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Graphical Abstract

Catalyst-free one-pot four-component domino reactions in water-PEG- 400: Highly efficient and convergent approach to thiazoloquinoline scaffolds

Anugula Nagaraju,[a] B. Janaki Ramulu,[a] Gaurav Shukla,[a] Abhijeet Srivastava,[a] Girijesh Kumar Verma,[a] Keshav Raghuvanshi[b] and Maya Shankar Singh*[a]

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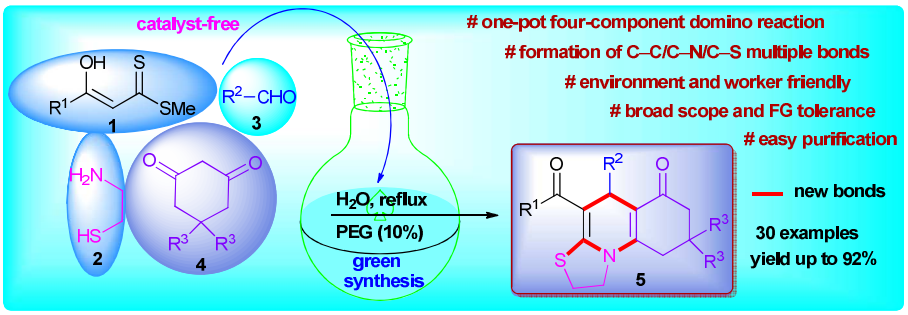

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A cost-effective and eco-friendly straightforward synthesis of highly diversified thiazoloquinoline scaffolds has been successfully achieved *via* one-pot four-component cascade reaction utilizing α-enolic dithioesters, cysteamine, aldehydes, and cyclic 1,3-diketones in water-PEG-400. The new efficient domino protocol generates two rings by the concomitant formation of C–C (two), C–N (two), and C–S multiple bonds presumably involving a sequence of *N,S*-acetal formation, Knoevenagel reaction, aza-ene reaction, imine-enamine/keto-enol tautomerization, and N-cyclization as key steps. The merit of this protocol is highlighted by its easily available and economical starting materials, operational simplicity, efficient utilization of all the reactants, clean reaction profile, simple workup procedure, and tolerance of a wide variety of functional groups.

Introduction

The field of organic synthesis has recently experienced numerous innovative scientific breakthroughs accompanied by improved and efficient synthetic protocols that avoid the use of toxic solvents and reagents. The realization of simple and sustainable green synthetic procedures constitute an important goal in organic synthesis.[1] Development of synthetic strategies able to furnish molecular diversity and complexity from easily available and economical starting materials, has become one of the main challenges for organic synthesis.[2] In this context, multicomponent coupling reactions[3] (MCRs) have emerged as a powerful tool to achieve synthetic efficiency. MCRs have unique advantages such as convergence, operational simplicity, flexibility, and pot, atom, step, and cost economy[4] (PASCE). They usually show a good stereocontrol and good overall yields with easy purification processes. MCRs enable the expedient assembly of complex molecules and also furnish structurally diverse libraries of drug-like scaffolds.[5,6] Therefore, MCRs play a pivotal role in lead identification and optimization processes in drug discovery programmes.[7]

Because of the increasing public concern for the harmful effects of organic solvents on the environment, recent years have witnessed an extensive use of water as reaction medium[8] for various organic transformations. It is known that water is a non-flammable, non-hazardous, non-toxic, uniquely redox-stable, inexpensive green solvent.[9] In addition, water facilitates novel solvation and molecular assembly processes leading to remarkable modes of reactivity and selectivity of a wide variety of organic reactions.[10] Combination of MCRs and water as a solvent has become a new research direction, which enables a simultaneous growth of both MCRs and green solvent toward ideal organic synthesis.[11] Therefore, the design of new MCRs with green procedure has attracted great attention, especially in the areas of drug discovery, and material science.[12]

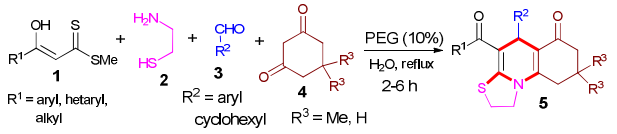
The use of Polyethylene glycol (PEG) as a greener alternative in organic synthesis is advantageous over toxic organic solvents because of its low toxicity and solubility in both aqueous and non-aqueous media.[13] Several organic reactions are reported in water in the presence of PEG, which solubilises organic components in water.[14] Herein, we report the direct synthesis of thiazoloquinoline derivatives employing PEG-400 as a solubilizing agent in water *via* one-pot four-component reaction involving α-enolic dithioesters, cysteamine, aldehydes and cyclic 1,3-diketones as coupling partners. In this domino reaction, two new rings are constructed by the formation of C–C (two), C–N (two), and C–S multiple bonds with all reactants efficiently utilized in the chemical transformation.

The thiazoloquinoline scaffold represents an interesting template in medicinal chemistry, and its derivatives possess useful biological and pharmacological properties.[15] The methods available for the synthesis of thiazoloquinolines include hydration/cyclodehydration of 3-substituted 2,4-dioxo-1,2,3,4-tetrahydroquinolin-3-yl-thiocyanates *via* thiocarbamates[16a] and a palladium-catalyzed reaction of ethyl 2-bromo-5-chlorothiazole-4-carboxylate with arylboronic acids.[16b] However, these methods suffer from one or more drawbacks such as lack of generality, require a number of steps, harsh reaction conditions, cumbersome workup procedure and the use of toxic organic solvents and catalysts. To the best of our knowledge, four-component reaction involving α-enolic dithioesters, cysteamine, aldehydes and cyclic

1,3-diketones as coupling partners for the synthesis of thiazoloquinoline derivatives till date is not known. In this context, in the present paper we describe a catalyst-free straightforward one-pot cost-effective and green procedure for the synthesis of thiazoloquinoline scaffolds *via* one-pot four-component domino reaction in water-PEG 400 with easily available starting materials. The present work forms a part of our ongoing research programme on the development of novel multi-component and domino reactions for the construction of important heterocyclic ring systems.[17,18]

Results and discussion

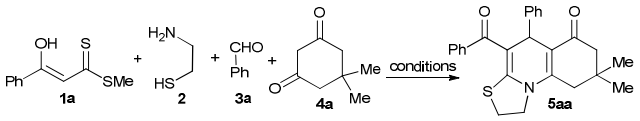
Simple molecules bearing diverse functionality are considered to be ideal starting materials in diversity oriented synthesis. One such polyfunctional simple molecule is α-enolic dithioester, a thio-analogue of β-ketoester. Owing to the presence of enolic and dithioester moieties, the reactions of α-enolic dithioesters with various reagents have been exploited to construct five-/six-membered and fused heterocycles depending on the reaction conditions during the past years.[19] In the course of our studies, we were interested to utilize α-enolic dithioester as one of the coupling partner in a four-component coupling reaction. Thus, upon treatment of α-enolicdithioesters **1** with cysteamine **2** followed by addition of aldehydes **3** and cyclohexane-1,3-diones **4** in water-PEG afforded the corresponding thiazoloquinolines **5** within 2-6 h in good to excellent yields. The desired products were purified by simple filtration and recrystallization from MeOH-DCM (1:1) mixture avoiding the conventional chromatographic separation (Scheme 1).



Scheme 1 One-pot four-component synthesis of thiazoloquinolines **5**.

We started our investigations with the optimization of four-component coupling reaction using equimolecular amounts of methyl 3-hydroxy-3-phenyl-prop-2-enedithioate **1a**, cysteamine **2**, benzaldehyde **3a** and dimedone **4a** as model substrates. The above model reaction was performed in the absence and presence of different catalysts in various solvents as well as under solvent-free conditions at different temperatures. The results are listed in Table 1. Initially, the above model reaction was performed without any catalyst under solvent-free conditions at 60 °C. The reaction did not proceed at all and the starting materials remained completely unconsumed even after 24 h (Table 1, entry 1). Next, we performed the model reaction at 100 °C under similar conditions, which afforded the desired compound **5aa** in 60 % yield (Table 1, entry 2). In order to check the efficacy of Lewis acid and base catalysts we performed the model reaction under solvent-free conditions at 100 °C by adding Lewis acid and base in catalytic amounts, but regretted results were obtained (Table 1 entries 3-5).

Table 1 Optimization of reaction conditions for the synthesis of **5aa**[a]



Entry	Solvent (v/v %)	Catalyst (mol %)	Temp. (°C)	Time[b] (h)	Yield (%)
1	None	None	60	24	-[c]
2	None	None	100	14	60
3	None	$FeCl_3$ (10)	100	12	55
4	None	$InCl_3$ (10)	100	12	55
5	None	DMAP (10)	100	11	45
6	MeOH	None	reflux	24	20[d]
7	EtOH	None	reflux	24	30[d]
8	CH_3CN	None	reflux	24	15[d]
9	Acetone	None	reflux	24	10[d]
10	DMF	None	110	9	55
11	DMSO	None	110	3	70
12	H_2O	None	reflux	24	trace
13	PEG 400	None	110	6	75
14	PEG/H_2O (50)	None	reflux	4	81
15	PEG/H_2O (33)	None	reflux	3	85
16	**PEG/H_2O (10)**	**None**	**reflux**	**2**	**92**
17	PEG/H_2O (15)	None	reflux	2	89
18	PEG/H_2O (5)	None	reflux	6	50[d]
19	PEG/EtOH (50)	None	reflux	12	40[d]
20	EtOH/H_2O (50)	None	reflux	12	30[d]

[a] Reaction conditions: **1a** (0.5 mmol) was treated with **2** (0.5 mmol) followed by addition of **3a** (0.5 mmol) and **4a** (0.5 mmol), [b] Total reaction time, [c] No reaction, [d] Reactants remained unconsumed.

In order to check the effect of solvent on the reaction, various protic polar and aprotic polar solvents were evaluated. It was found that protic polar (MeOH and EtOH) and low boiling aprotic solvents (acetone and CH_3CN) under reflux conditions afforded the low yield of the desired product **5aa**, and most of the reactants remained unconsumed even after 24 h (Table 1, entries 6-9). High boiling polar aprotic solvents like DMF and DMSO afforded the desired product in higher yield taking less time (Table 1, entries 10 and 11). From the economical and environmental point of view, H_2O was screened as the reaction medium but no improvement was observed due to solubility problem (Table 1, entry 12). In order to make the reaction more efficient, next we performed the model reaction in PEG-400 at 110 °C, and to our delight the desired product was obtained in 75% yield within 6 h (Table 1, entry 13). Encouraged by the above result, we carried out the reaction in a mixture of PEG-400 and H_2O (1:1), which afforded the desired product in 81% yield within 4 h (Table 1, entry 14).

PEG-400 is high boiling water soluble polyether, which has the ability to solubilize organic components in water, thus accelerating the rate of the reaction. The use of PEG-400 increases the solubility of reactants, which leads to larger interfacial area, lower mass transfer resistance.[20a] The promoting effects of water to the reaction could be attributed to its hydrophobic, polarity and hydrogen-bonding effects.[20b-d] After getting a suitable medium for the reaction, we optimized the ratio

of water and PEG-400 and it was found that H_2O-PEG-400 (9:1) afforded the desired product in 92% yield within 2 h (Table 1, entry 16). Further increase or decrease in the ratio of PEG-400 in water did not improve the result. These observations led to the conclusion that water-PEG-400 (9:1 at 100 °C) is the solvent of choice for this four-component coupling reaction under aerobic conditions. One clear advantage of the water-PEG-400 combination is that it afforded products that could be rendered very pure by simple recrystallization from a mixture of MeOH-DCM (1:1) avoiding conventional chromatographic purification.

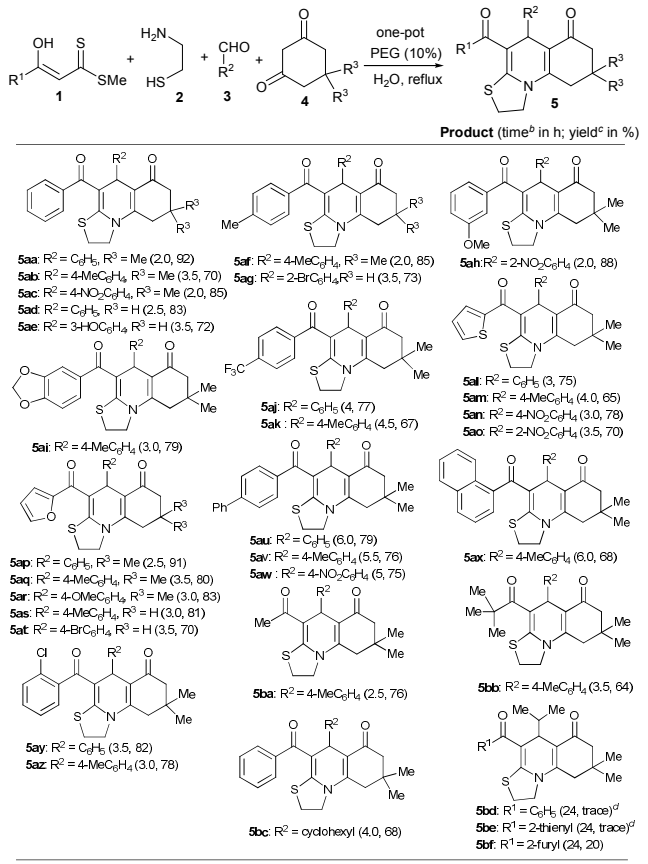
Once the feasibility of the proposed pathway had been validated, the scope and robustness of this one-pot four-component de novo thiazoloquinolines **5** synthesis was evaluated (Table 2) by employing a diverse range of α-enolic dithioesters, aldehydes, and cyclic 1,3-diketones. As shown in Table 2, this four-component cascade reaction of α-enolic dithioesters, cysteamine, aldehydes and cyclic 1,3-diketones in water-PEG-400 mixture under reflux for 2-6 h proceeded smoothly affording a series of thiazoloquinolines **5** in good to excellent yields. A broad spectrum of α-enolic dithioesters **1**, bearing R^1 as aryl (containing both electron-withdrawing and electron-donating substituents), hetaryl, extended aromatics and alkyl groups could be employed and tolerated well under the optimal reaction conditions. Diverse aromatic aldehydes, and 1,3-cyclohexanediones bearing R^3 as methyl or hydrogen were also tolerated well.

To explore the electronic influence on the aza-ene domino process, a wide range of dithioesters derived from acetophenones containing both electron-donating and electron-withdrawing groups on the phenyl ring were employed. α-Enolic dithioesters bearing R^1 as aryl group with electron-donating substituents gave considerably higher yields than those with electron-withdrawing groups (**5af**, **5ag, 5ah, 5ai** *vs* **5aj, 5ak**). After successful utilization of aromatic dithioesters, we next extended our study to various heteroaromatic dithioesters derived from 2-substituted heteroaromatic compounds such as 2-acetylthiophene and 2-acetylfuran, which were tolerated well and shown to be effective substrates affording the desired compounds in 65-91% yields (**5al-5at)**. We were pleased to find that extended aromatics such as biphenyl and 1-naphthyl as R^1 substituents were also tolerated well resulting in good yields of the products (**5au-5ax**). R^1 as *ortho*-chlorophenyl group also afforded the product in good yields (**5ay**, **5az**). Noticeably, alkyl-substituted dithioester derived from aliphatic ketone such as acetone also underwent smoothly to give desired compound **5ba** in 76% yield. However, when the more bulkier *tert*.-butyl group was installed, the reaction became slightly sluggish and afforded **5bb** in 64% yield.

In order to extend the reaction scope further, we turned our attention towards aromatic aldehydes bearing electron-withdrawing and electron-donating groups. Notably, aldehydes with electron-withdrawing groups furnished the product in higher yields than those of bearing electron-donating groups (**5ac** *vs* **5ab** and **5an** *vs* **5am**). The reaction with cyclohexyl carboxaldehyde also furnished the product in good yield (**5bc**). But in the case of isobutyraldehyde, the desired product was obtained in trace and reactants remained mostly unconsumed even after 24 h (**5bd** and **5be**). However, when R^1 is 2-furyl substituent, the desired product was obtained in 20% yield (**5bf**). This protocol has furnished comparably good result with methyl at R^3 on cyclohexane-1,3-dione than hydrogen (**5aa** *vs* **5ae**).

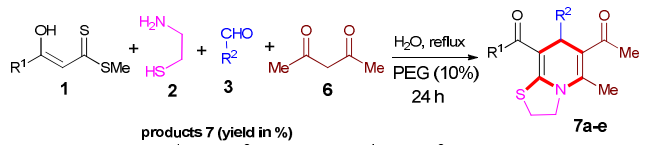
In the next attempt, we tried to synthesize oxazolo and imidazolo-quinolinones by treating dithioester separately with ethanolamine and ethylenediamine, respectively under the similar reaction conditions but we could not get the desired cyclic-*O,N* and *N,N*-acetals even after 6 h, thus, limiting the generality of the reaction to some extent.

Table 2 Substrate scope for synthesis of thiazoloquinolinones **5**[a]



[a] Reaction conditions: **1a** (0.5 mmol) was treated with **2** (0.5 mmol), after the formation of *N,S*-acetal, 0.5 mmol of **3** and 0.5 mmol of **4** was added, [b] total reaction time, [c] isolated yields, [d] not isolated.

Being inspired by the above results, we considered it worthwhile to replace the cyclic 1,3-diketones **4** with acyclic diketone like acetylacetone **6** to add further generality to our newly developed methodology. Thus, we treated **1**, **2**, **3** with **6** under the previously described reaction conditions. The workup of the reaction afforded the desired thiazolopyridines (**7a-e**) in low yields (20-30%) even after 24 h of reflux and most of the components remained unconsumed (Scheme 2).



Scheme 2 One-pot four-component synthesis of thiazolopyridines **7**.

The structures of all the newly synthesized thiazoloquinolines **5** and thiazolopyridines **7** are deduced by their satisfactory spectral (IR, ^{1}H, ^{13}C NMR, and mass) studies. The structures of three representative compounds **5ar**, **5ax**, and **5ba** (Figure 1) were explicitly established by the single crystal X-ray diffraction analysis (see the ESI). The mass spectra of these compounds displayed molecular ion peaks at the appropriate m/z values.

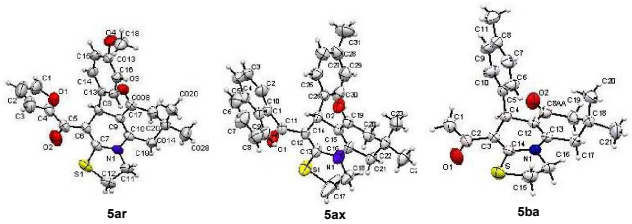
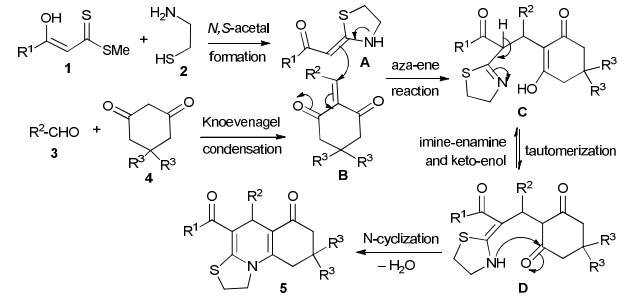


Fig. 1 ORTEP diagrams of **5ar**, **5ax** and **5ba**

By taking our entire experimental outcomes into consideration, a plausible mechanistic pathway for the formation of compound **5** is outlined in Scheme 3. The first step is believed to be the formation of cyclic *N,S*-acetal **A** by the reaction of *α*-enolic dithioester **1** with cysteamine **2**, which was isolated and fully characterized.[21] Next reaction of aldehyde **3** with cyclic 1,3-diketone **4** gave Knoevenagel product **B**, a highly reactive *ortho*-quinonemethide intermediate that could not be isolated. Subsequently, the *N,S*-acetal **A** undergoes a conjugate addition with *ortho*-quinonemethide intermediate **B** *via* aza-ene fashion to generate acyclic intermediate **C**. Intermediate **C** undergoes imine-enamine and keto-enol tautomerization to give intermediate **D**, which rapidly undergoes intramolecular dehydrative N-cyclization to give the desired triheterocyclic product **5**. It turns out that the intermediates **A** and **B** might be formed concomitantly and reacts instantly to limit the formation of byproducts.



Scheme 3 Plausible mechanism for formation of thiazoloquinolinone **5**.

Conclusions

In summary, we report a simple and straightforward one-pot four-component catalyst-free integrated protocol for the synthesis of thiazoloquinolinone and thiazolopyridine scaffolds in water-PEG-400 (9:1; v/v) at 100 °C for the first time. This convergent and versatile method, which exhibits an unusually high multiple bond-forming efficiency as well as structure and step economies, presents broad substrate scope and excellent functionality tolerance. This approach enables the rapid assembly of diverse thiazoloquinolinone-based frameworks utilizing all the four reactants efficiently. In addition, the method involves the use of readily available commercial reagents and operationally simple synthetic protocols and does not require advanced intermediates, anhydrous solvents or any catalysts. This approach therefore exemplifies the reconciliation of structural complexity and operational simplicity in an environmentally friendly time and cost effective manner. Significantly, the presence of acyclic and cyclic keto-groups at 4- and 6-positions, respectively on thiazoloquinolines makes these compounds excellent entrants as precursors for further synthetic renovations to meet the need for diverse useful purposes. The isolation and purification of compounds by simple filtration and water washing makes the process very simple avoiding conventional chromatographic separation. We hope this clean and green four-component coupling protocol may be of value for both synthetic and medicinal chemists for academic research and practical applications.

Experimental section

General information

The commercially available starting materials were used as received without further purification. *α*-Enolicdithioesters **1** were prepared by the reported procedure.[19c] ^{1}H and ^{13}C NMR spectra were recorded on NMR spectrometers operating at 300 and 75 MHz, respectively. Chemical shifts (δ) are given in parts per million (ppm) using the residual solvent peaks as reference relative to TMS. *J* values are given in Hz. Mass spectra were recorded using electrospray ionization (ESI) mass spectrometry.

General procedure for the synthesis of 4,5-disubstituted-thiazolo[3,2-*a*]quinolin-6-ones 5. A round bottom flask was charged with the appropriate *α*-enolicdithioesters **1** (0.5 mmol), cysteamine **2** (0.5 mmol), 2.7 ml water and 0.3 ml PEG-400, and set the reaction mixture at 100 °C over the pre-heated oil bath. The reaction mixture was stirred for 20 min till the formation of cyclic N,S-acetal (monitored by TLC), followed by addition of aldehyde **3** (0.5 mmol) and cyclohexane-1,3-dione **4** (0.5 mmol). The reaction mixture was further stirred for a stipulated period of time (Table 2). After completion of the reaction as shown by TLC, the reaction was quenched with distilled water. The yellow solid thus precipitated was collected by filtration. The crude product obtained was dried under vacuum, and recrystallized from MeOH-DCM (1:1) mixture to give the analytically pure compound **5**, except **5bf**, which was isolated by preparative chromatography using hexane-ethylacetate (60:40) as mobile phase.

The spectral and analytical data of all the compounds are given as follows:

4-Benzoyl-8,8-dimethyl-5-phenyl-1,2,5,7,9-pentahydro-thiazolo[3,2-*a*]quinolin-6-one (5aa). Yellow solid; mp 210-212 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.25 (m, 5H), 7.11-7.05 (m, 3H), 6.91 (d, J = 6.9 Hz, 2H), 5.23 (s, 1H), 4.09-3.95 (m, 2H), 3.23-3.18 (m, 2H), 2.46 (ABq, J^1 = 25.8 Hz, J^2 = 17.1 Hz, 2H), 2.21 (ABq, J^1 = 22.9 Hz, J^2 = 16.2 Hz, 2H), 1.09 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 194.5, 154.9, 148.1, 145.6, 139.5, 130.0, 128.1, 127.9, 127.2, 127.1, 126.1,

115.5, 107.7, 49.9, 49.6, 40.7, 37.0, 32.2, 29.9, 28.2, 26.7.

4-Benzoyl-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydro-thiazolo[3,2-*a*]quinolin-6-one (5ab). Yellow solid; mp 217-219 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.26 (m, 4H), 7.02-6.90 (m, 3H), 6.80 (d, J = 7.8 Hz, 2H), 5.20 (s, 1H), 4.08-3.98 (m, 2H), 3.23-3.18 (m, 2H), 2.47-2.38 (m, 2H), 2.26-2.22 (m, 5H), 1.09 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 194.5, 154.8, 148.1, 142.7, 139.5, 135.5, 130.0, 128.8, 127.9, 127.1, 127.0, 115.7, 107.8, 49.9, 49.6, 40.6, 36.5, 32.2, 29.9, 28.2, 26.8, 20.9.

4-Benzoyl-8,8-dimethyl-5-(4-nitrophenyl)-1,2,5,7,9-pentahydro-thiazolo[3,2-*a*]quinolin-6-one (5ac). Yellow solid; mp 207-208 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (d, J = 8.7 Hz, 2H), 7.44-7.18 (m, 5H), 7.04 (d, J = 8.7 Hz, 2H), 5.35 (s, 1H), 4.19-4.01 (m, 2H), 3.34-3.23 (m, 2H), 2.50 (ABq, J^1 = 28.9 Hz, J^2 = 16.9 Hz, 2H), 2.22 (ABq, J^1 = 28.8 Hz, J^2 = 16.2 Hz, 2H), 1.13 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0, 194.2, 155.3, 152.8, 148.7, 146.2, 139.3, 130.3, 128.3, 127.6, 126.7, 123.9, 123.4, 114.2, 106.8, 49.8, 40.8, 37.8, 32.9, 32.2, 29.9, 28.2, 26.7.

4-Benzoyl-5-phenyl-1,2,5,7,8,9-hexahydrothiazolo[3,2-*a*] quinolin-6-one (5ad). Yellow solid; mp 208-209 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36-7.22 (m, 5H), 7.13-7.05 (m, 3H), 6.91 (d, J = 7.2 Hz, 2H), 5.27 (s, 1H), 4.04-3.95 (m, 2H), 3.22-3.14 (m, 2H), 2.66-2.51 (m, 2H), 2.41-2.21 (m, 2H), 2.04-1.77 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.3, 194.4, 154.6, 149.8, 145.9, 139.4, 130.0, 128.1, 127,9, 127.2, 127.0, 126.1, 116.4, 107.5, 49.5, 36.9, 36.3, 28.1, 26.9, 20.6.

4-Benzoyl-5-(3-hydroxyphenyl)-1,2,5,7,8,9-hexahydrothiazolo[3,2-*a*]quinolin-6-one (5ae). Brown solid; mp 249-251 °C. ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO): δ 8.35 (s, 1H), 6.95-6.83 (m, 5H), 6.49-6.44 (m, 1H), 6.09-5.90 (m, 3H), 4.72 (s, 1H), 3.66-3.63 (m, 2H), 2.88-2.77 (m, 2H), 2.31-2.11 (m, 2H), 1.89-1.83 (m, 2H), 1.58-1.44 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO): δ 194.2, 192.8, 156.2, 153.8, 149.5, 146.5, 138.6, 129.1, 128.07, 128.02, 127.0, 126.1, 117.0, 116.8, 114.7, 113.1, 112.9, 112.3, 106.1, 48.7, 35.5, 35.4, 27.1, 25.8, 19.6.

8,8-Dimethyl-4-(4-methylbenzoyl)-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5af). Yellow solid; mp 188-200 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21 (d, J = 7.8 Hz, 2H), 7.09 (d, J = 7.8 Hz, 2H), 6.92 (d, J = 8.1 Hz, 2H), 6.83 (d, J = 7.8 Hz, 2H), 5.25 (s, 1H), 4.07-3.94 (m, 2H), 3.72-3.61 (m, 2H), 3.22-3.17 (m, 2H), 2.47-2.22 (m, 8H), 1.09 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 194.4, 154.4, 148.2, 142.7, 140.4, 136.6, 135.5, 128.8, 128.6, 127.4, 127.0, 126.4, 115.5, 107.9, 50.0, 49.6, 40.6, 36.5, 32.2, 29.9, 28.2, 26.8, 21.4, 20.9. HRMS (ESI$^+$): calcd for $C_{28}H_{29}NO_2S$ [M+H$^+$], 444.1992; found, 444.1993.

5-(2-Bromophenyl)-4-(4-methylbenzoyl)-1,2,5,7,8,9-hexahydrothiazolo[3,2-*a*]quinolin-6-one (5ag). Yellow solid; mp 137-139 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.12 (m, 5H), 6.94-6.75 (m, 3H), 5.59 (s, 1H), 4.17-3.97 (m, 2H), 3.08-3.04 (m, 2H), 2.70-2.58 (m, 2H), 2.36-2.23 (m, 5H), 2.04-1.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.19, 195.12, 152.1, 150.7, 143.6, 140.7, 136.6, 133.2, 132.1, 128.8, 127.4, 127.2, 126.5, 123.0, 113.9, 107.8, 49.6, 40.0, 36.1, 27.6, 27.2, 21.3, 20.5.

4-(3-Methoxybenzoyl)-8,8-dimethyl-5-(2-nitrophenyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ah). Brown solid; mp 101-103 °C.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (d, J = 7.8 Hz, 1H), 7.26-7.06 (m, 4H), 6.90 (d, J = 6.0 Hz, 1H), 6.78 (d, J = 7.5 Hz, 1H), 6.59 (s, 1H), 5.77 (s, 1H), 4.15-4.07 (m, 2H), 3.67 (s, 3H), 3.21-3.14 (m, 2H), 2.47 (s, 2H), 2.23-2.10 (m, 2H), 1.10 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0, 194.7, 159.4, 154.7, 149.4, 148.4, 140.9, 138.9, 132.4, 131.3, 129.3, 126.9, 123.9, 118.7, 116.4, 113.7, 111.4, 107.1, 55.1, 49.8, 49.6, 41.0, 36.2, 31.9, 29.5, 27.8, 27.0.

4-(Benzo[1,3]dioxole-5-carbonyl)-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ai). Yellow solid; mp 185-186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.96-6.83 (m, 6H), 6.70 (d, J = 8.1 Hz, 1H), 5.95 (s, 1H), 4.06-3.98 (m, 2H), 3.20-3.15 (m, 2H), 2.44 (ABq, J^1 = 26.2 Hz, J^2 = 16.5 Hz, 2H), 2.23 (m, 5H), 1.09 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 193.0, 154.4, 149.4, 148.2, 147.2, 142.6, 135.6, 133.4, 128.9, 126.9, 122.6, 115.4, 108.2, 107.7, 101.2, 50.0, 49.7, 40.6, 36.5, 32.2, 29.9, 28.2, 26.7, 20.8.

8,8-Dimethyl-5-phenyl-4-(4-trifluoromethylbenzoyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5aj). Brown solid; mp 143-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62-7.52 (m, 2H), 7.28-7.20 (m, 4H), 7.12-7.06 (m, 2H), 6.90 (d, J = 6.9 Hz, 1H), 5.09 (s, 1H), 4.16-3.92 (m, 2H), 3.29-3.14 (m, 2H), 2.57-2.40 (m, 2H), 2.26-2.13 (m, 2H), 1.08 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.1, 192.8, 162.2, 156.3, 147.9, 145.3, 143.0, 131.2 (q, J = 32.1 Hz, 1C), 128.1, 127.8, 127.1, 126.2, 125.4, 124.8, 115.5, 115.3, 106.9, 49.7, 49.6, 40.4, 36.8, 32.1, 29.6, 28.0, 26.5.

8,8-Dimethyl-5-*p*-tolyl-4-(4-trifluoromethylbenzoyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ak). Yellow solid; mp 148-150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 7.8 Hz, 2H), 6.93 (d, J = 7.5 Hz, 2H), 6.79 (d, J = 7.8 Hz, 2H), 5.06 (s, 1H), 4.16-3.96 (m, 2H), 3.29-3.24 (m, 2 H), 2.47-2.39 (m, 2H), 2.28-2.16 (m, 5H), 1.10 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 193.1, 156.2, 147.8, 143.0, 142.4, 135.9, 131.5 (q, J = 32.1 Hz, 1C), 129.0, 127.3, 127.1, 125.0 (q, J = 3.6 Hz, 1C), 116.1, 107.2, 49.9, 49.7, 40.6, 36.5, 32.3, 29.8, 28.3, 26.9, 20.9.

8,8-Dimethyl-5-phenyl-4-(thiophene-2-carbonyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5al). Yellow solid; mp 247-248 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J = 4.5 Hz, 1H), 7.36 (d, J = 3.6 Hz, 1H), 7.24-7.12 (m, 5H), 6.94-6.92 (m, 1H), 5.76 (s, 1H), 4.11-4.04 (m, 1H), 3.96-3.86 (m, 1H), 3.26-3.18 (m, 2H), 2.50-2.16 (m, 4H), 1.07 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.4, 183.0, 157.6, 148.7, 144.7, 144.0, 131.4, 130.6, 128.5, 127.7, 126.9, 126.3, 115.6, 106.2, 50.0, 49.8, 40.2, 35.5, 32.2, 29.9, 28.3, 26.4. HRMS (ESI$^+$): calcd for $C_{24}H_{23}NO_2S_2$ [M+H$^+$], 422.1243; found, 422.1247.

8,8-Dimethyl-4-(thiophene-2-carbonyl)-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5am). Yellow solid; mp 200-203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.36 (m, 2H), 7.12-6.92 (m, 5H), 5.69 (s, 1H), 4.11-3.87 (m, 2H), 3.21-3.13 (m, 2H), 2.51-2.24 (m, 7H), 1.06 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0, 182.5, 157.2, 148.4, 143.7, 141.5, 135.4, 131.0, 130.1, 128.9, 127.3, 126.4, 115.3, 105.9, 49.7, 49.5, 39.8, 34.8, 31.8, 29.5, 28.0, 26.2, 20.5.

8,8-Dimethyl-5-(4-nitrophenyl)-4-(thiophene-2-carbonyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5an).

Yellow solid; mp 201-203 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, J = 8.4 Hz, 2H), 7.50-7.29 (m, 4H), 6.99-6.96 (m, 1H), 5.88 (s, 1H), 4.20-4.13 (m, 1H), 4.04-3.95 (m, 1H), 3.32-3.23 (m, 2H), 2.49 (ABq, J^1 =36.3 Hz, J^2 = 17.4 Hz, 2H), 2.28 (Distorted ABq, 2H), 1.10 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.1, 182.7, 157.8, 152.0, 149.5, 146.2, 143.2, 131.6, 130.2, 127.9, 127.6, 123.8, 123.7, 114.0, 105.3, 49.8, 49.7, 40.3, 36.2, 32.1, 29.8, 28.2, 26.2.

8,8-Dimethyl-5-(2-nitrophenyl)-4-(thiophene-2-carbonyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ao). Brown solid; mp 245-247 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.46 (m, 3H), 7.33-7.26 (m, 2H), 7.18 (d, J = 7.8 Hz, 1H), 7.02 (s, 1H), 6.15 (s, 1H), 4.20-3.98 (m, 2H), 3.69-3.45 (m, 2H), 2.47 (ABq, J^1 = 27 Hz, J^2 = 17.1 Hz, 2H), 2.18 (ABq, J^1 = 23.5 Hz, J^2 = 16.0 Hz, 2H), 1.09 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.8, 185.7, 153.4, 149.1, 148.7, 142.5, 138.4, 131.7, 131.4, 131.2, 130.7, 127.3, 127.2, 124.1, 113.4, 107.2, 50.0, 49.5, 41.0, 35.5, 31.9, 29.7, 27.8, 26.8.

4-(Furan-2-carbonyl)-8,8-dimethyl-5-phenyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ap). Brown solid; mp 237-238 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.26-7.08 (m, 5H), 6.97 (d, J = 3.3 Hz, 1H), 6.37 (s, 1H), 5.90 (s, 1H), 4.13-3.88 (m, 2H), 3.27-3.12 (m, 2H), 2.45-2.36 (m, 2H), 2.26-2.21 (m, 2H), 1.08 (s, 3H), 0.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.4, 178.0, 157.2, 152.6, 148.4, 145.4, 145.0, 128.3, 127.0, 126.1, 117.3, 115.9, 111.6, 106.6, 50.0, 49.7, 40.4, 34.9, 32.2, 29.8, 28.3, 26.7. HRMS (ESI$^+$): calcd for $C_{24}H_{23}NO_3S$ [M+H$^+$], 406.1471; found, 406.1471.

4-(Furan-2-carbonyl)-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5aq). Yellow solid; mp 221-222 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.10 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 7.5 Hz, 3H), 6.37 (s, 1H), 5.84 (s, 1H), 4.06-3.87 (m, 2H), 3.21-3.15 (m, 2H), 2.42 (ABq, J^1 = 27.4 Hz, J^2 = 17.1 Hz, 2H), 2.25-2.23 (m, 5H), 1.07 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.4, 178.0, 157.1, 152.5, 148.3, 144.9, 142.5, 135.5, 128.9, 126.9, 117.3, 116.0, 111.7, 111.5, 106.7, 50.0, 49.7, 40.3, 34.4, 32.2, 29.7, 28.2, 26.7, 20.9.

4-(Furan-2-carbonyl)-5-(4-methoxyphenyl)-8,8-dimethyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ar). Brown solid; mp 201-202 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.14 (d, J = 8.4 Hz, 2H), 6.96 (d, J = 3.3 Hz, 1H), 6.72 (d, J = 8.4 Hz, 2H), 6.38 (d, J = 1.8 Hz, 1H), 5.81 (s, 1H), 4.12-4.05 (m, 1H), 3.96-3.87 (m, 1H), 3.70 (s, 3H), 3.21-3.15 (m, 2H), 2.43 (ABq, J^1 = 27.7 Hz, J^2 = 17.1 Hz, 2H), 2.30-2.19 (m, 2H), 1.07 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.4, 178.0, 157.7, 157.0, 152.5, 148.2, 144.9, 137.9, 128.0, 117.3, 116.1, 113.5, 111.6, 106.8, 54.9, 50.0, 49.6, 40.3, 34.1, 32.2, 29.7, 28.2, 26.6. HRMS (ESI$^+$): calcd for $C_{25}H_{25}NO_4S$ [M+H$^+$], 436.1577; found, 436.1577.

4-(Furan-2-carbonyl)-5-*p*-tolyl-1,2,5,7,8,9-hexahydrothiazolo [3,2-*a*]quinolin-6-one (5as). Yellow solid; mp 125-127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.12-6.97 (m, 5H) 6.37 (s, 1H), 5.88 (s, 1H), 4.05-3.88 (m, 2H), 3.19-3.13 (m, 2H), 2.59-2.23 (m, 7H), 2.03-1.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.6, 177.9, 156.9, 152.3, 150.2, 144.9, 142.8, 135.5, 129.0, 126.9, 117.2, 117.0, 111.5, 106.6, 49.5, 36.3, 34.3, 28.1, 26.6, 20.8, 20.5.

5-(4-Bromophenyl)-4-(furan-2-carbonyl)-1,2,5,7,8,9-hexahydrothiazolo[3,2-*a*]quinolin-6-one (5at). Yellow solid; mp 143-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.31-7.26 (m, 2H), 7.11 (d, J = 8.1 Hz, 2H), 7.00 (d, J = 3.3 Hz, 1H), 6.40 (s, 1H), 5.92 (s, 1H), 4.14-3.92 (m, 2H), 3.23-3.18 (m, 2H), 2.69-2.26 (m, 3H), 2.08-1.86 (m, 1H), 1.75 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.5, 177.8, 157.0, 152.7, 150.3, 145.1, 131.3, 129.1, 120.0, 117.5, 116.6, 111.8, 111.7, 106.3, 49.6, 36.4, 34.7, 28.3, 26.8, 20.6.

4-(Biphenyl-4-carbonyl)-8,8-dimethyl-5-phenyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5au). Yellow solid; mp 194-195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60-7.34 (m, 10 H), 7.20-6.97 (m, 4H), 5.32 (s, 1H), 4.08-3.95 (m, 2H), 3.25-3.18 (m, 2H), 2.46 (ABq, J^1= 26.1Hz, J^2 = 17.1 Hz, 2H), 2.23 (Distorted ABq, 2H), 1.09 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 194.0, 155.0, 148.2, 145.6, 142.8, 140.3, 138.3, 128.7, 128.2, 127.8, 127.6, 127.2, 127.1, 126.7, 126.2, 115.5, 107.7, 50.0, 49.7, 40.7, 37.1, 32.2, 29.9, 28.2, 26.7. HRMS (ESI$^+$): calcd for $C_{32}H_{29}NO_2S$ [M+H$^+$], 492.1992; found, 492.1996.

4-(Biphenyl-4-carbonyl)-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5av). Yellow solid; mp 236-238 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61-7.36 (m, 9H), 6.95-6.86 (m, 4H), 5.29 (s, 1H), 4.09-4.00 (m, 2H), 3.27-3.23 (m, 2H), 2.54-2.40 (m, 2H), 2.30-2.23 (m, 5H), 1.11 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.2, 194.0, 154.9, 148.1, 142.9, 142.7, 140.4, 138.3, 135.6, 128.9, 128.7, 127.9, 127.5, 127.1, 126.7, 115.8, 107.8, 50.0, 49.7, 40.7, 36.5, 32.3, 29.9, 28.3, 26.8, 20.9. HRMS (ESI$^+$): calcd for $C_{33}H_{31}NO_2S$ [M+H$^+$], 506.2148; found, 506.2148.

4-(Biphenyl-4-carbonyl)-8,8-dimethyl-5-(4-nitrophenyl)-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5aw). Yellow solid; mp 235-236 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, J = 8.7 Hz, 2H), 7.61-7.29 (m, 9H), 7.12 (d, J = 8.4 Hz, 2H), 5.44 (s, 1H), 4.16-4.02 (m, 2H), 3.30-3.25 (m, 2H), 2.51 (ABq, J^1 = 29.7, J^2 = 17.4, 2H), 2.24 (ABq, J^1 = 28.2, J^2 = 16.2, 2H), 1.13 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0, 193.8, 155.3, 152.8, 148.8, 146.3, 143.2, 140.0, 138.0, 128.8, 128.3, 127.8, 127.5, 127.1, 126.9, 123.5, 114.2, 106.8, 49.8, 40.8, 37.8, 32.3, 29.9, 28.2, 26.7.

8,8-Dimethyl-4-(naphthalene-1-carbonyl)-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ax). Yellow solid; mp 222-224 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83-7.77 (m, 2H), 7.50-7.20 (m, 4H), 7.00 (d, J = 6.3 Hz, 1H), 6.71 (d, J = 7.5 Hz, 2H), 6.55 (d, J = 7.8 H, 2H), 4.81 (s, 1H), 4.13-3.95 (m, 2H), 3.27-3.21 (m, 2H), 2.53-2.39 (m, 2H), 2.21-2.06 (m, 5H), 1.08 (s, 3H), 0.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.3, 194.7, 164.9, 154.4, 147.3, 143.2, 137.9, 135.3, 133.5, 130.2, 129.1, 128.4, 127.9, 127.5, 126.1, 125.7, 125.0, 124.6, 124.0, 116.4, 110.1, 50.0, 49.6, 40.9, 37.3, 32.2, 29.8, 28.2, 27.0, 20.8. HRMS (ESI$^+$): calcd for $C_{31}H_{29}NO_2S$ [M+H$^+$], 480.1992; found, 480.1992.

4-(2-Chlorobenzoyl)-8,8-dimethyl-5-phenyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5ay). Yellow solid; mp 112-114 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31-7.22 (m, 3H), 7.08-7.01 (m, 4H), 6.78 (d, J = 3.6 Hz, 2H), 4.84 (s, 1H), 4.17-3.94 (m, 2H), 3.32-3.16 (m, 2H), 2.63-2.40 (m, 2H), 2.25-2.09 (m, 2H), 1.07 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.9, 192.1, 155.3, 147.5, 145.6, 139.2, 129.8, 129.3,

127.7, 126.3, 126.0, 116.1, 108.4, 49.8, 49.5, 40.6, 37.4, 32.1, 29.8, 28.1, 26.8.

4-(2-Chloro-benzoyl)-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5az). Yellow solid; mp 206-207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32-7.23 (m, 2H), 7.09-7.05 (m, 1H), 6.84 (d, J = 7.8 Hz, 2H), 6.65 (d, J = 7.5 Hz, 3H), 4.80 (s, 1H), 4.17-3.94 (m, 2H), 3.30-3.16 (m, 2H), 2.47 (ABq, J^1 = 26.1 Hz, J^2 = 17.1 Hz, 2H), 2.28-2.09 (m, 5H), 1.08 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.0, 192.2, 155.2, 147.4, 142.7, 139.2, 135.5, 129.8, 129.3, 128.4, 128.1, 127.5, 126.3, 116.3, 108.5, 49.8, 49.5, 40.6, 36.9, 32.2, 29.7, 28.1, 26.9, 20.9. HRMS (ESI$^+$): calcd for $C_{27}H_{26}ClNO_2S$ [M+H$^+$], 464.1446; found, 464.1453.

4-Acetyl-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo [3,2-*a*]quinolin-6-one (5ba). Yellow solid; mp 204-206 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12 (d, J = 7.8 Hz, 2H), 7.01 (d, J = 7.8 Hz, 2H), 5.14 (s, 1H), 4.12-4.04 (m, 1H), 3.91-3.82 (m, 1H), 3.26-3.14 (m, 2H), 3.49-2.37 (m, 2H), 2.25-2.22 (m, 5H), 2.10 (s, 3H), 1.08 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.1, 195.3, 152.4, 148.1, 142.3, 135.8, 128.9, 127.6, 115.8, 108.5, 49.9, 49.3, 40.6, 36.7, 32.2, 29.6, 28.1, 27.0, 26.9, 20.9. HRMS (ESI$^+$): calcd for $C_{22}H_{25}NO_2S$ [M+H$^+$], 368.1679; found, 368.1685.

4-(2,2-Dimethylpropionyl)-8,8-dimethyl-5-*p*-tolyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5bb). White solid; mp 277-278 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.98 (s, 4H), 5.77 (s, 1H), 3.97-3.93 (m, 2H), 3.15-3.10 (m, 2H), 2.47-2.24 (m, 7H), 1.15-1.09 (m, 12H), 0.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.4, 195.5, 155.2, 148.9, 142.2, 135.4, 128.9, 126.5, 115.6, 105.8, 50.0, 49.4, 43.1, 40.5, 34.4, 34.2, 32.3, 30.2, 28.2, 27.6, 26.59, 26.50, 20.8. HRMS (ESI$^+$): calcd for $C_{25}H_{31}NO_2S$ [M+H$^+$], 410.2148; found, 410.2154.

4-Benzoyl-5-cyclohexyl-8,8-dimethyl-1,2,5,7,9-pentahydro-thiazolo[3,2-*a*]quinolin-6-one (5bc). Yellow solid; mp 147-149 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, J = 7.5 Hz, 2H), 7.42-7.38 (m, 3H), 5.29 (s, 1H), 4.17-3.98 (m, 2H), 3.15-3.11 (m, 2H), 2.52 (s, 2H), 2.33 (s, 2H), 1.52-1.37 (m, 4H), 1.25 (s, 4H), 1.16 (d, J = 6 Hz, 6H), 1.03-0.76 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.7, 195.4, 153.2, 149.3, 139.0, 130.5, 128.2, 128.1, 113.2, 106.6, 50.2, 49.5, 46.0, 41.0, 37.1, 37.0, 32.1, 30.4, 29.0, 28.4, 27.8, 27.2, 27.1, 26.3.

4-(Furan-2-carbonyl)-5-isopropyl-8,8-dimethyl-1,2,5,7,9-pentahydrothiazolo[3,2-*a*]quinolin-6-one (5bf). Yellow solid; mp 203-205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.20 (s, 1H), 6.48 (s, 1H), 4.79 (d, J = 2.7 Hz, 1H), 4.02-3.98 (m, 2H), 3.14-3.09 (m, 2H), 2.56-2.39 (m, 2H), 2.33-2.25 (m, 2H), 1.70-1.62 (m, 1H), 1.17 (s, 3H), 1.15 (s, 3H), 0.74 (d, J = 5.4 Hz, 3H), 0.66 (d, J = 5.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.8, 179.1, 155.8, 153.5, 149.7, 144.7, 116.9, 113.4, 111.6, 106.8, 50.2, 49.4, 40.9, 36.2, 35.2, 31.9, 30.4, 28.0, 27.0, 18.7, 17.9.

General procedure for the synthesis of 5,6,7,8-tetrasubstituted-2,3-dihydro-*7H*-thiazolo[3,2-*a*]pyridines 7. A similar procedure as for compounds **5** was employed. A mixture of α-enolic dithioesters **1** (0.5 mmol), cysteamine **2** (0.5 mmol), 2.7 ml water and 0.3 ml PEG-400 was heated at 110 °C till the formation of cyclic N,S-acetal (monitored by TLC), followed by addition of aldehyde **3** (0.5 mmol) and acetyl acetone **7** (0.5 mmol). The reaction mixture was further stirred for 24 h. Then the reaction was quenched with distilled water followed by extraction with DCM. Finally, the desired compound was isolated by preparative chromatography using hexane-ethylacetate (65:35) as mobile phase.

1-(8-Benzoyl-5-methyl-7-phenyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6-yl)-ethanone (7a). Yellow solid; mp 150-152 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.39 (m, 5H), 7.12 (d, J = 6.6 Hz, 3H), 6.80-6.78 (m, 2H), 5.12 (s, 1H), 4.16-4.01 (m, 2H), 3.14 (t, J = 7.2 Hz, 2H), 2.50 (s, 3H), 2.15 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.4, 194.0, 154.1, 145.0, 143.4, 139.7, 130.2, 128.4, 128.2, 127.2, 126.59, 126.50, 116.2, 106.8, 50.2, 41.6, 29.9, 27.9, 17.1.

1-(8-Benzoyl-5-methyl-7-p-tolyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6-yl)-ethanone (7b). Yellow solid; mp 133-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (d, J = 7.2 Hz, 5H), 6.93 (d, J = 7.5 Hz, 2H), 6.67 (d, J = 7.8 Hz, 2H), 5.07 (s, 1H), 4.14-3.99 (m, 2H), 3.11 (t, J = 7.2 Hz, 2H), 2.48 (s, 3H), 2.23 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.6, 194.1, 154.1, 143.3, 142.1, 139.8, 136.2, 130.2, 129.1, 128.2, 127.3, 126.4, 116.4, 107.1, 50.3, 41.2, 29.9, 28.0, 20.9, 17.2.

1-[8-(Benzo[1,3]dioxole-5-carbonyl)-5-methyl-7-phenyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6-yl]-ethanone (7c). Yellow solid; mp 154-156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.18-7.10 (m, 3H), 7.02-6.96 (m, 2H), 6.89-6.78 (m, 3H), 6.00 (s, 2H), 5.19 (s, 1H), 4.19-3.97 (m, 2H), 3.09 (t, J = 7.2 Hz, 2H), 2.50 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.4, 192.9, 153.2, 149.6, 147.6, 145.0, 143.8, 133.6, 128.5, 126.6, 126.4, 122.5, 115.7, 108.2, 107.9, 107.1, 101.4, 50.3, 41.8, 30.0, 28.0, 17.2.

1-[8-(4-Chloro-benzoyl)-5-methyl-7-phenyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6-yl]-ethanone (7d). Yellow solid; mp 196-198 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.32 (m, 4H), 7.20-7.13 (m, 3H), 6.81 (d, J = 6.0 Hz, 2H), 5.06 (s, 1H), 4.18-4.02 (m, 2H), 3.15 (t, J = 7.2 Hz, 2H), 2.48 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.5, 192.8, 154.8, 144.9, 143.1, 138.2, 136.3, 128.8, 128.65, 128.60, 126.8, 126.5, 116.7, 106.7, 50.4, 41.7, 30.1, 28.1, 17.2.

1-[8-(Furan-2-carbonyl)-5-methyl-7-phenyl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6-yl]-ethanone (7e). Yellow solid; mp 162-164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 (s, 1H), 7.20-7.02 (m, 6H), 6.49 (d, J = 1.8 Hz, 1H), 5.91 (s, 1H), 4.05 (t, J = 6.8 Hz, 2H), 3.12 (t, J = 7.2 Hz, 2H), 2.44 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.7, 177.7, 156.9, 153.7, 145.2, 144.3, 142.8, 128.6, 126.5, 126.3, 117.6, 117.2, 112.0, 105.9, 50.3, 39.2, 30.2, 28.0, 17.0.

Acknowledgements

We gratefully acknowledge the financial support from the Science and Engineering Research Board (Grant No. SB/S1/OC-30/2013) and the Council of Scientific and Industrial Research (Grant No. 02(0072)/12/EMR-II), New Delhi, India. A.N. and G.K.V. are thankful to the UGC, and B.J.R. G.S. and A.S. are thankful to the CSIR, New Delhi, for research fellowship. K.R. is highly grateful to DAAD and George-August-Universität-Göttingen for financial support as DAAD fellowship.

† Dedication

This paper is dedicated to Prof. Ganesh Pandey on the occasion

of his 60th birthday.

Notes and references

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†Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectra of all compounds. CCDC reference numbers 960941 (**5ar**), 1012571 (**5ax**) and 1012297 (**5ba**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

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