

One-Pot Synthesis of Functionalized (4-Oxo-1,3-thiazinan-5-yl)acetic Acids from Isothiocyanates, Primary Alkylamines, and Ithaconic Anhydride

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A one-pot synthesis of 2-(4-oxo-1,3-thiazinan-5-yl)acetic acids is described *via* a three-component reaction between primary alkylamines and itaconic anhydride and phenyl isothiocyanate or benzoyl isothiocyanate.

Introduction. – Polyfunctionalized heterocyclic compounds play important roles in the drug discovery process. Analysis of drugs in late development or on the market shows that 68% of them are heterocycles [1][2]. Therefore, it is not surprising that research in the field of synthesis of heterocyclic compounds has received special attention.

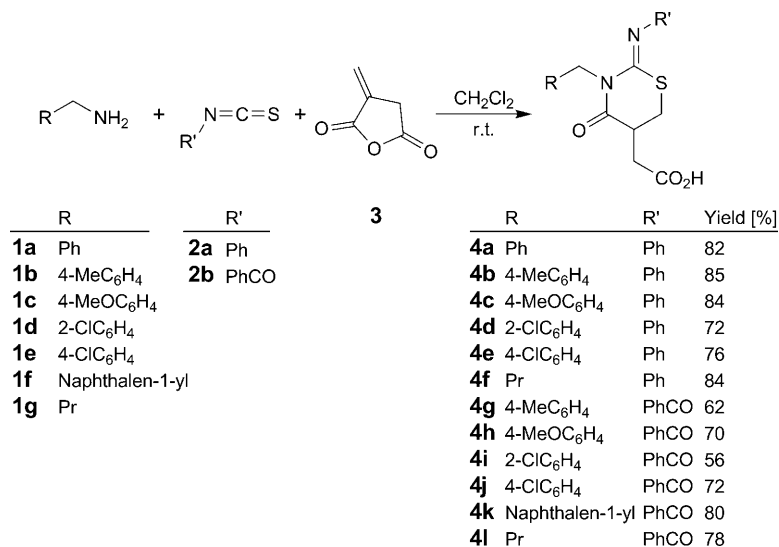
Multicomponent reactions (MCRs), because of their productivity, simple procedures, convergence, and facile execution, are one of the best tools in combinatorial chemistry [3]. Therefore, the design of novel MCRs has attracted great attention from research groups working in various areas such as drug discovery, organic synthesis, and material science. As a result, the number of new MCRs in recent years is growing rapidly [4–7].

As part of our current studies on the development of new routes in heterocyclic synthesis [8–12], we report a three-component synthesis to (4-oxo-1,3-thiazinan-5-yl)acetic acids.

Results and Discussion. – The reaction of primary amines (**1**) with phenyl isothiocyanate (**2a**) or benzoyl isothiocyanate (**2b**) in the presence of itaconic anhydride (= dihydro-3-methylidenefuran-2,5-dione, **3**) proceeded smoothly in CH₂Cl₂ and was complete within 2–5 h. The ¹H- and ¹³C-NMR spectra of the crude products clearly indicated the formation of (4-oxo-1,3-thiazinan-5-yl)acetic acids (**4a–4l**) in 56–85% yield (*Scheme 1*).

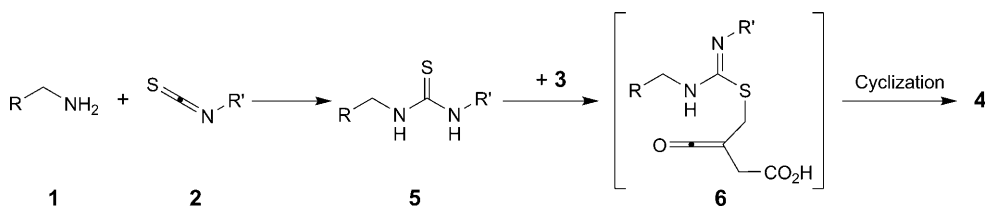
The structures of compounds **4a–4l** were deduced from their IR, ¹H- and ¹³C-NMR spectra. For example, the ¹H-NMR spectrum of **4a** in CDCl₃ showed an *AB* system for the CH₂–N group together with two *AMX* systems for CH₂ H-atoms and a *multiplet* for the CH H-atom. The ¹H-decoupled ¹³C-NMR spectrum of **4a** showed 15 distinct resonances in agreement with the proposed structure. The IR spectrum of **4a** displayed characteristic C=O (1724 and 1710 cm^{–1}) and C=N (1689 cm^{–1}) bands. The ¹H- and ¹³C-NMR spectra of **4b–4l** were similar to those for **4a**, except for the substituents on the N-atoms, which exhibited characteristic resonances in the appropriate regions of the spectrum.

Scheme 1



Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation (*Scheme 2*). Presumably, the initial event is the formation of thiourea **5** from the amine and heterocumulene **2**. Compound **5** subsequently attacks **3** to produce intermediate **6**, which undergoes cyclization to generate product **4**.

Scheme 2



In summary, we report a three-component synthesis of new compounds from primary alkylamines, itaconic anhydride, and phenylisothiocyanate or benzoylisothiocyanate. The present procedure has the advantage that the reactants can be mixed without any prior activation or modification.

Experimental Part

General. Compounds **1**, **2**, and **3** were obtained from *Merck* and used without further purification. M.p.: *Electrothermal 9100* apparatus; uncorrected. IR Spectra: *Shimadzu IR-460* spectrometer; in cm⁻¹. ¹H- and ¹³C-NMR Spectra: *Bruker DRX-500 AVANCE* instrument, in CDCl₃ at 500.1 and 125.7 MHz, resp.; δ in ppm, J in Hz. MS: *Finnigan-MAT-8430* mass spectrometer, at 70 eV; in m/z. Elemental analyses (C, H, N): *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Compounds 4. To the stirred soln. of 0.27 g of phenylisothiocyanate (**2a**, 2 mmol) and 0.22 g of benzylamine (**1a**, 2 mmol) in 10 ml of CH₂Cl₂ was added 0.22 g of itaconic anhydride (**3**, 2 mmol) at r.t. After completion of the reaction (2–5 h), as indicated by TLC (AcOEt/hexane, 2:1), the solvent was removed under reduced pressure, and the residue was purified by silica gel (SiO₂; Merck 230–240 mesh) column chromatography (CC) using a 5:1 hexane/AcOEt mixture as eluent to afford the pure product.

2-[(2Z)-3-Benzyl-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (4a). Yield: 0.58 g (82%). Pale yellow oil. IR (KBr): 3385 (br.), 1724, 1710, 1689, 1610, 1588, 1428, 1379, 1272, 1161, 988, 899, 765, 730. ¹H-NMR: 2.73 (dd, ³J = 6.2, ²J = 17.1, 1 H, CH); 2.85 (dd, ³J = 3.6, ²J = 12.5, 1 H, CH); 3.06–3.10 (m, 2 H, 2 CH); 3.38–3.43 (m, 1 H, CH); 5.46 (AB, Δν_{AB} = 68.4, ²J = 12.7, 2 H, CH₂); 6.85 (d, ³J = 7.8, 2 H, CH); 7.17 (t, ³J = 7.9, 1 H, CH); 7.33 (t, ³J = 7.8, 1 H, CH); 7.38–3.40 (m, 4 H, CH); 7.47 (t, ³J = 7.8, 2 H, CH); 10.06 (br. s, 1 H, OH). ¹³C-NMR: 26.1 (CH₂–S); 34.6 (CH₂); 40.8 (CH); 46.6 (CH₂–N); 120.3 (2 CH); 124.0 (CH); 127.0 (CH); 128.1 (2 CH); 128.2 (2 CH); 128.9 (2 CH); 137.3 (C); 147.6 (C); 150.1 (C=N); 170.5 (CO); 176.4 (CO₂). EI-MS: 154 (5), 77 (85), 59 (10), 45 (10). Anal. calc. for C₁₉H₁₈N₂O₃S (354.42): C 64.39, H 5.12, N 7.90; found: C 64.17, H 5.06, N 8.02.

2-[(2Z)-3-(4-Methylbenzyl)-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (4b). Yield: 0.62 g (85%). Yellow powder. M.p. 138–139°. IR (KBr): 3400 (br.), 1746, 1718, 1663, 1598, 1429, 1304, 1154, 996, 762. ¹H-NMR: 2.36 (s, 3 H, CH₃); 2.70 (dd, ³J = 6.5, ²J = 17.5, 1 H, CH); 2.84 (dd, ³J = 4.1, ²J = 12.5, 1 H, CH); 3.04–3.07 (m, 2 H, CH); 3.35–3.38 (m, 1 H, CH); 5.35 (AB, Δν_{AB} = 67.0, ²J = 17.8, 2 H, CH₂); 6.83 (d, ³J = 8.0, 2 H, CH); 7.15–7.18 (m, 2 H, CH); 7.35–7.37 (m, 5 H, CH); 10.40 (br. s, 1 H, OH). ¹³C-NMR: 20.6 (CH₂–S); 26.3 (Me); 34.9 (CH₂); 41.1 (CH); 46.6 (CH₂–N); 120.6 (2 CH); 124.2 (CH); 128.6 (2 CH); 129.0 (2 CH); 129.2 (2 CH); 134.6 (C); 136.9 (C); 148.0 (C); 150.4 (C=N); 170.7 (CO); 176.7 (CO₂). EI-MS: 153 (5), 91 (50), 77 (85), 59 (5), 45 (10). Anal. calc. for C₂₀H₂₀N₂O₃S (368.44): C 65.20, H 5.47, N 7.60; found: C 65.01, H 5.39, N 7.68.

2-[(2Z)-3-(4-Methoxybenzyl)-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (4c). Yield: 0.64 g (84%). Yellow oil. IR (KBr): 3382 (br.), 1733, 1703, 1606, 1582, 1508, 1378, 1293, 1266, 1177, 1107, 1029, 979. ¹H-NMR: 2.69 (dd, ³J = 6.5, ²J = 17.1, 1 H, CH); 2.83 (dd, ³J = 4.0, ²J = 13.0, 1 H, CH); 3.03–3.06 (m, 2 H, 2 CH); 3.34–3.37 (m, 1 H, CH); 3.80 (s, 3 H, CH₃); 5.35 (AB, Δν_{AB} = 71.0, ²J = 17.9, 2 H, CH₂); 6.82 (d, ³J = 7.5, 2 H, CH); 6.89 (d, ³J = 8.9, 2 H, CH); 7.14 (t, ³J = 8.7, 1 H, CH); 7.35 (t, 2 H, CH); 7.40 (d, ³J = 8.5, 2 H, CH); 10.01 (br. s, 1 H, OH). ¹³C-NMR: 26.3 (CH₂–S); 34.9 (CH₂); 41.0 (CH); 46.3 (CH₂–N); 55.3 (MeO); 113.7 (2 CH); 120.6 (2 CH); 124.2 (CH); 129.1 (2 CH); 129.8 (C); 130.3 (2 CH); 147.9 (C); 150.4 (C); 158.8 (C=N); 170.7 (CO); 176.6 (CO₂). EI-MS: 153 (5), 106 (55), 77 (80), 59 (5), 45 (10). Anal. calc. for C₂₀H₂₀N₂O₄S (384.45): C 62.48, H 5.24, N 7.29; found: C 62.40, H 5.15, N 7.31.

2-[(2Z)-3-(2-Chlorobenzyl)-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (4d). Yield: 0.56 g (72%). Yellow oil. IR (KBr): 3391 (br.), 1766, 1708, 1604, 1481, 1378, 1289, 1161, 1038, 993, 902, 764, 733. ¹H-NMR: 2.71 (dd, ³J = 6.9, ²J = 17.2, 1 H, CH); 2.91 (dd, ³J = 3.8, ²J = 12.9, 1 H, CH); 3.03 (dd, ³J = 5.8, ²J = 17.3, 1 H, CH); 3.15 (dd, ³J = 12.3, ²J = 12.5, 1 H, CH); 3.40–3.43 (m, 1 H, CH); 5.30 (AB, Δν_{AB} = 71.9, ²J = 15.5, 2 H, CH₂); 6.71 (d, ³J = 7.5, 2 H, CH); 7.11 (t, ³J = 7.5, 1 H, CH); 7.23–7.26 (m, 3 H, CH); 7.29 (t, ³J = 6.5, 2 H, CH); 7.35 (t, ³J = 7.8, 1 H, CH); 10.16 (br. s, 1 H, OH). ¹³C-NMR: 26.4 (CH₂–S); 34.6 (CH₂); 41.3 (CH); 46.6 (CH₂–N); 120.5 (2 CH); 124.2 (CH); 126.6 (CH); 128.2 (CH); 128.5 (CH); 129.1 (2 CH); 129.5 (CH); 133.1 (C); 134.5 (C); 147.6 (C); 150.0 (C=N); 170.6 (CO); 176.4 (CO₂). EI-MS: 153 (10), 112 (60), 77 (70), 59 (5), 45 (10). Anal. calc. for C₁₉H₁₇ClN₂O₃S (388.86): C 58.69, H 4.41, N 7.20; found: C 58.62, H 4.35, N 7.10.

2-[(2Z)-3-(4-Chlorobenzyl)-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (4e). Yield: 0.59 g (76%). Pale yellow oil. IR (KBr): 3389 (br.), 1765, 1708, 1601, 1487, 1431, 1377, 1274, 1159, 1102, 1012, 900, 798. ¹H-NMR: 2.73 (dd, ³J = 6.5, ²J = 17.2, 1 H, CH); 2.84 (dd, ³J = 4.0, ²J = 12.9, 1 H, CH); 2.99 (dd, ³J = 5.8, ²J = 17.3, 1 H, CH); 3.08 (dd, ³J = 12.3, ²J = 12.5, 1 H, CH); 3.35–3.57 (m, 1 H, CH); 5.37 (AB, Δν_{AB} = 74.5, ²J = 14.2, 2 H, CH₂); 6.79 (d, ³J = 7.5, 2 H, CH); 7.14 (t, ³J = 7.5, 1 H, CH); 7.30 (d, ³J = 8.0, 2 H, CH); 7.34 (t, ³J = 7.5, 2 H, CH); 7.40 (d, ³J = 8.4, 2 H, CH); 10.35 (br. s, 1 H, OH). ¹³C-NMR: 26.3 (CH₂–S); 34.9 (CH₂); 41.0 (CH); 46.2 (CH₂–N); 120.5 (2 CH); 124.4 (CH); 128.5 (2 CH); 129.2 (2 CH); 130.2 (2 CH); 133.1 (C); 136.1 (C); 147.7 (C); 150.2 (C=N); 170.7 (CO); 176.8

(CO₂). EI-MS: 153 (8), 112 (45), 77 (80), 59 (5), 45 (10). Anal. calc. for C₁₉H₁₇ClN₂O₃S (388.86): C 58.69, H 4.41, N 7.20; found: C 58.59, H 4.33, N 7.13.

2-[(2Z)-3-Butyl-4-oxo-2-(phenylimino)-1,3-thiazinan-5-yl]acetic Acid (**4f**). Yield: 0.54 g (84%). White powder. M.p. 108–110°. IR (KBr): 3385 (br.), 1705, 1700, 1668, 1584, 1435, 1390, 1304, 1181, 1121, 953, 767. ¹H-NMR: 0.95 (t, ³J = 7.5, 3 H, Me); 1.37–1.40 (m, 2 H, CH₂); 1.67–1.70 (m, 2 H, CH₂); 2.66 (dd, ³J = 6.7, ²J = 17.1, 1 H, CH); 2.84 (dd, ³J = 3.8, ²J = 12.8, 1 H, CH); 2.99 (dd, ³J = 6.0, ²J = 16.9, 1 H, CH); 3.10 (dd, ³J = 12.5, ²J = 12.8, 1 H, CH); 3.30–3.33 (m, 1 H, CH); 4.16–4.19 (m, 2 H, CH₂); 6.85 (d, ³J = 8.0, 2 H, CH); 7.12 (t, ³J = 7.4, 1 H, CH); 7.34 (t, ³J = 7.8, 2 H, CH); 10.70 (br. s, 1 H, OH). ¹³C-NMR: 13.8 (Me); 20.1 (CH₂); 26.5 (CH₂); 29.8 (CH₂–S); 35.0 (CH₂); 41.0 (CH); 44.3 (CH₂–N); 120.6 (2 CH); 124.2 (CH); 129.1 (2 CH); 148.1 (C); 150.4 (C=N); 170.6 (CO); 176.9 (CO₂). EI-MS: 153 (8), 134 (45), 77 (80), 59 (10), 45 (5). Anal. calc. for C₁₆H₂₀N₂O₃S (320.40): C 59.98, H 6.29, N 8.74; found: C 59.88, H 6.20, N 8.63.

2-[(2Z)-3-(4-Methylbenzyl)-4-oxo-2-(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4g**). Yield: 0.49 g (62%). Pale yellow powder. M.p. 129–131°. IR (KBr): 3395 (br.), 1732, 1712, 1696, 1636, 1584, 1433, 1409, 1302, 1266, 1215, 1181, 1058. ¹H-NMR: 2.25 (s, 3 H, Me); 2.84 (dd, ³J = 6.0, ²J = 17.1, 1 H, CH); 2.99 (dd, ³J = 5.0, ²J = 17.3, 1 H, CH); 3.15 (dd, ³J = 3.5, ²J = 12.5, 1 H, CH); 3.43 (dd, ³J = 13, ²J = 13.3, 1 H, CH); 3.48–3.51 (m, 1 H, CH); 5.40 (AB, Δν_{AB} = 82.4, ²J = 14.5, 2 H, CH₂); 7.12 (d, ³J = 8.0, 2 H, CH); 7.25 (d, ³J = 8.0, 2 H, CH); 7.39 (t, ³J = 7.5, 2 H, CH); 7.54 (t, ³J = 7.1, 1 H, CH); 7.84 (d, ³J = 7.1, 2 H, CH); 10.06 (br. s, 1 H, OH). ¹³C-NMR: 26.8 (CH₂–S); 35.1 (CH₂); 37.7 (Me); 41.7 (CH); 47.9 (CH₂–N); 128.2 (2 CH); 129.1 (2 CH); 129.8 (2 CH); 130.4 (2 CH); 133.6 (CH); 135.6 (C); 135.9 (C); 137.2 (C); 161.2 (C=N); 172.0 (C=O); 172.5 (CO₂); 176.3 (C=O). EI-MS: 153 (10), 150 (45), 136 (85), 77 (80), 59 (10), 45 (5). Anal. calc. for C₂₁H₂₀N₂O₄S (396.46): C 63.62, H 5.08, N 7.07; found: C 63.50, H 5.11, N 7.14.

2-[(2Z)-3-(4-Methoxybenzyl)-4-oxo-2-(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4h**). Yield: 0.57 g (70%). Pale yellow powder. M.p. 116–119°. IR (KBr): 3390 (br.), 1740, 1702, 1695, 1611, 1509, 1434, 1309, 1269, 1248, 1159, 902, 812. ¹H-NMR: 2.80 (dd, ³J = 6.4, ²J = 17.2, 1 H, CH); 2.90 (dd, ³J = 3.5, ²J = 12.8, 1 H, CH); 2.99 (dd, ³J = 4.9, ²J = 17.3, 1 H, CH); 3.22 (dd, ³J = 12.7, ²J = 12.9, 1 H, CH); 3.40–3.43 (m, 1 H, CH); 3.77 (s, 3 H, MeO); 5.40 (AB, Δν_{AB} = 46.9, ²J = 14.1, 2 H, CH₂); 6.83 (d, ³J = 8.0, 2 H, CH); 7.33 (d, ³J = 8.0, 2 H, CH); 7.39 (t, ³J = 7.4, 2 H, CH); 7.53 (t, ³J = 7.1, 1 H, CH); 7.95 (t, ³J = 7.6, 2 H, CH); 10.49 (br. s, 1 H, OH). ¹³C-NMR: 26.5 (CH₂–S); 34.7 (CH₂); 40.6 (CH); 47.4 (CH₂–N); 55.3 (MeO); 113.9 (2 CH); 128.4 (2 CH); 129.1 (C); 129.6 (2 CH); 129.9 (2 CH); 133.1 (CH); 134.5 (C); 159.0 (C=N); 160.3 (C–O); 171.2 (CO); 176.0 (CO₂); 176.4 (CO). EI-MS: 153 (5), 136 (80), 105 (50), 77 (85), 59 (5), 45 (10). Anal. calc. for C₂₁H₂₀N₂O₆S (412.46): C 61.15, H 4.89, N 6.79; found: C 61.02, H 4.85, N 6.85.

2-[(2Z)-3-(2-Chlorobenzyl)-4-oxo-2-(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4i**). Yield: 0.47 g (56%). Pale yellow powder. M.p. 125–127°. IR (KBr): 3432 (br.), 1722, 1708, 1694, 1631, 1470, 1434, 1405, 1303, 1269, 1216, 1167, 1083. ¹H-NMR: 2.87 (dd, ³J = 6.0, ²J = 17.3, 1 H, CH); 3.02 (dd, ³J = 4.9, ²J = 17.3, 1 H, CH); 3.22 (dd, ³J = 3.5, ²J = 12.5, 1 H, CH); 3.55 (dd, ³J = 15.1, ²J = 15.2, 1 H, CH); 3.63–3.65 (m, 1 H, CH); 5.50 (s, 2 H, CH₂); 7.23–7.28 (m, 3 H, CH); 7.3 (t, ³J = 7.4, 2 H, CH); 7.40 (t, ³J = 7.2, 1 H, CH); 7.51 (d, ³J = 7.1, 1 H, CH); 7.78 (d, ³J = 7.6, 2 H, CH); 10.35 (br. s, 1 H, OH). ¹³C-NMR: 26.9 (CH₂–S); 35.0 (CH₂); 41.7 (CH); 46.4 (CH₂–N); 127.9 (CH); 128.0 (CH); 129.1 (CH); 129.3 (2 CH); 130.1 (CH); 130.5 (2 CH); 133.7 (CH); 135.5 (C); 135.8 (C); 161.9 (C); 168 (C=N); 172.5 (CO); 172.8 (CO₂); 176.2 (CO). EI-MS: 171 (55), 153 (8), 136 (80), 77 (90), 59 (3), 45 (5). Anal. calc. for C₂₀H₁₇ClN₂O₃S (416.88): C 57.62, H 4.11, N 6.72; found: C 57.51, H 4.01, N 6.82.

2-[(2Z)-3-(4-Chlorobenzyl)-4-oxo-2-(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4j**). Yield: 0.60 g (72%). Yellow powder. M.p. 136–138°. IR (KBr): 3389 (br.), 1728, 1700, 1693, 1634, 1489, 1459, 1401, 1302, 1271, 1215, 1141, 1083. ¹H-NMR: 2.83 (dd, ³J = 6.7, ²J = 17.4, 1 H, CH); 2.94 (dd, ³J = 4.0, ²J = 13.0, 1 H, CH); 2.99 (dd, ³J = 5.1, ²J = 17.3, 1 H, CH); 3.27 (dd, ³J = 12.7, ²J = 12.9, 1 H, CH); 3.40–3.42 (m, 1 H, CH); 5.41 (AB, Δν_{AB} = 52.3, ²J = 14.5, 2 H, CH₂); 7.26 (d, ³J = 7.8, 2 H, CH); 7.36 (d, ³J = 7.8, 2 H, CH); 7.41 (t, ³J = 7.5, 2 H, CH); 7.50 (t, ³J = 7.1, 1 H, CH); 7.88 (t, ³J = 7.6, 2 H, CH); 10.51 (br. s, 1 H, OH). ¹³C-NMR: 29.6 (CH₂–S); 34.5 (CH₂); 40.7 (CH); 47.3 (CH₂–N); 127.3 (CH); 128.4 (2 CH); 128.7 (2 CH); 129.4 (2 CH); 129.8 (2 CH); 133.1 (C); 134.4 (C); 135.5 (C); 160.5 (C=N); 171.2

(CO); 174.2 (CO₂); 176.3 (CO). EI-MS: 171 (50), 153 (10), 136 (75), 77 (80), 59 (5), 45 (5). Anal. calc. for C₂₀H₁₇ClN₂O₄S (416.88): C 57.62, H 4.11, N 6.72; found: C 57.51, H 4.02, N 6.81.

2-[(2Z)-3-(Naphthalen-1-ylmethyl)-4-oxo-2-[(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4k**). Yield: 0.69 g (80%). Brown powder. M.p. 130–132°. IR (KBr): 3371 (br.), 1725, 1700, 1690, 1634, 1490, 1432, 1411, 1303, 1269, 1215, 1165, 1084. ¹H-NMR: 2.89 (dd, ³J = 6.0, ²J = 17.5, 1 H, CH); 3.04 (dd, ³J = 5.2, ²J = 17.5, 1 H, CH); 3.25 (dd, ³J = 3.5, ²J = 12.5, 1 H, CH); 3.58 (dd, ³J = 10.7, ²J = 11.1, 1 H, CH); 3.60–3.62 (m, 1 H, CH); 5.94 (AB, Δν_{AB} = 82.3, ²J = 17.8, 2 H, CH₂); 7.17 (t, ³J = 7.5, 2 H, CH); 7.33 (d, ³J = 7.0, 1 H, CH); 7.40–7.43 (m, 3 H, CH); 7.58–7.61 (m, 2 H, CH); 7.82 (d, ³J = 7.9, 1 H, CH); 7.95 (d, ³J = 7.5, 2 H, CH); 8.22 (d, ³J = 8.0, 1 H, CH); 10.49 (br. s, 1 H, OH). ¹³C-NMR: 26.8 (CH₂–S); 35.0 (CH₂); 41.8 (CH); 45.9 (CH₂–N); 123.3 (CH); 123.7 (CH); 126.2 (CH); 126.5 (CH); 127.1 (CH); 128.0 (CH); 128.9 (2 CH); 129.6 (CH); 130.2 (2 CH); 132.4 (C); 133.4 (C); 133.5 (CH); 134.7 (C); 135.9 (C); 161.5 (C=N); 167.7 (CO); 172.7 (CO₂); 176.2 (CO). EI-MS: 153 (5), 136 (80), 77 (85), 59 (5), 45 (10). Anal. calc. for C₂₄H₂₀N₂O₄S (432.49): C 66.65, H 4.66, N 6.48; found: C 66.52, H 4.51, N 6.52.

2-[(2Z)-3-Butyl-4-oxo-2-[(phenylcarbonyl)imino]-1,3-thiazinan-5-yl]acetic Acid (**4l**). Yield: 0.54 g (78%). White powder. M.p. 120–122°. IR (KBr): 3375 (br.), 1725, 1705, 1668, 1584, 1435, 1390, 1340, 1181, 1121, 953, 767, 689. ¹H-NMR: 0.95 (t, ³J = 7.5, 3 H, Me); 1.40–1.42 (m, 2 H, CH₂); 1.69–1.71 (m, 2 H, CH₂); 2.76 (dd, ³J = 6.1, ²J = 17.2, 1 H, CH); 2.96 (dd, ³J = 5.3, ²J = 17.2, 1 H, CH); 3.08 (dd, ³J = 3.5, ²J = 12.4, 1 H, CH); 3.33 (dd, ³J = 12.9, ²J = 13.1, 1 H, CH); 3.34–3.37 (m, 1 H, CH); 4.20–4.22 (m, 2 H, CH₂); 7.51 (t, ³J = 8.0, 2 H, CH); 7.60 (t, ³J = 7.9, 1 H, CH); 8.12–8.14 (d, ³J = 7.9, 2 H, CH); 10.72 (br. s, 1 H, OH). ¹³C-NMR: 20.8 (Me); 26.9 (CH₂); 29.3 (CH₂); 35.0 (CH₂–S); 37.6 (CH₂); 41.5 (CH); 45.6 (CH₂–N); 128.2 (CH); 129.3 (2 CH); 130.3 (2 CH); 135.9 (C); 162.8 (C=N); 172.0 (CO); 172.6 (CO₂); 176.3 (CO). EI-MS: 193 (55), 156 (8), 136 (75), 77 (80), 59 (10), 45 (10). Anal. calc. for C₁₇H₂₀N₂O₄S (348.41): C 58.60, H 5.79, N 8.04; found: C 58.54, H 5.71, N 8.11.

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