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 ithaconic 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.

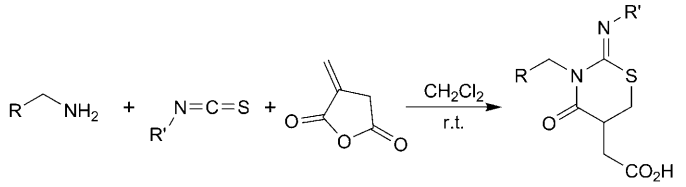
Multicomponent reactions (MCRs), because of their productivity, simple procedures, convergence, and facile execution, are one of the best tools in combinatorial chemistry [3]. Therefore, the design of novel MCRs has attracted great attention from research groups working in various areas such as drug 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 CH_2Cl_2 and was complete within 2–5 h. The ^{1}H- and ^{13}C-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, ^{1}H- and ^{13}C-NMR spectra. For example, the ^{1}H-NMR spectrum of **4a** in $CDCl_3$ showed an *AB* system for the CH_2–N group together with two *AMX* systems for CH_2 H-atoms and a *multiplet* for the CH H-atom. The ^{1}H-decoupled ^{13}C-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 ^{1}H- and ^{13}C-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

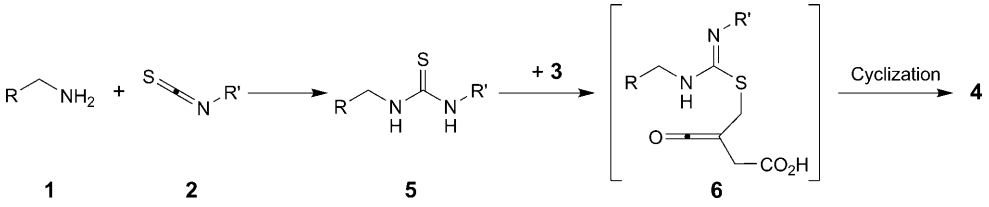


	R		R'		3
1a	Ph	**2a**	Ph		
1b	4-MeC_6H_4	**2b**	PhCO		
1c	4-$MeOC_6H_4$				
1d	2-ClC_6H_4				
1e	4-ClC_6H_4				
1f	Naphthalen-1-yl				
1g	Pr				

	R	R'	Yield [%]
4a	Ph	Ph	82
4b	4-MeC_6H_4	Ph	85
4c	4-$MeOC_6H_4$	Ph	84
4d	2-ClC_6H_4	Ph	72
4e	4-ClC_6H_4	Ph	76
4f	Pr	Ph	84
4g	4-MeC_6H_4	PhCO	62
4h	4-$MeOC_6H_4$	PhCO	70
4i	2-ClC_6H_4	PhCO	56
4j	4-ClC_6H_4	PhCO	72
4k	Naphthalen-1-yl	PhCO	80
4l	Pr	PhCO	78

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



1 **2** **5** **6**

In summary, we report a three-component synthesis of new compounds from primary alkylamines, ithaconic 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 ^{13}C-NMR Spectra: *Bruker DRX-500 AVANCE* instrument, in $CDCl_3$ 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 CH_2Cl_2 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 (SiO_2; *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. ^{1}H-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*, $\Delta\nu_{AB} = 68.4$, $^2J = 12.7$, 2 H, CH_2); 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). ^{13}C-NMR: 26.1 (CH_2–S); 34.6 (CH_2); 40.8 (CH); 46.6 (CH_2–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 (CO_2). EI-MS: 154 (5), 77 (85), 59 (10), 45 (10). Anal. calc. for $C_{19}H_{18}N_2O_3S$ (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. ^{1}H-NMR: 2.36 (*s*, 3 H, CH); 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*, $\Delta\nu_{AB} = 67.0$, $^2J = 17.8$, 2 H, CH_2); 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). ^{13}C-NMR: 20.6 (CH_2–S); 26.3 (Me); 34.9 (CH_2); 41.1 (CH); 46.6 (CH_2–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 (CO_2). EI-MS: 153 (5), 91 (50), 77 (85), 59 (5), 45 (10). Anal. calc. for $C_{20}H_{20}N_2O_3S$ (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. ^{1}H-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, CH); 5.35 (*AB*, $\Delta\nu_{AB} = 71.0$, $^2J = 17.9$, 2 H, CH_2); 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). ^{13}C-NMR: 26.3 (CH_2–S); 34.9 (CH_2); 41.0 (CH); 46.3 (CH_2–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 (CO_2). EI-MS: 153 (5), 106 (55), 77 (80), 59 (5), 45 (10). Anal. calc. for $C_{20}H_{20}N_2O_4S$ (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. ^{1}H-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*, $\Delta\nu_{AB} = 71.9$, $^2J = 15.5$, 2 H, CH_2); 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). ^{13}C-NMR: 26.4 (CH_2–S); 34.6 (CH_2); 41.3 (CH); 46.6 (CH_2–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 (CO_2). EI-MS: 153 (10), 112 (60), 77 (70), 59 (5), 45 (10). Anal. calc. for $C_{19}H_{17}ClN_2O_3S$ (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. ^{1}H-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*, $\Delta\nu_{AB} = 74.5$, $^2J = 14.2$, 2 H, CH_2); 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). ^{13}C-NMR: 26.3 (CH_2–S); 34.9 (CH_2); 41.0 (CH); 46.2 (CH_2–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

(CO_2). EI-MS: 153 (8), 112 (45), 77 (80), 59 (5), 45 (10). Anal. calc. for $C_{19}H_{17}ClN_2O_3S$ (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. ^{1}H-NMR: 0.95 (*t*, ^3J = 7.5, 3 H, Me); 1.37–1.40 (*m*, 2 H, CH_2); 1.67–1.70 (*m*, 2 H, CH_2); 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, CH_2); 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). ^{13}C-NMR: 13.8 (Me); 20.1 (CH_2); 26.5 (CH_2); 29.8 (CH_2–S); 35.0 (CH_2); 41.0 (CH); 44.3 (CH_2–N); 120.6 (2 CH); 124.2 (CH); 129.1 (2 CH); 148.1 (C); 150.4 (C=N); 170.6 (CO); 176.9 (CO_2). EI-MS: 153 (8), 134 (45), 77 (80), 59 (10), 45 (5). Anal. calc. for $C_{16}H_{20}N_2O_3S$ (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. ^{1}H-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*, $\Delta\nu_{AB}$ = 82.4, ^2J = 14.5, 2 H, CH_2); 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). ^{13}C-NMR: 26.8 (CH_2–S); 35.1 (CH_2); 37.7 (Me); 41.7 (CH); 47.9 (CH_2–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 (CO_2); 176.3 (C=O). EI-MS: 153 (10), 150 (45), 136 (85), 77 (80), 59 (10), 45 (5). Anal. calc. for $C_{21}H_{20}N_2O_4S$ (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. ^{1}H-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*, $\Delta\nu_{AB}$ = 46.9, ^2J = 14.1, 2 H, CH_2); 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). ^{13}C-NMR: 26.5 (CH_2–S); 34.7 (CH_2); 40.6 (CH); 47.4 (CH_2–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 (CO_2); 176.4 (CO). EI-MS: 153 (5), 136 (80), 105 (50), 77 (85), 59 (5), 45 (10). Anal. calc. for $C_{21}H_{20}N_2O_6S$ (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. ^{1}H-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, CH_2); 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). ^{13}C-NMR: 26.9 (CH_2–S); 35.0 (CH_2); 41.7 (CH); 46.4 (CH_2–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 (CO_2); 176.2 (CO). EI-MS: 171 (55), 153 (8), 136 (80), 77 (90), 59 (3), 45 (5). Anal. calc. for $C_{20}H_{17}ClN_2O_4S$ (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. ^{1}H-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*, $\Delta\nu_{AB}$ = 52.3, ^2J = 14.5, 2 H, CH_2); 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). ^{13}C-NMR: 29.6 (CH_2–S); 34.5 (CH_2); 40.7 (CH); 47.3 (CH_2–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 (CO_2); 176.3 (CO). EI-MS: 171 (50), 153 (10), 136 (75), 77 (80), 59 (5), 45 (5). Anal. calc. for $C_{20}H_{17}ClN_2O_4S$ (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. ^{1}H-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*, $\Delta\nu_{AB} = 82.3$, $^2J = 17.8$, 2 H, CH_2); 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). ^{13}C-NMR: 26.8 (CH_2–S); 35.0 (CH_2); 41.8 (CH); 45.9 (CH_2–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 (CO_2); 176.2 (CO). EI-MS: 153 (5), 136 (80), 77 (85), 59 (5), 45 (10). Anal. calc. for $C_{24}H_{20}N_2O_4S$ (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. ^{1}H-NMR: 0.95 (*t*, $^3J = 7.5$, 3 H, Me); 1.40–1.42 (*m*, 2 H, CH_2); 1.69–1.71 (*m*, 2 H, CH_2); 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, CH_2); 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). ^{13}C-NMR: 20.8 (Me); 26.9 (CH_2); 29.3 (CH_2); 35.0 (CH_2–S); 37.6 (CH_2); 41.5 (CH); 45.6 (CH_2–N); 128.2 (CH); 129.3 (2 CH); 130.3 (2 CH); 135.9 (C); 162.8 (C=N); 172.0 (CO); 172.6 (CO_2); 176.3 (CO). EI-MS: 193 (55), 156 (8), 136 (75), 77 (80), 59 (10), 45 (10). Anal. calc. for $C_{17}H_{20}N_2O_4S$ (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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