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Antiaggregating and Antithrombotic Activities of new 1,2,3-Triazolecarboxamides

Twenty five new triazolecarboxamides related to YC-1 were prepared and tested for their antiplatelet (*in vitro*) and antithrombotic (*in vivo*) activities. Five of them inhibited the aggregation of blood platelets (Born test, inducer collagen) with IC_{50} values between 90 and 130 μM. Nine compounds exhibited significant antithrombotic properties with an inhibition of thrombus formation between 11 and 7%. Only one compound (**8c**) showed both, *in vitro* and *in vivo* effects. *In vitro,* the most active compounds were **11c** and **12d.** They inhibit platelet aggregation with IC_{50} = 90 and 95 μM. *In vivo*, **10a** showed the strongest inhibition of thrombus formation with 11% in arterioles (5% in venules) after a single oral dose of 60 mg/kg. With serotonin as inducer both, **11c** and **12d,** showed lower IC_{50} values namely 25 or 30 μM, respectively. Additional antiplatelet activities were found for **11c** against adrenaline (IC_{50} = 25 μM) and for **12d** against platelet activating factor (PAF) (IC_{50} = 15 μM) as inducer.

Keywords: YC-1; Triazolecarboxamides; Antiplatelet effects; Antithrombotic properties

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Introduction

The concentration of cyclic GMP in platelets is regulated by soluble guanylate cyclase (sGC), which catalyzes the synthesis of cyclic GMP from GTP, and cyclic GMP phosphodiesterase, which degrades cyclic GMP to 5′-GMP. Agents that elevate the cyclic GMP level either by stimulating sGC or inhibiting cyclic GMP phosphodiesterase are powerful inhibitors of platelet aggregation. YC-1 activates sGC of human platelets by a NO-independent mechanism and exerts its antiplatelet effects through the sGC/cyclic GMP pathway. Surprisingly, YC-1 not only activated sGC, but also affected cyclic GMP metabolism, as it inhibits the activity of phosphodiesterase (PDE) isoforms 1−5 [1].

Therefore, we synthesized new compounds related to YC-1 (see Figure 1) in which the indazole heterocycle was replaced by triazoles, primaryly by 1H-1,2,3-triazoles. The benzyl residue at N-1 of indazole was modified using phenyl-, alkyl- and arylalkyl groups. The hydroxymethylfuryl residue of YC-1 was replaced by various carboxamide functions and the importance of the hydroxy group was investigated. Primarily, compounds with an additional basic centre within the amide function were investigated.

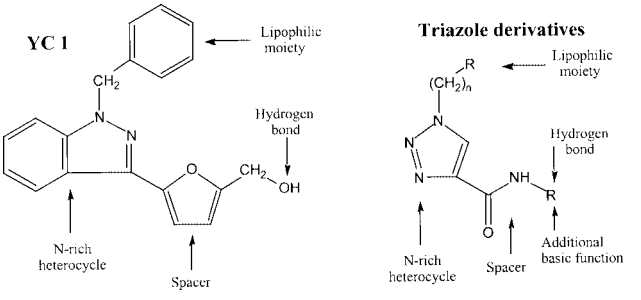

Figure 1. Triazole derivatives related to YC 1.

Chemistry

The most common method for the preparation of 1,2,3-triazoles is the 1,3-dipolar cycloaddition of azides with acetylenes (Scheme 1) [2]. Most of the azides were synthesized according to a procedure reported previously [3]. Alkylazides were prepared from corresponding iodides or bromides and sodium azide with methylcarbitol and water as solvent [4]. Arylalkylazides were prepared from the corresponding chlorides or bromides via the reaction with sodium azide in a mixture of carbitol and water as solvent. Phenyl azide has been prepared following a combination of the methods described by Noelting [5] and Lindsay [6].

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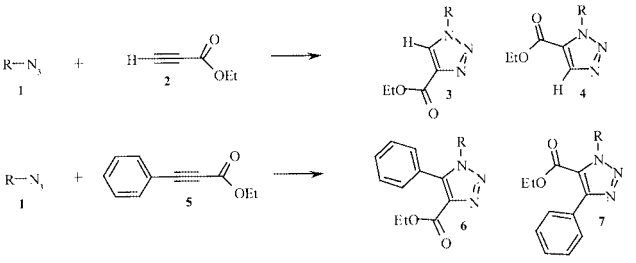
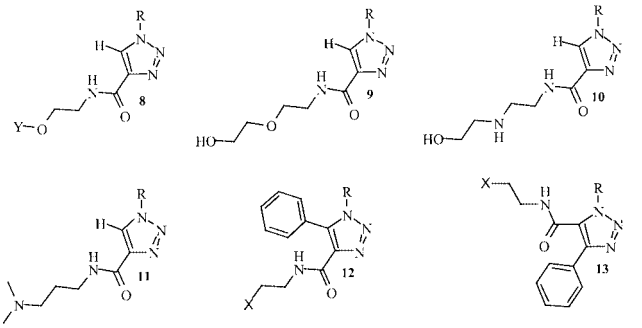


Scheme 1. Reaction between azides and acetylene derivatives. R is alkyl, arylalkyl or phenyl.

Azides **1** were reacted with ethyl propiolate (**2**) or ethyl phenylpropiolate (**5**) in boiling ethanol to give the 1H-1,2,3-triazoles **3/4** or **6/7** (Scheme 1). The products were characterized by ^{1}H-NMR spectroscopy. The reaction of azides with ethyl propiolate or ethyl phenylpropiolate is not regiospecific, i.e. mixtures are obtained. TLC using a mixture of petroleum ether or hexane with ethyl acetate (ratio 3:1) as eluent confirmed the presence of two products. These products are the isomeric triazole-4- and 5-carboxylates. The 1,4-isomer (**3**) is identified by the ^{1}H-NMR signal of the triazole-H (H-5), which appears upfield of the corresponding triazole-H (H-4) for the other isomer (**4**) [7]. For instance, in the 1-phenyl-1H-1,2,3-triazole-4-carboxylic acid ethylester **3d** the proton in 5-position appears at 8.47 ppm. In the corresponding 1-phenyl-1H-1,2,3-triazole 5-carboxylic acid the proton in 4-position resonates at 9.49 ppm. The mixtures were separated by column chromatography using silica gel as sorbent and a petroleum ether/ethyl acetate mixture (3:1) as eluent. First the 5-carboxylate (**4d**, 17%) and then the 4-carboxylate (**3d**, 83%) are obtained.

In general, the reaction of azides with ethyl propiolate (**2**) resulted in the 1,4-isomer (**3**) as the major product (83−100%), whereas the reaction with ethyl phenylpropiolate (**5**) afforded mixtures with the two isomers in approximately equal portions [8] (**6**/**7**). The isomeric products were separated by column chromatography too, using a silica gel and also a petroleum ether/ethyl acetate mixture. The compound appearing first in the eluent was claimed by Buckle et al. [8] to be the 5-carboxylate.

An unambiguous assignment can be made via the ^{1}H-NMR signal of N-CH_2 group in 1-position of the triazole. If the ester function is vicinal, i.e. in 5-position, its anisotropic effect causes a downfield shift to 5.94 ppm (**7c**, $CDCl_3$). A vicinal phenyl group (i.e. ester in 4-position) results in an upfield signal at 5.35 ppm (**6c**, $CDCl_3$). The same is true for **6d** (4.40 ppm, $CDCl_3$) and **7d** (4.96 ppm).



Scheme 2. Triazolecarboxamides from **3** (**8**-**11**) and **6**/**7** (**12**/**13**). R is alkyl, arylalkyl or phenyl, X = O-CH_2-CH_2-OH; NH-CH_2-CH_2-OH or CH_2-N(CH_3)$_2$; Y = H or CH_3.

The triazolecarboxylates where reacted with various amines in ethanol as solvent to give triazolecarboxamides **8**−**13** (Scheme 2).

Biology

Inhibition of platelet aggregation in vitro (Born test)

The platelet aggregation experiments were carried out as already described [9]. The standard drug acetylsalicylic acid (**asa**) showed an IC_{50} = 175 ± 20 μM. This percentage of deviation from the mean is typical for these antiplatelet experiments. The results of the Born test are given in column 4 of all three Tables 1, 2 and 3.

The compounds **10d**, **11c**, **12c,** and **12d** with one voluminous substituent on the N-1 of the triazole or with an alkyl or cycloalkyl substituent at N-1 and a phenylgroup at the triazole C-5 combined with a basic moiety within the amide function showed antiaggregating effects (IC_{50} = 90−125 μM). The lipophilicity of these substituents plays a major role. On the other hand, compound **8c** with 4-methylbenzyl substituent at the N-1 of the triazole without a basic portion in the amide function showed some antiaggregating activity (IC_{50} = 130 μM). The introduction of the basic NH instead of the O-moiety in **9f** lead to an antiaggregating compound **10d** with IC_{50} = 100 μM. Similiarly appears the change from **9f** to **11c** (see Table 1). There are no significant results for the compounds **10d** and **11c** *in vivo*. An additional phenyl-substituent in triazole C-5 of **11a** results in compound **12d** with IC_{50} = 95 μM. The same effect is observed by variation of **10a** to **12c**. The hydroxy group is not essential for the antiplatelet activity. The compounds **11c** and **12d** were tested *in vitro* (Born test) with other inducers (ADP, adrenaline,

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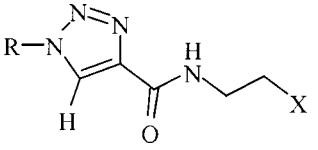
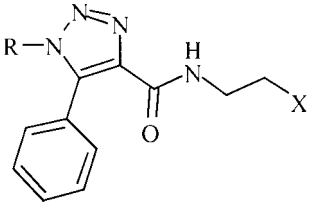
Table 1. *In vitro* (Born test, inducer collagen) antiplatelet and *in vivo* antithrombotic properties of triazolecarboxamides **8**–**11**. Statistics: Wilcoxon Man Whitney U test, n. s. = not significant.



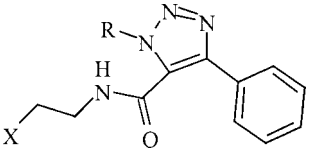
			Inhibition of thrombus formation		
			Born test	venules	arterioles
Cpd.	**R**	**X**	**IC_{50} (μmol/L)**	**% ± s_x (α)**	**% ± s_x (α)**
8a	cyclohexyl	OH	> 300	n.s.	n.s.
8b	benzyl	OH	> 300	n.s.	4 ± 1 (0,05)
8c	4-methylbenzyl	OH	130	n.s.	7 ± 1 (0,05)
8d	benzyl	OCH_3	> 300	n.s.	7 ± 3 (0,01)
9a	heptyl	O-CH_2-CH_2-OH	> 300	not tested	
9b	cyclohexyl	O-CH_2-CH_2-OH	> 300	n.s.	n.s.
9c	benzyl	O-CH_2-CH_2-OH	> 300	n.s.	n.s.
9d	4-methylbenzyl	O-CH_2-CH_2-OH	> 300	n.s.	10 ± 1 (0,002)
9e	4-fluorbenzyl	O-CH_2-CH_2-OH	> 300	n.s.	9 ± 1 (0,02)
9f	biphenylmethyl	O-CH_2-CH_2-OH	> 300	n.s.	n.s.
10a	heptyl	NH-CH_2-CH_2-OH	> 300	5 ± 2 (0,05)	11 ± 2 (0,002)
10b	benzyl	NH-CH_2-CH_2-OH	> 300	4 ± 1 (0,05)	7 ± 1 (0,01)
10c	4-methylbenzyl	NH-CH_2-CH_2-OH	> 300	n.s.	n.s.
10d	biphenylmethyl	NH-CH_2-CH_2-OH	100	n.s.	n.s.
10e	phenyl	NH-CH_2-CH_2-OH	> 300	3 ± 1 (0,1)	10 ± 1 (0,002)
11a	cyclohexyl	CH_2-N(CH_3)$_2$	> 300	not tested	
11b	benzyl	CH_2-N(CH_3)$_2$	> 300	n.s.	9 ± 2 (0,01)
11c	biphenylmethyl	CH_2-N(CH_3)$_2$	90	n.s.	n.s.

Table 2. *In vitro* (Born test, inducer collagen) antiplatelet and in vivo antithrombotic properties of triazolecarboxamides **12**. Statistics: Wilcoxon Man Whitney U test, n. s. = not significant.



			Inhibition of thrombus formation		
			Born test	venules	arterioles
Cpd.	**R**	**X**	**IC_{50} (μmol/L)**	**% ± s_x (α)**	**% ± s_x (α)**
12a	benzyl	OH	> 300	n.s.	n.s.
12b	phenylethyl	O-CH_2-CH_2-OH	> 300	n.s.	n.s.
12c	heptyl	NH-CH_2-CH_2-OH	125	not tested	
12d	cyclohexyl	CH_2-N(CH_3)$_2$	95	n.s.	n.s.
12e	biphenylmethyl	CH_2-N(CH_3)$_2$	250	not tested	

Table 3. *In vitro* (Born test, inducer collagen) antiplatelet and *in vivo* antithrombotic properties of triazolecarboxamides **13**. Statistics: Wilcoxon Man Whitney U test, n. s. = not significant.



			Inhibition of thrombus formation		
			Born test	venules	arterioles
Cpd.	**R**	**X**	**IC_{50} (μmol/L)**	**% ± s_x (α)**	**% ± s_x (α)**
13a	benzyl	OH	> 300	n. s.	8 ± 1 (0,1)
13b	phenylethyl	O-CH_2-CH_2-OH	> 300	3 ± 1 (0,1)	9 ± 1 (0,1)

Table 4. *In vitro* antiplatelet properties of compounds **11c** and **12d** with different inducers of the platelet aggregation.

Compd.	IC_{50} (μmol/L)				
	Collagen	ADP	Serotonin	Adrenaline	PAF
11c	90	200	25	25	250
12d	95	80	30	145	15

PAF (platelet activating factor), and serotonin). The results are shown in Table 4. Obviously, **11c** is most active against serotonin and adrenaline. Compound **12d** has its peak activity against PAF with an IC_{50} = 15 μM.

Inhibition of thrombus formation *in vivo* (laser-thrombosis model)

The influence of the test compounds on the formation of thrombi was assayed in a laser-thrombosis model [9]. The results are compiled in the last column of Tables 1, 2 and 3 each. In general, triazolecarboxamides selected for Table 1 exhibit a moderate (≤11 %) inhibition of thrombus formation in arterioles. The effects in venules are weaker. This is not surprising, because it is more difficult to inhibit the formation of thrombi in venules. The reason is that the blood flow in venules is much slower than in arterioles, and therefore, thrombus formation is easier induced, but harder to inhibit.

In the triazolecarboxamides the results present a mixed picture. Nearly all antithrombotic compounds are without basic centre in the amide moiety. Surprisingly, **8c** with a 4-methylbenzyl-substituent at the N-1 of the triazole and missing a basic center in the amide function showed both, antiaggregating activity (IC_{50} = 130 μM) and a small but significant antithrombotic effect in arterioles (7 %). Compounds with voluminous substituents like biphenylmethyl at the triazole N-1 showed no activity *in vivo.* Among the isomeric amides **12** and **13** (**a**/**b**), only the 5-carboxylates exhibited antithrombotic properties, whereas the 4-carboxylates are without activity.

Activation of sGC and inhibition of phosphodiesterases

The activation of soluble guanylate cyclase (sGC) was determined as described previously [10]. Compounds **8**, **9a**, **10d**, **11a**, **12a,** and **12b** were tested in concentrations of 10 and 100 μM and exhibited no activity.

The inhibition of PDE 1, 2, 3, 5, and 9 was as determined in c-GMP-SPA-test. Compounds **8**, **9a**, **10d**, **11a**, **12a,** and **12b** showed no activity in a concentration of 10 μM. These observations strongly suggest a mechanism for the antiplatelet effects different from YC-1.

Acknowledgments

We thank J.-P. Stasch and E. Bischoff, Institute of Cardiovascular Research, Bayer AG, Wuppertal, Germany, for testing the compounds on sGC activation and PDE inhibition.

Experimental

Chemistry

The full set of data is given in the PhD thesis Anke Cwiklicki, FU Berlin 2002.

Mp (uncorr.), Linström. – Elemental analysis: Elementar Vario EL. – IR: ATI Mattson Genesis Serie FTIR – NMR: Bruker Advance DPX 400, (Bruker, Rheinstetten, Germany). – EI-MS: CH-7A-Varian MAT (70 eV), (Varian, Braunschweig, Germany).

Procedure for the synthesis of phenylazide (**1**)

6.2 g (0.07 mol) aniline was suspended in 50 mL of water. After addition of 25 g conc. H_2SO_4 the mixture was stirred while cooling with ice-water and a solution of 5.25 g $NaNO_2$ in 31 mL water was added dropwise. 100 mL of hexane were added, followed by dropwise addition of a solution of 4.6 g NaN_3 in water. After stirring for 3 h, the organic phase was separated, dried with anhydrous Na_2SO_4, filtered and the solvent removed *in vacuo*. Yellow liquid, yield 7.0 g (96%). – Anal. $C_6H_5N_3$. – ^{1}H-NMR ([D$_6$]DMSO): δ = (ppm) 7.12 (m, 2H), 7.20 (m, 1H), 7.42 (m, 2H).

General procedure for the synthesis of 1H-1,2,3-triazolecarboxylicacidesters

To 10 mmol of the azide in 50 mL ethanol, 10 mmol of the alkine are added. The mixture is refluxed for at least 8 h (TLC monitoring). Then the solvent is removed *in vacuo*. The residue is recrystallized from petrolether/methanol.

1-Heptyl-1H-1,2,3-triazole-4-carboxylicacidethylester (**3a**)

from 1 g (7.1 mmol) azidoheptane and ethylpriolate. Crystals, yield 0.9 g (53%). – Anal. $C_{12}H_{21}N_3O_2$. – **1H-NMR** ($CDCl_3$): δ (ppm) = 0.88 (t, *J* = 7.0 Hz, 3H, CH_2CH_3), 1.28 (m, 4H), 1.32 (m, 4H) 1.42 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.93 (m, 2H, NCH_2CH_2), 4.41 (m, 4H, NCH_2, OCH_2), 8.05 (s, 1H, tr-H).

1-Cyclohexyl-1H-1,2,3-triazole-4-carboxylicacidethylester (**3b**)

from 0.44 g (3.5 mmol) azidocyclohexane and ethylpropiolate, Crystals, yield 0.5 g (65%). – Anal. $C_{11}H_{17}N_3O_2$. – **^{1}H-NMR** ([D$_6$]DMSO): δ (ppm) = 1.25 (m, 1H, CH), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 1.66 (m, 1H, CH), 1.82 (m, 4H, $(CH_2)_2$), 2.06 (m, 2H, CH_2), 4.30 (q, 2H, *J* = 7.1 Hz, OCH_2CH_3), 4.54 (m, 1H), 8.82 (s, 1H, tr-H).

1-(4-Phenyl)-benzyl-1H-1,2,3-triazole-4-carboxylicacidethylester (**3c**)

from 0.5 g (2.4 mmol) azido-4-phenylbenzene and ethylpropiolate. Powder, mp 148°C, yield 0.65 g (88%). – Anal. $C_{18}H_{17}N_3O_2$. – **IR** (KBr): ν = 1724 cm^{-1} (C=O), 1226 (C–O), 743 (aromatic). – **^{1}H-NMR** ([D$_6$]DMSO): δ (ppm) = 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 4.30 (q, *J* = 7.1 Hz, 2H, CH_3CH_2O), 5.70 (s, 2H, CH_2N), 7.37 (m, 1H, 4′-ph-H), 7.45 (m, 4H, ph-H), 7.66 (m, 4H, ph-H), 8.90 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 307 (11) [M$^{+\bullet}$], 278 (3) [M$^{+\bullet}$–C_2H_5], 167 (100) [M$^{+\bullet}$–N_3].

1-Phenyl-1H-1,2,3-triazole-4-(and-5-)carboxylicacidethylester (**3d**/**4d**)

from 2.4 g (0.02 mol) azidobenzene and ethylpropiolate. Powder, mixture of isomers, yield 3.0 g (69%). Column chromatography (hexane/ethylacetate 3:1) gave 2.5 g (83%) **3d** (crystals, mp 86°C) and 0.5 g (17%) **4d** (yellow oil). – Anal. $C_{11}H_{11}N_3O_2$. – **^{1}H-NMR** ([D$_6$]DMSO) **3d**: δ (ppm) = 1.35 (t, *J* = 7.1 Hz, 3H, CH_3), 4.37 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 7.54 (m, 1H, 4-ph-H), 7.62 (m, 2H, ph-H), 7.99 (m, 2H, ph-H), 9.49 (s, 1H, tr-H). – **1H-NMR** ([D$_6$] DMSO) **4d**: δ (ppm) = 1.17 (t, *J* = 7.1 Hz, 3H, CH_3), 4.22 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 7.59 (m, 5H, ph-H),8.47 (s, 1H, tr-H).

1-Heptyl-5-phenyl-1H-1,2,3-triazole-4-carboxylicacidethylester (**6a**)

from 2.6 g (18.4 mmol) azidoheptane and 3-phenylpropiolicacidethylester. Crystals, yield 3.0 g (52%). – Anal. $C_{18}H_{25}N_3O_2$. – **^{1}H-NMR** ([D$_6$]DMSO): δ (ppm) = 0.80 (t, 3H, CH_2CH_3), 1.08–1.24 (m, 11H, $(CH_2)_4$, OCH_2CH_3), 1.62 (m, 2H, $CH_2CH_2CH_2N$),4.14 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 4.23 (t, 2H, *J* = 7.0 Hz, CH_2N), 7.49 (m, 2H, ph-H), 7.54 (m, 3H, ph-H)

1-Cyclohexyl-5-phenyl-1H-1,2,3-triazole-4-carboxylicacidethylester (**6b**)

from 1g (8 mmol) azidocyclohexane and 3-phenylpropiolicacidethylester. Crystals, yield 1.3 g (56%). – Anal. $C_{17}H_{21}N_3O_2$. – **^{1}H-NMR** ([D$_6$]DMSO): δ (ppm) = 1.07 (t, *J* = 7.1 Hz, 3H, CH_3), 1.20 (m, 3H, CH, CH_2), 1.59 (m, 1H, CH), 1.78 (m, 2H, CH_2), 1.94 (m, 4H, $(CH_2)_4$), 4.00 (m, 1H, CH_2CHCH_2), 4.12 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 7.47 (m, 2H, ph-H), 7.56 (m, 3H, ph-H).

1-Benzyl-5(and-4)-phenyl-1H-1,2,3-triazole-4(and-5)-carboxylicacidethylester (**6c**/**7c**)

from 1.5 g (10 mmol) azidomethylbenzene and 3-phenylpropiolicacidethylester. Powder, yield 2.8 g (91%), mixture of isomers (45% **7c**/55% **6c**). – Anal. $C_{18}H_{17}N_3O_2$. – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 1.17 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3 **7c**), 1.25 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3 **6c**), 5.43 (s, 2H, CH_2N, **6c**), 5.94 (s, 2H, CH_2N, **7c**), 6.99 (m, 2H, aromat., 2 × 4-ph-H), 7.18–7.51 (m, 16H, aromat., 4 × 4 ph-H, **6c**+**7c**), 7.25 (m, 4H, 2 × OCH_2CH_3, **6c+7c**), 7.71 (m, 2H, 2 × 4-ph-H).

1-Phenylethyl-5(and-4)-phenyl-1H-1,2,3-triazole-4(and-5)-carbxylicacidethylester (**6d**/**7d**)

from 0.85 g (5.8 mmol) azidoethylbenzene and 3-phenylpropiolicacidethaclester. Crystals and oil, yield 1.3 g (70%) – Column chromatography gave **6d** 40% and **7d** 60%. – Anal. $C_{19}H_{19}N_3O_2$. – **^{1}H-NMR** ($CDCl_3$) **6d**: δ (ppm) = 1.24 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 3.16 (t, *J* = 7.2 Hz, 2H, CH_2CH_2N), 4.27 (q, *J* = 7.1 Hz, 2H, OCH_2CH_3), 4.40 (t, *J* = 7.2 Hz, 2H, CH_2N), 6.88 (m, 2H, ph-H), 6.95 (m, 2H, ph-H), 7.21 (m, 3H, ph-H), 7.38-7.48 (m, 3H, ph-H). – ^{1}H-NMR ($CDCl_3$) **7d**: δ (ppm) = 1.23 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3) 3.24 (t, *J* = 7.8 Hz, 2H, CH_2CH_2N), 4.27 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 4.96 (t, *J* = 7.8 Hz, 2H, CH_2N), 7.20-7.33 (m, 5H, ph-H), 7.42 (m, 3H, ph-H), 7.69 (m, 2H, ph-H).

General procedure for the synthesis of the type **8** *carboxamides*

The ester and a three- to fivefold amount of the amine are heated in methanol to 50°C (DC control with hexane/ethylacetate 3:1). After about 24 h the solvent is removed *in vacuo* and the carboxamide precipitated with water. In case no precipitate forms, the mixture should be extracted with trichloromethane, dried over Na_2SO_4, filtered, and concentrated. At 5°C the carboxamides often crystallized; if not, the crystallization is induced by a suitable amount of petrolic ether or diisopropylether.

1-Cyclohexyl-1H-1,2,3-triazole-N-(2-hydroxyethyl)-4-carboxamide (**8a**)

from 0.45 g (2 mmol) **3b**. Crystals, mp 135°C, yield 0.3 g (62%). – Anal. $C_{11}H_{18}N_4O_2$. – **IR** (KBr): ν = 3427 cm^{-1} (OH), 1648 (C=O), 1576 (C=N), 1053 (C=C). – **^{1}H-NMR** ($CDCl_3$):

δ (ppm) = 1.31 (m, 2H, CH_2), 1.46 (m, 2H, CH_2), 1.74 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 2.23 (m, 2H, CH_2), 3.63 (m, 2H, CH_2CH_2OH), 3.83 (m, 2H, CH_2CH_2OH), 4.48 (m, 1H, CHN), 7.52 (s, br, 1H, NH), 8.07 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 237 (<1) $[M^{+\bullet}-H]^+$, 220 (11) $[M^{+\bullet}-H_2O]^+$, 208 (100) $[M^{+\bullet}-CH_2O]^+$, 207 (89) $[M^{+\bullet}-CH_2OH]^+$, 195 (30), 178 (82) $[R-Cs\equiv O]^+$, 125 (92) $[C_6H_{11}N_3]^+$, 96 (63), 83 (54) $[C_6H_{11}]^+$, 55 (78) $[C_4H_7]^+$, 41 (65) $[C_3H_5]^+$.

1-Benzyl-1H-1,2,3-triazole-N-(2-hydroxyethyl)-4-carboxamide (**8b**)

from 0.5 g (2.2 mmol) 1-benzyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 124 °C (C_2H_5OH/H_2O), yield 0.3 g (56 %). – Anal. $C_{12}H_{14}N_4O_2$. **IR** (KBr): ν = 3416 cm^{-1} (OH); 3106 (NH); 1654 (C=O); 1576 (C=N); 1051 (C=C); 719 (aromat.). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 2.56 (s, br, -OH, D_2O ex.), 3.62 (q, *J* = 5.3 Hz, 2H, CH_2CH_2OH) 3.81 (t, *J* = 4.5 Hz, 2H, CH_2CH_2OH) 5.55 (s, 2H, CH_2N), 7.28 (m, 2H, ph-H), 7.39 (m, 3H, ph-H), 7.52 (s, br, 1H, NH, D_2O ex.), 7.96 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 228 (3) $[M^{+\bullet}-H_2O]^{+\bullet}$, 216 (29), 186 (29) $[M^{+\bullet}-NH(CH_2)_2OH]^+$, 91 (100) $[C_7H_7]^+$.

1-(4-Methylphenylmethyl)-1H-1,2,3-triazole-N-(2-hydroxyethyl)-4-carboxamide (**8c**)

from 0.45 g (1.8 mmol) 1-(4-methylphenyl)-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 151 °C, yield 0.3 g (64 %) – Anal. $C_{13}H_{16}N_4O_2$. – **IR** (KBr): ν = 3275 cm^{-1} (OH); 1666 (C=O); 1578 (C=N); 1063 (C=C). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 2.36 (s, 3H, CH_3), 2.60 (s, br., 1H, OH, D_2O ex.), 3.61 (m, 2H, CH_2OH), 3.82 (t, *J* = 5 Hz, 2H, NCH_2), 5.50 (s, 2H, CH_2N), 7.18 (m, 4H), 7.52 (s, br, 1H, NH, D_2O ex.), 7.93 (s, 1H, tr-H).**MS** (70 eV): *m/z* (%) = 261(<1) $[M+H]^+$, 230 (18), $[M^{+\bullet}-CH_2OH]^+$, 105 (100) $[CH_3\text{-}C_6H_4\text{-}CH_2]^+$, 77 (13), 31 (6) $[H_2C{=}OH]^+$.

1-Benzyl-1H[1,2,3]-triazole-N-(2-methoxyethyl)-4-carboxamide (**8d**)

from 0.45 g (1.9 mmol) 1-benzyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 138 °C, yield 0.35 g (71 %) – Anal. $C_{13}H_{16}N_4O_2$. – **IR** (KBr): ν = 3311 (NH) cm^{-1}; 1580 (C=N); 1055 (C=O). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 3.25 (s, 3H, OCH_3), 3.42 (m, 4H, $CH_2CH_2OCH_3$), 5.64 (s, 2H, $phCH_2N$), 7.38 (m, 5H, ph-H), 8.40 (t, *J* = 5.7 Hz, 1H, O=C-NH), 8.62 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 260 (3) $[M^{+\bullet}]$, 228 (24), 215 (19), 186 (32), 91 (100).

1-Heptyl-1H-[1,2,3]-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9a**)

from 0.45 g (1.9 mmol) **3a**. Crystals, mp 72-74 °C, yield 0.26 g (46 %) – Anal. $C_{14}H_{26}N_4O_3$. – **IR** (KBr): ν = 3433 cm^{-1} (OH): 1648 (C=O): 1576 (C=N): 1050 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.24 (m, 8H, $(CH_2)_4$), 0.85 (t, *J* = 6.9 Hz, 3H, CH_3), 1.83 (m, 2H, $CH_2CH_2CH_2$), 3.42 (m, 4H, CH_2OCH_2), 3.50 (m, 4H, $NHCH_2$, CH_2OH), 4.39 (t, *J* = 7.0 Hz, 2H, CH_2N), 4.59 (t, *J* = 5.4 Hz, 1H, OH, D_2O ex.), 8.37 (t, *J* = 5.7 Hz, 1H, O=C-NH, D_2O ex.), 8.56 (s, 1H, tr-H) – **MS** (70 eV): *m/z* (%) = 298 $[M^{+\bullet}]$, 236 (32), 223 (93) $[M^{+\bullet}-CH_2O(CH_2)_2OH]^+$, 194 (100) $[RC{\equiv}O]^+$, 57 (66).

1-Cyclohexyl-1H-[1,2,3]-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9b**)

from 0.5 g (2.2 mmol) **3b**. Crystals, mp 65 °C, yield 0.35 g (56 %) – Anal. $C_{13}H_{22}N_4O_3$. – **IR**: ν = 3317 cm^{-1} (OH); 1658 (C=O); 1575 (C=N); 1060 (C=C). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 1.30 (m, 2H, CH_2), 1.45 (m, 2H, CH_2), 1.77 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 2.22 (m, 2H, CH_2), 2.90 (t, *J* = 5.1 Hz, 1H, OH, D_2O ex.), 3.62 (m, 4H, CH_2OCH_2), 3.75 (m, 4H, $NHCH_2$, CH_2OH), 4.47 (m, 1H, CHN), 7.52 (s, br., 1H, NH), 8.06 (s, 1H, tr-H) – **MS** (70 eV): *m/z* (%) = 282 (<1) $[M^{+\bullet}]$, 221 (27), 207 (87) $[M^{\bullet+}-CH_2O(CH_2)_2OH]^+$, 178 (76) $[RC{\equiv}O]^+$, 125 (100) $[C_6H_{11}N_3]^+$, 96 (55).

1-Phenylmethyl-1H-[1,2,3-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9c**)

from 0.5 g (2.2 mmol) 1-phenylmethyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 115 °C, yield 0.35 g (55 %). – Anal. $C_{14}H_{18}N_4O_3$. – **IR**(KBr): ν = 3327 cm^{-1} (OH); 1650 (C=O); 1578 (C=N); 1055 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 3.39-3.52 (m, 8H, $HN(CH_2)_2O(CH_2)_2OH$), 4.60 (s, br., 1H, OH, D_2O ex.), 5.65 (s, 2H, $phCH_2N$), 7.35 (m, 5H, ph-H), 8.43 (t, *J* = 5.7 Hz, 1H, O=C−NH, D_2O ex.), 8.62 (s, 1H, tr-H) – **MS** (70 eV): *m/z* (%) = 291 (<1) $[M+H]^{+\bullet}$, 260 (6) $[M^{+\bullet}-CH_2OH]^+$, 229 (10) $[M^+\text{-}OCH_2CH_2OH]^+$, 215 (21), 186 (31) $[RC-O]^+$, 91 (100) $[C_7H_7]^+$.

1-(4-Methylbenzyl)-1H-1,2,3-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9d**)

from 0.45 g (1.8 mmol) 1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 129 °C, yield 0.3 g (55 %). – Anal. $C_{15}H_{20}N_4O_3$. – **IR** (KBr): ν = 3327 (OH) cm^{-1}; 1652 (C=O); 1578 (C=N); 1053 (C=O). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 2.36 (s, 3H, CH_3), 3.61 (m, 2H, OCH_2), 3.65 (m, 4H, $HNCH_2$, OCH_2), 3.75 (m, 2H, CH_2OH), 5.50 (s, 2H, CH_2N), 7.18 (m, 4H, ph-H), 7.50 (s, 1H, NH), 7.92 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 304 (<1) $[M^+]$, 105 (100) $[CH_3C_7H_6]^+$.

1-(4-Fluorobenzyl)-1H-1,2,3-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9e**)

from 0.45 g (1.8 mmol) 1-(4-fluorobenzyl)-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 157 °C, yield 0.34 g (61 %) – Anal. $C_{14}H_{17}FN_4O_3$. – **IR** (KBr): ν = 3314 cm^{-1} (OH): 1654 (C=O): 1579 (C=N): 1058 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 3.41 (m, 4H, CH_2OCH_2), 3.49 (m, 4H, 2 x CH_2), 4.59 (t, *J* = 5.4 Hz, 1H, OH), 5.64 (s, 2H, CH_2N), 7.22 (m, 2H, ph-H), 7.42 (m, 2H, ph-H), 8.42 (t, *J* = 5.5 Hz, 1H, O=C-NH), 8.63 (s, 1H, tr-H) – **MS** (70 eV): *m/z* (%) = 308 (<1) $[M^{+\bullet}]$, 233 (11), 204 (14), 109 (100).

1-(4-Phenylbenzyl)-1H-1,2,3-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**9f**)

from 0.35 g (1.1 mmol) **3c**. Crystals, mp 178 °C, yield 0.25 g (60 %). – Anal. $C_{20}H_{22}N_4O_3$. – **IR** (KBr): ν = 3400 cm^{-1} (OH); 1648 (C=O); 1574 (C=N); 1067 (C=O). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 3.62 (m, 2H, $HNCH_2$), 3.67 (m, 4H, CH_2OCH_2), 3.76 (m, 2H, CH_2OH), 5.59 (s, 2H, CH_2N), 7.37 (m, 2H, ph-H), 7.45 (m, 2H, ph-H), 7.57 (m, 5H, ph-H), 8.00 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 366 (<1) $[M^{+\bullet}]$, 167 (100).

1-Heptyl-1H-1,2,3-triazole-N-[2-(2-hydroxyethylamino)-ethyl]-4-carboxamide (**10a**)

from 0.5 g (2.1 mmol) **3a**. Crystals, mp 107−110 °C, yield 0.4 g (64 %) – Anal. $C_{14}H_{27}N_5O_2$. – **IR** (KBr): ν = 3340 (OH) cm^{-1}; 1648 (C=O); 1576 (C=N); 1069 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 0.88 (m, 3H, CH_3), 1.27 (m, 4H, $(CH_2)_2$), 1.86 (quint, *J* = 7.1 Hz, 2H, $CH_2CH_2CH_2$), 2.61 (t,

J = 5.7 Hz, 2H, CH_2NH), 2.70 (t, J = 6.4 Hz, 2H, HNCH_2), 3.35 (m, 2H, O=C-HNCH_2), 3.46 (t, J = 5.7 Hz, CH_2OH), 4.41 (t, J = 7.0 Hz, 2H, CH_2CH_2N), 8.39 (t, J = 5,7 Hz, 1H, O=C-NH, D_2O ex.), 8.58 (s, 1H, tr-H) – **MS** (70 eV): *m/z* (%) = 297 (<1) [$M^{+\bullet}$], 87 (40), 74 (100).

1-Benzyl-1H-1,2,3-triazole-N-[2-(2-hydroxyethylamino)-ethyl]-4-carboxamide (**10b**)

from 0.45 g (1.9 mmol) 1-benzyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 136-138 °C ($CHCl_3$/petrolic ether), yield 0.3 g (54 %). – Anal. $C_{14}H_{19}N_5O_2$. – **IR** (KBr): ν = 3339 cm^{-1} (OH); 1649 (C=O); 1577 (C=N): 1068 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 2.58 (t, J = 5.8 Hz, 2H, NHCH_2), 2.66 (t, J = 6.5 Hz, 2H, CHNH), 3.32 (2H, O=C-NHCH_2), 3.43 (m, 2H, CH_2OH), 5.65 (s, 2H, CH_2N), 7.35 (m, 3H, ph-H), 7.39 (m, 2H, ph-H), 8.39 (s, br., 1H, NH, D_2O ex.), 8.60 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 290 (1) $[M+H]^+$, 271 (8) $[M^{+\bullet}-H_2O]^{+\bullet}$, 258 (21) $[M^{+\bullet}-CH_2OH]^+$, 187 (9) [R-Cs≡O]$^+$, 159 (20) $[C_6H_5CH_2Tr]^+$, 91 (74), 87 (71), 74 (100) $[CH_2NH(CH_2)_2OH]^+$, 30 (22) $[CH_2NH_2]^+$.

1-(4-Methylbenzyl)-1H-1,2,3-triazole-N-[2-(2-hydroxyethylamino)-ethyl]-4-carboxamide (**10c**)

from 0.5 g (2 mmol) 1-(4-methylbenzyl)-1H-1,2,3-triazole-4-carboxylicacidethylester. Column chromatography: eluent $CHCl_3$ / CH_3OH (1:2). Crystals, mp 132 °C, yield 0.25 g (41 %). – Anal. $C_{15}H_{21}N_5O_2$. – **IR** (KBr): ν = 3345 cm^{-1} (OH); 1648 (C=O); 1577 (C=N); 1068 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 2.57 (t, J = 5.7 Hz, 2H, CH_2NH), 2.66 (t, J = 6.4 Hz, 2H, HNCH_2), 3.30 (O=C-HNCH_2), 3.41 (m, 2H, CH_2OH), 4.43 (m, 1H, OH, D_2O ex.), 5.58 (s, 2H, CH_2N), 7.19 ("d", J = 7,9 Hz, 2H, ph-H), 7.23 ("d", J = 7,9 Hz, 2H, ph-H), 8.37 (t, J = 5.3 Hz, 1H, O=C-NH, D_2O ex.), 8.57 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 304 (<1) $[M+H]^+$, 272 (14), 105 (100), 87 (50), 74 (85).

1-(4-Phenylbenzyl)-1H-1,2,3-triazole-N-[2-(2-hydroxyethylamino)-ethyl]-4-carboxamide (**10d**)

from 0.35 g (1.1 mmol) **3c**. Crystals, mp 187-189 °C, yield 0.2 g (50 %). – Anal. $C_{20}H_{23}N_5O_2$. – **IR** (KBr): ν = 3331 (OH) cm^{-1}; 1650 (C=O); 1574 (C=N); 1067 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 2.60 (t, J = 5.7 Hz, 2H, CH_2NH), 2.69 (t, J = 6.4 Hz, 2H, HNCH_2), 3.33 (m, 2H, O=C-NHCH_2), 3.43 (m, 2H, CH_2OH), 4.45 (s, br., 1H, OH, D_2O ex.), 5.69 (s, 2H, CH_2N), 7.37 (m, 4H, ph-H), 7.46 (m, 4H, ph-H), 7.66 (m, 4H, ph-H), 8.39 (t, J = 5.6 Hz, 1H, O=C-NH, D_2O ex.), 8.65 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 364 (<1) [$M^{+\bullet}$], 167 (100), 87 (51), 74 (91).

1-Phenyl-1H-1,2,3-triazole-N-[2-(2-hydroxyethylamino)-ethyl]-4-carboxamide (**10e**)

from 0.45 g (2.1 mmol) **3d**. Crystals, mp 140 °C, yield 0.3 g (53 %). – Anal. $C_{13}H_{17}N_5O_2$. – **IR** (KBr): ν = 3431 (OH) cm^{-1}; 1652 (C=O); 1578 (C=N); 1061 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 2.60 (t, J = 5.8 Hz, 2H, HNCH_2), 2.71 (t, J = 6.5 Hz, 2H, CH_2NH), 3.38 (t, J = 6.2 Hz, 2H, O=CHNCH_2), 3.45 (t, J = 5.8 Hz, 2H, CH_2OH) 4.45 (s, br., 1H, OH, D_2O ex.), 7.53 (t, J = 7.4 Hz, 1H, 4-ph-H), 7.62 (m, 2H, 3-, 5-ph-H), 7.98 (m, 2H, 2-, 6-ph-H), 8.53 (t, J = 5.6 Hz, 1H, O=C-NH), 9.26 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 257 (2) $[M^{+\bullet}-H_2O]^{+\bullet}$, 87 (37), 74 (100).

1-Cyclohexyl-1H-[1,2,3]-triazole-N-(3-dimethylaminopropyl)-4-carboxamide (**11a**)

from 0.45 g (2 mmol) **3b**. Crystals, mp 125 °C, yield 0.4 g (72 %). – Anal. $C_{14}H_{25}N_5O$. – **IR** (KBr): ν = 3433 cm^{-1}; 1658 (C=O); 1573 (C=N); 1057 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.22 (m, 1H, *H*CH), 1.41 (m, 2H, CH_2), 1.63 (m, 3H, HC*H*, CH_2), 1.77 (m, 2H, CH_2), 2.07 (m, 2H, CH_2), 2.12 (s, 6H, N(CH_3)$_2$), 2.23 (m, 2H, CH_2N(CH_3)$_2$), 3.26 (m, 2H, HNCH_2), 4.51 (m, 1H, CHN), 8.53 (t, J = 5.8 Hz, 1H, O=C-NH), 8.57 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 279 (5) [$M^{+\bullet}$], 58 (100) [CH_2=N^+(CH_3)$_2$].

1-Phenylmethyl-1H-1,2,3-triazole-N-(3-dimethylaminopropyl)-4-carboxamide (**11b**)

from 0.45 g (1.9 mmol) 1-phenylmethyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 140 °C, yield 0.39 g (71 %). – Anal. $C_{15}H_{21}N_5O$. – **IR** (KBr): ν = 3325 (NH) cm^{-1}; 1648 (C=O); 1577 (C=N); 1048 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.62 (dt, J = 7.0/7.0 Hz, 2H, CH_2CH_2CH$_2$), 2.11 (s, 6H, N(CH_3)$_2$), 2.22 (t, J = 7.0 Hz, 2H, CH_2N(CH_3)$_2$), 3.26 (m, 2H, HNCH_2), 5.64 (s, 2H, phCH_2N), 7.37 (m, 5H, ph-H), 8.57 (m, 1H, O=C-NH, D_2O ex.), 8.60 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 287 (4) [$M^{+\bullet}$], 91 (17), 58 (100) [CH_2=N^+(CH_3)$_2$].

1-(4-Phenylbenzyl)-1H-1,2,3-triazole-N-(3-dimethylaminopropyl)-4-carboxamide (**11c**)

from 0.5 g (1.6 mmol) **3c**. Crystals, mp 190 °C, yield 0.36 g (62 %). – Anal. $C_{21}H_{25}N_5O$. – **IR** (KBr): ν = 3327 (NH) cm^{-1}; 1648 (C=O); 1575 (C=N); 1046 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.62 (tt, J = 7.0/7.0 Hz, 2H, CH_2CH_2CH$_2$), 2.11 (s, 6H, N(CH_3)$_2$), 2.23 (t, J = 7.0 Hz, 2H, CH_2N(CH_3)$_2$), 3.26 (q, J = 6.6 Hz, HNCH_2), 5.69 (s, 2H, phCH_2N), 7.37 (m, 1H, ph-H), 7.45 (m, 4H, ph-H), 7.66 (m, 4H, ph-H), 8.58 (t, J = 5.8 Hz, 1H, O=C-NH, D_2O ex.), 8.64 (s, 1H, tr-H). – **MS** (70 eV): *m/z* (%) = 363 (5) [$M^{+\bullet}$], 167 (17), 58 (100) [CH_2=N^+(CH_3)$_2$].

1-Benzyl-5-phenyl-1H-1,2,3-triazole-N-(2-hydroxyethyl)-4-carboxamide (**12a**)

from **6c**/**7c.** – Anal. $C_{18}H_{18}N_4O_2$. – **IR** (KBr): ν = 3549 cm^{-1} (OH); 1622 (C=O). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 3.57 (q, 2H, CH_2CH$_2$OH), 3.79 (t, 2H, CH_2CH_2OH), 5.43 (s, 2H, CH_2N), 7.01 (m, 4H, ph-H), 7.45 (m, 6H, ph-H), 7.64 (s, 1H, O=C-NH). – **MS** (70 eV): *m/z* (%) = 322 (1) [M^+], 304 (2) $[M^{+\bullet}-H_2O]^{+\bullet}$, 292 (17) $[M^{+\bullet}-CH_2O]^{+\bullet}$, 291 (12) $[M^{+\bullet}-CH_2OH]^+$, 262 (25) [R−C≡O]$^+$, 91 (100) $[C_7H_7]^+$.

1-Phenylethyl-5-phenyl-1H-[1,2,3]-triazole-N-[2-(2-hydroxyethoxy)-ethyl]-4-carboxamide (**12b**)

from 0.5 g (1.6 mmol) **6d**. Yellow oil, yield 0.3 g (50 %). – Anal. $C_{21}H_{24}N_4O_3$. – **IR** (film): ν = 3413 cm^{-1} (OH); 1668 (C=O); 1572 (C=N); 1070 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 3.00 (t, J = 7.0 Hz, 2H, CH_2CH$_2$N), 3.30 (2H, CH_2O), 3.41 (m, 2H, CH_2O), 3.48 (m, 4H, CH_2OH, CH_2NH), 4.49 (t, J = 7.1 Hz, 2H, CH_2N), 4.59 (t, J = 5.5 Hz, 1H, OH, D_2O ex.), 6.91 (m, 2H, ph-H), 7.19 (m, 5H, ph-H), 7.47 (m, 3H, ph-H), 8.36 (t, J = 5.8 Hz, 1H, O=C-NH). – **MS** (70 eV): *m/z* (%) = 381 (2) $[M+H]^+$, 380 (2) [$M^{+\bullet}$], 350 (9) $[M^{+\bullet}-CH_2O]^{+\bullet}$, 335 (17), 319 (13) $[M^+-O(CH_2)_2OH]^+$, 306 (23), 277 (45) [RC≡O]$^+$, 105 (100) $[C_8H_9]^+$, 91 (8) $[C_7H_7]^+$, 45 (16) $[CH_3-O^+=CH_2]$.

*1-Heptyl-5-phenyl-1H-1,2,3-triazole-N-[2-(2-hydroxyethyl-amino)-ethyl]-4-carboxamide (***12c**)

from 0.6 g (1.9 mmol) **6a**. Crystals, mp 50–52 °C, yield 0.42 g (59 %). – Anal. $C_{20}H_{31}N_5O_2$. – **IR** (KBr): ν = 3439 cm^{-1} (OH); 1662 (C=O); 1570 (C=N); 1065 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 0.80 (s, 3H, CH_3), 1.09 (m, 6H, □CH_2□$_3$), 1.17 (m, 2H, CH_2) 1.61 (t, *J* = 6.8 Hz, 2H, C*H*$_2$$CH_2$N), 2.57 (m, 2H, C*H*$_2$NH), 2.64 (t, *J* = 6.5 Hz, 2H, NHC*H*$_2$), 3.30 (NHC*H*$_2$), 3.42 (m, 2H, C*H*$_2$OH), 4.23 (t, *J* = 7.1 Hz, 2H, CH_2C*H*$_2$N), 7.48 (m, 5H, ph-H), 8.32 (t, *J* = 5.7 Hz, 1H, O=C-NH, D_2O ex.). – **MS** (70 eV): *m/z* (%) = 373 (1) [$M^{+\bullet}$], 342 (28), 300 (77), 287 (100), 270 (20) [RC≡O]$^+$, 159 (55), 117 (29), 87 (69), 74 (98) [CH_2=NH^+(CH_2)$_2$OH].

1-Cyclohexyl-5-phenyl-1H-1,2,3-triazole-N-(3-dimethyl-aminopropyl)-4-carboxamide (**12d**)

from 0.5 g (1.7 mmol) **6b**. Crystals, mp 105 °C, yield 0.45 g (74 %). υ Anal. $C_{20}H_{29}N_5O$. – **IR** (KBr): ν = 3327 (OH) cm^{-1}; 1666 (C=O); 1569 (C=N); 1042 (C=C). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.21 (m, 3H, $CHCH_2$), 1.58 (m, 1H, CH), 1.58 (tt, *J* = 6.9/6.9 Hz, 2H, CH_2C*H*$_2$$CH_2$), 1.77 (m, 2H, CH_2), 1.90 (m, 4H, CH_2CH_2), 2.10 (s, 6H, N(CH_3)$_2$), 2.20 (t, *J* = 7.0 Hz, 2H, CH_2C*H*$_2$N(CH_3)$_2$), 3.19 (q, *J* = 6.5 Hz, 2H, NHC*H*$_2$$CH_2$), 4.00 (m, 1H, CH), 7.43 (m, 2H, ph-H), 7.52 (m, 3H, ph-H), 8.52 (t, *J* = 5.7 Hz, 1H, C=O-NH, D_2O ex.). **MS** (70 eV): *m/z* (%) = 355 (9) [M^+], 58 (100) [CH_2=N^+(CH_3)$_2$].

1-Biphenyl-5-phenyl-1H-1,2,3-triazole-N-(3-dimethylamino-propyl)-4-carboxamide (**12e**)

from 0.5 g (1.3 mmol) 1-biphenyl-5-phenyl-1H-1,2,3-triazole-4-carboxylicacidethylester. Crystals, mp 105 °C, yield 0.28g (49 %). – Anal. $C_{27}H_{29}N_5O$. – **IR** (KBr): ν = 3329 (NH) cm^{-1}; 1664 (C=O); 1570 (C=N). – **^{1}H-NMR** ([D_6]DMSO): δ (ppm) = 1.60 (tt, *J* = 7.0/7.0 Hz, 2H, CH_2C*H*$_2$$CH_2$), 2.10 (s, 6H, N($CH_3$)$_2$), 2.21 (t, *J* = 7.0 Hz, 2H, C*H*$_2$N), 3.20 (q, *J* = 6.6 Hz, 2H, HNC*H*$_2$), 5.54 (s, 2H, phCH_2N),7.03 (m, 1H, 4′-ph-H), 7.41 (m, 4H, ph-H), 7.60 (m, 4H, ph-H), 8.60 (t, *J* = 5.8 Hz, 1H, O=C-NH). – **MS** (70 eV): *m/z* (%) = 439 (15) [M^+], 167 (36), 58 (100) [CH_2=N^+(CH_3)$_2$].

1-Benzyl-4-phenyl-1H-1,2,3-triazole-N-(2-hydroxyethyl)-5-carboxamide (**13a**)

from 1.5 g (4.9 mmol) **6c**/**7c** mixture of isomers (1:1) Separation from 1-benzyl-5-phenyl-1H-1,2,3-triazole-N-(2-hydroxyethyl)-4-carboxamide by column chromatography on silicagel: eluent $CHCl_3$/C_2H_5OH (3:1). Crystals, mp 123/140 °C, yield 0.25 g (32 %). – Anal. $C_{18}H_{18}N_4O_2$. – **IR** (KBr): ν = 3468 cm^{-1} (OH); 1641 (C=O); 1561 (C=N); 1069 (C=C). – **^{1}H-NMR** ($CDCl_3$): δ (ppm) = 3.39 (dt, *J* = 6.5/6.5 Hz, 2H, C*H*$_2$$CH_2$OH), 3.57 (t, *J* = 6.5 Hz, 2H, CH_2C*H*$_2$OH), 5.89 (s, 2H, CH_2N), 7.32 (m, 5H, ph-H), 7.45 (m, 3H, ph-H), 7.66 (m, 2H, ph-H). – **MS** (70 eV): *m/z* (%) = 322 (<1) [M^+], 262 (<1) [R-C≡O]$^+$, 116 (7), 91 (100) [$C_6H_5CH_2$]$^+$.

1-Phenylethyl-4-phenyl-1H-1,2,3-triazole-N-[2-(2-hydroxy-ethoxy)-ethyl]-5-carboxamide (**13b**)

from 0.5 g (1.6 mmol)**7d**. Oil, yield 0.3 g (50 %). – Anal. $C_{21}H_{24}N_4O_3$. – **IR** (film): ν = 3554 (OH) cm^{-1}; 1640 (C=O). – **^{1}H-NMR** ($CDCl_3$): δ = 3.26 (t, *J* = 7.6 Hz,2H, phC*H*$_2$$CH_2$N) 3.40 (m, 2H, CH_2O), 3.46 (m, 4H, OCH_2, HNC*H*$_2$), 3.54 (m, 2H, C*H*$_2$OH), 4.92 (t, *J* = 7.6 Hz, 2H, PhCH_2C*H*$_2$N), 6.02 (s, br., 1H, O=C-NH), 7.22 (m, 3H, ph-H), 7.29 (m, 2H, ph-H), 7.47 (m, 3H, ph-H) 7.65 (m, 2H, ph-H). – **MS** (70 eV): *m/z* (%) = 380 (13) [$M^{+\bullet}$], 105 (100).

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