of phthalazinone derivatives. (i) a) Hydrazine derivatives, THF or MeOH, b) $SOCl_2$, THF or benzene, 56–80%; (ii) a) KOH, THF/MeOH/H_2O (74–98%); (iii) $(COCl)_2$, DMF, CH_2Cl_2, and NaN_3, acetone (75–97%); (iv) benzene, reflux, and MeOH (80–99%); (v) benzene, reflux, 8 M HCl, and 2 M NaOH (80–98%).

ethyl acetate (100 mL). The solvent was evaporated and the crude product was purified by column chromatography (silica gel) eluting with hexane/ethyl acetate (2:1) to give oxidized diester **17** as a brown oil (1.25 g, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.61 (d, J=5.1 Hz, 1H, H-5), 7.43 (d, J=5.1 Hz, 1H, H-4), 3.85 (s, 3H, −OCH_3), 3.80 (s, 3H, −OCH_3); ^{13}C NMR δ_C (100.6 MHz, $CDCl_3$) 179.6, 162.8, 162.1, 142.0, 136.7, 132.9, 129.9, 53.1, 52.5; ν_{max} (ATR) 3110, 2954, 1758, 1717, 1668, 1262, 1170, 1151 cm^{-1}; [found: C, 46.99; H, 3.54; S, 14.27. $C_9H_8O_5S$ requires C, 47.36; H, 3.53; S, 14.05%].

*4.1.3. 2-(Carboxycarbonyl)-3-furoic acid (**18**).* A solution of KOH (28.3 mL, 56.6 mmol, 2 M) in methanol was added to a stirred solution of oxidized diester **16** (4.0 g, 18.9 mmol) in THF (60 mL), MeOH (30 mL), and H_2O (4 mL). The mixture was stirred at 50 °C for 4 h and monitored on TLC. After the completion of the reaction, the mixture was cooled on an ice bath and a solid precipitated. The precipitate was filtered, washed with ethyl acetate, and then dissolved in water (30 mL). The solution was acidified with aq HCl (1 M) to pH=2 and then extracted with ethyl acetate (3×400 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated to give diacid **18** as a white solid (2.96 g, 85%), mp 187–189 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.60 (br s, 2H, −COOH), 8.18 (d, J=1.7 Hz, 1H, C=CH), 7.00 (d, J=1.7 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 177.1, 163.7, 162.9, 148.9, 147.5, 127.5, 113.2; ν_{max} (ATR) 3441, 3154, 2957, 1638, 1478, 1430, 1377, 1269, 1208, 1151, 1076 cm^{-1}; [found: C, 45.54; H, 2.19. $C_7H_4O_6$ requires C, 45.67; H, 2.19%].

*4.1.4. 2-(Carboxycarbonyl)-3-thienoic acid (**19**).* The same procedure was used as described above using oxidized diester **17** (4.0 g, 17.5 mmol) to give diacid **19** as a white solid (3.1 g, 90%), mp 153–155 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.50 (br s, 2H, −COOH), 8.07 (d, J=5.0 Hz, 1H, C=CH), 7.47 (d, J=5.0 Hz, 1H, C=CH); ^{13}C NMR δ (100.6 MHz, DMSO-d_6) 181.9, 163.8, 162.8, 140.8, 138.6, 134.2, 129.5; ν_{max} (ATR) 3118, 1719, 1685, 1663, 1526, 1402, 1259, 12,043 cm^{-1}; [found: C, 42.04; H, 2.13; S, 16.02. $C_7H_4O_5S$ requires C, 42.00; H, 2.01; S, 16.02%].

*4.1.5. 2-[Methoxy(oxo)acetyl]-3-furoic acid (**20**).* Concd HCl (20 drops) was added to a stirred solution of diacid **18** (2.0 g, 10.87 mmol) in MeOH (20 mL) and CH_2Cl_2 (40 mL) and the mixture was stirred at 40 °C for 15 h. The solvents were evaporated and the residue was purified and separated by column chromatography (silica gel) eluting with hexane/ethyl acetate (2:1) and then only with ethyl acetate to give monoester **20** as a white solid (1.51 g, 70%), mp 64–65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.5 (br s, 1H, −COOH), 7.72 (d, J=1.7 Hz, 1H, C=CH), 7.14 (d, J=1.7 Hz, 1H, C=CH), 3.96 (s, 3H, −OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 177.0, 161.6 (2C), 148.8, 147.3, 129.3, 116.3, 53.6; ν_{max} (ATR) 3128, 2916, 1744, 1704, 1670, 1578, 1477, 1423, 1385, 1296, 1232, 1217, 1077 cm^{-1}; [found: C, 48.49; H, 3.01. $C_8H_6O_6$ requires C, 48.50; H, 3.05%].

*4.1.6. 2-[Methoxy(oxo)acetyl]-3-thienoic acid (**21**).* The same procedure was used as described above using diacid **19** (3.1 g, 15.5 mmol) to give monoester **21** as a white solid (2.2 g, 66%), mp 98–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.5 (br s, 1H, −COOH), 7.71 (d, 1H, J=5.1 Hz, C=CH), 7.64 (d, J=5.1 Hz, 1H, C=CH), 3.89 (s, 3H, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 179.6, 166.6, 162.0, 142.5, 136.1, 133.7, 131.2, 53.3; ν_{max} (ATR) 3117, 2960, 1723, 1690, 1664, 1518, 1403, 1312, 1290, 1274, 1172 cm^{-1}; [found: C, 44.44; H, 2.76; S, 14.93. $C_8H_6O_5S$ requires C, 44.86; H, 2.82; S, 14.97%].

*4.1.7. Methyl 5-methyl-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26a**).* A solution of methyl hydrazine (0.37 mL, 7.07 mmol) in dry THF (5 mL) was added to a stirred solution of the monoester **20** (1.4 g, 7.07 mmol) in dry THF (75 mL) and the mixture was stirred at 50 °C for 2 h. Thionyl chloride (1.03 mL, 14.14 mmol) was added to the reaction mixture and stirred at 50 °C for 16 h. The solvent was evaporated and the residue was purified by column chromatography (silica gel) eluting with ethyl acetate/chloroform/hexane (3:3:2) to give pyridazine **26a** as a white solid (1.25 g, 85%), mp 207–208 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=2.0 Hz, 1H, C=CH), 7.10 (d, J=2.0 Hz, 1H, C=CH), 4.06 (s, 3H, −OCH_3), 3.98 (s, 3H, N−CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.2, 158.8, 151.3, 147.6, 126.6, 122.9, 107.2, 53.0, 40.4; ν_{max} (ATR) 3126, 3108, 2960, 1739, 1674, 1505, 1428, 1331, 1231, 1155, 1056 cm^{-1}; [found: C, 51.81; H, 3.83; N, 13.37. $C_9H_8N_2O_4$ requires C, 51.93; H, 3.87; N, 13.46%].

*4.1.8. Methyl 5-methyl-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylate (**27a**).* The same procedure was used as described above using monoester **21** (1.4 g, 6.5 mmol) to give pyridazine **27a** as a white solid (1.43 g, 91%), mp 200–202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, A-part of AB-system, J=5.4 Hz, 1H, C=CH), 7.68 (d, B-part of AB-system, J=5.4 Hz, 1H, C=CH), 4.00 (s, 3H, −OCH_3), 3.92 (s, 3H, −NCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.2, 157.6, 138.5, 135.3, 133.9, 131.5, 124.3, 53.3, 40.2; ν_{max} (ATR) 3085, 3070, 2964, 1710, 1683, 1451, 1432, 1354, 1256, 1211, 1056 cm^{-1}; [found: C, 48.42; H, 3.59; N, 12.49; S, 14.68. $C_9H_8N_2O_3S$ requires C, 48.21; H, 3.60; N, 12.49; S, 14.30%].

*4.1.9. Methyl 4-oxo-5-phenyl-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26b**).* A solution of phenyl hydrazine (0.99 mL, 10.1 mmol) in dry THF (5 mL) was added to a stirred solution of the monoester **20** (2.0 g, 10.1 mmol) in dry THF (40 mL) and dry benzene (40 mL) and the mixture was stirred at 80 °C for 4 h. Thionyl chloride (1.5 mL, 20.2 mmol) was added to the reaction mixture and stirred at 80 °C for 16 h. The solvents were evaporated and the residue was purified by column chromatography (silica gel) eluting with ethyl acetate/hexane (1:1) and then ethyl acetate/dichloromethane (1:1) to give pyridazine **26b** as a white solid (2.46 g, 90%), mp 201–202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J=2.0 Hz, 1H, C=CH), 7.61–7.58 (m, 2H, arom.), 7.53–7.49 (m, 2H, arom.), 7.44 (tt, J=6.8, 1.2 Hz, 1H), 7.16 (d, J=2.0 Hz, 1H), 4.05 (s, 3H, −OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.3, 158.4, 151.0, 147.8, 141.1, 129.0, 128.7, 127.6, 126.1, 123.9, 107.9, 53.1; ν_{max} (ATR) 3156, 3099, 2957, 1739, 1687, 1627, 1580, 1510, 1434, 1334, 1263, 1179, 1136, 1121, 1079 cm^{-1}; [found: C, 62.36; H, 3.64; N, 10.32. $C_{14}H_{10}N_2O_4$ requires C, 62.22; H, 3.73; N, 10.37%].

*4.1.10. Methyl 4-oxo-5-phenyl-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylate (**27b**).* The same procedure was used as described above using monoester **21** (2.0 g, 6.3 mmol) to give pyridazine **27b** as a white solid (2.1 g, 81%), mp 246–248 °C. ^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.74 (s, 2H, thiophene), 7.58–7.55 (m, 2H, arom.), 7.46–7.42 (m, 2H, arom.), 7.36 (tt, *J*=7.4, 1.2 Hz, 1H, arom.), 3.98 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.4, 157.0, 141.1, 138.1, 136.2, 134.2, 132.2, 129.0, 128.6, 126.0, 125.0, 53.4; ν_{max} (ATR) 3102, 3083, 1709, 1681, 1500, 1453, 1356, 1192, 1155, 1045 cm^{-1}; [found: C, 58.90; H, 3.67; N, 9.82; S, 11.57; $C_{14}H_{10}N_2O_3S$ requires C, 58.73; H, 3.52; N, 9.78; S, 11.20%].

4.2. General procedure for the synthesis of furopyridazine derivatives (26c–g)

The monoester **20** (1.0 g, 5.05 mmol) and phenyl hydrazinium chloride derivatives (5.3 mmol) were dissolved in dry THF (30 mL) and MeOH (30 mL) and the mixture was stirred at 60 °C for 3 h. The solvents were evaporated and the residue was dissolved in dry THF (40 mL). Thionyl chloride (1.3 mL, 17.8 mmol) was added to the reaction mixture and stirred at 60 °C for 16 h. The solvent was evaporated and the residue was purified by column chromatography eluting with ethyl acetate/hexane (1:1) and then ethyl acetate/dichloromethane (1:1) to give furopyridazine derivatives **26c–g** as a white solid.

*4.2.1. Methyl 5-(4-methylphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26c**).* (1.30 g, 91%), mp 205–206 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J*=2.0 Hz, 1H, –C=CH), 7.39 (br d, *J*=7.6 Hz, 2H, arom.), 7.23 (br d, *J*=7.6 Hz, 2H, arom.), 7.08 (d, *J*=2.0 Hz, 1H, C=CH), 3.97 (s, 3H, $-OCH_3$), 2.35 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.3, 158.5, 151.0, 147.8, 138.8, 138.6, 129.6, 127.4, 125.9, 123.8, 107.8, 53.0, 21.2; ν_{max} (ATR) 3153, 3100, 2960, 1743, 1687, 1509, 1436, 1336, 1260, 1133, 1121, 1076 cm^{-1}; [found: C, 63.06; H, 4.11; N, 9.61. $C_{15}H_{12}N_2O_4$ requires C, 63.38; H, 4.25; N, 9.85%].

*4.2.2. Methyl 5-(4-methoxyphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26d**).* (1.36 g, 90%), mp 203–204 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J*=2.0 Hz, 1H, C=CH), 7.46–7.42 (m, A-part of AA′BB′ system, 2H, arom.), 7.08 (d, *J*=2.0 Hz, 1H, C=CH), 6.96–6.92 (m B-part of-AA′BB′ system, 2H, arom.), 3.97 (s, 3H, $-OCH_3$), 3.79 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.3, 159.6, 158.5, 151.0, 147.7, 134.1, 127.3, 127.2, 123.8, 114.2, 107.8, 55.6, 53.0; ν_{max} (ATR) 3142, 3104, 2966, 1741, 1720, 1682, 1506, 1435, 1334, 1253, 1134, 1118, 1076 cm^{-1}; [found: C, 59.64; H, 4.06; N, 9.20. $C_{15}H_{12}N_2O_5$ requires C, 60.00; H, 4.03; N, 9.33%].

*4.2.3. Methyl 5-(4-chlorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26e**).* (1.33 g, 86%), mp 192–193 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J*=2.0 Hz, 1H, C=CH), 7.61–7.58 (m, A-part of AA′BB′ system, 2H, arom.), 7.52–7.50 (m, B-part of AA′BB′ system, 2H, arom.), 7.18 (d, *J*=2.0 Hz, 1H, C=CH), 4.07 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.1, 158.2, 150.9, 148.0, 139.5, 134.5, 129.1, 127.9, 127.4, 123.9, 107.9, 53.2; ν_{max} (ATR) 3148, 3130, 2968, 1744, 1702, 1504, 1488, 1437, 1332, 1258, 1180, 1172, 1136, 1116, 1083, 1074 cm^{-1}; [found: C, 54.85; H, 2.79; N, 8.87. $C_{14}H_9ClN_2O_4$ requires C, 55.19; H, 2.98; N, 9.19%].

*4.2.4. Methyl 5-(4-fluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26f**).* (1.32 g, 91%), mp 214–215 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=2.0 Hz, 1H, C=CH), 7.54–7.49 (m, A-part of AA′BB′ system, 2H, arom.), 7.19–7.10 (m, B-part of AA′BB′ system, 2H, arom.), 7.08 (d, *J*=2.0 Hz, 1H, C=CH), 3.98 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.8 (d, *J*=248.6 Hz), 161.1, 158.3, 150.9, 148.0, 137.0 (d, *J*=3.1 Hz), 128.0 (d, *J*=8.8 Hz), 127.7, 123.9, 115.9 (d, *J*=23.2 Hz), 107.9, 53.1; ν_{max} (ATR) 3174, 3150, 2971, 1740, 1686, 1505, 1435, 1336, 1277, 1215, 1177, 1135, 1112, 1076 cm^{-1}; [found: C, 58.44; H, 3.03; N, 9.67. $C_{14}H_9FN_2O_4$ requires C, 58.34; H, 3.15; N, 9.72%].

*4.2.5. Methyl 5-(2,4-difluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylate (**26g**).* (1.32 g, 85%), mp 181–182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J*=2.0 Hz, 1H, C=CH), 7.50–7.45 (m, 1H, arom.), 7.16 (d, *J*=2.0 Hz, 1H, C=CH), 7.07–7.00 (m, 2H, arom.), 4.06 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.1 (dd, *J*=252.1 and 11.3 Hz), 160.9, 157.9, 157.6 (dd, *J*=255.8 and 12.8 Hz), 151.0, 148.1, 129.9 (dd, *J*=10.3 and 1.3 Hz), 128.4, 125.2 (dd, *J*=12.9 and 4.0 Hz), 123.6, 112.0 (dd, *J*=22.7 and 3.6 Hz), 107.8, 105.1 (dd, *J*=26.7 and 23.4 Hz), 53.2; ν_{max} (ATR) 3174, 3072, 2970, 1736, 1702, 1619, 1506, 1435, 1344, 1291, 1229, 1176, 1139, 1105, 1071 cm^{-1}; [found: C, 54.71; H, 2.60; N, 9.08. $C_{14}H_8F_2N_2O_4$ requires C, 54.91; H, 2.63; N, 9.15%].

4.3. General procedure for the synthesis of thienopyridazine derivatives (27c–g)

The monoester **21** (1.0 g, 4.67 mmol) and phenyl hydrazinium chloride derivatives (5.1 mmol) were dissolved in dry MeOH (50 mL) and the mixture was stirred at 50 °C for 2 h. The solvent was evaporated and the residue was dissolved in dry benzene (50 mL). Thionyl chloride (1.0 mL, 14.0 mmol) was added to the reaction mixture and stirred at 50 °C for 16 h. The solvent was evaporated and the residue was purified by column chromatography eluting with ethyl acetate/dichloromethane (1:1) to give thienopyridazine derivatives **27c–g** as a white solid.

*4.3.1. Methyl 5-(4-methylphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylate (**27c**).* (1.33 g, 95%), mp 251–253 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, A-part of AB-system *J*=5.5 Hz, 1H, C=CH), 7.72 (d, B-part of AB-system, *J*=5.5 Hz, 1H, C=CH), 7.45–7.42 (m, A-part of AA′BB′ system, 2H, arom.), 7.25–7.22 (m, B-part of AA′BB′ system, 2H, arom.), 3.97 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 164.1, 157.7, 139.3, 139.2, 138.7, 136.8, 134.7, 132.7, 130.2, 126.4, 125.6, 53.9, 21.8; ν_{max} (ATR) 3102, 3083, 2959, 1746, 1710, 1679, 1487, 1453, 1442, 1405, 1356, 1270, 1145, 1111, 1086, 1046 cm^{-1}; [found: C, 59.78; H, 4.11; N, 9.43; S, 10.82. $C_{15}H_{12}N_2O_3S$ requires C, 59.99; H, 4.03; N, 9.33; S, 10.68%].

*4.3.2. Methyl 5-(4-methoxyphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxy-late (**27d**).* (1.26 g, 85%), mp 189–191 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J*=5.5 Hz, 1H, C=CH), 7.72 (d, *J*=5.5 Hz, 1H, C=CH), 7.50–7.46 (m, A-part of AA′BB′ system, 2H, arom.), 6.97–6.91 (m, B-part of AA′BB′ system, 2H, arom.), 3.97 (s, 3H, $-OCH_3$), 3.79 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.5, 159.6, 157.1, 138.1, 136.2, 134.1, 134.0, 132.0, 127.2, 125.0, 114.2, 55.6, 53.3; ν_{max} (ATR) 3075, 2954, 2839, 1720, 1671, 1511, 1454, 1437, 1358, 1234, 1175, 1147, 1047 cm^{-1}; [found: C, 56.65; H, 3.81; N, 8.81; S, 9.82. $C_{15}H_{12}N_2O_4S$ requires C, 56.95; H, 3.82; N, 8.86; S, 10.14%].

*4.3.3. Methyl 5-(4-chlorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylate (**27e**).* (1.47 g, 98%), mp 195–197 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J*=5.3 Hz, 1H, C=CH), 7.73 (d, *J*=5.3 Hz, 1H, C=CH), 7.59–7.52 (m, A-part of AA′BB′ system, 2H, arom.), 7.44–7.38 (m, B-part of AA′BB′ system, 2H, arom.), 3.98 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.2, 156.8, 139.5, 138.1, 136.1, 134.5, 134.3, 132.4, 129.1, 127.3, 125.0, 53.4; ν_{max} (ATR) 3103, 3087, 2919, 2849, 1745, 1717, 1686, 1486, 1452, 1405, 1358, 1270, 1143, 1135, 1087, 1011 cm^{-1}; [found: C, 52.39; H, 3.15; N, 8.44; S, 10.35. $C_{14}H_9ClN_2O_3S$ requires C, 52.42; H, 2.83; N, 8.73; S, 10.00%].

*4.3.4. Methyl 5-(4-fluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylate (**27f**).* (1.26 g, 89%), mp 201–203 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J*=5.3 Hz, 1H, C=CH), 7.73 (d, *J*=5.3 Hz, 1H, C=CH), 7.57 (m, A-part of AA′BB′ system, 2H, arom.), 7.55 (m, B-part of AA′BB′ system, 2H, arom.), 3.98 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.3, 161.3 (d, *J*=248.7 Hz), 157.0, 138.1, 137.1 (d, *J*=3.4 Hz), 136.2, 134.43, 132.3, 127.9 (d, *J*=8.7 Hz), 125.0, 115.9 (d, *J*=23.0 Hz), 53.41; ν_{max} (ATR) 3105, 3084, 2964, 1746, 1716, 1682, 1453,

1435, 1358, 1235, 1144, 1042 cm^{-1}; [found: C, 55.32; H, 3.04; N, 9.10; S, 11.02. $C_{14}H_9FN_2O_3S$ requires C, 55.26; H, 2.98; N, 9.21; S, 10.54%].

*4.3.5. Methyl 5-(2,4-difluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d] pyridazine-7-carboxylate (**27g**).* (1.46 g, 97%), mp 224–226 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J=5.3 Hz, 1H, C=CH), 7.73 (d, J=5.3 Hz, 1H, C=CH), 7.48–7.38 (m, 1H, arom.), 7.00–6.92 (m, 2H, arom.), 3.98 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.1, 163.0 (dd, J=251.7 and 11.1 Hz), 157.7 (dd, J=257.0 and 13.0 Hz), 156.5, 138.3, 135.7, 134.7, 133.0, 129.9 (dd, J=10.3 and 1.4 Hz), 125.3 (dd, J=13.0 and 4.2 Hz), 125.0, 112.0 (dd, J=22.8 and 3.8 Hz), 105.2 (dd, J=26.5 and 23.5 Hz), 53.5; ν_{max} (ATR) 3104, 3085, 2963, 1746, 1717, 1687, 1485, 1452, 1435, 1359, 1271, 1143, 1110, 1087 cm^{-1}; [found: C, 52.17; H, 2.50; N, 8.66; S, 10.35. $C_{14}H_8F_2N_2O_3S$ requires C, 52.17; H, 2.50; N, 8.69; S, 9.95%].

4.4. General procedure for the hydrolysis of pyridazine derivatives (26a–g and 27a–g)

A solution of KOH (4.8–3.1 mL, 2 mol equiv, 2 M) in methanol was added to a stirred solution of esters **26a–g** and **27a–g** (1.0 g, 4.8–3.1 mmol) in THF (60 mL), chloroform (80 mL) and H_2O (0.5 mL). The mixture was stirred at 50 °C for 90 min and monitored on TLC. After the completion of the reaction, the mixture was cooled, hexane (50 mL) added and a solid precipitated. The precipitate was filtered, washed with ethyl acetate, and then dissolved in water (40 mL). The solution was acidified with aq HCl (1 M) to pH=2 and a white solid precipitated. The precipitate was filtered on filter paper and allowed to dry at ambient temperature to give acids **28a–g** and **29a–g** as white solids.

*4.4.1. 5-Methyl-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylic acid (**28a**).* (0.73 g, 78%), mp 258–260 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 13.3 (br s, 1H, –COOH), 8.29 (d, J=2.0 Hz, 1H, C=CH), 7.20 (d, J=2.0 Hz, 1H, C=CH), 3.80 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.6, 158.1, 151.0, 148.9, 127.0, 122.1, 106.7, 39.7; ν_{max} (ATR) 3125, 3109, 2875, 1733, 1634, 1572, 1506, 1424, 1370, 1315, 1216, 1165, 1069 cm^{-1}; [found: C, 49.25; H, 3.07; N, 14.37. $C_8H_6N_2O_4$ requires C, 49.49; H, 3.12; N, 14.43%].

*4.4.2. 4-Oxo-5-phenyl-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylic acid (**28b**).* (0.82 g, 87%), mp 231–233 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 13.98 (br s, 1H, –COOH), 8.37 (d, J=1.6 Hz, 1H, C=CH), 7.56–7.49 (m, 5H, arom.), 7.29 (d, J=1.6 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.6, 157.9, 150.8, 149.2, 141.3, 128.7, 128.4, 128.1, 126.5, 123.1, 107.3; ν_{max} (ATR) 3140, 3113, 3069, 2913, 1727, 1639, 1526, 1510, 1489, 1421, 1314, 1228, 1184, 1157, 1123, 1082 cm^{-1}; [found: C, 61.19; H, 3.01; N, 10.91. $C_{13}H_8N_2O_4$ requires C, 60.94; H, 3.15; N, 10.93%].

*4.4.3. 5-(4-Methylphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazi-ne-7-carboxylic acid (**28c**).* (0.82 g, 86%), mp 225–227 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 13.96 (br s, 1H, –COOH), 8.36 (d, J=2.0 Hz, 1H, C=CH), 7.44–7.41 (m, A-part of AA′BB′ system, 2H, arom.), 7.36–7.33 (m, B-part of AA′BB′ system, 2H, arom.), 7.27 (d, J=2.0 Hz, 1H, C=CH), 2.39 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.6, 157.9, 150.8, 149.1, 138.8, 138.0, 129.1, 127.9, 126.2, 123.0, 107.3, 20.8; ν_{max} (ATR) 3149, 3113, 2919, 1732, 1641, 1526, 1510, 1420, 1312, 1218, 1155, 1121 cm^{-1}; [found: C, 61.85; H, 3.64; N, 10.12. $C_{14}H_{10}N_2O_4$ requires C, 62.22; H, 3.73; N, 10.37%].

*4.4.4. 5-(4-Methoxyphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazine-7-carboxylic acid (**28d**).* (0.81 g, 85%), mp 212–214 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.34 (br s, 1H, C=CH), 7.46 (br d, J=6.6 Hz, 2H, arom.), 7.25 (br s, 1H, C=CH), 7.06 (br d, J=6.6 Hz, 2H, arom.), 3.86 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.6, 158.9, 158.0, 150.7, 149.2, 134.1, 127.8, 127.7, 123.0, 113.8, 107.3, 55.6; ν_{max} (ATR) 3141, 3113, 2910, 2834, 1728, 1642, 1525, 1507, 1423, 1370, 1254, 1229, 1157, 1124 cm^{-1}; [found: C, 58.36; H, 3.43; N, 9.42. $C_{14}H_{10}N_2O_5$ requires C, 58.74; H, 3.52; N, 9.79%].

*4.4.5. 5-(4-Chlorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyrida-zine-7-carboxylic acid (**28e**).* (0.80 g, 84%), mp 226–227 °C. ^1H NMR δ (400 MHz, DMSO-d_6) 8.37 (d, J=1.7 Hz, 1H, C=CH), 7.62 (br s, 4H, arom.), 7.29 (d, J=1.7 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.5, 157.8, 150.7, 149.3, 140.0, 132.9, 128.7, 128.3, 128.2, 123.1, 107.4; ν_{max} (ATR) 3148, 3112, 2934, 1730, 1640, 1525, 1510, 1491, 1421, 1315, 1230, 1185, 1154, 1120, 1093, 1018 cm^{-1}; [found: C, 53.39; H, 2.42; N, 9.44. $C_{13}H_7ClN_2O_4$ requires C, 53.72; H, 2.43; N, 9.64%].

*4.4.6. 5-(4-Fluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyrida-zine-7-carboxylic acid (**28f**).* (0.82 g, 86%), mp 244–245 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 13.82 (br s, 1H, –COOH), 8.36 (d, J=2.0 Hz, 1H), 7.65–7.60 (m, A-part of AA′BB′ system, 2H, arom.), 7.41–7.36 (m, B-part of AA′BB′ system, 2H, arom.), 7.28 (d, J=2.0 Hz, 1H); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.6, 161.5 (d, J=245.6 Hz), 157.9, 150.8, 149.2, 137.5 (d, J=2.9 Hz), 128.7 (d, J=8.9 Hz), 128.1, 123.1, 115.5 (d, J=22.9 Hz), 107.3; ν_{max} (ATR) 3140, 3114, 2926, 1729, 1651, 1608, 1526, 1423, 1317, 1231, 1185, 1158, 1123, 1022 cm^{-1}; [found: C, 56.77; H, 2.46; N, 10.07. $C_{13}H_7FN_2O_4$ requires C, 56.94; H, 2.57; N, 10.22%].

*4.4.7. 5-(2,4-Difluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-]pyrida-zine-7-carboxylic acid (**28g**).* (0.76 g, 80%), mp 224–225 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.41 (d, J=2.0 Hz, 1H, C=CH), 7.74–7.68 (m, 1H, arom.), 7.60–7.54 (m, 1H, arom.), 7.34–7.30 (1H, m), 7.32 (d, J=2.0 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 162.3 (dd, J=248.9 and 11.4 Hz), 161.4, 157.6, 157.0 (dd, J=252.9 and 13.3 Hz), 150.9, 149.6, 130.9 (d, J=10.4 Hz), 129.1, 125.4 (dd, J=12.9 and 3.9 Hz), 122.8, 122.2 (dd, J=22.7 and 3.4 Hz), 107.3, 104.9 (dd, J=27.2 and 23.9 Hz); ν_{max} (ATR) 3145, 3120, 2919, 1730, 1656, 1615, 1526, 1506, 1439, 1421, 1369, 1275, 1214, 1145, 1124, 1077 cm^{-1}; [found: C, 53.27; H, 1.97; N, 9.44. $C_{13}H_6F_2N_2O_4$ requires C, 53.44; H, 2.07; N, 9.59%].

*4.4.8. 5-Methyl-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29a**).* (0.53 g, 57%), mp 276–278 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 13.90 (br s, 1H, –COOH), 8.15 (d, J=5.3 Hz, 1H, C=CH), 7.66 (d, J=5.3 Hz, 1H, C=CH), 3.82 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.9, 156.8, 138.1, 135.5, 134.6, 131.7, 123.5, 39.6; ν_{max} (ATR) 3073, 2957, 1705, 1619, 1456, 1396, 1189, 1033 cm^{-1}; [found: C, 45.39; H, 2.55; N, 12.97; S, 14.89. $C_8H_6N_2O_3S$ requires C, 45.71; H, 2.88; N, 13.33; S, 15.25%].

*4.4.9. 4-Oxo-5-phenyl-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29b**).* (0.69 g, 73%), mp 245–247 °C ^1H NMR (400 MHz, DMSO-d_6) δ 14.20 (br s, 1H, –COOH), 8.22 (d, J=5.3 Hz, 1H, C=CH), 7.73 (d, J=5.3 Hz, 1H, C=CH), 7.63–7.47 (m, 5H, arom.); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 164.6, 157.0, 141.9, 138.5, 136.6, 136.1, 133.1, 129.3, 129.0, 127.1, 124.7; ν_{max} (ATR) 3109, 3076, 2959, 2834, 1714, 1536, 1456, 1401, 1393, 1153, 1126, 1036 cm^{-1}; [found: C, 57.07; H, 3.09; N, 10.63; S, 12.11. $C_{13}H_8N_2O_3S$ requires C, 57.35; H, 2.96; N, 10.29; S, 11.78%].

*4.4.10. 5-(4-Methylphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyri-dazine-7-carboxylic acid (**29c**).* (0.83 g, 87%), mp 233–235 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 14.10 (br s, 1H, –COOH), 8.20 (d, J=5.3 Hz, 1H, C=CH), 7.72 (d, J=5.3 Hz, 1H, C=CH), 7.48 (br d, J=8.3 Hz, 2H, arom.), 7.35 (br d, J=8.3 Hz, 2H, arom.), 2.40 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.9, 156.4, 138.8, 137.9, 137.8, 135.8, 135.5, 132.4, 129.1, 126.2, 124.1, 20.7; ν_{max} (ATR) 3102, 2918, 1746, 1716, 1687, 1623, 1487, 1453, 1434, 1359, 1270, 1146, 1039 cm^{-1}; [found: C, 58.41;

H, 3.59; N, 9.53; S, 11.58. $C_{14}H_{10}N_2O_3S$ requires C, 58.73; H, 3.52; N, 9.78; S, 11.20%].

*4.4.11. 5-(4-Methoxyphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29d**).* (0.83 g, 87%), mp 230–232 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.05 (br s, 1H, –COOH), 8.20 (d, J=5.3 Hz, 1H, C=CH), 7.71 (d, J=5.3 Hz, 1H, C=CH), 7.55–7.49 (m, A-part of AA′BB′ system, 2H, arom.), 7.11–7.06 (m, B-part of AA′BB′ system, 2H, arom.), 3.83 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 164.0, 158.9, 156.5, 137.8, 135.8, 135.4, 134.1, 132.2, 127.7, 124.1, 113.8, 55.5; ν_{max} (ATR) 3111, 3075, 2961, 2834, 1714, 1624, 1609, 1508, 1456, 1330, 1252, 1218, 1155, 1127, 1031 cm^{-1}; [found: C, 55.28; H, 3.38; N, 9.30; S, 10.61. $C_{14}H_{10}N_2O_4S$ requires C, 55.62; H, 3.33; N, 9.27; S, 10.61%].

*4.4.12. 5-(4-Chlorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29e**).* (0.67 g, 70%), mp 244–246 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.10 (br s, 1H, –COOH), 8.22 (d, J=5.3 Hz, 1H, C=CH), 7.73 (d, J=5.3 Hz, 1H, C=CH), 7.70–7.65 (m, A-part of AA′BB′ system, 2H, arom.), 7.65–7.60 (m, B-part of AA′BB′ system, 2H, arom.); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.9, 156.3, 140.0, 137.9, 136.1, 135.5, 132.8, 132.7, 128.7, 128.2, 124.1; ν_{max} (ATR) 3074, 2956, 1714, 1626, 1492, 1394, 1309, 1217, 1155 cm^{-1}; [found: C, 50.71; H, 2.29; N, 8.85; S, 11.18. $C_{13}H_7ClN_2O_3S$ requires C, 50.91; H, 2.30; N, 9.13; S, 10.45%].

*4.4.13. 5-(4-Fluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29f**).* (0.58 g, 61%), mp 255–257 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.10 (br s, 1H, –COOH), 8.22 (d, J=5.3 Hz, 1H, C=CH), 7.73 (d, J=5.3 Hz, 1H, C=CH), 7.70–7.64 (m, A-part of AA′BB′ system 2H, arom.), 7.43–7.36 (m, B-part of AA′BB′ system, 2H, arom.); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.9, 161.4 (d, J=245.4 Hz), 156.4, 137.9, 137.5 (d, J=3.1 Hz), 136.0, 135.5, 132.5, 128.7 (d, J=8.9 Hz), 124.1, 115.5 (d, J=23.1 Hz); ν_{max} (ATR) 3112, 3074, 2960, 1716, 1628, 1604, 1510, 1240, 1218, 1157 cm^{-1}; [found: C, 53.27; H, 2.34; N, 9.61; S, 11.38. $C_{13}H_7FN_2O_3S$ requires C, 53.79; H, 2.43; N, 9.65; S, 11.05%].

*4.4.14. 5-(2,4-Difluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carboxylic acid (**29g**).* (0.65 g, 68%), mp 240–242 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.15 (br s, 1H, –COOH), 8.27 (d, J=5.3 Hz, 1H, C=CH), 7.76 (d, J=5.3 Hz, 1H, C=CH), 7.79–7.73 (m, 1H, arom.), 7.58 (ddd, J=10.4, 9.2, and 2.7 Hz, 1H, arom.), 7.37–7.30 (m, 1H, arom.); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.6, 162.3 (dd, J=248.9 and 11.7 Hz), 157.0 (dd, J=252.9 and 13.3 Hz), 156.0, 138.1, 136.6, 134.9, 133.5, 131.0 (d, J=10.3 Hz), 125.5 (dd, J=13.0 and 3.9 Hz), 123.9, 112.2 (dd, J=22.8 and 3.5 Hz), 104.9 (dd, J=27.1 and 24.1 Hz); ν_{max} (ATR) 3079, 2930, 1725, 1639, 1534, 1404, 1278, 1163, 1149, 1134 cm^{-1}; [found: C, 50.42; H, 2.03; N, 9.37; S, 10.67. $C_{13}H_6F_2N_2O_3S$ requires C, 50.65; H, 1.96; N, 9.09; S, 10.49%].

4.5. 5-Methyl-4-oxo-4,5-dihydrofuro[2,3-*d*]pyridazine-7-carbonyl azide (30a)

Thionyl chloride (2.5 mL) was added to a stirred suspension of acid **28a** (0.5 g, 2.85 mmol) in chloroform (50 mL) and heated at reflux for 1 h. Since, a clear solution did not form acetonitrile (30 mL) and further thionyl chloride (5 mL) were added and heated at reflux. After 30 min, a clear solution was formed and heating was continued for additional 20 min. The solvent and excess thionyl chloride were evaporated. The residue was dissolved in acetone (50 mL) and cooled to 2 °C. A solution of NaN_3 (0.32 g, 4.92 mmol) in H_2O (3 mL) was added and the resulting mixture was stirred for 70 min. Then, H_2O (80 mL) was added and extracted with ethyl acetate (3×100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography (silica gel) eluting with ethyl acetate/dichloromethane (1:1) to give acyl azide **30a** as a white solid (0.48 g, 84%), mp 134–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J=2.0 Hz, 1H, C=CH), 7.03 (d, J=2.0 Hz, 1H, C=CH), 3.91 (s, 3H $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.0, 158.7, 151.0, 147.9, 126.8, 122.9, 107.2, 40.5; ν_{max} (ATR) 3133, 3109, 2164, 1691, 1504, 1421, 1381, 1325, 1248, 1235, 1167, 1087 cm^{-1}.

4.6. General procedure for the synthesis of acyl azide derivatives (30b–g)

Oxalyl chloride (0.35 mL, 4.1 mmol) and then DMF (4 drops) were added to a stirred suspension of the acids **28b–g** (0.5 g, 1.7–2.0 mmol) in dichloromethane (60 mL) and the mixture was stirred at rt for 90 min. The solvent and excess oxalyl chloride were evaporated. The residue was dissolved in acetone (50 mL) and cooled to 2 °C. To this solution, a solution of NaN_3 (0.25 g, 3.85 mmol) in H_2O (3 mL) was added. Precipitation of inorganic salts was immediately observed. The resulting mixture was stirred for 1 h and then, H_2O (80 mL) was added. The mixture was extracted with ethyl acetate (2×150 mL), the combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography (silica gel) eluting with ethyl acetate/dichloromethane/hexane (2:2:1) to give acyl azides **30b–g** as white solids.

*4.6.1. 4-Oxo-5-phenyl-4,5-dihydrofuro[2,3-d]pyridazine-7-car-bonyl azide (**30b**).* (0.52 g, 95%), mp 114–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J=1.6 Hz, 1H, C=CH), 7.52–7.38 (m, 5H, arom.), 7.10 (d, J=1.6 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.2, 158.3, 150.6, 148.2, 140.9, 129.1, 128.9, 127.7, 125.9, 123.9, 107.9; ν_{max} (ATR) 3150, 3124, 2150, 1688, 1617, 1593, 1541, 1489, 1385, 1327, 1234, 1168, 1113, 1050 cm^{-1}.

*4.6.2. 5-(4-Methylphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyrida-zine-7-carbonyl azide (**30c**).* (0.48 g, 88%), mp 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=2.0 Hz, 1H, C=CH), 7.40–7.37 (m, A-part of AA′BB′ system, 2H, arom.), 7.26–7.23 (m, B-part of AA′BB′ system, 2H, arom.), 7.08 (d, J=2.0 Hz, 1H, C=CH), 2.35 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.2, 158.3, 150.6, 148.1, 139.0, 138.4, 129.7, 127.5, 125.7, 123.8, 107.8, 21.2; ν_{max} (ATR) 3136, 3118, 2153, 1685, 1504, 1385, 1322, 1232, 1162, 1115, 1052 cm^{-1}.

*4.6.3. 5-(4-Methoxyphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyri-dazine-7-carbonyl azide (**30d**).* (0.44 g, 81%), mp 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=2.0 Hz, 1H, C=CH), 7.45–7.41 (m, A-part of AA′BB′ system, 2H, arom.), 7.08 (d, J=2.0 Hz, 1H, C=CH), 6.97–6.93 (m, B-part of AA′BB′, 2H, arom.), 3.80 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.2, 159.8, 158.4, 150.6, 148.1, 133.8, 127.4, 127.1, 123.8, 114.3, 107.8, 55.6; ν_{max} (ATR) 3147, 3127, 2157, 1697, 1681, 1515, 1504, 1388, 1331, 1241, 1165, 1115 cm^{-1}.

*4.6.4. 5-(4-Chlorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyri-dazine-7-carbonyl azide (**30e**).* (0.47 g, 87%), mp 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J=2.0 Hz, 1H, C=CH), 7.51–7.48 (m, A-part of AA′BB′ system, 2H, arom.), 7.44–7.41 (m, B-part of AA′BB′ system, 2H, arom.), 7.09 (d, J=2.0 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.9, 158.0, 150.4, 148.3, 139.2, 134.7, 129.1, 127.8, 127.1, 123.8, 107.8. ν_{max} (ATR) 3151, 3127, 2153, 1710, 1693, 1506, 1489, 1407, 1385, 1325, 1239, 1168, 1105, 1088 cm^{-1}.

*4.6.5. 5-(4-Fluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyri-dazine-7-carbonyl azide (**30f**).* (0.49 g, 90%), mp 159–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J=2.0 Hz, 1H, C=CH), 7.53–7.49 (m, A-part of AA′BB′ system, 2H, arom.), 7.17–7.10 (m, B-part of AA′BB′ system, 2H, arom.), 7.09 (d, J=2.0 Hz, 1H, C=CH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.0, 162.4 (d, J=249.2 Hz), 158.2, 150.5, 148.4, 136.8 (d, J=3.2 Hz), 127.9 (d, J=8.9 Hz), 127.8, 123.9, 116.0 (d,

J=23.0 Hz), 107.9; ν_{max} (ATR) 3151, 3131, 2155, 1705, 1693, 1510, 1503, 1325, 1238, 1167, 1145, 1111, 1050 cm^{-1}.

*4.6.6. 5-(2,4-Difluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyri-dazine-7-carbonyl azide (**30g**).* (0.45 g, 83%), mp 101–102 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J=2.0 Hz, 1H, C=CH), 7.41–7.35 (m, 1H, arom.), 7.10 (d, J=2.0 Hz, 1H, C=CH), 7.01–6.93 (m, 2H, arom.); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.8, 162.3 (dd, J=152.4 and 11.1 Hz), 157.7, 157.6 (dd, J=256.1 and 12.6 Hz), 150.6, 148.5, 129.8 (d, J=10.3 Hz), 128.5, 124.9 (dd, J=13.0 and 4.4 Hz), 123.7, 112.1 (dd, J=23.0 and 3.8 Hz), 107.9, 105.3 (dd, J=26.7 and 23.4 Hz); ν_{max} (ATR) 3140, 3113, 3081, 2155, 1713, 1699, 1607, 1502, 1387, 1339, 1261, 1217, 1160, 1107, 1050 cm^{-1}.

4.7. General procedure for the synthesis of acyl azide derivatives (31a–g)

Oxalyl chloride (0.70 mL, 8.2 mmol) and then DMF (7 drops) were added to a stirred suspension of the acids **29a–g** (1.0 g, 3.25–4.76 mmol) in dichloromethane (120 mL) and the mixture was stirred at rt for 2 h. The reaction mixture was worked up as described above.

*4.7.1. 5-Methyl-4-oxo-4,5-dihydrothieno[2,3-d]pyridazine-7-carbonyl azide (**31a**).* (0.69 g, 62%), mp 137–139 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=5.3 Hz, 1H, C=CH), 7.68 (d, J=5.3 Hz, 1H, C=CH), 3.91 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.3, 157.5, 137.6, 135.2, 134.3, 131.9, 124.2, 40.3; ν_{max} (ATR) 3117, 3099, 3073, 2155, 1672, 1659, 1349, 1186 cm^{-1}.

*4.7.2. 4-Oxo-5-phenyl-4,5-dihydrothieno[2,3-d]pyridazine-7-carbonyl azide (**31b**).* (0.83 g, 75%), mp 152–154 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J=5.3 Hz, 1H, C=CH), 7.75 (d, J=5.3 Hz, 1H, C=CH), 7.58–7.54 (m, 2H, arom.), 7.49–7.43 (m, 2H, arom.), 7.39 (tt, J=7.4 and 1.2 Hz, 1H, arom.); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.6, 156.9, 140.9, 137.2, 136.2, 134.6, 132.6, 129.1, 128.8, 125.9, 125.0; ν_{max} (ATR) 3098, 3082, 2155, 1694, 1668, 1347, 1165 cm^{-1}.

*4.7.3. 5-(4-Methylphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyr-idazine-7-carbonyl azide (**31c**).* (0.71 g, 65%), mp 159–161 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J=5.3 Hz, 1H, C=CH), 7.74 (d, J=5.3 Hz, 1H, C=CH), 7.45–7.41 (m, A-part of AA′BB′ system, 2H, arom.), 7.26–7.24 (m, B-part of AA′BB′ system, 2H, arom.), 2.36 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.6, 157.0, 138.9, 138.4, 137.2, 136.1, 134.4, 132.4, 129.7, 125.6, 125.0, 21.2; ν_{max} (ATR) 3098, 3079, 2960, 2919, 2159, 1690, 1669, 1628, 1509, 1346, 1172 cm^{-1}.

*4.7.4. 5-(4-Methoxyphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyr-idazine-7-carbonyl azide (**31d**).* (0.66 g, 61%), mp 119–121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J=5.3 Hz, 1H, C=CH), 7.74 (d, J=5.3 Hz, 1H, C=CH), 7.50–7.45 (m, A-part of AA′BB′ system, 2H, arom.), 6.98–6.93 (m, B-part of AA′BB′ system, 2H, arom.), 3.80 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.5, 159.7, 157.0, 137.1, 136.0, 134.4, 133.8, 132.3, 127.0, 124.9, 114.3, 55.6; ν_{max} (ATR) 3083, 2921, 2835, 2151, 1668, 1507, 1349, 1250, 1166, 1105 cm^{-1}.

*4.7.5. 5-(4-Chlorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyri-dazine-7-carbonyl azide (**31e**).* (0.93 g, 86%), mp 128–130 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J=5.3 Hz, 1H, C=CH), 7.74 (d, J=5.3 Hz, 1H, C=CH), 7.57–7.52 (m, A-part of AA′BB′ system, 2H, arom.), 7.46–7.40 (m, B-part of AA′BB′ system, 2H, arom.); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.4, 156.8, 139.3, 137.2, 136.1, 134.9, 134.6, 132.8, 129.2, 127.1, 125.0; ν_{max} (ATR) 3118, 3101, 2158, 1692, 1671, 1488, 1350, 1260 cm^{-1}.

*4.7.6. 5-(4-Fluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyri-dazine-7-carbonyl azide (**31f**).* (0.85 g, 79%), mp 137–239 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=5.3 Hz, 1H, C=CH), 7.74 (d, J=5.3 Hz, 1H, C=CH), 7.59–7.53 (m, A-part of AA′BB′ system, 2H, arom.), 7.18–7.11 (m, B-part of AA′BB′ system, 2H, arom.); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.4, 162.4 (d, J=248.9 Hz), 156.8, 137.2, 136.9 (d, J=3.0 Hz), 136.1, 134.8, 132.7, 127.8 (d, J=8.9 Hz), 125.0, 116.0 (d, J=23.1 Hz); ν_{max} (ATR) 3125, 3109, 2155, 1682, 1671, 1506, 1353, 1247, 1160, 1151 cm^{-1}.

*4.7.7. 5-(2,4-Difluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyr-idazine-7-carbonyl azide (**31g**).* (0.83 g, 77%), mp 146–148 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J=5.3 Hz, 1H, C=CH), 7.74 (d, J=5.3 Hz, 1H, C=CH), 7.45–7.37 (m, 1H, arom.), 7.02–6.93 (m, 2H, arom.); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.3, 163.2 (dd, J=252.4 and 11.1 Hz), 157.6 (dd, J=256.1 and 12.6 Hz), 156.4, 137.3, 135.7, 135.1, 133.4, 129.7 (dd, J=10.3 and 1.0 Hz), 125.1 (d, J=4.0 Hz), 124.9, 112.1 (dd, J=22.7 and 3.7 Hz), 105.3 (dd, J=26.4 and 23.4 Hz); ν_{max} (ATR) 3107, 3083, 2960, 2163, 1698, 1680, 1613, 1510, 1485, 1173 cm^{-1}.

4.8. General procedure for the synthesis of urethane derivatives (32a–g)

The acyl azide derivatives **30a–g** (0.25 g, 0.8–1.1 mmol) were dissolved in dry benzene (40 mL) and heated at reflux temperature for 90 min. Dry MeOH (2 mL) was added and stirred at 50 °C for 1 h. The solvent was evaporated. The crude product was purified by column chromatography (silica gel) eluting with hexane/ethyl acetate/dichloromethane (2:1:1) to give the urethane derivatives **32a–g** as a white solids.

*4.8.1. Methyl 5-methyl-4-oxo-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32a**).* (0.21 g, 83%), mp 181–182 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J=2.0 Hz, 1H, C=CH), 7.10 (d, J=2.0 Hz, 1H, C=CH), 6.90 (br s, 1H, –NH), 3.86 (s, 3H, $-OCH_3$), 3.82 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.4, 153.8, 147.9, 147.0, 129.8, 124.0, 107.9, 53.2, 39.3; ν_{max} (ATR) 3183, 3135, 3053, 1694, 1664, 1588, 1556, 1506, 1400, 1251, 1211, 1055 cm^{-1}; [found: C, 48.63; H, 3.92; N, 18.90. $C_9H_9N_3O_4$ requires C, 48.43; H, 4.06; N, 18.83%].

*4.8.2. Methyl 4-oxo-5-phenyl-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32b**).* (0.20 g, 80%), mp 275–279 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J=2.0 Hz, 1H, C=CH), 7.61–7.58 (m, 2H, arom.), 7.51–7.48 (m, 2H, arom.), 7.41 (tt, J=7.4 and 1.2 Hz, 1H, arom.), 7.16 (d, J=2.0 Hz, 1H, C=CH), 6.98 (br s, 1H, –NH), 3.87 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.8, 153.7, 147.5, 147.2, 141.1, 130.6, 128.7, 127.9, 125.8, 124.7, 108.3, 53.2; ν_{max} (ATR) 3179, 3161, 3102, 3048, 1719, 1679, 1594, 1557, 1508, 1400, 1271, 1257, 1157, 1037 cm^{-1}; [found: C, 59.23; H, 3.65; N, 14.96. $C_{14}H_{11}N_3O_4$ requires C, 58.95; H, 3.89; N, 14.73%].

*4.8.3. Methyl 5-(4-methylphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyr-idazin-7-ylcarbamate (**32c**).* (0.21 g, 84%), mp 182–183 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J=2.0 Hz, 1H, C=CH), 7.46–7.43 (m, A-part of AA′BB′ system, 2H, arom.), 7.28–7.25 (m, B-part of AA′BB′ system, 2H, arom.), 7.21 (br s, 1H, –NH), 7.15 (d, J=2.0 Hz, 1H, C=CH), 3.85 (s, 3H, $-OCH_3$), 2.40 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.1, 154.1, 147.8, 147.2, 138.7, 138.0, 130.6, 129.4, 125.7, 124.7, 108.4, 53.2, 21.1; ν_{max} (ATR) 3149, 3127, 2925, 1729, 1654, 1592, 1551, 1507, 1431, 1252, 1163, 1042 cm^{-1}; [found: C, 59.95; H, 4.29; N, 13.94. $C_{15}H_{13}N_3O_4$ requires C, 60.20; H, 4.38; N, 14.04%].

*4.8.4. Methyl 5-(4-methoxyphenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32d**).* (0.21 g, 84%), mp 190–191 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J=2.0 Hz, 1H, C=CH), 7.51–7.47 (m, A-part of AA′BB′ system, 2H, arom.), 7.15 (d, J=2.0 Hz, 1H, C=CH), 7.06 (br s, 1H, –NH), 7.06–6.97 (m, B-part of AA′BB′ system, 2H, arom.), 3.86 (s, 6H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.1,

158.09, 154.0, 147.7, 147.2, 134.2, 130.5, 127.1, 124.7, 114.0, 108.4, 55.5, 53.3; ν_{max} (ATR) 3180, 3148, 3128, 3008, 2974, 1727, 1651, 1607, 1590, 1553, 1401, 1331, 1248, 1230, 1127, 1042 cm^{-1}; [found: C, 56.90; H, 3.94; N, 13.11. $C_{15}H_{13}N_3O_5$ requires C, 57.14; H, 4.16; N, 13.33%].

*4.8.5. Methyl 5-(4-chlorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32e**).* (0.20 g, 79%), mp 187–188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (br s, 1H, C=CH), 7.46 (br d, J=8.4 Hz, 2H, arom.), 7.32 (br d, J=8.4 Hz, 2H, arom.), 7.19 (br s, 1H, C=CH), 7.05 (br s, 1H, –NH), 3.76 (s, 3H, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.9, 153.8, 147.6, 147.4, 139.7, 133.6, 131.1, 128.8, 127.1, 124.7, 108.4, 53.3; ν_{max} (ATR) 3178, 3150, 3128, 3040, 2979, 1733, 1656, 1593, 1554, 1507, 1493, 1405, 1331, 1251, 1233, 1162, 1126, 1081 cm^{-1}; [found: C, 52.96; H, 3.28; N, 12.78. $C_{14}H_{10}ClN_3O_4$ requires C, 52.60; H, 3.15; N, 13.14%].

*4.8.6. Methyl 5-(4-fluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32f**).* (0.21 g, 83%), mp 181–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J=2.0 Hz, 1H, C=CH), 7.51–7.48 (m, A-part of AA′BB′ system, 2H, arom.), 7.10–7.05 (m, B-part of AA′BB′ system, 2H, arom.), 7.07 (d, J=2.0 Hz, 1H, C=CH), 6.95 (br s, 1H, –NH), 3.78 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.8 (d, J=247.9 Hz), 158.0, 153.9, 147.7, 147.4, 137.2 (d, J=3.3 Hz), 131.0, 127.7 (d, J=8.7 Hz), 124.7, 115.6 (d, J=22.9 Hz), 108.4, 53.3; ν_{max} (ATR) 3181, 3154, 3128, 2980, 1740, 1654, 1589, 1554, 1505, 1404, 1333, 1250, 1238, 1167, 1128, 1082 cm^{-1}; [found: C, 55.47; H, 3.39; N, 13.82. $C_{14}H_{10}FN_3O_4$ requires C, 55.45; H, 3.32; N, 13.86%].

*4.8.7. Methyl 5-(2,4-difluorophenyl)-4-oxo-4,5-dihydrofuro[2,3-d]pyridazin-7-ylcarbamate (**32g**).* (0.20 g, 79%), mp 171–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J=1.9 Hz, 1H, C=CH), 7.48–7.42 (m, 1H, arom.), 7.16 (d, J=1.9 Hz, 1H, C=CH), 7.05–6.98 (m 3H, arom. and –NH), 3.87 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.7 (dd, J=251.2 and 11.2 Hz), 157.6, 157.5 (dd, J=255.8 and 12.6 Hz), 153.7, 147.8, 147.4, 131.4, 129.9 (d, J=11.7 Hz), 125.3 (dd, J=12.9 and 4.2 Hz), 124.3, 111.8 (dd, J=22.7 and 3.6 Hz), 108.4, 105.0 (dd, J=26.4 and 23.5 Hz), 53.3; ν_{max} (ATR) 3182, 3155, 3128, 1974, 1738, 1659, 1653, 1506, 1404, 1249, 1225, 1177, 1039 cm^{-1}; [found: C, 52.63; H, 3.10; N, 12.85. $C_{14}H_9F_2N_3O_4$ requires C, 52.34; H, 2.82; N, 13.08%].

4.9. General procedure for the synthesis of urethane derivatives (33a–g)

The acyl azide derivatives **31a–g** (0.20 g, 0.60–0.85 mmol) were reacted with MeOH (6 h and 12 h) as described above. The solvent and excess MeOH were evaporated. The crude product was washed with hexane/ethyl acetate/dichloromethane (2:1:1) to give the urethane derivatives **33a–g** as white solids.

*4.9.1. Methyl 5-methyl-4-oxo-4,5-dihydrothieno[2,3-d]pyri-dazin-7-ylcarbamate (**33a**).* (87 mg, 43%), mp 171–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J=5.3 Hz, 1H, C=CH), 7.60 (d, J=5.3 Hz, 1H, C=CH), 7.14 (br s, 1H, –NH), 3.76 (s, 3H, $-OCH_3$), 3.71 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.2, 154.4, 137.3, 136.3, 135.3, 132.2, 124.9, 53.1, 38.9; ν_{max} (ATR) 3236, 3138, 2957, 2922, 2851, 1698, 1640, 1550, 1523, 1462, 1247, 1060 cm^{-1}; [found: C, 45.11; H, 3.91; N, 17.24; S, 13.65. $C_9H_9N_3O_3S$ requires C, 45.18; H, 3.79; N, 17.56; S, 13.40%].

*4.9.2. Methyl 4-oxo-5-phenyl-4,5-dihydrothieno[2,3-d]pyri-dazin-7-ylcarbamate (**33b**).* (119 mg, 59%), mp 186–188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J=5.3 Hz, 1H, C=CH), 7.67 (d, J=5.3 Hz, 1H, C=CH), 7.57–7.53 (m, 2H, arom.), 7.42 (br t, J=7.4 Hz, 2H, arom.), 7.32 (tt, J=7.4, 1.2 Hz, 1H, arom.), 6.97 (br s, 1H, –NH), 3.78 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.6, 154.4, 141.1, 138.2, 136.0, 135.9, 132.6, 128.8, 128.0, 125.8, 125.5, 53.2; ν_{max} (ATR) 3244, 3107, 2960, 2913, 1724, 1646, 1553, 1488, 1302, 1241, 1046 cm^{-1}; [found: C, 56.07; H, 3.99; N, 13.88; S, 11.02. $C_{14}H_{11}N_3O_3S$ requires C, 55.80; H, 3.68; N, 13.95; S, 10.64%].

*4.9.3. Methyl 5-(4-methylphenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazin-7-ylcarbamate (**33c**).* (95 mg, 47%), mp 172–174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=5.3 Hz, 1H, C=CH), 7.65 (d, J=5.3 Hz, 1H, C=CH), 7.43–7.37 (m, A-part of AA′BB′ system, 2H, arom.), 7.20–7.18 (m, B-part of AA′BB′ system, 2H, arom.), 7.03 (br s, 1H, –NH), 3.77 (s, 3H, $-OCH_3$), 2.33 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.6, 154.5, 138.6, 138.2, 138.0, 135.9, 135.8, 132.4, 129.4, 125.5, 53.2, 21.1; ν_{max} (ATR) 3246, 3107, 3087, 3031, 2959, 1725, 1653, 1552, 1481, 1240, 1135, 1044 cm^{-1}; [found: C, 56.78; H, 4.27; N, 13.05; S, 10.39. $C_{15}H_{13}N_3O_3S$ requires C, 57.13; H, 4.16; N, 13.33; S, 10.17%].

*4.9.4. Methyl 5-(4-methoxyphenyl)-4-oxo-4,5-dihydrothieno-[2,3-d]pyridazin-7-ylcarbamate (**33d**).* (91 mg, 45%), mp 167–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=5.3 Hz, 1H, C=CH), 7.66 (d, J=5.3 Hz, 1H, C=CH), 7.47–7.42 (m, A-part of AA′BB′ system, 2H, arom.), 6.99 (br s, 1H, –NH), 6.94–6.89 (m, B-part of AA′BB′ system, 2H, arom.), 3.78 (s, 3H, $-OCH_3$), 3.77 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.8, 154.4, 152.2, 135.9, 133.6, 133.5, 131.8, 130.2, 124.7, 123.2, 111.7, 53.3, 50.9; ν_{max} (ATR) 3327, 3105, 3089, 2922, 2850, 1735, 1657, 1560, 1512, 1484, 1456, 1098, 1019 cm^{-1}; [found: C, 54.25; H, 4.33; N, 12.31; S, 9.59. $C_{15}H_{13}N_3O_4S$ requires C, 54.37; H, 3.95; N, 12.68; S, 9.68%].

*4.9.5. Methyl 5-(4-chlorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazin-7-ylcarbamate (**33e**).* (109 mg, 54%), mp 156–158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=5.3 Hz, 1H, C=CH), 7.67 (d, J=5.3 Hz, 1H, C=CH), 7.54–7.49 (m, A-part of AA′BB′ system, 2H, arom.), 7.37–7.32 (m, B-part of AA′BB′ system, 2H, arom.), 7.14 (br s, 1H, –NH), 3.78 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.4, 154.3, 139.5, 138.0, 136.3, 135.9, 133.5, 132.8, 128.8, 126.9, 125.5, 53.3; ν_{max} (ATR) 3208, 3103, 3085, 2955, 2922, 1729, 1682, 1556, 1536, 1486, 1262, 1244, 1126 cm^{-1}; [found: C, 50.36; H, 3.18; N, 12.48; S, 10.16. $C_{14}H_{10}ClN_3O_3S$ requires C, 50.08; H, 3.00; N, 12.51; S, 9.55%].

*4.9.6. Methyl 5-(4-fluorophenyl)-4-oxo-4,5-dihydrothieno[2,3-d]pyridazin-7-ylcarbamate (**33f**).* (176 mg, 87%), mp 145–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=5.3 Hz, 1H, C=CH), 7.66 (d, J=5.3 Hz, 1H, C=CH), 7.55–7.48 (m, A-part of AA′BB′ system, 2H, arom.), 7.16 (br s, 1H, –NH), 7.10–7.03 (m, B-part of AA′BB′ system, 2H, arom.), 3.77 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.8 (d, J=248.0 Hz), 156.5, 154.3, 138.0, 137.0 (d, J=3.3 Hz), 136.1, 136.0, 132.7, 127.5 (d, J=8.6 Hz), 125.5, 115.6 (d, J=22.9 Hz), 53.2; ν_{max} (ATR) 3280, 3087, 1708, 1660, 1558, 1523, 1495, 1130 cm^{-1}; [found: C, 52.35; H, 3.32; N, 12.87; S, 10.50. $C_{14}H_{10}FN_3O_3S$ requires C, 52.66; H, 3.16; N, 13.16; S, 10.04%].

*4.9.7. Methyl 5-(2,4-difluorophenyl)-4-oxo-4,5-dihydrothieno-[2,3-d]pyridazin-7-ylcarbamate (**33g**).* (129 mg, 64%), mp 199–201 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=5.3 Hz, 1H, C=CH), 7.69 (d, J=5.3 Hz, 1H, C=CH), 7.41–7.34 (m, 1H, arom.), 7.00 (br s, 1H, –NH), 6.97–6.88 (m, 2H, arom.), 3.77 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.7 (dd, J=251.2 and 11.3 Hz), 157.6 (dd, J=255.7 and 12.6 Hz), 156.3, 154.3, 137.5, 136.5, 136.4, 132.9, 129.8 (dd, J=10.2 and 1.8 Hz), 125.5, 125.2 (dd, J=4.3 and 2.6 Hz), 111.8 (dd, J=22.6 and 3.7 Hz), 105.0 (dd, J=26.3 and 23.5 Hz), 53.7; ν_{max} (ATR) 3197, 3112, 3069, 2990, 2947, 1727, 1651, 1563, 1508, 1246, 1151 cm^{-1}; [found: C, 50.16; H, 2.74; N, 12.26; S, 9.57. $C_{14}H_9F_2N_3O_3S$ requires C, 49.85; H, 2.69; N, 12.46; S, 9.51%].

4.10. General procedure for the synthesis of aminopyridazinone derivatives (34a–g and 35a–g)

The acyl azide derivatives **30a–g** and **31a–g** (0.3 g, 1.0–1.4 mmol) were dissolved in dry benzene (40 mL) and heated at reflux for

90 min. The solution was cooled to 40 °C and HCl (10 mL, 8 M) was added. The mixture was stirred at 40 °C for 10 min and then the pH value was adjusted to pH=10 by addition of 10% NaOH solution at 10 °C. The mixture was extracted with ethyl acetate (3×100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography (silica gel) eluting with ethyl acetate/dichloromethane (1:1) to give the amine derivatives **34a**–**g** and **35a**–**g** as white solids.

*4.10.1. 7-Amino-5-methylfuro[2,3-d]pyridazin-4(5H)-one (**34a**).* (0.15 g, 68%), mp 187–188 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J=1.9 Hz, 1H, C=CH), 6.98 (d, J=1.9 Hz, 1H, C=CH), 4.31 (br s, 2H, $-NH_2$), 3.63 (s, 3H, OCH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.1, 146.5, 146.0, 138.1, 123.3, 108.4, 38.7; ν_{max} (ATR) 3474, 3308, 3185, 3116, 3093, 2920, 1625, 1590, 1533, 1475, 1412, 1342, 1225, 1136, 1085 cm^{-1}; [found: C, 51.09; H, 4.31; N, 25.10. $C_7H_7N_3O_2$ requires C, 50.91; H, 4.27; N, 25.44%].

*4.10.2. 7-Amino-5-phenylfuro[2,3-d]pyridazin-4(5H)-one (**34b**).* (0.17 g, 71%), mp 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J=2.0 Hz, 1H, C=CH), 7.61–7.58 (m, 2H, arom.), 7.50–7.46 (m, 2H, arom.), 7.37 (tt, J=7.4, 1.2 Hz, 1H, arom.), 7.15 (d, J=2.0 Hz, 1H, C=CH), 4.17 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.8, 146.8, 146.1, 142.1, 138.7, 129.0, 127.8, 126.4, 123.9, 108.9; ν_{max} (ATR) 3328, 3187, 3151, 3119, 1671, 1639, 1592, 1544, 1472, 1414, 1336, 1272, 1231, 1124, 1050 cm^{-1}; [found: C, 63.33; H, 3.83; N, 18.23. $C_{12}H_9N_3O_2$ requires C, 63.43; H, 3.99; N, 18.49%].

*4.10.3. 7-Amino-5-(4-methylphenyl)furo[2,3-d]pyridazin-4(5H)-one (**34c**).* (0.18 g, 73%), mp 204–205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=2.0 Hz, 1H, C=CH), 7.48–7.44 (m, A-part of AA′BB′ system, 2H, arom.), 7.29–7.26 (m, B-part of AA′BB′ system, 2H, arom.), 7.14 (d, J=2.0 Hz, 1H, C=CH), 4.46 (s, 2H, $-NH_2$), 2.41 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.6, 146.4, 145.8, 139.3, 138.3, 137.5, 129.4, 125.9, 123.6, 108.6, 21.1; ν_{max} (ATR) 3371, 3296, 3197, 3157, 2953, 1669, 1625, 1595, 1542, 1508, 1470, 1412, 1337, 1231, 1124, 1049 cm^{-1}; [found: C, 64.72; H, 4.49; N, 17.34. $C_{13}H_{11}N_3O_2$ requires C, 64.72; H, 4.60; N, 17.42%].

*4.10.4. 7-Amino-5-(4-methoxyphenyl)furo[2,3-d]pyridazin-4(5H)-one (**34d**).* (0.19 g, 77%), mp 172–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (br s, 1H, C=CH), 7.48 (br d, 2H, J=8.4 Hz, arom.), 7.13 (br s, 1H, C=CH), 6.98 (br d, J=8.4 Hz, 2H, arom.), 4.55 (br s, 2H, $-NH_2$), 3.85 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.8, 146.5, 145.8, 138.3, 134.8, 132.9, 127.4, 123.6, 114.0, 108.6, 55.5; ν_{max} (ATR) 3342, 3283, 3184, 3143, 3106, 1669, 1624, 1695, 1545, 1507, 1471, 1413, 1337, 1249, 1234, 1171, 1027 cm^{-1}; [found: C, 60.94; H, 4.40; N, 15.97. $C_{13}H_{11}N_3O_3$ requires C, 60.70; H, 4.31; N, 16.33%].

*4.10.5. 7-Amino-5-(4-chlorophenyl)furo[2,3-d]pyridazin-4(5H)-one (**34e**).* (0.17 g, 68%), mp 198–199 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J=1.6 Hz, 1H, C=CH), 7.51–7.48 (m, A-part of AA′BB′ system, 2H, arom.), 7.36–7.33 (m, B-part of AA′BB′ system, 2H, arom.), 7.05 (d, J=1.6 Hz, 1H, C=CH), 4.43 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.5, 146.7, 145.8, 140.3, 138.5, 133.0, 128.8, 127.3, 123.6, 108.7; ν_{max} (ATR) 3433, 3342, 3140, 3122, 1683, 1614, 1547, 1491, 1475, 1409, 1330, 1270, 1231, 1135, 1041 cm^{-1}; [found: C, 55.40; H, 2.97; N, 15.92. $C_{12}H_8ClN_3O_2$ requires C, 55.08; H, 3.08; N, 16.06%].

*4.10.6. 7-Amino-5-(4-fluorophenyl)furo[2,3-d]pyridazin-4(5H)-one (**34f**).* (0.16 g, 65%), mp 203–204 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J=1.9 Hz, 1H, C=CH), 7.52–7.46 (m, A-part of AA′BB′ system, 2H, arom.), 7.10–7.05 (m, B-part of AA′BB′ system, 2H, arom.), 7.05 (d, J=1.9 Hz, 1H, C=CH), 4.43 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.6 (d, J=246.9 Hz), 157.6, 146.6, 145.8, 138.3, 137.8 (d, J=2.8 Hz), 127.9 (d, J=8.5 Hz), 123.6, 115.5 (d, J=22.8 Hz), 108.7; ν_{max} (ATR) 3341, 3198, 3161, 3116, 3085, 1674, 1636, 1596, 1545, 1502, 1473, 1415, 1336, 1216, 1152, 1050 cm^{-1}; [found: C, 58.70; H, 3.23; N, 17.09. $C_{12}H_8FN_3O_2$ requires C, 58.78; H, 3.29; N, 17.14%].

*4.10.7. 7-Amino-5-(2,4-difluorophenyl)furo[2,3-d]pyridazin-4(5H)-one (**34g**).* (0.15 g, 60%), mp 232–233 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J=2.0 Hz, 1H, C=CH), 7.39–7.33 (m, 1H, arom.), 7.05 (d, J=2.0 Hz, 1H, C=CH), 6.95–6.88 (m, 2H, arom.), 4.41 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.5 (dd, J=247.3 and 11.4 Hz), 157.0 (dd, J=252.1 and 13.0 Hz), 156.4, 148.2, 146.2, 140.2, 131.0 (dd, J=10.3 and 1.7 Hz), 126.4 (dd, J=12.9 and 4.0 Hz), 121.9, 111.7 (dd, J=22.4 and 3.4 Hz), 107.7, 104.6 (dd, J=26.9 and 24.4 Hz); ν_{max} (ATR) 3343, 3195, 3162, 3121, 1678, 1637, 1598, 1547, 1505, 1473, 1415, 1347, 1267, 1236, 1134, 1046 cm^{-1}; [found: C, 54.38; H, 2.57; N, 15.70. $C_{12}H_7F_2N_3O_2$ requires C, 54.76; H, 2.68; N, 15.97%].

*4.10.8. 7-Amino-5-methylthieno[2,3-d]pyridazin-4(5H)-one (**35a**).* (80 mg, 42%), mp 165–167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J=5.2 Hz, 1H, C=CH), 7.52 (d, J=5.2 Hz, 1H, C=CH), 4.13 (br s, 2H, $-NH_2$), 3.65 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.6, 142.2, 137.2, 133.1, 129.6, 126.1, 38.4; ν_{max} (ATR) 3325, 3158, 3075, 1610, 1531, 1416, 1330, 1249, 1127, 1041 cm^{-1}; [found: C, 46.01; H, 3.87; N, 22.98; S, 18.10. $C_7H_7N_3OS$ requires C, 46.40; H, 3.89; N, 23.19; S, 17.69%].

*4.10.9. 7-Amino-5-phenylthieno[2,3-d]pyridazin-4(5H)-one (**35b**).* (94 mg, 46%), mp 187–189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J=5.1 Hz, 1H, C=CH), 7.57 (d, J=5.1 Hz, 1H, C=CH), 7.58–7.55 (m, 2H, arom.), 7.43–7.37 (m, 2H, arom.), 7.29 (tt, J=7.4 and 1.2 Hz, 1H, arom.), 4.21 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 156.2, 142.6, 141.7, 137.8, 133.4, 129.9, 128.7, 127.6, 126.7, 125.9; [ν_{max} (ATR) 3336, 3203, 3101, 1632, 1556, 1544, 1403, 1304, 1054 cm^{-1}; [found: C, 59.12; H, 3.85; N, 17.29; S, 13.61. $C_{12}H_9N_3OS$ requires C, 59.24; H, 3.73; N, 17.27; S, 13.18%].

*4.10.10. 7-Amino-5-(4-methylphenyl)thieno[2,3-d]pyridazin-4(5H)-one (**35c**).* (91 mg, 44%), mp 245–247 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.82 (d, J=5.2 Hz, 1H, C=CH), 7.54 (d, J=5.2 Hz, 1H, C=CH), 7.46–7.41 (m, A-part of AA′BB′ system, 2H, arom.), 7.13–7.11 (m, B-part of AA′BB′ system, 2H, arom.), 5.44 (br s, 2H, $-NH_2$), 2.24 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 155.0, 143.8, 139.5, 136.7, 136.1, 133.6, 132.1, 128.7, 125.8, 125.2, 20.6; ν_{max} (ATR) 3351, 3200, 3082, 1629, 1541, 1401, 1324, 1259, 1088 cm^{-1}; [found: C, 60.31; H, 4.40; N, 15.98; S, 12.10. $C_{13}H_{11}N_3OS$ requires C, 60.68; H, 4.31; N, 16.33; S, 12.46%].

*4.10.11. 7-Amino-5-(4-methoxyphenyl)thieno[2,3-d]pyridazin-4(5H)-one (**35d**).* (100 mg, 48%), mp 208–210 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.81 (d, J=5.1 Hz, 1H, C=CH), 7.54 (d, J=5.1 Hz, 1H, C=CH), 7.48–7.43 (m, A-part of AA′BB′ system, 2H, arom.), 6.89–6.82 (m, B-part of AA′BB′ system, 2H, arom.), 5.43 (s, 2H, $-NH_2$), 3.71 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 157.8, 155.0, 143.7, 136.9, 135.0, 133.5, 132.1, 127.2, 125.2, 113.4, 55.3; ν_{max} (ATR) 3326, 3184, 3078, 1630, 1606, 1506, 1325, 1030 cm^{-1}; [found: C, 56.81; H, 3.99; N, 15.29; S, 12.24. $C_{13}H_{11}N_3O_2S$ requires C, 57.13; H, 4.06; N, 15.37; S, 11.73%].

*4.10.12. 7-Amino-5-(4-chlorophenyl)thieno[2,3-d]pyridazin-4(5H)-one (**35e**).* (119 mg, 57%), mp 230–232 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.84 (d, J=5.2 Hz, 1H, C=CH), 7.68–7.63 (m, A-part of AA′BB′ system, 2H, arom.), 7.55 (d, J=5.2 Hz, 1H, C=CH), 7.38–7.30 (m, B-part of AA′BB′ system, 2H, arom.), 5.55 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 155.0, 144.1, 140.7, 136.7, 133.8, 132.3, 130.9, 128.2, 127.5, 125.2; ν_{max} (ATR) 3355, 3304, 3202, 3077, 1628, 1539, 1489, 1472, 1322, 1089 cm^{-1}; [found: C, 52.27; H, 2.86; N, 15.13; S, 11.68. $C_{12}H_8ClN_3OS$ requires C, 51.90; H, 2.90; N, 15.13; S, 11.55%].

*4.10.13. 7-Amino-5-(4-fluorophenyl)thieno[2,3-d]pyridazin-4(5H)-one (**35f**).* (125 mg, 60%), mp 241–243 °C. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.74 (d, J=5.2 Hz, 1H, C=CH), 7.59 (d, J=5.2 Hz, 1H, C=CH), 7.57–7.50 (m, A-part of AA′BB′ system, 2H, arom.), 7.11–7.04 (m, B-part of AA′BB′ system, 2H, arom.), 4.21 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 160.1 (d, J=243.8 Hz), 154.7, 143.7, 137.9 (d, J=2.8 Hz), 136.4, 133.4, 131.9, 127.7 (d, J=8.5 Hz), 124.8, 114.7 (d, J=22.6 Hz); ν_{max} (ATR) 3339, 3192, 3095, 3083, 1632, 1541, 1501, 1319, 1216, 1057 cm^{-1}; [found: C, 55.01; H, 3.03; N, 15.94; S, 12.84. $C_{12}H_8FN_3OS$ requires C, 55.16; H, 3.09; N, 16.08; S, 12.27%].

*4.10.14. 7-Amino-5-(2,4-difluorophenyl)thieno[2,3-d]pyridazin-4(5H)-one (**35g**).* (101 mg, 48%), mp 248–250 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.86 (d, J=5.2 Hz, 1H, C=CH), 7.54 (d, J=5.2 Hz, 1H, C=CH), 7.48 (dt, J=8.7 and 6.1 Hz, 1H, arom.), 7.10–6.98 (m, 2H, arom), 5.50 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 161.5 (dd, J=247.3 and 11.6 Hz), 157.0 (dd, J=252.3 and 13.1 Hz), 154.9, 144.3, 136.0, 134.3, 132.5, 130.9 (dd, J=10.3 and 1.7 Hz), 126.4 (dd, J=12.9 and 3.9 Hz), 125.0, 111.7 (dd, J=22.5 and 3.4 Hz), 104.6 (dd, J=26.8 and 24.4 Hz); ν_{max} (ATR) 3337, 3187, 3082, 1639, 1611, 1546, 1504, 1336 cm^{-1}; [found: C, 51.51; H, 2.73; N, 14.74; S, 11.21. $C_{12}H_7F_2N_3OS$ requires C, 51.61; H, 2.53; N, 15.05; S, 11.48%].

4.11. 2-[Methoxy(oxo)acetyl]benzoic acid (38)

The monoester **37**[24] (4.0 g, 20.61 mmol) was dissolved in anisole (40 mL) and SeO_2 (3.43 g, 30.93 mmol) was added. The mixture was heated at reflux temperature for 6 h. The reaction mixture was cooled, filtered, and washed with ethyl acetate (100 mL). The filtrate was evaporated. The crude product was purified by column chromatography (silica gel) eluting with hexane/EtOAc (5:1, 2:1) to give oxidized monoester **38** as a white solid (2.2 g, 51%), mp 72–73 °C (lit. mp 74–85 °C[25]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dt, J=7.6 and 0.8 Hz, 1H, arom.), 7.77 (dt, J=7.5 and 1.1 Hz, 1H, arom.), 7.68 (dt, J=7.5 and 1.0 Hz, 1H, arom.), 7.58 (dt, J=7.6 and 0.8 Hz, 1H, arom.), 3.82 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 168.3, 167.9, 167.8, 144.8, 134.9, 131.4, 127.0, 125.8, 122.9, 54.3; ν_{max} (ATR) 3507, 3431, 3046, 2853, 1770, 1735, 1465, 1289, 1230, 1149, 1112 cm^{-1}; [found: C, 57.83; H, 3.99. $C_{10}H_8O_5$ requires C, 57.70; H, 3.87%].

4.12. Methyl 3-methyl-4-oxo-3,4-dihydrophthalazine-1-carboxylate (39a)

Methyl hydrazine (0.35 mL, 6.7 mmol) was added to a stirred solution of the monoester **38** (1.4 g, 6.7 mmol) in dry THF (25 mL) and stirred at 50 °C for 3 h. The mixture was cooled to rt, thionyl chloride (1 mL, 13.5 mmol) was added dropwise and then stirred at 50 °C for 18 h. The reaction was monitored on TLC. After the completion of the reaction, the solvent was evaporated and the crude product was purified by column chromatography (silica gel) eluting with dichloromethane/ethylacetate/hexane (1:1:1) to give a white solid **39a** (1.0 g, 68%), mp 125–126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (ddd, J=8.2, 1.2, and 0.6 Hz, 1H, arom.), 8.40 (ddd, J=8.0, 1.4, and 0.4 Hz, 1H, arom.), 7.79 (ddd, J=8.4, 7.3, and 1.5 Hz, 1H, arom.), 7.73 (ddd, J=8.0, 7.7, and 1.3, 7.7 Hz, 1H, arom.), 3.96 (s, 3H, $-OCH_3$), 3.87 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.7, 159.7, 135.1, 133.6, 131.8, 128.1, 127.5, 126.9, 126.3, 53.0, 40.1; ν_{max} (ATR) 3046, 2952, 1720, 1675, 1443, 1321, 1288, 1213, 1159 cm^{-1}; [found: C, 60.19; H, 4.78; N, 12.31. $C_{11}H_{10}N_2O_3$ requires C, 60.55; H, 4.62; N, 12.31%].

4.13. General procedure for the synthesis of phthalazinone derivatives (39b–g)

Phenyl hydrazinium chloride derivatives (1.1 equiv) were added to a stirred solution of the monoester **38** (1.0 g, 4.8 mmol) in dry methanol (50 mL). This mixture was stirred at given temperature for a while (see Table). The solvent was evaporated and the residue was dissolved in dry benzene (70 mL). Thionyl chloride (4 equiv) was added dropwise and then the mixture was stirred for 18 h. The reaction was monitored on TLC. After the completion of the reaction, the solvent was evaporated and the crude product was purified by column chromatography (silica gel) eluting with suitable solvent mixture to give phthalazinone derivatives **39b–g** as white solids.

Compound number	Temperature (°C)	Time (h)	Column solvent		Yield (%)
			Hexane	EtOAc	
39b	70	4	4	1	74
39c	50	4	4	1	74
39d	50	2.5	9	1	56
39e	65	4	4	1	80
39f	65	4	3	1	73
39g	65	4	3	1	61

*4.13.1. Methyl 4-oxo-3-phenyl-3,4-dihydrophthalazine-1-carboxylate (**39b**).* (1.1 g, 74%), mp 111–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (ddd, J=8.2, 1.1, and 0.4 Hz, 1H), 8.56 (ddd, J=8.0, 1.1, and 0.4 Hz, 1H), 7.93 (ddd, J=8.2, 7.4, and 0.5 Hz, 1H), 7.86 (ddd, J=8.5, 7.3, and 1.2 Hz, 1H), 7.72–7.68 (m, 2H), 7.56–7.51 (m, 2H), 7.44 (tt, J=7.4 and 1.2 Hz, 1H), 4.04 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.8, 159.1, 141.4, 136.1, 134.0, 132.1, 128.9, 128.4, 128.3, 127.7, 127.6, 126.4, 125.8, 53.0; ν_{max} (ATR) 3040, 2954, 1719, 1666, 1595, 1427, 1321, 1234, 1175, 1143, 1027 cm^{-1}; [found: C, 68.45; H, 4.40; N, 9.95. $C_{16}H_{12}N_2O_3$ requires C, 68.56; H, 4.32; N, 9.99%].

*4.13.2. Methyl 3-(4-methylphenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylate (**39c**).* (2.1 g, 74%), mp 152–153 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (bdd, J=7.9 and 0.8 Hz, 1H), 8.47 (dd, J=7.9 and 1.0 Hz, 1H), 7.83 (ddd, J=8.3, 7.3, and 1.5 Hz, 1H), 7.76 (ddd, J=8.4, 7.4, and 1.2 Hz, 1H), 7.48–7.45 (m, 2H), 7.25–7.22 (m 2H), 3.94 (s, 3H, $-OCH_3$), 2.35 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.8, 159.1, 138.9, 138.3, 135.9, 133.9, 132.0, 129.5, 128.4, 127.7, 127.5, 126.3, 125.6, 53.0, 21.1; ν_{max} (ATR), 3050, 1720, 1679, 1647, 1515, 1329, 1238, 1142; [found: C, 69.04; H, 4.71; N, 9.40. $C_{17}H_{14}N_2O_3$ requires C, 69.38; H, 4.79; N, 9.52%].

*4.13.3. Methyl 3-(4-methoxyphenyl)-4-oxo-3,4-dihydro-phthalazine-1-carboxylate (**39d**).* (0.83 g, 56%), mp 181–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (br d, J=8.7 Hz, 1H), 8.47 (dd, J=8.0 and 1.2 Hz, 1H), 7.83 (ddd, J=8.7, 7.3, and 1.4 Hz, 1H), 7.77 (ddd, J=8.3, 7.7, and 1.2 Hz, 1H), 7.53–7.48 (m, A-part of AA′BB′ system, 2H), 6.97–6.93 (m, B-part of AA′BB′ system, 2H), 3.94 (s, 3H, $-OCH_3$), 3.80 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.8, 159.3, 159.2, 135.8, 134.4, 133.9, 132.0, 128.3, 127.7, 127.5, 127.1, 126.3, 114.1, 55.6, 53.0; ν_{max} (ATR) 3000, 2953, 1722, 1671, 1513, 1435, 1253, 1144, 1046 cm^{-1}; [found: C, 65.45; H, 4.84; N, 8.95. $C_{17}H_{14}N_2O_4$ requires C, 65.80; H, 4.55; N, 9.03%].

*4.13.4. Methyl 3-(4-chlorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylate (**39e**).* (0.65 g, 80%), mp 179–181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (br d, J=8.1 Hz, 1H), 8.55 (dd, J=7.9 and 0.8 Hz, 1H), 7.94 (ddd, J=8.2, 7.7, and 1.4 Hz, 1H), 7.87 (ddd, J=8.5, 7.6, and 1.2 Hz, 1H), 7.69–7.66 (m, A-part of AA′BB′ system, 2H), 7.52–7.48 (m, B-part of AA′BB′ system, 2H), 4.04 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.6, 159.0, 139.8, 136.4, 134.2, 134.0, 132.3, 129.0, 128.2, 127.6, 127.1 (2C), 126.5, 53.1; ν_{max} (ATR) 3085, 2952, 1723, 1683, 1489, 1481, 1435, 1323, 1235, 1171, 1143, 1091, 1064, 1046 cm^{-1}; [found: C, 60.79; H, 3.41; N, 8.83. $C_{16}H_{11}ClN_2O_3$ requires C, 61.06; H, 3.53; N, 8.90%].

*4.13.5. Methyl 3-(4-fluorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylate (**39f**).* (1.05 g, 73%), mp 125–127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (br d, J=8.0 Hz, 1H), 8.56 (dd, J=7.9 and 0.9 Hz, 1H), 7.93 (ddd, J=8.6, 7.4, and 1.4 Hz, 1H), 7.88 (ddd, J=8.3, 7.4, and 1.2 Hz, 1H), 7.71–7.66 (m, A-part of AA′BB′ system, 2H),

7.25–7.19 (m, B-part of AA′BB′ system, 2H), 4.05 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.6, 162.1 (d, J=248.1 Hz), 159.1, 137.3 (d, J=3.0 Hz), 136.2, 134.1, 132.2, 128.3, 127.8, 127.7, 127.6 (d, J=7.3 Hz), 126.5, 115.8 (d, J=22.8), 53.1; ν_{max} (ATR) 3089, 2953, 1723, 1683, 1505, 1483, 1349, 1233, 1143, 1046 cm^{-1}; [found: C, 64.04; H, 3.70; N, 9.22. $C_{16}H_{11}FN_2O_3$ requires C, 64.43; H, 3.72; N, 9.39%].

*4.13.6. Methyl 3-(2,4-difluorophenyl)-4-oxo-3,4-dihydro-phthalazine-1-carboxylate (**39g**).* (0.5 g, 61%), mp 120–121 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (br d, J=8.1 Hz, 1H), 8.54 (dd, J=7.7 and 1.2 Hz, 1H), 7.95 (dt, J=8.3 and 1.4 Hz, 1H), 7.88 (br dt, J=7.8 and 0.8 Hz, 1H), 7.56–7.50 (m, 1H), 7.09–7.01 (m, 2H), 4.04 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 163.4, 163.0 (dd, J=251.6 and 11.1 Hz), 158.7, 157.7 (dd, J=255.7 and 12.6 Hz), 137.0, 134.3, 132.4, 129.9 (dd, J=10.3 and 1.8 Hz), 127.8, 127.8, 127.5, 126.6, 125.5 (dd, J=13.0 and 4.1 Hz), 111.9 (dd, J=22.7 and 3.7 Hz), 105.1 (dd, J=26.4 and 23.5 Hz), 53.1; ν_{max} (ATR), 3021, 2970, 1742, 1679, 1605, 1533, 1434, 1352, 1330, 1274, 1230, 1170, 1143, 1073 cm^{-1}; [found: C, 60.59; H, 3.32; N, 8.76. $C_{16}H_{10}F_2N_2O_3$ requires C, 60.76; H, 3.19; N, 8.86%].

4.14. General procedure for the hydrolysis of phthalazinone derivatives (39a–g)

The esters **39a–g** (1.0 g, 3.16–4.59 mmol) were dissolved in THF (50 mL), methanol (25 mL), and water (1 mL). To the resulting solution, a solution of 2 M KOH in MeOH (3 equiv) was added and stirred at constant temperature and monitored on TLC. After the completion of the reaction, the solvent was evaporated and the residue was dissolved in water (15 mL) and extracted with ethyl acetate (3×50 mL). The water phase was acidified to pH=2 by addition of 1 M HCl and extracted with ethyl acetate (3×75 mL). The combined organic phases were dried ($MgSO_4$) and the solvent was evaporated and the acid derivatives **40a–g** were obtained as a white solids.

Compound number	Temperature (°C)	Time (h)	Yield (%)
40a	40	1.5	85
40b	40	1.5	85
40c	40	1.5	90
40d	45	16	87
40e	60	4	74
40f	60	2	77
40g	60	2	98

*4.14.1. 3-Methyl-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40a**).* (0.8 g, 85%), mp 246–247 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.53 (br d, J=8.1 Hz, 1H), 8.27 (br d, J=7.8 Hz, 1H), 7.94 (br t, J=7.7 Hz, 1H), 7.86 (br t, J=7.5 Hz, 1H), 3.77 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 164.4, 158.6, 135.4, 133.6, 131.9, 127.4, 126.8, 126.2, 126.0, 40.1; ν_{max} (ATR) 3017, 2875, 1716, 1624, 1575, 1489, 1415, 1346, 1311, 1209, 1186, 1063 cm^{-1}; [found: C, 58.49; H, 4.07; N, 13.43. $C_{10}H_8N_2O_3$ requires C, 58.82; H, 3.95; N, 13.72%].

*4.14.2. 4-Oxo-3-phenyl-3,4-dihydrophthalazine-1-carboxylic acid (**40b**).* (0.80 g, 85%), mp 217–218 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 9.13 (br d, J=8.2 Hz, 1H), 8.48 (dd, J=7.8 and 0.8 Hz, 1H), 7.90 (dt, J=7.6 and 1.4 Hz, 1H), 7.83 (dt, J=8.1 and 1.1 Hz, 1H), 7.56–7.54 (m, 2H), 7.51–7.47 (m, 2H), 7.42 (tt, J=7.2 and 1.1 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.6, 159.2, 140.1, 134.6, 133.1, 132.9, 129.2, 128.9, 128.4, 127.7, 127.6, 127.3, 125.7; ν_{max} (ATR) 2859, 1735, 1708, 1686, 1596, 1576, 1432, 1317, 1281, 1157, 1125 cm^{-1}; HRMS-ESI $[M+Na]^+$ calcd for $C_{15}H_{10}N_2NaO_3$ 267.0764, found: 267.0731.

*4.14.3. 3-(4-Methylphenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40c**).* (1.05 g, 90%), mp 204–205 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 9.11 (dd, J=8.3 and 0.6 Hz, 1H), 8.47 (dd, J=7.9 and 0.9 Hz, 1H), 7.89 (ddd, J=8.4, 7.2, and 1.2 Hz, 1H), 7.82 (ddd, J=8.3, 7.2, and 1.4 Hz, 1H), 7.43–7.40 (m, A-part of AA′BB′ system, 2H), 7.28–7.26 (m, B-part of AA′BB′ system, 2H), 2.38 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.0, 159.3, 139.0, 138.1, 134.6, 133.1, 132.8, 129.7, 128.3, 127.7, 127.4, 127.3, 125.5, 21.2; ν_{max} (ATR) 3003, 2970, 1738, 1705, 1682, 1510, 1433, 1320, 1250, 1183, 1171 cm^{-1}; HRMS-MALDI $[M-H]^+$ calcd for $C_{16}H_{11}N_2O_3$ 279.0769; found: 279.0779.

*4.14.4. 3-(4-Methoxyphenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40d**).* (1.01 g, 87%), mp 219–220 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.57 (br d, J=8.0 Hz, 1H), 8.37 (br dd, J=7.8 and 0.7 Hz, 1H), 8.02 (ddd, J=8.4, 7.4, and 1.3 Hz, 1H), 7.94 (dt, J=8.0 and 1.0 Hz, 1H), 7.56–7.52 (m, A-part of AA′BB′ system, 2H), 7.10–7.06 (m, B-part of AA′BB′ system, 2H), 3.83 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 164.5, 158.7, 158.4, 136.7, 134.3, 134.0, 132.2, 127.8, 127.5, 127.2, 126.7, 126.4, 113.8, 55.4; ν_{max} (ATR) 2989, 2839, 2560, 1701, 1609, 1511, 1436, 1313, 1248, 1160 cm^{-1}; [found: C, 64.52; H, 4.00; N, 9.28. $C_{16}H_{12}N_2O_4$ requires C, 64.86; H, 4.08; N, 9.46%].

*4.14.5. 3-(4-Chlorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40e**).* (1.0 g, 74%), mp 208–209 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.58 (br d, J=7.7 Hz, 1H), 8.39 (dd, J=8.8 and 0.9 Hz, 1H), 8.04 (dt, J=7.3 and 1.5 Hz, 1H), 7.96 (dt, J=8.0 and 1.2 Hz, 1H), 7.72–7.69 (m, A-part of AA′BB′ system, 2H) 7.74–7.61 (m, B-part of AA′BB′ system, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 164.3, 158.3, 140.1, 137.1, 134.2, 132.4, 132.3, 128.6, 127.9, 127.7, 127.2, 126.7, 126.5; ν_{max} (ATR) 3003, 2970, 1738, 1683, 1484, 1431, 1372, 1319, 1230, 1154 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{15}H_{10}ClN_2O_3$ 301.0380, found: 301.0371.

*4.14.6. 3-(4-Fluorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40f**).* (0.96 g, 77%), mp 215–217 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.58 (br d, J=8.2 Hz, 1H), 8.38 (dd, J=7.9 and 0.8 Hz, 1H), 8.04 (dt, J=7.4 and 1.4 Hz, 1H), 7.96 (dt, J=8.2 and 1.1 Hz, 1H), 7.71–7.68 (m, A-part of AA′BB′ system, 2H), 7.41–7.37 (m, B-part of AA′BB′ system, 2H); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 164.3, 161.2 (d, J=245.1 Hz), 158.3, 137.7 (d, J=2.8 Hz), 136.7, 134.2, 132.3, 128.4 (d, J=8.8 Hz), 127.8, 127.2, 126.7, 126.4, 115.5 (d, J=22.8 Hz); ν_{max} (ATR) 2980, 2643, 1736, 1672, 1629, 1602, 1507, 1481, 1404, 1346, 1294, 1234, 1216, 1174, 1151, 1130, 1015 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{15}H_{10}FN_2O_3$ 285.0675, found: 285.0666.

*4.14.7. 3-(2,4-Difluorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carboxylic acid (**40g**).* (0.93 g, 98%), mp 225–226 °C. ^1H NMR (400 MHz, DMSO-d_6) δ 8.57 (dd, J=8.2 and 0.4 Hz, 1H), 8.37 (dd, J=7.9 and 0.8 Hz, 1H), 8.07 (dt, J=7.9 and 1.4 Hz, 1H), 7.98 (dt, J=8.0 and 1.2 Hz, 1H), 7.76 (dt, J=8.8 and 6.1 Hz, 1H), 7.57 (ddd, J=10.4, 9.2, and 2.8 Hz, 1H), 7.35–7.30 (m, 1H); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 163.3, 161.3 (dd, J=248.7 and 11.5 Hz), 157.2, 156.2 (dd, J=252.7 and 13.2 Hz). 137.0, 133.7, 131.9, 130.1 (d, J=10.2 Hz), 126.5, 126.4, 125.9, 125.8, 124.8 (dd, J=13.0 and 4.1 Hz), 111.4 (dd, J=22.6 and 3.4 Hz), 104.0 (dd, J=27.1 and 24 Hz); ν_{max} (ATR) 3079, 1730, 1658, 1615, 1604, 1511, 1352, 1274, 1229, 1177, 1159, 1148 cm^{-1}; [found: C, 59.28; H, 2.74; N, 8.92. $C_{15}H_8F_2N_2O_3$ requires C, 59.61; H, 2.67; N, 9.27%].

4.15. General procedure for the synthesis of acyl azide derivatives (41a–g)

Oxalyl chloride (2 equiv) was added to a stirred suspension of acids **40a–g** (1.0 g) in dichloromethane at rt and then DMF (3 drops) were added. After 10 min, all acid dissolved and the solution was stirred at rt for 90 min. The solvent and excess oxalyl chloride were evaporated. The residue was dissolved in acetone (15 mL) and cooled in an ice bath. A solution of NaN_3 (2 equiv) in water (1 mL)

was added dropwise and stirred in an ice-cooled bath for 90 min. The mixture was extracted with ethyl acetate (200 mL) and water (100 mL). The combined water layers were extracted with EtOAc (3×75 mL), dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography eluting with ethyl acetate/dichloromethane/hexane (2:2:1) to give acyl azide derivatives **41a**–**g** as white solids.

*4.15.1. 3-Methyl-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41a**).* (0.90 g, 81%), mp 110–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (br d, J=7.9 Hz, 1H), 8.39 (dd, J=7.9 and 1.1 Hz, 1H), 7.82 (ddd, J=8.6, 7.3 and 1.5 Hz, 1H), 7.75 (ddd, J=8.2, 8.1 and 1.2 Hz, 1H), 3.88 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.3, 159.0, 133.3, 131.8, 131.3, 127.1, 126.5, 126.2, 125.4, 39.5; ν_{max} (ATR) 3123, 2162, 1673, 1603, 1447, 1346, 1322, 1289, 1201, 1044 cm^{-1}.

*4.15.2. 4-Oxo-3-phenyl-3,4-dihydrophthalazine-1-carbonyl azide (**41b**).* (0.82 g, 75%), mp 87–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (br d, J=8.2 Hz, 1H), 8.47 (dd, J=7.9 and 0.9 Hz, 1H), 7.87 (dt, J=7.3 and 1.4 Hz, 1H), 7.79 (dt, J=8.0 and 1.2 Hz, 1H), 7.62–7.58 (m, 2H), 7.48–7.43 (m, 2H), 7.37 (tt, J=7.6 and 1.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 169.3, 159.0, 133.3, 131.8, 131.3, 127.1, 126.5, 126.2, 125.4, 39.6; ν_{max} (ATR) 3038, 2924, 2140, 1681, 1595, 1488, 1344, 1318, 1227, 1185, 1126, 1075 cm^{-1}.

*4.15.3. 3-(4-Methylphenyl)-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41c**).* (1.05 g, 97%), mp 111–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (br d, J=8.3 Hz, 1H), 8.45 (br d, J=7.9 Hz, 1H), 7.87–7.83 (m, 1H), 7.80–7.75 (m, 1H), 7.47–7.44 (m, A-part of AA′BB′ system, 2H), 7.26–7.24 (m, B-part of AA′BB′ system, 2H), 2.35 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.3, 159.2, 138.7, 138.6, 134.6, 134.3, 132.2, 129.6, 128.1, 127.7, 127.5, 126.2, 125.4, 21.2; ν_{max} (ATR) 3110, 2917, 2121, 1793, 1752, 1681, 1604, 1510, 1346, 1181, 1127 cm^{-1}.

*4.15.4. 3-(4-Methoxyphenyl)-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41d**).* (1.01 g, 94%), mp 110–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (dd, J=8.3 and 0.5 Hz, 1H), 8.46 (dd, J=7.9 and 0.9 Hz, 1H), 7.86 (dt, J=7.3 and 1.4 Hz, 1H), 7.78 (dt, J=8.0 and 1.2 Hz, 1H), 7.52–7.48 (m, A-part of AA′BB′ system, 2H), 6.98–6.94 (m, B-part of AA′BB′ system, 2H), 3.80 (s, 3H, $-OCH_3$); ν_{max} (ATR) 3078, 2954, 2146, 1724, 1694, 1676, 1509, 1323, 1252, 1173, 1031 cm^{-1}.

*4.15.5. 3-(4-Chlorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41e**).* (1.0 g, 92%), mp 123–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, J=8.3 and 0.53 Hz, 1H), 8.46 (dd, J=7.9, 0.9 Hz, 1H), 7.87 (dt, J=7.3 and 1.4 Hz, 1H), 7.79 (dt, J=8.0 and 1.2 Hz, 1H), 7.60–7.56 (m, A-part of AA′BB′ system, 2H), 7.44–7.40 (m, B-part of AA′BB′ system, 2H); ν_{max} (ATR); 3093, 2969, 2146, 1735, 1691, 1608, 1449, 1439, 1347, 1319, 1276, 1201, 1129, 1069 cm^{-1}.

*4.15.6. 3-(4-Fluorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41f**).* (0.96 g, 89%), mp 117–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (dd, J=8.2 and 0.4 Hz, 1H), 8.46 (ddd, J=8.0, 0.7, and 0.6 Hz, 1H), 7.90–7.85 (m, 1H), 7.82–7.78 (m, 1H), 7.62–7.56 (m, A-part of AA′BB′ system, 2H), 7.17–7.11 (m, B-part of AA′BB′ system, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 170.2, 162.2 (d, J=248.7 Hz), 159.1, 137.1 (d, J=3.0 Hz), 135.0, 134.5, 132.4, 128.3, 128.0, 127.6 (d, J=15.3 Hz), 127.4, 126.3, 115.9 (d, J=22.9 Hz); ν_{max} (ATR), 3131, 2940, 2148, 1698, 1683, 1603, 1507, 1350, 1325, 1237, 1182, 1128, 1076 cm^{-1}.

*4.15.7. 3-(2,4-Difluorophenyl)-4-oxo-3,4-dihydrophthalazine-1-carbonyl azide (**41g**).* (0.93 g, 86%), mp 104–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (br d, J=8.4 Hz, 1H), 8.44 (dd, J=7.9 and 0.9 Hz, 1H), 7.87 (dt, J=7.8 and 1.4 Hz, 1H), 7.80 (dt, J=8.1 and 1.1 Hz, 1H), 7.45–7.40 (m, 1H), 7.00–6.92 (m, 2H); ν_{max} (ATR) 3092, 2969, 2146, 1692, 1607, 1507, 1481, 1346, 1319, 1276, 1201, 1179, 1129, 1109, 1069 cm^{-1}.

4.16. General procedure for the synthesis of urethane derivatives (42a–g)

The acyl azide derivatives **41a**–**g** (0.25 g) were dissolved in dry benzene (40 mL) and heated at reflux for 90 min. To this solution, dry MeOH (2 mL) was added and stirred at this temperature for 2–16 h. The reaction was monitored with TLC. The solvent and excess methanol were evaporated. The crude product was purified by column chromatography (silica gel) with suitable eluent to give urethane derivatives **42a**–**g** as white solids.

*4.16.1. Methyl (3-methyl-4-oxo-3,4-dihydrophthalazin-1-yl)carbamate (**42a**).* (0.24 g, 96%), mp 173–174 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38–8.35 (m, 1H), 7.73–7.71 (m, 3H), 6.81 (br s, 1H, –NH), 3.73 (s, 3H, $-OCH_3$), 3.73 (s, 3H, $-NCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.4, 155.4, 137.2, 132.9, 132.0, 128.6, 127.6, 127.1, 124.7, 53.1, 39.3; ν_{max} (ATR) 3218, 2950, 1734, 1626, 1578, 1556, 1489, 1452, 1353, 1230, 1060 cm^{-1}; [found: C, 56.45; H, 4.83; N, 17.94. $C_{11}H_{11}N_3O_3$ requires C, 56.65; H, 4.75; N, 18.02%].

*4.16.2. Methyl (4-oxo-3-phenyl-3,4-dihydrophthalazin-1-yl)carbamate (**42b**).* (0.21 g, 85%), mp 175–176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57–8.54 (m, 1H), 7.90–7.86 (m, 3H), 7.70–7.67 (m, 2H), 7.54–7.50 (m, 2H), 7.41 (tt, J=7.4 and 7.4 Hz, 1H), 6.77 (br s, 1H, –NH), 3.85 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.9, 155.5, 147.1, 141.4, 138.2, 133.3, 132.3, 128.8, 127.8, 127.8, 127.3, 125.7, 125.0, 53.2; ν_{max} (ATR) 3276, 3010, 2969, 2955, 1737, 1706, 1668, 1595, 1556, 1484, 1455, 1313, 1254, 1055 cm^{-1}; [found: C, 65.00; H, 4.27; N, 13.87. $C_{16}H_{13}N_3O_3$ requires C, 65.08; H, 4.44; N, 14.23%].

*4.16.3. Methyl [3-(4-methylphenyl)-4-oxo-3,4-dihydrophthalazin-1-yl]carbamate (**42c**).* (0.21 g, 80%), mp 195–196 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (m, 1H), 7.77–7.70 (m, 3H), 7.44–7.40 (m, A-part of AA′BB′ system, 2H), 7.17 (m, B-part of AA′BB′ system, 2H), 7.00 (br s, 1H, –NH), 3.72 (s, 3H, $-OCH_3$), 2.30 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.9, 155.6, 138.9, 138.1, 137.8, 133.2, 132.1, 129.4, 129.3, 127.7, 127.3, 125.4, 125.0, 53.1, 21.1; ν_{max} (ATR) 3206, 3112, 2915, 1709, 1668, 1591, 1512, 1469, 1447, 1354, 1332, 1313, 1180, 1064 cm^{-1}; [found: C, 65.98; H, 4.83; N, 13.23. $C_{17}H_{15}N_3O_3$ requires C, 66.01; H, 4.89; N, 13.58%].

*4.16.4. Methyl (3-(4-methoxyphenyl)-4-oxo-3,4-dihydrophthalazin-1-yl)carbamate (**42d**).* (0.21 g, 83%), mp 153–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46–8.44 (m, 1H), 7.80–7.74 (m, 3H), 7.50–7.46 (m, A-part of AA′BB′ system, 2H), 6.95–6.91 (m, B-part of AA′BB′ system, 2H), 6.67 (br s, 1H, –NH), 3.79 (s, 3H, $-OCH_3$), 3.75 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.8, 158.7, 155.3, 137.8, 134.2, 133.0, 131.9, 129.0, 127.5, 127.1, 126.6, 124.7, 113.7, 55.3, 52.9; ν_{max} (ATR) 3264, 3070, 2951, 1731, 1667, 1599, 1505, 1466, 1452, 1305, 1239, 1178, 1131, 1009 cm^{-1}; [found: C, 62.97; H, 4.70; N, 12.88. $C_{17}H_{15}N_3O_4$ requires C, 62.76; H, 4.65; N, 12.92%].

*4.16.5. Methyl (3-(4-chlorophenyl)-4-oxo-3,4-dihydrophthalazin-1-yl)carbamate (**42e**).* (0.23 g, 92%), mp 178–179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.43 (m, 1H), 7.82–7.74 (m, 3H), 7.60–7.56 (m, A-part of AA′BB′ system, 2H), 7.38–7.35 (m, B-part of AA′BB′ system, 2H), 6.83 (s, 1H, –NH), 3.75 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.8, 155.4, 139.9, 138.4, 133.5, 133.3, 132.4, 129.2, 128.8, 127.9, 127.2, 126.7, 124.9, 53.2; ν_{max} (ATR) 3221, 3053, 2969, 1705, 1668, 1597, 1524, 1485, 1327, 1249, 1173, 1132, 1069,

1041, 1021, 1009 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{16}H_{13}ClN_3O_3$ 330.0645, found : 330.0688.

*4.16.6. Methyl (3-(4-fluorophenyl)-4-oxo-3,4-dihydrophthalazin-1-yl)carbamate (**42f**).* (0.25 g, 99%), mp 190–192 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.44–8.42 (m, 1H), 7.79–7.74 (m, 3H), 7.58–7.54 (m, A-part of AA′BB′ system, 2H), 7.10–7.05 (m, B-part of AA′BB′ system, 2H), 6.90 (s, 1H, –NH), 3.74 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.7 (d, J=246.1 Hz), 158.9, 155.4, 138.2, 137.4 (d, J=3.0 Hz), 133.4, 132.4, 129.2, 127.8, 127.4 (d, J=8.7 Hz), 127.3, 125.0, 115.6 (d, J=22.7 Hz), 53.2; ν_{max} (ATR) 3221, 3072, 2923, 1705, 1665, 1587, 1556, 1504, 1454, 1324, 1256, 1213, 1140, 1058 cm^{-1}; [found: C, 61.08; H, 4.11; N, 13.09. $C_{16}H_{12}FN_3O_3$ requires C, 61.34; H, 3.86; N, 13.41%].

*4.16.7. Methyl (3-(2,4-difluorophenyl)-4-oxo-3,4-dihydro-phthalazin-1-yl)carbamate (**42g**).* (0.24 g, 97%), mp 202–203 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.45–8.42 (m, 1H), 7.85–7.76 (m, 3H), 7.45–7.40 (m, 1H), 6.97–6.90 (m, 2H), 6.65 (s, 1H, –NH), 3.75 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 162.7 (dd, J=249.7 and 11.0 Hz), 158.7, 156.6 (dd, J=254.1 and 12.6 Hz), 155.3, 138.8, 133.6, 132.5, 129.8 (dd, J=10.1 and 1.5 Hz), 128.7, 127.8, 127.5, 125.5 (dd, J=12.8 and 4.1 Hz), 125.3, 111.8 (dd, J=22.5 and 3.6 Hz), 105.0 (dd, J=26.3 and 23.6 Hz), 53.2; ν_{max} (ATR) 3198, 3062, 2970, 2948, 1730, 1650, 1606, 1589, 1509, 1486, 1238, 1216, 1148, 1056, cm^{-1}; [found: C, 58.30; H, 3.44; N, 12.27. $C_{16}H_{11}F_2N_3O_3$ requires C, 58.01; H, 3.35; N, 12.68%].

4.17. General procedure for the synthesis of amino-phthalazinone derivatives (43a–g)

The acyl azide derivatives **41a–g** (0.3 g, 0.92–1.3 mmol) were dissolved in dry benzene (30 mL) and heated at reflux for 90 min. The solution was cooled to 40 °C and HCl (10 mL, 8 M) was added. The mixture was stirred at rt for 15 min–4 h and then the pH value was adjusted to pH 10 by the addition of 10% NaOH solution. The mixture was extracted with ethyl acetate (3×100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The crude product was purified by column chromatography eluting with ethyl acetate/dichloromethane (1:2) to give amine derivatives **43a–g** as white solids.

*4.17.1. 4-Amino-2-methylphthalazin-1(2H)-one (**43a**).* (0.18 g, 79%), mp 151–153 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.44–8.39 (m, 1H), 7.75–7.71 (m, 2H), 7.62–7.58 (m, 1H), 3.65 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.3, 144.6, 132.5, 131.7, 128.8, 127.7, 124.4, 122.3, 38.5; ν_{max} (ATR) 3392, 3329, 3203, 1624, 1560, 1497, 1436, 1365, 1133, 1104, cm^{-1}; HRMS-ESI $[M+Na]^+$ calcd for $C_9H_9N_3NaO$ 198.0638, found: 198.0624.

*4.17.2. 4-Amino-2-phenylphthalazin-1(2H)-one (**43b**).* (0.19 g, 80%), mp 176–178 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50–8.48 (m, 1H), 7.80–7.73 (m, 2H), 7.67–7.63 (m, 1H), 7.62–7.59 (m, 2H), 7.43–7.38 (m, 2H), 7.27 (tt, J=7.4 and 1.1 Hz, 1H), 4.13 (br s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 157.8, 144.8, 141.7, 132.7, 131.6, 129.1, 128.4, 127.9, 127.1, 125.5, 124.2, 122.2; ν_{max} (ATR) 3421, 3319, 3212, 3064, 1609, 1592, 1578, 1552, 1494, 1455, 1342, 1311 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{14}H_{12}N_3O$ 238.0980, found: 238.0996.

*4.17.3. 4-Amino-2-(4-methylphenyl)phthalazin-1(2H)-one (**43c**).* (0.22 g, 95%), mp 208–209 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50–8.48 (m, 1H), 7.80–7.72 (m, 2H), 7.64–7.62 (m, 1H), 7.48–7.45 (m, A-part of AA′BB′ system, 2H), 7.23–7.20 (m, B-part of AA′BB′ system, 2H), 4.33 (br s, 2H, $-NH_2$), 2.32 (s, 3H, $-CH_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.1, 144.9, 139.6, 137.2, 132.9, 131.7, 129.4, 129.3, 128.2, 125.5, 124.5, 122.5, 21.1; ν_{max} (ATR) 3295, 3195, 3016, 2970, 1738, 1623, 1574, 1553, 1514, 1354, 1229, 1216, 1205 cm^{-1}; [found: C, 71.53; H, 5.09; N, 16.54. $C_{15}H_{13}N_3O$ requires C, 71.70; H, 5.21; N, 16.72%].

*4.17.4. 4-Amino-2-(4-methoxyphenyl)phthalazin-1(2H)-one (**43d**).* (0.23 g, 94%), mp 274–275 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, J=8.0 and 0.8 Hz, 1H), 7.79–7.73 (m, 2H), 7.57–7.54 (m, 1H), 7.55–7.51 (m, A-part of AA′BB′ system, 2H), 6.90–6.86 (m, B-part of AA′BB′ system, 2H), 3.76 (s, 3H, $-OCH_3$); ^{13}C NMR (100.6 MHz, DMSO-d_6) δ 160.0, 158.1, 153.7, 138.9, 134.6, 133.3, 132.4, 129.4, 128.1, 126.8, 123.5, 114.1, 55.5; ν_{max} (ATR) 3247, 3144, 2839, 1683, 1666, 1650, 1630, 1561, 1508, 1469, 1447, 1323, 1308, 1249, 1170, 1028 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{15}H_{14}N_3O_2$ 268.1086, found: 268.1112.

*4.17.5. 4-Amino-2-(4-chlorophenyl)phthalazin-1(2H)-one (**43e**).* (0.24 g, 98%), mp 214–215 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48–8.46 (m, 1H), 7.80–7.72 (m, 2H), 7.64–7.61 (m, 1H), 7.62–7.58 (m, A-part of AA′BB′ system, 2H), 7.36–7.32 (m, B-part of AA′BB′ system, 2H), 4.40 (s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 158.1, 145.1, 140.5, 133.2, 132.6, 132.0, 129.3, 128.7, 128.3, 126.8, 124.5, 122.4; ν_{max} (ATR) 3453, 3344, 3220, 3035, 1738, 1617, 1589, 1577, 1551, 1490, 1430, 1347, 1088, 683 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{14}H_{11}ClN_3O$ 272.0591, found: 272.0586.

*4.17.6. 4-Amino-2-(4-fluorophenyl)phthalazin-1(2H)-one (**43f**).* (0.22 g, 92%), mp 224–225 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.49–8.47 (m, 1H), 7.81–7.74 (m, 2H), 7.65–7.62 (m, 1H), 7.61–7.58 (m, A-part of AA′BB′ system, 2H), 7.10–7.06 (m, B-part of AA′BB′ system, 2H), 4.36 (s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.4 (d, J=246.8 Hz), 158.1, 145.0, 138.0 (d, J=3.1 Hz), 133.1, 131.9, 129.3, 128.3, 127.4 (d, J=8.6 Hz), 124.5, 122.4, 115.4 (d, J=22.8 Hz): ν_{max} (ATR) 3479, 3358, 3227, 3071, 1617, 1578, 1552, 1431, 1352, 1211, 1153 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{14}H_{11}FN_3O$ 256.0886, found : 256.0888.

*4.17.7. 4-Amino-2-(2,4-difluorophenyl)phthalazin-1(2H)-one (**43g**).* (0.23 g, 94%), mp 187–188 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48–8.46 (m, 1H), 7.83–7.75 (m, 2H), 7.65–7.63 (m, 1H), 7.44–7.39 (m, 1H), 6.97–6.87 (m, 2H), 4.34 (s, 2H, $-NH_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 161.4 (dd, J=245.7 and 11.1 Hz), 157.1, 156.7 (dd, J=253.8 and 12.6 Hz), 144.4, 132.3, 131.0, 128.9 (dd, J=10.2 and 2.1 Hz), 127.7, 127.2, 125.2 (dd, J=12.9 and 4.2 Hz), 123.8, 121.7, 110.7 (dd, J=22.5 and 3.7 Hz), 103.9 (dd, J=26.3 and 23.7 Hz); ν_{max} (ATR) 3469, 3343, 3220, 3071, 1738, 1621, 1579, 1553, 1507, 1453, 1429, 1357, 1269, 1253, 1141, 1099, 964 cm^{-1}; HRMS-MALDI $[M+H]^+$ calcd for $C_{14}H_{10}F_2N_3O$ 274.0792, found: 274.0790.

4.18. Crystallography

For the crystal structure determination, a single-crystal of compound **32a** was used for data collection on a four-circle Rigaku R-AXIS RAPID-S diffractometer (equipped with a two-dimensional area IP detector). Graphite-monochromated Mo-K_α radiation (λ=0.71073 Å) and oscillation scans technique with Δw=5° for one image were used for data collection. The lattice parameters were determined by the least-squares methods on the basis of all reflections with $F^2>2\sigma(F^2)$. Integration of the intensities, correction for Lorentz and polarization effects and cell refinement was performed using CrystalClear (Rigaku/MSC Inc., 2005) software.[26] The structures were solved by direct methods using SHELXS-97[27] and refined by a full-matrix least-squares procedure using the program SHELXL-97H atoms were positioned geometrically and refined using a riding model. The final difference Fourier maps showed no peaks of chemical significance. *Crystal data for* **32a**: $C_9H_9N_3O_4$, crystal system, space group: monoclinic, $P2_1/a$; (no: 14); unit cell

dimensions: a=8.1317(2), b=14.0449(2), c=8.8512(1)Å, α=90, β=94.48(2), γ=90 Å; volume: 1007.79(3) Å^3; Z=4; calculated density: 1.471 g/cm^3; absorption coefficient: 0.118 mm^{-1}; F(000): 464; θ-range for data collection 2.3–26.9°; refinement method: full matrix least-square on F^2; data/parameters: 2104/148; goodness-of-fit on F^2: 1.009; final R-indices [$I>2r(I)$]: R_1=0.0833, wR_2=0.233; largest diff. peak and hole: 0.518 and −0.544 e Å^{-3}; Crystallographic data that were deposited in CSD under CCDC registration number 890787 contain the supplementary crystallographic data for this Letter. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC) via www.ccdc.cam.ac.uk/data_request/cif and are available free of charge upon request to CCDC, 12 Union Road, Cambridge, UK (fax: +441223 336033, e-mail: deposit@ccdc.cam.ac.uk).

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Supplementary data

These data include the ^{1}H and ^{13}C NMR spectra of compounds (228 pages). Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.10.010.

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