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Friedel-Crafts chemistry. Part 50. Convergent and diversity-oriented constructions of polycyclic quinolines via Friedel-Crafts and Beckmann ring enlargement approaches

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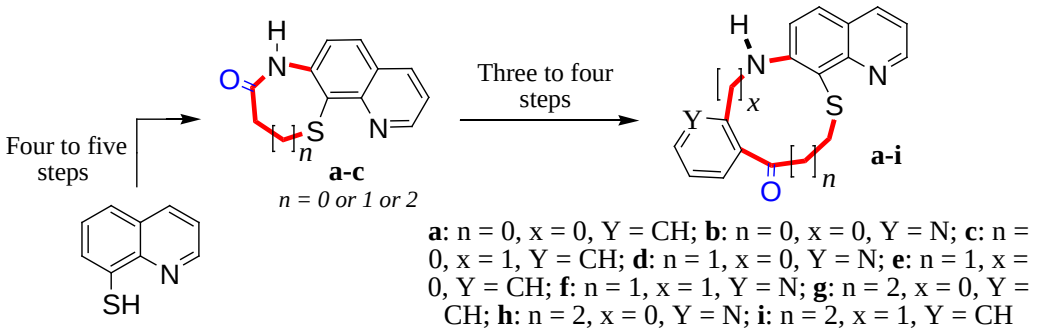
Abstract

Condensed heterocyclic systems containing N- & S-medium-sized rings, in particular, thiazepine, thiazocine, and thiazonine systems are important substructures present in a large variety of biologically active natural products. Methods for the formation of thiazonines and higher ring systems, however, remain largely unknown. The research presented addresses the synthesis and characterization of new heterocyclic skeletons incorporating N- & S-medium-sized-rings fused to quinolines to form the targeted tetracyclic 1,4-thiazocines, 1,4-thiazonines and 1,4-thiazecines by Friedel-Crafts cycliacylation and Beckmann-rearrangement sequences. The ambient conditions, short-reaction times and easy work-up procedures make this synthetic strategy a better protocol for the synthesis of medium-sized heterocyclic rings bearing nitrogen and sulphur atoms.

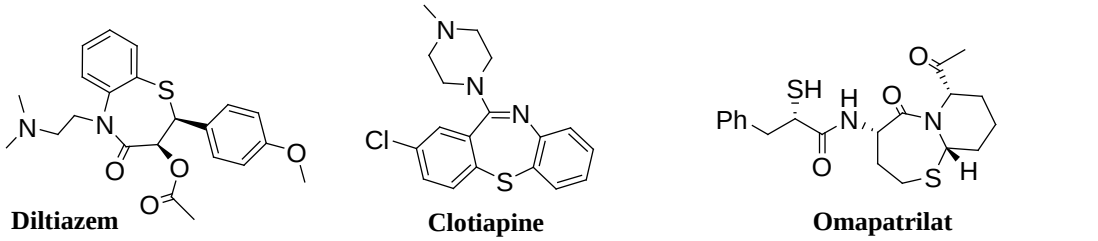


Keywords: Heteropolycycles, heterocyclic acids, 1,4-thiazocino[3,2-h]quinolinones, 1,4-thiazonino[3,2-h]quinolinones

Introduction

Condensed heterocycles containing N- and S- medium-sized rings, in particular thiazepine, thiazocine, and thiazonine systems, are receiving significant attention because of their presence in a wide range of natural products[1], and are often incorporated into biologically-active drugs and pharmaceuticals.[2] Literature perusal of pharmacological studies of such moieties reveals that these compounds possess immense chemotherapeutic significance and are present as the core in a variety of drugs[3] (Fig. 1), such as Prothioconazole-thiazocine, Diltiazem, Clotiapine, Omapatrilat, Promazine, Mesoridazine and Quetiapine, and exhibit a wide spectrum of pharmacological activities such as anticoagulant,[4] antiarterisoclerotic,[5] antihypertensive,[6] antidepressant,[7] antihistaminic,[8] anticonvulsant,[9] antidopaminergic,[10] tranquilizer,[11] antidepressant,[12] antihypertensive,[13] calcium channel blocker,[14] blood-platelet-aggregation inhibitors[15] and antiallergic agents.[16]

A search for the applied methods for synthesis of medium-sized N,S-heterocyclic systems demonstrated that several established protocols are in practice, and comprehensive reviews of the syntheses and biological activities of various benzo-condensed 1,3-, 1,4-, 1,5-thiazepine and thiazocine regioisomers have been published.[17-23] Formation of thiazonines and higher ring systems, however, remains unknown.



Diltiazem

cis-(+)-[2-(2-Dimethylaminoethyl)-5-(4-methoxyphenyl)-3-oxo-6-thia-2-azabicyclo[5.4.0]undeca-7,9,11-trien-4-yl]ethanoate

Clotiapine

8-chloro-6-(4-methylpiperazin-1-yl)benzo[b][1,5]benzothiazepine

Omapatrilat

(4S,7S,10aS)-5-oxo-4-{[(2S)-3-phenyl-2-sulfanylpropanoyl]amino}-2,3,4,7,8,9,10,10aoctahydropyrido[6,1-b][1,3]thiazepine-7-carboxylic acid

Figure 1. Fused medium-sized N,S-heterocycles-containing pharmaceuticals.

Most of the reported strategies for the synthesis of 1,4-thiazocine and higher ring frameworks are presented in a few select publications. For example, Yale *et al*.[24] reported that dihydrodibenzo[*b,f*]1,4]thiazocine was obtained from derived α,α`-dibromo-o-xylenes and 2-aminothiophenol in the presence of $NaHCO_3$ in DMF solution. In 2004, Bates *et al*.[25] reported a new strategy for the synthesis of several thiazocine-2-acetic acids from sulfoxide and sulfone analogues by ring-closing metathesis (RCM). They reported that a conjugate addition of allyl mercaptan to acrylate-containing olefinic intermediates, followed by RCM, provided the thiazocines in excellent yields.

Sashida *et al*.[26], on the other hand, reported interesting examples for the synthesis of eight-, nine-, and ten-membered rings of tetrahydro-1,2-thiazocines, hexahydro-1,2-thiazonines and 1,2-thiazecines through the 2,3-sigmatropic shifts of *S*-imides of (*Z*)-2-vinylthiacycloalkanes. They disclosed that the ten-membered ring is generated directly during the treatment of chloramine T with 2-vinylthiacycloheptane. Manhas *et al*.[27] synthesized several 6,7,8,9,10,11-hexahydro-10-methoxy-benzo[*j*][l,4]thiazonine-9,11-diones via enlargement (arynic condensation) by oxidation of the corresponding substituted *S*-lactam with $NaIO_4$ in a water-isopropanol solution. Lu *et al.*[28] reported the formation of dibenzo[*b,f*][1,4]thiazocin-11-ones via the Pd-catalyzed carbonylation reactions of 2-(2-iodobenzylthio)benzenamines in low overall yields.

Another isomerization–RCM strategy was carried out by van Otterlo et al.[29] who reported that the synthesis of benzothiazocine dioxide from the corresponding sulfone was carried out in high yield. In an alternative strategy, Lilly *et al*.[30] reported a simple protocol for the synthesis of various benzo-1,4-thiazocines via intramolecular cyclization of acyclic-thioether substrates. Mukherjee *et al*.[31] have applied the same intramolecular cyclization methodology to the synthesis of 2,3,4,5-tetrahydro-2*H*benzo[*b*][1,4]thiazocines by treatment of 3-(2-bromophenylthio)propan-1-amines (arenes) with lithium diisopropylamide (LDA). Federsel *et al.*[32] reported the formation of a *N*-formyl thiazocine series via the conversion of the thiazole and benzothiazole into the corresponding thiazolium salts, followed by ring expansion, which resulted in *N*-formyl thiazocine and benzothiazocine. Due to the wide range of biological, industrial and synthetic applications of these heterocyclic compounds, the development of a concise and efficient synthetic protocol for these moieties continues to challenge synthetic organic chemists.

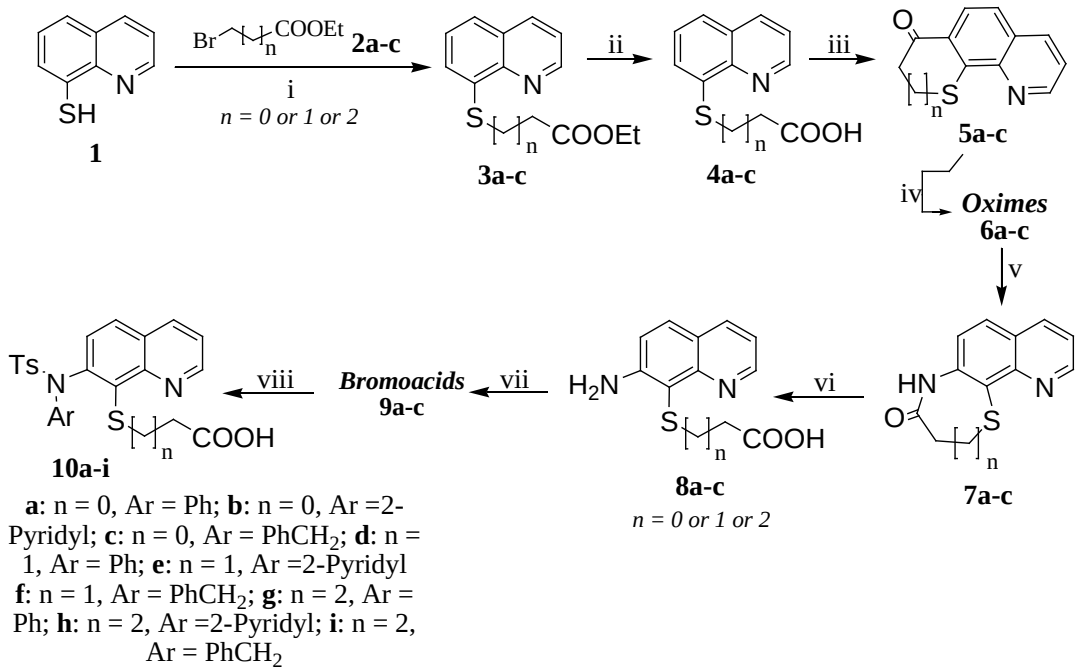
In our previous works of this series,[33,34] we described a straightforward synthesis of a novel series of *N*-carbocycles of various ring sizes via Friedel-Crafts[35] cycliacylation reactions. In a continuation of these studies, the present research addresses the synthesis and characterization of new heterocyclic skeletons, incorporating N-& S-medium-sized-rings nuclei fused to quinolines, to form the targeted tetracyclic 1,4-thiazocines, 1,4-thiazonines and 1,4-thiazecines by applying the ring enlargement approaches of Friedel-Crafts and Beckmann-rearrangement sequences.

Results and Discussion

Our synthetic route to the (*N*-aryl-*N*-tosylamino)quinolin-8-ylthio)carboxylic acids precursors **10a-i** required for this work proceeded via consecutive steps starting from quinoline-8-thiol (**1**) as depicted in Scheme 1. Initial optimization studies were directed toward the ring-closure of acyclic precursors **4a-c**, readily generated in a three-step sequence.

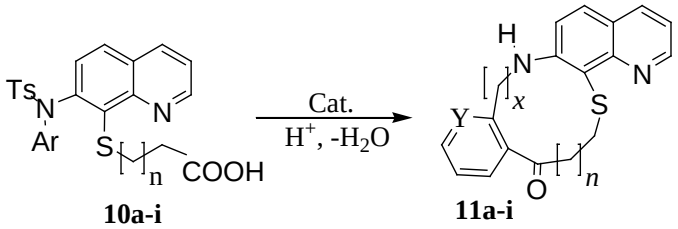
Synthesis was started by S-alkylation of quinoline-8-thiol (**1),** with different α-, β-, and γ-bromoesters as alkylating agents, in the presence of K_2CO_3 in acetone to give ethyl (quinolin-8-ylthio)alkanoates (**3a-c**). The resulting esters were hydrolyzed by NaOH to yield the corresponding substituted 2-(quinolin-8-yl)sulfanyl) acids **4a-c**.

Cyclization of the acids **4a-c** took place in the presence of polyphosphoric acid (PPA), producing the ketones thieno[3,2-*h*]quinolin-3(2*H*)-one (**5a**), 2,3-dihydrothiopyrano[3,2-*h*]quinolin-4-one (**5b**) and 3,4-dihydrothiepino[3,2-*h*]quinolin-5(2*H*)-one (**5c**) in moderate yields. Treatment of ketones **5a-c** with $NH_2OH.HCl$ in NaOH solution gave the corresponding oximes **6a-c**. The resulting oximes underwent ring enlargement induced by heating with PPA at 110–120 °C following Beckmann-rearrangement procedures[36] to afford the corresponding cyclic amides **7a-c**. These amides were hydrolyzed to the corresponding substituted (7-aminoquinolin-8-ylthio)alkanoic acids **8a-c** with NaOH in refluxing EtOH, which were subsequently converted to 7-bromoquinolin-8-ylthioalkanoic acids **9a-c** by Sandmeyer reaction.[37] Subsequent treatment of halo-acids **9a-c** with various aromatic tosylated amines (PhNHTs or N-tosylpyridin-2-amine or $TsNHCH_2Ph$) in the presence of K_2CO_3 in DMSO solution furnished (7-(*N*-phenyl-*N*-tosylamino)quinolin-8-ylthio)alkanoic acids (**10a-i**) in good overall yields.



Scheme 1. Reagents and conditions: (i) K_2CO_3/acetone, 15 h, reflux**,** (ii) NaOH, 2-3 h, reflux, (iii) polyphosphoric acid (PPA), 5h, 100-110 °C, (iv) NH_2OH. HCl/NaOH, 1h, 80-90 °C, (v) PPA, 5h, 110–120 °C, (vi) EtOH/NaOH, 10 h, reflux, (vii) HCl/$NaNO_2$/H_2O/KBr, 30 min, 100 °C, (viii) Aromatic amines (*PhNHTs or N-tosylpyridin-2-amine or TsNHCH₂Ph*), K_2CO_3/DMSO, 120-130 °C, 10 h.

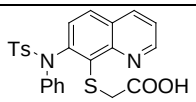
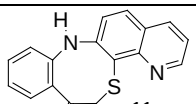
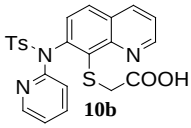
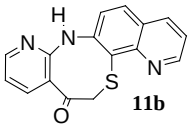
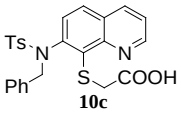
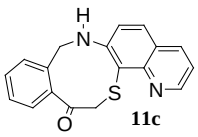
Cycloacylations of acids **10a-i** were carried out in the presence of $AlCl_3/CH_3NO_2$ or P_2O_5 or p-toluenesulfonic acid (PTSA) catalysts providing a series of nine tetracyclic benzo- and pyrido- 1,4-thiazocinoquinolinones, 1,4-thiazoninoquinolinones, 1,4-thiazecinoquinolinones and 1,4-thiazacyclododecano[3,2-*h*]quinolinones **11a-i** (Scheme 2 and Table 1). The structures of all ketones were confirmed by both analytical and spectral data.



Scheme 2. Cycloacylations of acids **10a-i** under Friedel-Crafts conditions.

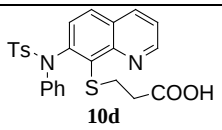
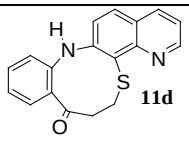
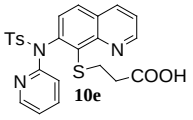
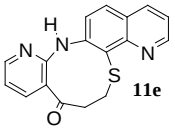
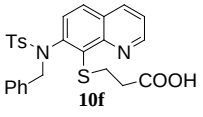
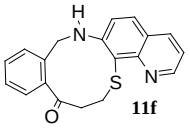
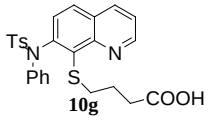
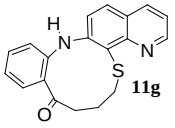
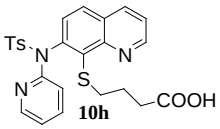
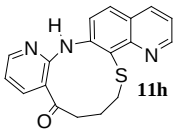
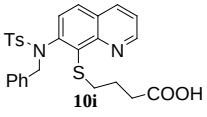
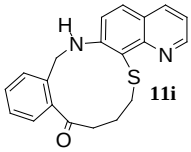
The acylation mechanism accounting for the ring closure products involves the generation of acyl carbocations by loss of water or alcohol upon treatment with acidic catalysts. The resulting acyl carbocations underwent ring closure to form the fused tetracyclic quinolinones **(11a-i)** (Tables 1 and 2). The removal of the Ts-group takes place concurrently with the closure step of heterocyclic acids as noted in different examples in the literature.[38]

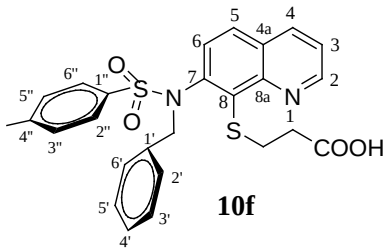
Table 1. Friedel-Crafts cycloacylations of heterocyclic acids **10a-c**

Entry	Substrate	Product	Conditions	Product (%)[a]
1	 **10a**	 **11a**	$AlCl_3/CH_3NO_2$[b], DCM[c], 15 h, reflux	**11a** (85)
			P_2O_5[d], toluene, 18 h, reflux	**11a** (90)
			PTSA[e], PhH, 12 h, reflux	**11a** (82)
2	 **10b**	 **11b**	$AlCl_3/CH_3NO_2$, DCM, 8 h, reflux	**11b** (90)
			P_2O_5, toluene, 10 h, reflux	**11b** (83)
			PTSA, PhH, 10 h, reflux	**11b** (85)
3	 **10c**	 **11c**	$AlCl_3/CH_3NO_2$, DCM, 4 h, reflux	**11c** (89)
			P_2O_5, toluene, 5 h, reflux	**11c** (92)
			PTSA, PhH, 10 h, reflux	**11c** (84)

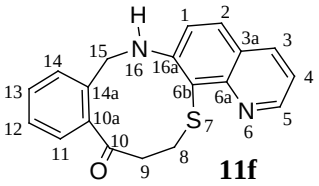
[a]Isolated yield relative to substrate. [b]With $AlCl_3/CH_3NO_2$ catalyst reactant proportions were: acid (0.002 mole), $AlCl_3$ (0.0024 mole), CH_3NO_2 (0.024 mole), solvent (10 mL). [c]Dichloromethane. [d]With P_2O_5 catalyst reactant proportions were: acid (0.4 g) and P_2O_5 (4 g) in anhydrous toluene (15 mL). [e]With PTSA catalyst reactant proportions were: acid (0.5 g), PTSA (3 g) and solvent (10 mL).

Table 2. Friedel-Crafts ring closures of acids **10d-i**

Entry	Substrate	Product	Conditions	Product (%)
1	 **10d**	 **11d**	$AlCl_3/CH_3NO_2$, DCM, 2 h, rt	**11d** (85)
			P_2O_5, toluene, 5 h, reflux	**11d** (90)
			PTSA, PhH, 15 h, reflux	**11d** (84)
2	 **10e**	 **11e**	$AlCl_3/CH_3NO_2$, DCM, 40 h, rt	**11e** (85)
			P_2O_5, toluene, 24 h, reflux	**11e** (82)
			PTSA, PhH, 10 h, reflux	**11e** (86)
3	 **10f**	 **11f**	$AlCl_3/CH_3NO_2$, DCM, 2 h, rt	**11f** (90)
			P_2O_5, toluene, 3 h, reflux	**11f** (91)
			PTSA, PhH, 8 h, reflux	**11f** (84)
4	 **10g**	 **11g**	$AlCl_3/CH_3NO_2$, DCM, 44 h, rt	**11g** (85)
			P_2O_5, toluene, 20 h, reflux	**11g** (84)
			PTSA, PhH, 8 h, reflux	**11g** (80)
5	 **10h**	 **11h**	$AlCl_3/CH_3NO_2$, DCM, 4 h, rt	**11h** (88)
			P_2O_5, toluene, 4 h, reflux	**11h** (83)
			PTSA, PhH, 6 h, reflux	**11h** (82)
6	 **10i**	 **11i**	$AlCl_3/CH_3NO_2$, DCM, 8 h, rt	**11i** (90)
			P_2O_5, toluene, 24 h, reflux	**11i** (84)
			PTSA, PhH, 8 h, reflux	**11i** (85)



3-(7-(*N*-benzyl-*N*-tosylamino)quinolin-8-ylthio)propanoic acid



8,9,10,15-tetrahydro-16H-benzo[6,7][1,4]thiazecino[3,2-h]quinolin-10-one

Figure 2. Structures of tetracyclic **11f** and its precursor heterocyclic acid **10f**.

The ^{1}H NMR data showed the obvious elucidation of the formation of condensed heteropolycycles. For example, the ^{1}H NMR spectrum for propanoic acid **10f** displayed six signals in which CH_3 protons showed as a singlet at δ 2.32 ppm, and two methylene groups appeared as two triplets at δ 2.76 and 3.40 ppm. The fourth signal appeared as singlet at δ 5.13 ppm for benzylic-CH_2 protons, while aromatic protons gave sets of multiplets in the area of 7.00-8.83 ppm. The sixth singlet proton, which appeared at δ 10.70 ppm, was assigned to carboxyl-group protons. In comparison with acid **10f**, tetracyclic thiazecino[3,2-*h*]quinolin-10-one **11f** showed ^{1}H NMR chemical shifts in $CDCl_3$ as a characteristic set of five signals. Three CH_2-groups appeared as two triplets at δ 2.87 & 3.93 ppm, and a singlet at δ 4.52 ppm was assigned to the down-field CH_2 protons, respectively. The aromatic protons exhibited a complex set of signals at δ 6.89-8.72 ppm and δ 9.95 ppm for the NH group.

Conclusions

The development of a new, concise, and efficient protocol with broad applicability for the preparation of a range of tetracyclic, medium-sized N- & S-heterocyclic rings fused to quinoline scaffolds using Friedel–Crafts ring closures of synthesized heterocyclic acids in the presence of $AlCl_3/CH_3NO_2$, P_2O_5 and PTSA catalysts, and Beckmann rearrangements has been achieved. The ambient conditions, short reaction times and easy work-up procedures make this synthetic strategy a better protocol for the synthesis of medium-sized heterocyclic rings bearing nitrogen and sulphur atoms. The results have demonstrated the significance of a Friedel-Crafts ring-closure approach in the synthesis of heteropolycycles.

Experimental Section

General. All melting points were determined with a digital Gallenkamp capillary melting point apparatus and are uncorrected. Infrared spectra were measured on a Mattson 5000 FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL LA 400 MHz FT-NMR (400 MHz for ^{1}H, 100 MHz for ^{13}C). Chemical shifts (δ) are reported in ppm downfield from TMS as the internal standard, and coupling constants are expressed as *J* values in Hz. Elemental analyses were carried out either by a Perkin-Elmer 2400 Series II instrument or by a microanalytical unit. Reactions were monitored by TLC using pre-coated silica plates (0.2 mm, Kiesel 60, F254, E. Merck) and visualized with UV light. Flash column chromatography was performed on silica gel (230–400 mesh, E. Merck).

General procedure for the synthesis of ethyl 2-(quinolin-8-ylthio)alkanoates (3a-c). A mixture of quinoline-8-thiol **1** (3.2 g, 20 mmol), (α-, β- or γ-) haloesters **2a** or **b** or **c** (25 mmol) and anhydrous K_2CO_3 (7.0 g, 50 mol) in dry acetone (50 mL) was refluxed in a water bath for 15h. On completion of the reaction, confirmed by TLC (20% ethyl acetate/*n*-hexane), the excess solvent was removed by distillation. The residue was diluted with water and finally extracted with ether (3×30 mL). The combined organic layers were washed with water and dried over anhydrous Na_2SO_4. Evaporation of the solvent *in vacuo* afforded crude products. Purification of the crude esters by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 1/3) gave pure esters **3a-c**. The yields, further purifications and spectral data are given in the following:

Ethyl 2-(quinolin-8-ylthio)acetate (3a). Yellow needles; 80 %; mp 70-2 °C (from n-hexane); IR (KBr, ν, cm^{-1}): 3065, 2920, 1745, 1600, 1575, 1492, 1440, 1345, 1234, 1178, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.17 (3H, t, *J* 6.8, and 7.6 Hz, CH_3), 3.95 (2H, s, CH_2), 4.12 (2H, q, *J* 7.2 , 7.2 and 6.8 Hz, CH_2), 7.37 (1H, q, *J* 4.8, 3.6 and 4.4 Hz), 7.60 (1H, dd, J 6.0, and 1.6 Hz), 7.81 (1H, t, *J* 7.6 Hz), 7.87 (1H, d, *J* 1.2 Hz), 8.09 (1H, app dt, *J* 8.0 Hz), 8.92 (1H, dd, *J* 2.0, 2.8 and 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 14.1, 36.4, 61.5, 122.1, 125.5, 126.6, 127.4, 127.9, 130.9, 134.4, 144.8, 148.7, 169.3. Anal. Calcd. for $C_{13}H_{13}NO_2S$ (247); C, 63.15; H, 5.26; N, 5.66; S, 12.95. Found; C, 63.24; H, 5.22; N, 5.74; S, 12.80 %.

Ethyl 3-(quinolin-8-ylthio)propanoate (3b). Yellowish viscous oil; 88%; n_D^{25} 1.586; IR (Film) ν_{max} 3020, 2968, 1740, 1590, 1570, 1460, 1440, 1330, 1282, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.32 (3H, t, *J* 7.2 Hz, CH_3), 2.66 (2H, t, *J* 6.8 and 6.4 Hz, CH_2), 3.28 (2H, t, *J* 6.8 and 7.2 Hz, CH_2), 4.07 (2H, q, *J* 7.2 Hz, CH_2), 7.36 (1H, q, *J* 4.8 and 3.2 Hz), 7.59 (1H, t, *J* 6.0 Hz), 7.81 (1H, t, *J* 8.0 Hz), 7.86 (1H, d, *J* 2.0 Hz), 8.09 (1H, td, *J* 8.4 and 1.2 Hz), 8.92 (1H, dd, *J* 2.0 and 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 34.5, 60.6, 122.1, 125.5, 126.6, 127.5, 127.9, 130.9, 134.4, 144.8, 148.7, 171.5. Anal. Calcd. for $C_{14}H_{15}NO_2S$ (261); C, 64.36; H, 5.74; N, 5.36; S, 12.26. Found; C, 64.34; H, 5.64; N, 5.50; S, 12.35 %.

Ethyl 4-(quinolin-8-ylthio)butanoate (3c). White crystals; 75%; mp 95-7 °C [from petroleum ether (60-80°C)]; IR (KBr) ν_{max} 3040, 2945, 1735, 1580, 1520, 1485, 1440, 1370, 1330, 1185, 742 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.13 (3H, t, *J* 7.2 and 6.8 Hz, CH_3), 1.86 (2H, sp, *J* 7.2, 7.2, 7.2 and 7.6 Hz, CH_2), 2.28 (2H, t, *J* 7.2 and 7.6 Hz, CH_2), 3.09 (2H, t, *J* 7.2 Hz, CH_2), 4.07 (2H, q, *J* 6.8, 7.2 Hz, CH_2), 7.37 (1H, q, *J* 3.2 and 4.8 Hz), 7.56 (1H, dd, *J* 6.0 and 1.6 Hz), 7.81 (1H, t, *J* 8.0 Hz), 7.87 (1H, d, *J* 2.0 Hz), 8.09 (1H, d, *J* 7.6 Hz), 8.91 (1H, dd, *J* 2.0 and 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 14.1, 24.8, 32.4, 33.2, 60.6, 122.1, 125.5, 126.7, 127.5, 127.9, 130.9, 134.4, 144.8, 148.7, 173.0. Anal. Calcd. for $C_{15}H_{17}NO_2S$ (275); C, 65.45; H, 6.18; N, 5.09; S, 11.63. Found; C, 65.61; H, 6.25; N, 5.12; S, 11.82%.

General procedure for the synthesis of propanoic acids (4a-c). A mixture of ester **3a** or **b** or **c** (5 mmol) and excess NaOH solution (15 mL, 20%) was stirred under reflux for 2-3 h. After cooling to room temperature, the clear solution was diluted with water (30 mL) and poured with occasionally stirring into an ice-cold diluted HCl solution (20 mL, 15%). After standing for 8 h in a refrigerator, the crude acid was filtered off and dissolved with slight warming in a $NaHCO_3$ solution (15 mL, 20 %), filtered and acidified with HCl solution (25 mL, 10%). The product was filtered, washed and dried to afford crude acids **4a,** or **b** or **c**. Purifications, yields and spectral data are presented in the following:

2-(Quinolin-8-ylthio)acetic acid (4a). White needles; 82%; mp 108-10 °C (from methanol); IR (KBr, ν, cm^{-1}): 3320, 3085, 2950, 2620, 1718, 1585, 1450, 1435, 1330, 750. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 3.97 (2H, s, CH_2), 7.36 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.58 (1H, dd, *J* 1.2, 4.0 and 1.6 Hz), 7.82 (1H, t, *J* 7.6 Hz), 7.87 (1H, app d, *J* 2.0 Hz), 8.07 (1H, d, *J* 8.0 Hz), 8.91 (1H, dd, *J* 2.0 and 1.6 Hz), 10.35 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 32.5, 122.1, 125.5, 126.6, 127.4, 127.9, 130.8, 134.4, 144.8, 148.7, 171.3. Anal. Calcd. for $C_{11}H_9NO_2S$ (219); C, 60.27; H, 4.10; N, 6.39; S, 14.61. Found; C, 60.41; H, 4.19; N, 6.43; S, 14.55%.

3-(Quinolin-8-ylthio)propanoic acid (4b). Pale yellow needles; 90%; mp 122-4 °C (from benzene); IR (KBr, ν, cm^{-1}): 3035, 2970, 2560, 1720, 1600, 1580, 1460, 1445, 1335, 1180, 748. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.69 (2H, t, *J* 6.8 Hz, CH_2), 3.25 (2H, t, *J* 6.8 Hz, CH_2), 7.37 (1H, app q, *J* 3.2, and 4.8 Hz), 7.56 (1H, dd, *J* 1.6 and 2.0 Hz), 7.81 (1H, t, *J* 8.0 Hz), 7.86 (1H, app d, *J* 2.0 Hz), 8.09 (1H, d, *J* 8.4 Hz), 8.91 (1H, dd, *J* 2.0 and 1.6 Hz), 11.25 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.7, 34.2, 122.1, 125.5, 126.7, 127.5, 127.9, 130.8, 134.4, 144.8, 148.7, 175.2. Anal. Calcd. for $C_{12}H_{11}NO_2S$ (233); C, 61.80; H, 4.72; N, 6.00; S, 13.73. Found; C, 61.84; H, 4.65; N, 6.17; S, 13.58 %.

4-(Quinolin-8-ylthio)butanoic acid (4c). Creamy plates; 90%; mp 155-7 °C (from methanol); IR (KBr, ν, cm^{-1}): 3030, 2940, 2560, 1718, 1610, 1570, 1455, 1440, 1380, 1140, 745; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.85 (2H, sp, *J* 7.2, and 7.6 Hz, CH_2), 2.41 (2H, t, *J* 7.2 Hz, CH_2), 3.08 (2H, t, *J* 7.6 Hz, CH_2), 7.37 (1H, app q, *J* 3.2, and 4.8 Hz), 7.56 (1H, dd, *J* 1.6 and 2.0 Hz), 7.81 (1H, t, *J* 8.0 Hz), 7.86 (1H, app d, *J* 1.2 Hz), 8.09 (1H, d, *J* 7.6 Hz), 8.91 (1H, dd, *J* 2.0 and 1.6 Hz), 10.57 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 24.8, 32.9, 33.2, 122.1, 125.5, 126.6, 127.4, 127.9, 130.8, 134.4, 144.8, 148.7, 177.6. Anal. Calcd. for $C_{13}H_{13}NO_2S$ (247); C, 63.15; H, 5.26; N, 5.66; S, 12.95. Found; C, 63.19; H, 5.32; N, 5.49; S, 13.05 %.

General procedure for cyclization of propanoic acids (4a-c). A mixture of acid **4a** or **b** or **c** (5 mmol) and freshly prepared PPA (15 g) was heated on an oil bath and kept at temperature 100-110 °C for 5h. Afterwards, the flask was cooled to room temperature and basified by addition of $NaHCO_3$ solution (25 mL, 30%). The residue was extracted with ether (3×20 mL) and the combined organic phases were washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated in *vacuo* to give the crude ketones **5a-c**.

Thieno[3,2-*h*]quinolin-3(2*H*)-one (5a). Yellow plates; 84%; mp 173-5 °C (ethanol); IR (KBr, ν, cm^{-1}): 3050, 2930, 1692, 1580, 1470, 1440, 1385, 1280, 1075, 749. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 4.73 (2H, s, CH_2), 7.40 (1H, q, *J* 3.6 and 3.2 Hz), 7.81 (1H, d, *J* 10.4 Hz), 8.28 (1H, td, *J* 1.6, 6.4 and 1.6 Hz), 8.49 (1H, app dd, *J* 1.6 Hz), 8.98 (1H, dd, *J* 2.0 and 1.6 Hz);^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 36.8, 122.1, 126.6, 127.8, 127.9, 130.8, 134.4, 135.5, 144.8, 150.8, 194.4. Anal. Calcd. for $C_{11}H_7NOS$ (201); C, 65.67; H, 3.48; N, 6.96; S, 15.92. Found; C, 65.60; H, 3.52; N, 6.87; S, 15.95%.

2,3-Dihydrothiopyrano[3,2-*h*]quinolin-4-one (5b). Creamy plates; 80%; mp 152-4 °C (from methanol); IR (KBr, ν, cm^{-1}): 3045, 2962, 1697, 1583, 1475, 1440, 1380, 1340, 1120, 760. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.79 (2H, sp, *J* 4.8, 4.8 4.4 and 4.8 Hz, CH_2), 4.01 (2H, app t, *J* 0.8, 3.6 and 36 Hz, CH_2), 7.40 (1H, q, *J* 3.6, 3.2 and 3.6 Hz), 7.67 (1H, d, *J* 8.8 Hz), 7.98 (1H, td, *J* 1.6, 1.6, 1.2 and 1.6 Hz), 8.48 (1H, app dd, *J* 1.2 Hz), 8.98 (1H, dd, *J* 2.0 and 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.8, 39.3, 122.1, 126.6, 127.8, 127.9, 129.7, 130.9, 134.4, 144.8, 148.7, 192.1. Anal. Calcd. for $C_{12}H_9NOS$ (215); C, 66.97; H, 4.18; N, 6.51; S, 14.88. Found; C, 67.07; H, 4.02; N, 6.58; S, 14.74%.

3,4-Dihydrothiepino[3,2-*h*]quinolin-5(2*H*)-one (5c). Yellow needles; 79%; mp 120-2 °C (from n-hexane); IR (KBr, ν, cm^{-1}): 3030, 2955, 1695, 1580, 1470, 1435, 1384, 1345, 1090, 754. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.02 (2H, quin, *J* 4.0, 2.0, 2.4, 4.4 and 4.0 Hz, CH_2), 2.71 (2H, t, *J* 4.4 and 3.6 Hz, CH_2), 3.75 (2H, t, *J* 4.4 and 3.6 Hz, CH_2), 7.40 (1H, q, *J* 3.6, 3.2 and 3.6 Hz), 7.74 (1H, d, *J* 8.8 Hz), 7.99 (1H, td, *J* 1.6, 2.4 and 1.6 Hz), 8.40 (1H, app dd, *J* 1.2 Hz), 8.98 (1H, app dd, *J* 1.6 and 3.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 30.0, 38.7, 122.1, 126.6, 127.8, 127.9, 129.7, 130.8, 134.4, 144.81, 148.7, 199.2. Anal. Calcd. for $C_{13}H_{11}NOS$ (229); C, 68.12; H, 4.80; N, 6.11; S, 13.97. Found; C, 68.20; H, 4.71; N, 6.16; S, 13.82 %.

General Procedure for the synthesis of cyclic amides (7a-c). The title compounds were obtained by applying Beckmann rearrangement of oximes **6a-c**. Hence, these skeletons were obtained in a series of two steps. A summary of the steps is given in the following:

Method (i) A solution of NH_2OH. HCl (0.68 g, 10 mmol) in water (4 mL) was added dropwise with stirring to an ice-cold solution of ketones **5a** or **b** or **c** (8 mmol) in ethanol (20 mL). Lastly, a solution of NaOH (4 mL, 4 N) was added gradually with efficient stirring during 5 min. The cooling bath was then removed and the reaction mixture was left to stir for 30 min at room temperature, and finally heated in a steam bath at 80-90 °C for 1 h. After cooling to room temperature, the reaction mixture was quenched by adding 50 mL of water. The resulting mixture was extracted with AcOEt (3×30 mL) and the combined organic layers were washed with HCl (2×30 mL, 5%) and water. The organic extracts were dried over anhydrous Na_2SO_4, filtered, and evaporated to afford the crude oxime. The residue was purified by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 1/1) resulting in the pure oximes **6a-c**. The yields and spectral data are given in the following:

Thieno[3,2-h]quinolin-3(2*H*)-one oxime (6a). White crystal, 88%; mp 98-100 °C (from ethanol); IR (KBr) 3175, 3160, 2940, 1664, 1476, 1380; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 4.89 (2H, s, CH_2), 7.42 (1H, q, *J* 3.6 Hz), 7.87 (1H, d, *J* 3.6 Hz), 8.24 (1H, app dd, *J* 1.6 Hz), 8.33 (1H, td, *J* 1.6, 1.6, 3.6 and 2.0 Hz), 8.93 (1H, dd, *J* 1.6 and 3.2 Hz), 10.42 (1H, s, *N*-OH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 36.8, 122.1, 126.6, 127.8, 127.9, 130.6, 130.9, 134.4, 144.8, 150.8, 153.8. Anal. Calcd. for $C_{11}H_8N_2OS$ (216); C, 61.11; H, 3.70; N, 12.96; S, 14.81. Found; C, 61.24; H, 3.85; N, 12.82; S, 14.74 %.

2,3-Dihydrothiopyrano[3,2-*h*]quinolin-4-one oxime (6b). Pale yellow plates, 90%; mp 111-13 °C (from ethanol); IR (KBr) 3250, 3180, 2960, 1595, 1485, 1267; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.84 (2H, app quin, *J* 4.0, 3.6, 1.2, 2.0, 2.8 and 4.8 Hz, CH_2), 3.98 (2H, t, *J* 4.8 and 4.4 Hz, CH_2), 7.42 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.64 (1H, d, *J* 7.2 Hz), 8.25 (1H, app sp, *J* 1.6, 1.6, 2.4 and 2.0 Hz), 8.40 (1H, q, *J* 2.0, 2.8 and 1.6 Hz), 8.93 (1H, app dd, *J* 2.0, 2.8 and 1.6 Hz), 10.73 (1H, s, *N*-OH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.0, 43.6, 122.1, 126.7, 127.8, 127.9, 130.6, 130.8, 134.4, 144.8, 148.7, 153.8. Anal. Calcd. for $C_{12}H_{10}N_2OS$ (230); C, 62.60; H, 4.34; N, 12.17; S, 13.91. Found; C, 62.46; H, 4.52; N, 12.04; S, 14.07 %.

3,4-Dihydrothiepino[3,2-*h*]quinolin-5(2*H*)-one oxime (6c). White plates, 90%; mp 160-2 °C (from methanol); IR (KBr) 3220, 3155, 2927, 1580, 1490, 1365; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.90 (2H, app quin, *J* 4.0, 2.8, 1.6, 1.6, 2.8, 3.2 and 3.2 Hz, CH_2), 2.91 (2H, app t, *J* 2.0, 2.4, 2.4 and 2.0 Hz, CH_2), 3.74 (2H, t, *J* 4.0 and 4.8 Hz, CH_2), 7.42 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.63 (1H, d, *J* 8.8 Hz), 8.24 (1H, app t, *J* 7.2 and 1.6 Hz), 8.33 (1H, quin, *J* 1.6, 1.6, 4.8 and 2.0 Hz), 8.93 (1H, app dd, *J* 1.6, 3.2 and 1.6 Hz), 10.20 (1H, s, *N*-OH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 28.3, 30.0, 122.1, 126.6, 127.8, 127.9, 130.6, 130.8, 134.4, 144.8, 148.7, 153.8. Anal. Calcd. for $C_{13}H_{12}N_2OS$ (244); C, 63.93; H, 4.91; N, 11.47; S, 13.11. Found; C, 63.95; H, 4.80; N, 11.55; S, 13.15 %.

Method (ii) A mixture of oximes **6a** or **b** or **c** (10 mmol) and polyphosphoric acid (20.0 g) was stirred at 110–120 °C for 5 h. The reaction mixture was cooled to room temperature, diluted with water (50 mL), saturated with $NaHCO_3$ solution (50 mL, 40%) and then left to stand overnight. The separated solid was filtered and washed with water to afford the respective cyclic amide. Recrystallization from ethanol gave the following:

2*H*-[1,4]Thiazino[3,2-*h*]quinolin-3(4*H*)-one (7a). White crystal, 76%; mp 96-8 °C (from acetone); IR (KBr) 3460, 3055, 2920, 1682, 1485**;** ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 4.07 (2H, s, CH_2), 7.32 (2H, q, *J* 4.8, 4.0 and 3.6 Hz), 7.90 (1H, dt, *J* 1.6 Hz), 7.92 (1H, d, *J* 1.6 Hz), 8.11 (1H, q, *J* 1.6, 7.2 and 2.0 Hz), 8.76 (1H, dd, *J* 1.6, 3.2 and 1.6 Hz), 10.04 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.8, 117.3, 122.1, 126.6, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7, 165.0. Anal. Calcd. for $C_{11}H_8N_2OS$ (216); C, 61.11; H, 3.70; N, 12.96; S, 14.81. Found; C, 61.19; H, 3.68; N, 12.82; S, 14.95 %.

2,3-Dihydro-[1,4]thiazepino[3,2-*h*]quinolin-4(5*H*)-one (7b). White crystal, 74%; mp 117-9 °C (from methanol); IR (KBr) 3440, 3070, 2930, 1690, 1515, 1432; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.71 (2H, app t, *J* 5.2, 4.8 and 4.4 Hz, CH_2), 3.88 (2H, t, *J* 5.6 and 5.2 Hz, CH_2), 7.32 (1H, q, *J* 4.4, 4.0 and 4.8 Hz), 7.56 (1H, d, *J* 8.8 Hz), 7.89 (1H, quin, *J* 2.0, 1.6, 7.2 and 1.2 Hz), 8.10 (1H, dd, *J* 1.6, and 7.6 Hz), 8.76 (1H, dd, *J* 2.0, 2.8 and 1.6 Hz), 10.51 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.0, 35.6, 117.3, 122.1, 126.6, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7,

170.6. Anal. Calcd. for $C_{12}H_{10}N_2OS$ (230); C, 62.60; H, 4.34; N, 12.17; S, 13.91. Found; C, 62.60; H, 4.47; N, 12.20; S, 13.82 %.

3,4-Dihydro-2*H*-[1,4]thiazocino[3,2-*h*]quinolin-5(6*H*)-one (7c). Brown crystal, 80%; mp 142-4 °C (from AcOEt); IR (KBr) 3420, 3050, 2957, 1700, 1520, 1450; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.90 (2H, quin, *J* 4.8, 2.4, 2.0, 3.2 and 1.2 Hz, CH_2), 2.47 (2H, sp, *J* 1.6, 3.2, 2.4 and 1.6 Hz, CH_2), 3.48 (2H, t, *J* 4.4 and 4.8 Hz, CH_2), 7.32- 7.36 (2H, m), 7.89 (1H, dt, *J* 2.0, 6.4, 2.4 and 1.2 Hz), 8.28 (1H, app dd, *J* 1.6, 7.2 and 2.0 Hz,), 8.76 (1H, dd, *J* 2.8 and 1.6 Hz,), 9.83 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 33.2 (2C), 117.3, 122.1, 126.6, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7, 174.0. Anal. Calcd. for $C_{13}H_{12}N_2OS$ (244); C, 63.93; H, 4.91; N, 11.47; S, 13.11. Found; C, 64.14; H, 4.84; N, 11.37; S, 13.15 %.

General Procedure for hydrolysis of cyclic amides 7a-c to aminoacids (8a-c). To a solution of cyclic amide **4a** or **b** or **c** (20 mmol) in ethanol (30 mL) was added NaOH solution (10 N, 3.5 mL); the resulting mixture was stirred under reflux for 10 h. The excess alcohol was removed by distillation and the residue was diluted with water (50 mL). The resulting solution was filtered, and the filtrate was cooled to room temperature and adjusted to pH 6-7 with HCl solution (30 mL, 20 %). The solution was left to stand at 0 °C overnight. The precipitate was collected, washed and dried to give the crude acids.

2-(7-Aminoquinolin-8-ylthio)acetic acid (8a). White plates; 82%, mp 110-12 °C (from benzene); IR (KBr) ν_{max} 3420, 3348, 3070, 2930, 2760, 1720,1600, 1580, 1460, 1438, 1385, 1220, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 3.95 (2H, s, CH_2), 4.35 (2H, s, NH_2), 7.36 (1H, q, *J* 4.4, 3.6 and 4.8 Hz), 7.54 (1H, d, *J* 8.0 Hz), 8.00 (1H, td, *J* 1.6, 1.2, 4.4, 2.0 and 1.2 Hz), 8.50 (1H, dd, *J* 1.2 and 1.6 Hz), 8.87 (1H, dd, *J* 1.6 and 1.6 Hz), 10.39 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 32.5, 122.1, 126.6, 127.4, 127.9, 130.8, 134.4 (2C), 144.8, 148.7, 171.3. Anal. Calcd. for $C_{11}H_{10}N_2O_2S$ (234); C, 65.41; H, 4.27; N, 11.96; S, 13.67. Found; C, 65.45; H, 4.39; N, 11.84; S, 13.78 %.

3-(7-Aminoquinolin-8-ylthio)propanoic acid (8b). White plates; 76%, mp 174-6 °C (from AcOEt); IR (KBr) ν_{max} 3380, 3320, 3050, 2960, 2784, 1718, 1610, 1590, 1470, 1445, 1381, 1230, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.75 (1H, t, *J* 6.4 Hz, CH_2), 3.35 (1H, t, *J* 6.4 Hz, CH_2), 4.51 (2H, s, NH_2), 7.42 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.54 (1H, d, *J* 8.0 Hz, CH_2), 7.98 (1H, app q, *J* 1.6, 2.0 and 6.4 Hz), 8.49 (1H, dd, *J* 1.6 and 1.6 Hz), 8.87 (1H, dd, *J* 1.6 and 1.6 Hz), 10.80 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.6, 34.2, 122.1, 126.6, 127.4, 127.9, 130.8, 134.4 (2C), 144.8, 148.7, 175.2. Anal. Calcd. for $C_{12}H_{12}N_2O_2S$ (248); C, 58.06; H, 4.83; N, 11.29; S, 12.90. Found; C, 58.14; H, 4.70; N, 11.41; S, 12.86 %.

4-(7-Aminoquinolin-8-ylthio)butanoic acid (8c). Pale yellow cryatals; 88%; mp 174-6 °C (from AcOEt); IR (KBr) ν_{max} 3410, 3350, 3040, 2954, 2757, 1720,1605, 1590, 1465, 1440, 1390, 1230, 742 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.86 (2H, sp, *J* 7.2, 7.2, 7.6 and 7.6 Hz, CH_2), 2.39 (1H, t, *J* 7.2 and 7.6 Hz, CH_2), 3.14 (1H, t, *J* 7.6 and 7.6 Hz, CH_2), 4.62 (2H, s, NH_2), 7.42 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.54 (1H, d, *J* 8.0 Hz), 7.98 (1H, td, *J* 2.0, 1.2, 2.8 and 1.6 Hz), 8.50 (1H, app t, *J* 6.8 and 1.6 Hz), 8.87 (1H, dd, *J* 2.0 and 1.6 Hz), 10.73 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 24.8, 32.9, 33.2, 122.1, 126.6, 127.4, 127.9, 130.8, 134.4 (2C), 144.8, 148.7, 177.6. Anal. Calcd. for $C_{13}H_{14}N_2O_2S$ (262); C, 59.54; H, 5.34; N, 10.68; S, 12.21. Found; C, 59.52; H, 5.48; N, 10.72; S, 12.05 %.

General Procedure for the synthesis of 7-bromoquinolin-8-ylthio)alkanoic acids (9a-c). To a stirred solution of amino acid **8a** or **b** or **c** (50 mmol) in water (50 mL) was added concentrated HCl (12 mL) at room temperature. The flask was warmed on a hot plate until no solids remained. The solution was then cooled in an ice bath and an aqueous solution of $NaNO_2$ (3.6 g, 53 mmol) in water (25 mL) was added slowly with stirring. The resulting solution was stirred for 10 minutes. A solution of KBr (8.5 g, 55 mmol) in water (12 mL) was added with occasional swirling and the solution was then heated at 100 °C for 30 min. The reaction mixture was cooled to

ambient temperature and the precipitate was filtered and washed with water to afford the crude acids **9a** or **b** or **c**. Purifications, yields and spectral data are given in the following:

2-(7-Bromoquinolin-8-ylthio)acetic acid (9a). Yellow solid; 82%, mp 139-41 °C (from AcOEt); IR (KBr) ν_{max} 3010, 2930, 2645, 1715, 1600, 1590, 1470, 1440, 1375, 1248, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 3.95 (2H, s, CH_2), 7.30 (1H, q, *J* 4.8, 3.2 and 4.0 Hz), 7.81 (1H, d, *J* 8.4 Hz), 8.07 (1H, td, *J* 1.6, 1.6, 1.2, 1.2 and 2.0 Hz), 8.40 (1H, app t, *J* 7.2 and 1.6 Hz), 8.89 (1H, dd, *J* 2.4 and 1.6 Hz), 10.52 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 32.5, 119.7, 122.1, 126.6, 127.9, 130.8, 131.8, 134.4, 144.8, 148.7, 171.3. Anal. Calcd. for $C_{11}H_8BrNO_2S$ (297); C, 44.44; H, 2.69; Br, 26.59; N, 4.71; S, 10.77. Found; C, 44.59; H, 2.75; Br, 26.46; N, 4.75; S, 10.61 %.

3-(7-Bromoquinolin-8-ylthio)propanoic acid (9b). Yellow crystals; 74%, mp 154-6 °C (from benzene); IR (KBr) ν_{max} 3035, 2960, 2585, 1720, 1590, 1464, 1440, 1390, 1235, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.71 (2H, t, *J* 6.4 and 6.4 Hz, CH_2), 3.32 (2H, t, *J* 6.8 and 6.4 Hz, CH_2), 7.29 (1H, q, *J* 4.4, 3.2 and 4.4 Hz), 7.81 (1H, d, *J* 8.4 Hz), 8.06 (1H, td, *J* 2.0, 1.2, 3.6, 2.0 and 1.2 Hz), 8.40 (1H, dd, *J* 1.2 and 1.6 Hz), 8.89 (1H, app dd, *J* 1.6 and 3.2 Hz), 9.77 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.7, 34.2, 119.7, 122.1, 126.6, 127.9, 130.8, 131.8, 134.4, 144.8, 148.7, 175.2. Anal. Calcd. for $C_{12}H_{10}BrNO_2S$ (311); C, 46.30; H, 3.21; Br, 25.40; N, 4.50; S, 10.28. Found; C, 46.39; H, 3.34; Br, 25.24; N, 4.61; S, 10.30 %.

4-(7-Bromoquinolin-8-ylthio)butanoic acid (9c). white plates; 78%, mp 125-7 °C (from benzene); IR (KBr) ν_{max} 3044, 2960, 2570, 1720, 1590, 1560, 1480, 1440, 1380, 1250, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 1.86 (2H, sp, *J* 3.2, 6.4, 7.6 and 7.6 Hz, CH_2), 2.40 (2H, t, *J* 7.2 and 7.6 Hz, CH_2), 3.13 (2H, t, *J* 7.6 and 7.6 Hz, CH_2), 7.29 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.81 (1H, d, *J* 8.4 Hz), 8.06 (1H, td, *J* 2.0, 1.2, 3.6, 2.0 and 1.2 Hz), 8.40 (1H, app t, *J* 6.8 and 1.6 Hz), 8.89 (1H, app dd, *J* 1.6 and 3.2 Hz), 10.20 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 24.8, 32.9, 33.2, 119.7, 122.1, 126.6, 127.9, 130.8, 131.8, 134.4, 144.8, 148.7, 177.6. Anal. Calcd. for $C_{13}H_{12}BrNO_2S$ (325); C, 48.00; H, 3.69; Br, 24.30; N, 4.30; S, 9.84. Found; C, 48.13; H, 3.52; Br, 24.28; N, 4.34; S, 9.78 %.

General procedure for arylation using (7-bromoquinolin-8-ylthio)carboxylic acids (9a-c). A mixture of bromo-carboxylic acids **9a** or **b** or **c** (20 mmol), K_2CO_3 (4.1 g, 50 mmol), tosylated arylamine (Ph*N*HTs or *N*-tosylpyridin-2-amine or Ts*N*HCH_2Ph) (22 mmol) in DMSO (20 mL) was heated with efficient stirring for 10 h at 120-30 °C. after which TLC analysis (EtOAc) indicated that the reaction was complete, the solution was cooled and treated with NaOH solution (40 mL, 10%). The solution was refluxed for 10 min then filtered by suction. The filtrate was concentrated and acidified with aqueous HCl solution (40 mL, 10%). The resulted precipitate was filtered, washed with water, dried to give the crude acids **10a-i**. The yields and spectral data are given in the following:

2-(7-(*N*-Phenyl-*N*-tosylamino)quinolin-8-ylthio)acetic acid (10a). White crystals; 79%, mp 182-4 °C (from benzene); IR (KBr) ν_{max} 3085, 2975, 2585, 1720, 1585, 1455, 1440, 1390, 1237, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.33 (3H, s, CH_3), 3.97 (2H, s, CH_2), 7.06 (1H, d, *J* 8.4 Hz), 7.12 (2H, dd, *J* 1.2 and 1.2 Hz), 7.19 (1H, app quin, *J* 6.4, 1.2, 1.6 and 6.0 Hz), 7.31 (1H, d, *J* 2.4 Hz), 7.33 (2H, t, *J* 2.8 and 4.8 Hz), 7.49 (2H, d, *J* 8.0 Hz), 7.65 (2H, t, *J* 7.6, 0.8 and 7.6 Hz), 8.06 (1H, dd, *J* 1.6 and 1.2 Hz), 8.21 (1H, app dt, *J* 1.6, 2.0, 2.0 and 1.2 Hz), 8.86 (1H, dd, *J* 2.0 and 1.2 Hz), 10.46 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 32.5, 117.2, 122.1, 122.9 (2C), 124.7, 125.3 (2C), 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8, 134.4, 135.0, 144.2, 144.8, 148.7, 171.3. Anal. Calcd. for $C_{24}H_{20}N_2O_4S_2$ (464); C, 62.06; H, 4.31; N, 6.03; S, 13.79. Found; C, 62.02; H, 4.38; N, 6.11; S, 13.65 %.

2-(7-(*N*-(Pyridin-2-yl)-*N*-tosylamino)quinolin-8-ylthio)acetic acid (10b). White crystals; 84%, mp 122-4 °C (from benzene); IR (KBr) ν_{max} 3074, 2983, 2580, 1718, 1593, 1563, 1475, 1440, 1380, 1244, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.33 (3H, s, CH_3), 3.96 (2H, s, CH_2), 7.05 (1H, d, *J* 8.4 Hz), 7.21 (1H, app dt, *J* 1.2, 0.8, 1.2, and 3.6 Hz), 7.31 (2H, d, *J* 8.4 Hz), 7.38 (1H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.49 (1H, d, *J* 8.0 Hz), 7.87-7.90 (2H, m), 8.07 (1H, dd, *J* 1.6, 7.2 and 2.0 Hz), 8.21 (1H, app dt, *J* 2.0, 1.2, 4.8 and 1.6 Hz), 8.44 (1H, dd, *J* 2.0 and 1.2 Hz), 8.86 (1H, dd, *J* 2.0 and 1.6 Hz), 11.16 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 32.5, 111.4, 117.2,

118.8, 122.1, 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8, 134.4, 135.0, 138.1, 140.4, 144.2, 144.8, 148.3, 148.7, 153.9, 171.3. Anal. Calcd. for $C_{23}H_{19}N_3O_4S_2$ (465); C, 59.35; H, 4.08; N, 9.03; S, 13.76. Found; C, 59.33; H, 4.14; N, 9.10; S, 13.55%.

2-(7-(*N*-Benzyl-*N*-tosylamino)quinolin-8-ylthio)acetic acid (10c). Yellow needles; 82%, mp 140-2 °C (from acetone); IR (KBr) ν_{max} 3030, 2980, 2750, 1720, 1605, 1581, 1440, 1375, 1237, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.32 (3H, s, CH_3), 3.95 (2H, s, CH_2), 5.15 (2H, s, CH_2), 7.01-7.06 (3H, m), 7.25-7.42 (6H, m), 7.40 (2H, d, *J* 8.0 Hz), 7.80 (1H, two t, *J* 2.0, 1.6 and 1.6 Hz), 8.05 (1H, dd, *J* 1.6 and 2.0 Hz), 8.83 (1H, dd, *J* 1.6 and 1.6 Hz), 10.82 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 32.5, 55.8, 117.2, 122.1, 126.6, 127.4 (2C), 127.7 (2C), 127.9, 128.5 (2C), 128.9, 129.7 (2C), 134.4, 134.8, 137.3, 140.4, 144.2, 144.8, 148.7, 171.3. Anal. Calcd. for $C_{25}H_{22}N_2O_4S_2$ (478); C, 62.76; H, 4.60; N, 5.85; S, 13.38. Found; C, 62.66; H, 4.64; N, 5.79; S, 13.42 %.

3-(7-(*N*-Phenyl-*N*-tosylamino)quinolin-8-ylthio)propanoic acid (10d). White crystals; 78%, mp 95-7 °C (from acetone); IR (KBr) ν_{max} 3040, 2960, 2620, 1720, 1610, 1585, 1460, 1445, 1385, 1270, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.33 (3H, s, CH_3), 2.74 (2H, t, *J* 6.8 Hz, CH_2), 3.41 (2H, t, *J* 6.8 and 6.4 Hz, CH_2), 7.04 (1H, d, *J* 8.4 Hz), 7.12 (2H, dd, *J* 1.2 and 1.6 Hz), 7.19-7.23 (1H, m), 7.31 (3H, app t, *J* 6.4, 1.2 and 6.4 Hz), 7.49 (2H, d, *J* 8.0 Hz), 7.65 (2H, t, *J* 7.6, 0.8 and 7.6 Hz), 8.06 (1H, dd, *J* 1.6 and 1.6 Hz), 8.21 (1H, two t, *J* 2.0, 1.2, 4.8, 1.6 and 2.0 Hz), 8.86 (1H, dd, *J* 2.0 and 1.6 Hz), 10.53 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 28.6, 34.29, 117.2, 122.1, 122.9 (2C), 124.7, 125.3 (2C), 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8, 134.4, 135.0, 144.2, 144.8, 148.7, 175.2. Anal. Calcd. for $C_{25}H_{22}N_2O_4S_2$ (478); C, 62.76; H, 4.60; N, 5.85; S, 13.38. Found; C, 62.74; H, 4.69; N, 5.93; S, 13.47 %.

3-(7-(*N*-(Pyridin-2-yl)-*N*-tosylamino)quinolin-8-ylthio)propanoic acid (10e). White plates; 85%, mp 113-5 °C (from benzene); IR (KBr) ν_{max} 3025, 2980, 2560, 1720, 1585, 1560, 1495, 1438, 1374, 1240, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.33 (3H, s, CH_3), 2.74 (2H, t, *J* 6.8 and 6.4 Hz, CH_2), 3.41 (2H, t, *J* 6.8 and 6.4 Hz, CH_2), 7.04 (1H, d, *J* 8.8 Hz), 7.20 (1H, ddd, *J* 3.6, 1.2, 0.8, 1.2, 3.6 and 2.0 Hz), 7.31 (2H, d, *J* 7.6 Hz), 7.39 (1H, q, *J* 3.6, 3.2 and 3.6 Hz), 7.49 (2H, d, *J* 8.0 Hz), 7.85-7.91 (2H, m), 8.06 (1H, dd, *J* 1.6 and 1.2 Hz), 8.21 (1H, two t, *J* 2.0, 1.2, 2.0 and 1.6 Hz), 8.44 (1H, dd, *J* 1.6 and 1.2 Hz), 8.86 (1H, dd, *J* 2.0 and 2.0 Hz), 10.41 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 28.6, 34.2, 111.4, 117.2, 118.8, 122.1, 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8, 134.4, 135.0, 138.1, 140.4, 144.2, 144.8, 148.3, 148.7, 153.9, 175.2. Anal. Calcd. for $C_{24}H_{21}N_3O_4S_2$ (479); C, 62.12; H, 4.38; N, 8.76; S, 13.36. Found; C, 62.31; H, 4.48; N, 8.85; S, 13.32 %.

3-(7-(*N*-Benzyl-*N*-tosylamino)quinolin-8-ylthio)propanoic acid (10f). White needles; 81%, mp 110-12 °C (from ethanol); IR (KBr) ν_{max} 3050, 2910, 2670, 1722, 1590, 1580, 1477, 1445, 1395, 1240, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 2.32 (3H, s, CH_3), 2.76 (2H, t, *J* 6.8 and 3.2 Hz, CH_2), 3.40 (2H, t, *J* 6.8 Hz, CH_2), 5.13 (2H, s, CH_2), 7.00-7.06 (H, m), 7.24-7.33 (6H, m), 7.40 (2H, d, *J* 8.0 Hz), 7.80 (1H, two t, *J* 3.2, 4.2, 1.6 and 1.6 Hz), 8.04 (1H, dd, *J* 1.6 and 2.0 Hz), 8.83 (1H, dd, *J* 1.6 and 1.6 Hz), 10.70 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 28.6, 34.2, 55.8, 117.2, 122.1, 126.6, 127.4 (2C), 127.7 (2C), 127.9, 128.5 (2C), 128.9, 129.7 (2C), 134.4, 134.8, 137.3, 144.2, 144.8, 148.7, 175.2. Anal. Calcd. for $C_{26}H_{24}N_2O_4S_2$ (492); C, 63.41; H, 4.87; N, 5.69; S, 13.00. Found; C, 63.49; H, 4.82; N, 5.74; S, 12.88 %.

4-(7-(*N*-Phenyl-*N*-tosylamino)quinolin-8-ylthio)butanoic acid (10g). White cryatals; 80%, mp 158-60 °C (from AcOEt); IR (KBr) ν_{max} 3045, 2965, 2620, 1720, 1587, 1550, 1440, 1435, 1385, 1290, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 1.87 (2H, quin, *J* 7.6, 7.6, 7.2 and 7.6 Hz, CH_2), 2.33 (3H, s, CH_3), 2.39 (2H, t, *J* 7.6 and 7.2 Hz, CH_2), 3.20 (2H, t, *J* 7.6 Hz, CH_2), 7.04 (1H, d, *J* 8.8 Hz), 7.12 (2H, dd, *J* 1.2, 2,8 and 1.6 Hz), 7.21-7.23 (1H, m), 7.31-7.35 (3H, m), 7.49 (2H, d, *J* 8.0 Hz), 7.65 (2H, t, *J* 7.6 and 8.4 Hz), 8.06 (1H, dd, *J* 1.6 and 1.6 Hz), 8.20 (1H, two t, *J* 1.6, 1.6, 1.6 and 1.6 Hz), 8.86 (1H, dd, *J* 2.0 and 1.6 Hz), 11.06 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 24.8, 32.9, 33.2, 117.2, 122.1, 122.9 (2C), 124.7, 125.3 (2C), 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8,

134.4, 135.0, 144.2, 144.8, 148.7, 177.6. Anal. Calcd. for $C_{26}H_{24}N_2O_4S_2$ (492); C, 63.41; H, 4.87; N, 5.69; S, 13.00. Found; C, 63.48; H, 4.95; N, 5.62; S, 13.13 %.

4-(7-(*N*-(Pyridin-2-yl)-*N*-tosylamino)quinolin-8-ylthio)butanoic acid (10h). White crystals; 82%, mp 140-2 °C (from benzene); IR (KBr) ν_{max} 3045, 2985, 2790, 1720, 1605, 1585, 1440, 1370, 1284, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 1.87 (2H, quin, *J* 7.2, 7.2, 7.6 and 7.6 Hz, CH_2), 2.33 (3H, s, CH_3), 2.39 (2H, t, *J* 7.6 and 7.2 Hz, CH_2), 3.20 (2H, t, *J* 7.6 and 7.6 Hz, CH_2), 7.04 (1H, d, *J* 8.8 Hz), 7.19 (1H, ddd, *J* 2.0, 3.6, 1.2, 0.8, 1.2, 3.6 and 2.0 Hz), 7.31 (2H, d, *J* 8.4 Hz), 7.39 (2H, q, *J* 4.8, 3.2 and 4.8 Hz), 7.49 (2H, d, *J* 8.0 Hz), 7.85-7.91 (2H, m), 8.06 (1H, dd, *J* 1.6 and 1.2 Hz), 8.21 (1H, two t, *J* 2.0, 1.2, 1.2, 2.0 and 1.2 Hz), 8.44 (1H, dd, *J* 1.6 and 1.2 Hz), 8.86 (1H, dd, *J* 2.0 and 1.6 Hz), 10.54 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2, 24.8, 32.9, 33.2, 111.4, 117.2, 118.8, 122.1, 126.6, 127.4 (2C), 127.9, 129.7 (2C), 130.8, 134.4, 135.0, 138.1, 140.4, 144.2, 144.8, 148.3, 148.7, 153.9, 177.6. Anal. Calcd. for $C_{25}H_{23}N_3O_4S_2$ (493); C, 60.85; H, 4.66; N, 8.51; S, 12.98. Found; C, 60.78; H, 4.56; N, 8.58; S, 12.84 %.

4-(7-(*N*-Benzyl-*N*-tosylamino)quinolin-8-ylthio)butanoic acid (10i). White crystals; 80%, mp 167-9 °C (from acetone); IR (KBr) ν_{max} 3025, 2947, 2670, 1720, 1600, 1565, 1444, 1373, 1286, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 1.87 (2H, quin, *J* 7.6, 7.2, 7.6 and 7.6 Hz, CH_2), 2.32 (3H, s, CH_3), 2.39 (2H, t, *J* 7.6 and 7.6 Hz, CH_2), 3.26 (2H, t, *J* 7.6 and 7.6 Hz, CH_2), 5.13 (2H, s, CH_2), 7.00-7.06 (3H, m), 7.24-7.33 (6H, m), 7.40 (2H, d, *J* 8.0 Hz), 7.80 (1H, two t, *J* 1.6, 1.6, 1.2, 1.6 and 1.6 Hz), 8.04 (1H, dd, *J* 1.6 and 1.6 Hz), 8.83 (1H, dd, *J* 1.6 and 1.6 Hz), 10.85 (1H, s, COOH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 1.2, 24.8, 32.9, 33.2, 55.8, 117.2, 122.1, 126.6, 127.4 (2C), 127.7 (2C), 127.9, 128.5 (2C), 128.9, 129.7 (2C), 134.4, 134.8, 140.4, 144.2, 144.8, 148.7, 177.6. Anal. Calcd. for $C_{27}H_{26}N_2O_4S_2$ (506); C, 64.03; H, 5.13; N, 5.53; S, 12.64. Found; C, 64.14; H, 5.02; N, 5.48; S, 12.75 %.

Friedel-Crafts cycliacylation procedures

Procedure A. Cycliacylations using $AlCl_3/CH_3NO_2$ catalyst. To a solution of $AlCl_3$ (2.4 mmol) in CH_3NO_2 (24 mmol) was added a solution of required acid precursor **3a**–**i** (2.0 mmol) in DCM (10 mL) dropwise with efficient stirring over 10–15 min. The reaction mixture was further stirred for a certain time at room temperature (Tables 1&2) and decomposed by careful addition of ice-cold HCl solution (20 mL, 10 %). The residue was extracted with ether (3×20 mL) and the combined organic phases were washed with Na_2CO_3 (20 mL, 10 %), water and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure to afford the crude products **10a**–**i**.

Procedure B. Cycliacylations using P_2O_5 catalyst. A solution of acid **3a-i** (0.5 g) and P_2O_5 (5 g) in dry benzene (10 mL) was refluxed for the required time (Tables 1&2) and, after cooling to room temperature, the reaction mixture was diluted with ether (40 mL). The organic layer was separated, washed successively with a saturated solution of $NaHCO_3$, water and dried over $MgSO_4$. The solvent was evaporated under reduced pressure to afford the crude products **10a-i**.

Procedure C. Cycliacylations using PTSA catalyst. A stirred mixture of acid **3a**–**i** (0.5 g) and PTSA (5.0 g) was heated on an oil bath and kept at the required temperature for a certain time as shown in Tables 1&2. Afterwards, the flask was cooled to room temperature and the reaction products basified by addition of $NaHCO_3$ solution (40 mL, 30 %). The residue was extracted with ether (3×20 mL) and the combined organic phases were washed with water, dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo* to give the crude products **10a**–**i**.

13,14-Dihydro-5*H*-benzo[5,6][1,4]thiazocino[3,2-*h*]quinolin-14(12H)-one (11a). Yellow crystals, mp 135-7 °C (from ethanol); IR (KBr, ν, cm^{-1}): 3450, 3030, 2980, 1740, 1580, 1465, 1440, 1373, 1260, 1133, 1075, 748; ^1H NMR (400 MHz, $CDCl_3$, ppm), δ 4.77 (2H, s, CH_2), 7.03 (1H, dd, *J* 1.2 and 1.6 Hz), 7.25-7.32 (2H, m), 7.37 (1H, dd, *J* 1.6 and 1.6 Hz), 7.46 (1H, dt, *J* 0.8 Hz), 7.54 (1H, dt, *J* 8.0 and 2.0 Hz), 7.88 (1H, two t, *J* 2.0, 1.6, 4.2, 2.0 and 1.2 Hz), 8.28 (1H, dd, *J* 1.2 and 1.6 Hz), 8.76 (1H, dd, *J* 2.0 and 1.6 Hz), 9.80 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ,

ppm): 38.2, 117.2, 117.6, 122.1, 122.2, 122.5, 126.6, 126.8, 127.9, 130.8, 131.5, 134.4, 140.7, 141.1, 144.8, 148.7, 194.4. Anal. Calcd. for $C_{17}H_{12}N_2OS$ (292); C, 69.86; H, 4.10; N, 9.58; S, 10.95. Found; C, 69.75; H, 4.18; N, 9.64; S, 10.81 %.

13,14-Dihydro-5*H*-pyrido[2',3'-5,6][1,4]thiazocino[3,2-*h*]quinolin-14(12*H*)-one (11b). Pale yellow solid, mp 177-9 °C (from ethanol); IR (KBr, ν, cm^{-1}): 3422, 3055, 2930, 1740, 1600, 1585, 1470, 1445, 1389, 1275, 1150, 755; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 4.80 (2H, s, CH_2), 6.92 (1H, q, *J* 4.8, 2.0 and 5.6 Hz), 7.30-7.34 (2H, m), 7.80 (1H, dd, *J* 1.6 and 2.0 Hz), 7.89 (1H, two t, *J* 1.6 Hz), 8.13 (1H, dd, *J* 2.0 and 2.0 Hz), 8.28 (1H, dd, *J* 1.6 and 2.0 Hz), 8.76 (1H, dd, *J* 2.0 and 1.6 Hz) 10.27 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 38.2, 117.2, 118.1, 122.1, 123.3, 126.6, 127.8, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7, 150.5, 156.9, 194.4. Anal. Calcd. for $C_{16}H_{11}N_3OS$ (293); C, 65.52; H, 3.75; N, 14.33; S, 10.92. Found; C, 65.66; H, 3.89; N, 14.42; S, 10.78 %.

8,13,14-Trihydro-7*H*-benzo[6,7][1,4]thiazonino[3,2-*h*]quinolin-13(15H)-one (11c). White crystals; mp 95-6 °C (from benzene); IR (KBr, ν, cm^{-1}): 3380, 3010, 2965, 1743, 1580, 1480, 1440, 1395, 1284, 1135, 1077, 752; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 4.48 (2H, s, CH_2), 4.61 (2H, s, CH_2), 6.88 (1H, d, *J* 8.8 Hz), 7.23-7.27 (2H, m), 7.36 (1H, dt, *J* 1.6 Hz), 7.46 (1H, dt, *J* 6.4 and 1.2 Hz), 7.71 (1H, two t, *J* 1.6, 1.6, 6.8 and 1.6 Hz), 7.81 (1H, dd, *J* 1.2 and 1.6 Hz), 8.31 (1H, dd, *J* 1.6 and 1.6 Hz), 8.69 (1H, dd, *J* 2.0 and 1.6 Hz), 9.75 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 38.2, 48.6, 117.2, 122.1, 125.8, 126.6, 126.6, 127.0, 127.9, 130.8, 131.4, 132.3, 133.1, 134.4, 140.7, 148.7, 194.4. Anal. Calcd. for $C_{18}H_{14}N_2OS$ (306); C, 70.58; H, 4.57; N, 9.15; S, 10.45. Found; C, 70.54; H, 4.61; N, 9.31; S, 10.29 %.

6,7,8-Trihydro-13*H*-benzo[5,6][1,4]thiazonino[3,2-*h*]quinolin-8-one (11d). Yellow needles; mp 138-40 °C (from acetone); IR (KBr) ν_{max} 3410, 3035, 2920, 1743, 1580, 1460, 1455, 1385, 1290, 1140, 1070, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.79 (2H, app quin, *J* 2.8, 1.6, 2.0 and 2.4 Hz, CH_2), 3.75 (2H, app quin, *J* 3.2, 1.2, 1.6 and 2.8 Hz, CH_2), 7.02 (1H, dd, *J* 1.2 and 1.2 Hz), 7.24-7.38 (4H, m), 7.55 (1H, dt, *J* 2.0, 1.6 and 2.0 Hz), 7.88 (1H, two t, *J* 1.6, 1.6 and 1.6 Hz), 8.09 (1H, dd, *J* 1.6 and 2.0 Hz), 8.75 (1H, dd, *J* 2.0 and 2.0 Hz), 10.28 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.0, 44.9, 117.2, 117.6, 122.1, 122.2, 124.5, 126.6, 127.9, 130.4, 130.8, 131.5, 134.4, 140.7, 141.1, 144.8, 148.7, 199.2. Anal. Calcd. for $C_{18}H_{14}N_2OS$ (306); C, 70.58; H, 4.57; N, 9.15; S, 10.45. Found; C, 70.44; H, 4.62; N, 9.27; S, 10.38 %.

13,14-Dihydro-5*H*-pyrido[2',3'-5,6][1,4]thiazonino[3,2-*h*]quinolin-15-one (11e). White needles; mp 143-5 °C (from acetone); IR (KBr) ν_{max} 3430, 3045, 2960, 1740, 1600, 1585, 1480, 1440, 1380, 1385, 1130, 744 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.80 (2H, app quin, *J* 2.4, 2.0, 1.6 and 2.8 Hz, CH_2), 3.81 (2H, app q, *J* 2.8, 2.0 and 4.0 Hz, CH_2), 6.90 (1H, q, *J* 5.2, 1.6 and 5.2 Hz), 7.29-7.33 (2H, m), 7.56 (1H, dd, *J* 2.0 and 1.6 Hz), 7.89 (1H, two t, *J* 2.0, 1.6, 2.0 and 1.6 Hz), 8.09 (1H, dd, *J* 1.6 and 1.6 Hz), 8.41 (1H, dd, *J* 2.0 and 2.0 Hz), 8.75 (1H, dd, *J* 2.0 and 1.6 Hz), 10.32 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.07, 44.9, 117.2, 118.1, 122.1, 123.3, 126.6, 127.8, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7, 150.5, 156.9, 199.2. Anal. Calcd. for $C_{17}H_{13}N_3OS$ (307); C, 66.44; H, 4.23; N, 13.68; S, 10.42. Found; C, 66.45; H, 4.36; N, 13.55; S, 10.50 %.

8,9,10,15-Tetrahydro-16*H*-benzo[6,7][1,4]thiazecino[3,2-*h*]quinolin-10-one (11f). Pale yellow crystals; mp 174-6 °C (from benzene); IR (KBr) ν_{max} 3370, 3015, 2975, 1745, 1600, 1590, 1470, 1440, 1381, 1276, 1132, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 2.87 (2H, t, *J* 6.0 and 5.6 Hz, CH_2), 3.93 (2H, t, *J* 5.2 and 6.0 Hz, CH_2), 4.52 (2H, s, CH_2), 6.89 (1H, d, *J* 8.8 Hz), 7.24-7.32 (3H, m), 7.46 (1H, app dt, *J* 6.8 and 1.2 Hz), 7.73 (1H, two t, *J* 2.0, 1.6 and 1.6 Hz), 7.83 (1H, dd, *J* 1.2 and 1.2 Hz), 8.28 (1H, dd, *J* 1.6 and 1.6 Hz), 8.72 (1H, dd, *J* 1.6 and 1.6 Hz), 9.95 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 30.0, 44.9, 48.6, 117.2, 122.1, 125.8, 126.6, 126.6, 127.0, 127.9, 130.8, 131.4, 132.3, 133.1, 140.7, 144.8, 148.7, 199.2. Anal. Calcd. for $C_{19}H_{16}N_2OS$ (320); C, 71.25; H, 5.00; N, 8.75; S, 10.00. Found; C, 71.33; H, 4.86; N, 8.78; S, 9.87 %.

2,3,4,5-Tetrahydro-10*H*-benzo[5,6][1,4]thiazecino[3,2-*h*]quinolin-5-one (11g). Yellow needles; mp 138-40 °C (from acetone); IR (KBr) ν_{max} 3374, 3072, 2952, 1740, 1580, 1496, 1440, 1365, 1290, 1137, 1095, 759 cm^{-1}; ^{1}H

NMR (400 MHz, $CDCl_3$, ppm), δ 1.93 (2H, quin, *J* 4.4, 4.4, 4.4 and 4.8 Hz, CH_2), 2.52 (2H, app q, *J* 7.6, 4.8 and 4.4 Hz, CH_2), 3.62 (2H, app q, *J* 4.4, 2.0 and 2.4 Hz, CH_2), 7.18 (1H, d, *J* 9.2 Hz), 7.28-7.40 (4H, m), 7.62 (1H, dt, *J* 1.6, 1.6, 4.2 and 1.6 Hz), 7.88 (1H, two t, *J* 1.6, 1.6, 1,6 and 1.6 Hz), 8.10 (1H, dd, *J* 1.2 and 1.2 Hz), 8.76 (1H, dd, *J* 2.0 and 2.0 Hz), 10.21 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 33.2, 38.7, 117.2, 117.6, 122.1, 122.2, 124.5, 126.6, 127.9, 130.4, 130.8, 131.5, 134.4, 140.7, 141.1, 144.8, 148.7, 204.3. Anal. Calcd. for $C_{19}H_{16}N_2OS$ (320); C, 71.25; H, 5.00; N, 8.75; S, 10.00. Found; C, 71.22; H, 5.14; N, 8.64; S, 10.05 %.

2,3,4,5-Tetrahydro-10*H*-pyrido[2',3'-5,6][1,4]thiazecino[3,2-*h*]quinolin-5-one (11h). White crystals; mp 150-2 °C (from acetone); IR (KBr) ν_{max} 3366, 3045, 2930, 1745, 1595, 1485, 1440, 1430, 1374, 1280, 1174, 760 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.89 (2H, m, CH_2), 2.54 (2H, app q, *J* 6.8, 5.2 and 4.4 Hz, CH_2), 3.50 (2H, app quin, *J* 2.4, 2.0, 2.4 and 2.0 Hz, CH_2), 6.91 (1H, q, *J* 5.2, 2.4 and 4.8 Hz), 7.24 (1H, d, *J* 9.2 Hz), 7.30 (1H, q, *J* 4.8, 3.6 and 4.8 Hz), 7.80 (1H, dd, *J* 2.0, 5.2 and 2.0 Hz), 7.89 (1H, two t, *J* 1.6, 1.6 and 1.6 Hz), 8.11 (1H, dd, *J* 1.6 and 1.2 Hz), 8.39 (1H, dd, *J* 2.0 and 2.0 Hz), 8.76 (1H, dd, *J* 2.0 and 2.0 Hz), 9.83 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 33.2, 38.7, 117.2, 118.1, 122.1, 123.3, 126.6, 127.8, 127.9, 130.8, 134.4, 140.7, 144.8, 148.7, 150.5, 156.9, 199.2. Anal. Calcd. for $C_{18}H_{15}N_3OS$ (321); C, 67.28; H, 4.67; N, 13.08; S, 9.96. Found; C, 67.41; H, 4.54; N, 13.14; S, 10.04 %.

8,9,10,11,16-Pentaahydro-17*H*-benzo[6,7][1,4]thiazacyclododecano[3,2-*h*]quinolin-11-one (11i). White needles; mp 132-4 °C (from acetone); IR (KBr) ν_{max} 3430, 3080, 2950, 1737, 1584, 1485, 1440, 1435, 1375, 1290, 1075, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, ppm), δ 1.87 (2H, sp, *J* 5.6, 4.4, 5.2 and 4.8 Hz, CH_2), 2.60 (2H, t, *J* 4.4, 3.2 and 1.6 Hz, CH_2), 3.64 (2H, t, *J* 5.2 and 5.6 Hz, CH_2), 4.78 (2H, s, CH_2), 7.07 (1H, d, *J* 8.8 Hz), 7.17 (1H, dd, *J* 1.6 and 1.2 Hz), 7.23 (1H, q, *J* 4.8, 3.6 and 4.8 Hz), 7.35 (1H, dt, *J* 1.3, 6.4 and 1.3 Hz), 7.46 (1H, dt, *J* 1.6, 6.4, 1.2 and 8.0 Hz), 7.73 (1H, two t, *J* 1.6, 1.6, 1.3, 1.6 and 1.6 Hz), 7.83 (1H, dd, *J* 1.2, 6.4 and 1.6 Hz), 8.29 (1H, dd, *J* 1.6 and 1.2 Hz), 8.72 (1H, dd, *J* 1.6 and 1.6 Hz), 10.15 (1H, s, NH); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.0, 33.2, 38.7, 48.6, 117.2, 122.1, 125.8, 126.6, 126.6, 127.0, 127.9, 130.8, 131.4, 132.3, 133.1, 134.4, 140.7, 148.7, 206.8. Anal. Calcd. for $C_{20}H_{18}N_2OS$ (334); C, 71.85; H, 5.38; N, 8.38; S, 9.58. Found; C, 72.02; H, 5.28; N, 8.44; S, 9.46 %.

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