

One-pot synthesis of functionalized 4-oxo-2-thioxo-1,3-thiazinanes from primary amines, CS₂, and itaconic anhydride

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Abstract An efficient synthesis of 2-(3-alkyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acids is described via a three-component reaction between primary amines, CS₂, and itaconic anhydride.

Keywords Itaconic anhydride · 4-Oxo-2-thioxo-1,3-thiazinane · Multicomponent reaction · Carbon disulfide

Introduction

Dithiocarbamates have received considerable attention due to their numerous biological activities, their pivotal role in agriculture, and as linkers in solid-phase organic synthesis [1–6]. In fact, few methods for the synthesis of dithiocarbamates have been employed, and among them, reactions of amines with costly and toxic reagents, such as thiophosgene and isothiocyanates, have been reported [7–9]. Recently, one-pot and catalyst-free reaction of amines, CS₂ and alkyl halides, or α , β -unsaturated compounds, in water or under solvent-free conditions have been developed for synthesis of dithiocarbamates [10, 11].

Attempts to discover potent and selective antiviral or anticancer agents have resulted in the design of nucleoside analogues with modification of the heterocyclic moiety. Results show that the structure of the nucleobase can be changed considerably while retaining the biological activity [12, 13]. Sulfur analogues of uracil and thymine have been proposed, in which the N1 atom of the pyrimidine base has been replaced by a sulfur atom. 3,4-Dihydro-4-oxo-2-thio-2H-1,3-thiazine and its *N*-methyl and *N*-ethyl

derivatives have been reported as a sulfur analogue of uracil [14].

As part of our current studies on the development of new routes in heterocyclic synthesis [15–17], we wish to report a new synthetic route to 2-(3-alkyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acids (**3**), as a precursor of new sulfur analogues of uracil, via the reaction between primary amines (**1**), CS₂, and itaconic anhydride (**2**) in MeCN (Scheme 1).

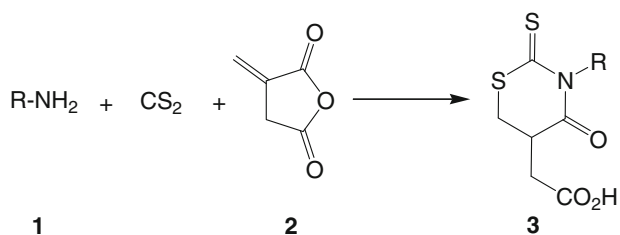
Results and discussion

A simple mixing of primary amines, carbon disulfide, and itaconic anhydride in MeCN produced 2-(3-alkyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acids (**3**) in 68–86% yields (see Scheme 1). This three-component reaction is completed in about 1 h at r.t. The structures of compounds **3a–k** were deduced from their IR, ¹H, and ¹³C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m/z* values. The ¹H NMR spectrum of **3a** in CDCl₃ has two (AB)X systems for the two methylene groups of the CH₂CHCH₂ moiety, together with a characteristic AB system for the CH₂N group. The methine proton appears as a multiplet at $\delta = 3.47 - 3.53$.

A tentative mechanism for this transformation is proposed in Scheme 2. It is conceivable that, the initial event is the formation of the alkylammonium dithiocarbamate salt **4** from the amine and CS₂, which subsequently attacks to itaconic anhydride to generate the acyclic dithiocarbamate **5**. This intermediate undergoes cyclization to produce **3** and the released amine reacts with CS₂ to initiate the next cycle of the reaction (Scheme 2).

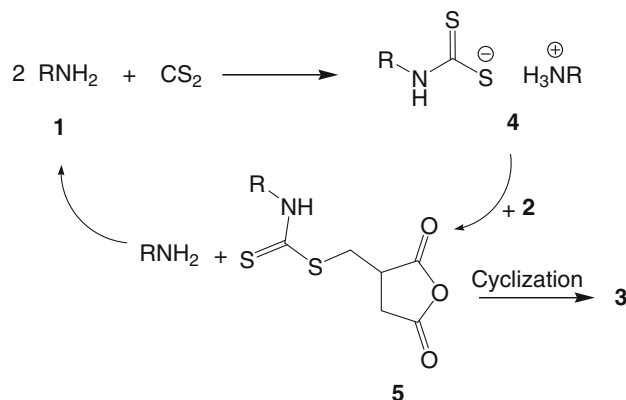
When arylamines or sterically hindered alkylamines were used, only a simple addition of the amine to anhydride moiety

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| 1, 3 | R | Yield/ % of 3 |
|------|--|---------------|
| a | Bn | 80 |
| b | 4-Me-C ₆ H ₄ -CH ₂ | 77 |
| c | 4-MeO-C ₆ H ₄ -CH ₂ | 80 |
| d | 4-Cl-C ₆ H ₄ -CH ₂ | 78 |
| e | 1-Naphthyl-CH ₂ | 81 |
| f | Allyl | 86 |
| g | <i>n</i> -Bu | 80 |
| h | 2-Ethylhexyl | 68 |
| i | HOCH ₂ CH ₂ | 75 |
| j | H(OCH ₂ CH ₂) ₂ | 70 |
| k | PhNH | 74 |

Scheme 1 Synthesis of 2-(3-alkyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acids



Scheme 2 Proposed mechanism for the synthesis of 2-(3-alkyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acids

of **2** was observed. Presence of a base such as Et₃N or DBU showed no significant effect on these results.

In conclusion, we have described reaction of itaconic anhydride with alkylammonium dithiocarbamates, produced in situ from primary amines and CS₂, which leads to functionalized 4-oxo-2-thioxo-1,3-thiazinanes. These products contain a dithiocarbamate moiety that has been found to play an important role when incorporated in a variety of biologically active agents and can be used as a precursor of new sulfur analogues of uracil. Neutral condition of the reaction, simple mixing of starting materials, and easy work up are the advantages of this procedure.

Experimental

All purchased solvents and chemicals were of analytical grade and used without further purification. Melting points

and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. The ¹H and ¹³C NMR spectra were recorded on a BRUKER DRX-500 AVANCE instrument using CDCl₃ as applied solvent and TMS as internal standard at 500 and 125.7 MHz, respectively. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer.

General procedure

A solution of 0.22 g of itaconic anhydride (**2**, 2 mmol) in 5 mL of MeCN was slowly added to a stirred solution of amine (**1**, 2.0 mmol) and 0.91 g of CS₂ (12 mmol) in 5 mL of MeCN at room temperature. The reaction mixture was then stirred for about 1 h. The solvent was removed under reduced pressure, and the yellow residue was purified by flash chromatography over silica gel (Merck 230–400 mesh) using an *n*-hexane–AcOEt mixture (4:1) as eluant.

2-(3-Benzyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acid (**3a**)

Yellow oil, yield: 0.47 g (80%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3080 (br), 1705 (C=O), 1700 (C=O), 1410, 1334, 1260, 1165, 1135, 1023, 970, 940, 795. ¹H NMR (500 MHz, CDCl₃): δ = 2.70 (dd, 1H, ³*J* 6.6 Hz, ²*J* 17.4 Hz, CH₂), 2.81 (dd, 1H, ³*J* 4.0 Hz, ²*J* 12.9 Hz, CH₂), 3.00 (dd, 1H, ³*J* 5.7 Hz, ²*J* 17.4 Hz, CH₂), 3.29 (dd, 1H, ³*J* 11.8 Hz, ²*J* 12.9 Hz, CH₂), 3.47–3.53 (m, 1H, CH), 5.51 (d, ²*J* 14.5 Hz, 1H, CH₂N), 5.71 (d, 1H, ²*J* 14.5 Hz, CH₂N), 7.12–7.25 (m, 5H, C₆H₅), 9.62 (br s, 1H, OH). ¹³C NMR (125.7 MHz, CDCl₃): δ = 29.5 (CH₂), 34.6 (CH₂), 40.0 (CH), 49.9 (CH₂N), 128.2 (2CH), 128.5 (2CH), 129.1 (CH), 133.5 (C), 168.5 (CON), 175.8 (CO₂), 200.0 (C=S). EI-MS: 295 (M⁺, 12), 262 (45), 148 (15), 105 (30), 91 (100). Anal. Calcd (%) for C₁₃H₁₃NO₃S₂ (295.38): C, 52.86, H, 4.44, N, 4.74. Found: C, 52.70, H, 4.35, N, 4.80.

2-[3-(4-Methylbenzyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (**3b**)

Yellow oil, yield: 0.48 g (77%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3040 (br), 1702 (C=O), 1690 (C=O), 1409, 1334, 1262, 1161, 1135, 1024, 973, 938, 797. ¹H NMR (500 MHz, CDCl₃): δ = 2.31 (s, 3H, Me), 2.71 (dd, 1H, ³*J* 6.6 Hz, ²*J* 17.4 Hz, CH₂), 2.82 (dd, 1H, ³*J* 4.0 Hz, ²*J* 12.9 Hz, CH₂), 3.00 (dd, 1H, ³*J* 5.7 Hz, ²*J* 17.4 Hz, CH₂), 3.29 (dd, 1H, ³*J* 11.9 Hz, ²*J* 12.9 Hz, CH₂), 3.46–3.52 (m, 1H, CH), 5.55 (d, 1H, ²*J* 14.3 Hz, CH₂N), 5.69 (d, 1H, ²*J* 14.3 Hz, CH₂N), 7.10 (d, 2H, ³*J* 7.6 Hz, C₆H₄), 7.21 (d, 2H, ³*J* 7.6 Hz, C₆H₄), 9.52

(br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 21.0 (Me), 29.7 (CH_2), 34.7 (CH_2), 39.9 (CH), 49.7 (CH_2N), 128.0 (2CH), 129.0 (2CH), 133.0 (C), 137.1 (C), 168.6 (CON), 175.9 (CO_2), 199.9 (C=S). EI-MS: 309 (M^+ , 10), 276 (20), 163 (25), 119 (15), 105 (100). Anal. Calcd (%) for $\text{C}_{14}\text{H}_{15}\text{NO}_3\text{S}_2$ (309.40): C, 54.35, H, 4.89, N, 4.53. Found: C, 54.29, H, 4.81, N, 4.55.

2-[3-(4-Methoxybenzyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3c)

Yellow oil, yield: 0.52 g (80%). IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3030 (br), 1705 (C=O), 1698 (C=O), 1502, 1420, 1334, 1297, 1242, 1167, 1024, 968, 928. ^1H NMR (500 MHz, CDCl_3): δ_{H} = 2.70 (dd, 1H, 3J 5.9 Hz, 2J 17.3 Hz, CH_2), 2.78 (dd, 1H, 3J 4.3 Hz, 2J 13.0 Hz, CH_2), 2.96 (dd, 1H, 3J 6.3 Hz, 2J 17.3 Hz, CH_2), 3.26 (dd, 1H, 3J 12.0 Hz, 2J 13.0 Hz, CH_2), 3.44–3.50 (m, 1H, CH), 3.76 (s, 3H, MeO), 5.50 (d, 1H, 2J 14.3 Hz, CH_2N), 5.65 (d, 1H, 2J 14.3 Hz, CH_2N), 6.81 (d, 2H, 3J 8.6 Hz, C_6H_4), 7.28 (d, 2H, 3J 8.6 Hz, C_6H_4), 10.15 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 30.6 (CH_2), 33.7 (CH_2), 40.8 (CH), 50.3 (CH_2N), 56.1 (MeO), 114.7 (2CH), 129.2 (C), 130.7 (2CH), 159.8 (C), 169.6 (CON), 177.2 (CO_2), 200.9 (C=S). EI-MS: 325 (M^+ , 10), 292 (32), 179 (40), 135 (50), 121 (100). Anal. Calcd (%) for $\text{C}_{14}\text{H}_{15}\text{NO}_4\text{S}_2$ (325.40): C, 51.68, H, 4.65, N, 4.30. Found: C, 51.80, H, 4.62, N, 4.44.

2-[3-(4-Chlorobenzyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3d)

Yellow oil, yield: 0.52 g (78%). IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3040 (br), 1700 (C=O), 1690 (C=O), 1395, 1340, 1277, 1150, 1034, 940, 770. ^1H NMR (500 MHz, CDCl_3): δ = 2.70 (dd, 1H, 3J 6.7 Hz, 2J 17.2 Hz, CH_2), 2.85 (dd, 1H, 3J 4.5 Hz, 2J 12.7 Hz, CH_2), 3.00 (dd, 1H, 3J 5.6 Hz, 2J 17.2 Hz, CH_2), 3.30 (dd, 1H, 3J 11.9 Hz, 2J 12.7 Hz, CH_2), 3.45–3.52 (m, 1H, CH), 5.55 (d, 1H, 2J 14.5 Hz, CH_2N), 5.70 (d, 1H, 2J 14.5 Hz, CH_2N), 7.16 (d, 2H, 3J 7.7 Hz, C_6H_4), 7.29 (d, 2H, 3J 7.7 Hz, C_6H_4), 9.70 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 29.5 (CH_2), 34.6 (CH_2), 40.0 (CH), 49.9 (CH_2N), 128.2 (2CH), 129.4 (2CH), 134.1 (C), 136.7 (C), 168.7 (CON), 175.8 (CO_2), 199.6 (C=S). EI-MS: 332 (M^+ +2, 2), 330 (M^+ , 7), 297 (27), 184 (100), 140 (40). Anal. Calcd (%) $\text{C}_{13}\text{H}_{12}\text{ClNO}_3\text{S}_2$ (329.82): C, 47.34, H, 3.67, N, 4.25. Found: C, 47.20, H, 3.80, N, 4.55.

2-[3-(1-Naphthylmethyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3e)

Yellow crystals, yield: 0.56 g (81%), mp 165–166 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3025 (br), 1700 (C=O), 1686 (C=O), 1406, 1341, 1319, 1256, 1166, 1109, 1072, 961, 766, 761.

^1H NMR (500 MHz, CDCl_3): δ = 2.77 (dd, 1H, 3J 6.6 Hz, 2J 17.4 Hz, CH_2), 2.91 (dd, 1H, 3J 4.1 Hz, 2J 12.9 Hz, CH_2), 3.02 (dd, 1H, 3J 5.6 Hz, 2J 17.4 Hz, CH_2), 3.43 (dd, 1H, 3J 11.9 Hz, 2J 12.9 Hz, CH_2), 3.57–3.63 (m, 1H, CH), 6.03 (d, 1H, 2J 15.7 Hz, CH_2N), 6.22 (d, 1H, 2J 15.7 Hz, CH_2N), 7.05 (d, 1H, 3J 7.0 Hz, C_{10}H_7), 7.38 (t, 1H, 3J 7.9 Hz, C_{10}H_7), 7.50 (t, 1H, 3J 7.8 Hz, C_{10}H_7), 7.54 (t, 1H, 3J 6.8 Hz, C_{10}H_7), 7.75 (d, 1H, 3J 7.9 Hz, C_{10}H_7), 7.87 (d, 1H, 3J 7.8 Hz, C_{10}H_7), 7.99 (d, 1H, 3J 8.1 Hz, C_{10}H_7), 10.22 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 29.7 (CH_2), 34.6 (CH_2), 40.2 (CH), 48.1 (CH_2N), 122.4 (CH), 122.6 (CH), 125.1 (CH), 125.8 (CH), 126.2 (CH), 127.7 (CH), 128.9 (CH), 130.6 (C), 131.2 (C), 133.7 (C), 168.6 (CON), 175.4 (CO_2), 199.7 (C=S). EI-MS: 345 (M^+ , 9), 312 (29), 199 (100), 155 (35), 141 (20). Anal. Calcd (%) $\text{C}_{17}\text{H}_{15}\text{NO}_3\text{S}_2$ (345.44): C, 59.11, H, 4.38, N, 4.05. Found: C, 58.90, H, 4.35, N, 4.12.

2-(3-Allyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acid (3f)

Yellow crystals, yield: 0.42 g (86%), mp 115–117 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3055 (br), 1704 (C=O), 1695 (C=O), 1415, 1328, 1256, 1169, 1134, 1029, 950, 929, 726. ^1H NMR (500 MHz, CDCl_3): δ = 2.75 (dd, 1H, 3J 6.2 Hz, 2J 17.3 Hz, CH_2), 2.85 (dd, 1H, 3J 3.8 Hz, 2J 12.9 Hz, CH_2), 2.98 (dd, 1H, 3J 5.9 Hz, 2J 17.3 Hz, CH_2), 3.32 (dd, 1H, 3J 11.9 Hz, 2J 12.9 Hz, CH_2), 3.44–3.50 (m, 1H, CH), 4.94 (1H, dd, 3J 4.5 Hz, 2J 14.6 Hz, CH_2N), 5.05 (dd, 1H, 3J 5.4 Hz, 2J 14.6 Hz, CH_2N), 5.12–5.20 (m, 2H, CH_2), 5.80–5.89 (m, 1H, CH), 10.27 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 29.7 (CH_2), 34.7 (CH_2), 39.7 (CH), 49.2 (CH_2N), 118.4 (CH_2), 130.8 (CH), 168.2 (CON), 176.4 (CO_2), 199.5 (C=S). EI-MS: 245 (M^+ , 10), 213 (15), 99 (100), 55 (50). Anal. Calcd (%) for $\text{C}_9\text{H}_{11}\text{NO}_3\text{S}_2$ (245.32): C, 44.07, H, 4.52, N, 5.71. Found: C, 44.16, H, 4.72, N, 5.80.

2-(3-Butyl-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acid (3g)

Yellow crystals, yield: 0.42 g (80%), mp 121–122 °C. IR (KBr) ($\nu_{\text{max}}/\text{cm}^{-1}$): 3010 (br), 1697 (C=O), 1691 (C=O), 1419, 1346, 1300, 1177, 1096, 1025, 920, 715. ^1H NMR (500 MHz, CDCl_3): δ = 0.92 (t, 3H, 3J 7.3 Hz, Me), 1.32–1.40 (m, 2H, CH_2), 1.57–1.70 (m, 2 H, CH_2), 2.72 (dd, 1H, 3J 6.2 Hz, 2J 17.3 Hz, CH_2), 2.81 (dd, 1H, 3J 3.7 Hz, 2J 12.9 Hz, CH_2), 2.98 (dd, 1H, 3J 6.0 Hz, 2J 17.3 Hz, CH_2), 3.29 (dd, 1H, 3J 12.0 Hz, 2J 12.9 Hz, CH_2), 3.43–3.49 (m, 1H, CH), 4.26–4.32 (m, 1 H, CH_2N), 4.40–4.46 (m, 1H, CH_2N), 10.42 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 14.5 (Me), 20.8 (CH_2), 30.1 (CH_2), 30.8 (CH_2), 35.8 (CH_2), 40.8 (CH), 48.6 (CH_2N), 169.3 (CON), 176.5 (CO_2), 200.5 (C=S). EI-MS: 261 (M^+ , 5), 228 (48), 114 (45), 94 (20), 72 (50), 41 (100). Anal. Calcd (%) for

$C_{10}H_{15}NO_3S_2$ (261.36): C, 45.95, H, 5.78, N, 5.36. Found: C, 46.05, H, 5.64, N, 5.55.

2-[3-(2-Ethylhexyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3h)

Yellow oil, yield: 0.43 g (68%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3050 (br), 1708 (C=O), 1698 (C=O), 1419, 1328, 1256, 1177, 1093, 961, 791. ^1H NMR (500 MHz, CDCl_3): δ = 0.79 (t, 3H, 3J 7.2 Hz, Me), 0.89 (t, 3H, 3J 7.1 Hz, Me), 1.22–1.32 (m, 8H, 4 CH_2), 1.88–1.93 (m, 1H, CH), 2.72 (dd, 1H, 3J 6.1 Hz, 2J 17.2 Hz, CH_2), 2.79 (dd, 1H, 3J 4.2 Hz, 2J 12.8 Hz, CH_2), 2.98 (dd, 1H, 3J 5.9 Hz, 2J 17.2 Hz, CH_2), 3.30 (dd, 1H, 3J 11.9 Hz, 2J 12.8 Hz, CH_2), 3.47–3.53 (m, 1H, CH), 4.22–4.31 (m, 1H, CH_2N), 4.50–4.56 (m, 1H, CH_2N), 10.85 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 10.6 (Me), 14.0 (Me), 23.0 (CH_2), 27.3 (CH_2), 29.0 (CH_2), 29.7 (CH_2), 30.4 (CH_2), 35.0 (CH_2), 37.2 (CH), 40.2 (CH), 50.6 (CH_2N), 169.0 (CON), 176.7 (CO_2), 200.3 (C=S). EI-MS: 317 (M^+ , 5), 284 (40), 171 (15), 127 (100), 113 (35). Anal. Calcd (%) for $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{S}_2$ (317.47): C, 52.97, H, 7.30, N, 4.41. Found: C, 52.90, H, 7.42, N, 4.59.

2-[3-(2-Hydroxyethyl)-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3i)

Yellow oil, yield: 0.37 g (75%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3390, 3012 (br), 1705 (C=O), 1696 (C=O), 1327, 1163, 1065, 808, 778. ^1H NMR (500 MHz, CDCl_3): δ = 2.72 (dd, 1H, 3J 6.2 Hz, 2J 17.3 Hz, CH_2), 2.95 (dd, 1H, 3J 3.7 Hz, 2J 12.9 Hz, CH_2), 3.05 (dd, 1H, 3J 6.0 Hz, 2J 17.3 Hz, CH_2), 3.29 (dd, 1H, 3J 12.0 Hz, 2J 12.9 Hz, CH_2), 3.55–3.61 (m, 1H, CH), 3.65–3.78 (m, 2H, CH_2O), 4.41–4.46 (m, 1H, CH_2N), 4.60–4.64 (m, 1H, CH_2N), 7.75 (br s, 1H, OH), 10.37 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 30.3 (CH_2), 35.0 (CH_2), 40.7 (CH), 49.5 (CH_2N), 59.0 (CH_2O), 170.1 (CON), 172.4 (CO_2), 202.7 (C=S). EI-MS: 249 (M^+ , 10), 216 (20), 102 (20), 85 (23), 59 (100). Anal. Calcd (%) for $\text{C}_8\text{H}_{11}\text{NO}_4\text{S}_2$ (249.31): C, 38.54, H, 4.45, N, 5.62. Found: C, 38.70, H, 4.35, N, 5.83.

2-[3-[2-(2-Hydroxyethoxy)ethyl]-4-oxo-2-thioxo-1,3-thiazinan-5-yl]acetic acid (3j)

Yellow oil, yield: 0.41 g (70%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3390, 3024 (br), 1697 (C=O), 1685 (C=O), 1419, 1327, 1256, 1177, 1093, 1050, 961, 868. ^1H NMR (500 MHz, CDCl_3): δ = 2.73 (dd, 1H, 3J 6.1 Hz, 2J 17.3 Hz, CH_2), 2.94 (dd, 1H, 3J 3.7 Hz, 2J 12.9 Hz, CH_2), 3.06 (1H, dd, 3J 6.0 Hz, 2J 17.3 Hz, CH_2), 3.29 (dd, 1H, 3J 12.0 Hz, 2J 12.9 Hz, CH_2), 3.50–3.56 (m, 1H, CH), 3.62–3.72 (m, 4H, 2 CH_2O), 3.75–3.84 (m, 2H, CH_2O), 4.61–4.65 (m, 1H, CH_2N), 4.77–4.82 (m, 1H, CH_2N), 6.50 (br s, 1H, OH), 10.64 (br s, 1H, OH). ^{13}C

NMR (125.7 MHz, CDCl_3): δ = 29.8 (CH_2), 34.9 (CH_2), 39.9 (CH), 45.8 (CH_2N), 61.5 (CH_2O), 64.6 (CH_2O), 72.0 (CH_2O), 169.3 (CON), 174.4 (CO_2), 200.4 (C=S). EI-MS: 293 (M^+ , 5), 260 (25), 128 (50), 85 (100). Anal. Calcd (%) for $\text{C}_{10}\text{H}_{15}\text{NO}_5\text{S}_2$ (293.36): C, 40.94, H, 5.15, N, 4.77. Found: C, 40.71, H, 5.29, N, 4.80.

2-(3-Anilino-4-oxo-2-thioxo-1,3-thiazinan-5-yl)acetic acid (3k)

Yellow oil, yield: 0.44 g (74%). IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3265 (br), 3030 (br), 1706 (C=O), 1692 (C=O), 1592, 1522, 1487, 1429, 1297, 1185, 1037, 883, 748. ^1H NMR (500 MHz, CDCl_3): 2.05 (dd, 1H, 3J 6.6 Hz, 2J 17.4 Hz, CH_2), 2.82 (dd, 1H, 3J 4.0 Hz, 2J 12.9 Hz, CH_2), 3.00 (dd, 1H, 3J 5.7 Hz, 2J 17.4 Hz, CH_2), 3.62 (dd, 1H, 3J 11.9 Hz, 2J 12.9 Hz, CH_2), 3.93–3.99 (m, 1H, CH), 5.29 (s, 1H, NH), 6.76 (d, 2H, 3J 7.7 Hz, 2CH), 6.96 (t, 1H, 3J 7.4 Hz, CH), 7.25 (t, 2H, 3J 7.4 Hz, 2CH), 9.52 (br s, 1H, OH). ^{13}C NMR (125.7 MHz, CDCl_3): δ = 29.6 (CH_2), 34.7 (CH_2), 41.3 (CH), 114.8 (2CH), 122.5 (CH), 129.2 (2CH), 144.3 (C), 167.5 (CON), 174.9 (CO_2), 197.7 (C=S). EI-MS: 296 (M^+ , 15), 263 (50), 150 (44), 106 (100). Anal. Calcd (%) for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_3\text{S}_2$ (296.36): C, 48.63, H, 4.08, N, 9.85. Found: C, 48.40, H, 4.20, N, 10.05.

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