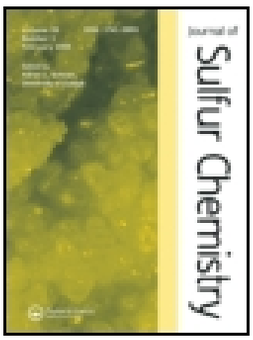

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# Yield of benzothiazine derivatives and catalysis by heteropolyacids

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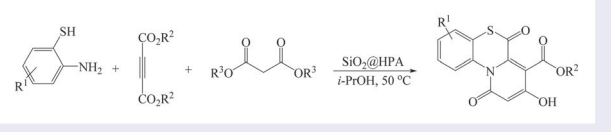
**ABSTRACT**

An efficient heteropolyacid-catalyzed reaction for the synthesis of benzothiazine derivatives is reported. In this transformation, $H_3PW_{12}O_{40}$ was employed as a catalyst in a reaction involving 2-aminobenzenethiols, acetylenic esters, and malonate esters. Optimum conditions are developed in *i*-PrOH at 50˚C for 7 h.

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**KEYWORDS**
Heteropolyacid; multicomponent reaction; heterogeneous catalyst; 1; 4-benzothiazine; heterocycles



## 1. Introduction

Multicomponent reactions (MCR) are efficient methods in diversity-oriented synthesis of heterocycles.[1–3] Among the various types of MCR, reactions promoted by catalysts have served as powerful tools for the rapid and efficient syntheses of highly demanding heterocyclic compounds.[4,5] In particular, heteropolyacids (HPAs)-catalyzed reactions have gained considerable interest for the synthesis of heterocyclic compounds.[6] Among the heterocycles, 1,4-benzothiazine derivatives possess numerous biological activities such as antibiotic, anticancer, antiviral, antifungal, antimicrobial, antiarrhythmic, and anti HIV antiallergic.[7,8] 1,4-Benzothiazine structures are typically synthesized by cyclocondensation of 2-aminobenzothiazole with α, β-unsaturated acids or esters, electron deficient alkynes; cyclocondensations of 2-aminobenzothiaoles with $\alpha$-haloketones; condensation and oxidative cyclization of N-unsubstituted and N,N-dialkyldithioanilines with 1,3-dicarbonyls or esters; ring expansions of benzothiazolines by using different oxidants such as iodine and sulfuryl chloride.[7,9–13] Yavari and coworkers have reported a novel route for the synthesis of benzoxazine and quinioxaline derivatives in a reaction involving 2-aminophenols or 1,2-benzene diamine, acetylenic esters, and malonyl chloride. While the importance of this reaction cannot be overstated, the main drawbacks of this protocol are using malonyl chloride and chlorinated solvent. As part of our ongoing research toward heterocycles syntheses,[14–17] we report a simple and greener protocol for the preparation

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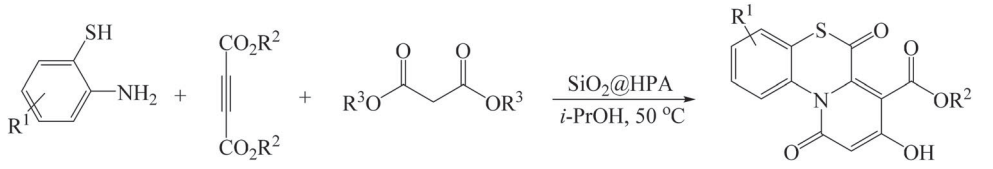



**Scheme 1.** Synthesis of 1,4-benzothiazine derivatives.

of the 1,4-benzothiazine skeletons from readily available 2-aminobenzenethiols, acetylenic esters, and malonate esters catalytic in HPAs (Scheme 1).

## 2. Results and discussion

The catalytic reaction was initially examined (2-aminobenzenethiol (**1a**), dimethyl acetylenedicarboxylate (**2a**, DMAD), and dimethyl malonate (**3a**)) in the presence of $H_4PMo_{12}O_{40}$ as a model reaction to assess the reaction efficiency. Stirring in toluene at 50°C for 4 h gave **4a** in 11% yield. To develop the reaction conditions, a variety of catalysts and solvents were examined (Table 1). No desired product formation took place in the absence of a HPA source even at higher temperatures and for longer reaction times, and methyl-2-(3-oxo-3,4-dihydro-2H-benzo[b][1,4]thiazin-2-ylidene)acetate was obtained (**5**) in 93% yield instead (Table 1, Entry 14). This result supports the suggested mechanism pathway. The influence of the different metals on the HPAs efficiency was then examined (Table 1, Entries 1–5). The study indicated that HPAs with tungsten as central atom resulted in comparatively higher yields than those composed of molybdenum, which is most likely due to the greater acidity of W-containing HPA.[18] A modest decrease in yield occurred using Cs salt of HPA (Table 1, Entry 6). Supported $H_3PW_{12}O_{40}$ on conventional amorphous silica required longer reaction times to give the desired product in comparable yields (Figure 1 and Table 1, Entry 7). It is worth mentioning that silica materials alone as the catalyst did not promote the desired product formation (not shown in Table 1).

Reactions conducted in alcoholic solvents resulted in high conversions (Table 1, Entries 2, 7–8). Reaction in polar-aprotic solvents occurred to lower conversions, likely due to the leaching of catalyst (Table 1, Entries 9–10). Reaction conducted in an etheric solvent such as THF occurred to low conversion (Table 1, Entry 12). It is worth mentioning that the desired product obtained only in 22% yield when deionized water was used as the solvent (Table 1, Entry 13). The study indicated that the presence of the catalyst was necessary to form the desired product (Table 1, Entry 14). Finally, a catalyst loading screen indicated that the yield remained almost unchanged by decreasing the catalyst amount to 60 mg; however, the yield was observed to decrease as the catalyst amount reduced further (Table 1, Entries 15–16).

The optimum reaction conditions proved to be effective in the preparation of a number of substituted 1,4-benzothiazines (Table 2). Electron-natural substrates **1a–1b** afforded the desired products in good yields (© 2016 Tom Stewart, Entries 1–2). 2-aminobenzenethiol containing chloro group gave the corresponding product in comparatively lower yields (Table 2, Entries 3–4). The reactions conducted with methyl substituted 2-aminobenzenethiol proceeded in high conversion (Table 2, Entries 5–6). Reaction of

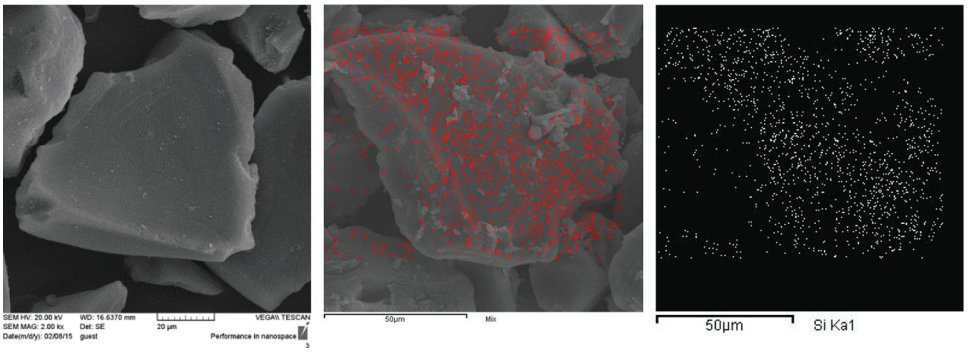
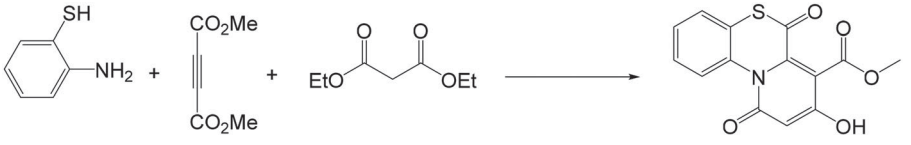



**Figure 1.** SEM of silica (left), SEM of supported HPA on silica (middle and right).

**Table 1.** Optimization of the reaction conditions[a].



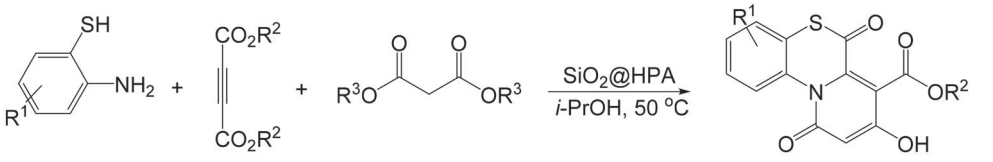

**1a** **2a** **3a** **4a**

| Entry | Catalyst | Solvent | Yield (%) |
|---|---|---|---|
| 1 | $H_4SiW_{12}O_{40}$ | *i*-PrOH | 50 |
| 2 | $H_3PW_{12}O_{40}$ | *i*-PrOH | 86 |
| 3 | $H_4PMo_{12}O_{40}$. | *i*-PrOH | 48 |
| 4 | $H_3PMo_{10}W_2O_{40}$ | *i*-PrOH | 62 |
| 5 | $H_4SiMo_{12}O_{40}$ | *i*-PrOH | 37 |
| 6 | $Cs_2HPW_{12}O_{40}$ | *i*-PrOH | 39 |
| 7 | $H_3PW_{12}O_{40}$-Silica | *i*-PrOH | 84[b] |
| 8 | $H_3PW_{12}O_{40}$ | EtOH | 71 |
| 9 | $H_3PW_{12}O_{40}$ | DMSO | traces |
| 10 | $H_3PW_{12}O_{40}$ | DMF | traces |
| 11 | $H_3PW_{12}O_{40}$ | Toluene | 23 |
| 12 | $H_3PW_{12}O_{40}$, | THF | 13 |
| 13 | $H_3PW_{12}O_{40}$, | $H_2O$ | 22 |
| 14 | – | *i*-PrOH | trace[c] |
| 15 | $H_3PW_{12}O_{40}$-Silica | *i*-PrOH | 84[d] |
| 16 | $H_3PW_{12}O_{40}$-Silica | i-PrOH | 70[e] |

[a]For all entries except stated otherwise: 1a (1.0 mmol), 2a (1.0 mmol), 3a (3.0 mmol), catalyst (0.1 mmol), solvent (3 mL), 50°C, 4 h.
[b]h, 100 mg supported catalyst.
[c]**5** was obtained in 96% yield.
[d]7 h, 60 mg supported catalyst.
[e]7 h, 50 mg supported catalyst.

electron-rich aminobenzenethiol occurred to excellent conversion (Table 2, Entry 7). Substrate containing bromo moiety was also tolerated. Notably, the tolerance for bromide on the aromatic ring offers an opportunity for subsequent cross-coupling, facilitating expedient synthesis of highly complex 1,4-bezoxthiazines (Table 2, Entry 8). This reaction was sensitive to steric effects as 2-amino-6-(tert-butyl)benzenethiol did not give the desired product (not shown in Table 2); however, 2-amino-4-(tert-butyl)benzenethiol (**1i)**

**Table 2.** Synthesis of 1,4-benzothiazine derivatives[a].




**1** $R^2$ = Me, **2a**; $R^2$ = Et, **2b**; $R^2$ = *t*-Bu, **2c** **3** **4**

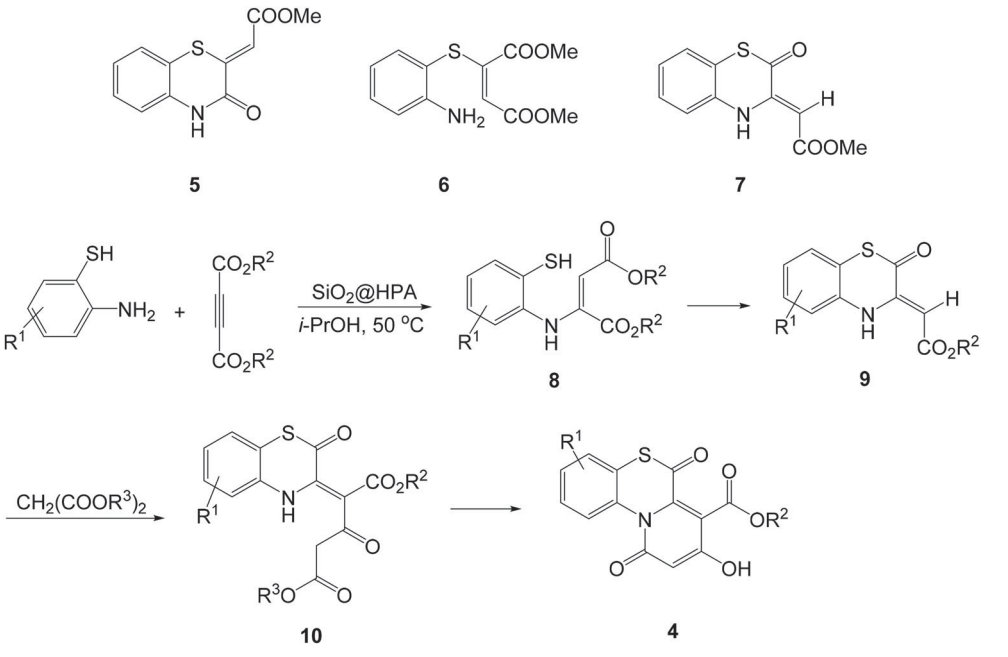
| Entry | Amine | $R^1$ | 2 | Malonate | $R^2$ | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | **2a** | **3a** | Et, Et | **4a**, 89 |
| 2 | **1b** | $C_4H_4$ | **2a** | **3a** | Et, Et | **4b**, 92 |
| 3 | **1c** | 5-Cl | **2a** | **3a** | Et, Et | **4c**, 85 |
| 4 | **1d** | 4-Cl | **2a** | **3a** | Et, Et | **4d**, 82 |
| 5 | **1e** | 5-$CH_3$ | **2a** | **3a** | Et, Et | **4e**, 89- |
| 6 | **1f** | 4-$CH_3$ | **2a** | **3a** | Et, Et | **4f**, 90 |
| 7 | **1g** | 4-$OCH_3$ | **2a** | **3a** | Et, Et | **4g**, 96 |
| 8 | **1h** | 4-Br | **2a** | **3a** | Et, Et | **4h**, 81 |
| 9 | **1i** | 4-*t*-Bu | **2a** | **3a** | Et, Et | **4i**, 87 |
| 10 | **1a** | H | **2b** | **3a** | Et, Et | **4j**, 86 |
| 11 | **1a** | H | **2c** | **3a** | Et, Et | **4k**, 92 |
| 12 | **1a** | H | **2a** | **3b** | Me, Me | **4a**, 69 |
| 13 | **1a** | H | **2a** | **3c** | Bn, Bn | **4a**, 54 |
| 14 | **1a** | H | **2a** | **3d** | *i*-Pr, *i*-Pr | **4a**, 89 |
| 15 | **1a** | H | **2a** | **3e** | *t*-Bu, *t*-Bu | **4a**, 80 |
| 16 | **1a** | H | **2a** | **3f** | H, H | **4a**, 60 |
| 17 | **1a** | H | **2a** | **3a** | Et, Et | **4a**, 87[d] |
| 18 | **1a** | H | **2a** | **3a** | Et, Et | **4a**, 80 |
| 19 | **1a** | H | **2a** | **3a** | Et, Et | **4a**, 67 |

[a]For all entries except stated otherwise: **1** (1.0 mmol), **2** (1.0 mmol), **3** (3.0 mmol), catalyst (60 mg), in *i*-PrOH (3 mL) at 50˚C for 7 h.
[b]1.0 mmol of diethyl acetylenedicarboxylate (**2b**) was used.
[c]At 100°C for 11 h.
[d]Entries 17–19 indicate the yield of the product in recycling tests, second through fourth runs.



afforded the desired product in acceptable yields (Table 2, Entry 9). The presence of electron-withdrawing groups such as nitro or cyano on 2-aminobenzenethiol ring was not compatible with this transformation. Diethyl and di-*tert*-butyl acetylenedicarboxylates also afforded the corresponding 1,4-benzothiazine structures in good yields (Table 2, Entries 10–11). Other malonate esters were also examined and gave the desired product in acceptable yields; however, diethyl malonate (**3a**) was selected as the malonate of choice based on the cost and efficiency (Table 2, Entries 12–15). Malonic acid (**3f**) gave the desired product in competitively lower yield even at higher temperatures (Table 2, Entries 16).

The recyclability of the heterogeneous catalyst is one of the most important issues for practical applications. For this reason, the recyclability of the catalyst was then examined using the model reaction (Table 2, Entries 17–19). After the completion of the reaction, the catalyst was recovered by filtration, followed by washing with ethanol (10 mL × 3). After drying (80°C for 6 h in vacuo), the catalyst was reused directly for the next reaction. The catalytic activity remained almost unchanged after three catalytic cycles, indicating that the catalyst is stable and can be regenerated for repeated use. However, the yield decreased when the catalyst was used for the fourth run.




**Scheme 2.** Proposed mechanism for the synthesis of 1,4-benzothiazine derivatives.

As reported in previous reports, compounds **5** and **6** are obtained by treating **1a** and **2a**.[19,20] Liso and coworkers have reported that the thiol group reacts first, in contrast with results reported by Fomum, et al. When we treated **1a** with **2a** in the absence of the catalyst, **5** was obtained in 96% yield (Table 1, Entry 14), which is in favor of Liso's results. However, the reaction conducted with **1a** and **2a** using $SiO_2@H_3PW_{12}O_{40}$ resulted in formation of methyl-2-(2-oxo-2H-benzo[b][1,4]thiazin-3(4H)-ylidene)acetate (**7**) in 93% yield, which indicates the reaction starts with the amine attack. It could be deduced that the presence of catalyst is necessary to form the intermediate **8** and **9**. We could not isolate the intermediate **10** from the reaction mixture. Based on these findings, a tentative mechanism for this transformation is proposed in Scheme 2. It is conceivable that the initial event is the formation of intermediate **8,** which is converted to alkylidene **9**. This adduct is subsequently attacked by malonate ester to produce **10**, followed by cyclization reaction, alcohol elimination, and keto-enol tautomerism to generate the desired product.

In conclusion, we have described a green and efficient procedure for the synthesis of 1,4-benzothiazine derivatives. To our knowledge, this work was the first example of the utilizing $SiO_2$@HPAs as reusable catalyst for the synthesis of 1,4-benzothiazines in a reaction involving 2-aminobenzenethiols, acetylenic esters, and dialkyl malonates. The optimized reaction conditions reported herein are compatible with the presence of functional groups such as OMe, Cl, Br, and *t*-Bu.

## 2.1. Experimental

All reagents were purchased from the Merck chemical companies and used without further purification. Products were characterized by different spectroscopic methods (FT–IR,

GC-Mass, and $^1$H NMR spectra), elemental analysis (CHN), and melting points. The NMR spectra were recorded in DMSO-$d_6$. $^1$H NMR spectra were recorded on a Bruker Avance DRX 500 MHz instrument. The chemical shifts ($\delta$) are reported in ppm relative to the TMS as internal standard. *J* values are given in Hz. IR (KBr) spectra were recorded on a Perkin-Elmer 781 spectrophotometer. Melting points were taken in open capillary tubes with a BUCHI 510 melting point apparatus and were uncorrected. The elemental analysis was performed using Heraeus CHN-O-Rapid analyzer. TLC was performed on silica gel polygram SIL G/UV 254 plates. Morphology and particle dispersion was investigated by scanning electron microscopy (SEM) (Cam scan MV2300).

### 2.1.1. General procedure for the preparation of $SiO_2$@$H_3PW_{12}O_{40}$

The HPAs were prepared by a hydrothermal synthesis method.[21] As an example, $H_4PMo_{12}O_{40}$ was prepared according to the following procedure: A mixture of phosphoric acid (0.98 g) and of molybdenum trioxide (14.4 g) was suspended in distilled $H_2O$ (150 mL) and the mixture stirred for 6 h at 80°C. After cooling to 20°C and removal of insoluble molybdates, the HPA solution was evaporated and dried at 85°C for 24 h to give orange crystals. Silica-supported HPA was prepared by the standard literature procedure.[22] A mixture of silica (DavisilTM, 200–425 mesh, 150) and HPA in $H_2O$–*i*-PrOH or MeCN was stirred at 25°C for 24 h. The catalyst was washed with deionized $H_2O$ and dried at 110°C for 12 h. The supported catalyst was then calcinated at 200°C for 3 h.

### 2.1.2. Typical procedure for preparation of 4

A mixture of acetylenic ester (1.0 mmol) and 2-aminobenzenethiol (1.0 mmol) was stirred at 0°C for 20 min. A solution of malonate source (3.0 mmol) and HPA (0.1 mmol or 100 mg of supported HPA) in *i*-PrOH (3 ml) was then added to the initial mixture in one portion. The resulting mixture was heated to 50°C for 7 h. After completion of the reaction, it was filtered and then diluted by EtOAc (5 mL) and saturated $NH_4Cl$ solution (5 mL). The mixture was stirred for additional 30 min and two layers were separated. The aqueous layer was extracted with EtOAc (7 mL × 3). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuum. The residue was purified by chromatography (silica gel, hexane:EtOAc 3:1) to give the pure product (see ESI for characterization data for all products).

***2.1.2.1. Methyl 8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4a).*** Pale yellow powder, m.p.: 267–270°C; yield: 0.27 g (89%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3490, 1745, 1675, 1620, 1533, 1226. $^1$H NMR (500.1 MHz, DMSO): $\delta_H$ = 3.76 (3 H, s, $OCH_3$), 6.18 (H, s, CH), 7.25–7.48 (3 H, m, 3 CH), 8.17 (H, d, $^3J$ = 6.7 Hz, CH), 12.06 (H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 53.7 ($OCH_3$), 105.2 (CH), 114.1 (C), 117.2 (CH), 120.4 (CH), 125.8 (CH), 127.4 (CH), 128.2 (C), 136.1 (C), 149.7 (C), 161.3 (C), 164.2 (C), 169.5 (C), 181.7 (C). MS: *m/z* (%) = 303 (M+, 5), 289 (26), 244 (43), 186 (49), 110 (67), 77 (100), 43 (12). Anal. Calcd for $C_{14}H_9NO_5S$ (303.29): C, 55.44; H, 2.99; N, 4.62. Found: C, 55.67; H, 3.17; N, 4.57%.

***2.1.2.2. Methyl 3-hydroxy-1,5-dioxo-1,5-dihydronaphtho[2,3-b]pyrido[1,2- d][1,4]thiazine-4-carboxylate (4b).*** Pale yellow powder, m.p.: 318–321°C; yield: 0.32 g (92%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3467, 1740, 1654, 1607, 1524, 1220. $^1$H NMR (500.1 MHz, DMSO):

$\delta_H$ = 3.84 (3 H, s, $OCH_3$), 6.12 (1 H, s, CH), 6.86 (1 H, s, CH), 7.19–7.28 (2 H, m, 2 CH), 7.51–7.63 (2 H, m, 2 CH), 8.19 (1 H, d, $^3J$ = 6.7 Hz, CH), 11.25 (1 H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 53.7 ($OCH_3$), 97.8 (CH), 111.3 (C), 122.2 (CH), 123.1 (CH), 126.4 (C), 126.8 (CH), 127.1 (C), 127.7 (C), 128.3 (CH), 130.2 (C), 131.0 (C), 139.7 (C), 154.1 (C), 162.8 (C), 165.4 (C), 171.6 (C), 180.9 (C). MS: *m/z* (%) = 353 (M+, 2), 339 (17), 294 (33), 236 (61), 127 (100), 110 (72). Anal. Calcd for $C_{18}H_{11}NO_5S$ (353.35): C, 61.19; H, 3.14; N, 3.96. Found: C, 61.36; H, 3.28; N, 4.03%.

***2.1.2.3. Methyl 3-chloro-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4] thiazine-7-carboxylate (4c).*** Pale yellow powder, m.p.: 289–292°C; yield: 0.29 g (85%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3467, 1751, 1647, 1607, 1524, 1213. $^1$H NMR (500.1 MHz, DMSO): $\delta_H$ = 3.82 (3 H, s, $OCH_3$), 6.17 (1 H, s, CH), 7.24 (1 H, d, $^3J$ = 7.0 Hz, CH), 7.41 (1 H, s, 1 CH), 8.27 (1 H, d, $^3J$ = 7.0 Hz, CH), 12.17 (1 H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 53.5 ($OCH_3$), 105.4 (CH), 116.7 (C), 123.2 (CH), 123.6 (CH), 125.4 (CH), 127.9 (C), 132.8 (C), 140.6 (C), 155.2 (C), 161.4 (C), 165.3 (C), 169.2 (C), 181.3 (C). MS: *m/z* (%) = 337 (M+, 2), 321 (14), 278 (24), 220 (35), 111 (100), 110 (78). Anal. Calcd for $C_{14}H_8ClNO_5S$ (337.73): C, 49.79; H, 2.39; N, 4.15. Found: C, 49.94; H, 2.46; N, 4.29%.

***2.1.2.4. Methyl 2-chloro-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4] thiazine-7-carboxylate (4d).*** Pale yellow powder, m.p.: 281–284°C; yield: 0.28 g (82%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3469, 1748, 1662, 1611, 1541, 1215. $^1$H NMR (500.1 MHz, DMSO): $\delta_H$ = 3.79 (3 H, s, $OCH_3$), 6.17 (1 H, s, CH), 7.27–7.38 (2 H, m, 2 CH), 8.07 (1 H, s, CH), 12.22 (1 H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 53.5 ($OCH_3$), 106.3 (CH), 115.6 (C), 119.2 (CH), 122.1 (CH), 130.4 (CH), 131.3 (C), 136.5 (C), 140.2 (C), 155.7 (C), 161.2 (C), 165.4 (C), 170.1 (C), 183.7 (C). MS: *m/z* (%) = 337 (M+, 2), 321 (28), 278 (37), 220 (40), 111 (100), 110 (78). Anal. Calcd for $C_{14}H_8ClNO_5S$ (337.73): C, 49.79; H, 2.39; N, 4.15. Found: C, 49.87; H, 2.58; N, 4.21%.

***2.1.2.5. Methyl 3-methyl-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4] thiazine-7-carboxylate (4e).*** Pale yellow powder, m.p.: 273–276°C; yield: 0.28 g (89%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3476, 1751, 1660, 1606, 1545, 1211. $^1$H NMR (500.1 MHz, DMSO): $\delta_H$ = 2.32 (3 H, s, $CH_3$), 3.72 (3 H, s, $OCH_3$), 6.15 (1 H, s, CH), 7.06 (1 H, d, $^3J$ = 6.8 Hz, CH), 7.12 (1 H, s, CH), 8.11 (1 H, d, $^3J$ = 6.9 Hz, CH), 12.06 (1 H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 20.4 ($CH_3$), 52.9 ($OCH_3$), 103.5 (CH), 116.3 (C), 118.5 (CH), 121.2 (CH), 126.7 (CH), 133.2 (C), 137.5 (C), 138.0 (C), 154.4 (C), 161.2 (C), 164.8 (C), 170.1 (C), 183.9 (C). MS: *m/z* (%) = 317 (M+, 3), 303 (14), 258 (37), 200 (41), 110 (100), 91 (56). Anal. Calcd for $C_{15}H_{11}NO_5S$ (317.32): C, 56.78; H, 3.49; N, 4.41. Found: C, 56.94; H, 3.59; N, 4.43%.

***2.1.2.6. Methyl 2-methyl-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4] thiazine-7-carboxylate (4f).*** Pale yellow powder, m.p.: 280–283°C; yield: 0.29 g (90%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3462, 1741, 1652, 1608, 1547, 1236. $^1$H NMR (500.1 MHz, DMSO): $\delta_H$ = 2.30 (3 H, s, $CH_3$), 3.80 (3 H, s, $OCH_3$), 6.11 (1 H, s, CH), 7.21–7.29 (2 H, m, 2 CH), 8.01 (1 H, s, CH), 11.97 (1 H, br s, OH). $^{13}$C NMR(125.7 MHz, DMSO): $\delta_C$ = 21.7 ($CH_3$), 53.5 ($OCH_3$), 106.1 (CH), 114.7 (C), 120.8 (CH), 123.4 (CH), 127.6 (CH), 133.1 (C), 135.6 (C), 139.6 (C), 154.7 (C), 161.3 (C), 164.9 (C), 171.8 (C), 184.5 (C). MS: *m/z* (%) = 317

(M+, 8), 303 (24), 258 (46), 200 (72), 110 (100), 91 (42). Anal. Calcd for $C_{15}H_{11}NO_5S$ (317.32): C, 56.78; H, 3.49; N, 4.41. Found: C, 57.05; H, 3.67; N, 4.40%.

***2.1.2.7. Methyl 8-hydroxy-2-methoxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4g).*** Pale yellow powder, m.p.: 302–305°C; yield: 0.32 g (96%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3457, 1747, 1656, 1607, 1546, 1211. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 3.65$ (3 H, s, $OCH_3$), 3.69 (3 H, s, $OCH_3$), 6.04 (1 H, s, CH), 6.79 (1 H, d, $^3J = 7.0$ Hz, CH), 7.14 (1 H, d, $^3J = 7.1$ Hz, CH), 7.76 (1 H, s, CH), 10.76 (H, br s, OH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 54.6$ ($OCH_3$), 56.1 ($OCH_3$), 98.6 (CH), 108.9 (CH), 112.6 (CH), 116.3 (C), 128.3 (CH), 129.7 (C), 137.6 (C), 154.4 (C), 157.8 (C), 160.2 (C), 167.0 (C), 172.5 (C), 184.8(C). MS: *m/z* (%) = 333 (M+, 2), 319 (12), 275 (35), 216 (47), 275 (35), 110 (69), 108 (100). Anal. Calcd for $C_{15}H_{11}NO_6S$ (333.31): C, 54.05; H, 3.33; N, 4.20. Found: C, 54.28; H, 3.52; N, 4.31%.

***2.1.2.8. Methyl 2-bromo-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4h).*** Pale yellow powder, D.p: 350°C; yield: 0.31 g (81%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3380, 1746, 1652, 1612, 1546, 1217. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 3.68$ (3 H, s, $OCH_3$), 6.02 (1 H, s, CH), 7.29 (1 H, d, $^3J = 6.8$ Hz, CH), 7.53 (1 H, d, $^3J = 6.9$ Hz, CH), 7.93 (1 H, s, CH), 11.87 (H, br s, OH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 54.7$ ($OCH_3$), 102.7 (CH), 116.7 (C), 120.6 (CH), 124.0 (C), 128.4 (CH), 129.7 (CH), 134.2 (C), 138.7 (C), 154.2 (C), 161.1 (C), 165.8 (C), 172.0 (C), 183.5 (C). MS: *m/z* (%) = 382 (M+, 5), 367 (14), 323 (37), 265 (52), 155 (52), 110 (100). Anal. Calcd for $C_{14}H_8BrNO_5S$ (382.182): C, 44.00; H, 2.11; N, 3.66. Found: C, 44.12; H, 2.27; N, 3.82%.

***2.1.2.9. Methyl 3-(tert-butyl)-8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4i).*** Pale yellow powder, m.p.: 316–319°C; yield: 0.31 g (87%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3380, 1751, 1656, 1611, 1547, 1223. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 1.32$ (9 H, s, 3 $CH_3$), 3.62 (3 H, s, $OCH_3$), 6.21 (1 H, s, CH), 7.26–7.37 (2 H, m, 2 CH), 7.96 (1 H, d, $^3J = 6.9$ Hz, CH), 11.79 (1 H, br s, OH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 27.4$ (3 $CH_3$), 45.1 (C), 56.4 ($OCH_3$), 103.8 (CH), 112.6 (C), 119.1 (CH), 121.5 (CH), 123.9 (CH), 133.5 (C), 137.2 (C), 145.1 (C), 154.7 (C), 162.5 (C), 166.1 (C), 171.7 (C), 183.3 (C). MS: *m/z* (%) = 359 (M+, 4), 345 (17), 301 (25), 242 (35), 133 (86), 110 (76), 57 (100). Anal. Calcd for $C_{18}H_{17}NO_5S$ (359.40): C, 60.16; H, 4.77; N, 3.90. Found: C, 60.32; H, 4.93; N, 4.05%.

***2.1.2.10. Ethyl 8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4j).*** Pale yellow powder, m.p.: 279–282°C; yield: 0.27 g (86%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3368, 1744, 1668, 1601, 1526, 1217. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 1.29$ (3 H, t, $^3J = 6.4$ Hz, $CH_3$), 4.27 (2 H, q, $^3J = 6.7$ Hz, $CH_2$), 6.14 (1 H, s, CH), 7.11 (1 H, t, $^3J = 7.0$ Hz, CH), 7.18 (1 H, t, $^3J = 7.1$ Hz, CH), 7.41 (1 H, d, $^3J = 6.7$ Hz, CH), 8.17 (1 H, d, $^3J = 6.8$ Hz, CH), 12.11 (1 H, s, OH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 15.2$ ($CH_3$), 62.6 ($CH_2$), 104.4 (CH), 112.7 (C), 122.1 (CH), 124.6 (CH), 124.8 (CH), 125.7 (CH), 135.1 (C), 137.5 (C), 152.6 (C), 161.8 (C), 165.4 (C), 173.5 (C), 183.6 (C). MS: *m/z* (%) = 317 (M+, 1), 289 (15), 245 (27), 186 (34), 110 (100), 77 (78). Anal. Calcd for $C_{15}H_{11}NO_5S$ (317.32): C, 56.78; H, 3.49; N, 4.41. Found: C, 56.95; H, 3.64; N, 4.38%.

***2.1.2.11. Tert-butyl 8-hydroxy-6,10-dioxo-6,10-dihydrobenzo[b]pyrido[1,2-d][1,4]thiazine-7-carboxylate (4k).*** Pale yellow powder, m.p.: 313–316°C; yield: 0.32 g (92%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3379, 1751, 1646, 1611, 1547, 1213. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 1.61$ (9 H, s, 3 $CH_3$), 6.16 (1 H, s, CH), 7.11–7.26 (3 H, m, 3 CH), 7.98 (1 H, d, $^3J = 6.8$ Hz, CH), 11.89 (1 H, s, OH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 29.8$ (3 $CH_3$), 80.2 (C), 101.8 (CH), 112.3 (C), 121.1 (CH), 122.5 (CH), 123.6 (CH), 123.9 (CH), 134.1 (C), 137.5 (C), 155.7 (C), 160.9 (C), 166.3 (C), 170.6 (C), 182.2 (C). MS: *m/z* (%) = 345 (M+, 2), 289 (19), 245 (33), 186 (51), 110 (69), 77 (86), 57 (100). Anal. Calcd for $C_{17}H_{15}NO_5S$ (345.37): C, 59.12; H, 4.38; N, 4.06. Found: C, 59.21; H, 4.56; N, 4.12%.

***2.1.2.12. Methyl-2-(2-oxo-2H-benzo[b][1,4]thiazin-3(4H)-ylidene)acetate (7).*** Yellow powder, m.p.: 143–146.5°C; yield: 0.22 g (93%). IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3371, 1740, 1628, 1531, 1134. $^1H$ NMR (500.1 MHz, DMSO): $\delta_H = 3.67$ (3 H, s, $OCH_3$), 6.87 (H, s, CH), 6.31 (H, d, $^3J = 6.7$ Hz, CH), 7.06–7.13 (2 H, m, 2 CH), 7.56 (H, d, $^3J = 7.1$ Hz, CH), 12.24 (H, br s, NH). $^{13}C$ NMR(125.7 MHz, DMSO): $\delta_C = 54.1$ ($OCH_3$), 111.8 (CH), 115.6 (CH), 119.9 (CH), 123.5 (CH), 134.1 (CH), 137.0 (C), 148.1 (C), 163.1 (C), 167.4 (C), 184.1 (C). Anal. Calcd for $C_{11}H_9NO_3S$ (235.26): C, 56.16; H, 3.86; N, 5.95. Found: C, 57.00; H, 4.41; N, 5.78%.

## Disclosure statement

No potential conflict of interest was reported by the author.

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