Full Paper

New 2-Amino-thiazole-4-acetamides with Antiplatelet Activity

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In the Born test, 23 title compounds were synthesized and investigated for their antiplatelet activities against collagen, ADP, adrenaline, and platelet-activating factor (PAF) as inducers of the aggregation. Using collagen, three compounds with IC_{50} values below 10 μM were found (**3a**, **3b**, **3c**) and 15 compounds with IC_{50} values between 10 and 100 μM were determined. In general, a cyclohexylamino rest on an 4-carboxamide moiety is a pre-requisite for this pharmacological activity. A clear dependence from the substituent R^1 in the structural element Y is observed. The same is true for the spacer n in the 4-carboxamide substituent. Compound **3e** showed strong ADP-antagonistic effects (IC_{50} = 2.2 nM); **3c** antagonized adrenaline (IC_{50} = 2.8 nM), while **3n** was highly effective against platelet-activating factor (IC_{50} = 0.2 μM).

Keywords: ADP / Antiplatelet properties / Born test with Adrenaline / PAF / Thiazole acetamides

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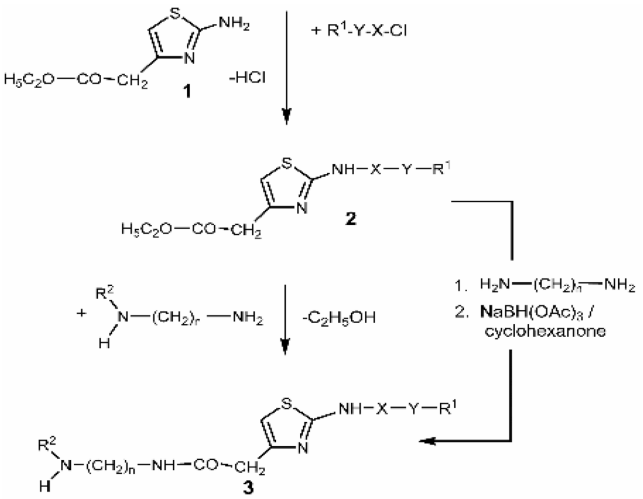
Introduction

In a number of publications, we have shown that the substitution of heterocycles rich in nitrogen-like purines [1], indazoles [2], triazoles [3], oxadiazoles [4], imidazoles [5], pyrimidocinnolines [6], or phthalazines [7] with a carboxamide partial structure, a hydrophobic moiety and basic groups leads to a wide variety of compounds with antiplatelet activities in micromolar concentrations. In this paper, we wish to report a number of thiazole derivatives fulfilling these structural requirements and, consequently, were promising to show remarkable antiplatelet activities.

Results and discussion

Chemistry

The synthesis of the title 2-amino-thiazole-4-acetamides is summarized in Scheme 1. Starting material is the commercially available 2-amino-thiazol-4-acetic acid ethylester **1**. This compound is converted with sulfonic acid chlorides (X = SO_2) or carboxylic acid chlorides (X = CO) to the corresponding sulfonamide or carboxamide derivatives of type **2**. The substituent Y was phenyl, 2-naphthyl, phenylalkyl, or cyclohexyl. The rest R^1 is 4-H, 4-F, 4Cl, 3-Cl, 2-Cl, 3,4-Cl_2, 2,4-Cl_2, 4-Br, 4-I, 4-CH_3, or 4-phenyl. The



For X, Y, R1, R2 and n see Table 1.

Scheme 1. Synthesis of 2-amino-thiazole-4-acetamides (type-**3**).

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Abbreviation: platelet-activating factor (PAF)

Table 1. Antiplatelet activity of **3a**–**w** in the Born test with collagen as inducer.

Compound	R^1	Y	X	n	R^2	IC_{50} (μM)
3a	4-F	phenyl	SO_2	3	cyclohexyl	1
3b	4-Cl	phenyl	SO_2	5	cyclohexyl	6
3c	4-F	phenyl	CO	3	cyclohexyl	9
3d	4-phenyl	phenyl	SO_2	3	cyclohexyl	14
3e	4-Cl	phenyl	SO_2	2	cyclohexyl	15
3f	2-Cl	phenyl	SO_2	3	cyclohexyl	19
3g	–	cyclohexyl	CO	3	cyclohexyl	19
3h	4-I	phenyl	CO	3	cyclohexyl	21
3i	H	phenylCH_2	CO	3	cyclohexyl	22
3j	H	phenyl$(CH_2)_2$	CO	3	cyclohexyl	22
2k	4-phenyl	phenyl	CO	–	–	26
3l	–	2-naphthyl	SO_2	3	cyclohexyl	28
3m	4-Cl	phenyl	CO	3	cyclohexyl	33
3n	4-Cl	phenyl	SO_2	3	-CH_2-cyclohexyl	36
3o	4-Br	phenyl	CO	3	cyclohexyl	44
3p	3-Cl	phenyl	SO_2	3	cyclohexyl	46
3q	4-phenyl	phenyl	CO	3	cyclohexyl	53
3r	4-Cl	phenyl	SO_2	3	cyclohexyl	57
3s	4-I	phenyl	SO_2	3	cyclohexyl	100
3t	4-Cl	phenyl	SO_2	6	cyclohexyl	126
3u	H	phenyl	CO	3	cyclohexyl	137
3v	4-Cl	phenyl	SO_2	4	cyclohexyl	204
3w	H	phenyl	SO_2	3	cyclohexyl	282

successful synthesis is indicated in the ^{1}H-NMR spectrum by the shift of the NH_2-Signal from 6.87 ppm to 12.3–12.8 (N*H*SO_2) or 12.0–13.0 ppm (N*H*CO). The 5-H thiazole proton is shifted from 6.30 to 6.6–6.7 ppm (sulfonamides) or to 6.95–7.1 ppm (carboxamides). Aminolysis of type **2** esters with suitable primary amines yielded the desired test compounds of type **3**. Some of them were obtained by aminolysis with twofold primary diamines followed by reductive alkylation with cyclohexanone and sodium-triacetoxy boron hydride. The number of methylene groups varied from n = 2–6. For R^2 a variety of alkyl, alkyloxy, or carboxylic acid groups were used. Surprisingly, however, all pharmacologically active compounds were substituted by a cyclohexyl- or cyclohexylmethyl group; consequently, we will only discuss these substances here.

Biology

Due to the limited space of the paper, only compounds which showed an inhibition of the platelet aggregation in the Born test [8] (induced by collagen) with an IC_{50} below 300 μM were included in the discussion. For the same reason, only for these compounds the synthetic and analytical data are given in the experimental part. The full set of data can be found in the PhD thesis of T. Baselt [9]. To identify the favorable structural elements, a ranking of the substances was performed according to their IC_{50} values. This is shown in Table 1. Unexpectedly, already one type (ester **2**), *i.e.* the biphenylcarboxamide **2k**, showed antiplatelet activity (IC_{50} = 26 μM). We suppose that this is due to the high lipophilicity of the biphenyl group which had turned out to be favorable in other heterocycles [3, 4]. The additional introduction of a suitable basic function which yielded compound **3q** leads, however, to decreased activity (**3q**: IC_{50} = 53 μM). In contrast in the corresponding sulfonamide **2d** (IC_{50} = 212 μM), the same procedure leads to the highly active compound **3d** (IC_{50} = 14 μM). The same is true for all other compounds for which the introduction of a cyclohexyl-(methyl)-aminoalkyl rest in 4-position is a prerequisite for pharmacological activity.

The substituent R^1 in the phenyl group has a decisive influence on the antiplatelet activity. If R^1 is hydrogen, only small effects are seen (**3w**: X = SO_2, IC_{50} = 282 μM; **3u**: X = CO, IC_{50} = 137 μM). If R^1 is fluorine in 4-position, the most active compound **3a** (X = SO_2) is obtained showing an IC_{50} = 1 μM. If X is CO (see **3c**) high activity (IC_{50} = 9 μM) is still observed. If, however, there are one or two methylene groups between the phenyl ring and the CO group (see **3i** and **3j**, respectively), no fluorine substitution is needed for a remarkable effect of 22 μM in each case. If Y is 2-naphthyl (see **3l**), also no further substituent R^1 is necessary for an activity of 28 μM. If the phenyl group is replaced by a cyclohexyl moiety (compare **3u**: 137 μM with **3g**: 19 μM), a strong increase in activity is seen. If R^1 is a chlorine atom (n = 3 and Y = SO_2 held constant) a decrease of the IC_{50} from 4-Cl (**3r**: 57 μM) via 3-Cl (**3p**:

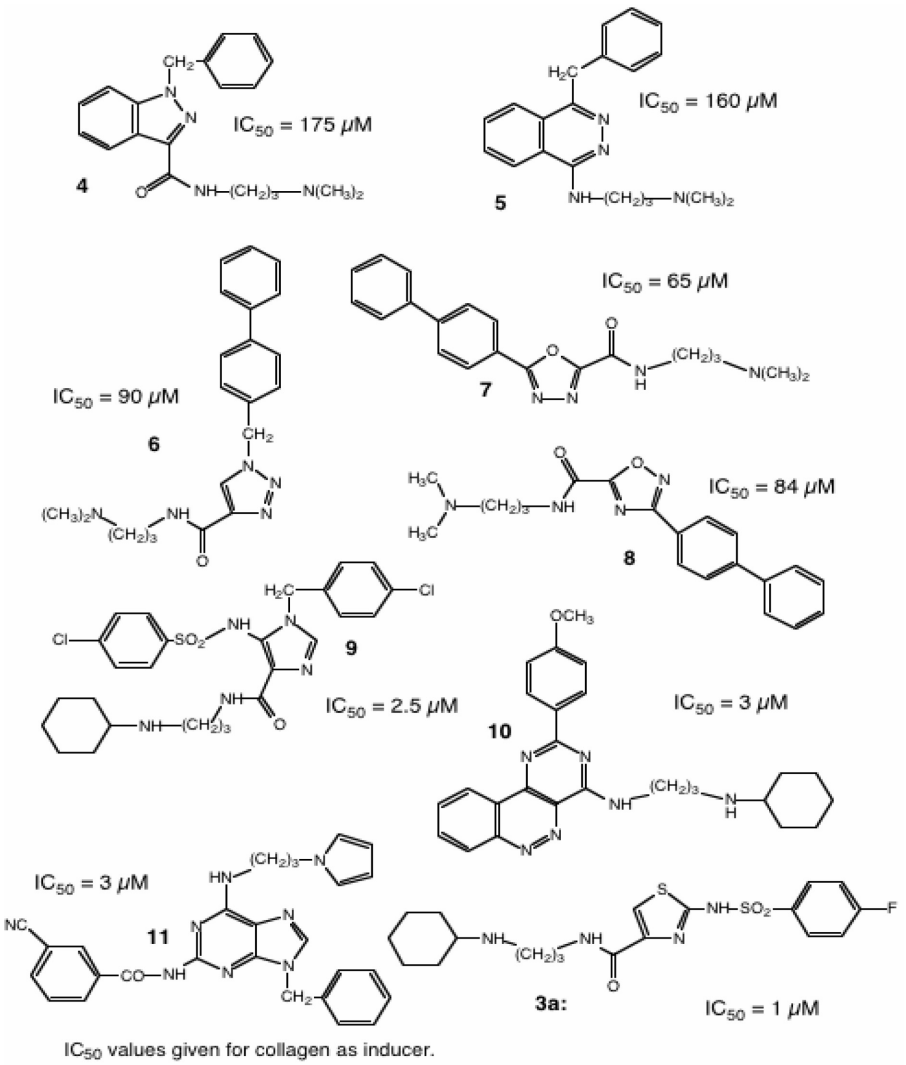

Figure 1. Most active platelet-aggregation inhibitors in each class of heterocycles.

46 μM) to 2-Cl (**3f**: 19 μM) is observed. A 4-Br or 4-I substitution (**3o**: 44 μM, **3h**: 21 μM, **3s**: 100 μM) results active compounds as well.

With R^1 = 4-Cl, the influence of the spacer n was investigated. Comparison of **3b** (n = 5, IC_{50} = 6 μM) with **3e** (n = 2, IC_{50} = 15 μM) and **3r** (n = 3, IC_{50} = 57 μM) shows that the number of methylene groups has a strong influence on the activity. Surprisingly, for n = 4 (**3v**: 204 μM) and n = 6 (**3t**: 126 μM) only small activities could be observed.

The question whether sulfonamides or carboxamides are the superior class of compounds should be answered by comparing pairs of compounds which only differ with respect to this structural element. This is possible with five pairs of compounds; see Table 1. Comparison of **3a** (1 μM) with **3c** (9 μM) and **3d** (14 μM) with **3q** (53 μM) suggests an advantage for sulfonamides. Unfortunately, with the pairs **3s** (100 μM) vs **3h** (21 μM), **3r** (57 μM) vs **3m** (33 μM), and **3w** (282 μM) vs **3u** (137 μM), it is just the other way round.

In summary, a 4-fluorophenylsulfonylamino rest in 2-position of the thiazoles combined with a cylohexylaminopropyl acetamide in 4-position exhibits the strongest antiplatelet activity with an IC_{50} = 1 μM against collagen as inducer of the aggregation.

To compare structure and activity of the thiazole derivatives **3** with the other heterocycles already investigated, we have compiled the most effective inhibitory compound of each series in Fig. 1 (**3** – **11**).

Concerning the activity, there is an obvious difference between compounds **4** – **8** (IC_{50} = 65 to 160 μM) and **9** – **11** (2.5 to 3 μM). The latter compounds are joined by the thiazole **3a** with an IC_{50} = 1 μM. The reason for this difference is the basic substituent. Since Steege [5] discovered the enormous influence of the 3-cyclohexylaminopropyl-

moiety in the imidazole derivatives **9**, the way for getting strong antiplatelet activity was opened (see **10** and **3a**). The purine derivative **11**, however, shows that the pyrrol moiety can substitute the cyclohexylamino rest (IC_{50} = 3 μM). In this case, the cyclohexylamino compound reached rang two with an IC_{50} = 17 μM [1]. The carboxamide structure of **11** corresponds to the sulfonamide group in **9** or **3a**. In conclusion, the differentiation by the heterocyclic moiety in **9**–**11** is small provided that the heterocyclic system is rich in nitrogen and combined with the most suitable basic substituent.

The same is true for the upper compounds of Fig. 1, where the *N*,*N*-dimethylaminopropyl-group (**4**, **5**, **6**, **7**, **8**) had been taken for the basic substituent. The (most effective) hydrophobic substituent in **6**, **7**, and **8** is 4,4′-biphenyl. These three compounds show nearly the same antiplatelet activity despite different heterocycles.

The indazole **4** and the phthalazine **5** even exhibit nearly the same antiplatelet activity, which is equal to acetylsalicylic acid (175 μM). When the indazole **4** is substituted by a fluorine atom in 2-position of the benzyl group, a slight improvement (85 μM) is obtained. The structure of **3a** finally and surprisingly shows that a thiazole is a sufficient frame for the two substituents needed for strong antiplatelet activity. A special hydrophobic substitution seems not to be necessary.

To get a more complete idea concerning the mechanism of action, the effects using other inducers of the platelet aggregation were investigated with selected compounds.

The criteria-of-choice were: (i) High activity against collagen (**3a**, **3b**, **3c**, **3e**); (ii) influence of the spacer n (**3e**, **3r**, **3v**, **3b**, **3t)** (n = 2-6); (iii) exchange of R^1 = 4-Cl against 4-F (**3a** / **3r**); (iv) exchange of X = SO_2 against CO (**3a**, **3c**, **3m**, **3r);** (v) an example for Y = 2-naphthyl (**3l**): (vi) an example for Y = phenylethyl (**3j**); (vii) an example for R^2 = cyclohexylmethyl (**3n**).

The results obtained with the inducers adenosinediphosphate (ADP), adrenaline, or PAF are summarized in Table 2. The results with collagen are added once more for better comparison.

Considering firstly the influence of the spacer (n = 2–6) on ADP-induced platelet aggregation this can be achieved by R^1 YX = 4-Cl-phenyl-SO_2 held constant for the row **3e** (IC_{50} = 2.2 nM, n = 2), **3v** (5.3 nM, n = 4), **3t** (0.9 μM, n = 6), **3b** (31 μM, n = 5), and **3r** (106 μM, n = 3). It is obvious that two or four methylene groups between the sulfonamide and the nitrogen function are most suitable and show inhibitory effects in the lower nanomolar range. By enlarging the spacer to five or six methylene groups, a decrease in activity by three orders of magnitude is observed. The same is even more evident for n = 3 where the ADP antagonism is nearly lost (see **3r**). Altogether, the spacer n plays a crucial role in ADP-mediated platelet aggregation.

Table 2. Selected compounds for the investigation of other inducers than collagen in the platelet aggregation.

Compound	Collagen IC_{50} (μM)	ADP IC_{50} (μM)	Adrenaline IC_{50} (μM)	PAF IC_{50} (μM)
3a	1	27	0.0027	40
3b	6	31	0.44	53
3c	9	43	0.0028	42
3e	15	0.0022	1.1	106
3j	22	0.82	14	58
3l	28	39	22	3
3m	33	11	0.59	12
3n	36	26	106	0.2
3r	57	106	14	106
3t	126	0.9	0.53	106
3v	204	0.0053	53	15

Contrary to the collagen-induced aggregation, the exchange of chlorine by fluorine in R^1 has only a small effect [**3r** (106 μM) 1 **3a** (27 μM)]. The exchange of X = SO_2 against X = CO (**3r** = 106 μM; **3m** = 11 μM) increases the activity tenfold, while the same procedure in **3a** (27 μM) gives **3c** with similar activity. The Y-part phenylethyl is accepted (see **3j** = 0.82 μM) while the naphthyl group provides only small activity (see **3l** = 39 μM). The cylohexylmethyl group instead of cyclohexyl as R^2 is a possibility (**3r**: 106 μM; **3n**: 26 μM).

The influence of the selected compounds on the aggregation induced by adrenaline shows a different pattern of activity. Concerning the spacer, similar effects are found for **3e**: n = 2 (1.1 μM), **3b**: n = 5 (0.44 μM), and **3t**: n = 6 (0.53 μM). Medium distances **3r**: n = 3, (14 μM) and **3v**: n= 4 (53 μM) generate smaller activities. Altogether, a dependence of the effects from the number of methylene groups is seen. If **3r** is slightly modified by exchange of R^1 = 4-Cl against R^1 = 4-F, a dramatic increase in activity by more than three orders of magnitude is observed (**3a**: 2.7 nM) which stresses the importance of a highly electronegative rest in R^1. Instead of X = SO_2 the rest X = CO is as well accepted as compound **3c** (2.8 nM) is showing. R^2 = cyclohexylmethyl is less suitable as the comparison of **3r** (14 μM) with **3n** (106 μM) indicates.

This is in strong contrast to the influence on PAF-induced aggregation where **3n** is the most powerful inhibitor with an IC_{50} = 200 nM. The naphthyl derivative **3l** follows with an IC_{50} = 3 μM which is one order of magnitude weaker but still tenfold stronger than all other compounds so that **3n** and **3l** probably can by classified as rather specific PAF antagonists.

The authors have declared no conflict of interest.

Experimental

Chemistry

M.p. (uncorr.), Linström (Bühler, Tübingen Germany). – Elementary analysis, Elementar Vario EL-IR (Elementaranalysen Systeme, Hanau, Germany), ATI Mattson Genesis Serie FTIR (Unicam Analytische Systeme, Kassel, Germany). – ^{1}H-NMR: Bruker DPX 400 in [d_6]DMSO (Bruker, Bioscience, USA).

General procedure for the synthesis of type-2 acylesters

The corresponding acid chloride (10 mmol) was dissolved in 10 mL pyridine while the mixture was cooled with ice. 10 mmol of **1** were slowly added and heated for 10 min at 120°C. Then the mixture was poured on 400 mL ice water. The solution was acidified with hydrochloric acid to pH 2. Meanwhile, an oily product separated and crystallized. The crystals were sucked off and recrystallized from ethanol (sulfonamides) or ethanol / water (80 : 20, v/v) (carboxamides). The purity of the products was confirmed by elementary analysis within the usual (± 0.4%) limits. The full set of IR, NMR, and MS data is given in the PhD thesis of Baselt [9].

Compounds **2a**, **2b**, **2d**, **2f**, and **2p** have already been described in the literature [10, 11].

*2-[[(4-Fluorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2a***

From 1.9 g (10.2 mmol) **1** and 2.0 g 4-fluorophenylsulfonic acid chloride. Beige crystals, m.p. 122°C, yield 2.5 g (71%).

*2-[[(4-Chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2b***

From 1.9 g (10.2 mmol) **1** and 2.15 g 4-chlorophenylsulfonic acid chloride. Light beige crystals, m.p. 173°C, yield 2.9 g (79%).

*2-[[(4-Fluorophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2c***

From 1.9 g (10.2 mmol) **1** and 1.62 g (10.2 mmol) 4-fluorobenzoic acid chloride. Light beige crystals, m.p. 104 – 107°C (decomp.), yield 2.1 g (67%).

*2-[[1,1′-(Biphenyl-4-yl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2d***

From 1.9 g (10.2 mmol) **1** and 2.6 g biphenyl-4-sulfonic acid chloride. Light beige crystals, m.p. 172°C, yield 2.6 g (63%).

*2-[[(2-Chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2f***

From 1.9 g (10.2 mmol) **1** and 2.15 g 2-chlorophenylsulfonic acid chloride. Light brown crystals, m.p. 172°C, yield 2.7 g (74%).

*2-[(Cyclohexylcarbonyl)amino]-1,3-thiazol-4-yl-acetic acid ethylester **2g***

From 1.9 g (10.2 mmol) **1** and 1.5 g cyclohexylcarboxylic acid chloride. Needles, m.p. 188°C, yield 2.4 g (80%).

*2-[[(4-Iodophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2h***

From 1.9 g (10.2 mmol) **1** and 2.7 g (10.2 mmol) 4-iodobenzoic acid chloride. Light beige crystals, m.p. 119°C, yield 2.7 g (63%).

*2-[(Phenylacetyl)amino]-1,3-thiazol-4-yl-acetic acid ethylester **2i***

From 1.9 g (10.2 mmol) **1** and 1.6 g 2-phenylacetic acid chloride. Light yellow crystals, m.p. 90 – 92°C, yield 2.1 g (68%).

*2-[[(2-Phenylethyl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2j***

From 1.9 g (10.2 mmol) **1** and 1.7 g 2-phenylethanecarboxylic acid chloride. Light yellow crystals, m.p. 84°C, yield 2.25 g (69%).

*2-[[1,1′-(Biphenyl-4-yl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2k***

From 1.9 g (10.2 mmol) **1** and 2.0 g biphenyl-4-carboxylic acid chloride. Light beige crystals, m.p. 191 – 194°C, yield 3.0 g (73%).

*2-[(2-Naphthylsulfonyl)amino]-1,3-thiazol-4-yl-acetic acid ethylester **2l***

From 1.9 g (10.2 mmol) **1** and 2.3 g 2-naphthylsulfonic acid chloride. Light beige crystals, m.p. 159 – 160°C, yield 2.75 g (71%).

*2-[[(4-Chlorophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2m***

From 1.9 g (10.2 mmol) **1** and 1.8 g (10.2 mmol) 4-chlorophenylcarboxylic acid chloride. Light beige crystals, m.p. 130°C, yield 2.6 g (79%).

*2-[[(4-Bromophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2o***

From 1.9 g (10.2 mmol) **1** and 2.2 g (10.2 mmol) 4-bromophenylcarboxylic acid chloride. Light beige crystals, m.p. 119 – 121°C, yield 2.45 g (65%).

*2-[[(3-Chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2p***

From 1.9 g (10.2 mmol) **1** and 2.15 g 3-chlorophenylcarboxylic acid chloride. Light red crystals, m.p. 143 – 144°C, yield 2.15 g (60%).

*2-[[(4-Iodophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetic acid ethylester **2s***

From 1.9 g (10.2 mmol) **1** and 3.1 g 4-iodophenylsulfonic acid chloride. Light beige crystals, m.p. 162°C, yield 3.8 g (83%).

*2-Benzoylamino-1,3-thiazol-4-yl-acetic acid ethylester **2u***

From 1.9 g (10.2 mmol) **1** and 1.44 g benzoylchloride. Crystals, m.p. 92 – 95°C, yield 1.8 g (60%).

*2-Phenylsulfonylamino-1,3-thiazol-4-yl-acetic acid ethylester **2w***

From 1.9 g (10.2 mmol) **1** and 1.8 g phenylsulfonic acid chloride. Light beige crystals, m.p. 129°C, yield 2.65 g (80%).

General procedure for the synthesis of 2-acylamino-1,3-thiazol-4-yl-acetamides (see type-3 in Scheme 1)

Procedure A: The suitable type-**2** acetic acid ethylester (10 mmol) is suspended in the desired diamine (at least 50 mmol) and kept 1.5 h at 120°C or at 70°C overnight. Then, the mixture is diluted with ethylene, diethylene, or triethylene glycol (about 80 mL). Now, the solvent and the excess of the diamine are removed *in vacuo* at 1 mm Hg. The temperature should not exceed 130°C.

A 1: The residue is mixed with water (70°C). The crystals formed are sucked off and recrystallized from a small amount of methanol.

A 2: The residue is mixed with ethanol and 3 mL isopropanolic HCl are added. The mixture is concentrated and mixed with ethylacetate / methanol (3 : 1). A precipitate of crystals forms and is sucked off. If necessary, the crystals are purified by column chromatography or recrystallization with the solvent stated.

Procedure B (**3b**, **3e**, **3t**, **3v**): When the suitable diamine (n = 2, 4, 5, 6) was not commercially available or the purification of the type-**3** compound was difficult, these complications could be circumvented by procedure B via type-**3** compounds with R^2 = H.

The aminolysis follows procedure A. Then, these compounds were transformed by reductive alkylation with cyclohexanone and sodiumtriacetoxy boron hydride to the test compounds of Table 1 (R^2 = cyclohexyl). The reductive alkylation is described below. The intermediate primary aminoalkylamide **3** (R^2 = H, 10 mmol) and 10 mmol cyclohexanone get dissolved in 35 mL dry 1,2-dichloroethane, 10 mL dry methanol, 2 mL acetic acid, and 4 mL DMSO. Then, 14 mmol $NaBH(OAc)_3$ are added and the mixture is stirred under nitrogen at r.t. When the reaction is completed (TLC control), the mixture is poured into 2 N HCl, twice extracted with ether, and brought to pH 8. After extraction with dichloromethane / methanol (1 : 1), the organic layer is dried with Na_2SO_4, acidified with 3 mL isopropanolic HCl, and the solvent removed. The crystallizing hydrochloride is suspended in ethylacetate / methanol (3 : 1) and sucked off.

*N-[3-(Cyclohexylamino)propyl]-2-[[(4-fluorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide semihydrate **3a***

From 2.5 g (7.26 mmol) **2a** and 4.0 g *N*-cyclohexyl-1,3-propanediamine, procedure A2, column chromatography ($CHCl_3$ / CH_3OH saturated with NH_3 = 3 : 1). Crystals, m.p. 182–187°C, yield 0.21 g (6%). – Anal. $C_{20}H_{28}FN_4O_{3.5}S_2$ (454.58). – IR (KBr): ν = 3434 cm^{-1}; 3096; 3067; 2938; 2859; 2554; 2454; 1648 (CO); 1591; 1539; 1492; 1454; 1353; 1326; 1297; 1257 (SO_2); 1234; 1155; 1138 (SO_2); 1086; 1045; 1021. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.03–1.12 (m, 1H, 4a-chex-H), 1.16–1.33 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.58 (m, 1H, 4e-chex-H), 1.72-1.81 (m, 4H, 3e, 5e-chex-H, $CONHCH_2CH_2CH_2$), 1.99 (m, 2H, 2e, 6e-chex-H), 2.88 (brs, 3H, 1chex-H, $CONHCH_2CH_2CH_2$), 3.13 (dt, 2H, J = 6.2/6.2 Hz, $CONHCH_2$), 3.40 (s, 2H, thiaCH_2), 6.58 (s, 1H, thia-H), 7.56 ("d", J = 8.4 Hz, 2H, 3,5 ph-H), 7.92 ("d", J = 8.4 Hz, 2H, 2,6 ph-H), 8.34 (t, J = 5.6 Hz, 1H, D_2O exchange, CONH), 8.77 (brs, D_2O exchange, NH-chex), 12.84 (brs, 1H, D_2O exchange, thia-$NHSO_2$). – MS (70 eV, 220°C): m/z (%) = 454 (23) [$M^{+\bullet}$], 411 (36), 316 (19), 295 (21), 198 (15), 175 (47), 159 (61), 112 (72), 95 (100), 56 (41).

*N-[5-(Cyclohexylamino)pentyl]-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide hydrochloride hydrate **3b***

From **2b** and 1,5-pentanediamine (first step) and cyclohexanone (second step) by procedure B. Crystals, m.p. 196°C, yield 15% (both steps). – Anal. $C_{22}H_{32}Cl_2N_4O_3S_2$ (535.55). – IR (KBr): ν = 3434 cm^{-1}; 3300; 3086; 2939; 2860; 2820; 1654; (CO); 1611; 1582; 1533; 1476; 1454; 1429; 1393; 1376; 1351; 1310 (SO_2); 1273; 1174; 1146 (SO_2); 1089; 1012. – ^{1}HNMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.07–1.13 (m, 1H, 4a-chex-H), 1.17–1.32 (m, 6H, 2a, 3a, 5a, 6a-chex-H, $CONHCH_2CH_2CH_2$), 1.38-1.48 (m, 2H, $CONH(CH_2)_3CH_2$), 1.50–1.67 (m, 3H, $CONHCH_2CH_2$, 4e-chex-H), 1.75 (m, 2H, 3e, 5e-chex-H), 2.01 (m, 2H, 2e, 6echexH), 2.84 (brs, 2H, $CH_2CH_2N^+H_2$-chex), 2.93 (brs, 1H, 1-chex-H), 3.04 (dt, J = 6.2/6.2 Hz, 2H, $CONHCH_2CH_2$), 3.39 (s, 2H, thia-CH_2, visible after CF_3COOD exchange), 6.55 (s, 1H, thiaH), 7.61 ("d", J = 8.5 Hz, 2H, 3,5-ph-H), 7.80 ("d", J = 8.4 Hz, 2H, 2,6-ph-H), 8.10 (t, J = 5.0 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.57 (brs, 2H, D_2O exchange, -N^+H_2-chex), 12.78 (brs, 1H, D_2O exchange, thia-$NHSO_2$). – MS (70 eV, 210°C): M/z (%) = 498 (27) [$M^{+\bullet}$], 455 (49), 413 (12), 398 (24), 287 (13), 314 (28), 323 (57), 288 (28), 224 (19), 191 (16), 175 (27), 124 (57), 112 (100), 98 (50), 84 (58), 56 (49), 30 (42).

*N-[3-(Cyclohexylamino)propyl]-2-[[(4-fluorophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetamide dihydrochloride **3c***

From 2.5 g (8.1 mmol) **2c** and 4.0 g *N*-cyclohexylpropane-1,3-diamine, procedure A2. Crystals, m.p. 200–205°C, yield 0.95 g (24%). – Anal. $C_{21}H_{29}Cl_2FN_4O_2S$ (491.45). – IR (KBr): ν = 3411 cm^{-1}; 3326; 3247; 3058; 2939; 2859; 2818; 2787; 2739; 2546; 2429; 1681 (CO); 1661 (CO); 1598; 1556; 1528; 1456; 1414; 1369; 1316; 1300; 1274; 1236; 1190; 1163; 1132; 1089; 1046; 1033; 1013. – ^{1}H–NMR / 400 MHz ([d_6]DMSO): (ppm) = 1.00–1.09 (m, 1H, 4a-chex-H), 1.13–1.41 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.55 (m, 1H, 4e-chex-H, 1.71 (m, 2H, 3e, 5e-chex-H), 1.83 (tt, J = 7.0/7.0 Hz, 2H, $CONHCH_2CH_2$), 2.0 (m, 2H, 2e, 6e-chex-H), 2.87 (brs, 3H, 1-chex-H, $CONHCH_2CH_2CH_2$), 3.17 (dt, J = 6.2/6.2 Hz, 2H, $CONHCH_2CH_2$), 3.56 (s, 2H, thia-CH_2), 7.02 (s, 1H, thia-H), 7.39 (dd, J = 8.8/8.8 Hz, 2H, 3,5-ph-H), 8.18–8.21 (m, 2H, 2,6-ph-H), 8.37 (t, J = 5.7 Hz, 1H, D_2O exchange, $CONHCH_2$), 9.02 (brs, 2H, D_2O exchange, -N^+H_2-chex), 12.73 (brs, 1H, D_2O exchange, thia-NHCO). – MS (70 eV, 220°C): m/z (%) = 418 (23) [$M^{+\bullet}$], 376 (810), 375 (45), 321 (32), 320 (18), 307 (14), 280 (49), 262 (41), 236 (13), 139 (10), 123 (100), 112 (24), 98 (41), 95 (24), 56 (17), 30 (20).

*2-[-(1,1′-Biphenyl-4-yl)sulfonyl]amino-1,3-thiazol-4-yl-N-[3-(cyclohexylamino)propyl]-acetamide **3d***

From 2.5 g **2d** and 4.0 g *N*-cyclohexylpropane-1,3-diamine, procedure A1. Light yellow powder, m.p. 162°C, yield 0.22 g (7%). – Anal. $C_{26}H_{32}N_4O_3S_2$ (512.69). – IR (KBr): ν = 3392 cm^{-1}; 3060; 3029; 2933; 2857; 1650 (CO); 1595; 1450; 1348; 1271 (SO_2); 1256; 1133 (SO_2); 1089; 1024; 1006. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.03–1.11 (m, 1H, 4a-chex-H), 1.14–1.33 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.56 (m, 1H, 4e-chex-H), 1.60–1.77 (m, 4H, 3e, 5e-chex-H, $CONHCH_2$-CH_2), 1.92 (m, 2H, 2e, 6e-chex-H), 2.90 (t, J = 7.4 Hz, 2H, $CONHCH_2CH_2CH_2$), 2.97–3.05 (m, 1H, 1-chex-H), 3.14 (dt, J = 6.1/6.1 Hz, 1H, $CONHCH_2CH_2$), 3.21 (s, 2H, thia-CH_2), 6.19 (s, 1H, thia-H), 7.38 (t, J = 7.6 Hz, 1H, 4′biph-H), 7.47 (t, J = 7.6 Hz, 2H, 3′,5′-biph-H), 7.62-7.71 (m, 4H, 3, 5, 2′, 6′-biph.–H), 7.81 (d, J = 8.2 Hz, 2H, 2,6-biph-H), 8.17 (t, J = 5.8 Hz, 1H, D_2O exchange, $CONHCH_2$),

12.9 (brs, 1H, D_2O exchange, thia-$NHSO_2$). – MS (70 eV, 220°C): m/z (%) = 512 (2) [$M^{+\bullet}$], 330 (23), 266 (51), 233 (32), 217 (19), 153 (100), 112 (19), 56 (52).

*N-[2-(Cyclohexylamino)ethyl]-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide hydrochloride **3e***

From **2b** and 1,2-ethanediamine (1st step) and cyclohexanone (2nd step) by procedure B. Crystals, m.p. 172 – 175°C, yield 35% (both steps). – Anal. $C_{19}H_{26}Cl_2N_4O_3S_2$ (493.47). – IR(KBr): ν = 3413 cm^{-1}; 3248; 3216; 3071; 2939; 2859; 2816; 2654; 2432; 1663 (CO); 1609; 1581; 1533; 1476; 1453; 1424; 1393; 1351; 1310 (SO_2); 1174; 1146 (SO_2); 1088; 1025; 1012. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.07 – 1.13 (m, 1H, 4a-chex-H), 1.11.35 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.59 (m, 1H, 4e-chex-H), 1.74 (m, 2H, 3e, 5e-chex-H), 2.00 (m, 2H, 2e, 6e-chex-H), 2.97 (brs, 3H, 1-chex-H, $CONHCH_2CH_2$), 3.39 (t, J = 5.9 Hz, 2H, $CONHCH_2$-CH_2, visible after D_2O exchange), 3.43 (s, 2H, thia-CH_2), 6.59 (s, 1H, thia-H), 7.61 ("d", J = 8.1 Hz, 2H, 3,5-ph-H), 7.79 ("d", J = 8.1 Hz, 2H, 2,6-ph-H), 8.40 (t, J = 5,4 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.75 (brs, 2H, D_2O exchange, $CON^+H_2CH_2$), 12.80 (brs, 1H, D_2O exchange, thia-$NHSO_2$). – MS (70 eV, 210°C): m/z (%) = 456 (3) [$M^{+\bullet}$], 438 (39), 263 (44), 231 (14), 223 (15), 191 (21), 175 (23), 166 (58), 123 (100), 112 (53), 55 (19), 36 (64).

*N-[3-(Cyclohexylamino)propyl]-2-[[(2-chlorophenyl)sulfonyl]amino]-1,3-thiazolyl-4-yl-acetamide hydrochloride **3f***

From 2.5 g (7 mmol) **2f** and 4.0 g *N*-cyclohexylpropane-1,3-diamine by procedure A2. Crystals, m.p. 172 – 176°C, yield 0.4 g (11%). – Anal. $C_{20}H_{29}Cl_2N_4O_3S_2$ (507.50). – IR (KBr): ν = 3370 cm^{-1}; 3274; 3066; 2939; 2859; 2818; 2791; 2564; 2505; 2453; 1650 (CO); 1607; 1527; 1453; 1434; 1375; 1354; 1312 (SO_2); 1297; 1252; 1193; 1148 (SO_2); 1129; 1108; 1046; 1018. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.05 – 1.13 (m, 1H, 4a-chex-H), 1.17 – 1.32 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.59 (m, 1H, 4e-chex-H), 1.73 – 1.80 (m, 4H, 3e, 5echex-H, $CONHCH_2CH_2CH_2$), 1.99 (m, 2H, 2e, 6e-chex-H), 2.89 (brs, 3H, 1-chex-H, $CONHCH_2CH_2CH_2$), 3.41 (s, 2H, thia-CH_2), 6.57 (s, 1H, thia-H), 7.49 – 7.55 (m, 1H, 5phH), 7.57 – 7.62 (m, 2H, 3, 4-ph-H), 8.05 ("d", J = 7.1 Hz, 6-ph-H), 8.28 (t, J = 5,6 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.62 (brs, 2H, D_2O exchange $-N^+H_2$-chex), 12.84 (brs, 1H, D_2O exchange, thia-$NHSO_2$). – MS (70 eV, 220°C): m/z (%) = 470 (23) [$M^{+\bullet}$], 427 (43), 295 (46), 253 (12), 190 (18), 175 (13), 155 (44), 112 (100), 138 (29), 98 (49), 56 (95).

*N-[(3-Cyclohexylamino)propyl]-2-[(cyclohexylcarbonyl)amino]-1,3-thiazol-4-yl-acetamide dihydrochloride **3g***

From 2.5 g (7.5 mmol) **2g** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 197 205°C, yield 1.5 g (49%). – Anal. $C_{21}H_{36}Cl_2N_4O_2S$ (479.51). – IR (KBr): ν = 3405 cm^{-1}; 3253; 3058; 2935; 2856; 2810; 2431; 2364; 1708 (CO); 1657 (CO); 1601; 1551; 1451; 1386; 1348; 1334; 1302; 1302; 1258; 1212; 1189; 1162; 1123; 1077; 1046; 1032. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.05 – 1.11 (m, 1H, 4a-chex-H-amino), 1.15-1.32 (m, 7H, 2a, 3a, 5a, 6a, chex-H-amino, 4a-chex-H-CO, 3a, 5a-chex-H-CO), 1.351.43 (m, 2H, 2a, 6a-chex-H-CO), 1.56 – 1.65 (m, 2H, 4e-chex-H-amino, 4echexHCO), 1.72 – 1.83 (m, 8H, 2e, 3e, 5e, 6e-chex-H-amino, 3e, 5e-chex-H-CO, $CONHCH_2CH_2$), 1.98 (m, 2H, 2e, 6e-chex-H-CO), 2.86 (brs, 3H, 1-chex-H-amino, $CONHCH_2CH_2CH_2$), 3.15 (dt, J = 6.2/6.2 Hz, $CONHCH_2CH_3$), 3.47 (s, 2H, thia-CH_2), 6.88 (s, 1H, thia-H), 8.26 (t, J = 5.6 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.85 (brs, 2H, D_2O exchange, -N^+H_2-chex), 12.06 (brs, 1H, D_2O exchange, thia-NHCO). – MS (70 eV, 210°C): m/z (%) = 406 (46) [$M^{+\bullet}$], 363 (100), 323 (30), 309 (73), 295 (14), 268 (81), 250 (40), 224 (11), 140 (16), 98 (11).

*N-[3-(Cyclohexylamino)propyl]-2-[(4-iodophenylcarbonyl)amino]-1,3-thiazol-4-yl-acetamide dihydrochloride **3h***

From 2.5 g (6 mmol) **2h** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 198 – 201°C, yield 1.1 g (30%). – Anal. $C_{21}H_{29}Cl_2IN_4O_2S$. – IR (KBr): ν = 3411 cm^{-1}; 3248; 3123; 3057; 2938; 2857; 2793; 2371; 1679 (CO); 1587; 1556; 1482; 1453; 1397; 1368; 1353; 1316; 1302; 1264; 1189; 1095; 1058; 1033; 1007. – ^{1}H-NMR /400 MHz ([d_6]DMSO): δ (ppm) = 1.00 – 1.07 (m, 1H, 4a-chex-H), 1.13 – 1.33 (m, 4H, 2a, 3a, 5a, 6achexH), 1.56 (m, 1H, 4e-chex-H), 1.71 (m, 2H, 3e, 5e-chex-H), 1.81 (tt, J = 7.0/7.0 Hz, 2H, $CONHCH_2$-CH_2-CH_2), 1.99 (m, 2H, 2e, 6e-chex-H), 2.86 (brs, 3H, 1-chex-H, $CONHCH_2CH_2CH_2$), 3.16 (dt, J = 6.2/6.2 Hz, 2H, $CONHCH_2CH_2$), 3.55 (s, 2H, thia-CH_2), 7.02 (s, 1H, thia-H), 7.76 ("d", J = 8.5 Hz, 2H, 3,5-ph-H), 8.04 ("d", J = 8.5 Hz, 2H, 2,6phH), 8.33 (t, J = 5.7 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.95 (brs, 2H, D_2O exchange, N^+H_2chex), 12.76 (brs, 1H, D_2O exchange, thia-NHCO). – MS (70 eV, 220°C): m/z (%) = 526 (23) [$M^{+\bullet}$], 483 (54), 443 (11), 429 (41), 415 (17), 388 (59), 369 (42), 344 (12), 231 (100), 203 (25), 112 (38), 98 (66), 76 (34), 56 (29), 30 (25).

*N-[3-(Cyclohexylamino)propyl]-2-[(phenylacetyl)amino]-1,3-thiazol-4-yl-acetamide hydrochloride hydrate **3i***

From 2.5 g (8 mmol) **2i** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 130 – 137°C, yield 0.6 g (15%). – Anal. $C_{23}H_{33}ClN_4O_3S$ (469.04). – IR (KBr): ν = 3381 cm^{-1}; 3247; 3030; 2940; 2858; 2544; 2433; 1651 (CO); 1543; 1453; 1312; 1274; 1190; 1143; 1087; 1031. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.05 – 1.10 (m, 1H, 4achex-H), 1.14 – 1.28 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.57 (m, 1H, 4e-chex-H), 1.70 – 1.77 (m, 4H, 3e, 5e-chex-H, $CONHCH_2CH_2CH_2$), 1.95 (m, 2H, 2e, 6e-chex-H), 2.77 (brs, 3H, 1chexH, $CONHCH_2CH_2CH_2$), 3.15 (dt, J = 6.4/6.4 Hz, 2H, $CONHCH_2$-CH_2), 3.47 (s, 2H, thiaCH_2), 3.75 (s, 2H, $COCH_2$-ph), 6.89 (s, 1H, thia-H), 7.23 – 7.33 (m, 5H, ph-H), 8.19 (t, J = 5.7 Hz, 1H, D_2O exchange, $CONHCH_2$), 8.54 (brs, 2H, D_2O exchange, -N^+H_2-chex), 12.35 (brs, 1H D_2O exchange, thia-NHCO). – MS (70 eV, 200°C): m/z (%) = 414 (52) [$M^{+\bullet}$], 371 (86), 32 (26), 317 (100), 303 (32), 289 (14), 276 (95), 259 (34), 258 (73), 231 (17), 158 (13), 140 (52), 112 (54), 98 (89), 91 (88), 56 (48), 55 (41), 30 (91).

*N-[3-(Cyclohexylamino)propyl]-2-[[(2-phenylethyl)carbonyl]amino]-1,3-thiazol-4-yl-acetamide dihydrochloride **3j***

From 2.5 g (8 mmol) **2f** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 197 – 205°C, yield 0.6 g (15%). – Anal. $C_{23}H_{34}Cl_2N_4O_2S$ (501.51). – IR (KBr): ν = 3408 cm^{-1}; 3282; 3059; 3024; 2938; 2858; 2814; 2436; 2370; 1713; 1713 (CO); 1644 (CO); 1592; 1547; 1497; 1453; 1420; 1380; 1353; 1301; 1263; 1206; 1187; 1142; 1077; 1044; 1030; 1004. – ^{1}H-NMR / 400 MHz ([d_6]DMSO); δ (ppm) = 1.12 – 1.17 (m, 1H, 4a-chex-H), 1.21 – 1.38 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.64 (m, 1H, 4e-chex-H), 1.77 – 1.84 (m, 4H, 3e, 5e-chex-H, CONH-$CH_2CH_2CH_2$), 2.02 (m, 2H, 2e, 6e-chex-H), 2.79 (t, J = 7.7 Hz, 2H, $COCH_2CH_2$-ph), 2.93 – 3.09 (m, 5H,

COC*H*$_2$-CH$_2$-ph, 1-chex-H, CONHCH$_2$CH$_2$C*H*$_2$), 3.19 (dt, J = 6.3/6.3 Hz, 2H, CONHC*H*$_2$CH$_2$CH$_2$), 3.52 (s, 2H, thia-CH$_2$), 6.94 (s, 1H, thia-H), 7.237.36 (m, 5H, ph-H), 8.26 (t, J = 5.7 Hz, 1H, D$_2$O exchange, CON*H*CH$_2$), 8.68 (brs, D$_2$O exchange, 2H, N$^+$H$_2$-chex), 12.10 (brs, D$_2$O exchange, 1H, thia-NHCO). – MS (70 eV, 220°C): m/z (%) = 484 (22) [M$^{+\bullet}$], 428 (45), 385 (88), 345 (20), 331 (89), 317 (27), 290 (92), 272 (60), 246 (21), 198 (17), 158 (22), 139 (62), 112 (51), 105 (58), 98 (67), 91 (100), 80 (26), 56 (65), 41 (44), 30 (68).

*N-[3-(Cyclohexylamino)propyl]-2-[(2-naphthylsulfonyl)amino]-1,3-thiazol-4-yl-acetamide hydrochloride **3l***

From 2.5 g (6 mmol) **2l** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 212 – 213°C, yield 2.9 g (80%). – Anal. $C_{24}H_{31}ClN_4O_3S_2$ (523.11). – IR (KBr): ν = 3401 cm^{-1}; 2163; 3056; 2938; 2858; 2448; 1648 (CO); 1608; 1593; 1524; 1454; 1424; 1346; 1309; 1264 (SO$_2$); 1146 (SO$_2$); 1073; 1022. – ^{1}H-NMR / 400 MHz ([d$_6$]DMSO): δ (ppm) = 1.07 – 1.16 (m, 1H, 4a-chex-H), 1.20-1.36 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.62 (m, 1H, 4e-chex-H), 1.77 – 1.84 (m, 4H, 3e, 5e-chex-H, CONHCH$_2$-C*H*$_2$), 2.03 (m, 2H, 2e, 6echex-H), 2.93 (brs, 3H, 1-chex-H, CONHCH$_2$CH$_2$C*H*$_2$), 3.18 (dt, J = 6.2/6.2 Hz, 2H, CONHC*H*$_2$), 3.44 (s, 2H, thia-CH$_2$), 6.61 (s, 1H, thia-H), 7.69 – 7.76 (m, 2H, 6,7-naph-H), 7.86 ("d", J = 8.6 Hz, 1H, 5-naph-H), 8.07 ("d", J = 7.9 Hz, 1H, 8-naph-H), 8.13 ("d", J = 8.7 Hz, 1H, 4-naph-H), 8.22 ("d", J = 7.6 Hz, 1H, 3-naph-H), 8.34 (t, J = 5.4 Hz, 1H, D$_2$O exchange, CON*H*CH$_2$), 8.52 (s, 1H, 1-naph-H), 8.69 (brs, 2H, D$_2$O exchange, N$^+$H$_2$-chex), 12.82 (brs, 1H, D$_2$O exchange, thia-NH-SO$_2$). – MS (70 eV, 240°C): m/z (%) = 486 (6) [M$^{+\bullet}$], 443 (10), 348 (10), 295 (11), 261 (10), 207 (59), 191 (10), 160 (28), 127 (100), 98 (26), 56 (54), 41 (14).

*N-[3-(Cyclohexylamino)propyl]-2-[[(4-chlorophenyl)carbonyl]amino]-1,3-thiazol-4-yl-acetamide dihydrochloride **3m***

From 2.5 g **2m** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. – Crystals, m.p. 227°C, yield 1.3 g (36%). – Anal. $C_{21}H_{29}Cl_3N_4O_2S$ (507.90). – IR (KBr): ν = 3428 cm^1; 3256; 3058; 3025; 2938; 2818; 2550; 2435; 1685 (CO); 1648 (CO); 1594; 1556; 1490; 1455; 1404; 1367; 1316; 1301; 1291; 1270; 1243; 1187; 1162; 1098; 1045; 1033; 1013. – ^{1}HNMR / 400 MHz ([d$_6$]DMSO): δ (ppm) = 1.03 – 1.09 (m, 1H, 4a-chex-H), 1.13 – 1.32 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.56 (m, 1H, 4e-chex-H), 1.71 (m, 2H, 3e, 5e-chexH), 1.81 (tt, J = 7.1/7.1 Hz, 2H, CONHCH$_2$C*H*$_2$CH$_2$), 1.98 (m, 2H, 2e, 6e-chex-H), 2.86 (brs, 3H, 1chexH, CONHCH$_2$CH$_2$C*H*$_2$), 3.16 (dt, J = 6.1/6.1 Hz, 2H, CONHC*H*$_2$CH$_2$CH$_2$), 3.54 (s, 2H, thia-CH$_2$), 7.01 (s, 1H, thia-H), 7.62 ("d", J = 8.5 Hz, 2H, 3,5-ph-H), 8.12 ("d", J = 8.5 Hz, 2H, 2,6-ph-H), 8.31 (t, J = 5.1 Hz, D$_2$O exchange, 1H, CON*H*CH$_2$CH$_2$CH$_2$), 8.88 (brs, D$_2$O exchange, 2H, -N$^+$H$_2$-chex), 12.58 (brs, D$_2$O exchange, 1H, thia-NHCO). – MS (70 eV, 200°C): m/z (%) = 434 (20) [M$^{+\bullet}$], 391 (40), 337 (27), 336 (15), 323 (11), 296 (42), 280 (17), 252 (11), 139 (100), 112 (33), 98 (64), 56 (31), 30 (39).

*N-[[(3-Cyclohexylmethyl)amino]propyl]-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide hydrochloride **3n***

From **2b** and 1,3-propanediamine (1st step) and cyclohexane aldehyde (2nd step) by procedure B. Crystals, m.p. 179 – 181°C, yield 15% (both steps). – Anal. $C_{21}H_{29}Cl_2N_4O_3S_2$ (521.52). – IR (KBr): ν = 3306 cm^{-1}; 3087; 2958; 2087; 1919; 1638 (CO); 1581; 1536; 1454; 1392; 1324; 1281 (SO$_2$); 1261; 1174; 1131 (SO$_2$); 1087; 1023; 1010. – ^{1}H-NMR / 400 MHz ([d$_6$]DMSO): δ (ppm) = 0.89 – 0.97 (m, 2H, 2a, 6a-chex-H), 1.11 – 1.24 (m, 3H, 3a, 4a, 5a-chex-H), 1.53 – 1.85 (m, 8H, 1e, 2e, 3e, 4e, 5e, 6e-chex-H, CONHCH$_2$C*H*$_2$CH$_2$), 2.70 (brs, 2H, NH$_2$C*H*$_2$-chex), 2.86 (brs, 2H, CONHCH$_2$CH$_2$C*H*$_2$), 3.12 (dt, J = 6.2/6.2 Hz, 2H, CONHC*H*$_2$CH$_2$), 3.40 (s, 2H, thia-CH$_2$), 6.57 (s, 1H, thia-H), 7.61 ("d", J = 8.5 Hz, 2H, 3,5ph-H), 7.80 ("d", J = 8.4 Hz, 2H, 2,6-ph-H), 8.26 (t, J = 5.5 Hz, D$_2$O exchange, 1H, CON*H*CH$_2$CH$_2$CH$_2$), 8.46 (brs, 2H, D$_2$O exchange, -N$^+$H$_2$-chex), 12.80 (brs, 1H, D$_2$O exchange, thia-NHSO$_2$). – MS (70 eV, 220°C): m/z (%) = 484 (34) [M$^{+\bullet}$], 468 (74), 401 (55), 358 (10), 227 (23), 191 (13), 175 (17), 113 (29), 111 (27), 36 (100), 28 (52).

*N-[3-(Cyclohexylamino)propyl]-2-[[(4-bromophenyl)carbonyl]amino]-1,3-thiazol-4-yl- acetamide dihydrochloride **3o***

From 2.5 g **2o** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 203 – 204°C, yield 0.95 g (25%). – Anal. $C_{21}H_{29}BrCl_2N_4O_2S$ (552.36). – IR (KBr): ν = 3347 cm^{-1}; 3247; 3053; 3023; 2937; 2858; 2819; 2792; 2546; 2434; 1686 (CO); 1648 (CO); 1590; 1556; 1486; 1456; 1400; 1366; 1317; 1303; 1269; 1243; 1187; 1160; 1160; 1098; 1071; 1046; 1033; 1010. – ^{1}H-NMR / 400 MHz ([d$_6$]DMSO): δ (ppm) = 1.00 – 1.09 (m, 1H, 4achex-H), 1.13 – 1.33 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.55 (m, 1H, 4e-chex-H), 1.71 (m, 2H, 3e, 5e-chex-H), 1.81 (tt, J = 7.0/7.0 Hz, 2H, CONHCH$_2$C*H*$_2$CH$_2$), 1.99 (m, 2H, 2e, 6echex-H), 2.86 (m, 2H, 1-chex-H, CONHCH$_2$-CH$_2$-C*H*$_2$), 3.16 (dt, J = 6.2/6.2 Hz, 2H, CONHC*H*$_2$CH$_2$), 3.54 (s, 2H, thia-CH$_2$), 7.01 (s, 1H, thia-H), 7.86 ("d", J = 8.4 Hz, 2H, 3,5ph-H), 7.93 ("d", J = 8.3 Hz, 2H, 2,6-ph-H), 8.33 (t, J = 5.6 Hz, D$_2$O exchange, 1H, CON*H*CH$_2$CH$_2$CH$_2$), 8.95 (brs, D$_2$O exchange, 2H, -N$^+$H$_2$-chex), 12.75 (brs, D$_2$O exchange, 1H, thia-NHCO). – MS (70 eV, 100°C): m/z (%) = 480/478 (23) [M$^{+\bullet}$], 437/435 (50), 383/381 (31), 380 (17), 367 (14), 342/340 (50), 325/323 (20), 322 (38), 295 (19), 261 (34), 185/183 (100), 179 (14), 155 (24), 139 (19), 112 (46), 98 (86), 56 (33), 30 (29).

*N-[3-(Cyclohexylamino)propyl]-2-[[(3-chlorophenylsulfonyl)]amino]-1,3-thiazol-4-yl- acetamide monohydrate **3p***

From 2.5 g (6.9 mmol) **2p** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2, column chromatography (chloroform / methanol saturated with NH$_3$ = 4 : 1). Crystals, m.p. 132 – 137°C, yield 0.1 g (3%). – Anal. $C_{20}H_{29}ClN_4O_4S_2$ (489.05). – IR (KBr): ν = 3420 cm^{-1}; 3064; 2938; 2859; 1648 (CO); 1540; 1456; 1408; 1354; 1326; 1259 (SO$_2$); 1140 (SO$_2$); 1106; 1079; 1021. – ^{1}HNMR / 400 MHz ([d$_6$]DMSO): δ (ppm) = 1.04 – 1.12 (m, 1H, 4a-chex-H), 1.16 – 1.32 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1,57 (m, 1H, 4e-chex-H), 1.72 – 1.80 (m, 4H, 3e, 5echex-H, CONH-CH$_2$-C*H*$_2$-CH$_2$), 1.99 (m, 2H, 2e, 6e-chex-H), 2.89 (brs, 3H, 1-chex-H, CONHCH$_2$CH$_2$-C*H*$_2$), 3,13 (dt, J = 6.3/6.3 Hz, 2H, CONH-C*H*$_2$-CH$_2$), 3.41 (s, 2H, thiaCH$_2$), 6.59 (s, 1H, thia-H), 7.59 (dd, J = 8.2 Hz, 1H, 5-ph-H), 7.67-7.90 (m, 1H, 4ph-H), 7.75 – 7.77 (m, 2H, 2,6-ph-H), 8.31 (t, J = 5.4 Hz, D$_2$O exchange, 1H, CON*H*-CH$_2$), 8.67 (brs, 2H, D$_2$O exchange, -N$^+$H$_2$-chex), 12.87 (brs, D$_2$O exchange, 1H, thia-NH-SO$_2$). – MS (70 eV, 200°C): m/z (%) = 470 (61) [M$^{+\bullet}$], 427 (94), 372 (19), 332 (40), 295 (59), 253 (11), 191 (52), 190 (35), 175 (31), 139 (19), 127 (47), 111 (100), 98 (42), 74 (28), 56 (44).

*N-[(3-Cyclohexylamino)propyl]-2-[[(1,1′-biphenyl-4-yl)carbonyl]amino]-1,3-thiazol-4-yl- acetamide **3q***

From 2.5 g (7 mmol) **2k** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A1. Light yellow powder, m.p. 156 – 157°C, yield 0.2 g (7%). – Anal. $C_{27}H_{32}N_4O_2S$ (476.63). – IR (KBr): ν = 3419 cm^{-1}; 3251; 3059; 2939; 2859; 2818; 1680 (CO); 1606; 1554; 1512; 1489; 1450; 1408; 1371; 1324; 1302; 1277; 1240; 1203; 1163; 1127; 1092; 1050; 1007. – ^{1}HNMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.03 – 1.12 (m, 1H, 4a-chex-H), 1.12 – 1.36 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.56 (m, 1H, 4e-chex-H), 1,71 (m, 2H, 3e, 5e-chex-H), 1.77 (tt, J = 6.9/6.9 Hz, 2H, CONHCH$_2$C*H*$_2$-CH$_2$), 1.96 (m, 2H, 2e, 6e-chex-H), 2.88 (brs, 3H, 1chexH, CONHCH$_2$CH$_2$C*H*$_2$), 3.18 (dt, J = 6.3/6.3 Hz, 2H, CONHC*H*$_2$CH$_2$CH$_2$), 3.55 (s, 2H, thia-CH$_2$), 7.00 (s, 1H, thia-H), 7.44 (t, J = 7.6 Hz, 1H, 4′-biph-H), 7.52 (dd, J = 7.6/7.6 Hz, 2H, 3′,5′biphH), 7.77 (d, J = 7.4 Hz, 2H, 2′,6′-biph-H), 7.85 (d, J = 8.4 Hz, 2H, 3,5-biph-H), 8.20 (d, J = 8.3 Hz, 2H, 2,6-biph-H), 8.24 (t, J = 5.5 Hz, D_2O exchange, 1H, CON*H*-CH$_2$), 8.57 (brs, D_2O exchange, 1H, NH-chex-H), 12.69 (brs, D_2O exchange, 1H, thiaNHCO). – MS (70 eV, 220°C): m/z (%) = 476 (10) [$M^{+\bullet}$], 433 (15), 379 (18), 338 (21), 320 (17), 294 (10), 181 (100), 152 (40), 98 (12), 36 (27).

*N-[3-(Cyclohexylamino)-propyl-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl- acetamide hydrochloride **3r***

From 2.5 g (7 mmol) **2b** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A1. Crystals, m.p. 191°C, yield 0.4 g (12%). – Anal. $C_{20}H_{28}Cl_2N_4O_3S_2$ (507.50). – IR (KBr): ν = 3363 cm^{-1}; 3267; 3084; 2939; 2859; 2818; 1649 (CO); 1607; 1529; 1475; 1455; 1424; 1393; 1352; 1316 (SO_2); 1174; 1146 (SO_2); 1088; 1025; 1011. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.06 – 1.12 (m, 1H, 4a-chex-H), 1.16 – 1.31 (m, 4H, 2a, 3a, 5a, 6achexH), 1.59 (m, 1H, 4e-chex-H), 1.73 – 1.81 (m, 4H, 3e, 5e-chex-H, CONHCH$_2$C*H*$_2$CH$_2$), 1.98 (m, 2H, 2e, 6e-chex-H), 2.88 (brs, 3H, 1-chex-H, CONHCH$_2$CH$_2$-C*H*$_2$), 3.13 (dt, J = 6.3/6.3 Hz, 2H, CONH-C*H*$_2$-CH$_2$), 3.39 (s, 2H, thia-CH$_2$), 6.57 (s, 1H, thia-H), 7.61 ("d", J = 8.6 Hz, 3,5-ph-H), 7.80 ("d", J = 8.6 Hz, 2H, 2,6-ph-H), 8.28 (t, J = 5.6 Hz, D_2O exchange, 1H, CON*H*-CH$_2$), 8.60 (brs, 2H, D_2O exchange, N^+H_2chex-H), 12.49 (brs, 1H, D_2O exchange, thia-NHSO$_2$). – MS (70 eV, 220°C): m/z (%) = 470 (14) [$M^{+\bullet}$], 427 (26), 332 (17), 295 (26), 188 (10), 277 (11), 261 (17), 219 (12), 191 (36), 175 (47), 113 (65), 112 (100), 98 (42), 75 (43), 56 (58).

*N-[3-(Cyclohexylamino)propyl]-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide hydrochloride **3s***

From 2.5 g (5 mmol) **2s** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 210°C, yield 1.2 g (28%). – Anal. $C_{20}H_{28}ClIN_4O_3S_2$ (598.95). – IR (KBr): ν = 3432 cm^{-1}; 3276; 3086; 2938; 2858; 2816; 2454; 1649 (CO); 1607; 1567; 1529; 1454; 1434; 1382; 1352; 1314 (SO_2); 1268; 1181; 1147; (SO_2); 1085; 1054; 1024; 1004. – ^{1}HNMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.03 – 1.12 (m, 1H, 4a-chex-H), 1.16 – 1.33 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.58 (m, 1H, 4e-chex-H), 1.72 – 1.81 (m, 4H, 3e, 5e-chex-H, CONHCH$_2$C*H*$_2$), 1.99 (m, 2H, 2e, 6e-chex-H), 2.88 (brs, 3H, 1-chex-H, CONHCH$_2$CH$_2$C*H*$_2$), 3.13 (dt, J = 6.2/6.2 Hz, 2H, CONHC*H*$_2$CH$_2$), 3.40 (s, 2H, thia-CH$_2$), 6.58 (s, 1H, thia-H), 7.56 ("d", J = 8.4 Hz, 2H, 3,5-ph-H), 7.92 ("d", J = 8.4 Hz, 2H, 2,6-ph-H), 8.34 (t, J = 5.6 Hz, D_2O exchange, 1H, CON*H*CH$_2$), 8.77 (brs, 2H, D_2O exchange, N^+H_2-chex-H), 12.84 (brs, 1H, D_2O exchange, thia-NHSO$_2$). – MS (70 eV, 220°C): m/z (%) = 562 (26) [$M^{+\bullet}$], 519 (38), 424 (26), 407 (14), 380 (11), 295 (36), 283 (100), 267 (37), 203 (15), 139 (25), 112 (38), 98 (52), 56 (54).

*N-(6-Cyclohexylaminohexyl-2-[(4-chlorophenylsulfonyl)amino]-1,3-thiazol-4-yl)-acetamide hydrochloride **3t***

From **2b** and 1,6-hexanediamine (first step) and cyclohexanone (second step) by procedure B. Crystals, m.p. 190 – 191°C, yield 35% (both steps). – Anal. $C_{23}H_{34}Cl_2N_4O_3S_2$ (549.15). – IR (KBr): ν = 3417 cm^{-1}; 3081; 2938; 2859; 2819; 1655 (CO); 1533; 1476; 1455; 1429; 1393; 1376; 1353; 1307 (SO_2); 1274; 1172; 1145 (SO_2); 1088; 1011. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.07 – 1.13 (m, 1H, 4a-chex-H), 1.17 – 1.34 (m, 8H, 2a, 3a, 5a, 6achex-H, CONHCH$_2$CH$_2$C*H*$_2$C*H*$_2$), 1.36-1.43 (m, 2H, C*H*$_2$CH$_2$N$^+$H$_2$-chex), 1.53 – 1.67 (m, 3H, CONHCH$_2$C*H*$_2$CH$_2$, 4e-chex-H), 1.75 (m, 2H, 3e, 5e-chex-H), 2.02 (m, 2H, 2e, 6echexH), 2.84 (brs, 2H, CH$_2$C*H*$_2$N$^+$H$_2$-chex), 2.93 (brs, 1H, 1-chex-H), 3.03 (dt, J = 6.4/6.4 Hz, CONHC*H*$_2$CH$_2$), 3.39 (s, 2H, thia-CH$_2$, visible after addition of CF_3COOD), 6.55 (s, 1H, thia-H), 7.61 ("d", J = 8.6 Hz, 2H, 3,5-ph-H), 7.80 ("d", J = 8.5 Hz, 2H, 2,6-ph-H), 8.11 (t, J = 5.5 Hz, 1H, D_2O exchange, CON*H*CH$_2$), 8.68 (brs, 2H, D_2O exchange, N^+H_2chex), 12.79 (brs, 1H, D_2O exchange, thia-NHSO$_2$). – MS (70 eV, 220°C): m/z (%) = 512 (34) [$M^{+\bullet}$], 469 (71), 412 (12), 401 (12), 337 (84), 314 (12), 226 (16), 175 (12), 168 (21), 156 (29), 138 (18), 112 (100), 98 (56), 56 (25), 28 (18).

*N-(3-Cyclohexylaminopropyl)-2-phenylcarbonylamino-1,3-thiazol-4-yl-acetamide dihydrochloride **3u***

From 2,5 g (8.6 mmol) **2u** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2. Crystals, m.p. 217 – 221°C, yield 0.5 (10%). – Anal. $C_{21}H_{30}Cl_2N_4O_2S$ (472.15). – IR (KBr): ν = 3425 cm^{-1}; 3251; 3060; 2938; 2858; 2795; 2544; 2434; 2362; 2340; 1683 (CO); 1650 (CO); 1597; 1552; 1450; 1370; 1303; 1277; 1243; 1189; 1145; 1089; 1029. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.00 – 1.09 (m, 1H, 4a-chex-H), 1.13 – 1.30 (m, 4H, 2a, 3a, 5a, 6achex-H), 1.55 (m, 1H, 4e-chex-H), 1.71 (m, 2H, 3e, 5e-chex-H), 1.79 (tt, J = 7.1/7.1 Hz, 2H, CONHCH$_2$C*H*$_2$CH$_2$), 1.97 (m, 2H, 2e, 6e-chex-H), 2.87 (brs, 3H, 1-chex-H, CONHCH$_2$CH$_2$C*H*$_2$), 3.17 (dt, J = 6.3 Hz, 2H, CONHC*H*$_2$CH$_2$CH$_2$), 3.54 (s, 2H, thiaCH$_2$), 6.99 (s, 1H, thia-H), 7.54 (dd, J = 7.6 Hz, 2H, 3,5-ph-H), 7.63 (t, J = 7.3 Hz, 1H, 4-ph-H), 8.10 (d, J = 7.8 Hz, 2H, 2,6-ph-H), 8.24 (t, J = 5.7 Hz, 1H, D_2O exchange, CON*H*CH$_2$), 8.73 (brs, 2H, D_2O exchange, N^+H_2-chex), 12.6 (brs, 1H, D_2O exchange, thiaNHCO). – MS (70 eV, 200°C): m/z (%) = 400 (25) [$M^{+\bullet}$], 357 (39), 303 (39), 289 (15), 262 (46), 245 (24), 244 (51), 217 (10), 112 (20), 105 (100), 98 (38), 77 (38), 56 (23), 38 (22), 35 (68), 30 (42).

*N-(4-Cyclohexylamino-butyl)-2-[[(4-chlorophenyl)sulfonyl]amino]-1,3-thiazol-4-yl-acetamide hydrochloride **3v***

From **2b** and 1,4-butanediamine (first step) and cyclohexanone (second step) by procedure B. Crystals, m.p. 186 – 187°C, yield 50% (both steps). – Anal. $C_{21}H_{30}Cl_2N_4O_3S_2$ (521.53). – IR (KBr): ν = 3329 cm^{-1}; 3086; 2939; 2861; 2801; 2556; 2506; 2432; 2046; 1910; 1655 (CO); 1609; 1582; 1533; 1475; 1453; 1453; 1423; 1393; 1377; 1352; 1318 (SO_2); 1174; 1146 (SO_2); 1089; 1055; 1023; 1012. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.07 – 1.13 (m, 1H, 4a-chex-H), 1.17-1.32 (m, 4H, 2a, 3a, 5a, 6a-chex-H), 1.43 – 1.48 (m, 2H, CONHCH$_2$CH$_2$C*H*$_2$CH$_2$), 1.53 – 1.64 (m, 3H, CONHCH$_2$C*H*$_2$CH$_2$,

4e-chex-H), 1.74 (m, 2H, 3e, 5e-chex-H), 2.00 (m, 2H, 2e, 6e-chex-H), 2.87 (brs, 3H, 1-chex-H, CH_2-C*H*$_2$$N^+H_2$-chex), 3.06 (dt, J = 6.3 Hz, 2H, CONHC*H*$_2$$CH_2$), 3.38 (s, 2H, thia-$CH_2$), 6.56 (s, 1H, thia-H), 7.61 ("d", J = 8.6 Hz, 2H, 3,5-ph-H), 7.80 ("d", J = 8.6 Hz, 2H, 2,6-ph-H), 8.16 (brs, 1H, D_2O exchange, CON*H*CH_2), 8.57 (brs, 2H, D_2O exchange, N^+H_2-chex), 1.78 (brs, 1H, D_2O exchange, thia-NHCO). – MS (70 eV, 220°C): m/z (%) = 484 (48) [$M^{+\bullet}$], 441 (100), 384 (45), 373 (25), 314 (28), 309 (76), 210 (26), 175 (16), 123 (100), 112 (67), 110 (47), 98 (46), 70 (61), 56 (56), 36 (39), 28 (64).

N-[(3-Cyclohexylamino)propyl]-2-(phenylsulfonylamino)-1,3-thiazol-4-yl-acetamide hydrate ***3w***

From 2.5 g (6 mmol) **2w** and 4.0 g *N*-cyclohexyl-propane-1,3-diamine by procedure A2, column chromatography (chloroform / methanol saturated with NH_3 = 85 : 15). Crystals, m.p. 147°C, yield 0,3 g (10%). – Anal. $C_{20}H_{30}N_4O_2S_2$. – IR (KBr): ν = 3411 cm^{-1}; 3062; 2938; 2859; 2169; 1648 (CO); 1538; 1456; 1326; 1257 (SO_2); 1131 (SO_2); 1087; 1017. – ^{1}H-NMR / 400 MHz ([d_6]DMSO): δ (ppm) = 1.03 – 1.09 (m, 1H, 4a-chex-H-), 1.13 – 1.30 (m, 4H, 2a, 3a, 5a, 6achex-H), 1.55 (m, 1H, 4e-chex-H), 1.71 (m, 2H, 3e, 5e-chex-H), 1.79 (tt, J = 7.0/7.0 Hz, 2H, $CONHCH_2CH_2CH_2$), 1.97 (m, 2H, 2e, 6e-chex-H), 2.87 (brs, 3H, 1-chex-H, $CONHCH_2CH_2CH_2$), 3.17 (dt, J = 6.4/6.4 Hz, 2H, CONHC*H*$_2$$CH_2$), 3.54 (s, 2H, thia-$CH_2$), 7.00 (s, 2H, thia-H), 7.54 (dd, J = 7.6/7.6 Hz, 2H, 3,5-ph-H), 7.64 (t, J = 7.3 Hz, 1H, 4-ph-H), 8.10 ("d", J = 7.1 Hz, 2H, 2,6-ph-H), 8.25 (t, J = 5.7 Hz, 1H, D_2O exchange, CON*H*$CH_2CH_2CH_2$), 8.71 (brs, 2H, D_2O exchange, N^+H_2-chex), 12.6 (brs, 1H, D_2O exchange, thia-$NHSO_2$. – MS (70 eV, 210°C): m/z (%) = 436 (18) [$M^{+\bullet}$], 393 (39), 295 (25), 280 (13), 198 (13), 141 (35), 112 (44), 77 (100).

Biology

The Born test was carried out as recently reported in detail in this journal [8].

References

[1] K. Märschenz, K. Rehse, *Arch. Pharm. Chem. Life Sci.* **2006**, *339*, 115 – 122.

[2] A. K. Yildiz, K. Rehse, J.-P. Stasch, E. Bischoff, *Arch. Pharm. Pharm. Med. Chem.* **2004**, *337*, 311 – 316.

[3] A. Cwiklicki, K. Rehse, *Arch. Pharm. Pharm. Med. Chem.* **2004**, *337*, 156 – 163.

[4] K. Bethge, H. H. Pertz, K. Rehse, *Arch. Pharm. Chem. Life Sci*. **2005**, *338*, 78 – 86.

[5] K. Rehse, J. Steege, *Arch. Pharm. Chem. Life Sci.* **2005**, *338*, 539 – 547.

[6] K. Rehse, H. Gonska, *Arch. Pharm. Chem. Life Sci*. **2005**, *338,* 590 – 597.

[7] M. Johnsen, K. Rehse, H. Pertz, J.-P. Stasch, E. Bischhoff, *Arch. Pharm. Med. Chem.* **2003**, *336*, 1 – 7.

[8] K. Bethge, H. H. Pertz, K. Rehse, *Arch. Pharm. Chem. Life Sci*. **2005**, *338*, 78 – 86.

[9] T. Baselt, PhD thesis, Freie Universität Berlin **2006**.

[10] C. Nilsson, C. Dreifeldt, PCT WO 2004/112782 A1.

[11] T. Barf, R. Emond, G. Kurz, J. Vallgarda, *et al*., Biovitrum AB, PCT WO 03/043999 A1, **2003**.

