# SUPPORTING INFORMATION

# Thiazolidinone–Peptide Hybrids as Dengue Virus Protease Inhibitors with Antiviral Activity in Cell Culture

*Christoph Nitsche,*[†] *Verena N. Schreier,*[†] *Mira A. M. Behnam,*[†] *Anil Kumar,*[‡] *Ralf Bartenschlager,*[‡] *Christian D. Klein**[,†]

[†]Medicinal Chemistry, Institute of Pharmacy and Molecular Biotechnology IPMB, Heidelberg University, Im Neuenheimer Feld 364, 69120 Heidelberg, Germany

[‡]Molecular Virology, Department of Infectious Diseases, Heidelberg University, Im Neuenheimer Feld 345, 69120 Heidelberg, Germany

*To whom correspondence should be addressed: Prof. C. Klein, Tel.: (+)49-6221-544875; Fax: (+)49-6221-546430; E-mail address: c.klein@uni-heidelberg.de

**CONTENTS:**


1. Aprotinin Competition Assay (Figure S1) S3

2. Inhibitory Activity of Representative Capping Molecules (Table S1) S4

3. Effects on the Renilla and Firefly Luciferase Activities (Figure S2) S6

4. Detailed Procedure for the Synthesis of N-Terminal Capped Peptide Hybrids S9

5. HRMS and HPLC Data S11

6. Experimental Procedures and Analytical Data for Synthetic Intermediates S14

## 1. Aprotinin Competition Assay

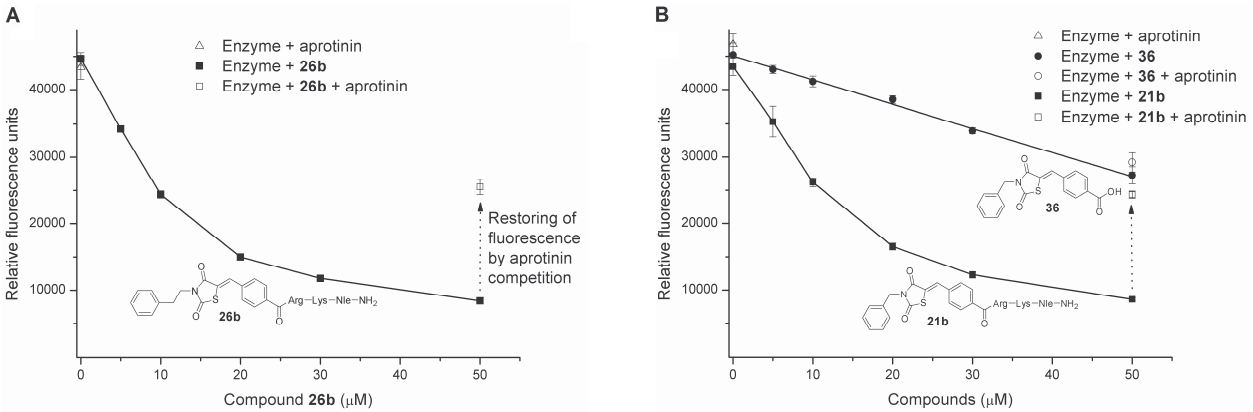
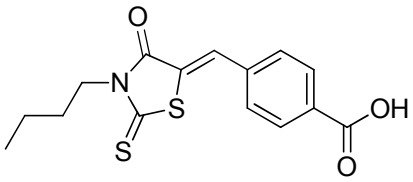
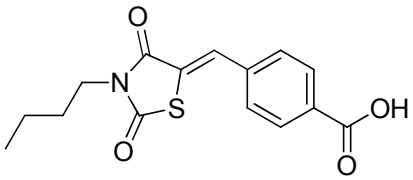
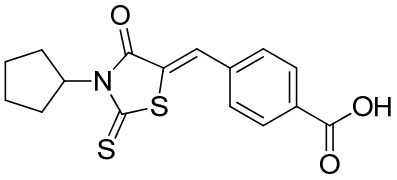
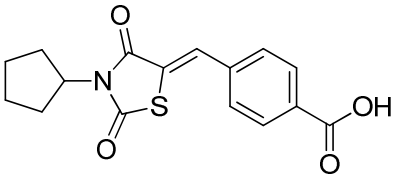
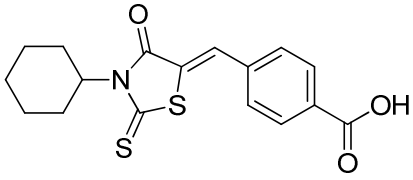
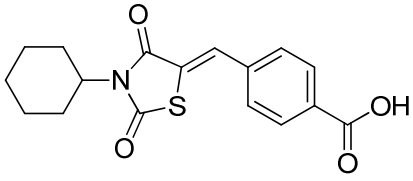
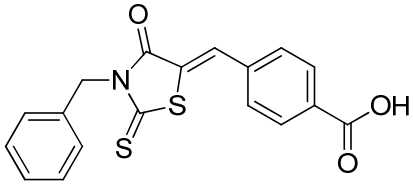
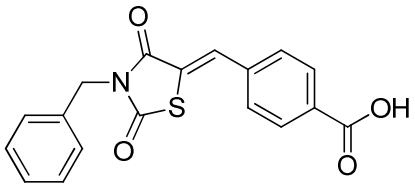
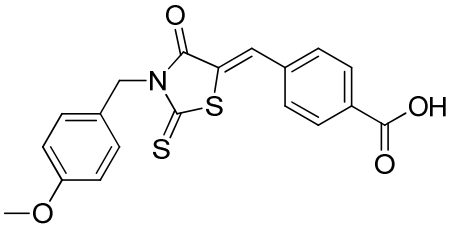
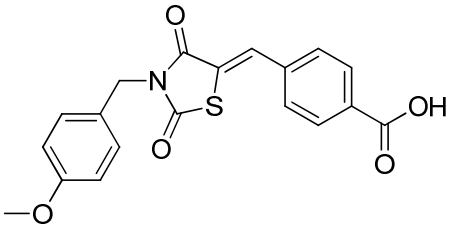
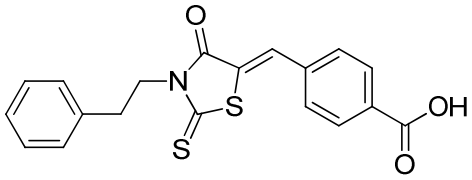
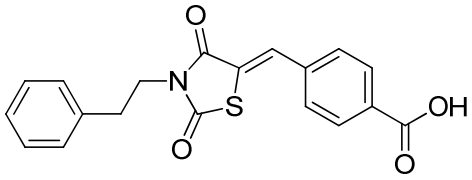



**Figure S1.** Results of the aprotinin competition assay are illustrated. The dengue virus protease is autofluorescent due to tryptophan residues. In Graph **A** the concentration dependent nonlinear quenching of the autofluorescence by inhibitor **26b** is shown. This effect is due to FRET interaction of the inhibitor and Trp50 near the active site. Fluorescence intensity is restored upon addition of aprotinin. Graph **B** shows the analogous experiment for compound **21b**, but additionally the results for the corresponding chromophore moiety without peptide sequence (compound **36**) are shown. For this compound only a weakly linear decrease of the fluorescence was found. No significant increase was observed upon addition of aprotinin, which indicates that **21b** does not bind to the active site. It is most likely that the linear decrease of fluorescence is due to the "inner filter effect" (non-FRET absorption).

## 2. Inhibitory Activity of Representative Capping Molecules

**Table S1.** Inhibitory Activity of Representative Capping Molecules at the dengue Virus Protease, West Nile Virus Protease and Thrombin.

| **Structure** | **DEN**[a] | **WNV**[b] | **THR**[c] |
|---|---|---|---|
|  | 31.2 ± 3.6 | 30.3 ± 4.2 | 8.3 ± 1.1 |
|  | 29.3 ± 2.9 | 43.5 ± 7.0 | 7.0 ± 0.6 |
|  | 32.5 ± 2.6 | 26.7 ± 5.4 | 7.0 ± 1.9 |
|  | 24.8 ± 0.4 | 30.9 ± 7.8 | 6.9 ± 1.5 |
|  | 33.0 ± 3.1 | 23.0 ± 7.1 | 7.3 ± 1.0 |
|  | 23.4 ± 3.6 | 38.8 ± 3.8 | 9.4 ± 2.4 |
|  | 26.4 ± 0.6 | 26.7 ± 1.7 | 8.1 ± 0.3 |

| | | | |
|---|---|---|---|
|  | 18.9<br>± 1.5 | 24.6<br>± 5.9 | 8.8<br>± 1.2 |
|  | 29.8<br>± 5.3 | 22.6<br>± 2.9 | 6.8<br>± 1.2 |
|  | 24.6<br>± 3.3 | 39.5<br>± 7.1 | 7.7<br>± 1.4 |
|  | 32.2<br>± 4.7 | 25.5<br>± 1.6 | 6.7<br>± 0.3 |
|  | 30.3<br>± 5.4 | 32.1<br>± 6.6 | 5.4<br>± 2.2 |

[a] % inhibition of the DEN NS2B-NS3 protease serotype 2 (enzyme: 100 nM, inhibitor 50 µM, substrate 50 µM, $K_m$ = 105 µM). None of the compounds showed significant inhibition in a HPLC-based assay.

[b] % inhibition of the WNV NS2B-NS3 protease (enzyme: 150 nM, inhibitor 50 µM, substrate 50 µM, $K_m$ = 212 µM).

[c] % inhibition of thrombin (enzyme: 10 nM, inhibitor 25 µM, substrate 50 µM, $K_m$ = 16 µM).

**3. Effects on the Renilla and Firefly Luciferase Activities**

Huh-7 cells stably expressing firefly luciferase or renilla luciferase were seeded into white clear-bottom 96-well plates (10000 cells/well) in a volume of 100 µl complete DMEM. To eliminate edge effects due to medium evaporation, the outer wells were seeded with cells but were not used for the experiment. After overnight incubation of the cells at 37 °C, the medium was replaced by DMEM containing appropriate concentration of compound stock. One hour later the medium was removed, 50 µl of luciferase lysis buffer were added (1% Triton X-100, 25 mM glycylglycine, 15 mM $MgSO_4$, 4 mM EGTA and 1 mM DTT, pH 7.8) and kept frozen at -20 °C until measured.

The luciferase reporter activity was measured using a luminometer capable of measuring 96-well plates (Mithras LB940). The plates were thawed and kept at 4 °C until measurement was done. For firefly reporter assay each well was injected with 75 µl assay buffer (25 mM glycylglycine, 15 mM $MgSO_4$, 4 mM EGTA, 1 mM DTT, 2 mM ATP and 15 mM $K_2PO_4$, pH 7.8) containing 70 µM luciferin and measured for 1 second. Renilla reporter activity was induced by injecting 50 µl assay buffer (25 mM glycylglycine, 15 mM $MgSO_4$, 4 mM EGTA and 15 mM $K_2PO_4$, pH 7.8) containing 5 µg/ml coelenterazine and measured for 0.1 second.

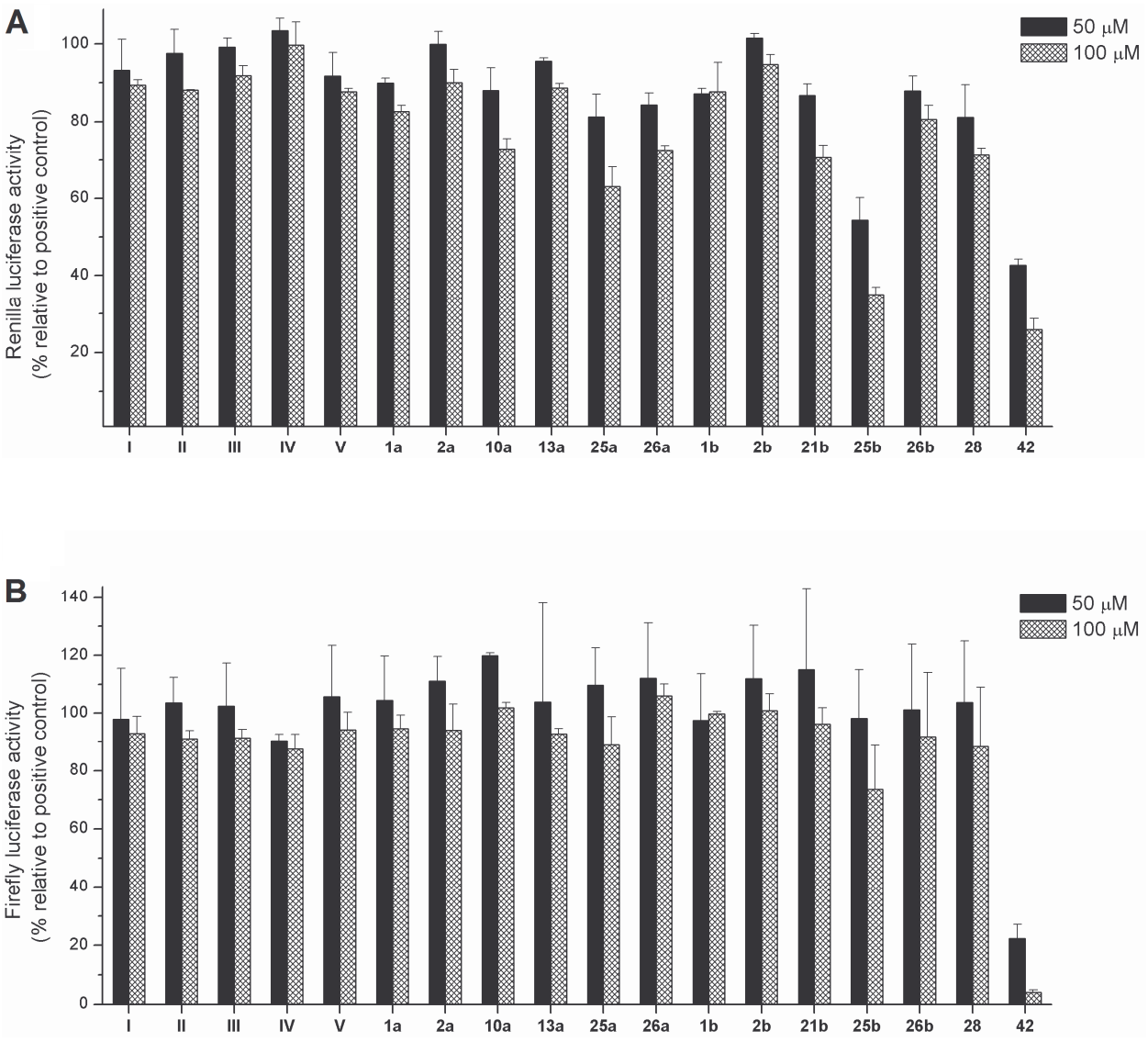



**Figure S2.** Effect of selected compounds on the renilla (diagram **A**) and firefly (diagram **B**) luciferase activity. Results are shown as %-activity compared to a positive control without test compounds. Measurements were done at compound concentrations of 50 and 100 µM, respectively. Only for compound **42** a significant interference with the firefly luciferase was observed, leading to false positive results in the cytotoxicity reporter gene assay. Compounds **42** and **25b** show significant interferences with the renilla luciferase, leading to the possibility of false-positive results in the dengue virus reporter gene assay. For the other compounds,

interferences were absent or of very minor degree at high concentrations with the renilla luciferase.

**4. Detailed Procedure for the Synthesis of N-Terminal Capped Peptide Hybrids**

The short peptides with different N-terminal caps were manually prepared by solid phase peptide synthesis according to the Fmoc protocol. The Rink amide resin was washed with DMF (2 x 15 min) to swell the resin. Fmoc deprotection was carried out with a solution of 30% piperidine in DMF (2 x 10 min). After washing with DMF (3 x), DCM (3 x) and DMF (3 x) a solution of the *N*-α-Fmoc-protected amino acid (3 equivalents), HBTU (3 equivalents) and DIPEA (3 equivalents) in DMF (<1.0 ml per 100 mg resin) was added for the coupling step. The reaction time was 90 min per coupling and then the resin was washed with DMF (4 x). The Fmoc deprotection and the washing procedures were repeated as described, until the completion of the synthesis of the desired peptide sequence. Finally, the cap molecule (3 equivalents) was coupled in an analogous procedure and the resin was washed with DMF (2 x), DCM (2 x) and diethyl ether (2 x). The peptide was cleaved from the resin using a mixture of 95% TFA, 2.5% triisopropylsilane and 2.5% water (2 h, 1.0 ml per 100 mg resin). The cleavage solution was filtered into ice-cold diethyl ether (10-20 ml per 100 mg resin) and the precipitate was centrifuged, washed with diethyl ether and dried in vacuum. All crude peptides were purified by preparative HPLC on an ÄKTA Purifier (GE Healthcare, Germany), with an RP-18 pre and main column (Rephospher, Dr. Maisch GmbH, Germany, C18-DE, 5 µm, 30 x 16 mm and 120 x 16 mm). The conditions were: eluent A: 0.1 % TFA in water, eluent B: 0.1 % TFA in methanol, flow rate: 8 ml/min, gradient: 10% B (2.5 min), 100% B (23.5 min), 100% B (26 min) 10% B (26.1 min), 10% B (30 min). Detection was performed at 214 nm, 254 nm and 280 nm. After freeze-drying, the peptides were stored at –20 °C. Identity and purity were determined by LC-HRMS, using an Agilent 1200 HPLC system with a multiple-wavelength detector combined with the Bruker micrOTOF-Q II instrument on an RP-18 column (ReproSil-Pur-ODS-3, Dr. Maisch

GmbH, Germany, 3 µm, 50 x 2 mm). The conditions were: eluent A: water (0.1% $HCO_2H$), eluent B: acetonitrile (0.1% $HCO_2H$), flow rate: 0.4 ml/min, gradient: 5% B (1 min), 95% B (6 min), 95% B (10 min), 5% B (10.1 min), 5% B (12 min). UV-detection was performed at 214 nm, 254 nm and 280 nm. Compounds were used at a concentration of 100 µM in water/acetonitrile (9:1).

## 5. HRMS and HPLC Data

| No. | HRMS (ESI) for $[M+H]^+$ | | | HPLC purity (254 nm) |
|---|---|---|---|---|
| | Formula | Calcd. | Found | |
| **1a** | $C_{29}H_{44}N_9O_5S_2$ | 662.2901 | 662.2913 | >95% |
| **2a** | $C_{30}H_{46}N_9O_5S_2$ | 676.3058 | 676.3056 | >95% |
| **3a** | $C_{31}H_{48}N_9O_5S_2$ | 690.3214 | 690.3222 | >95% |
| **4a** | $C_{32}H_{48}N_9O_5S_2$ | 702.3214 | 702.3226 | >95% |
| **5a** | $C_{32}H_{50}N_9O_5S_2$ | 704.3371 | 704.3380 | >95% |
| **6a** | $C_{32}H_{50}N_9O_5S_2$ | 704.3371 | 704.3381 | >95% |
| **7a** | $C_{33}H_{52}N_9O_5S_2$ | 718.3527 | 718.3544 | >95% |
| **9a** | $C_{34}H_{52}N_9O_5S_2$ | 730.3527 | 730.3545 | >95% |
| **10a** | $C_{35}H_{54}N_9O_5S_2$ | 744.3684 | 744.3689 | >95% |
| **11a** | $C_{34}H_{52}N_9O_6S_2$ | 746.3476 | 746.3489 | >95% |
| **12a** | $C_{36}H_{56}N_9O_7S_2$ | 790.3739 | 790.3748 | >95% |
| **13a** | $C_{32}H_{48}N_9O_5S_2$ | 702.3214 | 702.3231 | >95% |
| **14a** | $C_{31}H_{48}N_9O_6S_2$ | 706.3163 | 706.3165 | >95% |
| **15a** | $C_{33}H_{50}N_9O_7S_2$ | 748.3269 | 748.3282 | 93% |
| **16a** | $C_{35}H_{48}N_9O_5S_2$ | 738.3214 | 38.3242 | >95% |
| **17a** | $C_{36}H_{50}N_9O_5S_2$ | 752.3371 | 752.3384 | >95% |
| **18a** | $C_{36}H_{50}N_9O_6S_2$ | 768.3320 | 768.3338 | >95% |
| **19a** | $C_{35}H_{47}FN_9O_5S_2$ | 756.3120 | 756.3118 | >95% |
| **20a** | $C_{35}H_{47}ClN_9O_5S_2$ | 772.2825 | 772.2843 | >95% |

| | | | | |
|---|---|---|---|---|
| **21a** | $C_{36}H_{50}N_9O_5S_2$ | 752.3371 | 752.3383 | >95% |
| **22a** | $C_{37}H_{52}N_9O_5S_2$ | 766.3527 | 766.3537 | >95% |
| **23a** | $C_{37}H_{52}N_9O_6S_2$ | 782.3476 | 782.3498 | >95% |
| **24a** | $C_{36}H_{49}FN_9O_5S_2$ | 770.3277 | 770.3296 | >95% |
| **25a** | $C_{36}H_{49}ClN_9O_5S_2$ | 786.2981 | 786.3004 | >95% |
| **26a** | $C_{37}H_{52}N_9O_5S_2$ | 766.3527 | 766.3530 | >95% |
| **1b** | $C_{29}H_{44}N_9O_6S$ | 646.3130 | 646.3133 | >95% |
| **2b** | $C_{30}H_{46}N_9O_6S$ | 660.3286 | 660.3288 | 90% |
| **3b** | $C_{31}H_{48}N_9O_6S$ | 674.3443 | 674.3465 | >95% |
| **5b** | $C_{32}H_{50}N_9O_6S$ | 688.3599 | 688.3613 | >95% |
| **6b** | $C_{32}H_{50}N_9O_6S$ | 688.3599 | 688.3608 | >95% |
| **7b** | $C_{33}H_{52}N_9O_6S$ | 702.3756 | 702.3772 | >95% |
| **8b** | $C_{41}H_{68}N_9O_6S$ | 814.5008 | 814.5001 | 95% |
| **9b** | $C_{34}H_{52}N_9O_6S$ | 714.3756 | 714.3764 | >95% |
| **10b** | $C_{35}H_{54}N_9O_6S$ | 728.3912 | 728.3925 | >95% |
| **13b** | $C_{32}H_{48}N_9O_6S$ | 686.3443 | 686.3453 | >95% |
| **14b** | $C_{31}H_{48}N_9O_7S$ | 690.3392 | 690.3389 | >95% |
| **15b** | $C_{33}H_{50}N_9O_8S$ | 732.3498 | 732.3508 | >95% |
| **17b** | $C_{36}H_{50}N_9O_6S$ | 736.3599 | 736.3609 | >95% |
| **21b** | $C_{36}H_{50}N_9O_6S$ | 736.3599 | 736.3607 | >95% |
| **22b** | $C_{37}H_{52}N_9O_6S$ | 750.3756 | 750.3762 | 90% |
| **23b** | $C_{37}H_{52}N_9O_7S$ | 766.3705 | 766.3726 | >95% |
| **24b** | $C_{36}H_{49}FN_9O_6S$ | 754.3505 | 754.3501 | >95% |

| | | | | |
|---|---|---|---|---|
| **25b** | $C_{36}H_{49}ClN_9O_6S$ | 770.3210 | 770.3202 | >95% |
| **26b** | $C_{37}H_{52}N_9O_6S$ | 750.3756 | 750.3762 | >95% |
| **27** | $C_{36}H_{50}N_9O_6S$ | 736.3599 | 736.3613 | >95% |
| **28** | $C_{35}H_{48}N_9O_6S$ | 722.3443 | 722.3461 | >95% |
| **29** | $C_{36}H_{50}N_{11}O_6S$ | 764.3661 | 764.3662 | >95% |
| **30** | $C_{36}H_{49}N_8O_6S$ | 721.3490 | 721.3514 | >95% |
| **31** | $C_{36}H_{50}N_7O_6S$ | 708.3538 | 708.3545 | >95% |
| **32** | $C_{36}H_{50}N_9O_6S$ | 736.3599 | 736.3610 | >95% |
| **33** | $C_{36}H_{50}N_9O_6S$ | 736.3599 | 736.3628 | >95% |
| **34** | $C_{30}H_{39}N_8O_5S$ | 623.2759 | 623.2775 | >95% |
| **35** | $C_{24}H_{27}N_6O_4S$ | 495.1809 | 495.1838 | >95% |
| **36** | $C_{18}H_{14}NO_4S$ | 340.0638 | 340.0626 | >95% |
| **37** | $C_{29}H_{44}N_9O_5S_2$ | 662.2901 | 662.2922 | >95% |
| **38** | $C_{34}H_{52}N_9O_6S$ | 714.3756 | 714.3768 | >95% |
| **39** | $C_{32}H_{50}N_9O_7S_2$ | 736.3269 | 736.3269 | >95% |
| **40** | $C_{39}H_{56}N_9O_7S_2$ | 826.3739 | 826.3718 | >95% |
| **41** | $C_{31}H_{50}N_9O_6S_2$ | 708.3320 | 708.3316 | >95% |
| **42** | $C_{31}H_{48}N_9O_6S_2$ | 706.3163 | 706.3168 | >95% |
| **43** | $C_{35}H_{49}N_{10}O_5S$ | 721.3603 | 721.3606 | >95% |
| **44** | $C_{36}H_{51}N_{10}O_5S$ | 735.3759 | 735.3757 | >95% |

## 6. Experimental Procedures and Analytical Data for Synthetic Intermediates

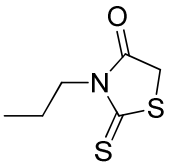
**3-Methyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (69% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.37 (s, 3H), 3.99 (s, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 31.3, 35.6, 173.7, 201.3 ppm; MS (EI, 70 eV): *m/z* (%): 147.0 (100) [$M^+$]; Anal. calcd for $C_4H_5NOS_2$: C, 32.63; H, 3.42; N, 9.51. Found: C, 32.63; H, 3.57; N, 9.40.

**3-Ethyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (71% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.21 (t, $J$ = 7.2 Hz, 3H), 3.95 (s, 2H), 4.05 (q, $J$ = 7.2 Hz, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 12.0, 35.4, 39.9, 173.6, 200.9 ppm; MS (EI, 70 eV): *m/z* (%): 161.0 (95) [$M^+$]; Anal. calcd for $C_5H_7NOS_2$: C, 37.24; H, 4.38; N, 8.69. Found: C, 37.33; H, 4.51; N, 8.68.

**3-Cyclopropyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a colorless solid (65% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 0.94 (m, 2H), 1.12 (m, 2H), 2.72 (m, 1H), 3.89 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 7.2, 27.6, 35.1, 174.0, 202.3 ppm; MS (EI, 70 eV): *m/z* (%): 173.0 (95) [$M^+$]; Anal. calcd for $C_6H_7NOS_2$: C, 41.59; H, 4.07; N, 8.08. Found: C, 41.65; H, 4.22; N, 8.05.

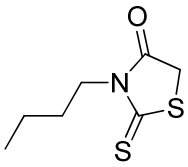
**3-Isopropyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (69% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.47 (d, $J$ = 6.9 Hz, 6H), 3.82 (s, 2H), 5.22 (sept, $J$ = 6.9 Hz, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 18.2, 34.0, 50.4, 174.2, 202.1 ppm; MS (EI, 70 eV): *m/z* (%): 175.0 (93) [$M^+$]; Anal. calcd for $C_6H_9NOS_2$: C, 41.12; H, 5.18; N, 7.99. Found: C, 41.26; H, 5.25; N, 7.99.

**3-Propyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a



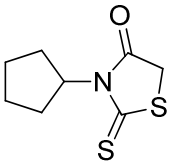
yellow liquid (58% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 0.93 (t, $J$ = 7.4 Hz, 3H), 1.66 (m, 2H), 3.93 (m, 2H), 3.96 (s, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 11.2, 20.1, 35.3, 46.2, 173.9, 201.2 ppm; MS (EI, 70 eV): *m/z* (%): 175.0 (100) [$M^+$]; Anal. calcd for $C_6H_9NOS_2$: C, 41.12; H, 5.18; N, 7.99. Found: C, 41.04; H, 5.22; N, 8.36.

3-**Butyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a



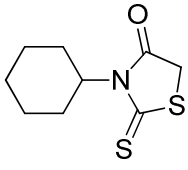
yellow liquid (58% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 0.94 (t, $J$ = 7.3 Hz, 3H), 1.35 (m, 2H), 1.61 (m, 2H), 3.95 (s, 2H), 3.97 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 13.6, 20.0, 28.8, 35.3, 44.6, 173.9, 201.2 ppm; MS (EI, 70 eV): *m/z* (%): 189.0 (100) [$M^+$]; Anal. calcd for $C_7H_{11}NOS_2$: C, 44.41; H, 5.86; N, 7.40. Found: C, 44.59; H, 5.78; N, 8.05.

**3-Cyclopentyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting



in a colorless solid (59% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.53-1.67 (m, 2H), 1.80-2.00 (m, 4H), 2.03-2.17 (m, 2H), 3.81 (s, 2H), 5.31 (quint, $J$ = 8.7 Hz, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 25.5, 27.5, 34.2, 57.8, 173.8, 202.5 ppm; MS (EI, 70 eV): *m/z* (%): 201.0 (76) [$M^+$]; Anal. calcd for $C_8H_{11}NOS_2$: C, 47.73; H, 5.51; N, 6.96. Found: C, 47.73; H, 5.58; N, 6.97.

**3-Cyclohexyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in



a colorless solid (37% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.15-1.42 (m, 3H), 1.58-1.71 (m, 3H), 1.80-1.90 (m, 2H), 2.21-2.37 (m, 2H), 3.81 (s, 2H), 4.85 (td, $J$ = 12.3, 3.8 Hz, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 25.0, 26.0, 27.5, 33.9, 58.4, 174.2, 202.3 ppm; MS (EI, 70 eV): *m/z* (%): 215.0 (76) [$M^+$].

**3-(Tetrahydrofuran-2-ylmethyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (68% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.65 (m, 1H), 1.80-2.07 (m, 3H), 3.72 (m, 1H), 3.82-3.95 (m, 2H), 3.98 (d, $J$ = 3.8 Hz, 2H), 4.09 (m, 1H), 4.36 (m, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 25.2, 29.1, 35.3, 47.9, 67.9, 74.6, 173.9, 201.6 ppm; MS (EI, 70 eV): *m/z* (%): 217.0 (18) [$M^+$]; Anal. calcd for $C_8H_{11}NO_2S_2$: C, 44.22; H, 5.10; N, 6.45. Found: C, 44.53; H, 5.24; N, 6.39.

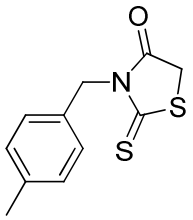
**3-Allyl-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (77% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.97 (s, 2H), 4.57 (dt, $J$ = 6.0, 1.4 Hz, 2H), 5.18-5.28 (m, 2H), 5.77 (m, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.7, 46.4, 119.5, 129.3, 173.3, 200.6 ppm; MS (EI, 70 eV): *m/z* (%): 173.1 (96) [$M^+$]; Anal. calcd for $C_6H_7NOS_2$: C, 41.59; H, 4.07; N, 8.08. Found: C, 41.66; H, 3.98; N, 8.05.

**3-(2-Phenylethyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B resulting in a pale yellow solid (65% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 2.93 (m, 2H), 3.92 (s, 2H), 4.19 (m, 2H), 7.20-7.33 (m, 5H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 32.6, 35.2, 45.7, 126.8, 128.5, 128.9, 137.3, 173.4, 200.9 ppm; MS (EI, 70 eV): *m/z* (%): 236.9 (76) [$M^+$]; Anal. calcd for $C_{11}H_{11}NOS_2$: C, 55.67; H, 4.67; N, 5.90. Found: C, 55.67; H, 4.82; N, 5.88.

**3-Benzyl-2-thioxo-1,3-thiazolidin-4-one**. Synthesis according to procedure B resulting in a pale yellow solid (81% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.98 (s, 2H), 5.18 (s, 2H), 7.30 (m, 3H), 7.42 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.4, 47.6, 128.2, 128.6, 129.0, 134.7, 173.8, 201.0 ppm; MS (EI, 70 eV): *m/z*

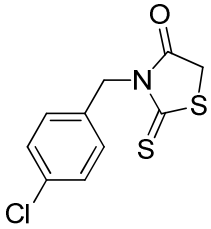
(%): 222.9 (88) [$M^+$]; Anal. calcd for $C_{10}H_9NOS_2$: C, 53.78; H, 4.06; N, 6.27. Found: C, 53.92; H, 4.13; N, 6.23.

**3-(4-Methylbenzyl)-2-thioxothiazolidin-4-one.** Synthesis according to procedure B resulting



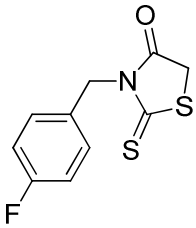

in a pale yellow oil (86% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 2.31 (s, 3H), 3.96 (s, 2H), 5.14 (s, 2H), 7.10 (m, 2H), 7.32 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 21.2, 35.4, 47.4, 129.1, 129.2, 131.7, 138.0, 173.8, 201.0 ppm; MS (EI, 70 eV): *m/z* (%): 237.0 (84) [$M^+$].

**3-(4-Chlorobenzyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B



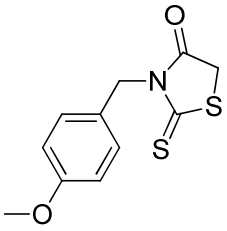

resulting in a pale yellow solid (80% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.98 (s, 2H), 5.13 (s, 2H), 7.27 (m, 2H), 7.38 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.6, 46.9, 128.7, 130.6, 133.1, 134.2, 173.7, 200.8 ppm; MS (EI, 70 eV): *m/z* (%): 256.8 (85) [$M^+$]; Anal. calcd for $C_{10}H_8ClNOS_2$: C, 46.60; H, 3.13; N, 5.43. Found: C, 46.48; H, 3.43; N, 5.23.

**3-(4-Fluorobenzyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure B



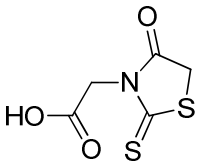

resulting in a pale yellow solid (85% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.97 (s, 2H), 5.14 (s, 2H), 6.98 (m, 2H), 7.44 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.4, 46.8, 115.3 + 115.6 (d, $J_{CF}$ = 21.6 Hz), 130.5 + 130.6 (d, $J_{CF}$ = 3.5 Hz), 131.1 + 131.3 (d, $J_{CF}$ = 8.1 Hz), 160.9 + 164.2 (d, $J_{CF}$ = 247 Hz), 173.8, 200.9 ppm; MS (EI, 70 eV): *m/z* (%): 240.9 (84) [$M^+$]; Anal. calcd for $C_{10}H_8FNOS_2$: C, 49.77; H, 3.34; N, 5.80. Found: C, 50.30; H, 3.71; N, 5.38.

**3-(4-Methoxybenzyl)-2-thioxo-1,3-thiazolidin-4-one**. Synthesis according to procedure B



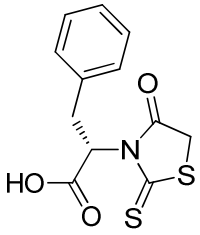
resulting in a pale yellow solid (20% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.77 (s, 3H), 3.95 (s, 2H), 5.11 (s, 2H), 6.83 (m, 2H), 7.41 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.4, 47.1, 55.2, 113.8, 127.0, 130.8, 159.5, 173.9, 201.0 ppm; MS (EI, 70 eV): *m/z* (%): 252.9 (81) [$M^+$]; Anal. calcd for $C_{11}H_{11}NO_2S_2$: C, 52.15; H, 4.38; N, 5.53. Found: C, 53.78; H, 4.88; N, 5.04.

**2-(4-Oxo-2-thioxothiazolidin-3-yl)acetic acid.** Synthesis according to procedure B resulting



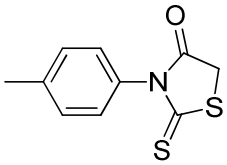
in a crude product as pale yellow solid (86% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.08 (s, 2H), 4.77 (s, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.6, 44.4, 171.0, 173.1, 200.2 ppm; MS (EI, 70 eV): *m/z* (%): 191.0 (94) [$M^+$].

**(*S*)-2-(4-Oxo-2-thioxothiazolidin-3-yl)-3-phenylpropanoic acid.** Synthesis according to



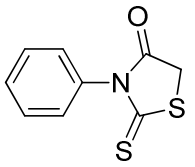
procedure B resulting in a crude product as orange oil (97% yield). $^{1}$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.49-3.56 (m, 2H), 4.13 (m, 2H), 5.84 (m, 1H), 7.13-7.29 (m, 5H) ppm; $^{13}$C-NMR (75 MHz, acetone-$d_6$): $\delta$ = 34.1, 35.1, 58.9, 127.6, 129.1, 130.0, 137.6, 169.1, 174.6, 203.3 ppm; MS (EI, 70 eV): *m/z* (%): 280.9 (58) [$M^+$].

**3-(4-Methylphenyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure C

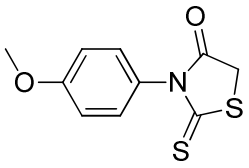


resulting in a pale yellow solid (54% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 2.41 (s, 3H), 4.17 (s, 2H), 7.07 (m, 2H), 7.33 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 21.4, 36.3, 128.0, 130.4, 132.2, 140.0, 173.5, 201.3 ppm; MS (EI, 70 eV): *m/z* (%): 223.1 (100) [$M^+$]; Anal. calcd for $C_{10}H_9NOS_2$: C, 53.78; H, 4.06; N, 6.27. Found: C, 55.92; H, 4.28; N, 6.84.

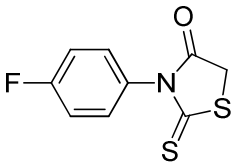
**3-Phenyl-2-thioxo-1,3-thiazolidin-4-one**. Synthesis according to procedure C resulting in a pale yellow solid (32% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.18 (s, 2H), 7.19 (m, 2H), 7.52 (m, 3H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 36.3, 128.3, 129.6, 129.8, 134.9, 173.4, 201.1 ppm; MS (EI, 70 eV): *m/z* (%): 208.9 (100) [$M^+$]; Anal. calcd for $C_9H_7NOS_2$: C, 51.65; H, 3.37; N, 6.69. Found: C, 50.51; H, 3.42; N, 6.33.



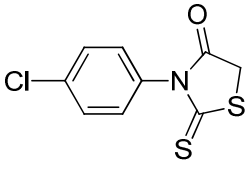
**3-(4-Methoxyphenyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure C resulting in a pale yellow solid (39% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.84 (s, 3H), 4.16 (s, 2H), 7.02 (m, 2H), 7.10 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 36.2, 55.5, 114.9, 127.2, 129.4, 160.3, 173.5, 201.5 ppm; MS (EI, 70 eV): *m/z* (%): 238.9 (100) [$M^+$]; Anal. calcd for $C_{10}H_9NO_2S_2$: C, 50.19; H, 3.79; N, 5.85. Found: C, 50.24; H, 3.73; N, 5.82.



**3-(4-Fluorophenyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure C resulting in a pale yellow solid (38% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.18 (s, 2H), 7.15-7.25 (m, 4H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 36.2, 116.6 + 116.9 (d, $J_{CF}$ = 23.3 Hz), 130.2 + 130.4 (d, $J_{CF}$ = 9.2 Hz), 130.5 + 130.6 (d, $J_{CF}$ = 3.2 Hz), 161.3 + 164.6 (d, $J_{CF}$ = 250 Hz), 173.3, 201.0 ppm; MS (EI, 70 eV): *m/z* (%): 227.1 (100) [$M^+$]; Anal. calcd for $C_9H_6FNOS_2$: C, 47.56; H, 2.66; N, 6.16. Found: C, 47.68; H, 2.41; N, 6.17.

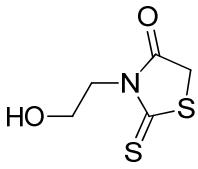


**3-(4-Chlorophenyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure C resulting in a pale yellow solid (47% yield). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.18 (s, 2H), 7.14 (m, 2H), 7.50 (m, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 36.3, 129.7, 129.9, 133.1, 135.8, 173.1, 200.7 ppm; MS (EI, 70



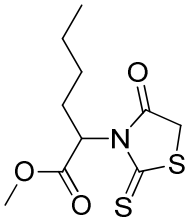
eV): *m/z* (%): 242.9 (100) [$M^+$]; Anal. calcd for $C_9H_6ClNOS_2$: C, 44.35; H, 2.48; N, 5.75. Found: C, 45.76; H, 2.51; N, 6.23.

**3-(2-Hydroxyethyl)-2-thioxo-1,3-thiazolidin-4-one.** Synthesis according to procedure C



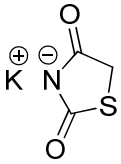
resulting in a pale yellow oil (17% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.90 (t, $J$ = 5.5 Hz, 2H), 4.01 (s, 2H), 4.25 (t, $J$ = 5.5 Hz, 2H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 35.4, 46.6, 59.9, 174.6, 201.9 ppm; MS (EI, 70 eV): *m/z* (%): 177.0 (60) [$M^+$]; Anal. calcd for $C_5H_7NO_2S_2$: C, 33.88; H, 3.98; N, 7.90. Found: C, 33.29; H, 4.12; N, 7.20.

**Methyl 2-(4-oxo-2-thioxo-1,3-thiazolidin-3-yl)hexanoate.** Synthesis according to procedure



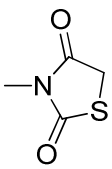
C resulting in a pale yellow oil (15% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 0.87 (t, $J$ = 7.1 Hz, 3H), 1.10-1.38 (m, 4H), 2.13-2.29 (m, 2H), 3.72 (s, 3H), 3.98 (s, 2H), 5.51 (dd, $J$ = 9.3, 5.9 Hz, 1H) ppm; $^{13}$C-NMR (75 MHz, $CDCl_3$): $\delta$ = 13.8, 22.3, 27.6, 28.2, 34.6, 52.7, 57.6, 168.7, 173.3, 201.0 ppm; MS (EI, 70 eV): *m/z* (%): 261.0 (55) [$M^+$]; Anal. calcd for $C_{10}H_{15}NO_3S_2$: C, 45.95; H, 5.78; N, 5.36. Found: C, 47.24; H, 6.12; N, 5.84.

**Potassium 2,4-dioxothiazolidin-3-ide.** Synthesis according to procedure D resulting in a



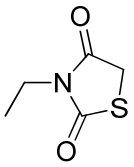
colorless solid (94% yield). $^1$H-NMR (300 MHz, DMSO-$d_6$): $\delta$ = 3.53 (s, 3H) ppm; HRMS (ESI): *m/z* [M–H]$^-$ calcd for $C_3H_2NO_2S$: 115.9812, found: 115.9804.

**3-Methylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale

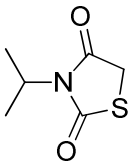


yellow solid (89% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.12 (s, 3H), 3.95 (s, 2H) ppm; HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_4H_5NNaO_2S$: 153.9933, found: 153.9943.

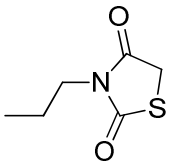
**3-Ethylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (66% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.20 (t, $J$ = 7.2 Hz, 3H), 3.68 (q, $J$ = 7.2 Hz, 2H), 3.93 (s, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 145.0 (78) [$M^+$].



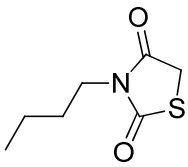
**3-Isopropylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (75% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.41 (d, $J$ = 6.9 Hz, 6H), 3.87 (s, 2H), 4.52 (sept, $J$ = 7.0 Hz, 1H) ppm; HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_6H_9NNaO_2S$: 182.0246, found: 182.0254.



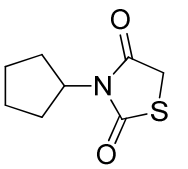
**3-Propylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (82% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.91 (t, $J$ = 7.4 Hz, 3H), 1.62 (m, 2H), 3.39 (s, 2H), 3.58 (m, 2H) ppm; HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_6H_9NNaO_2S$: 182.0246, found: 182.0254.



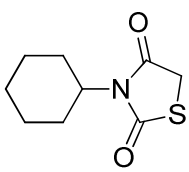
**3-Butylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (71% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 0.93 (t, $J$ = 7.3 Hz, 3H), 1.33 (m, 2H), 1.58 (m, 2H), 3.62 (m, 2H), 3.93 (s, 2H) ppm; HRMS (ESI): *m/z* [M+Na]$^+$ calcd for $C_7H_{11}NNaO_2S$: 196.0403, found: 196.0428.



**3-Cyclopentylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a colorless oil (54% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.56-1.65 (m, 2H), 1.78-1.93 (m, 4H), 1.95-2.07 (m, 2H), 3.88 (s, 2H), 4.62 (quint, $J$ = 8.7 Hz, 1H) ppm; MS (EI, 70 eV): *m/z* (%): 185.0 (2) [$M^+$].

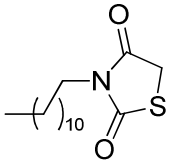


**3-Cyclohexylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a colorless solid (9% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.14-1.38 (m, 4H), 1.57-1.67 (m, 2H), 1.82-1.87 (m, 2H), 2.10-2.24 (m, 2H), 3.87 (s, 2H), 4.06-

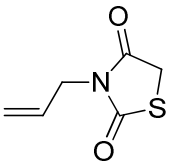


4.16 (m, 1H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_9H_{13}NNaO_2S$: 222.0559, found: 222.0571.

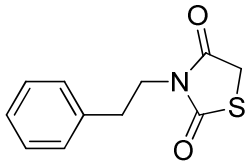
**3-Dodecylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow solid (80% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.88 (t, $J$ = 6.9, 3H), 1.25-1.28 (m, 18H), 1.58 (m, 2H), 3.61 (m, 2H), 3.93 (s, 2H) ppm; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{15}H_{28}NO_2S$: 286.1835, found: 286.1835.



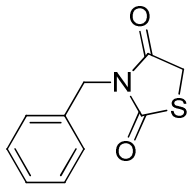
**3-Allylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a colorless solid (90% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.96 (s, 2H), 4.22 (dt, $J$ = 6.0, 1.4 Hz, 2H), 5.20-5.30 (m, 2H), 5.79 (m, 1H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_6H_7NNaO_2S$: 180.0090, found: 180.0127.



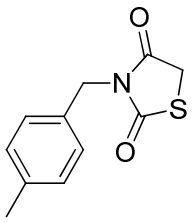
**3-Phenylethylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow solid (78% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.91 (m, 2H), 3.86 (m, 2H), 3.89 (s, 2H), 7.21-7.34 (m, 5H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{11}H_{11}NNaO_2S$: 244.0403, found: 244.0411.



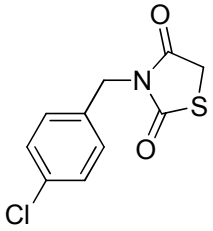
**3-Benzylthiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (85% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.94 (s, 2H), 4.77 (s, 2H), 7.29-7.35 (m, 3H), 7.36-7.41 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{10}H_9NNaO_2S$: 230.0246, found: 230.0253.



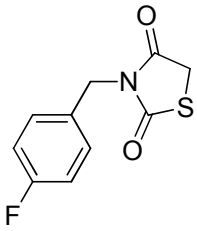
**3-(4-Methylbenzyl)thiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow oil (88% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 2.32 (s, 3H), 3.92 (s, 2H), 4.73 (s, 2H), 7.13 (m, 2H), 7.30 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{11}H_{12}NO_2S$: 222.0583, found: 222.0583.



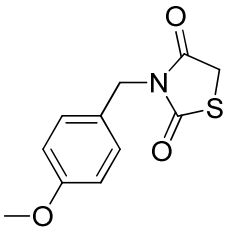
**3-(4-Chlorobenzyl)thiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a colorless solid (64% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.94 (s, 2H), 4.72 (s, 2H), 7.30 (m, 2H), 7.34 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{10}H_8ClNNaO_2S$: 263.9856, found: 263.9859.



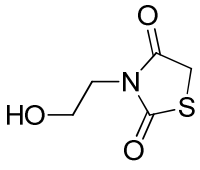

**3-(4-Fluorobenzyl)thiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a colorless solid (93% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.94 (s, 2H), 4.72 (s, 2H), 7.00 (m, 2H), 7.39 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{10}H_8FNNaO_2S$: 248.0152, found: 248.0164.



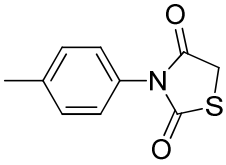

**3-(4-Methoxybenzyl)thiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a pale yellow solid (84% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.79 (s, 3H), 3.92 (s, 2H), 4.70 (s, 2H), 6.85 (m, 2H), 7.35 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{11}H_{11}NNaO_3S$: 260.0352, found: 260.0347.



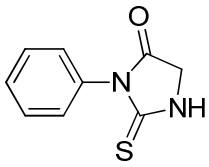

**3-(2-Hydroxyethyl)thiazolidine-2,4-dione.** Synthesis according to procedure D resulting in a crude product as pale yellow oil (80% yield). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 3.81 (m, 4H), 3.98 (s, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_5H_7NNaO_3S$: 184.0039, found: 184.0086.



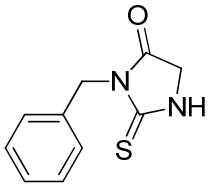

**3-(4-Methylphenyl)thiazolidine-2,4-dione.** Synthesis according to procedure E resulting in a colorless solid (14% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 2.40 (s, 3H), 4.12 (s, 2H), 7.13 (m, 2H), 7.31 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{10}H_9NNaO_2S$: 230.0246, found: 230.0289.



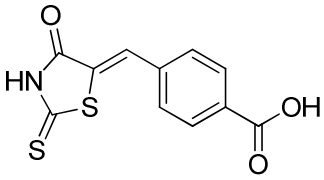
**3-Phenyl-2-thioxoimidazolidin-4-one.** Synthesis according to procedure F resulting in crude product as a pale pink solid (85% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.29 (s, 2H), 7.30-7.33 (m, 2H), 7.42-7.54 (m, 3H) ppm; HRMS (ESI): *m/z* $[M–H]^–$ calcd for $C_9H_7N_2OS$: 191.0285, found: 191.0267.



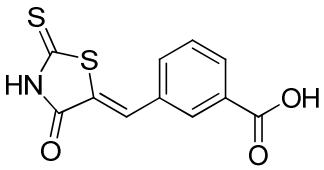

**3-Benzyl-2-thioxoimidazolidin-4-one.** Synthesis according to procedure F resulting in crude product as a colorless solid (90% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 4.08 (s, 2H), 5.00 (s, 2H), 7.28-7.34 (m, 3H), 7.47-7.50 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^–$ calcd for $C_{10}H_9N_2OS$: 205.0441, found: 205.0393.



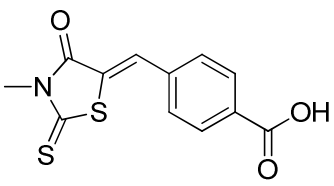

**4-[(4-Oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (98% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 7.69 (s, 1H), 7.76 (m, 2H), 8.19 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{11}H_7NNaO_3S_2$: 287.9760, found: 287.9755.



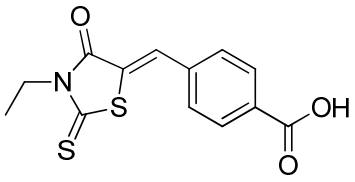

**3-[(4-Oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (96% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 7.21 (t, *J* = 7.8 Hz, 1H), 7.27 (s, 1H), 7.40 (m, 1H), 7.57 (m, 1H), 7.67 (m, 1H) ppm; MS (EI, 70 eV): *m/z* (%): 264.9 (33) $[M^+]$.



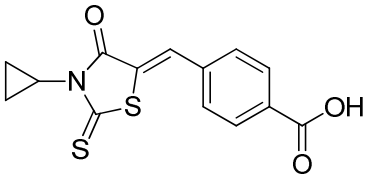

**4-[(3-Methyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (quant.). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.50 (s, 3H), 7.77 (m, 2H), 7.82 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 279.0 (35) $[M^+]$.



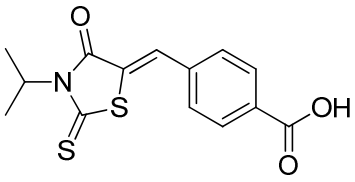
**4-[(3-Ethyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (99% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.26 (t, $J$ = 7.2 Hz, 3H), 4.17 (q, $J$ = 7.2 Hz, 2H), 7.77 (m, 2H), 7.81 (s, 1H), 8.18 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 293.0 (75) [$M^+$].



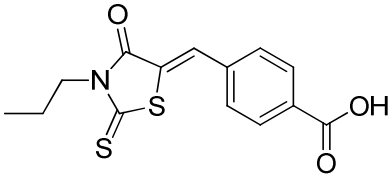

**4-[(3-Cyclopropyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (97% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.04-1.14 (m, 4H), 2.93 (m, 1H), 7.72 (m, 2H), 7.75 (s, 1H), 8.17 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 304.9 (75) [$M^+$].



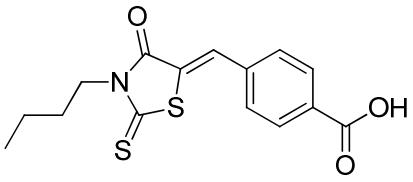

**4-[(3-Isopropyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (88% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.55 (d, $J$ = 7.0 Hz, 6H), 5.38 (sept, $J$ = 7.0 Hz, 1H), 7.72 (m, 2H), 7.76 (s, 1H), 8.18 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 307.0 (80) [$M^+$].



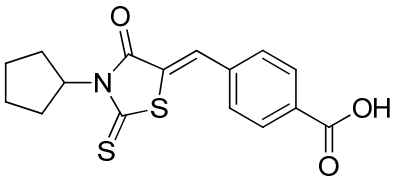

**4-[(4-Oxo-3-propyl-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (93% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 0.95 (t, $J$ = 7.5 Hz, 3H), 1.75 (m, 2H), 4.09 (m, 2H), 7.79 (m, 2H), 7.81 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 307.0 (76) [$M^+$].



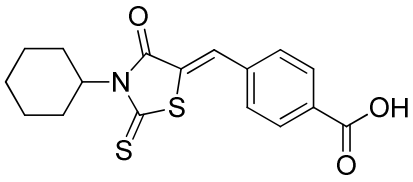
**4-[(3-Butyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (98% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 0.95 (t, $J$ = 7.3 Hz, 3H), 1.39 (m, 2H), 1.70 (m, 2H), 4.13 (m, 2H), 7.77 (m, 2H), 7.81 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 321.0 (49) [$M^+$].



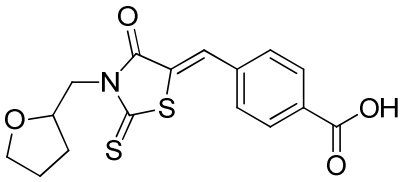

**4-[(3-Cyclopentyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (92% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.61-1.76 (m, 2H), 1.86-2.05 (m, 4H), 2.14-2.29 (m, 2H), 5.51 (m, 1H), 7.73 (s, 1H), 7.75 (m, 2H), 8.18 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 333.0 (72) [$M^+$].



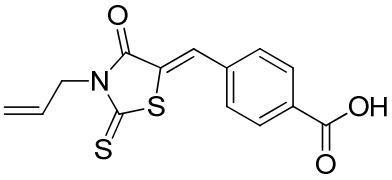

**4-[(3-Cyclohexyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (98% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.20-1.47 (m, 3H), 1.65-1.79 (m, 3H), 1.82-1.94 (m, 2H), 2.34-2.49 (m, 2H), 5.03 (m, 1H), 7.71 (s, 1H), 7.75 (m, 2H), 8.18 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 347.0 (60) [$M^+$].



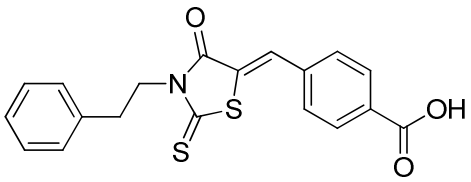

**4-[(4-Oxo-3-((tetrahydrofuran-2-yl)methyl)-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (87% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.70-2.07 (m, 4H), 3.67 (m, 1H), 3.82 (m, 1H), 4.05 (dd, $J$ = 13.2, 4.9 Hz, 1H), 4.25 (dd, $J$ = 13.2, 8.4 Hz, 1H), 4.40 (m, 1H), 7.78 (m, 2H), 7.81 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 348.9 (54) [$M^+$].



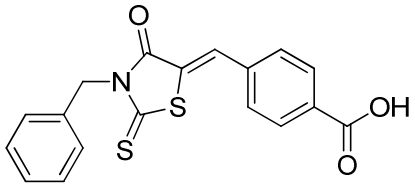
**4-[(3-Allyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (98% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 4.74 (dt, $J$ = 5.5, 1.5 Hz, 2H), 5.23 (m, 2H), 5.90 (m, 1H), 7.78 (m, 2H), 7.83 (s, 1H), 8.19 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{14}H_{10}NO_3S_2$: 304.0108, found: 304.0121.



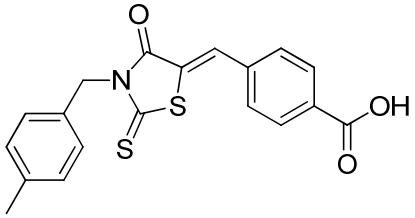

**4-[(4-Oxo-3-phenethyl-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (quant.). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.04 (m, 2H), 4.34 (m, 2H), 7.19-7.35 (m, 5H), 7.77 (m, 2H), 7.79 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 368.9 (66) $[M^+]$.



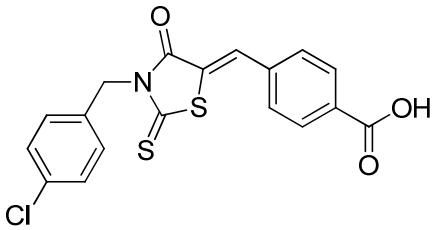

**4-[(3-Benzyl-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (93% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 5.34 (s, 2H), 7.27-7.37 (m, 3H), 7.40-4.45 (m, 2H), 7.79 (m, 2H), 7.85 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 354.9 (78) $[M^+]$.




**4-[(3-(4-Methylbenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (quant.). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 2.28 (s, 3H), 5.29 (s, 2H), 7.14 (m, 2H), 7.31 (m, 2H), 7.78 (m, 2H), 7.85 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 369.0 (63) $[M^+]$.

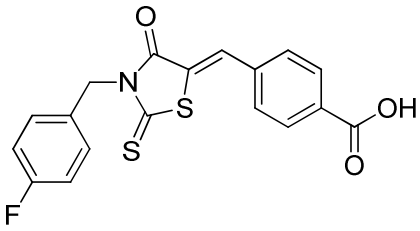


**4-[(3-(4-Chlorobenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis



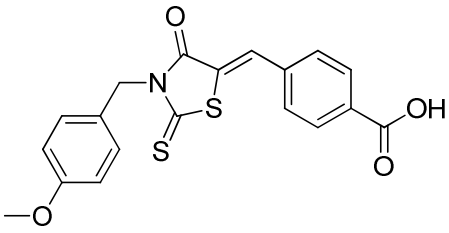
according to procedure G resulting in a yellow solid (96% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 5.33 (s, 2H), 7.37 (m, 2H), 7.46 (m, 2H), 7.79 (m, 2H), 7.86 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 388.9 (76) [$M^+$].

**4-[(3-(4-Fluorobenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis



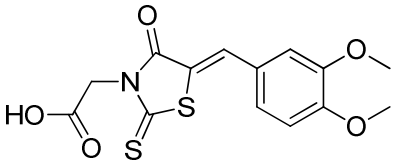
according to procedure G resulting in a yellow solid (83% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 5.32 (s, 2H), 7.11 (m, 2H), 7.50 (m, 2H), 7.78 (m, 2H), 7.85 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 372.9 (72) [$M^+$].

4-**[(3-(4-Methoxybenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.**

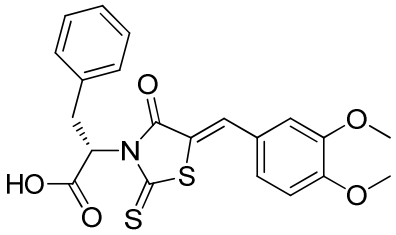


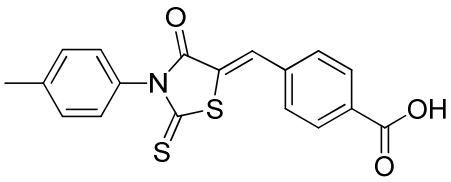
Synthesis according to procedure G resulting in a yellow solid (75% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.76 (s, 3H), 5.26 (s, 2H), 6.88 (m, 2H), 7.39 (m, 2H), 7.78 (m, 2H), 7.84 (s, 1H), 8.19 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 384.9 (68) [$M^+$].

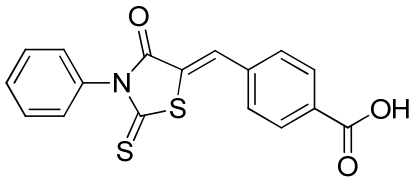
**2-[5-(3,4-Dimethoxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl]acetic acid.** Synthesis

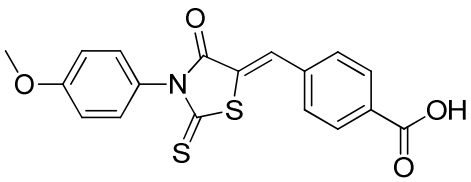


according to procedure G resulting in a yellow solid (87% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.91 (s, 3H), 3.92 (s, 3H), 4.87 (s, 2H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 2.0 Hz, 1H), 7.28 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.76 (s, 1H) ppm; MS (EI, 70 eV): *m/z* (%): 338.9 (80) [$M^+$].

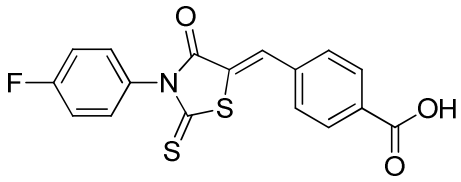
**(*S*)-2-[5-(3,4-Dimethoxybenzylidene)-4-oxo-2-thioxothiazolidin-3-yl]-3-phenylpropanoic acid.**  Synthesis according to procedure G resulting in a yellow solid (34% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.56-3.71 (m, 2H), 3.91 (s, 6H), 6.02 (m, 1H), 7.13-7.25 (m, 8H), 7.66 (s, 1H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{21}H_{19}NNaO_5S_2$: 452.0597, found: 452.0592.

**4-[(4-Oxo-2-thioxo-3-(*p*-tolyl)thiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (80% yield).  $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 2.42 (s, 3H), 7.30 (m, 2H), 7.38 (m, 2H), 7.81 (m, 2H), 7.82 (s, 1H), 8.21 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 354.9 (62) $[M^+]$.

**4-[(4-Oxo-3-phenyl-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid**. Synthesis according to procedure G resulting in a yellow solid (86% yield).  $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 7.44-7.47 (m, 2H), 7.51-7.62 (m, 3H), 7.82 (m, 2H), 7.84 (s, 1H), 8.21 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 341.0 (51) $[M^+]$.

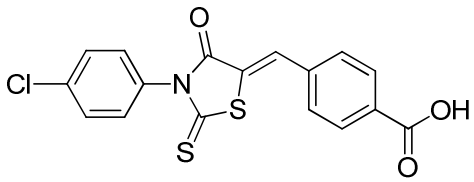
**4-[(3-(4-Methoxyphenyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a yellow solid (62% yield).  $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.88 (s, 3H), 7.10 (m, 2H), 7.35 (m, 2H), 7.81 (m, 2H), 7.82 (s, 1H), 8.21 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 370.8 (77) $[M^+]$.

**4-](3-(4-Fluorophenyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis



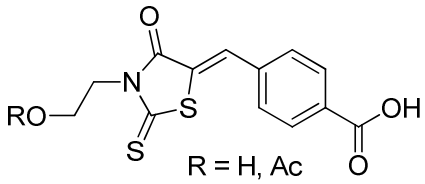
according to procedure G resulting in a yellow solid (86% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 7.36 (m, 2H), 7.54 (m, 2H), 7.82 (m, 2H), 7.84 (s, 1H), 8.21 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 358.9 (23) [$M^+$].

**4-[(3-(4-Chlorophenyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid.**



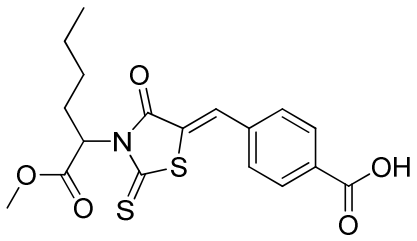
Synthesis according to procedure G resulting in a yellow solid (77% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 7.51 (m, 2H), 7.63 (m, 2H), 7.82 (m, 2H), 7.84 (s, 1H), 8.21 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 374.9 (68) [$M^+$].

**4-[(3-(2-Hydroxyethyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid (R = H) and 4-[(3-(2-acetoxyethyl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic acid (R = Ac).** Synthesis according to procedure G resulting in a



mixture of products (2/3:1/3 R = H, Ac) as a yellow solid (93% yield). $^1$H-NMR (300 MHz, DMSO-$d_6$): $\delta$ = 1.93 (s, 3H, R = Ac), 3.65 (m, 2H, R = H), 4.12 (m, 2H, R = H), 4.31 (m, 4H, R = Ac), 7.74 (m, 4H, R = H, Ac), 7.83 (s, 1H, R = H), 7.86 (s, 1H, R = Ac), 8.06 (m, 4H, R = H, Ac) ppm; MS (EI, 70 eV): *m/z* (%): 308.9 (19) [$M^+$ (R = H)], 350.9 (52) [$M^+$ (R = Ac)].

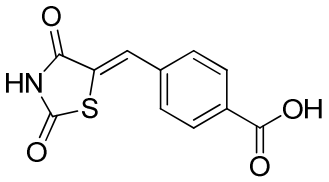
**4-[(3-(1-Methoxy-1-oxohexan-2-yl)-4-oxo-2-thioxothiazolidin-5-ylidene)methyl]benzoic**



**acid.** Synthesis according to procedure G resulting in a yellow solid (83% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 0.86 (t, *J* = 7.0 Hz, 3H), 1.22-1.44 (m, 4H), 2.28 (m, 2H), 3.70 (s, 3H), 5.70 (t, *J* = 7.5 Hz, 1H), 7.80 (m, 2H), 7.83 (s, 1H), 8.20

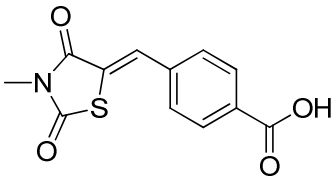
(m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 392.9 (59) [$M^+$].

**4-[(2,4-Dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G



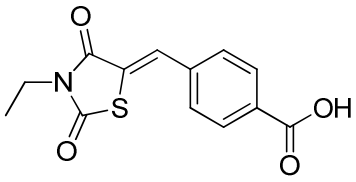
resulting in a pale yellow solid (95% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 7.76 (m, 2H), 7.85 (s, 1H), 8.17 (m, 2H) ppm; HRMS (ESI): *m/z* [M–H]$^-$ calcd for $C_{11}H_6NO_4S$: 248.0023, found: 249.9967.

**4-[(3-Methyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to



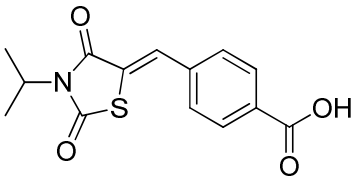
procedure G resulting in a crude product as colorless solid (56% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 3.21 (s, 3H), 7.78 (m, 2H), 7.95 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* [M–H]$^-$ calcd for $C_{12}H_8NO_4S$: 262.0180, found: 262.0192.

**4-[(3-Ethyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to



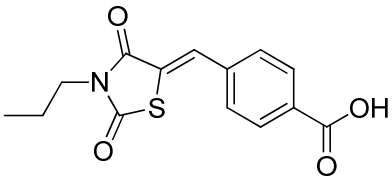
procedure G resulting in a colorless solid (52% yield). $^1$H NMR (300 MHz, acetone-$d_6$): $\delta$ = 1.23 (t, *J* = 7.2 Hz, 3H), 3.78 (q, *J* = 7.2 Hz, 2H), 7.76 (m, 2H), 7.93 (s, 1H), 8.17 (m, 2H) ppm; HRMS (ESI): *m/z* [M–H]$^-$ calcd for $C_{13}H_{10}NO_4S$: 276.0336, found: 276.0342.

**4-[(3-Isopropyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to

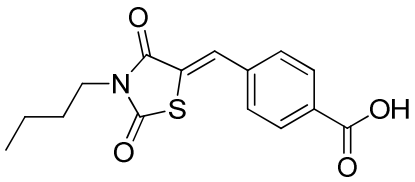


procedure G resulting in a pale yellow solid (63% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 1.47 (d, *J* = 6.9 Hz, 6H), 4.65 (sept, *J* = 6.9 Hz, 1H), 7.76 (m, 2H), 7.90 (s, 1H), 8.17 (m, 2H) ppm; HRMS (ESI): *m/z* [M–H]$^-$ calcd for $C_{14}H_{12}NO_4S$: 290.0496, found: 290.0416.

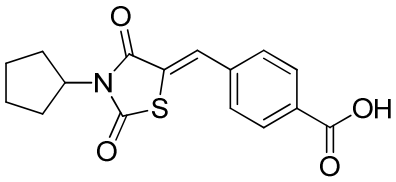
**4-[3-Propyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a pale yellow solid (58% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 0.93 (t, $J$ = 7.5 Hz, 3H), 1.70 (m, 2H), 3.72 (m, 2H), 7.78 (m, 2H), 7.94 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{14}H_{14}NO_4S$: 292.0638, found: 292.0682.



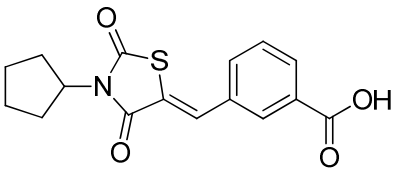

**4-[(3-Butyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a colorless solid (45% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 0.94 (t, $J$ = 7.3 Hz, 3H), 1.37 (m, 2H), 1.66 (m, 2H), 3.75 (m, 2H), 7.77 (m, 2H), 7.94 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M-H]^-$ calcd for $C_{15}H_{14}NO_4S$: 304.0649, found: 304.0655.



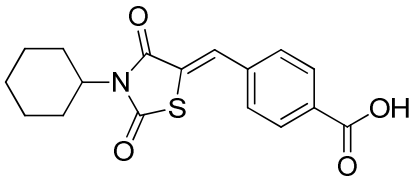

**4-[(3-Cyclopentyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a pale yellow solid (31% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 1.58-1.71 (m, 2H), 1.83-1.98 (m, 4H), 2.04-2.14 (m, 2H), 4.77 (quint, $J$ = 8.4 Hz, 1H), 7.76 (m, 2H), 7.90 (s, 1H), 8.17 (m, 2H) ppm; HRMS (ESI): *m/z* $[M-H]^-$ calcd for $C_{16}H_{14}NO_4S$: 316.0649, found: 316.0669.



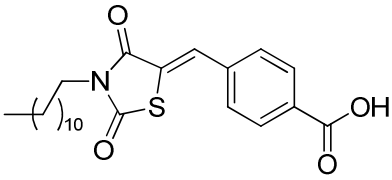

**3-[(3-Cyclopentyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid**. Synthesis according to procedure G resulting in a colorless solid (41% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 1.58-1.71 (m, 2H), 1.84-1.99 (m, 4H), 2.05-2.15 (m, 2H), 4.78 (quint, $J$ = 8.2 Hz, 2H), 7.70 (t, $J$ = 7.7 Hz, 1H), 7.89 (m, 1H), 7.93 (s, 1H), 8.12 (m, 1H), 8.27 (m, 1H) ppm; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{16}H_{16}NO_4S$: 318.0795, found: 318.0787.



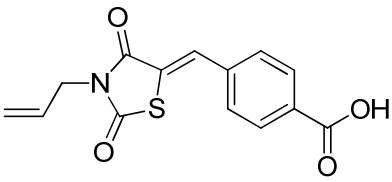
**4-[(3-Cyclohexyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a crude product as a pale yellow solid (32% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 1.15-1.46 (m, 4H), 1.59-1.69 (m, 2H), 1.84-1.89 (m, 2H), 2.14-2.27 (m, 2H), 4.19-4.30 (m, 1H), 7.76 (m, 2H), 7.90 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{17}H_{16}NO_4S$: 330.0806, found: 330.0498.



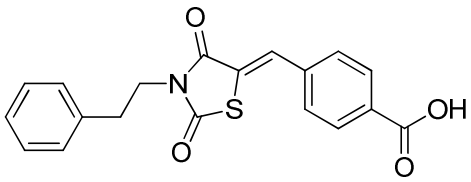
**4-[(3-Dodecyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a crude product as a pale yellow solid (92% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 0.87 (m, 3H), 1.23-1.36 (m, 18H), 1.67 (m, 2H), 3.74 (m, 2H), 7.77 (m, 2H), 7.94 (s, 1H), 8.17 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{23}H_{30}NO_4S$: 416.1901, found: 416.1775.



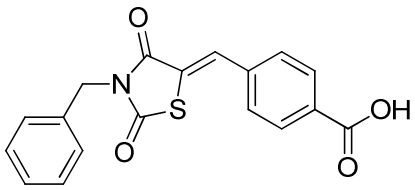
**4-[(3-Allyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a colorless solid (60% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 4.22 (dt, *J* = 5.6, 1.5 Hz, 2H), 5.19-5.28 (m, 2H), 5.91 (m, 1H), 7.79 (m, 2H), 7.97 (s 1H), 8.19 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{11}NNaO_4S$: 312.0301, found: 312.0355.



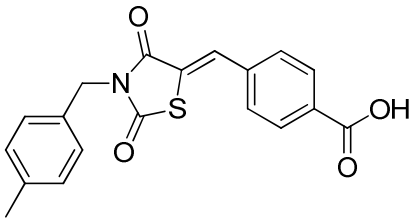
**4-[(3-Phenylethyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a colorless solid (13% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 3.01 (m, 2H), 3.99 (m, 2H), 7.20-7.34 (m, 5H), 7.77 (m, 2H), 7.92 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{19}H_{14}NO_4S$: 352.0649, found: 352.0598.



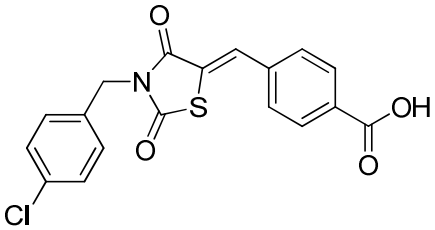
**4-[(3-Benzyl-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a pale yellow solid (77% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 4.93 (s, 2H), 7.31-7.42 (m, 5H), 7.79 (m, 2H), 7.99 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^–$ calcd for $C_{18}H_{12}NO_4S$: 338.0493, found: 338.0507.



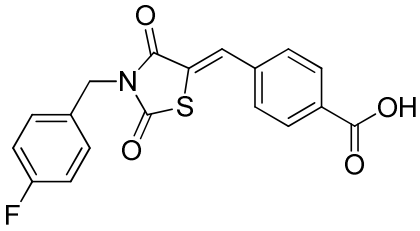

**4-[(3-(4-Methylbenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a crude product as colorless solid **(**quant.). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 2.30 (s, 3H), 4.88 (s, 2H), 7.11-7.31 (m, 4H), 7.78 (m, 2H), 7.98 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^–$ calcd for $C_{19}H_{14}NO_4S$: 352.0649, found: 352.0696.



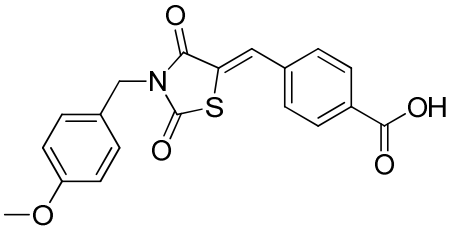

**4-[(3-(4-Chlorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a colorless solid (82% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 4.93 (s, 2H), 7.36-7.46 (m, 4H), 7.78 (m, 2H), 7.99 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{12}ClNNaO_4S$: 396.0068, found: 396.0030.




**4-[(3-(4-Fluorobenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to procedure G resulting in a pale yellow solid (76% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 4.92 (s, 2H), 7.13 (m, 2H), 7.48 (m, 2H), 7.78 (m, 2H), 7.98 (s, 1H), 8.18 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^–$ calcd for $C_{18}H_{11}FNO_4S$: 356.0398, found: 356.0125.

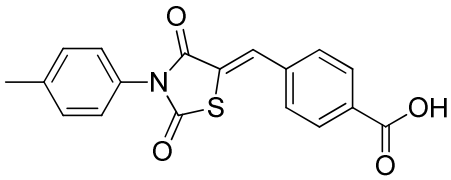


**4-[(3-(4-Methoxybenzyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis



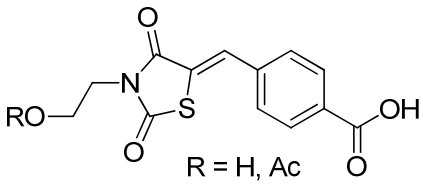
according to procedure G resulting in a pale yellow solid (54% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 3.77 (s, 3H), 4.84 (s, 2H), 6.89 (m, 2H), 7.34 (m, 2H), 7.76 (m, 2H), 7.96 (s, 1H), 8.16 (m, 2H) ppm; HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{19}H_{15}NNaO_5S$: 392.0563, found: 392.0650.

**4-[(3-(*p*-Tolyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid.** Synthesis according to



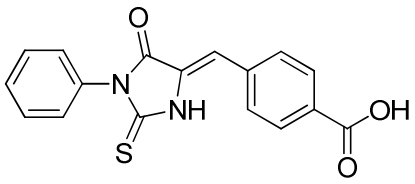
procedure G resulting in a colorless solid (23% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 2.41 (s, 3H), 7.36 (m, 4H), 7.83 (m, 2H), 8.00 (s, 1H), 8.21 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{18}H_{12}NO_4S$: 338.0493, found: 338.0408.

**4-[(3-(2-Hydroxyethyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid (R = H) and 4-[(3-(2-Acetoxyethyl)-2,4-dioxothiazolidin-5-ylidene)methyl]benzoic acid (R = Ac).** Synthesis



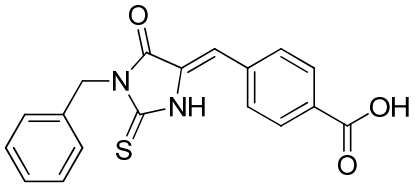
according to procedure G resulting in a mixture of products (2/3:1/3 R = H, Ac) as a pale yellow solid (42% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 1.96 (s, 3H, R = Ac), 3.78 (m, 2H, R = H), 3.88 (m, 2H, R = H), 4.01 (m, 2H, R = Ac), 4.31 (m, 2H, R = Ac), 7.77 (m, 4H, R = H, Ac), 7.93 (s, 1H, R = H), 7.96 (s, 1H, R = Ac), 8.17 (m, 4H, R = H, Ac) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{13}H_{10}NO_5S$ (R = H): 292.0285, found: 292.0210, $[M–H]^-$ calcd for $C_{15}H_{12}NO_6S$ (R = Ac): 334.0391, found: 334.0299.

**4-[(5-Oxo-1-phenyl-2-thioxoimidazolidin-4-ylidene)methyl]benzoic acid.** Synthesis



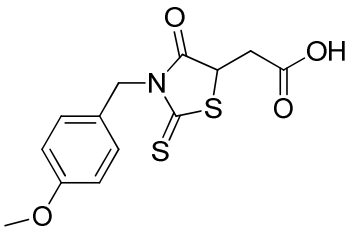
according to procedure G resulting in a yellow solid (38% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 6.76 (s, 1H), 7.44-7.57 (m, 5H), 7.91 (m, 2H), 8.10 (m, 2H) ppm; HRMS (ESI): *m/z* $[M–H]^-$ calcd for $C_{17}H_{11}N_2O_3S$: 323.0496, found: 323.0144.

**4-[(1-Benzyl-5-oxo-2-thioxoimidazolidin-4-ylidene)methyl]benzoic acid.** Synthesis

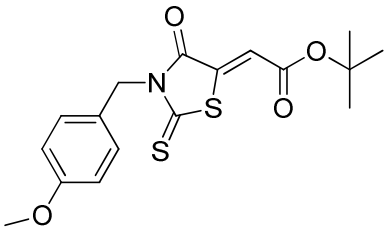


according to procedure G resulting in a yellow solid (28% yield). $^1$H NMR (300 MHz, acetone-$d_6$) $\delta$ = 5.11 (s, 2H), 6.74 (s, 1H), 7.28-7.37 (m, 3H), 7.43-7.45 (m, 2H), 7.87 (m, 2H), 8.08 (m, 2H) ppm; MS (EI, 70 eV): *m/z* (%): 338.0 (82) $[M^+]$.

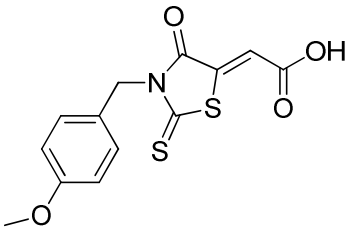
**2-[3-(4-Methoxybenzyl)-4-oxo-2-thioxothiazolidin-5-yl]acetic acid.** Synthesis according to procedure H resulting in a pale brown gum (26% yield). $^1$H-NMR (300 MHz, acetone-$d_6$): $\delta$ = 3.15 (dd, *J* = 17.9, 8.5 Hz, 1H), 3.30 (dd, *J* = 17.9, 3.8 Hz, 1H), 3.76 (s, 3H), 4.75 (dd, *J* = 8.5, 3.9 Hz, 1H), 5.02 (d, *J* = 14.4 Hz, 1H), 5.14 (d, *J* = 14.4 Hz, 1H), 6.83 (m, 2H), 7.33 (m, 2H) ppm; MS (EI, 70 eV): m/z (%): 311.0 (73) $[M^+]$.



***Tert*-butyl 2-[3-(4-methoxybenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene]acetate.** Synthesis according to procedure I resulting in a yellow oil (96% yield). $^1$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 1.51 (s, 9H), 3.77 (s, 3H), 5.20 (s, 2H), 6.74 (s, 1H), 6.82 (m, 2H), 7.37 (m, 2H) ppm; MS (EI, 70 eV): m/z (%): 365.0 (65) $[M^+]$.



**2-[3-(4-Methoxybenzyl)-4-oxo-2-thioxothiazolidin-5-ylidene]acetic acid.** Synthesis




according to procedure I resulting in an orange solid (quant.). $^{1}$H-NMR (300 MHz, $CDCl_3$): $\delta$ = 3.77 (s, 3H), 5.21 (s, 2H), 6.82 (m, 2H), 6.84 (s, 1H), 7.38 (m, 2H) ppm; MS (EI, 70 eV): m/z (%): 309.0 (71) [$M^+$].