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# Multicomponent Synthesis of Novel Amino Acid–Nucleobase Chimeras: a Versatile Approach to PNA-Monomers

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**Abstract**—This paper describes a multicomponent approach to novel totally protected precursors of PNA-monomers via Ugi 4CC. The obtained bisamides are converted into several partially protected PNA-monomers or derivatives thereof using three different procedures. Methods for hydrolysis are shown to be dependent on the nature of the isocyano component required for Ugi 4CC. Several novel monomers suitable for oligomer synthesis are prepared demonstrating the high versatility of the reaction sequence.


## Introduction

The design and synthesis of structurally modified oligonucleotides has attracted much interest since some of them show high affinity and sequence specific binding to RNA and DNA. Therefore, they represent promising drug candidates in the antisense and antigene therapy, and may also provide new tools in molecular biology and diagnostics.[1] A large number of structurally modified oligonucleotides has been reported throughout the last years, either modified at the sugar-phosphate backbone or at the nucleobases in order to optimize their properties.[2] Nielsen and co-workers reported a radically changed structure of a nucleic acid mimic called Peptide Nucleic Acids (PNAs). In these compounds the sugar-phosphate backbone of DNA is completely substituted by a pseudo-peptide structure (Fig. 1).[3]

These oligonucleotide analogues showed a high binding affinity to complementary single stranded DNA, mRNA and PNA by duplex formation as well as to double stranded DNA by triplex formation.[4] In vitro studies demonstrated both good antisense and antigene activity of PNAs.[5] Furthermore PNA is not known to be a substrate for any enzymes which degrade peptides or nucleic acids.[6] However there are some limitations for the use of PNAs in diagnostic and research applications, for example their low solubility in water and their tendency towards self-aggregation.[7] Many efforts were made to circumvent these drawbacks and to optimize the properties of PNAs and lead to the synthesis of a number of new structures,[8] e.g., side chain-modified polyamide backbones and terminal substituted derivatives.[9]

Also changes in PNA-structure leading to PNA analogues like retro-inverso PNA,[10] Aromatic Peptide Nucleic Acids (APNAs),[11] Phosphonic Ester Nucleic Acids (PHONAs)[12] and several other derivatives built up from α- or β-amino acids were investigated, some of them showing interesting properties.[13] Since research in this area is still an ongoing challenge a systematic investigation of structure–function relationships using combinatorial libraries seems to be attractive.[14] Having these considerations in mind we focussed our studies on the design of a general and versatile synthetic route to PNA-monomers. The Ugi four component condensation (Ugi 4CC) serves as a powerful tool in combinatorial and peptide chemistry.[15,18] Herein we describe the synthesis of a novel class of totally protected PNA-monomers and some analogues thereof via Ugi 4CC. The obtained bisamides could be selectively hydrolyzed under acidic or alkaline conditions to give N-terminal protected PNA-monomers or their derivatives, respectively.

## Results and Discussion

The usefulness of the Ugi 4CC in the synthesis of nucleobase–amino acid chimeras was recently demonstrated.[16] The use of a functionalized amine, a carboxylic acid, a suitable oxo compound and an isocyanide as starting materials generates bisamides of type **A** for the synthesis of PNA-monomers. Employment of different

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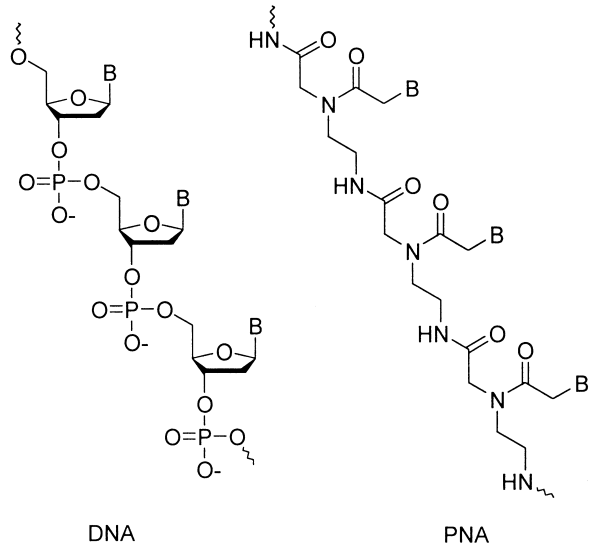



**Figure 1.** B = adenine, cytosine, guanine, thymine.

reactants determines the generation of precursors of PNA-monomers, known structural derivatives, or completely new analogues, respectively. However, application of the generated α-amino acid derivatives in peptide coupling reactions suffers from a big problem since the generated secondary amide 'protecting' the amino acid carboxyl function in **A** is usually difficult to cleave in a selective manner to give carboxylic acid **B**.[17] Most methods reported for the cleavage of secondary amides require harsh conditions and are incompatible with many functional groups within the same molecule (Scheme 1).[18]

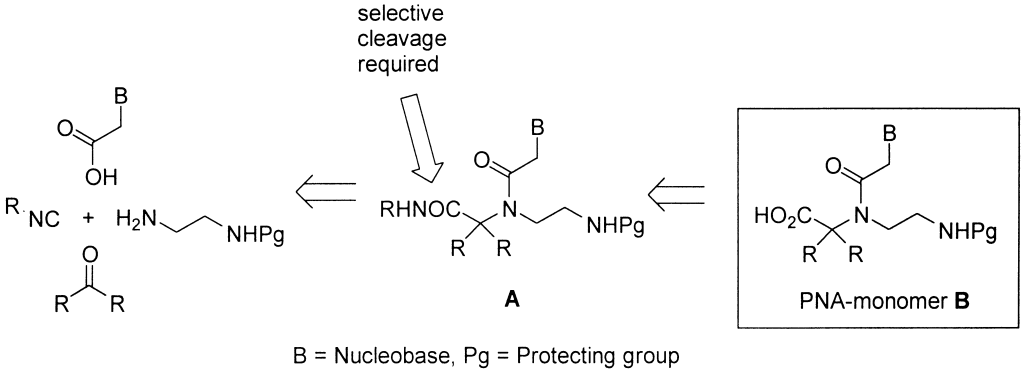
Two routes seem to be promising for the selective cleavage of secondary amides: acid mediated hydrolysis of **A** or alkaline mediated hydrolysis. However, both routes require the synthesis of suitable isocyanides needed for the generation of bisamides **A** via Ugi 4CC.

## Synthesis of totally protected PNA-monomers with an acid labile C-terminal protecting group

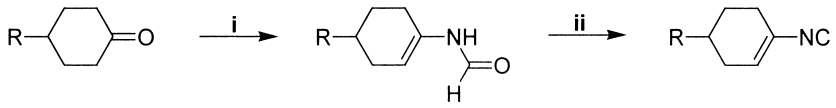
Recently Keating demonstrated cyclohexenyl isocyanide to be a suitable isocyano compound in Ugi 4CC reactions.[19] This attracted our interest because the obtained bisamides can be converted to different carboxylic acid derivatives by nucleophilic attack under acidic conditions. However, the common procedures for the preparation of cyclohexenyl isocyanide were not practical for large scale synthesis.[19,20,24] Besides the large number of steps the overall yields are also lowered because of decomposition during distillation or difficulties arising from coevaporation of the product while the solvent is removed after chromatography. To overcome these problems we first developed a shorter route to some derivatives of cyclohexenyl isocyanide (Scheme 2).

The starting cyclohexanones were converted into their corresponding cyclohexen-1-yl derivatives **1** in high yields by treatment with formamide. It is equally important to note that these reactions could be performed in large scale. These were easily dehydrated using the phosgene method[21] to give the desired isocyanides **2**. Compared to **2a** the new isocyanides **2b**, **c** are much more easy to handle because of their less extensive odour. They are stable solids which can be stored under argon at 0 °C for several months. Application of the vinylic isocyanides **2** to Ugi 4CC as outlined in Table 1 yielded the bisamides **6** in moderate to excellent yields.

The versatility of the Ugi 4CC in the synthesis of totally protected PNA-monomers is demonstrated by the structural variety of the obtained bisamides **6**. Ugi-adducts were generally obtained in high yields. Lower yield of compound **6d** was due to the low solubility of the required $G^{Bn}$-AcOH in organic solvents. It should be noted that the preparative versatility is accompanied by the ease of purification either by recrystallization or column chromatography on silica gel. All four natural nucleobases were incorporated into the totally protected PNA-monomers **6a–d** starting from the corresponding nucleobase acetic acids in the Ugi 4CC. The substitution pattern of the generated aminoethylglycine (aeg) derivatives was varied by employment of different aldehydes or ketones as oxo components to obtain novel mono- or dialkylated glycinederivatives **6b–m**. Even unusual or sterically crowded α-amino acid analogues like **6b** or **6e** were accessible by this one pot process. Common protecting groups for the second amino function in ethylendiamine derivatives **4a–d** were tolerated resulting in the synthesis of bisamides **6e–f** and **j** (Scheme 3).




**Scheme 1.** Ugi 4CC and regioselective hydrolysis to mono-protected PNA-monomers.

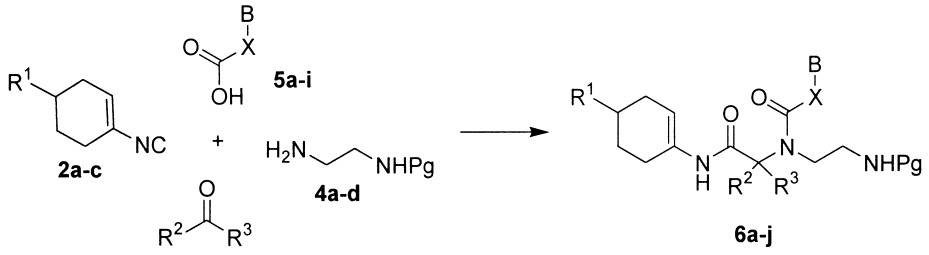



**1a**, R = H, 76 %
**1b**, R = *t*-Bu, 81 %
**1c**, R = Ph, 80 %

**2a**, R = H, 71 %
**2b**, R = *t*-Bu, 80 %
**2c**, R = Ph, 71 %

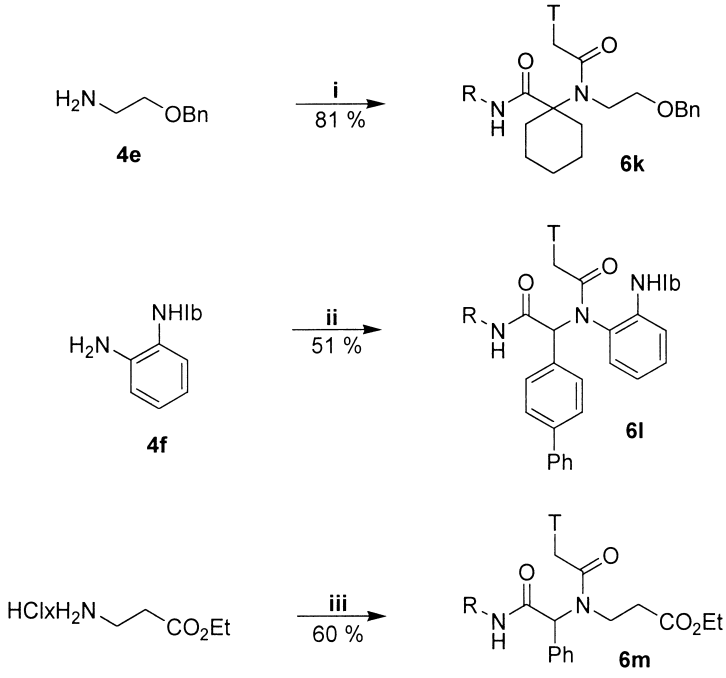
**Scheme 2.** Synthesis of vinylic isocyanides **2a**–**c**. Reagents and conditions: (**i**) formamide, $H_2SO_4$, toluene, Dean–Stark conditions; (**ii**) phosgene, $NEt_3$, 0 °C.

**Table 1.** Totally protected PNA-monomers **6** obtained from isocyanides **2**




| Educt | Product | $R^1$ | $R^2$ | $R^3$ | B | X | Pg[a] | Yield (%) |
|---|---|---|---|---|---|---|---|---|
| **2a, 4a, 5a** | **6a** | H | H | H | T | $CH_2$ | Boc | 76 |
| **2b, 4a, 5c** | **6b** | *t*-Bu | *t*-Bu | H | $C^Z$ | $CH_2$ | Boc | 97 |
| **2a, 4a, 5d** | **6c** | H | 2-Cl-Ph | H | $A^Z$ | $CH_2$ | Boc | 78 |
| **2a, 4a, 5f** | **6d** | H | 2-Cl-Ph | H | $G^{Bn}$ | $CH_2$ | Boc | 31 |
| **2c, 4b, 5a** | **6e** | Ph | $-(CH_2)_5-$ | | T | $CH_2$ | Etoc | 98 |
| **2c, 4c, 5a** | **6f** | Ph | $-(CH_2)_5-$ | | T | $CH_2$ | Z | 80 |
| **2c, 4a, 5a** | **6g** | Ph | $-(CH_2)_5-$ | | T | $CH_2$ | Boc | 90 |
| **2a, 4a, 5g** | **6h** | H | 2-Cl-Ph | H | T | CH-*n*-Bu | Boc | 39 |
| **2b, 4a, 5h** | **6i** | *t*-Bu | *t*-Bu | H | T | *o*-Bz | Boc | 52 |
| **2b, 4d, 5i** | **6j** | *t*-Bu | Ph | H | $C^Z$ | *o*-Bz | Ac | 55 |

[a]Pg, protecting group.




**Scheme 3.** Examples of totally protected PNA-monomers (R = 4-*tert*-butyl-cyclohex-1-enyl). Reagents and conditions: (**i**) cyclohexane, **5a**, **2b**, MeOH, rt; (**ii**) 4-biphenylcarbaldehyde, **5a**, **2b**, MeOH, rt; (**iii**) benzaldehyde, **5a**, **2b**, triethylamine, MeOH, rt.

Apart from classical nucleobase acetyl-aeg PNA-structures, many modified analogues may be synthesized using our one pot procedure. Among them the derivatives **6h–j** comprise a nucleobase linker-modified aeg-structure. These derivatives were synthesized using novel nucleobase derivatives **5g–i**. Incorporation of an aromatic ring system into backbone structures was performed by employment of mono-Ib-phenylen diamine **4f** as a diamino compound in the Ugi 4CC to give **6l**. Use of *O*-benzyl-ethanolamine **4e** as a functionalized amino compound gave rise to the synthesis of **6k**.

### Synthesis of totally protected PNA-monomers with a base labile C-terminal protecting group

As mentioned above, the cleavage of secondary amides under mild conditions is still a challenge in modern chemistry since it needs rigorous conditions in general.[17] The alkaline saponification of **A** offers an alternative access to the carboxylic deprotected monomer **B** (Scheme 1). As the cleavage is initiated by nucleophilic attack of a hydroxy ion at the amide carbonyl, the alkaline sensitivity of the amide depends on the location of the lone pair of the corresponding nitrogen atom. The substitution pattern of phenylamides allows modulation of the location of the nitrogen lone pair via π electron communication. In order to take advantage of this effect we used two nitro substituted phenyl isocyanides **3a, b** as precursors for the formation of electron depleted amides. The isocyanides were synthesized according to Ugi's method.[21] Unfortunately destabilization of the formed amide with further electron withdrawing groups attached to the phenyl moiety (i.e., a second nitro substituent) proved to go along with rising problems in synthesis and stability of the corresponding isocyanide. However, isocyanides **3a**, **b** were easily accessible and fairly stable in ambient conditions.

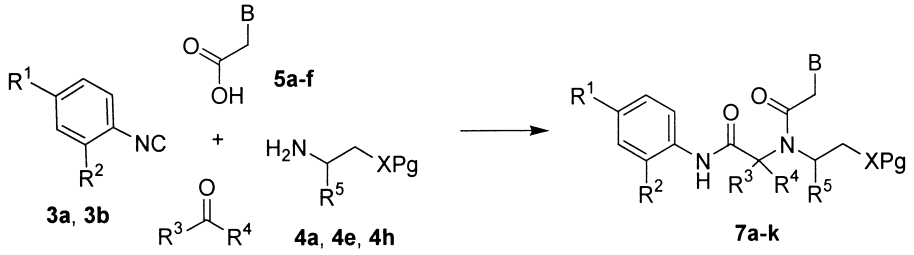
Employment of the nitrophenyl isocyanides **3a**, **b** in the one pot Ugi 4CC procedure described above gave rise to the totally protected PNA monomers **7**.

Again, variation of the remaining three components (oxo compound, amino compound, acid compound) could be utilized to get a wide variety of products. Monomers **7a–f** with a conventional aminoethylglycine (aeg) structure were generally synthesized in good yields, using formaldehyde as the oxo compound, mono-Boc ethylendiamine **4a** and a nucleobase acetic acid **5a–f** (Table 2). All natural nucleobases were incorporated by variation of the acid compound. The lower yields of the guanine containing structures **7e**, **7f** reflect the hindered reaction due to low solubility of $G^{Z}$-AcOH. Unfortunately the use of $G^{Bn}$-AcOH seemed to produce some by-products during Ugi reaction because of competitive aminal formation of the free amino group of guanine and formaldehyde.

Variation of the amino compound allowed modification of the aminoethyl unit (Scheme 4). In this way PNA monomers with a wide variety of diamino and amino-alcohol units were accessible in good yield. Alkylated, cyclic and aromatic mono-protected diamino units were incorporated in **7k–m**. **7g** represents an example of the utilization of *O*-protected aminoalcohols in Ugi 4CC, thus providing a protected, hydroxy terminus for a possible coupling to DNA monomers to generate DNA–PNA-chimeras.[22]

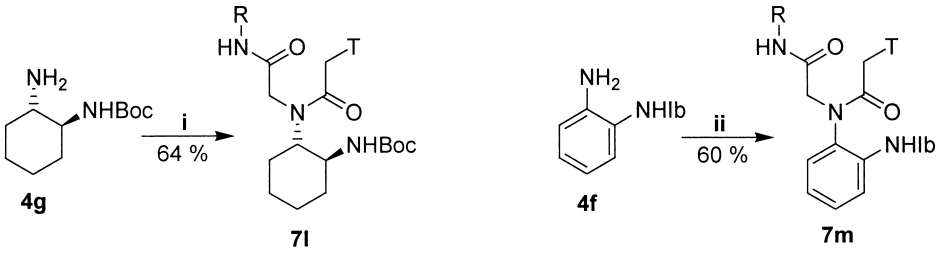
In case of Ugi reactions involving mono-Boc-ethylendiamine and formaldehyde formation of a by-product Mom-**7a** was observed. Excess of formaldehyde lead to methoxymethylenation of Boc-NH (Scheme 5). Since the resulting Boc-Mom-protection of the amino group is acid sensitive, the by-product shows the same

**Table 2.** Totally protected PNA-monomers **7** obtained from isocyanides **3**

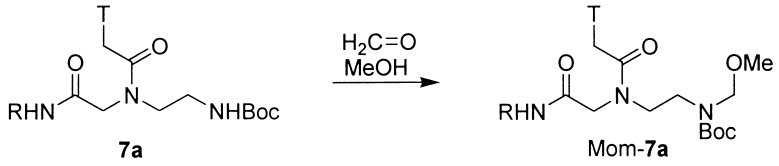



| Educt | Product | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | B | XPg[a] | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| **3a, 4a, 5a** | **7a** | $OCH_3$ | $NO_2$ | H | H | H | T | NHBoc | 64 |
| **3a, 4a, 5c** | **7b** | $OCH_3$ | $NO_2$ | H | H | H | $C^{Z}$ | NHBoc | 64 |
| **3a, 4a, 5b** | **7c** | $OCH_3$ | $NO_2$ | H | H | H | U | NHBoc | 64 |
| **3a, 4a, 5d** | **7d** | $OCH_3$ | $NO_2$ | H | H | H | $A^{Z}$ | NHBoc | 69 |
| **3a, 4a, 5f** | **7e** | $OCH_3$ | $NO_2$ | H | H | H | $G^{Bn}$ | NHBoc | 32 |
| **3a, 4a, 5e** | **7f** | $OCH_3$ | $NO_2$ | H | H | H | $G^{Z}$ | NHBoc | 20 |
| **3a, 4e, 5a** | **7g** | $OCH_3$ | $NO_2$ | H | H | H | T | OBn | 85 |
| **3a, 4a, 5a** | **7h** | $OCH_3$ | $NO_2$ | 1,4-DOSD[b] | | H | T | NHBoc | 83 |
| **3b, 4a, 5a** | **7i** | $NO_2$ | $OCH_3$ | 1,4-DOSD[b] | | H | T | NHBoc | 70 |
| **3a, 4a, 5a** | **7j** | $OCH_3$ | $NO_2$ | H | Ph | H | T | NHBoc | 41 |
| **3a, 4h, 5a** | **7k** | $OCH_3$ | $NO_2$ | H | H | $CH_3$ | T | NHBoc | 64 |

[a]Pg, protecting group.
[b]1,4-DOSD, 1,4-Dioxaspiro[4.5]dec-8-yl-.




**Scheme 4.** Employment of cyclic diamines in the 4CC; only one enantiomer for racemic **7l** is shown (R = 4-methoxy-2-nitro-phenyl). Reagents and conditions: (**i**) formaldehyde, **5a**, **3a**, MeOH, rt; (**ii**) formaldehyde, **5a**, **3a**, MeOH, rt.




**Scheme 5.** Methoxymethylenation of aeg-monomers (R = 4-methoxy-2-nitro-phenyl).

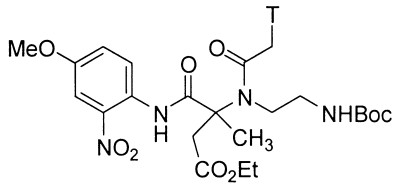
behaviour as the Boc protected monomer and may not be separated.

As the use of formaldehyde lead to the formation of a glycine unit in **7a**–**g** and **7k**–**m** almost any other α-amino acid unit is accessible through variation of the oxo compound in the Ugi 4CC. As examples, we would like to present compounds **7h**–**j** and **7n** leading to natural and unnatural amino acid units in totally protected PNA-monomers (Fig. 2).

Furthermore oxo compounds with additional (protected) functional groups allow the generation of polyfunctional PNA-monomers. The totally protected PNA-monomer **7n** contains a further carboxylic ending in the amino acid side chain as an additional coupling moiety for oligomerization or linkage of useful subunits. **7n** resulted from ethyl laevulinate as starting material in the Ugi transformation.

## Acidic hydrolysis to partially protected monomers

Vinylic amides **6** serve as versatile precursors of *N*-protected PNA-monomers and structural analogues thereof. We exposed compounds **6** to hydrolysis analogous to Keating's procedure[19] by treatment with THF/concd HCl to obtain the partially protected PNA-monomers **8**. Hydrolysis of Ugi-adduct **6a** lead to the formation of the known Boc-protected PNA-monomer **8a**[28] in moderate yield (Table 3).



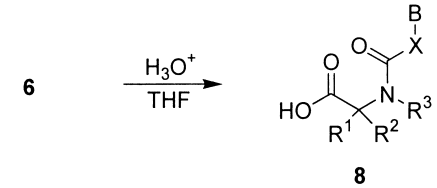

**7n**, 76 %

**Figure 2.** Polyfunctional PNA-monomer (R = 4-methoxy-2-nitro-phenyl).

In general, the synthesis of Boc-protected monomers requires special precautions. In some cases instability of Boc-amides under acidic reaction conditions leads to partial removal of the Boc-protecting group. As a consequence side reactions occur since free amino functions may act as nucleophiles, resulting in complex product mixtures.[19,23] Boc removal largely depends on acid concentration and reaction temperature. However, we succeeded in the synthesis of compounds **8a**, **8c**, **8g**, **8i** at 0 °C in moderate to good yields.

Some other Ugi-adducts like **6b** failed to give the corresponding Boc-protected PNA-monomers upon acidic hydrolysis and only complex product mixtures were obtained. Therefore, substitution of Boc-protecting group by acid stable protecting groups lead to the formation of **8e, 8f**, **8k, 8l** in high yields at room temperature. **8k**

**Table 3.** Yields of partially protected PNA-monomers **8**




| Educt | | PNA-monomer **8** | | | | | |
|---|---|---|---|---|---|---|---|
| | | $R^1$ | $R^2$ | $R^3$ | B | X | Yield (%) |
| **6a** | **8a** | H | H | Boc-ae[b] | T | $CH_2$ | 63[28] |
| **6c** | **8c** | 2-Cl-Ph | H | Boc-ae[b] | A[z] | $CH_2$ | 38 |
| **6e** | **8e** | $-(CH_2)_5-$ | | Etoc-ae[b] | T | $CH_2$ | 78 |
| **6f** | **8f** | $-(CH_2)_5-$ | | Z-ae[b] | T | $CH_2$ | 82 |
| **6g** | **8g** | $-(CH_2)_5-$ | | Boc-ae[b] | T | $CH_2$ | 82 |
| **6i** | **8i** | *t*-Bu | H | Boc-ae[b] | T | *o*-Bn | 47 |
| **6k** | **8k** | $-(CH_2)_5-$ | | Bn-oe[d] | T | $CH_2$ | 91 |
| **6l** | **8l** | 4-biPh[a] | H | *O*-Ib-An[c] | T | $CH_2$ | 66 |

[a]4-biPh, 4-biphenyl.
[b]ae: aminoethyl.
[c]*o*-Ib-An, *o*-*N*-isobutyryl-aniline.
[d]oe, oxyethyl.

Especially is an interesting monomer for the possible conjunction of PNA and DNA fragments in the synthesis of PNA-DNA–chimeras.[22]

When Ugi first reported on the synthesis of cyclohexenyl isocyanide and its use in the Ugi 4CC he observed an acid promoted conversion of the vinylic amide of the obtained bisamides to primary amides, which is in contrast to Keating's results.[24] Keating explained these contrasting observations by means of structural assignments of the starting Ugi-adducts.[19] Another factor influencing the course of the reaction may be the concentration of the desired nucleophile. In order to examine this we started some corresponding experiments. Treatment of **6m** with TFA in THF containing exactly one equivalent of water gave the primary amide **10** in good yield. Further hydrolysis of the carbamoyl group in **10** was not observed. Thus, no carboxylic acid was obtained upon hydrolysis of **6m**. The TFA mediated cleavage of Ugi-adducts like **6m** lead to interesting precursors **10** for novel aminals like **11**. The aminal **11** may serve as educt for the synthesis of retro-inverso PNAs. The synthesis of **11** starting from **10** should be possible following generally known Hofmann rearrangement and subsequent Boc-protection (Scheme 6).[25]

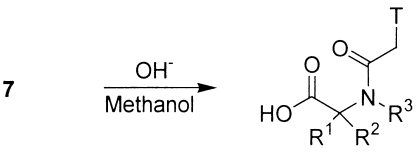
### Alkaline hydrolysis to partially protected monomers

In order to obtain the PNA-monomers **8a**, **9g**, **9j**, **9l** and **9m**, we have studied the alkaline deprotection of the corresponding Ugi products **7a**, **7g**, **7j**, **7l** and **7m**. Hydrolysis of the anilides was performed in methanol with six equivalents of KOH at room temperature and was monitored by TLC (Table 4).

We found that glycine containing bisamides **7a** and **7g** could easily be hydrolyzed to give the mono-protected monomers **8a**[28] and **9g** with a free carboxylic acid within a few hours. The quality of the *N*-alkyl/aryl linker section did not influence the success of alkaline hydrolysis, but it prolonged the reaction time with increasing steric demands (**9l**, **9m** versus **8a**, **9g**). Table 4 shows some synthesized glycine containing monomers with a free carboxylic acid obtained via alkaline hydrolysis.

The α-substituted species **7h–j** and **7n** proved to be much more resistant against alkaline hydrolysis compared to their glycine analogues, e.g., **7g**. In particular the anilides **7h** and **7i** with $R^3$ and $R^4 \neq H$ (see Table 2) were remarkably resistant to alkaline hydrolysis. As a consequence no regioselective cleavage of the amide bond was observed.[26]

**Table 4.** Yields of partially protected PNA-monomers **9** (R = 4-methoxy-2-nitrophenyl)




**9**

| Educt | | PNA-monomer **9** $R^1$ | $R^2$ | $R^3$ | Time (h)[a] | Yield (%) |
|---|---|---|---|---|---|---|
| **7g** | **9g** | H | H | Bn-oe[c] | 4 | 71 |
| **7j** | **9j** | H | Ph | Boc-ae[b] | 72 | 80 |
| **7l** | **9l** | H | H | Boc-ac[d] | 20 | 68[29] |
| **7m** | **9m** | H | H | *o*-Ib-An[e] | 19 | 83 |

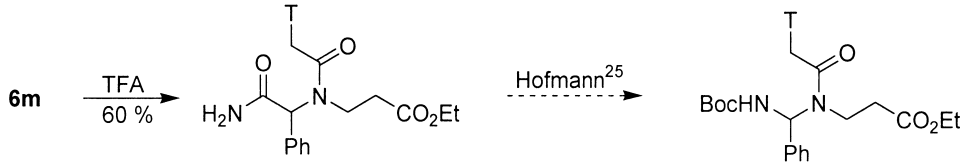
[a]Reaction time according to **GP6**.
[b]ae, aminoethyl.
[c]oe, oxyethyl.
[d]*o*-Ib-An, *o*-*N*-isobutyryl-aniline.
[e]ac, 2-aminocyclohexyl.

A convincing workaround for the synthesis of sterically crowded PNA-monomers was found in the substitution of the nucleobase by a hydroxy group in the carboxylic acid component for the Ugi 4CC. Scheme 7 shows the totally protected monomer **12** derived from glycolic acid with a hydroxy group as a nucleobase synthon.

The Ugi reaction with glycolic acid caused no problems and formed the totally protected PNA-precursor **12** in high yield. The regioselective alkaline cleavage to **13** was rapidly performed under standard conditions due to a stabilized transition state. In comparison the related thymine containing monomers lacking the hydroxy group in the side chain, like **7h**, were stable under these conditions for several weeks. The conversion of protected precursors for PNA-monomers like **13** via Mitsunobu reaction as outlined in Scheme 7 should be possible according to known protocols.[27]

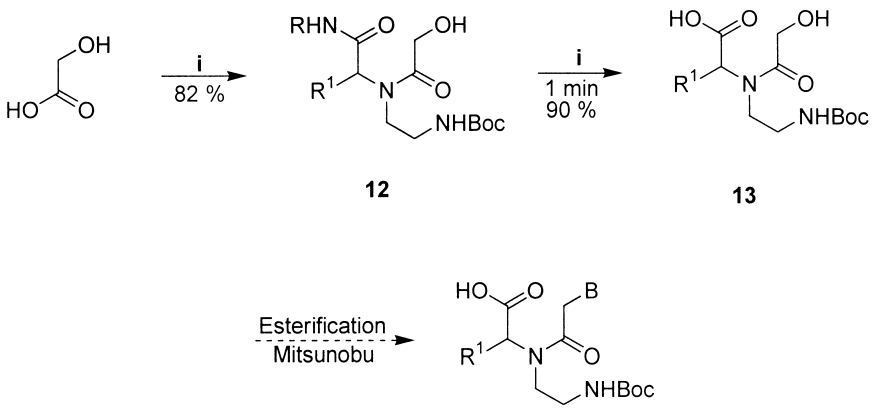
## Conclusion

In this article we described the synthesis of a novel class of totally protected monomers **6**, **7** for the preparation of PNAs or derivatives thereof. The protected PNA-monomers **6**, **7** are formed in a one pot procedure via Ugi–4CC with variable substitution pattern. They are converted to the mono-protected PNA-monomers **8** and **9** via regioselective acidic or alkaline hydrolysis.




**10** **11**

**Scheme 6.** Synthesis of a 'retro-inverso' PNA-monomer.




**Scheme 7.** Synthesis of PNA-monomers via precursors **12** and **13** (R = 4-methoxy-2-nitro-phenyl, $R^1$ = *t*-butyl). Reagents and conditions: **(i)** pivalaldehyde, **3a**, **4a**, MeOH, rt; **(ii)** 6 equiv KOH, MeOH.

The obtained cyclohexenyl amides **6** offer two routes of acid mediated conversions. The first route, a HCl-mediated hydrolysis with an excess of water, lead to *N*-protected PNA-monomers **8**. A lot of acid stable *N*-protecting groups are tolerated within the reaction sequence as demonstrated with the synthesis of **8e–f** and **8k–l**. In some cases even requirement of the acid labile Boc-protecting group lead to the formation of the desired *N*-protected monomers. The second route, a TFA-mediated cleavage of the secondary amides, lead to primary amides like **10**. These are useful precursors for monomers like **11** required for the synthesis of 'retro-inverso' PNAs.

The nitrophenyl amides **7a**, **7g**, **7j**, **7l** and **7m** were hydrolyzed to the corresponding PNA-monomers **8a**, **9g**, **9j**, **9l** and **9m** under alkaline conditions in case of the glycine derivatives. Hydrolysis of α-substituted monomers has not been successful yet. However, a workaround was found by the substitution of the nucleobase acetic acid by glycolic acid. The introduction of the nucleobase into the resulting carboxylic acid **13** should be possible according to known protocols.

Further routes for the alkaline[38] and acidic[39] cleavage of Ugi products have recently been reported and may provide attractive alternatives. Investigations in this direction are in progress.

## Experimental

### General remarks

If indicated with 'abs.', solvents were purified prior to use as follows: dichloromethane was distilled from $CaCl_2$, THF and $Et_2O$ were distilled from sodium and benzophenone, MeOH was distilled from magnesium turns. The following abbreviations are employed: thymin-1-yl (T), $N^2$-Z-guanin-9-yl ($G^Z$), 2-amino-6-benzyloxy-purin-9-yl ($G^{Bn}$), $N^6$-Z-adenin-9-yl ($A^Z$), $N^4$-Z-cytosin-1-yl ($C^Z$), trifluoroacetic acid (TFA), *tert*-butyloxycarbonyl (Boc), ethoxycarbonyl (Etoc), benzyloxycarbonyl (Z), acetyl (Ac), isobutyryl (Ib). The following compounds were prepared according to literature procedures: 4-methoxy-2-nitrophenyl isocyanide **3a**,[21b] 2-methoxy-4-nitrophenyl isocyanide **3b**,[21b] mono-Boc-ethylendiamine **4a**,[37] mono-Etoc-ethylendiamine **4b**,[30] mono-Z-ethylendiamine **4c**,[31] mono-acetyl-ethylendiamine **4d**,[32] *O*-benzyl-ethanolamine **4e**,[33] mono-Boc-cyclohexylendiamine **4g**,[29] *N*-1-carboxymethylthymine **5a**,[36] *N*-1-carboxymethyluracil **5b**,[34] $N^4$-Z-*N*-1-carboxymethylcytosine **5c**,[28] $N^6$-Z-*N*-9-carboxymethyladenine **5d**,[28] $N^2$-Z-*N*-9-carboxymethylguanine **5e**,[35] 2-amino-6-benzyloxy-*N*-9-carboxymethylpurine **5f**.[28] Thin layer chromatography (TLC) analyses were performed on silica gel Polygram® plates and fluorescence indicator from Macherey Nagel Co., Düren. For preparative chromatography Merck silica gel 60, 230–400 mesh, was used. Melting points were determined in open capillaries in a Dr. Lindström instrument and are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker-Karlsruhe AM 300 spectrometer (300 MHz/75 MHz) and on a Bruker-Karlsruhe ARX 500 spectrometer (500 MHz). Chemical shifts, δ, are presented in part per million (ppm) and coupling constants, *J*, in Hertz (Hz) from tetramethylsilane (TMS) as the internal standard in deuterated solvents such as $CDCl_3$ and DMSO-$d_6$. The NMR spectral assignments were established by analysis of the H,H-COSY, HMQC, HMBC NMR spectra. Mass spectra were obtained on a Finnigan-MAT 212 instrument in CI mode with *iso*-butane or $NH_3$ as reactant gas. Elemental analyses were performed on a C, H, N-Analyser EA 1108 from Fisons Instruments.

### General procedure for the synthesis of cyclohex-1-enyl-formamides 1 (GP1)

The appropriate cyclohexanone derivative (2 mol) and 99.1 g (2.2 mol) formamide were dissolved in 1000 mL toluene and treated with 1 mL concd $H_2SO_4$. The mixture was heated to reflux under Dean–Stark-conditions for 12 h. The solution was washed with water (200 mL) and brine (200 mL) and subsequently dried over $MgSO_4$. The solvent was removed under reduced pressure and the obtained crude product recrystallized from a suitable solvent.

### General procedure for the preparation of isocyanides 2 (GP2)

The appropriate formamide **1** (0.2 mol) and 64 ml abs. triethylamine were dissolved in 500 mL dichloromethane. The solution was cooled to 0 °C and 20 g (0.202 mol) phosgene were introduced over a period of about 2 min. After stirring for 1 h at 0 °C 140 mL water were added and the layers were separated. The organic layer was washed with 140 mL water two times and dried over $MgSO_4$. After evaporation of the solvent in vacuo the residue was subjected to flash chromatography on silica gel.

### General procedure for the preparation of totally protected PNA-monomers 6 (GP3)

The appropriate amino (2.5 mmol) and oxo compound (2.0 mmol) were dissolved in 7 mL abs. MeOH. The carboxylic acid (2.5 mmol) and isocyanide (2.0 mmol) were added and the solution was stirred for 48 h at room temperature. The solvent was removed in vacuo and the resulting crude product purified by column chromatography.

### General procedure for hydrolysis of vinylic amides 6 to *N*-protected PNA-monomers 8 (GP4)

Vinyl amide **6** was dissolved in a stock solution of 1 mL concd HCl and 9 mL THF at 0 °C. The solution was stirred for 5 h while slowly warming up to room temperature. Solid $Na_2CO_3$ was added for neutralization and the solution was filtered. The filtrate was evaporated to dryness in vacuo and the residue recrystallized from a suitable solvent to give the *N*-protected PNA-monomers **8**.

### General procedure for the preparation of totally protected PNA-monomers 7 (GP5)

Each 2.00 mmol of an amino compound and an oxo compound were dissolved in 7 mL of abs. MeOH. After a few minutes 2.00 mmol of a nitrophenylisocyanide and 2.00 mmol of a carboxylic acid were added and the mixture was stirred at room temperature for 48 h. After evaporation of the solvents in vacuo, the crude product was stirred in dichloromethane and formed amide by-product of compounds **4** and **5** was removed by filtration. The concentrated filtrate was precipitated from ether or purified via column chromatography on silica gel with dichloromethane:methanol (95:5).

### General procedure for the alkaline hydrolysis of nitro anilides 7a, 7g, 7j, 7l, 7m to *N*-protected PNA-monomers 8a, 9g, 9j, 9l, 9m (GP6)

0.30 mmol of a nitro anilide protected monomer **7** was dissolved in 6 mL of MeOH and 0.90 mL of a 2 N solution of KOH in MeOH (6 equiv of KOH) was added. The mixture was stirred at room temperature and TLC monitored. After complete hydrolysis, 20 mL of water was added, the mixture was washed three times, each with 20 mL of ether, slightly acidified with HCl and extracted five times with 20 mL of dichloromethane. The combined dichloromethane phases were dried and evaporated in vacuo. If necessary the products were recrystallized from dichloromethane to give the *N*-protected PNA-monomers.

***N*-Cyclohex-1-enyl-formamide 1a.** The title compound was prepared according to **GP1** using 196.3 g (2 mol) cyclohexanone as starting material. The enamide was recrystallized from *n*-hexane to yield 190.3 g (76%) of a colourless solid. Analytical data were consistent with literature data.[19]

***rac*-*N*-4-*tert*-Butyl-cyclohex-1-enyl-formamide 1b.** The title compound was prepared according to **GP1** using 308.5 g (2 mol) 4-*tert*-butylcyclohexanone as starting material. The enamide was recrystallized from *n*-hexane to yield 293.7 g (81%) of a colourless solid, mp: 108–110 °C. $^1$H NMR (300 MHz, $CDCl_3$, due to the existence of two rotamers in a 70:30 ratio several signals were doubled): δ 0.86 (ma.), 0.87 (mi.) (2s, 9H, *tert*-butyl-$CH_3$), 1.2–1.6 (m, 7H, CH, $CH_2$), 5.29 (ma.), 6.09 (mi.) (2m, 1H, C=CH), 6.59 (mi.), 7.74 (ma.) (br, 1H, NH), 8.14 (mi.), 8.32 (ma.) (s, d, 1H, OCH, $^3J = 11.6$ Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 23.51, 25.34, 27.15, 27.55, 27.98, 43.76, 110.73, 132.33, 161.27. MS (CI-isobutane): $m/z$ (%) = 182 (100) [$MH^+$]. $C_{11}H_{19}NO$ (181.3): calcd C 72.88, H 10.56, N 7.73; found C 73.08, H 10.62, N 7.81.

***rac*-*N*-4-Phenyl-cyclohexen-1-yl-formamide 1c.** The title compound was prepared according to **GP1** using 348.4 g (2 mol) 4-phenyl-cyclohexanone as starting material. The resulting crude product was stirred with hot *n*-hexane and filtered off after cooling to yield 322.0 g (80%) of a white solid, mp: 128–129 °C. $^1$H NMR (300 MHz, $CDCl_3$, due to the existence of isomers in a 56:22:22 ratio several signals were trebled): δ 1.5–2.8 (m, 7H, CH + $CH_2$), 5.37 (ma.), 6.18 (mi.), 6.59 (mi.) (3m, 1H, C=CH), 7.1–7.3 (m, 5H, arH), 7.99 (br, 1H, NH), 7.76 (mi.), 8.14 (mi.) (s, 0.44H, OCH), 8.36 (ma.) (d, 0.56H, OCH, $^3J = 11.6$ Hz). $^{13}$C NMR (75 MHz, $CDCl_3$, major isomer): δ 27.06, 29.11, 31.83, 39.51, 109.98, 126.28, 126.71, 128.42, 132.43, 145.66, 161.43. MS (CI-isobutane): $m/z$ (%) = 202 (100) [$MH^+$]. $C_{13}H_{15}NO$ (201.3): calcd C 77.58, H 7.51, N 6.96; found C 77.32, H 7.43, N 7.03.

**Cyclohexen-1-yl-isocyanide 2a.** The title compound was prepared according to **GP2** using 25.0 g (0.2 mol) of formamide **1a** as starting material. The resulting crude product was purified by flash chromatography (*n*-hexane:ethyl acetate, 95:5) to yield 15.2 g (71%) of a colourless liquid. Analytical data were consistent with literature data.[19]

***rac*-4-*tert*-Butyl-cyclohexen-1-yl-isocyanide 2b.** The title compound was prepared according to **GP2** using 36.3 g (0.2 mol) of formamide **1b** as starting material. The resulting crude product was purified by flash chromatography (*n*-hexane:ethyl acetate, 95:5) to yield 26.1 g (80%) of a colourless solid, mp: ~30 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.87 (s, 9H, $CH_3$), 1.2–1.4 (m, 7H,

cyclohexenyl-CH + $CH_2$), 6.02 (m, 1H, cyclohexenyl-C=CH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 23.13, 23.41, 25.68, 26.99, 27.20, 29.60, 31.98, 32.16, 38.45, 42.71, 45.98, 115.77, 129.05, 160.44. MS (CI-isobutane): *m*/*z* (%) = 164 (100) [$MH^+$]. $C_{11}H_{17}N$ (163.3): calcd C 80.93, H 10.50, N 8.59; found C 80.03, H 11.01, N 8.64.

***rac*-4-Phenyl-cyclohexen-1-yl-isocyanide 2c.** The title compound was prepared according to **GP2** using 40.2 g (0.2 mol) of formamide **1c** as starting material. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 99:1) to yield 26.0 g (71%) of a colourless solid, mp: ~40 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.8–2.8 (m, 7H, cyclohexenyl-CH + $CH_2$), 6.10 (m, 1H, cyclohexenyl-C=CH), 7.1–7.3 (m, 5H, arH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 28.86, 28.90, 31.94, 38.54, 124.65, 124.80, 126.54, 126.65, 128.41, 128.57, 144.88, 160.96. MS (CI-isobutane): *m*/*z* (%) = 184 (100) [$MH^+$]. $C_{13}H_{13}N$ (183.3): calcd C 85.21, H 7.15, N 7.64; found C 86.12, H 7.31, N 7.71.

***N*-2-Amino-phenyl-isobutyramide 4f.** To a well stirred solution of 2.16 g (20 mmol) *ortho*-phenylendiamine in 150 ml dichloromethane (abs.) was added a mixture of 1.07 g (10 mmol) isobutyryl chloride and 50 ml dichloromethane (abs.) at room temperature via a dropping funnel (time: 30 min). The resulting suspension was stirred overnight at room temperature, filtered off and the filtrate was evaporated to dryness in vacuo. The resulting yellowish precipitate was identified as the mono-protected diamine **4f**. Yield: 1.48 g (83%). $^1$H NMR ($CDCl_3$/DMSO-$d_6$): δ 1.16 (d, 6H, CH–($CH_3$)$_2$), 2.71 (m, 1H, C*H*-($CH_3$)$_2$), 6.44–7.42 (m, 4H, arH), 8.97 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$): δ 18.25, 33.25, 115.01, 115.53, 123.51, 123.95, 124.43, 140.16, 174.21. MS (CI-isobutane): *m*/*z* = 179 (100) [$MH^+$].

***rac*-1-Boc-amino-2-aminopropane 4h.** To a well stirred solution of 62 g (836 mmol) *rac*-1,2-propylendiamine in 200 mL abs. dimethylformamide was added a solution of 20 g (83,6 mmol) *tert*-butyl-4-nitrophenyl-carbonate in 150 mL abs. dimethylformamide at room temperature via a dropping funnel (time: 1 h). The yellowish solution was stirred overnight at room temperature. The solution was evaporated to dryness in vacuo and the residue was dissolved in 150 mL water. The solution was adjusted to pH 4 at 0 °C and extracted three times with 50 mL dichloromethane. After extraction the water phase was adjusted to pH 10 and extracted three times with 50 mL chloroform. The combined organic extracts were dried with $MgSO_4$, filtered off and evaporated to dryness in vacuo. The resulting yellowish oil was identified as the mono-protected diamine **4h**. Yield: 5.56 g (38%). $^1$H NMR ($CDCl_3$): δ 0.97 (d, 3H, $CH_2$–CH–C*H*$_3$), 1.38 (s, 9H, (C*H*$_3$)$_3$), 2.71–3.10 (m, 3H, C*H*$_2$–C*H*–$CH_3$), 5.18 (s, 1H, NH). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ 21.22, 28.20, 46.71, 48.35, 78.83, 156.12.

***rac*-2-(Thymin-1-yl)-hexanoic acid 5g.** 6.3 g (50 mmol) Thymine, 10.45 g methyl *rac*-2-bromocapronate and 7.5 g potassium carbonate were suspended in 250 mL abs. dimethylsulfoxide and heated to reflux for 2 h. The yellowish solution was stirred for 20 h at room temperature. The solution was evaporated to dryness in vacuo and the residue was dissolved in 200 mL dichloromethane and 200 mL water. After separation of the two phases the water phase was extracted three times with 50 mL dichloromethane. The combined organic extracts were dried with $MgSO_4$, filtered off and evaporated to dryness in vacuo. The resulting yellowish oil was dissolved in 100 mL 2 N NaOH and heated to reflux for 2 h. After cooling to room temperature the solution was adjusted to pH 1 with 4 N HCl. The resulting precipitate was filtered off, washed with ether and dried in vacuo. The product was obtained as a colourless solid in 8.77 g (73%) yield, mp: 192 °C. $^1$H NMR ($CDCl_3$/DMSO-$d_6$): δ 0.84 (t, 3H, ($CH_2$)$_3$C*H*$_3$), 1.27 (m, 4H, ($CH_2$)$_2$), 1.79 (s, 3H, thyminyl-$CH_3$), 1.95 (m, 2H, C*H*$_2$–($CH_2$)$_2$–C*H*$_3$), 4.97 (q, 1H, CH), 7.33 (s, 1H, C=CH). $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$): δ 11.98, 12.62, 21.42, 27.55, 28.79, 57.02, 108.96, 138.60, 151.07, 163.79, 171.35. MS (CI-isobutane): *m*/*z* (%) = 241 (100) [$MH^+$]. $C_{11}H_{16}N_2O_4$ (240.3): calcd C 54.99, H 6.71, N 11.66; found C 55.23, H 6.79, N 11.81.

**2-(Thymin-1-yl)-methyl-benzoic acid 5h.** 10.1 g (80 mmol) Thymine, 21.28 g methyl *ortho*-bromomethylen-benzoate and 13 g potassium carbonate were suspended in 300 mL abs. dimethylformamide and heated to reflux for 2 h. The yellowish solution was stirred for 2 days at room temperature. The solution was filtered off and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in 150 mL dichloromethane and 150 mL water. After separation of the two phases the water phase was extracted three times with 50 mL dichloromethane. The combined organic extracts were dried over $MgSO_4$, filtered off and evaporated to dryness in vacuo. The resulting yellowish oil was dissolved in 150 mL 2 N NaOH and stirred for 2 days. The solution was adjusted to pH 1 with 4 N HCl. The resulting precipitate was filtered off, washed with ether and dried in vacuo. The product was obtained as a colourless solid in 6.70 g (32%) yield, mp: 249 °C (dec.). $^1$H NMR ($CDCl_3$/DMSO-$d_6$): δ 1.81 (s, 3H, thyminyl-$CH_3$), 5.30 (s, 2H, $CH_2$–Ph), 7.14–7.98 (m, 4H, arH), 7.42 (s, 1H, thyminyl-H). $^{13}$C NMR ($CDCl_3$/DMSO-$d_6$): δ 11.99, 49.16, 109.06, 126.29, 127.23, 129.21, 130.79, 132.51, 138.32, 141.79, 151.14, 164.40, 168.09. MS (CI-isobutane): *m*/*z* (%) = 261 (100) [$MH^+$]. $C_{13}H_{12}N_2O_4$ (260.3): calcd C 60.00, H 4.65, N 10.76; found C 60.21, H 4.86, N 10.89.

**2-($N^4$-Z-Cytosin-1-yl)-methyl-benzoic acid 5i.** 19.6 g (80 mmol) $N^4$-Z-cytosine, 21.28 g methyl *ortho*-bromomethylen-benzoate and 13 g potassium carbonate were suspended in 300 mL dimethylformamide (abs.) and heated to reflux for 2 h. The suspension was stirred for 2 days at room temperature. The solution was filtered off and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in 150 mL dichloromethane and 150 mL water. After separation of the two phases the water phase was extracted three times with 50 mL dichloromethane. The combined organic extracts were dried over $MgSO_4$, filtered off and evaporated to dryness in vacuo. The resulting yellowish oil was dissolved in 150 mL 2 N NaOH and stirred for two days. The

solution was adjusted to pH 1 with 4 N HCl. The resulting precipitate was filtered off, washed with ether and dried in vacuo. The product was obtained as a colourless solid in 15.48 g (51%) yield, mp: 197–199 °C (dec.). $^1$H NMR (DMSO-$d_6$): δ 5.21 (s, 2H, $CH_2$–Ph), 5.38 (s, 2H, Z–$CH_2$), 6.96–8.12 (m, 9H, arH), 7.06 (d, 1H, cytosine-CH), 7.96 (d, 1H, cytosine-CH). $^{13}$C NMR (DMSO-$d_6$): δ 51.22, 66.48, 94.41, 126.88, 127.33, 127.92, 128.15, 128.47, 129.48, 130.72, 132.39, 135.98, 137.85, 150.37, 153.21, 155.12, 163.06, 168.09. MS (CI-isobutane): $m/z$ (%) = 380 (100) [$MH^+$]. $C_{13}H_{12}N_2O_4$ (379.4): calcd C 63.32, H 4.52, N 11.08; found C 63.30, H 4.57, N 11.21.

**2-[(2-Boc-aminoethyl)-thyminacetyl-amino]-acetic acid-(cyclohexen-1-yl)-amide 6a.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2 mmol) paraformaldehyde, 0.46 g (2.5 mmol) *N*-1-carboxymethyl-thymine **5a**, and 0.21 g (2.0 mmol) isocyanide **2a** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane: methanol, 95:5) to yield 0.70 g (76%) of a colourless solid, mp: 154 °C. $^1$H NMR (300 MHz, DMSO-$d_6$, due to the existence of two rotamers in a 60:40 ratio several signals were doubled): δ 1.32 (s, 9H, Boc-$CH_3$), 1.4–2.1 (m, 8H, cyclohexenyl-$CH_2$), 1.71, 1.73 (2s, 3H, T-Ac-$CH_3$), 2.8–3.2 (m, 4H), 3.91 (ma.), 4.05 (mi.) (s, 2H, $CH_2$), 4.48 (mi.), 4.62 (ma.) (s, 2H, $CH_2$), 6.00 (ma.), 6.08 (mi.) (m, 1H, cyclohexenyl-C=CH), 6.92 (mi.), 7.07 (ma.) (br, 1H, Boc-NH), 7.30 (mi.), 7.35 (ma.) (s, 1H, T-Ac-C = CH), 8.86 (ma.), 9.25 (mi.) (s, 1H, cyclohexenyl-NH), 11.25 (br, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$, due to the existence of two rotamers in a 60:40 ratio several signals were doubled): δ 11.85, 15.12, 21.73, 22.11, 23.49, 27.13, 28.16, 30.76, 35.78, 37.30, 37.92, 45.12, 47.27, 47.61, 49.31, 50.15, 62.80, 64.90, 77.68, 78.00, 107.26, 108.08, 110.29, 110.83, 133.27, 142.10, 142.81, 151.04, 155.61, 161.29, 162.31, 164.40, 166.32, 167.07, 167.85, 170.44. MS (CI-$NH_3$): $m/z$ (%) = 481 (15) [$MH^+ + NH_3$]. $C_{22}H_{33}N_5O_6$ (463.5): calcd C 57.01, H 7.18, N 15.11; found C 57.06, H 7.24, N 15.16.

**2-[(2-Boc-aminoethyl)-($N^4$-Z-cytosinacetyl)-amino]-3,3-dimethyl-butyric acid-(4-*tert*-butyl-cyclohexen-1-yl)-amide 6b.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.17 g (2 mmol) pivalaldehyde, 0.76 g (2.5 mmol) $N^4$-Z-*N*-1-carboxymethyl cytosine **5c**, and 0.33 g (2.0 mmol) isocyanide **2b** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 1.35 g (97%) of a colourless solid. $^1$H NMR (300 MHz, $CDCl_3$, due to the existence of two diastereomers in a 63:37 ratio several signals were doubled): δ 0.81 (s, 9H, 4-*tert*-butyl-cyclohexenyl-$CH_3$), 0.98 (ma.), 1.07 (mi.) (2s, 9H, $C(CH_3)_3$), 1.35 (mi.), 1.36 (ma.) (2s, 9H, Boc-$CH_3$), 1.7–2.2 (m, 7H, 4-*tert*-butyl-cyclohexenyl-CH, $CH_2$), 3.1–4.0 (m, 4H), 4.04 (ma.), 4.38 (mi.) (2s, 1H, C*H*C$(CH_3)_3$), 4.76 (m, 1H, C-Z-Ac-$CH_2$), 5.07 (m, 1H, C-Z-Ac-$CH_2$), 5.15 (ma.), 5.17 (mi.) (2s, 2H, Z-$CH_2$), 5.94 (ma.), 6.08 (2m, 1H, 4-*tert*-butyl-cyclohexenyl-C=CH), 7.18 (d, 1H, C-Z-Ac-CH=CH, $^3J$ = 7.0 Hz), 7.32 (m, 5H, arH), 7.63 (ma.), 7.90 (mi.) (2d, 1H, C-Z-Ac-CH=CH, $^3J$ = 7.0 Hz), 7.97 (br, 1H, 4-*tert*-butyl-cyclohexenyl-NH), 8.6 (br, 1H, Z-NH). MS (CI-$NH_3$): $m/z$ (%) = 695 (50) [$MH^+$], 712 (40) [$MH^+ + NH_3$]. $C_{37}H_{54}N_6O_7$ (694.9): calcd C 63.96, H 7.83, N 12.09; found C 63.78, H 7.91, N 12.03.

***rac*-2-[(2-Boc-aminoethyl)-$N^6$-Z-adeninacetyl-amino]-*ortho*-chlorophenylacetic acid-(cyclohexen-1-yl)-amide 6c.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.28 g (2 mmol) 2-chlorobenzaldehyde, 0.65 g (2 mmol) $N^6$-Z-*N*-9-carboxymethyl adenine **5d**, and 0.21 g (2.0 mmol) isocyanide **2a** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 1.12 g (78%) of a colourless solid, mp: 154–155 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): δ 1.33 (s, 9H, Boc-$CH_3$), 1.50 (m, 4H, cyclohexenyl-$CH_2$), 2.02 (m, 4H, cyclohexenyl-$CH_2$), 2.61 (m, 1H, $NCH_2CH_2$), 3.18 (m, 1H, $NCH_2CH_2$), 3.34 (m, 1H, $NCH_2CH_2$), 3.54 (m, 1H, $NCH_2CH_2$), 5.23 (s, 2H, Z-$CH_2$), 5.46 (s, 2H, cyclohexenyl-C=CH, NCH), 6.02 (d, 1H, A-Z-Ac-$CH_2$, $^2J$ = 14.9 Hz), 6.17 (d, 1H, A-Z-Ac-$CH_2$, $^2J$ = 14.9 Hz), 6.83 (br, 1H, Boc-NH), 7.39 (m, 9H, arH), 8.42 (s, 1H, A-Z-Ac-N=CH), 8.63 (s, 1H, A-Z-Ac-NCH), 9.63 (s, 1H, cyclohexenyl-NH), 10.63 (br, 1H, Z-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 21.60, 22.03, 23.49, 26.93, 28.80, 43.98, 44.22, 48.57, 59.96, 66.22, 77.92, 111.23, 122.94, 127.77, 127.89, 128.34, 129.72, 129.97, 130.33, 132.99, 133.23, 134.82, 136.35, 145.31, 149.37, 151.52, 152.13, 152.33, 155.54, 166.74, 166.97, 167.19. MS (CI-$NH_3$): $m/z$ (%) = 735 (15) [$MH^+ + NH_3$]. $C_{36}H_{41}N_8O_6Cl$ (717.2): calcd C 60.29, H 5.76, N 15.62; found C 60.25, H 5.72, N 15.62.

***rac*-2-[(2-Boc-aminoethyl)-(2-amino-6-benzyloxy-*N*-9-purinacetyl)-amino]-*ortho*-chlorophenylacetic acid-(cyclohexen-1-yl)-amide 6d.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.28 g (2 mmol) 2-chlorobenzaldehyde, 0.75 g (2.5 mmol) 2-amino-6-benzyloxy-*N*-9-carboxymethyl purine **5f**, and 0.21 g (2.0 mmol) isocyanide **2a** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 0.43 g (31%) of a colourless solid, mp: 120–121 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.39 (s, 9H, Boc-$CH_3$), 1.5–2.0 (m, 8H, cyclohexenyl-$CH_2$), 2.8–3.6 (m, 4H, $NCH_2CH_2$), 4.84 (d, 2H, G-Bz-Ac-$CH_2$, $^3J$ = 16.5 Hz), 5.02 (m, 2H, G-Bz-Ac-$CH_2$, Boc-NH), 5.49 (s, 2H, Z-$CH_2$), 5.94 (m, 1H, cyclohexenyl-C=CH), 6.07 (s, 1H, NCH), 6.12 (br, 2H, $NH_2$), 7.1–7.5 (m, 9H, arH), 7.86 (s, 1H, G-Bz-Ac-CH). MS (CI-$NH_3$): $m/z$ (%) = 707 (20) [$MH^+ + NH_3$]. $C_{35}H_{41}N_8O_5Cl$ (689.2): calcd C 60.99, H 6.00, N 16.26; found C 60.86, H 5.89, N 16.30.

***rac*-1-[(2-Etoc-aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid-(4-*tert*-butyl cyclohexen-1-yl-amide 6e.** The title compound was prepared according to **GP3** using 0.33 g (2.5 mmol) mono-Etoc-ethylendiamine **4b**, 0.20 g (2 mmol) cyclohexanone, 0.46 g (2.5 mmol) *N*-1-carboxymethylthymine **5a**, and 0.33 g (2.0 mmol)

isocyanide **2c** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 1.10 g (98%) of a colourless solid, mp: 165 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.82 (s, 9H, $C(CH_3)_3$), 1.25 (t, 3H, $CH_2CH_3$, $^3J$ = 7.6 Hz), 1.4–2.4 (m, 17H), 1.87 (s, 3H, T-Ac-CH=C), 3.27–3.61 (m, 4H), 4.12 (q, 2H, $CH_2CH_3$, $^3J$ = 7.6 Hz), 4.64 (br, 2H, T-Ac-$CH_2$), 5.78 (br, 1H, Etoc-NH), 6.17 (m, 1H, 4-*tert*-Bu-cyclohexenyl-C=CH), 6.94 (s, 1H, T-Ac-CH=$CCH_3$), 7.74 (br, 1H, NH), 9.94 (br, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.07, 14.51, 22.37, 23.63, 25.38, 27.00, 27.34, 28.91, 31.91, 32.37, 41.29, 43.38, 49.93, 53.34, 61.00, 66.40, 109.98, 113.57, 132.89, 141.49, 151.19, 157.53, 164.58, 168.77, 171.81. MS (CI-$NH_3$): *m*/*z* (%) = 577 (10)[$MH^+ + NH_3$]. $C_{29}H_{45}N_5O_6$ (559.4): calcd C 62.23, H 8.10, N 12.51; found C 62.68, H 7.95, N 12.62.

***rac*-1-[(2-Z-Aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid-(4-phenyl cyclohexen-1-yl)-amide 6f.** The title compound was prepared according to **GP3** using 0.49 g (2.5 mmol) *mono*-Z-ethylendiamine **4c**, 0.20 g (2 mmol) cyclohexanone, 0.46 g (2.5 mmol) *N*-1-carboxymethylthymine **5a**, and 0.37 g (2.0 mmol) isocyanide **2c** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane: methanol, 95:5) to yield 1.02 g (80%) of a colourless solid, mp: 154 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$, due to the existence of two rotamers in a 60:40 ratio several signals were doubled and extremely broadened): δ 1.3–2.7 (m, 17H), 1.81 (s, 3H, T-Ac-CH=C), 3.39–3.72 (m, 4H), 4.52 (m, 0.8H, T-Ac-$CH_2$), 5.12 (m, 1.2H, T-Ac-$CH_2$), 5.5–5.7 (m, 1H, Z-NH), 6.0–6.5 (m, 3H, Z-$CH_2$ + 4-phenyl-cyclohexenyl-C=CH), 6.81 (s, 0.6H, T-Ac-C*H*=$CCH_3$), 7.00 (s, 0.4H, T-Ac-C*H*=$CCH_3$), 7.1–7.4 (m, 10H, ar-H), 7.80 (br, 1H, NH), 9.76 (br, 0.6H, T-Ac-NH), 10.84 (br, 0.4H, T-Ac-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.16, 22.46, 25.19, 28.37, 29.31, 30.46, 32.36, 33.44, 33.82, 36.64, 39.50, 41.24, 42.60, 43.52, 49.84, 52.59, 53.37, 66.07, 66.81, 109.66, 110.09, 110.84, 113.13, 125.96, 126.14, 126.68, 128.23, 128.47, 128.77, 128.99, 132.78, 133.56, 136.19, 137.09, 141.48, 146.38, 147.04, 151.11, 151.87, 157.22, 158.39, 164.56, 167.14, 169.00, 171.11, 171.98. MS (CI-$NH_3$): *m*/*z* (%) = 660 (10) [$MH^+ + NH_3$]. $C_{36}H_{43}N_5O_6$ (641.8): calcd C 67.38, H 6.75, N 10.91; found C 65.98, H 6.87, N 11.03.

***rac*-1-[(2-Boc-aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid-(4-phenyl cyclohexen-1-yl)-amide 6g.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.20 g (2 mmol) cyclohexanone, 0.46 g (2.5 mmol) *N*-1-carboxymethylthymine **5a**, and 0.37 g (2.0 mmol) isocyanide **2c** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 1.10 g (90%) of a colourless solid, mp: 115 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.45 (s, 9H, Boc-$CH_3$), 1.4–2.4 (m, 16H, $CH_2$), 1.89 (s, 3H, T-Ac-CH=C), 2.75 (m, 1H, CH-phenyl), 3.39, 3.56 (m, 4H, $NCH_2CH_2$), 4.62 (s, 2H, T-Ac-$CH_2$), 5.51 (m, 1H, Boc-NH), 6.03 (m, 1H, cyclohexenyl-C=CH), 6.98 (s, 1H, T-Ac-CH=$CCH_3$), 7.87 (br, 1H, NH), 9.68 (br, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.16, 22.44, 25.21, 26.87, 28.28, 29.40, 32.33, 32.57, 39.56, 41.12, 41.82, 43.61, 49.94, 50.43, 66.58, 79.91, 110.30, 113.63, 125.98, 126.66, 128.26, 128.47, 132.82, 141.39, 146.36, 151.22, 156.58, 164.49, 169.04, 172.09. MS (CI-$NH_3$): *m*/*z* (%) = 626 (10) [$MH^+ + NH_3$]. $C_{33}H_{45}N_5O_6$ (607.8): calcd C 65.22, H 7.46, N 11.52; found C 65.10, H 7.44, N 11.49.

**2-[(2-Boc-aminoethyl)-(2-thyminhexanoyl)-amino]-*ortho*-chlorophenyl-acetic acid-(cyclohexen-1-yl)-amide 6h.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.28 g (2 mmol) 2-chlorobenzaldehyde, 0.60 g (2.5 mmol) *rac*-2-(thyminyl-1-yl)-hexanoic acid **5g**, and 0.21 g (2.0 mmol) isocyanide **2a** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 0.49 g (39%) of a colourless solid (mixture of two diastereomers in a 50:50 ratio). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.81 (m, 3H, $C_3H_6$–C*H*$_3$), 1.12–1.40 (m, 4H, $CH_2$–($CH_2$)$_2$–$CH_3$), 1.31, 1.35 (2 s, 9H, Boc-$CH_3$), 1.49–1.68, 1.99–2.18 (2m, 8H, cyclohexenyl-$CH_2$), 1.71–1.95 (m, 2H, C*H*$_2$–($CH_2$)$_2$–$CH_3$), 1.76, 1.81 (2s, 3H, thyminyl-$CH_3$), 2.89–3.46 (m, 4H), 4.86 (m, 1H, $C_4H_9$–C*H*), 6.00, 6.02 (2s, 1H, cyclohexenyl-C=CH), 6.43, 6.45 (2s, 1H), 7.29–7.54 (m, 5H, thyminyl-H, ar-H). MS (CI-$NH_3$): *m*/*z* (%) = 648 (10) [$MH^+ + NH_3$]. $C_{32}H_{44}ClN_5O_6$ (630.18): calcd C 60.99, H 7.04, N 11.11; found C 60.62, H 7.17, N 11.09.

***rac*-2-[(2-Boc-aminoethyl)-(2-thymin-methyl-benzoyl)-amino]-3,3-dimethyl-butyric acid-(cyclohexen-1-yl)-amide 6i.** The title compound was prepared according to **GP3** using 0.40 g (2.5 mmol) mono-Boc-ethylendiamine **4a**, 0.15 g (2 mmol) pivalaldehyde, 0.65 g (2.5 mmol) 2-(thymin-1-yl)-methyl-benzoic acid **5h**, and 0.21 g (2.0 mmol) isocyanide **2b** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 0.56 g (52%) of a colourless solid, mp: 164–166 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): (the title compound exists as a 90:10 mixture of rotamers in $CDCl_3$ at room temperature) δ 0.99, 1.15 (2s, 9H, CH–C(C*H*$_3$)$_3$), 1.32, 1.41 (2s, 9H, C–($CH_3$)$_3$), 1.56–1.65, 2.07–2.18 (2m, 8H, ($CH_2$)$_4$), 1.80, 1.83 (2s, 3H, thyminyl-$CH_3$), 2.91–3.96 (m, 4H), 4.82 (br, 1H), 5.00, 5.30, 5.51 (br, 2H, Ph-$CH_2$), 6.09 (br, 1H, cyclohexenyl-C=CH), 7.23–7.58 (m, 5H, thyminyl-H, ar-H), 8.52 (br, 1H, cyclohexenyl-NH). MS (CI-$NH_3$): *m*/*z* (%) = 557 (25) [$MH^+$ + $NH_3$]. $C_{28}H_{37}N_5O_6$ (539.30): calcd C 62.36, H 6.91, N 12.99; found C 62.31, H 6.94, N 13.41.

**2-[(2-Acetyl-aminoethyl)-(2-$N^4$-Z-cytosin-methyl-benzoyl)-amino]-phenyl-acetic acid-(4-*tert*-butyl-cyclohexen-1-yl)-amide 6j.** The title compound was prepared according to **GP3** 0.25 g (2.5 mmol) *mono*-acetyl-ethylendiamine **4d**, 0.21 g (2 mmol) benzaldehyde, 0.95 g (2.5 mmol) 2-($N^4$-Z-cytosin-1-yl)-methyl-benzoic acid **5i**, and 0.33 g (2 mmol) isocyanide **2b** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 0.70 g (48%) of a colourless solid (racemic mixture of two diastereomers in a 50:50 ratio). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.82 (s, 9H, (C*H*$_3$)$_3$), 1.12–1.36, 1.70–2.31

(2m, 10H, ($CH_2$)$_3$, ($CH_3$)$_3$–C*H*, CO–C$H_3$), 2.92–3.41 (m, 4H), 5.23–5.49 (m, 5H, Z-$CH_2$, Ph-$CH_2$, CH-Ph), 6.10 (br, 1H, cyclohexenyl-C=CH), 7.28–7.94 (m, 16H, arH, cytosine-H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 23.16, 23.64, 25.45, 28.95, 28.95, 29.60, 27.12, 32.06, 38.27, 43.44, 67.67, 95.27, 114.27, 126.63, 127.42, 128.19, 128.59, 128.93, 129.25, 129.78, 132.46, 133.02, 134.07, 149.93, 168.33, 170.18. MS (CI-$NH_3$): *m*/*z* (%) = 750 (15) [$MH^+ + NH_3$]. $C_{42}H_{47}N_6O_6$ (731.87): calcd C 68.93, H 6.47, N 11.48; found C 68.96, H 6.37, N 11.31.

***rac*-2-[(2-Benzyloxyethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid-(4-*tert*-butyl cyclohexen-1-yl)-amide 6k.** The title compound was prepared according to **GP3** using 0.38 g (2.5 mmol) *O*-benzyl ethanolamine **4e**, 0.20 g (2 mmol) cyclohexanone, 0.46 g (2.5 mmol) *N*-1-carboxymethylthymine **5a**, and 0.33 g (2.0 mmol) isocyanide **2b** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 95:5) to yield 0.94 g (81%) of a colourless solid, mp: 234 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 0.84 (s, 9H, C($CH_3$)$_3$), 1.3–2.2 (m, 17H), 1.78 (s, 3H, T-Ac-CH=C), 3.69 (m, 4H), 4.45–4.61 (m, 4H, Bz-$CH_2$ + T-Ac-$CH_2$), 6.01 (m, 1H, 4-*tert*-Bu-cyclohexenyl-C=CH), 7.25–7.39 (m, 6H, arH + T-Ac-CH=C$CH_3$), 8.32 (br, 1H, NH), 9.01 (br, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.20, 22.17, 23.65, 25.24, 25.45, 27.15, 27.56, 32.07, 32.96, 41.29, 43.57, 50.76, 66.46, 68.59, 73.97, 110.16, 112.68, 127.95, 128.15, 128.48, 132.81, 137.64, 141.19, 150.98, 164.22, 170.49. MS (CI-$NH_3$): *m*/*z* (%) = 597 (10) [$MH^+ + NH_3$]. $C_{33}H_{46}N_4O_5$ (578.8): calcd C 68.49, H 8.01, N 9.68; found C 67.10, H 7.98, N 9.79.

***rac*-2-[(2-Ib-Aminophenyl)-thyminacetyl-amino]-biphenyl-4-yl-acetic acid-(cyclohexen-1-yl)-amide 6l.** The title compound was prepared according to **GP3** using 0.45 g (2.5 mmol) mono-Ib-*ortho*-phenylendiamine **4f**, 0.36 g (2 mmol) 4-phenyl benzaldehyde, 0.46 g (2.5 mmol) *N*-1-carboxymethylthymine **5a**, and 0.21 g (2.0 mmol) isocyanide **2a** as starting materials. The resulting crude product was purified by flash chromatography (dichloromethane:methanol, 90:10) to yield 0.65 g (51%) of a colourless solid, mp: > 250 °C. $^1$H NMR (300 MHz, DMSO-$d_6$): δ 1.21 (d, 3H, CH(C$H_3$)$_2$, $^3J$ = 6.6 Hz), 1.24 (d, 3H, CH(C$H_3$)$_2$, $^3J$ = 6.6 Hz), 1.50 (m, 4H, $CH_2$), 1.73 (s, 3H, T-Ac-$CH_3$), 2.08 (m, 4H, $CH_2$), 2.90 (m, 1H, C*H*($CH_3$)$_2$, $^3J$ = 6.6 Hz), 3.92 (d, 1H, T-Ac-$CH_2$, $^2J$ = 16.5 Hz), 4.00 (d, 1H, T-Ac-$CH_2$, $^2J$ = 16.5 Hz), 5.88 (s, 1H, NCH), 6.10 (s, 1H, cyclohexenyl-C=CH), 6.7–8.3 (m, 14H, arH, T-Ac-C=CH), 9.47 (s, 1H, NH), 11.22 (s, 1H, NH), 11.32 (s, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 11.84, 19.39, 19.60, 21.22, 21.99, 23.51, 26.90, 35.32, 48.80, 65.66, 107.83, 111.54, 120.19, 122.63, 125.78, 126.25, 126.39, 127.05, 127.66, 128.84, 129.28, 130.10, 131.83, 133.29, 138.42, 138.85, 139.97, 142.01, 150.76, 150.99, 164.34, 167.28, 169.69, 170.02, 175.81. MS (CI-$NH_3$): *m*/*z* (%) = 651 (10) [$MH^+ + NH_3$]. $C_{37}H_{39}N_5O_5$ (633.6): calcd C 70.12, H 6.20, N 11.05; found C 70.49, H 6.24, N 11.07.

**3-[(2-Ethoxycarbonylethyl)-thyminacetyl-amino]-phenylacetic acid-(4-*tert*-butyl-cyclohexen-1-yl)-amide 6m.** 1.54 g (10 mmol) β-Alaninethylester-hydrochloride, 1.06 g (10 mmol) benzaldehyde, and 1.56 ml (12 mmol) triethylamine were dissolved in 40 mL toluene and stirred for 24 h at room temperature. The solvent was evaporated and the residue dissolved in 40 mL abs. MeOH. After addition of 1.84 g (10 mmol) *N*-1-carboxymethylthymine **5a** and 1.64 g (10 mmol) isocyanide **2b** the reaction mixture was stirred for 48 h at room temperature. The solvent was removed in vacuo and the crude product purified by flash chromatography to yield 3.34 g (60%) of a colourless solid (racemic mixture of two diastereomers in a 60:40 ratio). $^1$H NMR (300 MHz, $CDCl_3$): δ 0.73–0.89, 1.29–1.61, 1.99–2.63 (3m, 9H, C$H_2$–COOEt, ($CH_2$)$_3$, ($CH_3$)$_3$–C*H*), 0.91 (s, 9H, (C$H_3$)$_3$), 1.21 (m, 3H, COO–$CH_2$–C$H_3$), 1.87 (s, 3H, thyminyl-$CH_3$), 3.47–3.79 (m, 2H, N–C$H_2$–$CH_2$–COOEt), 4.07 (m, 2H, COO–C$H_2$–$CH_3$), 4.58, 4.83 (2d, 2H, T-$CH_2$), 5.71, 5.79, 5.83, 5.88 (4s, 1H, NCH), 6.02, 6.12, 6.29, 6.33 (4bs, 1H, cyclohexenyl-C=CH), 7.02 (2s, 1H, thyminyl-H), 7.28–7.53 (m, 5H, arH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.24, 14.01, 22.66, 23.62, 25.39, 27.12, 27.44, 28.92, 32.05, 32.23, 32.41, 32.72, 33.88, 34.02, 34.82, 41.00, 41.25, 41.41, 43.44, 46.61, 47.04, 48.32, 48.75, 50.56, 60.37, 60.73, 63.17, 63,71, 69.80, 110.37, 113.31, 126.60, 128.12, 129.11, 129.63, 129.70, 132.32, 133.67, 141.39, 151.17, 151.39, 164.52, 167.33, 167.67, 169.26, 171.15, 171.72. MS (CI-$NH_3$): *m*/*z* (%) = 571 (15) [$MH^+ + NH_3$]. $C_{30}H_{40}N_4O_6$ (552.67): calcd C 65.17, H 7.29, N 10.14; found C 65.17, H 7.38, N 10.34.

**2-[(2-Boc-aminoethyl)-thyminacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7a.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by chromatography to yield 0.68 g (64%) **7a** as an orange powder. $^1$H NMR (300 MHz, DMSO-$d_6$, rotamer ratio: ma.:mi. = 64:36): δ 1.38 (s, 0.64 · 9H, Boc-$CH_3$, ma.), 1.43 (s, 0.36 · 9H, Boc-$CH_3$, mi.), 1.76 (s, 3H, T-$CH_3$), 3.01–3.62 (m, 4H, $NCH_2CH_2$, rot.), 3.84, 3.85 (2 s, 3H, ar-O-$CH_3$, rot.), 4.13 (s, 0.64 · 2H, NCH, ma.), 4.32 (s, 0.36 · 2H, NCH, mi.), 4.50 (s, 0.36 2H, T-Ac-$CH_2$, mi.), 4.69 (s, 0.64 · 2H, T-Ac-$CH_2$, ma.), 6.73 (s, 0.36 · 1H, Boc-NH, mi.), 6.96 (s, 0.64 · 1H, Boc-NH, ma.), 7.21–7.38 (m, 2H, T-CH=C, ar-H, rot.), 7.46–7.64 (m, 2H, ar-H, ar-H, rot.), 10.12 (s, 0.64 · 1H, ar-NH, ma.), 10.39 (s, 0.36 · 1H, ar-NH, mi.), 11.27 (s, 1H, T-NH). $C_{23}H_{30}N_6O_9$ (534.5): calcd C 51.68, H 5.66, N 15.72; found C 51.53, H 5.79, N 15.56.

**2-[(2-Boc-aminoethyl)-($N^4$-Z-cytosinacetyl)-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7b.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.61 g (2.00 mmol) $N^4$-*Z*-*N*-1-carboxymethylcytosine **5c** as starting materials and purified by chromatography to yield 0.83 g (64%) **7b** as an orange powder, mp: 169 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$, rotamer ratio: ma.:mi. = 83:17): δ 1.42 (s, 9H, Boc-$CH_3$), 3.25–3.35, 3.56–3.64 (2 m, 0.17 · 4H, $NCH_2CH_2$, mi.), 3.36–3.48, 3.65–3.76 (2 m,

0.83 · 4H, $NCH_2CH_2$, ma.), 3.85 (s, 3H, ar-O-$CH_3$), 4.16 (s, 0.83 · 2H, NCH, ma.), 4.50 (s, 0.17 · 2H, NCH, mi.), 4.69 (s, 0.17 · 2H, $C^Z$-Ac-$CH_2$, mi.) , 4.89 (s, 0.83 · 2H, $C^Z$-Ac-$CH_2$, ma.), 5.22 , 5.77 (2 s, 3H, Z-$CH_2$-Ph, Boc-NH, rot.), 7.19 (dd, 1H, ar-H), 7.23 (m, 1H, $C^Z$-C*H*=CH, rot.), 7.32–7.42 (m, 5H, Z-Ph), 7.60 (d, 1H, ar-H), 7.68 (m, 1H, $C^Z$-CH=C*H*, rot.), 8.25–8.38 (m, 1H, $C^Z$-NH, rot.), 8.43 (d, 1H, ar-H), 10.29–10.40 (m, 1H, ar-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 28.34, 38.91, 39.55, 43.60, 48.88, 49.95, 52.14, 53.30, 55.89, 67.76, 79.85, 95.18, 108.78, 122.89, 124.48, 127.15, 128.14, 128.60, 135.09, 138.12, 149.88, 152.36, 155.53, 156.24, 162.99, 167.33, 167.87. $C_{30}H_{35}N_7O_{10}$ (653.6): calcd C 55.13, H 5.40, N 15.00; found C 55.21, H 5.38, N 15.12.

**2-[(2-Boc-aminoethyl)-uracilacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7c.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.34 g (2.00 mmol) *N*-1-carboxymethyluracil **5b** as starting materials and purified by chromatography to yield 0.67 g (64%) **7c** as an orange powder. $^1$H NMR (300 MHz, $CDCl_3$, rotamer ratio: ma.:mi. = 55:45): δ 1.40–151 (m, 9H, Boc-$CH_3$, rot.), 3.29–3.93 (m, 4H, $NCH_2CH_2$, rot.), 3.87 (s, 3H, ar-O-$CH_3$), 4.22 (s, 0.55 · 2H, NCH, ma.), 4.71 (s, 0.55 · 2H, T-Ac-$CH_2$, ma.), 4.14–4.96 (m, 0.45 · 4H, NCH, T-Ac-$CH_2$, mi.), 5.16, 5.55 (2 m, 1H, Boc-NH, rot.), 5.70 (d, 1H, U-C=CH), 7.19–7.28 (m, 2H, U-CH=C, ar-H, rot.), 7.62 (2 d, 1H, ar-H, rot.), 8.50 (d, 0.55 · 1H, ar-H, ma.), 8.57 (d, 0.45 · 1H, ar-H, mi.), 8.91 (s, 0.45 · 1H, U-NH, mi.), 9.10 (s, 0.55 · 1H, U-NH, ma.), 10.29 (s, 0.55 · 1H, ar-NH, ma.), 10.36 (s, 0.45 · 1H, ar-NH, mi.). $C_{22}H_{28}N_6O_9$ (520.5): calcd C 50.77, H 5.42, N 16.15; found C 50.79, H 5.38, N 16.01.

**2-[(2-Boc-aminoethyl)-($N^6$-Z-adeninacetyl)-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7d.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.65 g (2.00 mmol) $N^6$-Z-*N*-9-carboxymethyladenine **5d** as starting materials and purified by chromatography to yield 0.94 g (69%) **7d** as an orange powder. $^1$H NMR (300 MHz, $CDCl_3$, rotamer ratio: ma.:mi. = 55:45): δ 1.39–1.48 (m, 9H, Boc-$CH_3$, rot.), 3.24–3.48, 3.57–3.91 (2 m, 4H, $NCH_2CH_2$, rot.), 3.83 (m, 3H, ar-O-$CH_3$, rot.), 4.20, 4.24, 4.41 (3 s, 2H, NCH, rot.), 4.72, 4.95, 5.04 (3 s, 2H, $A^Z$-Ac-$CH_2$, rot.), 5.21–5.28 (m, 2H, Z-$CH_2$-Ph, rot.), 5.35, 5.70 (s, m, 1H, Boc-NH, rot.), 7.12–7.20 (m, 1H, ar-H, rot.), 7.30–7.40 (m, 5H, Z-Ph), 7.58–7.62 (m, 1H, ar-H, rot.), 8.10 (m, 1H, $A^Z$-CH=N, rot.), 8.44 (d, 0.55 · 1H, ar-H, ma.), 8.50 (d, 0.45 · 1H, ar-H, mi.), 8.60, 8.69 (m, 1H, $A^Z$-CH=N, rot.), 8.92–9.20 (m, 1H, $A^Z$-NH, rot.), 10.29 (s, 0.55 1H, ar-NH, ma.), 10.36 (s, 0.45 · 1H, ar-NH, mi.). $C_{31}H_{35}N_9O_9$ (677.7): calcd C 54.94, H 5.21, N 18.60; found C 54.82, H 5.18, N 18.51.

**2-[(2-Boc-aminoethyl)-(2-amino-6-benzyloxy-*N*-9-purinacetyl)-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7e.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) *mono*-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.60 g (2.00 mmol) 2-amino-6-benzyloxy-*N*-9-carboxymethylpurine **5f** as starting materials and purified by chromatography to yield 0.41 g (32%) **7e** as a yellow powder, mp: 115 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.38–1.49 (m, 9H, Boc-$CH_3$, rot.), 3.28–3.42, 3.55–3.70 (2 m, 4H, $NCH_2CH_2$, rot.), 3.82 (s, 3H, ar-O-$CH_3$), 4.12–4.40 (m, 2H, NCH, rot.), 4.73–5.18 (m, 3H, $G^{Bn}$-Ac-$CH_2$, Boc-NH, rot.), 5.44–5.85 (m, 2H, Bz-$CH_2$-Ph, rot.), 5.96–6.15 (m, 2H, $G^{Bn}$-$NH_2$, rot.), 7.11 (dd, 1H, ar-H), 7.28–7.50 (m, 5H, Bz-Ph), 7.55 (d, 1H, ar-H), 7.70 (s, 1H, $G^{Bn}$-CH=N), 8.40 (d, 1H, ar-H), 10.29 (s, 1H, ar-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 28.25, 38.63, 43.47, 48.69, 51.77, 55.78, 68.02, 79.85, 108.60, 114.54, 122.83, 124.08, 126.98, 127.90, 128.10, 128.27, 128.74, 137.71, 136.22, 140.31, 154.06, 155.36, 156.16, 159.27, 160.82, 167.14, 167.58. $C_{30}H_{35}N_9O_8$ (649.7): calcd C 55.46, H 5.47, N 19.40; found C 55.42, H 5.38, N 19.31.

**2-[(2-Boc-aminoethyl)-($N^2$-Z-guaninacetyl)-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7f.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.69 g (2.00 mmol) $N^2$-Z-*N*-9-carboxymethylguanine **5e** as starting materials and purified by chromatography to yield 0.27 g (20%) **7f** as a yellow powder, mp: 190 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.34, 1.44 (2 s, 9H, Boc-$CH_3$, rot.), 3.21–3.32, 3.42–3.60, 3.68–3.77 (3 m, 4H, $NCH_2CH_2$, rot.), 3.80 (s, 3H, ar-O-$CH_3$), 4.19, (2 s, 2H, NCH, rot.), 4.89, 5.04, 5.08 (3 s, 2H, $G^Z$-Ac-$CH_2$, rot.), 5.21 (m, 2H, Z-$CH_2$-Ph), 5.44, 6.00, 6.08 (3 s, 1H, Boc-NH, rot.), 7.11 (dd, 1H, ar-H), 7.31–7.39 (m, 5H, Z-Ph), 7.53 (m, 1H, ar-H, rot.), 7.70 (s, 1H, $G^Z$-CH=N), 8.11, 8.31 (2 d, 1H, ar-H, rot.), 9.56, 9.87, 10.87 (3 s, 1H, $G^Z$-NH, rot.), 10.20, 10.35 (2 s, 1H, ar-NH, rot.), 11.26, 11.31 (2 s, 1H, Z-NH, rot.). $C_{31}H_{35}N_9O_{10}$ (693.7): calcd C 53.68, H 5.09, N 18.17; found C 53.62, H 5.07, N 18.08.

**2-[(2-Benzyloxyethyl)-thyminacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7g.** The title compound was prepared according to **GP5** using 0.30 g (2.00 mmol) *O*-benzyl ethanolamine **4e**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by chromatography to yield 0.89 g (85%) **7g** as a yellow powder, mp: 162 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$, rotamer ratio:ma.:mi. = 56:44): δ 1.69 (s, 0.56 · 3H, T-$CH_3$, ma.), 1.75 (s, 0.44 · 3H, T-$CH_3$, mi.), 3.55, 3.68 (2 s, 4H, $NCH_2CH_2$), 3.81, 3.82 (2 s, 3H, ar-O-$CH_3$, rot.), 4.17 (s, 0.56 · 2H, NCH, ma.), 4.29, 4.32 (2 s, 0.44 · 4H, NCH, $CH_2$-Ph, mi.), 4.50 (s, 2H, T-Ac-$CH_2$), 4.74 (s, 0.56 · 2H, $CH_2$-Ph, ma.), 7.03 (s, 0.56 · 1H, T-CH=C, ma.), 7.19 (s, 0.44 · 1H, T-CH=C, mi.), 7.21–7.33 (m, 6H, Ph, ar-H), 7.44 (d, 1H, ar-H), 7.59 (d, 0.44 · 1H, ar-H, mi.), 7.70 (d, 0.56 · 1H, ar-H, ma.), 10.05 (s, 0.56 · 1H, ar-NH, ma.), 10.28 (s, 0.44 · 1H, ar-NH, mi.),

11.21 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 10.11, 45.43, 45.96, 46.22, 48.12, 49.40, 54.04, 65.93, 66.12, 70.35, 70.71, 106.53, 107.07, 118.50, 118.87, 122.02, 122.69, 124.72, 126.34, 125.49, 125.62, 126.28, 136.13, 139.85, 141.01, 149.22, 154.05, 154.43, 162.50, 165.32, 166.05. $C_{25}H_{27}N_5O_8$ (525.5): calcd C 57.14, H 5.18, N 13.33; found C 57.28, H 5.21, N 13.14.

**8-[(2-Boc-aminoethyl)-thyminacetyl-amino]-1,4-dioxaspiro-(4.5)decan-8-carboxylic acid-4-methoxy-2-nitro-phenyl-amide 7h.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.31 g (2.00 mmol) 1,4-cyclohexandione monoethylenacetal, 0.36 g (2.00 mmol) 4-methoxy-2-nitrophenyl-isocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by washing the crude product twice with diethylether to yield 1.09 g (83%) **7h** as a yellow powder, mp: 230 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 9H, Boc-$CH_3$), 1.63–1.70, 1.95–2.18, 2.34–2.40 (3 m, 8H, $(CH_2)_2C(CH_2)_2$), 1.79 (s, 3H, T-$CH_3$), 3.35–3.47, 3.53–3.62 (m, 4H, $NCH_2CH_2$), 3.85 (s, 3H, ar-O-$CH_3$), 3.93 (s, 4H, $OCH_2CH_2O$), 4.67 (s, 2H, T-Ac-$CH_2$), 6.69 (s, 1H, Boc-NH), 6.99 (s, 1H, T-CH=C), 7.20 (dd, 1H, ar-H), 7.55 (d, 1H, ar-H), 7.76 (s, 1H, T-NH), 8.10 (d, 1H, ar-H), 9.48 (s, 1H, ar-NH). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 11.73, 27.97, 29.03, 30.76, 42.50, 49.11, 55.58, 63.63, 107.13, 108.21, 120.58, 125.97, 127.10, 141.50, 141.53, 150.84, 155.42, 164.25, 168.17, 171.20. $C_{30}H_{40}N_6O_{11}$ (660.7): calcd C 54.54, H 6.10, N 12.72; found C 53.97, H 5.83, N 12.51.

**8-[(2-Boc-aminoethyl)-thyminacetyl-amino]-1,4-dioxaspiro-(4.5)decan-8-carboxylic acid-2-methoxy-4-nitro-phenyl-amide 7i.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.31 g (2.00 mmol) 1,4-cyclohexandione monoethylenacetal, 0.36 g (2.00 mmol) 2-methoxy-4-nitrophenyl-isocyanide **3b**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by chromatography to yield 0.93 g (70%) **7i** as a yellow powder, mp: 169 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$): δ 1.42 (s, 9H, Boc-$CH_3$), 1.59–1.69, 1.78–2.12, 2.23–2.35 (3 m, 8H, $(CH_2)_2C(CH_2)_2$), 1.74 (s, 3H, T-$CH_3$), 3.25–3.36, 3.49–3.57 (2 m, 4H, $NCH_2CH_2$), 3.90 (s, 4H, $OCH_2CH_2O$), 3.99 (s, 3H, ar-O-$CH_3$), 4.70 (s, 2H, T-Ac-$CH_2$), 6.88 (s, 1H, Boc-NH), 7.15 (s, 1H, T-CH=C), 7.72 (d, 1H, ar-H), 7.80 (dd, 1H, ar-H), 8.22 (d, 1H, ar-H), 8.72 (s, 1H, ar-NH), 11.10 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 11.70, 27.94, 29.06, 30.75, 42.67, 49.04, 56.30, 63.67, 64.57, 64.87, 78.09, 105.06, 106.90, 108.26, 116.41, 118.85, 133.89, 141.34, 142.49, 148.40, 150.71, 155.67, 164.24, 169.05, 171.17. $C_{30}H_{40}N_6O_{11}$ (660.7): calcd C 54.54, H 6.10, N 12.72; found C 54.21, H 6.03, N 12.85.

***rac*-2-[(2-Boc-aminoethyl)-thyminacetyl-amino]-2-phenyl-acetic acid-4-methoxy-2-nitro-phenylamide 7j.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.21 g (2.00 mmol) benzaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitro-phenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by chromatography to yield 0.41 g (41%) **7j** as an orange powder, mp: 115 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.42 (s, 9H, Boc-$CH_3$), 1.90 (s, 3H, T-$CH_3$), 3.20–3.51, 3.79–3.89 (2 m, 4H, $NCH_2CH_2$), 3.83 (s, 3H, ar-O-$CH_3$), 4.59, 4.80 (2 d, 2H, T-Ac-$CH_2$), 5.49 (s, 1H, Boc-NH), 5.77 (s, 1H, NCH), 7.00 (s, 1H, T-CH=C), 7.21 (dd, 1H, ar-H), 7.40–7.49 (m, 5H, Ph), 7.60 (d, 1H, ar-H), 8.59 (d, 1H, ar-H), 8.95 (s, 1H, T-NH), 10.11 (s, 1H, ar-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 12.30, 28.39, 39.40, 45.51, 48.72, 55.89, 65.97, 79.92, 108.68, 110.70, 123.01, 123.93, 127.47, 129.57, 129.77, 129.88, 132.51, 137.57, 141.00, 150.97, 155.45, 155.92, 164.05, 167.99, 168.67. $C_{29}H_{34}N_6O_9$ (610.6): calcd C 57.04, H 5.61, N 13.76; found C 57.12, H 5.69, N 13.59.

***rac*-2-[(2-Boc-amino-1-methyl-ethyl)-thyminacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7k.** The title compound was prepared according to **GP5** using 0.35 g (2.00 mmol) *rac*-1-Boc-amino-2-aminopropane **4h**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitro-phenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials to yield 0.60 g (55%) **7k** as an orange powder, $^1$H NMR ($CDCl_3$, 300 MHz): δ 1.31, 1.42 (2 d, 3H, NCHC$H_3$, rot.), 1.50 (s, 9H, Boc-$CH_3$), 1.90 (s, 3H, T-$CH_3$), 3.29–3.31 (m, 2H, NCH), 3.38–3.47 (m, 1H, NC$H$CH$_3$), 3.85 (s, 3H, ar-O$CH_3$), 4.25, 4.36–4.82 (m, 5H, 2-H, T-Ac-$CH_2$, Boc-NH, rot.), 7.02, 7.09 (2 s, 1H, T-CH=C, rot.), 7.21 (dd, 1H, ar-H), 7.62, 7.66 (2 d, 1H, ar-H, rot.), 8.45, 8.58 (d, 1H, ar-H), 8.61 (s, 1H, T-NH), 10.30, 10.38 (2 s, 1H, C-1-NH, rot.). $C_{24}H_{32}N_6O_9$ (548.6): calcd C 52.55, H 5.88, N 15.32; found C 52.32, H 5.80, N 15.26.

***rac*-2-[(*trans*-2-Boc-aminocyclohexyl)-thyminacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7l.** The title compound was prepared according to **GP5** using 0.43 g (2.00 mmol) mono-Boc-cyclohexylendiamine **4g**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitro-phenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials to yield 0.75 g (64%) **7l** as a yellow powder, mp: 130 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$, rotamer ratio: ma.:mi. = 55:45): δ 1.31 (s, 0.55 · 9H, Boc-$CH_3$, ma.), 1.35–1.45 (m, 0.45 · 9H, Boc-$CH_3$, mi.), 1.10–2.02 (m, 8H, $(CH_2)_4$), 1.78 (s, 3H, T-$CH_3$), 3.30–3.95 (m, 2H, NCHCH, rot.), 3.82, 3.84 (2 s, 3H, ar-O-$CH_3$, rot.), 4.12–4.39 (m, 0.45 · 2H, NCH, mi.), 4.33 (s, 0.55 · 2H, NCH, ma.), 4.48–4.82 (m, 0.45 · 2H, T-Ac-$CH_2$, mi.), 4.73, 4.91 (2 d, 0.55 · 2H, T-Ac-$CH_2$, ma.), 6.49–6.62 (m, 0.45 · 1H, Boc-NH, mi.), 6.92 (d, 0.55 · 1H, Boc-NH, ma.), 7.03–7.24 (m, 0.45 · 1H, T-CH=C, mi.), 7.12 (s, 0.55 · 1H, T-CH=C, ma.), 7.31 (dd, 1H, ar-H), 7.47 (d, 0.55 · 1H, ar-H, ma.), 7.49–7.59 (m, 0.45 · 2H, ar-H, ar-H, mi.), 7.72 (d, 0.55 · 1H, ar-H, ma.), 10.05 (s, 0.55 · 1H, ar-NH, ma.), 9.93, 10.36, 10.46 (3 s, 0.45 · 1H, ar-NH, mi.), 11.17–11.31 (m, 1H, T-NH, rot.). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 12.20, 12.81, 24.70, 24.97, 28.45, 30.01, 32.40, 46.48, 48.48, 49.00, 50.33, 56.33, 60.18, 78.23, 107.94, 108.47, 109.28, 120.61, 121.23, 123.85, 125.21, 126.66, 141.53, 141.96, 142.14, 142.32, 151.29,

155.36, 156.06, 156.76, 164.71, 167.96, 168.53, 169.98. $C_{27}H_{36}N_6O_9$ (588.6): calcd C 55.09, H 6.16, N 14.28; found C 55.18, H 6.12, N 14.11.

**2-[(2-Ib-Aminophenyl)-thyminacetyl-amino]-acetic acid-4-methoxy-2-nitro-phenylamide 7m.** The title compound was prepared according to **GP5** using 0.36 g (2.00 mmol) mono-Ib-*ortho*-phenylendiamine **4f**, 0.06 g (2.00 mmol) paraformaldehyde, 0.36 g (2.00 mmol) 4-methoxy-2-nitro-phenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials and purified by chromatography to yield 0.66 g (60%) **7m** as an orange powder, mp: 170 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$): δ 1.29 (t, 6H, Ib-$CH_3$), 1.71 (s, 3H, T-$CH_3$), 2.69 (sept, 1H, Ib-CH), 3.80 (s, 3H, ar-O-$CH_3$), 4.05–4.16 (2 d, 2H, NCH), 4.00, 4.77 (2 d, 2H, T-Ac-$CH_2$), 6.99 (s, 1H, T-CH=C), 7.09–7.19 (m, 2H, ar-H, ar-H), 7.31–7.38 (m, 2H, ar-H, ar-H), 7.41 (d, 1H, ar-H), 7.70 (d, 1H, ar-H), 8.21 (d, 1H, ar-H), 10.22 (s, 1H, Ib-NH), 10.36 (s, 1H, ar-NH), 11.08 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 10.83, 18.13, 18.27, 34.23, 47.18, 52.27, 54.58, 107.82, 119.24, 121.64, 122.83, 123.43, 125.48, 127.53, 128.49, 129.48, 135.14, 139.85, 149.70, 155.13, 163.36, 166.27, 167.32, 175.12. $C_{26}H_{28}N_6O_8$ (552.5): calcd C 56.52, H 5.11, N 15.21; found C 56.48, H 5.18, N 15.19.

***rac*-2-[(2-Boc-aminoethyl)-thyminacetyl-amino]-4-ethoxycarbonyl-2-methyl-butyric acid-4-methoxy-2-nitro-phenylamide 7n.** The title compound was prepared according to **GP5** using 0.32 g (2.00 mmol) mono-Boc-ethylendiamine **4a**, 0.29 g (2.00 mmol) ethyl-laevulinate, 0.36 g (2.00 mmol) 4-methoxy-2-nitro-phenylisocyanide **3a**, and 0.37 g (2.00 mmol) *N*-1-carboxymethylthymine **5a** as starting materials to yield 0.98 g (76%) **7n** as an orange powder, mp: 147 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.25 (t, 3H, C(O)O–$CH_2$–C$H_3$), 1.41 (s, 9H, Boc-$CH_3$), 1.60 (s, 3H, $CCH_3$), 1.84 (s, 3H, T-$CH_3$), 2.20–2.30, 2.39–2.53 (2 m, 4H, $CCH_2CH_2$), 3.40–3.77 (m, 4H, $NCH_2CH_2$), 3.85 (s, 3H, ar-O-$CH_3$), 4.12 (q, 2H, C(O)O-$CH_2$), 4.79 (s, 2H, T-Ac-$CH_2$), 5.38 (s, 1H, Boc-NH), 6.91 (s, 1H, T-CH=C), 7.21 (dd, 1H, ar-H), 7.61 (d, 1H, ar-H), 8.46 (d, 1H, ar-H), 8.65 (s, 1H, T-NH), 10.29 (s, 1H, ar-NH). $C_{29}H_{40}N_6O_{11}$ (648.7): calcd C 53.70, H 6.22, N 12.96; found C 53.75, H 6.28, N 12.88.

***rac*-2-[(2-Boc-aminoethyl)-$N^6$-Z-adeninacetyl-amino]-*ortho*-chlorophenylacetic acid 8c.** The title compound was prepared according to **GP4** using 0.30 g (0.42 mmol) **6c** as starting material. The resulting crude product was recrystallized from dichloromethane to yield 0.21 g (38%) of a colourless solid, mp: >102 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$, due to the existence of two rotamers in a 78:22 ratio several signals were doubled): δ 1.36 (ma.), 1.41 (mi.) (2s, 9H, Boc-$CH_3$), 3.1–3.4 (m, 4H), 5.19 (br, 1H, Boc-NH), 5.30 (m, 3H, 2H, Z-$CH_2$), 5.52 (m, 2H, A-Z-Ac-$CH_2$), 7.3–7.6 (m, 9H, ar-H), 7.98 (mi.), 8.17 (ma.) (2s, 1H, A-Z-Ac-N=CH), 8.72 (s, 1H, A-Z-Ac-N=CH), 9.3 (br, 1H, COOH). MS (CI-isobutane): *m*/*z* (%) = 639 (10) [$MH^+$]. $C_{30}H_{32}N_7O_7Cl$ (638.1): calcd C 56.47, H 5.05, N 15.37; found C 56.49, H 5.04, N 15.30.

**1-[(2-Etoc-aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid 8e.** The title compound was prepared according to **GP4** using 0.70 g (1.25 mmol) **6e** as starting material. The resulting crude product was recrystallized from $Et_2O$ to yield 0.41 g (78%) of a colourless solid, mp: 198 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$): δ 0.91 (t, 3H, Etoc-$CH_3$), 1.2–2.2 (m, 10H, $CH_2$), 1.76 (s, 3H, T-Ac-CH=CC$H_3$), 3.2–3.4 (m, 4H), 4.03 (q, 2H, Etoc-$CH_2$), 4.63 (s, 2H, T-Ac-$CH_2$), 7.21 (br, 1H, Etoc-NH), 7.36 (s, 1H, T-Ac-CH=$CCH_3$), 11.29 (s, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 11.87, 14.97, 22.55, 25.12, 28.15, 29.34, 32.23, 42.39, 49.18, 60.21, 108.20, 142.46, 151.34, 154.72, 164.76, 172.08. MS (CI-isobutane): *m*/*z* (%) = 426 (40) [$MH^+$]. $C_{19}H_{28}N_4O_7$ (424.5): calcd C 53.77, H 6.65, N 13.20; found C 53.69, H 6.72, N 12.97.

**1-[(2-Z-Aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid 8f.** The title compound was prepared according to **GP4** using 0.25 g (0.39 mmol) **6f** as starting material. The resulting crude product was recrystallized from $Et_2O$ to yield 0.16 g (82%) of a colourless solid, mp: 205 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$): δ 1.2–2.1 (m, 10H, $CH_2$), 1.74 (s, 3H, T-Ac-CH=CC$H_3$), 3.2–3.5 (m, 4H), 4.68 (s, 2H, T-Ac-$CH_2$), 5.02 (s, 2H, Z-$CH_2$), 7.26 (s, 1H, T-Ac-CH=$CCH_3$), 7.35 (m, 5H, arH), 11.12 (s, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 12.23, 22.97, 25.78, 28.15, 29.34, 42.39, 49.28, 60.21, 65.69, 108.06, 127.96, 128.04, 128.68, 137.34, 142.75, 151.36, 156.64, 164.78, 172.18. MS (CI-isobutane): *m*/*z* (%) = 488 (40) [$MH^+$]. $C_{24}H_{30}N_4O_7$ (486.5): calcd C 59.25, H 6.22, N 11.52; found C 60.12, H 6.34, N 11.89.

**1-[(2-Boc-aminoethyl)-thyminacetyl-amino]-cyclohexancarboxylic acid 8g.** The title compound was prepared according to **GP4** using 0.50 g (0.94 mmol) **6g** as starting material. The resulting crude product was recrystallized from dichloromethane to yield 0.35 g (82%) of a colourless solid, mp: 185 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$, due to the existence of two rotamers in a 70:30 ratio several signals were doubled): δ 1.41 (s, 9H, Boc-$CH_3$), 1.2–2.05 (m, 10H, $CH_2$), 1.79 (s, 3H, T-Ac-CH=CC$H_3$), 3.2, 3.57 (2m, 4H), 4.35 (mi.), 4.64 (ma.) (s, 2H, T-Ac-$CH_2$), 6.85 (ma.), 7.19 (mi.) (b, 1H, BocNH), 7.32 (ma.), 7.51 (mi.) (s, 1H, T-Ac-C*H*=$CCH_3$), 11.18 (ma.), 11.29 (mi.) (s, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$, due to the existence of two rotamers in a 70:30 ratio several signals were doubled): δ 11.87, 21.42, 22.19, 24.85, 25.12, 28.15, 31.61, 41.98, 48.40, 48.86, 63.75, 64.90, 67.02, 78.02, 107.87, 108.30, 141.81, 142.33, 150.98, 155.70, 164.43, 167.19, 169.53, 173.68. MS (CI-isobutane): *m*/*z* (%) = 454 (60) [$MH^+$]. $C_{21}H_{32}N_4O_7$ (452.5): calcd C 55.74, H 7.13, N 12.38; found C 55.49, H 7.12, N 12.45.

**2-[(2-Boc-aminoethyl)-2-thymine-methyl-benzoyl-amino]-3,3-dimethyl-butyric acid 8i.** The title compound was prepared according to **GP4** using 0.24 g (0.45 mmol) **6i** as starting material. The resulting crude product was recrystallized from $Et_2O$ to yield 0.11 g (47%) of a colourless solid, mp: 116 °C. $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$): δ 1.18 (s, 9H, *t*-Bu-$CH_3$), 1.21 (s,

9H, Boc-$CH_3$), 1.84 (m, 3H), 3.49–3.81 (m, 4H), 4.50 (br, 1H, CH-*t*-Bu), 5.07–5.41 (m, 2H), 7.20–7.61 (m, 5H). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 12.13, 28.17, 28.39, 36.22, 41.52, 47.42, 48.99, 60.42, 79.57, 110.95, 126.27, 126.97, 128.04, 129.11, 130.03, 134.02, 141.39, 151.50, 151.78, 155.67, 156.03, 164.81, 169.61, 172.42. MS (CI-isobutane): *m*/*z* (%) = 517 (80) [$MH^+$]. $C_{26}H_{36}N_4O_7$ (516.6): calcd C 60.45, H 7.02, N 10.85; found C 61.78, H 7.52, N 10.87.

**1-[(2-Benzyloxyethyl)-thyminacetyl-amino]-cyclohexan-carboxylic acid 8k.** The title compound was prepared according to **GP4** using 0.85 g (1.47 mmol) **6k** as starting material. The resulting crude product was recrystallized from dichloromethane to yield 0.59 g (91%) of a colourless solid, mp: 245 °C (dec.). $^1$H NMR (300 MHz, DMSO-$d_6$): δ 1.10–2.05 (m, 10H, $CH_2$), 1.72 (s, 3H, T-Ac-CH=CC$H_3$), 3.35 (m, 2H, $NCH_2$), 3.71 (m, 2H, O-C$H_2$CH$_2$), 4.57 (s, 2H, T-Ac-$CH_2$), 4.76 (s, 2H, Bz-$CH_2$), 6.97 (s, 1H, T-Ac-C*H*=C$CH_3$), 7.2–7.4 (m, 5H, ar-H), 11.29 (s, 1H, T-Ac-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 12.24, 22.56, 25.05, 31.93, 42.59, 49.40, 64.19, 69.89, 72.80, 108.21, 127.95, 128.11, 128.64, 138.48, 142.34, 151.28, 164.737, 167.76, 174.13. MS (CI-$NH_3$): *m*/*z* (%) = 445 (80) [$MH^+$]. $C_{23}H_{29}N_3O_6$ (443.5): calcd C 62.29, H 6.59, N 9.47; found C 63.34, H 6.78, N 9.56.

***rac*-2-[(2-Ib-Amino-phenyl)-thyminacetyl-amino]-biphen-4-yl-acetic acid 8l.** The title compound was prepared according to **GP4** using 0.35 g (0.55 mmol) **6l** as starting material. The resulting crude product was recrystallized from dichloromethane to yield 0.20 g (66%) of a colourless solid, mp: > 250 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.21 (d, 6H, CH(C$H_3$)$_2$, $^3J$ = 6.6 Hz), 1.73 (s, 3H, T-Ac-$CH_3$), 2.91 (m, 1H, C*H*(CH$_3$)$_2$, $^3J$ = 6.6 Hz), 3.91 (d, 1H, T-Ac-$CH_2$, $^2J$ = 16.5 Hz), 4.00 (d, 1H, T-Ac-$CH_2$, $^2J$ = 16.5 Hz), 5.86 (s, 1H, NCH), 6.7–8.5 (m, 15H, arH, T-Ac-C=CH, COOH), 11.22 (s, 1H, T-Ac-NH), 11.65 (s, 1H, NH-Ib). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 11.82, 19.55, 35.15, 48.68, 64.99, 107.77, 114.05, 120.26, 122.57, 125.45, 125.88, 126.18, 126.38, 126.92, 127.62, 128.46, 128.83, 129.08, 129.18, 130.36, 131.85, 132.11, 132.78, 138.49, 138.67, 139.88, 141.96, 150.73, 164.29, 167.08, 173.92, 175.83. MS (CI-isobutane): *m*/*z* (%) = 555 (100) [$MH^+$]. $C_{31}H_{30}N_4O_6$ (554.6): calcd C 67.14, H 5.45, N 10.10; found C 67.18, H 5.29, N 10.03.

**2-[(2-Benzyloxyethyl)-thyminacetyl-amino]-acetic acid 9g.** The title compound was prepared according to **GP6** using 0.16 g (0.30 mmol) of the totally protected monomer **7g** as starting material to yield 0.08 g (71%) **9g** as a colourless solid, mp: 147 °C. $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$, rotamer ratio: ma.:mi. = 65:35): δ 1.78 (s, 0.65 · 3H, T-$CH_3$, ma.), 1.85 (s, 0.35 · 3H, T-$CH_3$, mi.), 3.59–3.72 (m, 4H, $NCH_2CH_2$), 4.09 (s, 0.65 · 2H, NCH, ma.), 4.28, 4.47, 4.51 (3 s, 0.35 · 6H, NCH, T-Ac-$CH_2$, $CH_2$-Ph, mi.), 4.54 (s, 0.65 · 2H, T-Ac-$CH_2$, ma.), 4.71 (s, 0.65 · 2H, $CH_2$-Ph, ma.), 6.80 (s, 0.35 · 1H, T-CH=QC, mi.), 7.10 (s, 0.65 · 1H, T-CH=C, ma.), 7.27–7.39 (m, 5H, Ph), 11.24 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 10.79, 46.26, 46.34, 46.60, 46.86, 48.81, 66.70, 67.42, 70.35, 70.77, 107.78, 107.89, 126.13, 126.36, 126.90, 126.99, 136.61, 136.70, 139.90, 140.02, 149.88, 163.41, 166.26, 169.07. $C_{18}H_{21}N_3O_6$ (375.4): calcd C 57.59, H 5.64, N 11.19; found C 57.75, H 5.48, N 11.38.

***rac*-2-[(2-Boc-aminoethyl)-thyminacetyl-amino]-2-phenyl-acetic acid 9j.** The title compound was prepared according to **GP6** using 0.18 g (0.30 mmol) of the totally protected monomer **7j** as starting material to yield 0.11 g (80%) **9j** as a colourless solid, mp: 182 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$): δ 1.39 (s, 9H, Boc-$CH_3$), 1.85 (s, 3H, T-$CH_3$), 2.66–2.80, 3.00–3.15, 3.19–3.41 (3 m, 4H, $NCH_2CH_2$), 4.74 (s, 2H, T-Ac-$CH_2$), 5.79 (s, 1H, NCH), 6.43 (m, 1H, Boc-NH), 7.26 (s, 1H, T-CH=C), 7.31–7.45 (m, 5H, Ph), 11.30 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 10.72, 26.82, 43.10, 46.85, 60.72, 77.20, 107.45, 126.94, 127.14, 128.08, 132.73, 140.21, 149.72, 154.30, 163.31, 166.41, 169.93. $C_{22}H_{28}N_4O_7$ (460.5): calcd C 57.38, H 6.13, N 12.17; found C 57.23, H 6.03, N 12.35.

**2-[(2-Ib-Aminophenyl)-thyminacetyl-amino]-acetic acid 9m.** The title compound was prepared according to **GP6** using 0.17 g (0.30 mmol) of the totally protected monomer **7m** as starting material to yield 0.10 g (83%) **9m** as a colourless solid, mp: 215 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$): δ 1.22 (2 t, 6H, Ib-$CH_3$), 1.81 (s, 3H, T-$CH_3$), 2.73 (sept, 1H, Ib-CH), 4.18 (s, 2H, NCH), 3.99, 4.52 (2 d, 2H, T-Ac-$CH_2$), 7.14 (s, 1H, T-CH=C), 7.20 (t, 1H, ar-H), 7.38–7.45 (m, 2H, ar-H, ar-H), 8.21 (d, 1H, ar-H), 9.89 (s, 1H, Ib-NH), 11.21 (s, 1H, T-NH). $^{13}$C NMR (75 MHz, $CDCl_3$/DMSO-$d_6$): δ 10.65, 18.00, 34.11, 47.02, 49.99, 107.51, 121.71, 123.47, 127.52, 128.24, 129.64, 134.79, 139.83, 149.59, 163.16, 166.07, 170.78, 174.61. $C_{19}H_{22}N_4O_6$ (402.4): calcd C 56.71, H 5.51, N 13.92; found C 56.65, H 5.46, N 13.23.

***rac*-2-[(2-Ethoxycarbonyl-ethyl)-thyminacetyl-amino]-phenyl-acetic acid-amide 10.** 2.3 g (4.2 mmol) of the vinyl amide **6m** were dissolved in 50 mL abs. THF and 80 μL water and treated with 2 mL TFA. After stirring the solution for 2 h at room temperature the solvent was removed in vacuo and the crude product purified by flash chromatography to yield 1.12 g (64%) of a colourless solid. $^1$H NMR (300 MHz, $CDCl_3$/DMSO-$d_6$, due to the existence of two rotamers in a 60:40 ratio several signals were doubled): δ 1.10 (dt, 3H, COO–$CH_2$–C$H_3$), 1.79 (s, 3H, thyminyl-$CH_3$), 1.91, 2.50 (2m, 2H, C$H_2$–COOEt), 3.49 (m, 2H, N–C$H_2$–$CH_2$–COOEt), 3.91 (dq, 2H, COO–C$H_2$–$CH_3$), 4.66 (m, 2H, T-$CH_2$), 5.68, 5.98 (2s, 1H, NCH), 7.07–7.72 (m, 8H, thyminyl-H, ar-H, $CONH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 11.88, 13.79, 32.01, 33.41, 48.18, 59.49, 59.75, 60.87, 61.64, 108.19, 128.00, 128.34, 128.42, 129.27, 135.29, 141.75, 141.92, 151.00, 164.42, 167.13, 167.42, 170.15, 170.32, 170.86. MS (CI-isobutane): *m*/*z* (%) = 417 (40) [$MH^+$]. $C_{20}H_{24}N_4O_6$ (416.43): calcd C 57.69, H 5.81, N 13.45; found C 57.76, H 5.78, N 13.44.

**2-[(2-Boc-aminoethyl)-hydroxyacetyl-amino]-3,3-dimethyl-butyric acid-4-methoxy-2-nitro-phenylamide 12.** The title

compound was prepared according to **GP5** using 0.96 g (6.00 mmol) mono-Boc-ethylendiamine **4a**, 0.51 g (6.00 mmol) pivalaldehyde, 1.08 g (6.00 mmol) 4-methoxy-2-nitrophenylisocyanide **3a**, and 0.46 g (6.00 mmol) glycolic acid as starting materials and purified by chromatography to yield 2.38 g (82%) **12** as an orange solid, mp: 61 °C. $^1$H NMR (300 MHz, $CDCl_3$, rotamer ratio: ma.:mi. = 80:20): δ 1.15 (s, 9H, Boc-$CH_3$), 1.31, 1.40 (2 s, 9H, *tert*.butyl-$CH_3$, rot.), 1.78 (s, br, 1H, OH), 3.02–3.53, 3.68–3.82 (2 m, 5H, $NCH_2CH_2$, NCH), 3.89 (s, 3H, ar-O-$CH_3$), 4.30–4.50 (m, 2H, HO-Ac-$CH_2$, rot.), 4.85 (s, 0.80 · 1H, Boc-NH, ma.), 5.04 (s, 0.20 · 1H, Boc-NH, mi.), 7.23 (dd, 1H, ar-H), 7.64 (d, 1H, ar-H), 8.40 (d, 0.80 · 1H, ar-H, ma.), 8.58 (d, 0.20 · 1H, ar-H, mi.), 10.23 (s, 0.80 · 1H, ar-NH, ma.), 10.35 (s, 0.20 · 1H, ar-NH, mi.). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 28.20, 28.39, 28.68, 36.91, 37.13, 39.71, 40.27, 45.77, 46.47, 56.35, 60.90, 62.24, 67.04, 67.96, 80.18, 109.35, 110.65, 120.56, 122.93, 123.28, 124.95, 127.07, 127.49, 138.57, 139.21, 156.19, 167.64, 168.89, 174.99. MS (CI, $NH_3$): *m*/*z* (%) = 483 (13) [$MH^+$], 427 (24) [$MH^+$−isobutene], 383 (17) [$MH^+$−isobutene −$CO_2$], 315 (100) [$MH^+$−ar-$NH_2$], 259 (80) [$MH^+$−ar-$NH_2$−isobutene], 215 (19) [$MH^+$−ar-$NH_2$−isobutene−$CO_2$]. $C_{22}H_{34}N_4O_8$ (482.5): calcd C 54.76, H 7.10, N 11.61; found C 54.68, H 7.12, N 11.58.

**2-[(2-Boc-aminoethyl)-hydroxyacetyl-amino]-3,3-dimethyl-butyric acid 13.** The title compound was prepared according to **GP6** using 0.15 g (0.30 mmol) of the totally protected monomer **12** as starting material to yield 0.09 g (90%) **13** as a colourless solid, mp 115 °C (dec.). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.12 (s, 9H, Boc-$CH_3$), 1.44 (s, 9H, *tert*.butyl-$CH_3$), 3.02–3.15, 3.21–3.38 (2 m, 4H, $NCH_2CH_2$), 3.90 (s, 1H, NCH), 4.70, 4.87 (2 d, 2H, HO-Ac-$CH_2$), 4.99 (s, 1H, Boc-NH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ 26.56, 27.26, 36.95, 38.47, 47.80, 66.90, 68.32, 78.98, 155.33, 163.95. MS (CI, $NH_3$): *m*/*z* (%) = 333 (19) [$MH^+$], 315 (4) [$MH^+$−$H_2O$], 277 (100) [$MH^+$−isobutene], 259 (84) [$MH^+$−isobutene−$H_2O$], 233 (20) [$MH^+$−isobutene−$CO_2$], 215 (15) [$MH^+$−isobutene−$CO_2$−$H_2O$]. $C_{15}H_{28}N_2O_6$ (332.4): calcd C 54.20, H 8.49, N 8.43; found C 54.16, H 8.40, N 8.56.

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