A Manifold Three-Step Synthetic Route to Polycyclic Annulated Hydantoins *via* Cyclic Imines

by **Fabian Brockmeyer**, **Denis Kröger**, **Timo Stalling**, **Pasqual Ullrich**, and **Jürgen Martens***

Institut für Reine und Angewandte Chemie der Carl von Ossietzky Universität Oldenburg, Carl-von-Ossietzky-Str. 9–11, D-26129 Oldenburg
(phone: +49-441-798-3837; fax: +49-441-798 3329; e-mail: juergen.martens@uni-oldenburg.de)

Dedicated to Professor *Dieter Seebach* on the occasion of his 75th birthday

A new three-step synthetic pathway to generate polycyclic annulated hydantoins *via* rarely investigated heterocyclic imines is described. This procedure includes a one-pot reaction forming imines as precursor structures (*e.g.*, *Asinger* reaction), followed by an *Ugi* reaction to build up a bisamide structure that allows a ring-closing reaction to the targeted hydantoins *via* substitution. This pathway leads to a multiplicity of substances with a potential pharmacological activity.

Introduction. – Hydantoins (= imidazolidine-2,4-diones) are a very interesting and well-known substance class [1]. A plenty of this cyclic ureides are important compounds because of their industrial relevance as intermediates in the production of α-amino acids [2] and their frequent use in a plethora of pharmaceutical products [3][4]. Those derivatives with an annulated five-membered thiazolidine ring show activities against neurodegenerative diseases, such as morbus *Alzheimer* [5]. Also anticancer activity was reported [6]. Therefore, we focused our attention to the synthesis of polycyclic hydantoins. For this purpose, we developed a sequential combination of reactions which involves the utilization of the rarely investigated heterocyclic imines 2,5-dihydro-1,3-oxazole [7] and 1,4-benzothiazine [8], in addition to the known 2,5-dihydro-1,3-thiazole [9][10]. The cyclic amine parts of these species are also privileged scaffolds in an array of different biologically and pharmaceutically active compounds [10][11][12]. For example linezolid, which is a famous antibacterial [12a], is a 1,3-oxazolidine derivative. The 3,4-dihydrobenzothiazine substructure builds the skeleton of some antibiotica and potent potassium and calcium channel openers [11b–e][13]. The biological and pharmacological activities of the hydantoins and the mentioned heterocycles, respectively, suggests that the combination of both structures would lead to compounds with interesting properties. Therefore, we developed a sequential three-step synthetic route to the target structures depicted in the *Figure*.

On the basis of the retrosynthetic consideration outlined in *Scheme 1*, the target annulated hydantoins can be synthesized from bisamides [14]. The required bisamides starting from the cyclic imines can be obtained by an *Ugi* three-component reaction (*U-3CR*) [15]. Leading to our research on cyclic imines, the above mentioned imines are accessible by one-pot conversion of α-halo aldehydes [8][16]. In the case of the thia- and oxazoles, this strategy results in the combination of two multicomponent reactions.

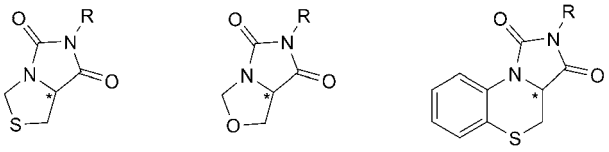
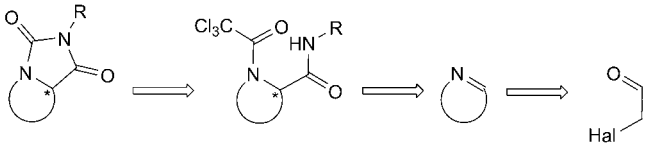


Figure. *The target structures*

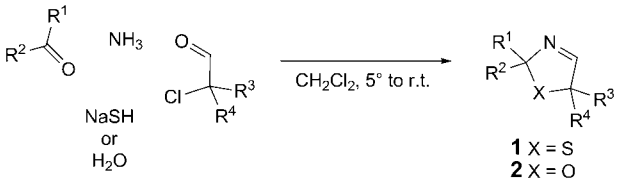
Displaying a high substrate tolerance, the developed synthetic sequence provides products that are characterized by a high diversity.

Scheme 1. *Retrosynthetic Consideration of the Target Structure*



Results and Discussion. – *Synthesis of the Cyclic Imines.* The first of the three-step synthesis sequence to polycyclic hydantoines was the preparation of the cyclic imines. To investigate the diversity of our route, three different types of cyclic imines were prepared as precursors for the further reaction steps. Two of them, *i.e.*, the five-membered 2,5-dihydro-1,3-thiazoles **1** and 2,5-dihydro-1,3-oxazole **2**, were prepared by a modified *Asinger* reaction [7][16]. This multicomponent reaction is well-known for its efficient manifold synthesis of cyclic imines [17]. Following the prevalent procedure [16], an α-chloro aldehyde was treated with a second variable carbonyl compound, NH_3, and NaHS or H_2O in CH_2Cl_2 to generate the imines **1** and **2** (*Scheme 2*).

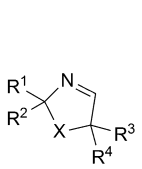
Scheme 2. *Four-Component Reaction to Form the 2,5-Dihydro-1,3-thiazoles* [16] **1** *and 2,5-Dihydro-1,3-oxazole* [7] **2**



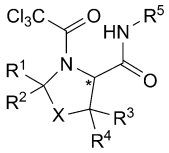
By means of the modified *Asinger* reaction, three different 2,5-dihydro-1,3-thiazoles **1** and one 2,5-dihydro-1,3-oxazole **2** were prepared as precursors (*Table 1*). The common cyclic imines **1a** [9], **1b** [18], and **2** [7], as well as the cyclic imine **1c**, which is reported for the first time, were obtained in moderate-to-good yields (up to 67%).

The annulated six-membered 2*H*-1,4-benzothiazine **3** [19] was synthesized from an α-bromo aldehyde, 2-aminothiophenol, and NaH in anhydrous THF (*Scheme 3*).

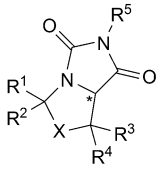
Table 1. *Preparation of Hydantoins* **7** *and* **8** via *Five-Membered Cyclic Imines* **1** *and* **2**



1, **2**



4, **5**

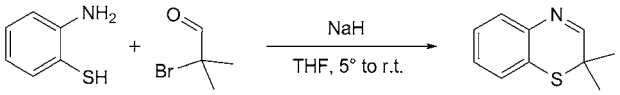


7, **8**

Entry	X	R^1	R^2	R^3	R^4	R^5	Imine	Yield[a]) [%]	Bisamide	Yield[a]) [%]	Hydantoin	Yield[a]) [%]
1	S	Me	Me	Me	Me	CH_2=$CHCH_2$	**1a**	64	**4a**	53	**7a**	85
2	S	Me	Me	Me	Me	4-MeO–$C_6H_4CH_2$	**1a**	64	**4b**	52	**7b**	74
3	S	Me	Me	Me	Me	Cyclohexyl	**1a**	64	**4c**	30	**7c**	63
4	S	Me	Me	Me	Me	(Napthalen-2-yl)methyl	**1a**	64	**4d**	58	**7d**	84
5	S	–$(CH_2)_5$–		–$(CH_2)_5$–		(Napthalen-2-yl)methyl	**1b**	67	**4e**	39	**7e**	94
6	S	–$(CH_2)_2O(CH_2)_2$–		Me	Me	CH_2=$CHCH_2$	**1c**	45	**4f**	45	**7f**	69
7	S	–$(CH_2)_2O(CH_2)_2$–		Me	Me	4-MeO–$C_6H_4CH_2$	**1c**	45	**4g**	32	**7g**	70
8	S	–$(CH_2)_2O(CH_2)_2$–		Me	Me	$PhCH_2CH_2$	**1c**	45	**4h**	56	**7h**	57
9	O	Me	Me	Me	Me	CH_2=$CHCH_2$	**2**	40	**5a**	55	**8a**	71
10	O	Me	Me	Me	Me	4-MeO–$C_6H_4CH_2$	**2**	40	**5b**	46	**8b**	52
11	O	Me	Me	Me	Me	Cyclohexyl	**2**	40	**5c**	52	**8c**	76
12	O	Me	Me	Me	Me	(Napthalen-2-yl)methyl	**2**	40	**5d**	68	**8d**	78

[a]) Isolated yields.

Scheme 3. *Synthesis of the 2*H*-1,4-Benzothiazines* **3** [19]

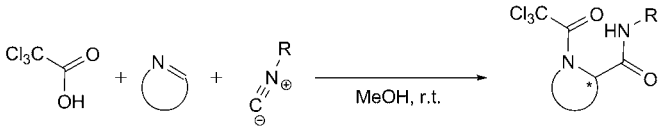


3

All three types of cyclic imines, **1**–**3**, are known for their reactivity, and they have been successfully utilized in the synthesis of different amides [7][20] and polycyclic structures [9][19][21].

Synthesis of the Bisamides. Adequate precursors for the final ring closure to the polycyclic hydantoins are α-bisamides containing at least one secondary amide, whereas the second amide group has to be affected by its electrophilicity and the presence of a leaving group [14]. An appropriate and efficient way to such structures is the *Ugi* reaction [14][22][23], which is one of the most efficient multicomponent reactions. In 1959, this reaction was described as a four-component reaction (*U-4CR*) to prepare bisamides from an amine, a carbonyl compound, a carboxylic acid, and an isocyanide [22]. Later, the *U-3CR* was developed to reduce the by-products [15][23]. Instead of the amine and the carbonyl compound, which were used in the *U-4CR* for the *in situ* formation of an imine compound, a pre-built imine was treated with a carboxylic acid and an isocyanide. The *U-3CR* was applied to the cyclic imines **1**–**3** in the recent past, too [8][18]. Following this strategy, the cyclic imines **1**–**3**, respectively, were reacted with Cl_3CCOOH and several isocyanides, which were commercially available or readily accessible, in anhydrous MeOH (*Scheme 4*). To amplify the scope of isocyanides, 2-(isocyanomethyl)naphthalene, which has never been reported before, was prepared from naphthalene-2-carbaldehyde.

Scheme 4. Ugi *Three-Component Reaction* [23] *of the Imines* **1**–**3** *to Prepare the Desired Bisamides* **4**–**6**, *Respectively*

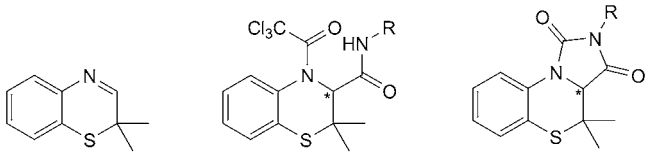


1–**3** **4**–**6**

As disclosed in *Table 1*, the imines **1** and **2** could be converted to the desired bisamides **4** and **5**, respectively, in moderate-to-good yields. Even when sterically hindered substrates, such as the imines **1b** and **1c**, or cyclohexyl isocyanide, were used in the reaction, the corresponding bisamides were obtained in moderate yields (*i.e.*, compounds **4c**, **4e**, **4f**, **4g**, **4h**, and **5c**). The *U-3CR* of the annulated six-membered imines **6** did not proceed in such high yields, but the expected bisamides **6a**–**6c** were obtained in all cases (*Table 2*). It is noteworthy to mention that the use of the new 2-(isocyanomethyl)naphthalene resulted in the highest yields (*i.e.*, compounds **4d** and **5d**).

Cyclization to the Polycyclic Hydantoins. The synthetic route to the polycyclic hydantoins was finalized by a ring closure of the bisamides **4**–**6**. A deprotonation of the secondary amide group is prerequisite for the desired cyclization. Treatment of the

Table 2. *Preparation of Hydantoins* **9** via *Annulated Six-Membered Cyclic Imines* **3**



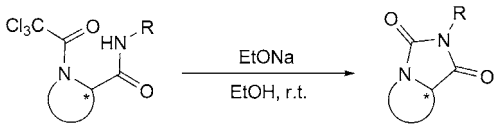
3 **6** **9**

Entry	R	Imine	Yield[a]) [%]	Bisamide	Yield[a]) [%]	Hydantoin	Yield[a]) [%]
13	CH_2=$CHCH_2$	**3**	57	**6a**	12	**9a**	67
14	4-MeO–$C_6H_4CH_2$	**3**	57	**6b**	6	**9b**	78
15	$PhCH_2CH_2$	**3**	57	**6c**	7	**9c**	63

[a]) Isolated yields.

bisamides **4**–**6** with freshly prepared EtONa is a suitable procedure to realize this initiation step of the ring closure (*Scheme 5*). As a result of this deprotonation, the hydantoins **7**–**9** were generated *via* a replacement of the leaving group Cl_3C^-.

Scheme 5. *Final Cyclization of the Bisamides* **4**–**6** *to the Polycyclic Hydantoins* **7**–**9**, *Respectively*



4 – 6 **7 – 9**

Starting from the bisamides **4** and **5**, the aimed products **7** and **8**, respectively, were obtained in good-to-excellent yields as compiled in *Table 1*. The cyclization of the bisamides **6** occurred in good yields, too (*Table 2*). Surprisingly, the best result for the final cyclization was accomplished starting from the bisamide **4e** (*Table 1*, *Entry 5*; 94%).

The structures of the products were verified by IR, ^{1}H- and ^{13}C-NMR, and mass spectra. The shift of the signal arising from the methine group in the imine ring strongly evidenced the formation of the hydantoins. For example, the ^{1}H-NMR spectrum of the bisamide **4d** exhibited one signal of the methine group at 5.16 ppm, whereas the spectrum of the corresponding hydantoin **7d** displayed that signal at 4.43 ppm. Moreover, the presence of the hydantoins is substantiated by the finding that the signals arising from the NH and the CCl_3 moiety were missing in the ^{1}H- and ^{13}C-NMR spectrum, respectively.

The obtained results (*Tables 1* and *2*) indicate the variability of the three-step synthesis sequence leading to polycyclic hydantoins. The cyclic imines, prepared in the first step, as well as the isocyanide compound, used in the second step, are variable in a wide range. It could be established that both five-membered cyclic imines containing S or O, *i.e.*, (**1** and **2**, resp.) and the six-membered annulated 2*H*-1,4-benzothiazine **3** could be converted to the desired hydantoins **7**–**9**. In addition to that, the applicability of five different isocyanides in the reaction sequence was also successfully examined.

Conclusions. – In summary, we developed a new three-step synthetic route to polycyclic hydantoins containing S or O in the annulated heterocycles. Starting from commercially available simple starting materials, the heterocyclic imines **1**–**3** were prepared in one-pot reactions. By functionalizing the highly reactive C=N bond of these precursors in the *Ugi* three-component reaction, we obtained the bisamides **4**–**6** characterized by a leaving group for a ring-closing reaction. In the final cyclization, initiated by treatment with EtONa, the annulated hydantoins **7**–**9** were synthesized. By following this synthetic route, it is possible to prepare a great number of products with high diversity.

Experimental Part

General. Synthetic procedures under Ar: vacuum line using standard *Schlenk* techniques. TLC: *Merck* SiO_2 F_{254} plates on aluminium sheets. Column chromatography (CC): *Grace* SiO_2 (0.035–0.070 mm, type *KG 60*). M.p.: *Laboratory Devices*; uncorrected. IR Spectra: *Bruker Tensor 27* spectrometer, '*Golden Gate*' diamond-ATR (attenuated total reflection) unit; in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Bruker AMX R 500* instrument (at 500.1 and 125.8 MHz, resp.) or *Bruker Avance III 500* instrument (at 499.9 and 125.7 MHz, resp.), in $CDCl_3$, (D_6)DMSO, or CD_3OD; multiplicity of C-atoms from DEPT spectra; assignments from COSY techniques; δ in ppm rel. to the solvent signal ($CDCl_3$: 7.26 and 77.16 ppm, resp.; (D_6)DMSO: 2.50 and 39.52 ppm, resp.; CD_3OD: 3.31 and 49.00 ppm, resp.) [24], *J* in Hz; in case of phenylene compounds, the assignments (*o*-, *m*-) refer to the methylene group. MS: *Finnigan MAT 95* (EI, 70 eV, or CI (isobutane or NH_3)) or *Waters Q-TOF Premier* (ESI, pos.-ion mode) instrument; in *m*/*z* (rel. %).

2-Chloro-2-methylpropanal [7], 1-chlorocyclohexane-1-carbaldehyde [25], 2-bromo-2-methylpropanal [26], allyl isocyanide [27][28], 1-(isocyanomethyl)-4-methoxybenzene [29][30], cyclohexyl isocyanide [31][32], and (2-isocyanoethyl)benzene [33] were prepared according to published procedures. All other chemicals were commercially available (*Aldrich* and *Merck*) and used without further purification. MeOH was refluxed with Mg and freshly distilled prior to use. EtOH was refluxed with Na and freshly distilled prior to use.

2-(Isocyanomethyl)naphthalene. A soln. of naphthalene-2-carbaldehyde (675 mg, 4.3 mmol) and HCOOH (1.66 g, 36.1 mmol) in $HCONH_2$ (30 ml) was heated at 140–150° for 5 h. The mixture was poured into 35 ml of ice-water and basified with 2N NaOH soln. to pH 9. The soln. was extracted with CH_2Cl_2 (2 × 25 ml). The org. layer was washed with H_2O, dried ($MgSO_4$), and the solvent was removed at a rotary evaporator to afford a yellow solid. The crude *N*-(naphthalen-2-ylmethyl)formamide was used in the next step without further purification.

A soln. of the crude product, Ph_3P (1.36 g, 5.2 mmol), CCl_4 (664 mg, 4.3 mmol), and Et_3N (437 mg, 4.3 mmol) in 1,2-dichloroethane (5 ml) was heated at 60° for 3 h. The solvent was removed at a rotary evaporator. The residue was taken up in MeCN, cooled to −30° for 5 h, and filtered. The filtrate was concentrated at a rotary evaporator. The crude product was purified by CC (CH_2Cl_2/hexane 1:1). Yield: 328 mg (45%). Brown solid. M.p. 67°. R_f (CH_2Cl_2/hexane 1:2) 0.31. IR (ATR): 3057, 3024, 2966, 2919, 2850. ^1H-NMR (500.1 MHz, $CDCl_3$): 4.79 (*s*, CH_2); 7.40–7.42 (*m*, 1 arom. H); 7.51–7.55 (*m*, 2 arom. H); 7.83–7.89 (*m*, 4 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 45.81 (CH_2); 124.16, 125.74, 126.69, 126.85, 127.87, 128.01, 129.05 (7 arom. CH); 129.72, 133.10, 133.28 (3 arom. C); 158.02 (NC). CI-MS: 185 (5, $[M + H + NH_3]^+$). HR-CI-MS: 185.1077 ($[M + H + NH_3]^+$, $C_{12}H_{13}N_2^+$; calc. 185.1079).

2,5-Dihydro-2,2,5,5-tetramethylthiazole (**1a**) [9]. Acetone (22.54 g, 0.388 mol) was added dropwise to a soln. of $NaHS \cdot H_2O$ (14.37 g, 0.194 mol) and aq. NH_3 soln. (26.43 g, 0.388 mol, 25%). To this soln., 2-chloro-2-methylpropanal (20.67 g, 0.194 mol) was added dropwise at 5–10°. After diluting with CH_2Cl_2 (20 ml), the soln. was stirred overnight at r.t. The phases were separated, and the aq. phase was extracted with CH_2Cl_2 (2 × 20 ml). The recombined org. phases were dried ($MgSO_4$), and the solvent was removed at a rotary evaporator. The crude product was purified by recrystallization from hexane. Yield: 17.78 g (64%). Colorless solid.

7-Thia-14-azadispiro[5.1.5.2]pentadec-14-ene (**1b**) [18]. Cylohexanone (8.19 g, 83.4 mol) was added dropwise to a soln. of $NaHS \cdot H_2O$ (3.07 g, 41.4 mmol) and aq. NH_3 soln. (5.68 g, 83.4 mmol, 25%). To this soln., 1-chlorocyclohexane-1-carbaldehyde (6.07 g, 41.4 mol) was added dropwise at 5–10°. After diluting with CH_2Cl_2 (20 ml), the soln. was stirred overnight at r.t. The phases were separated, and the aq. phase was extracted with CH_2Cl_2 (2 × 20 ml). The recombined org. phases were dried ($MgSO_4$), and the solvent was removed at a rotary evaporator. The crude product was purified by distillation (110°/0.067 mbar). Yield: 6.20 g (67%). Colorless oil.

2,2-Dimethyl-8-oxa-1-thia-4-azaspiro[4.5]dec-3-ene (**1c**). Oxan-4-one (2.50 g, 25.0 mmol) was added dropwise to a soln. of $NaHS \cdot H_2O$ (926 mg, 12.5 mmol) and aq. NH_3 soln. (426 mg, 25.0 mmol, 25%). To this soln., 2-chloro-2-methylpropanal (1.33 g, 12.5 mmol) was added dropwise at 5–10°. After diluting with CH_2Cl_2 (20 ml), the soln. was stirred overnight at r.t. The phases were separated, and the aq. phase was extracted with CH_2Cl_2 (2 × 20 ml). The recombined org. phases were dried ($MgSO_4$), and the solvent was removed at a rotary evaporator. The crude product was purified by distillation (95–100°/1.0 mbar). Yield: 960 mg (45%). Colorless solid. M.p. 45–46°. IR (ATR): 2962, 2944, 2917, 2847, 1651. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.78 (*s*, 2 Me); 2.03–2.06, 2.43–2.49 (2*m*, CH_2CCH_2); 3.82–3.86, 4.19–4.25 (2*m*, CH_2OCH_2); 7.49 (*s*, CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 30.26 (2 Me); 42.36 (CH_2CCH_2); 63.72 ($SCMe_2$); 66.06 (CH_2OCH_2); 92.10 ($SC(CH_2)_2N$); 166.85 (CH). CI-MS: 186 (100, $[M + H]^+$). HR-CI-MS: 186.0955 ($[M + H]^+$, $C_9H_{16}NOS^+$; calc. 186.0953).

2,5-Dihydro-2,2,5,5-tetramethyloxazole (**2**) [7]. 2-Chloro-2-methylpropanal (21.31 g, 0.200 mol) was added dropwise to a soln. of H_2O (14.23 g, 0.790 mol), aq. NH_3 soln. (53.81 g, 0.790 mol, 25%), and acetone (45.88 g, 0.790 mol) at 0–5°. After stirring for 1 h at 5°, the soln. was stirred overnight at r.t. The phases were separated, and the aq. phase was extracted with CH_2Cl_2 (2 × 30 ml). The recombined org. phases were dried ($MgSO_4$), and the solvent was removed at a rotary evaporator. The crude product was purified by distillation (47–55°/150 mbar). Yield: 10.17 g (40%). Colorless oil.

*2,2-Dimethyl-2*H*-1,4-benzothiazine* (**3**) [19]. Under Ar, a soln. of 2-aminothiophenol (6.00 g, 48.0 mmol) in 20 ml anh. THF was added to a suspension of NaH (2.00 g, 50.0 mmol, 60% in oil) in 70 ml anh. THF at 0°. The resulting foamy white/violet colored mixture was stirred for 2 h at r.t. 2-Bromo-2-methylpropanal (7.63 g, 50.5 mmol), dissolved in 15 ml anh. THF, was added dropwise. After stirring overnight at r.t., molecular sieves were added, and the mixture was stirred for 3 h. After filtration, the solvent was removed at a rotary evaporator. The crude product was purified by recrystallization from petroleum ether 40–60°. Yield: 4.84 g (57%). Colorless solid. M.p. 56–58°.

General Procedure (*GP 1*) *for the Synthesis of the Bisamides* **4**, **5**, *and* **6**. A soln. of 1 equiv. of the respective isocyanide and 1 equiv. of Cl_3CCOOH in anh. MeOH (3 ml per mmol imine) was added to a soln. of 1 equiv. of the respective cyclic imine **1**, **2**, or **3** in anh. MeOH (3 ml per mmol imine). The progress of the reaction was monitored by TLC. The solvent was removed at the rotary evaporator. The purification of the crude product is described in the experiments.

*(*RS*)-2,2,5,5-Tetramethyl-*N*-(prop-2-en-1-yl)-3-(trichloroacetyl)-1,3-thiazolidine-4-carboxamide* (**4a**). According to *GP 1:* **1a** (286 mg, 2.00 mmol), allyl isocyanide (134 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 2 d. Purification by washing with $^iPr_2O$ and pentane. Yield: 395 mg (53%). Colorless solid. M.p. 122°. IR (ATR): 3363, 2993, 2973, 2941, 2859, 1687, 1650. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.45, 1.71, 2.01, 2.07 (4*s*, 4 Me); 3.80–3.85, 3.95–4.00 (2*m*, $NHCH_2$); 5.11 (*s*, NCH); 5.14–5.17, 5.23–5.27 (2*m*, $CH{=}CH_2$); 5.77–5.85 (*m*, $CH{=}CH_2$); 5.96–5.97 (*m*, NH). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 25.87, 29.72, 31.26, 33.01 (4 Me); 42.30 (CH_2); 51.77 ($SCMe_2CH$); 76.96 ($SCMe_2N$); 77.16 (NCH); 94.22 (CCl_3); 117.64 ($CH{=}CH_2$); 133.43 ($CH{=}CH_2$); 158.51 (NCO); 168.46 (NHCO). CI-MS: 373 (100, $[M + H]^+$). HR-CI-MS: 372.0229 ($[M + H]^+$, $C_{13}H_{19}Cl_3N_2O_2S^+$; calc. 372.0233).

*(*RS*)-*N*-(4-Methoxybenzyl)-2,2,5,5-tetramethyl-3-(trichloroacetyl)-1,3-thiazolidine-4-carboxamide* (**4b**). According to *GP 1:* **1a** (286 mg, 2.00 mmol), 1-(isocyanomethyl)-4-methoxybenzene (294 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 5 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 470 mg (52%). Colorless solid. M.p. 163–165°. R_f (^{t}BuOMe/hexane 3:7) 0.18. IR (ATR): 3300, 3073, 2971, 2937, 2842, 1687, 1656, 1612, 1548, 1515. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.45, 1.70, 1.99, 2.00 (4*s*, 2 Me_2C); 3.79 (*s*, MeO); 4.25 (*dd*, $^2J = 14.4$, $^3J = 5.0$, 1 H, CH_2); 4.48 (*dd*, $^2J = 14.4$, $^3J = 6.0$, 1 H, CH_2); 5.11 (*s*, NCH); 6.09–6.11 (*m*, NH); 6.84–6.86 (*m*, 2 *m*-CH); 7.17–7.19 (*m*, 2 *o*-CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.90, 29.46, 31.26, 32.96 (2 CMe_2); 43.70 (CH_2); 51.81 ($SCMe_2CH$); 55.41 (MeO);

76.95 (NCH); 76.98 (S*C*Me$_2$N); 94.15 (CCl_3); 114.34 (2 *m*-CH); 129.22 (*C*(Ar)CH_2); 129.48 (2 *o*-CH); 158.37 (NCO); 159.34 (*C*(Ar)OMe); 168.42 (NHCO). CI-MS: 453 (99, $[M + H]^+$). HR-CI- MS: 453.0563 ($[M + H]^+$, $C_{18}H_{24}Cl_3N_2O_3S^+$; calc. 453.0573).

*(*RS*)-*N*-Cyclohexyl-2,2,5,5-tetramethyl-3-(trichloroacetyl)-1,3-thiazolidine-4-carboxamide* (**4c**). According to *GP 1:* **1a** (286 mg, 2.00 mmol), cyclohexyl isocyanide (218 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 3 d. Purification by CC (AcOEt/hexane 3:7). Yield: 246 mg (30%). Colorless solid. M.p. 126°. R_f (AcOEt/hexane 3:7) 0.62. IR (ATR): 3333, 2930, 2855, 1687, 1522. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.10–1.22 (*m*, 3 H, 2 CH_2); 1.30–1.40 (*m*, CH_2); 1.44 (*s*, Me); 1.57–1.62 (*m*, 1 H, CH_2); 1.66–1.69 (*m*, CH_2); 1.69 (*s*, Me); 1.87–1.90 (*m*, CH_2); 2.00, 2.08 (2*s*, 2 Me); 3.74–3.82 (*m*, NHC*H*); 5.04 (*s*, NCH); 5.74 (*d*, $^3J = 7.8$, NH). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 23.81, 24.56 (3 CH_2); 24.87, 28.72, 30.26 (3 Me); 31.89 (2 CH_2); 32.06 (Me); 47.79 (NHCH); 50.75 (S*C*Me$_2$CH); 75.82 (S*C*Me$_2$N); 76.13 (NCH); 93.28 (CCl_3); 157.51 (NCO); 166.48 (NHCO). CI-MS: 415 (98, $[M + H]^+$). HR-EI-MS: 414.0712 (M^+, $C_{16}H_{25}Cl_3N_2O_2S^+$; calc. 414.0702).

*(*RS*)-2,2,5,5-Tetramethyl-*N*-(naphthalen-2-ylmethyl)-3-(trichloroacetyl)-1,3-thiazolidine-4-carboxamide* (**4d**). According to *GP 1:* **1a** (286 mg, 2.00 mmol), 2-(isocyanomethyl)naphthalene (334 mg, 2.00 mmol) and Cl_3CCOOH (327 mg, 2.00 mmol); 2 d. Purification by washing with ^{i}Pr$_2$O and pentane. Yield: 545 mg (58%). Colorless solid. M.p. 198°. IR (ATR): 3304, 2971, 2938, 1685, 1657, 1543. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.48, 1.72, 2.01, 2.03 (4*s*, 4 Me); 4.49 (*dd*, $^2J = 14.7$, $^3J = 5.1$, 1 H, CH_2); 4.74 (*dd*, $^2J = 14.7$, $^3J = 5.1$, 1 H, CH_2); 5.16 (*s*, NCH); 6.22–6.24 (*m*, NH); 7.36–7.38 (*m*, 1 arom. H); 7.46–7.51 (*m*, 2 arom. H); 7.73–7.74 (*m*, 1 arom. H); 7.79–7.83 (*m*, 3 arom. H). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 25.95, 29.61, 31.30, 33.03 (4 Me); 44.32 (CH_2); 51.87 (S*C*Me$_2$CH); 77.05 (S*C*Me$_2$N); 77.16 (NCH); 94.22 (CCl_3); 125.90, 126.30, 126.59, 126.86, 127.86, 127.89, 128.92 (7 arom. CH); 132.99, 133.48, 134.74 (3 arom. C); 158.45 (NCO); 168.49 (NHCO). CI-MS: 473 (99, $[M + H]^+$). HR-EI-MS: 472.0540 (M^+, $C_{21}H_{23}Cl_3N_2O_2S^+$; calc. 472.0546).

*(*RS*)-*N*-(Naphthalen-2-ylmethyl)-14-(trichloroacetyl)-7-thia-14-azadispiro[5.1.5.2]pentadecane-15-carboxamide* (**4e**). According to *GP 1:* **1b** (670 mg, 3.00 mmol), 2-(isocyanomethyl)naphthalene (502 mg, 3.00 mmol) and Cl_3CCOOH (490 mg, 3.00 mmol); 3 d. Purification by crystallization from hexane. Yield: 646 mg (39%). Colorless solid. M.p. 220°. IR (ATR): 3315, 3060, 2931, 2855, 1682, 1652. ^{1}H-NMR (500.1 MHz, (D_6)DMSO): 1.04–2.03 (*m*, 17 H, CH_2, c-Hex); 2.57–2.63 (*m*, 1 H, CH_2, c-Hex); 2.80–2.90 (*m*, 2 H, CH_2, c-Hex); 4.28 (*dd*, $^2J = 14.4$, $^3J = 4.9$, 1 H, NHCH_2); 4.53 (*dd*, $^2J = 14.4$, $^3J = 6.4$, 1 H, NHCH_2); 5.28 (*s*, NCH); 7.37–7.39 (*m*, 1 arom. H); 7.47–7.53 (*m*, 2 arom. H); 7.75–7.76 (*m*, 1 arom. H); 7.85–7.90 (3*m*, 3 arom. H); 8.69–8.72 (*m*, NH). ^{13}C-NMR (125.8 MHz, (D_6)DMSO): 21.95, 24.23, 24.27, 24.96, 25.12, 25.59, 34.35, 35.09, 35.46, 37.90 (10 CH_2, c-Hex); 42.99 ($NHCH_2$); 57.44 (S*C*(CH_2)$_5$CH); 75.32 (NCH); 83.14 (S*C*(CH_2)$_5$N); 94.35 (CCl_3); 125.88, 126.35, 126.63, 126.69, 127.53, 127.60, 127.96 (7 arom. CH); 132.13, 132.83, 136.25 (3 arom. C); 157.44 (NCO); 166.95 (NHCO). CI-MS: 554 (98, $[M + H]^+$). HR-CI-MS: 553.1242 ($[M + H]^+$, $C_{27}H_{32}Cl_3N_2O_2S^+$; calc. 553.1245).

*(*RS*)-2,2-Dimethyl-*N*-(prop-2-en-1-yl)-4-(trichloroacetyl)-8-oxa-1-thia-4-azaspiro[4.5]decane-3-carboxamide* (**4f**). According to *GP 1:* **1c** (278 mg, 1.50 mmol), allyl isocyanide (109 mg, 1.50 mmol), and Cl_3CCOOH (245 mg, 1.50 mmol); 4 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 282 mg (45%). Colorless solid. M.p. 201–202°. R_f (^{t}BuOMe/hexane 3:7) 0.08. IR (ATR): 3317, 2967, 2913, 2856, 1687, 1660, 1537. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.49 (*s*, Me); 1.59–1.62 (*m*, 1 H, CH_2CCH$_2$); 1.67 (*s*, Me); 2.28–2.30 (*m*, 1 H, CH_2CCH_2); 3.34–3.44 (*m*, 3 H, CH_2CCH_2, CH_2OCH$_2$); 3.71–3.76 (*m*, 1 H, CH_2OCH_2); 3.81–3.86, 3.94–3.99 (2*m*, NHCH_2); 4.03–4.09 (*m*, 2 H, CH_2OCH_2); 5.15 (*s*, NCH); 5.15–5.17, 5.22–5.25 (2*m*, CH=CH_2); 5.76–5.83 (*m*, 2 H, C*H*=CH$_2$, NH). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 26.09, 33.11 (2 Me); 36.18 (*C*H$_2$CCH$_2$); 37.57 (CH$_2$*C*CH$_2$); 42.47 ($NHCH_2$); 51.36 (S*C*Me$_2$CH); 67.09 (*C*H$_2$OCH$_2$); 67.56 (CH$_2$O*C*H$_2$); 76.43 (NCH); 81.64 (S*C*(CH_2)$_2$N); 94.53 (CCl_3); 117.97 (CH=*C*H$_2$); 133.33 (*C*H=CH$_2$); 158.43 (NCO); 167.96 (NHCO). CI-MS: 415 (96, $[M + H]^+$). HR-CI-MS: 432.0674 ($[M + H + NH_3]^+$, $C_{15}H_{25}Cl_3N_3O_3S^+$; calc. 432.0682).

*(*RS*)-*N*-(4-Methoxybenzyl)-2,2-dimethyl-4-(trichloroacetyl)-8-oxa-1-thia-4-azaspiro[4.5]decane-3-carboxamide* (**4g**). According to *GP 1:* **1c** (278 mg, 1.50 mmol), 1-(isocyanomethyl)-4-methoxybenzene (221 mg, 1.50 mmol), and Cl_3CCOOH (245 mg, 1.50 mmol); 6 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 237 mg (32%). Colorless solid. M.p. 218–219°. R_f (^{t}BuOMe/hexane 3:7) 0.05. IR (ATR): 3299, 2962, 2932, 2856, 2839, 1689, 1656, 1612, 1544, 1513. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.49 (*s*, 3 H,

Me_2C); 1.58–1.61 (*m*, 1 H, CH_2CCH_2); 1.65 (*s*, 3 H, Me_2C); 2.30–2.32 (*m*, 1 H, CH_2CCH_2); 3.33–3.35 (*m*, CH_2CCH_2, CH_2O); 3.37–3.40 (*m*, 1 H, CH_2CCH_2); 3.70–3.74 (*m*, 1 H, CH_2O); 3.80 (*s*, MeO); 3.99–4.00, 4.05–4.09 (2*m*, CH_2O); 4.24 (*dd*, $^2J = 14.3$, $^3J = 4.9$, 1 H, $NHCH_2$); 4.50 (*dd*, $^2J = 14.3$, $^3J = 6.2$, 1 H, $NHCH_2$); 5.12 (*s*, NCH); 5.85–5.87 (*m*, NH); 6.84–6.86 (*m*, 2 *m*-CH); 7.17–7.18 (*m*, 2 *o*-CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 26.17, 33.08 (CMe_2); 36.24 (CH_2CCH_2); 37.29 (CH_2CCH_2); 43.78 ($NHCH_2$); 51.36 ($SCMe_2CH$); 55.46 (MeO); 67.10, 67.58 (CH_2OCH_2); 76.29 (NCH); 81.68 ($SC(CH_2)_2N$); 94.48 (CCl_3); 114.39 (2 *m*-CH); 129.24 (*C*(Ar)CH_2); 129.65 (2 *o*-CH); 158.30 (NCO); 159.44 (*C*(Ar)OMe); 167.72 (NHCO). CI-MS: 496 (100, $[M + H]^+$). HR-CI-MS: 495.0690 ($[M + H]^+$, $C_{20}H_{26}Cl_3N_2O_4S^+$; calc. 495.0679).

*(*RS*)-2,2-Dimethyl*-N-*(2-phenylethyl)-4-(trichloroacetyl)-8-oxa-1-thia-4-azaspiro[4.5]decane-3-carboxamide* (**4h**). According to *GP 1:* **1c** (278 mg, 1.50 mmol), (2-isocyanoethyl)benzene (197 mg, 1.50 mmol), and Cl_3CCOOH (245 mg, 1.50 mmol); 8 d. Purification by CC (^{t}BuOMe/hexane 2:3). Yield: 390 mg (56%). Colorless solid. M.p. 179–181°. R_f (^{t}BuOMe/hexane 2:3) 0.16. IR (ATR): 3323, 3030, 2966, 2858, 1686, 1654, 1538. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.43 (*s*, Me); 1.49–1.55 (*m*, 2 H, CH_2CCH_2); 1.62 (*s*, Me); 2.80–2.83 (*m*, $PhCH_2$); 3.10–3.21 (*m*, 2 H, CCH_2, CH_2OCH_2); 3.23–3.29 (*m*, 1 H, CCH_2); 3.55–3.70 (*m*, 3 H, CH_2OCH_2, $NHCH_2$); 3.81–3.84 (*m*, 1 H, CH_2OCH_2); 4.01–4.05 (*m*, 1 H, CH_2OCH_2); 5.07 (*s*, NCH); 5.72–5.74 (*m*, NH); 7.17–7.19 (*m*, 2 *o*-CH); 7.21–7.24 (*m*, 1 *p*-CH); 7.29–7.32 (*m*, 2 *m*-CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.98, 33.04 (2 Me); 35.28 ($PhCH_2$); 35.79, 37.32 (CH_2CCH_2); 40.48 ($NHCH_2$); 51.34 ($SCMe_2CH$); 66.99 (CH_2OCH_2); 67.41 (CH_2OCH_2); 76.47 (NCH); 81.29 ($SC(CH_2)_2N$); 94.43 (CCl_3); 127.00 (*p*-CH); 128.94, 129.04 (4 arom. CH); 138.15 (1 arom. C); 158.47 (NCO); 168.14 (NHCO). CI-MS: 479 (98, $[M + H]^+$). HR-CI-MS: 496.0999 ($[M + H + NH_3]^+$, $C_{20}H_{29}Cl_3N_3O_3S^+$; calc. 496.0995).

*(*RS*)-2,2,5,5-Tetramethyl*-N-*(prop-2-en-1-yl)-3-(trichloroacetyl)-1,3-oxazolidine-4-carboxamide* (**5a**). According to *GP 1:* **2** (254 mg, 2.00 mmol), allyl isocyanide (134 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 4 d. Purification by CC (AcOEt). Yield: 390 mg (55%). Colorless solid. M.p. 157°. R_f (AcOEt) 0.82. IR (ATR): 3383, 2981, 2935, 1713, 1776. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.09, 1.41, 1.44, 1.72 (4*s*, 4 Me); 3.99–4.01 (*m*, $NHCH_2$); 4.10 (*s*, NCH); 5.13–5.15, 5.19–5.23 (2*m*, $CH{=}CH_2$); 5.69–5.78 (*m*, $CH{=}CH_2$); 6.10–6.11 (*m*, NH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 23.02, 25.88, 27.81, 30.51 (4 Me); 40.94 (CH_2); 69.91 (NCH); 79.44 ($OCMe_2CH$); 93.92 (CCl_3); 99.34 ($OCMe_2N$); 118.68 ($CH{=}CH_2$); 130.86 ($CH{=}CH_2$); 155.43 (NCO); 169.13 (NHCO). CI-MS: 357 (100, $[M + H]^+$). HR-CI-MS: 357.0541 ($[M + H]^+$, $C_{13}H_{20}Cl_3N_2O_3^+$; calc. 357.0534).

*(*RS*)*-N-*(4-Methoxybenzyl)-2,2,5,5-tetramethyl-3-(trichloroacetyl)-1,3-oxazolidine-4-carboxamide* (**5b**). According to *GP 1:* **2** (336 mg, 2.65 mmol), 1-(isocyanomethyl)-4-methoxybenzene (389 mg, 2.65 mmol), and Cl_3CCOOH (433 mg, 2.65 mmol); 6 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 528 mg (46%). Colorless solid. M.p. 167–168°. R_f (^{t}BuOMe/hexane 3:7) 0.11. IR (ATR): 3289, 3087, 2978, 2941, 1687, 1657, 1610, 1556, 1511. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.38, 1.49, 1.74, 1.80 (4*s*, 2 Me_2C); 3.79 (*s*, MeO); 4.24 (*dd*, $^2J = 14.3$, $^3J = 5.0$, 1 H, CH_2); 4.47 (*dd*, $^2J = 14.3$, $^3J = 6.2$, 1 H, CH_2); 4.78 (*s*, NCH); 5.91–5.92 (*m*, NH); 6.84–6.86 (*m*, 2 *m*-CH); 7.16–7.18 (*m*, 2 *o*-CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.79, 27.15, 27.60, 29.47 (2 Me_2C); 43.60 (CH_2); 55.44 (MeO); 70.67 (NCH); 82.53 ($OCMe_2CH$); 93.64 (CCl_3); 99.47 ($OCMe_2N$); 114.40 (2 *m*-CH); 129.27 (*C*(Ph)CH_2); 129.63 (2 *o*-CH); 157.76 (NCO); 159.42 (*C*(Ph)OMe); 168.35 (NHCO). CI-MS: 437 (17, $[M + H]^+$). HR-CI-MS: 454.1071 ($[M + H + NH_3]^+$, $C_{18}H_{27}Cl_3N_3O_4^+$; calc. 454.1067).

*(*RS*)*-N-*Cyclohexyl-2,2,5,5-tetramethyl-3-(trichloroacetyl)-1,3-oxazolidine-4-carboxamide* (**5c**). According to *GP 1:* **2** (254 mg, 2.00 mmol), cyclohexyl isocyanide (218 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 3 d. Purification by crystallization from AcOEt and hexane. Yield: 414 mg (52%). Colorless solid. M.p. 198°. IR (ATR): 3358, 3007, 2973, 2932, 2858, 1689, 1656, 1533. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.06–1.18 (*m*, 3 H, 2 CH_2); 1.29–1.35 (*m*, CH_2); 1.36, 1.48 (2*s*, 2 Me); 1.59–1.61 (*m*, 1 H, CH_2); 1.67–1.69 (*m*, CH_2); 1.74, 1.85 (2*s*, 2 Me); 1.87–1.88 (*m*, CH_2); 3.72–3.80 (*m*, NHC*H*); 4.73 (*s*, NCH); 5.66 (*d*, $^3J = 7.9$, NH). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 24.84, 25.48 (2 CH_2); 25.71, 27.12, 27.71, 29.50 (4 Me); 32.89, 33.11 (2 CH_2); 48.67 (NHCH); 70.66 (NCH); 82.50 ($OCMe_2CH$); 93.69 (CCl_3); 99.29 ($OCMe_2N$); 157.83 (NCO); 167.57 (NHCO). CI-MS: 399 (100, $[M + H]^+$). HR-EI-MS: 398.0936 (M^+, $C_{16}H_{25}Cl_3N_2O_3^+$; calc. 398.0931).

*(*RS*)-2,2,5,5-Tetramethyl-*N*-(naphthalen-2-ylmethyl)-3-(trichloroacetyl)-1,3-oxazolidine-4-carboxamide* (**5d**). According to *GP 1:* **2** (254 mg, 2.00 mmol), 2-(isocyanomethyl)naphthalene (334 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 2 d. Purification by washing with $^iPr_2O$ and pentane. Yield: 625 mg (68%). Colorless solid. M.p. 209°. IR (ATR): 3303, 3082, 2987, 2947, 1687, 1658, 1554. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.41, 1.49, 1.75, 1.82 (4*s*, 4 Me); 4.44 (*dd*, $^2J = 14.5$, $^3J = 5.0$, 1 H, CH_2); 4.71 (*dd*, $^2J = 14.5$, $^3J = 6.4$, 1 H, CH_2); 4.84 (*s*, NCH); 6.11–6.14 (*m*, NH); 7.33–7.35 (*m*, 1 arom. H); 7.46–7.51 (*m*, 2 arom. H); 7.69–7.70 (*m*, 1 arom. H); 7.78–7.83 (*m*, 3 arom. H). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 25.82, 27.15, 27.65, 29.48 (4 Me); 44.25 (CH_2); 70.75 (NCH); 82.56 ($OCMe_2CH$); 93.70 (CCl_3); 99.54 ($OCMe_2N$); 125.97, 126.37, 126.63, 127.08 (4 arom. CH); 127.87 (2 arom. CH); 128.99 (1 arom. CH); 133.01, 133.46, 134.67 (3 arom. C); 157.75 (NCO); 168.59 (NHCO). CI-MS: 457 (100, $[M + H]^+$). HR-EI-MS: 456.0780 (M^+, $C_{21}H_{23}Cl_3N_2O_3^+$; calc. 456.0774).

*(*RS*)-3,4-Dihydro-2,2-dimethyl-*N*-(prop-2-en-1-yl)-4-(trichloroacetyl)-2*H*-1,4-benzothiazine-3-carboxamide* (**6a**). According to *GP 1:* **3** (354 mg, 2.00 mmol), allyl isocyanide (154 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 12 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 99 mg (12%). Yellow solid. M.p. 135–137°. R_f (^{t}BuOMe/hexane 3:7) 0.13. IR (ATR): 3302, 1681, 1661, 1578, 1538. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.11, 1.71 (2*s*, 2 Me); 3.86–3.88 (*m*, $NHCH_2$); 5.01 (*s*, NCH); 5.10–5.16 (*m*, $CH{=}CH_2$); 5.73–5.81 (*m*, $CH{=}CH_2$); 6.03–6.04 (*m*, NH); 7.26–7.29 (*m*, 2 arom. H); 7.37–7.40, 7.66–7.68 (2*m*, 2 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 26.76, 30.12 (2 Me); 41.98 ($NHCH_2$); 50.35 (Me_2C); 73.03 (NCH); 92.64 (CCl_3); 116.92 ($CH{=}CH_2$); 127.29, 128.22, 128.52, 130.75 (4 arom. CH); 132.68 (C(8a)); 133.57 ($CH{=}CH_2$); 136.06 (C(4a)); 162.49 (NCO); 167.42 (NHCO). CI-MS: 407 (94, $[M + H]^+$). HR-CI-MS: 424.0421 ($[M + H + NH_3]^+$, $C_{16}H_{23}Cl_3N_3O_2S^+$; calc. 424.0420).

*(*RS*)-3,4-Dihydro-*N*-(4-methoxybenzyl)-2,2-dimethyl-4-(trichloroacetyl)-2*H*-1,4-benzothiazine-3-carboxamide* (**6b**). According to *GP 1:* **3** (382 mg, 2.15 mmol), 1-(isocyanomethyl)-4-methoxybenzene (317 mg, 2.15 mmol), and Cl_3CCOOH (351 mg, 2.15 mmol); 5 d. Purification by CC (AcOEt/hexane 3:7). Yield: 60 mg (6%). Colorless solid. M.p. 148–150°. R_f (AcOEt/hexane 3:7) 0.44. IR (ATR): 3287, 3069, 3013, 2967, 2930, 2837, 1677, 1659, 1614, 1544, 1515. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.14, 1.68 (2*s*, Me_2C); 3.79 (*s*, MeO); 4.31 (*dd*, $^2J = 14.6$, $^3J = 5.4$, 1 H, CH_2); 4.39 (*dd*, $^2J = 14.6$, $^3J = 5.7$, 1 H, CH_2); 5.00 (*s*, NCH); 6.01–6.02 (*m*, NH); 6.82–6.83 (*m*, 2 *m*-CH); 7.10–7.11 (*m*, 2 *o*-CH); 7.21–7.28 (*m*, CH(6), CH(7)); 7.37 (*dd*, $^3J = 7.4$, $^4J = 1.2$, CH(8)); 7.56–7.58 (*m*, CH(5)). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 26.78, 30.23 (Me_2C); 43.33 (CH_2); 50.14 (Me_2C); 55.44 (MeO); 72.64 (NCH); 92.63 (CCl_3); 114.28 (2 *m*-CH); 127.20, 128.15, 128.31 (CH(5), CH(6), CH(7)); 129.13 (2 *o*-CH); 129.68 (C(Ar)CH_2); 130.65 (C(8)); 132.44 (C(8a)); 135.83 (C(4a)); 159.24 (C(Ar)OMe); 162.61 (NCO); 167.26 (NHCO). CI-MS: 487 (95, $[M + H]^+$). HR-CI-MS: 487.0429 ($[M + H]^+$, $C_{21}H_{22}Cl_3N_2O_3S^+$; calc. 487.0417).

*(*RS*)-3,4-Dihydro-2,2-dimethyl-*N*-(2-phenylethyl)-4-(trichloroacetyl)-2*H*-1,4-benzothiazine-3-carboxamide* (**6c**). According to *GP 1:* **3** (354 mg, 2.00 mmol), (2-isocyanoethyl)benzene (262 mg, 2.00 mmol), and Cl_3CCOOH (327 mg, 2.00 mmol); 8 d. Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 63 mg (7%). Yellow solid. M.p. 112–113°. R_f (^{t}BuOMe/hexane 3:7) 0.19. IR (ATR): 3317, 3065, 2968, 2930, 1671, 1523. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.00, 1.63 (2*s*, 2 Me); 2.77–2.80 (*m*, $PhCH_2$); 3.46–3.52, 3.61–3.69 (2*m*, $NHCH_2$); 4.94 (*s*, NCH); 5.79–5.80 (*m*, NH); 7.14–7.35 (*m*, 9 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 26.51, 29.95 (2 Me); 35.36 ($PhCH_2$); 40.25 ($NHCH_2$); 50.55 (Me_2C); 73.21 (NCH); 92.59 (CCl_3); 126.85, 127.31, 128.17, 128.24 (4 arom. CH); 128.85, 128.97 (4 arom. CH); 130.86 (1 arom. CH); 132.91 (C(8a)); 135.98 (C(4a)); 138.41 (1 arom. C); 162.27 (NCO); 167.55 (NHCO). CI-MS: 471 (96, $[M + H]^+$). HR-CI-MS: 488.0742 ($[M + H + NH_3]^+$, $C_{21}H_{25}Cl_3N_3O_2S^+$; calc. 488.0733).

General Procedure (*GP 2*) *for the Synthesis of the Hydantoines* **7**–**9**. One equiv. of a EtONa soln. (1M) was added to a suspension of 1 equiv. of the respective bisamide **4**, **5**, or **6** in anh. EtOH (10 ml per mmol bisamide). After stirring at r.t. for 1 h, the solvent was removed at the rotary evaporator. The purification of the crude product is described in the experiments.

*(*RS*)-1,1,3,3-Tetramethyl-6-(prop-2-en-1-yl)-1*H*-imidazo[1,5-*c*][1,3]thiazole-5,7(6*H*,7a*H*)-dione* (**7a**). According to *GP 2*, with **4a** (250 mg, 0.67 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 144 mg (85%). Orange solid. M.p. 40°. IR (ATR): 2992, 2972, 2927, 1758, 1703. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.39, 1.60, 1.72, 2.04 (4*s*, 4 Me); 4.03–4.05 (*m*, NCH_2); 4.42–4.43 (*m*, NCH); 5.18–5.20, 5.23–5.26 (*m*, $CH{=}CH_2$); 5.75–5.83 (*m*, $CH{=}CH_2$). ^{13}C-NMR (125.8 MHz, $CDCl_3$):

25.75, 25.89, 30.16, 33.35 (4 Me); 40.96 (NCH_2); 53.27 ($SCMe_2CH$); 69.46 ($SCMe_2N$); 74.27 (NCH); 118.53 ($CH{=}CH_2$); 131.20 ($CH{=}CH_2$); 152.78 (NCON); 168.63 (NCOCH). CI-MS: 255 (100, $[M+H]^+$). HR-EI-MS: 254.1092 (M^+, $C_{21}H_{23}Cl_3N_2O_3^+$; calc. 254.1089).

*(*RS*)-6-(4-Methoxybenzyl)-1,1,3,3-tetramethyl-1*H*-imidazo[1,5-*c*][1,3]thiazole-5,7(6*H*,7a*H*)-dione* (**7b**). According to *GP 2*, with **4b** (154 mg, 0.34 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 85 mg (74%). Yellow solid. M.p. 145–147°. IR (ATR): 2965, 2930, 2836, 1711, 1599, 1510. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.37, 1.51, 1.74, 1.83 (4*s*, 2 Me_2C); 3.73 (*s*, MeO); 4.21 (*d*, ^2J = 14.5, 1 H, CH_2); 4.27 (*d*, ^2J = 15.4, 1 H, CH_2); 4.30 (*s*, NCH); 6.76–6.78 (*m*, 2 *m*-CH); 7.11–7.12 (*m*, 2 *o*-CH). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 26.71, 31.42, 32.58, 32.64 (2 Me_2C); 44.29 (CH_2); 48.48 ($SCMe_2CH$); 55.35 (OMe); 70.44 ($SCMe_2N$); 77.36 (NCH); 114.13 (2 *m*-CH); 129.05 (2 *o*-CH); 131.13 (C(Ar)CH_2); 157.46 (NCON); 158.89 (C(Ar)OMe); 177.01 (NCOCH). CI-MS: 352 (71, $[M+H+NH_3]^+$). HR-CI-MS: 352.1691 ($[M+H+NH_3]^+$, $C_{17}H_{26}N_3O_3S^+$; calc. 352.1695).

*(*RS*)-6-Cyclohexyl-1,1,3,3-tetramethyl-1*H*-imidazo[1,5-*c*][1,3]thiazole-5,7(6*H*,7a*H*)-dione* (**7c**). According to *GP 2*, with **4c** (200 mg, 0.48 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 89 mg (63%). Orange solid. M.p. 86°. IR (ATR): 2928, 2858, 1767, 1750, 1704, 1672, 1599. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.13–1.33; 1.63–1.65; 1.79–1.82; 2.07–2.16 (4*m*, 5 CH_2); 1.36, 1.58, 1.70, 2.03 (4*s*, 4 Me); 3.78–3.84 (*m*, NC*H*CH_2); 4.30 (*s*, NCHCO). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.15 (CH_2); 25.42, 25.81 (2 Me); 25.95, 29.38, 29.47 (3 CH_2); 30.11, 33.49 (2 Me); 51.83 (N*C*HCH_2); 53.49 ($SCMe_2CH$); 69.63 ($SCMe_2N$); 73.45 (N*C*HCO); 153.34 (NCON); 168.82 (N*C*OCH). ESI-MS: 321 (31, $[M+Li^+ + H_2O]^+$). HR-CI-MS: 297.1639 ($[M+H]^+$, $C_{15}H_{25}N_2O_2S^+$; calc. 297.1637).

*(*RS*)-1,1,3,3-Tetramethyl-6-(naphthalen-2-ylmethyl)-1*H*-imidazo[1,5-*c*][1,3]thiazole-5,7(6*H*,7a*H*)-dione* (**7d**). According to *GP 2*, with **4d** (250 mg, 0.53 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 158 mg (84%). Orange solid. M.p. 58°. IR (ATR): 3340, 2984, 1673, 1606, 1510. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.30, 1.60, 1.71, 2.04 (4*s*, 4 Me); 4.43 (*s*, NCH); 4.76–4.77 (*m*, CH_2); 7.45–7.49 (*m*, 2 arom. H); 7.50–7.52 (*m*, 1 arom. H); 7.79–7.83 (*m*, 3 arom. H); 7.85–7.86 (*m*, 1 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.69, 25.87, 30.18, 33.37 (4 Me); 42.71 (CH_2); 53.35 ($SCMe_2CH$); 69.53 ($SCMe_2N$); 74.29 (NCH); 126.29, 126.37, 126.57, 127.78, 128.00, 128.14, 128.65 (7 arom. CH); 133.04, 133.36, 133.55 (3 arom. C); 152.96 (NCON); 168.57 (N*C*OCH). CI-MS: 355 (100, $[M+H]^+$). HR-EI-MS: 354.1405 (M^+, $C_{20}H_{22}N_2O_2S^+$; calc. 354.1402).

*(*RS*)-6′-(Naphthalen-2-ylmethyl)dispiro[cyclohexane-1,1′-imidazo[1,5-*c*][1,3]thiazole-3′,1″-cyclohexane]-5′,7′(6′*H*,7a′*H*)-dione* (**7e**). According to *GP 2*, with **4e** (277 mg, 0.50 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 205 mg (94%). Colorless solid. M.p. 168°. IR (ATR): 2939, 2857, 1755, 1700. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.11–2.12 (*m*, 19 H, CH_2, c-Hex); 2.96–3.02 (*m*, 1 H, CH_2, c-Hex); 4.38 (*s*, NCH); 4.76–4.77 (*m*, NCH_2); 7.45–7.51 (*m*, 3 arom. H); 7.79–7.84 (*m*, 4 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 22.38, 24.12, 24.67, 25.37, 25.44, 25.52, 32.64, 36.56, 37.62, 42.06 (10 CH_2, c-Hex); 42.58 (NCH_2); 58.93 ($SC(CH_2)_5CH$); 73.97 (NCH); 75.62 ($SC(CH_2)_5N$); 126.25, 126.35, 126.58, 127.78, 127.92, 128.13, 128.61 (7 arom. CH); 133.03, 133.38, 133.65 (3 arom. C); 152.82 (NCON); 168.97 (N*C*OCH). CI-MS: 435 (100, $[M+H]^+$). HR-CI-MS: 435.2100 ($[M+H]^+$, $C_{26}H_{31}N_2O_2S^+$; calc. 435.2101).

*(*RS*)-1,1-Dimethyl-6-(prop-2-en-1-yl)tetrahydro-1*H*-spiro[imidazo[1,5-*c*][1,3]thiazole-3,4′-pyran]-5,7(6*H*,7a*H*)-dione* (**7f**). According to *GP 2*, with **4f** (163 mg, 0.39 mmol). Purification by washing with CH_2Cl_2 and drying in vacuum. Yield: 79 mg (69%). Colorless solid. M.p. 107–112°. IR (ATR): 2964, 2859, 1711, 1597, 1512. ^{1}H-NMR (499.9 MHz, CD_3OD): 1.44, 1.60 (2*s*, 2 Me); 1.67–1.70 (*m*, 1 H, CH_2CCH_2); 2.39–2.42, 3.11–3.17 (2*m*, CH_2CCH_2); 3.35–3.45 (*m*, 2 H, CH_2CCH_2, CH_2OCH_2); 3.62–3.70 (*m*, 1 H, CH_2OCH_2); 3.75–3.76 (*m*, NCH_2); 3.91–3.99 (*m*, 2 H, CH_2OCH_2); 4.14 (*s*, NCH); 5.04–5.06, 5.18–5.21 (2*m*, $CH{=}CH_2$); 5.83–5.90 (*m*, $CH{=}CH_2$). ^{13}C-NMR (125.7 MHz, CD_3OD): 26.19, 34.91 (2 Me); 38.75 (CH_2CCH_2); 40.91 (CH_2CCH_2); 43.94 (NCH_2); 50.06 ($SCMe_2CH$); 68.60 (CH_2OCH_2); 68.98 (CH_2OCH_2); 78.35 ($SC(CH_2)_2N$); 79.28 (NCH); 115.54 ($CH{=}CH_2$); 136.56 ($CH{=}CH_2$); 157.95 (NCON); 176.45 (N*C*OCH). CI-MS: 297 (69, $[M+H]^+$). HR-CI-MS: 314.1541 ($[M+H+NH_3]^+$, $C_{14}H_{24}N_3O_3S^+$; calc. 314.1538).

*(*RS*)-6-(4-Methoxybenzyl)-1,1-dimethyltetrahydro-1*H*-spiro[imidazo[1,5-*c*][1,3]thiazole-3,4′-pyran]-5,7(6*H*,7a*H*)-dione* (**7g**). According to *GP 2*, with **4g** (201 mg, 0.40 mmol). Purification by washing with cold EtOH and crystallization from AcOEt. Yield: 106 mg (70%). Colorless oil. M.p. 171–175°. IR

(ATR): 2960, 2855, 1710, 1601, 1511. ^{1}H-NMR (499.9 MHz, CD_3OD): 1.44, 1.60 (2*s*, Me_2C); 1.68–1.71 (*m*, 1 H, CH_2CCH_2); 2.42–2.44, 3.13–3.19 (2*m*, CH_2CCH_2); 3.36–3.54 (*m*, 2 H, CH_2CCH_2, OCH_2); 3.62–3.67 (*m*, 1 H, OCH_2); 3.76 (*s*, OMe); 3.91–3.99 (*m*, 2 H, CH_2OCH_2); 4.14 (*s*, NCH); 4.27–4.28 (*m*, NCH_2); 6.85–6.86 (*m*, 2 *m*-CH); 7.22–7.23 (*m*, 2 *o*-CH). ^{13}C-NMR (125.7 MHz, CD_3OD): 26.20, 34.92 (CMe_2); 38.79 (CH_2CCH_2); 40.95 (CH_2CCH_2); 44.84 (NCH_2); 50.08 ($SCMe_2CH$); 55.68 (MeO); 68.62, 68.99 (CH_2OCH_2); 78.40 ($SC(CH_2)_2N$); 79.33 (NCH); 114.93 (2 *m*-CH); 129.54 (2 *o*-CH); 132.84 (C(Ar)CH_2); 158.06 (NCON); 160.24 (C(Ar)OMe); 176.41 (N*C*OCH). CI-MS: 395 (6, $[M + H + NH_3]^+$). HR-CI-MS: 394.1796 ($[M + H + NH_3]^+$, $C_{19}H_{28}N_3O_4S^+$; calc. 394.1801).

*(*RS*)-1,1-Dimethyl-6-(2-phenylethyl)tetrahydro-1*H*-spiro[imidazo[1,5-*c*][1,3]thiazole-3,4′-pyran]-5,7(6*H*,7a*H*)-dione* (**7h**). According to *GP 2*, with **4h** (141 mg, 0.29 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 60 mg (57%). Colorless solid. M.p. 129°. IR (ATR): 2962, 2945, 2913, 2842, 1763, 1702. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.20, 1.58 (2*s*, 2 Me); 1.73–1.76 (*m*, 1 H, CH_2CCH_2); 1.92–1.95 (*m*, 1 H, CH_2CCH_2); 2.31–2.37 (*m*, 1 H, CH_2CCH_2); 2.89–2.99 (*m*, $PhCH_2$); 3.33–3.42 (*m*, 2 H, CH_2CCH_2, CH_2OCH_2); 3.50–3.55 (*m*, 1 H, CH_2OCH_2); 3.65–3.71, 3.73–3.79 (2*m*, NCH_2); 3.97–3.99 (*m*, 1 H, CH_2OCH_2); 4.10–4.12 (*m*, 1 H, CH_2OCH_2); 4.35 (*s*, NCH); 7.19–7.24 (*m*, 3 arom. H); 7.26–7.30 (*m*, 2 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 25.73, 26.02 (2 Me); 33.98 ($PhCH_2$); 37.55 (CH_2CCH_2); 39.82 (NCH_2); 42.32 (CH_2CCH_2); 52.35 ($SCMe_2CH$); 65.83 (CH_2OCH_2); 67.18 (CH_2OCH_2); 72.91 ($SC(CH_2)_2N$); 73.45 (NCH); 126.86 (1 arom. CH); 128.67, 129.03 (4 arom. CH); 137.67 (1 arom. C); 152.93 (NCON); 168.57 (N*C*OCH). CI-MS: 362 (100, $[M + H]^+$). HR-CI-MS: 361.1584 ($[M + H]^+$, $C_{19}H_{25}N_2O_3S^+$; calc. 361.1586).

*(*RS*)-1,1,3,3-Tetramethyl-6-(prop-2-en-1-yl)-1*H*-imidazo[1,5-*c*][1,3]oxazole-5,7(6*H*,7a*H*)-dione* (**8a**). According to *GP 2*, with **5a** (358 mg, 1.00 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 170 mg (71%). Colorless solid. M.p. 197°. IR (ATR): 2991, 2942, 1639, 1591. ^{1}H-NMR (500.1 MHz, CD_3OD): 1.34, 1.44, 1.62, 1.71 (4*s*, 4 Me); 3.75–3.76 (*m*, CH_2); 3.95 (*s*, NCH); 5.03–5.05, 5.16–5.20 (2*m*, CH=CH_2); 5.81–5.88 (*m*, CH=CH_2). ^{13}C-NMR (125.8 MHz, CD_3OD): 25.81, 28.11, 28.88, 31.12 (4 Me); 43.43 (CH_2); 72.02 (NCH); 81.13 ($OCMe_2CH$); 96.49 ($OCMe_2N$); 115.40 (CH=CH_2); 136.35 (CH=CH_2); 156.78 (NCON); 176.44 (N*C*OCH). CI-MS: 239 (100, $[M + H]^+$). HR-CI-MS: 239.1392 ($[M + H]^+$, $C_{12}H_{19}N_2O_3^+$; calc. 239.1390).

*(*RS*)-6-(4-Methoxybenzyl)-1,1,3,3-tetramethyl-1*H*-imidazo[1,5-*c*][1,3]oxazole-5,7(6*H*,7a*H*)-dione* (**8b**). According to *GP 2*, with **5b** (184 mg, 0.42 mmol). Purification by CC (AcOEt/EtOH 4 : 1). Yield: 71 mg (52%). Colorless solid. M.p. 126–131°. R_f (AcOEt/EtOH 4 : 1) 0.58. IR (ATR): 2985, 2939, 2835, 1711, 1667, 1642, 1510. ^{1}H-NMR (499.9 MHz, CD_3OD): 1.33, 1.46, 1.64, 1.70 (4*s*, 2 Me_2C); 3.76 (*s*, MeO); 4.17 (*d*, ^2J = 15.4, 1 H, CH_2); 4.37–4.39 (*m*, 2 H, CH_2, NCH); 6.83–6.85 (*m*, 2 *m*-CH); 7.19–7.20 (*m*, 2 *o*-CH). ^{13}C-NMR (125.7 MHz, CD_3OD): 25.71, 28.15, 28.93, 30.83 (2 Me_2C); 44.34 (CH_2); 55.69 (MeO); 69.41 (NCH); 81.08 ($OCMe_2CH$); 96.90 ($OCMe_2N$); 114.76 (2 *m*-CH); 129.29 (2 *o*-CH); 133.23 (C(Ar)CH_2); 156.97 (NCON); 160.11 (C(Ar)OMe); 173.31 (N*C*OCH). CI-MS: 336 (5, $[M + H + NH_3]^+$). HR-CI-MS: 336.1930 ($[M + H + NH_3]^+$, $C_{17}H_{26}N_3O_4^+$; calc. 336.1923).

*(*RS*)-6-Cyclohexyl-1,1,3,3-tetramethyl-1*H*-imidazo[1,5-*c*][1,3]oxazole-5,7(6*H*,7a*H*)-dione* (**8c**). According to *GP 2*, with **5c** (200 mg, 0.50 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 107 mg (76%). Colorless solid. M.p. 57°. IR (ATR): 2978, 2932, 2857, 1765, 1705, 1603. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.12 (*s*, Me); 1.15–1.33 (*m*, 2 CH_2); 1.44, 1.47 (2*s*, 2 Me); 1.62–1.67 (*m*, 2 CH_2); 1.75 (*s*, Me); 1.79–1.82, 2.05–2.16 (2*m*, CH_2); 3.80–3.86 (*m*, NCH); 4.02 (*s*, NCH). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 22.87 (Me); 25.14 (CH_2); 25.93 (2 CH_2); 27.91 (Me); 29.16, 29.38 (2 CH_2); 30.70 (Me); 51.92 ($NCHCH_2$); 69.37 (NCH); 79.66 ($OC(Me)_2CH$); 94.13 ($OC(Me)_2N$); 156.11 (NCON); 169.72 (N*C*OCH). CI-MS: 281 (100, $[M + H]^+$). HR-CI-MS: 281.1858 ($[M + H]^+$, $C_{15}H_{25}N_2O_3^+$; calc. 281.1860).

*(*RS*)-1,1,3,3-Tetramethyl-6-(naphthalen-2-ylmethyl)-1*H*-imidazo[1,5-*c*][1,3]oxazole-5,7(6*H*,7a*H*)-dione* (**8d**). According to *GP 2*, with **5d** (300 mg, 0.66 mmol). Purification by washing with cold EtOH and drying in vacuum. Yield: 175 mg (78%). Colorless solid. M.p. 114°. IR (ATR): 2981, 2932, 1771, 1708. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.04, 1.46, 1.49, 1.77 (4*s*, 4 Me); 4.15 (*s*, NCH); 4.78–4.79 (*m*, CH_2); 7.45–7.49 (*m*, 2 arom. H); 7.51–7.53 (*m*, 1 arom. H); 7.79–7.83 (*m*, 3 arom. H); 7.86–7.87 (*m*, 1 arom. H). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 23.02, 26.00, 27.89, 30.59 (4*s*, 4 Me); 42.81 (CH_2); 70.03 (NCH); 79.64 ($OC(Me)_2CH$); 94.07 ($OC(Me)_2N$); 126.30, 126.36, 126.54, 127.76, 128.06, 128.12, 128.64 (7 arom. CH);

133.03 (1 arom. C); 133.34 (2 arom. C); 155.73 (NCON); 169.41 (N*C*OCH). CI-MS: 339 (100, $[M + H]^+$). HR-EI-MS: 338.1627 (M^+, $C_{20}H_{22}N_2O_3^+$; calc. 338.1630).

*(*RS*)-4,4-Dimethyl-2-(prop-2-en-1-yl)-3a,4-dihydro-1*H*-imidazo[5,1-*c*][1,4]benzothiazine-1,3(2*H*)-dione* (**9a**). According to *GP 2*, with **6a** (62 mg, 0.15 mmol). Purification by CC (CH_2Cl_2). Yield: 30 mg (67%). Colorless solid. M.p. 84–89°. R_f (CH_2Cl_2) 0.30. IR (ATR): 2990, 2966, 2927, 2880, 1775, 1704. ^{1}H-NMR (500.1 MHz, $CDCl_3$): 1.34, 1.74 (2*s*, 2 Me); 4.14–4.24 (*m*, NCH_2); 4.28 (*s*, NCH); 5.23–5.25, 5.29–5.33 (2*m*, CH=CH_2); 5.80–5.88 (*m*, C*H*=CH_2); 7.01–7.04 (*m*, CH(7)); 7.08–7.10 (*m*, CH(6)); 7.13–7.16 (*m*, CH(8)); 8.22–8.24 (*m*, CH(9)). ^{13}C-NMR (125.8 MHz, $CDCl_3$): 23.93, 24.87 (2 Me); 41.17 (CH_2); 42.29 (Me_2C); 64.91 (NCH); 119.10 (CH=*C*H_2); 121.03 (C(9)); 122.18 (C(5a)); 124.74, 125.49, 126.54 (C(6), C(7), C(8)); 130.62 (C(9a)); 130.67 (*C*H=CH_2); 153.42 (NCON); 167.66 (N*C*OCH). EI-MS: 228 (100, M^+). HR-EI-MS: 288.0939 (M^+, $C_{15}H_{16}N_2O_3S^+$; calc. 288.0933).

*(*RS*)-2-(4-Methoxybenzyl)-4,4-dimethyl-3a,4-dihydro-1*H*-imidazo[5,1-*c*][1,4]benzothiazine-1,3(2*H*)-dione* (**9b**). According to *GP 2*, with **6b** (70 mg, 0.14 mmol). Purification by CC (^{t}BuOMe/hexane 3:7). Yield: 40 mg (78%). Colorless solid. M.p. 120°. R_f (^{t}BuOMe/hexane 3:7) 0.52. IR (ATR): 3000, 2967, 2932, 2835, 1771, 1704, 1614, 1586, 1515. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.19, 1.71 (2*s*, 2 Me_2C); 3.78 (*s*, MeO); 4.23 (*s*, NCH); 4.65–4.71 (*m*, CH_2); 6.83–6.85 (*m*, 2 *m*-CH); 7.00–7.03 (*m*, CH(7)); 7.07–7.08 (*m*, CH(6)); 7.12–7.15 (*m*, CH(8)); 7.37–7.38 (*m*, 2 *o*-CH); 8.21–8.23 (*m*, CH(9)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 23.83, 24.87 (2 *Me*$_2$C); 42.23 (CH_2); 42.41 (Me_2C); 55.39 (MeO); 64.88 (NCH); 114.20 (2 *m*-CH); 121.13 (C(9)); 122.28 (C(5a)); 124.73, 125.45, 126.55 (C(6), C(7), C(8)); 127.95 (C(9a)); 130.42 (2 *o*-CH); 130.68 (*C*(Ar)CH_2); 153.70 (NCON); 159.61 (*C*(Ar)OMe); 167.85 (N*C*OCH). CI-MS: 370 (100, $[M + H]^+$). HR-CI-MS: 369.1270 ($[M + H]^+$, $C_{20}H_{21}N_2O_3S^+$; calc. 369.1273).

*(*RS*)-4,4-Dimethyl-2-(2-phenylethyl)-3a,4-dihydro-1*H*-imidazo[5,1-*c*][1,4]benzothiazine-1,3(2*H*)-dione* (**9c**). According to *GP 2*, with **6c** (44 mg, 0.09 mmol). R_f (CH_2Cl_2) 0.65. Yield: 20 mg (63%). Colorless oil. IR (ATR): 2958, 2928, 2857, 1771, 1715. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.17, 1.69 (2*s*, 2 Me); 3.01–3.02 (*m*, PhCH_2); 3.79–3.85, 3.89–3.95 (2*m*, NCH_2); 4.21 (*s*, NCH); 7.02–7.05, 7.08–7.09 (2*m*, 2 arom. H); 7.13–7.31 (*m*, 6 arom. H); 8.21–8.23 (*m*, CH(9)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 23.76, 24.90 (2 Me); 33.82 (Ph*C*H_2); 40.13 (NCH_2); 42.28 (Me_2C); 64.91 (NCH); 121.04 (C(9)); 122.33 (C(5a)); 124.73, 125.50, 126.58, 126.98 (4 arom. CH); 128.79, 129.05 (4 arom. CH); 130.74 (C(9a)); 137.59 (Ph*C*H_2); 153.72 (NCON); 167.92 (N*C*OCH). EI-MS: 352 (100, M^+). HR-EI-MS: 352.1242 (M^+, $C_{20}H_{20}N_2O_2S^+$; calc. 352.1246).

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