Preparation of Cyclopropane Analogues of the Natural Antibiotic TAN 1057 A/B[‡]

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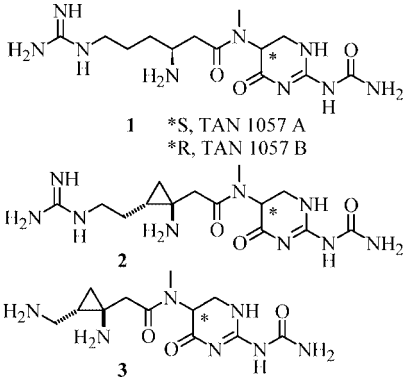
The two new analogues **2** and **3** of the natural dipeptide antibiotic TAN 1057 A/B (**1**), both with cyclopropyl containing β-amino acid side chains, were prepared. The synthesis of the corresponding β-amino acids in appropriately protected form (**4**-Z_3 and **5**-Z_2, respectively) from the correspondingly protected (hydroxyethyl)- (**7a**) and (hydroxymethyl)-substituted cyclopropylideneacetate (**7b**), prepared in two steps each from homoallyl and allyl benzyl ether, respectively, was achieved in nine and seven steps, respectively, with overall yields of 17 (**4**-Z_3) and 9.3 % (**5**-Z_2), respectively. Coupling with the *N*-methyldihydropyrimidinone **22** and deprotection gave the compounds **2** and **3**, which turned out to be active against methicillin resistant strains of *Staphylococcus aureus*, albeit to a lesser extent than TAN 1057 itself.

Introduction

The cyclopropane moiety is a common motif in nature.[1] It is present in such important compounds as e. g. the insecticidal chrysanthemum acid esters and in (1-aminocyclopropane)carboxylic acid (1-ACC), the biosynthetic precursor of the plant hormone ethylene. The importance of cyclopropyl-group containing compounds for industrial applications is also apparent, reflected for example by the tremendously successful class of pyrethroid insecticides[2] or pharmaceutical blockbusters like the antiinfectives ciprofloxacin and moxifloxacin.[3]

Several natural and non-natural products with interesting biological activities comprising a cyclopropane moiety are amino acids or derivatives thereof.[4] Among those, β-amino acids have gained increasing attention over the past years, not only as conformationally restricted analogues of natural amino acids in peptide/protein synthesis[5] but also in terms of developing new synthetic methodology.[6,7] Cyclopropyl analogues of non-cyclopropyl-group containing amino acids also have been used to modify or even improve the selectivity of biologically active compounds.[8]

The potent antiinfective TAN 1057 A/B, which had first been isolated by scientists at the Takeda company from *Flexibacter sp.* PK-74,[9] had attracted the attention of several groups around the world with respect to total and/or core unit synthesis.[10] Quite a few structural variations on either the urea or the β-amino acid moiety have also been reported.[11] Whereas replacement of the guanidinylpropyl unit in the homoarginine side chain of **1** by different heterocyclic groups led to vastly decreased activity, analogues with other basic substituents mimicking a guanidinyl moiety, even with only an amino group, had shown equivalent or even better antibiotic activity than the parent compound **1**. In view of this, we embarked on a project to synthesize the analogue **2** with a cyclopropyl-group containing β-amino acid side chain as well as the stripped version **3** with a terminal primary amino group (Figure 1). The versatility of



1 *S, TAN 1057 A
*R, TAN 1057 B

2

3

Figure 1. The natural antibiotic TAN 1057 A/B (**1**) and cyclopropyl analogues **2** and **3**.

[‡] Part 114 in the series "Cyclopropyl Building Blocks for Organic Synthesis". Part 113: M. Schelper, O. Buisine, S. I. Kozhushkov, C. Aubert, A. de Meijere, M. Malacria, *Eur. J. Org. Chem.* **2005**, in press; Part 112: F. Brackmann, D. S. Yufit, A. de Meijere, *Synthesis* **2005**, in press.

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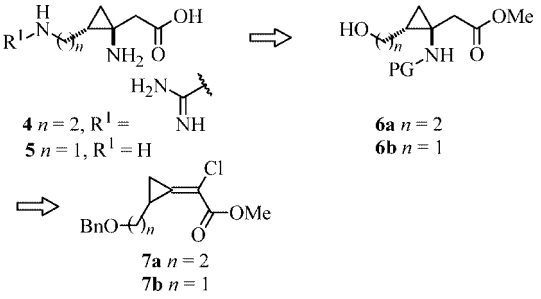
(2-chlorocyclopropylidene)acetates of type **7** towards the synthesis of various (aminocyclopropane)carboxylic acids had previously been demonstrated.[12] Thus, appropriately substituted building blocks of this type were chosen as suitable precursors to the envisaged methanohomoarginine and -lysine components in **2** and **3** (Scheme 1), and these β-amino acids would finally be converted into the target products **2** and **3** by simple peptide coupling with the racemic dihydropyrimidinone derivative **22** for which a productive synthesis has been reported before.[10b]

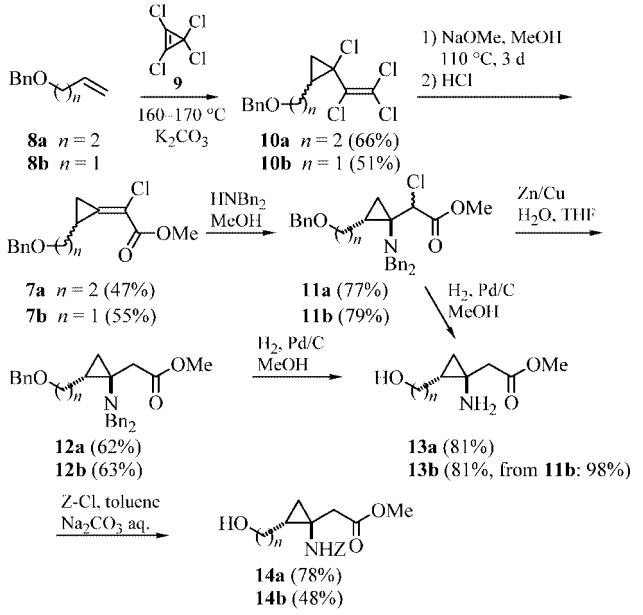


Scheme 1. Retrosynthetic considerations towards analogues **4** and **5** of the homoarginine side chain of TAN 1057 (PG = protecting group).

Results and Discussion

Methyl 2′-benzyloxyethyl- (**7a**) and methyl 2′-benzyloxymethyl-substituted (2-chlorocyclopropylidene)acetate (**7b**) were prepared by reaction of the correspondingly 2-substituted 1-chloro-1-(trichloroethenyl)cyclopropanes **10a**,**b**, obtained by addition of thermally ring-opened tetrachlorocyclopropene (**9**)[13] to 3-buten-1-yl benzyl ether (**8a**) and allyl benzyl ether (**8b**), respectively, with sodium methoxide in methanol and subsequent acidic work-up, according to a previously published general protocol.[14,15] Since the applied benzyl ethers **8a**,**b** have boiling points well above the temperature required for the ring opening of **9** to perchlorovinylcarbene (≥ 130 °C), these carbene additions could be performed in common laboratory glassware by simply heating **8a**,**b** under reflux with tetrachlorocyclopropene (**9**) in an inert gas atmosphere.[16] Transformation of **10a**,**b** to the (chlorocyclopropylidene)acetates **7a**,**b** was accomplished in reasonable yields as described before (Scheme 2).[12a,17]

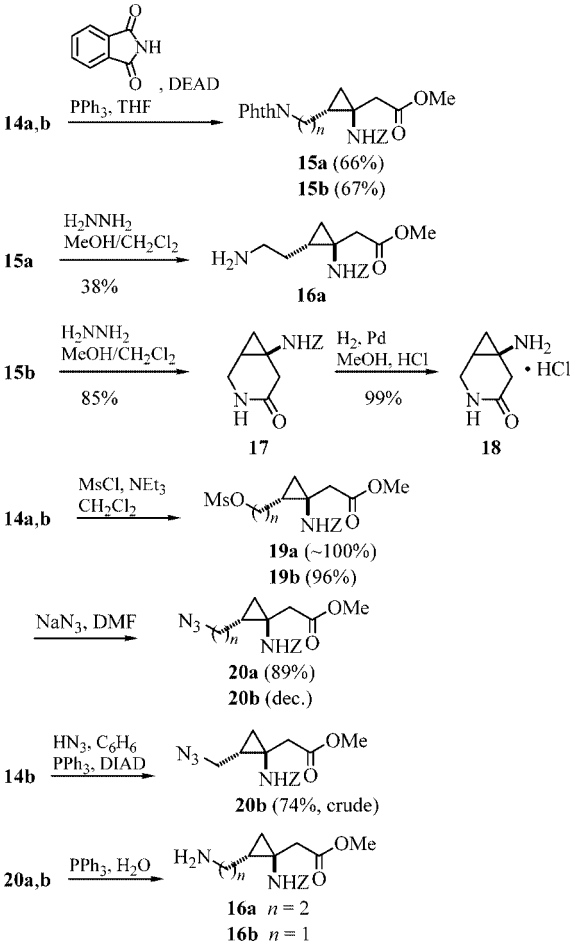
Since benzyl protecting groups can be removed under mild conditions without cleavage of the cyclopropane ring, as had been demonstrated in aminocyclopropanecarboxylic acid syntheses before,[18] *N*,*N*-dibenzylamine was used as the ammonia equivalent in the Michael addition to the cyclopropylideneacetates **7a**,**b** to furnish the protected [1′-amino-2′-(hydroxyalkyl)cyclopropyl]acetates **11a**,**b** in good yields (Scheme 2). An additional advantage of the relatively bulky *N*,*N*-dibenzylamine is that it adds to 2′-substituted cyclopropylideneacetates **7a**,**b** with complete diastereoselectivity placing the dibenzylamino substituent *trans* with respect to the benzyloxyalkyl group. The thus obtained (*E*)-diastereoisomers **11a** and **11b** were reductively dehalogenated by treatment with zinc/copper couple and water in tetrahydrofuran.[19] Subsequent catalytic hydrogenation led to the completely debenzylated β-amino esters **13a**,**b**. The same products can also be obtained by direct catalytic hydrogenation with prolonged reaction times of the α-chloro esters **11**, as demonstrated with **11b** to furnish **13b** in almost quantitative yield (98%). The primary amino groups in **13a**,**b** were *Z*-protected by treatment with benzyl chloroformate to give **14a**,**b** in reasonable yields.



Scheme 2. Preparation of [1′-amino-2′-(hydroxyalkyl)cyclopropyl]-acetates **14a**,**b** from homoallyl and allyl benzyl ethers **8a**,**b** via (2-chloro-2-cyclopropylidene)acetates **7a**,**b**.

The (2′-hydroxyalkyl-1′-aminocyclopropyl)acetates **14a**,**b** were ideal precursors to a variety of (aminocyclopropane)-carboxylic acids. Towards the synthesis of the TAN 1057 analogues **2** and **3**, the hydroxy groups in **14a** and **14b** had to be converted to a guanidine and an amino group, respectively (Scheme 3). Since the guanidinyl substituent can also be generated from an amino group, the hydroxyalkyl derivatives **14a**,**b** were first converted with phthalimide applying a Mitsunobu-type protocol that had been utilized in the synthesis of carnosadine [*cis*-1-amino-2-(guanidinomethyl)-cyclopropanecarboxylic acid].[20] Although the phthalimidoalkyl derivatives **15a**,**b** could be obtained in reasonable yields (66 and 67%, respectively), this route did not prove to be satisfactory, since hydrazinolysis either proceeded with low yield (38% for **16a**) or with immediately ensuing cyclization to the bicyclic aminolactam **17**. While the latter is not uninteresting and could be deprotected to 3-amino-3,4-methanovalerolactam, obtained by catalytic hydrogenation of **17** in methanol as the hydrochloride **18**, it is not very helpful towards the synthesis of **3**. Therefore, the amino groups in **16a** and **16b** were introduced via the azidoalkyl derivatives **20a** and **20b**. Conversion of **14a**,**b** to the corresponding mesylates **19a**,**b** was accomplished in excellent yields. Using a fivefold excess of sodium azide in DMF, **20a** was obtained in 89% yield. The mesylate **19b**, however,

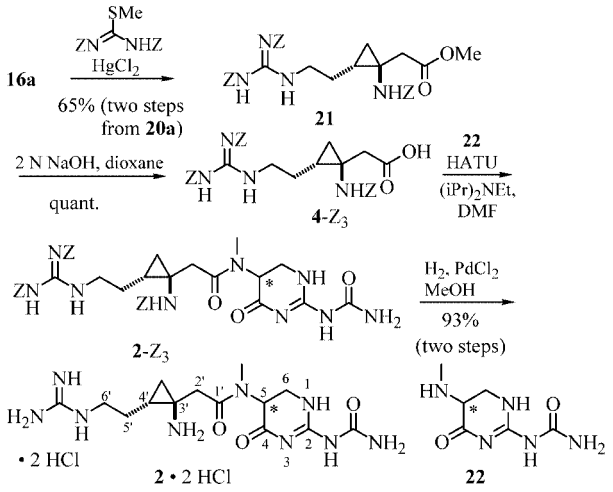
could not be completely converted into the azide **20b** before it underwent decomposition. Alternatively, the hydroxymethyl derivative **14b** could be converted into the azidomethyl compound **20b** using hydrazoic acid (solution in benzene)[21] according to a Mitsunobu protocol.[22] Crude **20b** (impurified by the hydrazine resulting from the DIAD coupling reagent) was obtained in approx. 74% yield, and it could be used without further purification for the next step.



Scheme 3. Synthesis of [1-amino-2′-(aminoalkyl)cyclopropyl]acetates **16a**,**b**.

The Staudinger reaction, due to its mild conditions, was successfully applied to reduce the azido to aminoalkyl functionalities in **20a**,**b**, and the resulting amines **16a** and **16b** could be used without isolation for the next step (Scheme 4). Upon treatment with *S*-methylthiourea in its bis(benzyloxycarbonyl)-protected form, **16a** was converted into the correspondingly protected methanohomoarginine methyl ester **21**, albeit under more rigorous conditions than usual, applying a stoichiometric amount of mercuric chloride.[23]

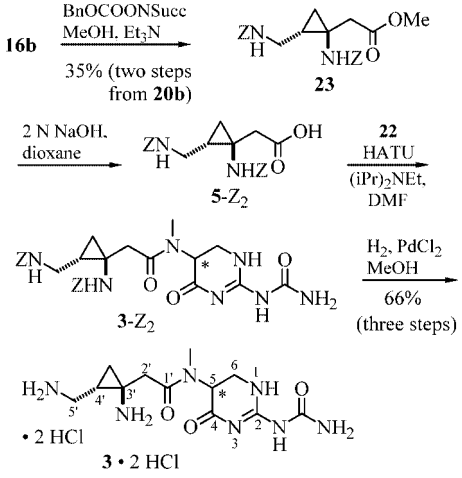
Under mild conditions, i.e. by treatment with benzyl *N*-oxysuccinimidyl carbonate and triethylamine in methanol, the free amino group in **16b** could be Z-protected and the ester groups in **21** and **23** saponified with 2 N NaOH in dioxane without loss of the protecting groups.



Scheme 4. Preparation of tris-protected 3,4-methanohomoarginine **4**-Z_3 and the TAN 1057 A/B analogue **2**·2 HCl.

Coupling of the tris-Z-protected **4**-Z_3, and the bis-Z-protected diamino acid **5**-Z_2 with the tetrahydropyrimidinone **22** was accomplished with the powerful coupling reagent HATU [*O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate].

Finally, deprotection by hydrogenation using one equivalent of palladium chloride per equiv. of **2**-Z_3 and **3**-Z_2, respectively, gave the desired TAN 1057 A/B derivatives **2** and **3** as their bis-hydrochloride salts in respectable yields (Scheme 4, Scheme 5).



Scheme 5. Synthesis of bis-protected 3,4-methanohomoornithine **5**-Z_2 and the TAN 1057 A/B analogue **3**.

In vitro tests of these new analogues **2** and **3** disclosed an antibiotic activity for both, yet it was neither any higher nor any more selective than that of TAN 1057 itself.[24]

Conclusions

The successful preparation of the cyclopropyl-group containing analogues **2** and **3** of the natural antibiotic TAN 1057 A/B (**1**) once again demonstrates the versatility of 2-chlorocyclopropylideneacetates of type **7** as building blocks

in the synthesis of aminocyclopropanecarboxylic acids. It also once more confirms the successful application of the principle of modifying biologically compounds by the incorporation of cyclopropyl groups.

Experimental Section

NMR spectra were recorded with Bruker AM 250, Varian UNITY-300 or Varian VXR 500 S instruments. Multiplicities were determined by DEPT (Distortionless Enhancement by Polarisation Transfer) or APT (Attached Proton Test) techniques. Chemical shifts refer to δ_{TMS} = 0.00 ppm according to the chemical shifts of residual solvent signals. IR: Bruker IFS 66 (FT-IR) spectrometer, measured as KBr pellets or films between KBr plates. MS (EI at 70 eV, DCI with NH_3, FAB (glycerine matrix) or ESI^+): Finnigan MAT 95, 70 eV. High resolution EI-MS spectra with perfluorokerosene as reference substance; pre-selected ion peak matching at $R >> 10000$ to be within ±2 ppm of the exact masses. TLC: Macherey–Nagel, precoated sheets, 0.25 mm Sil G/UV_{254}. Column chromatography: Merck silica gel, grade 60 (70–230 mesh) or Macherey–Nagel silica gel, grade 60, 230–400 mesh. Elemental analyses: Mikroanalytisches Laboratorium des Instituts für Organische und Biomolekulare Chemie, Universität Göttingen. All reactions were carried out under nitrogen or argon. DEAD = diethyl azodicarboxylate; DIAD = diisopropyl azodicarboxylate; HATU = *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate; Hünig's base = ethyldiisopropylamine.

3-Buten-1-yl benzyl ether (**8a**)[25] and allyl benzyl ether (**8b**)[25] as well as tetrachlorocyclopropene[26] were prepared according to known procedures.

2-(2′-Benzyloxyethyl)-1-chloro-1-(trichloroethenyl)cyclopropane (10a): A mixture of 3-buten-1-yl benzyl ether (**8a**) (32.4 g, 200 mmol), tetrachlorocyclopropene (**9**) (35.6 g, 200 mmol) and potassium carbonate (2.8 g, 20 mmol) was heated under reflux with vigorous stirring at 160–170 °C for 16 h. Distillation of the crude product yielded 44.9 g (66%) of **10a** (1:2 mixture of *E* and *Z* isomers) as a slightly yellow oil, b.p. 72 °C/0.04 Torr. The spectroscopic data of **10a** were identical with those previously reported for this compound.[12a]

2-(1′-Benzyloxymethyl)-1-chloro-1-(trichloroethenyl)cyclopropane (10b): From allyl benzyl ether (**8b**) (37.7 g, 254 mmol), **9** (44.5 g, 250 mmol) and potassium carbonate (3.5 g, 25 mmol), **10b** was obtained in the same way as **10a**, yield 41.6 g (51%), b.p. 140–150 °C/0.04 Torr as a 1:1.3 mixture of *E* and *Z* isomers. IR (film): $\tilde{\nu}$ = 3064 cm^{-1}, 3030, 2922, 1587, 1495, 1453, 1360, 1102, 1028, 736, 698. **Major Isomer:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.10–1.25 (m, 1 H, cPr-H), 1.50–1.70 (m, 1 H, cPr-H), 1.8–2.1 (m, 2 H), 2.2–2.35 (m, 1 H), 3.64 (t, J = 6.3 Hz, 2 H), 4.53 (s, 2 H, CH_2Ph), 7.24–7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 25.9 (–, cPr-C), 27.1 (+, cPr-C), 34.0 (–), 48.0 (C_{quat}, cPr-C), 68.9 (–), 73.1 (–, CH_2Ph), 116.5 (C_{quat}), 127.6 (+), 128.4 (+), 134.8 (C_{quat}, CCl), 138.2 (C_{quat}, CCl_2) ppm. **Second Isomer:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.0–1.2 (m, 1 H, cPr-H), 1.51–1.70 (m, 2 H), 1.8–2.1 (m, 2 H), 3.51–3.54 (m, 2 H), 4.51 (s, 2 H, CH_2Ph), 7.24–7.38 (m, 5 H, Ph-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 25.9 (–, cPr-C), 27.1 (+, cPr-C), 34.0 (–), 48.0 (C_{quat}, cPr-C), 68.9 (–), 73.1 (–, CH_2Ph), 116.4 (C_{quat}), 127.4 (+), 128.1 (+), 134.9 (C_{quat}, CCl), 138.4 (C_{quat}, CCl_2) ppm.

Methyl 2-[(2′-Benzyloxyethyl)cyclopropylidene]-2-chloroacetate (7a): A freshly prepared solution of sodium methoxide (34.0 g sodium, 1.48 mol) in MeOH (250 mL) was added at 0 °C under nitrogen to a solution of **10a** (62.9 g, 185 mmol) in MeOH (50 mL), and the mixture heated under reflux for 3 d. After cooling to room temperature, water (700 mL) was added, and the mixture extracted with Et_2O (3 × 250 mL). The collected organic phases were concentrated under reduced pressure. The residue was taken up in MeOH (300 mL). Hydrochloric acid (10%, 25 mL) was added, and the mixture stirred for 45 min, saturated sodium carbonate solution (300 mL) was added with care, the mixture extracted with Et_2O (3 × 250 mL), dried with $CaCl_2$, and the solvent evaporated. Purification by column chromatography on silica gel (300 g), eluting with light petroleum/Et_2O, 10:1, yielded 24.4 g, (47%) of **7a** as a 1:1.6 mixture of two diastereomers as a yellow oil. IR (film): $\tilde{\nu}$ = 2950 cm^{-1}, 2859, 1731 (C=O), 1267, 738 (arom.), 698 (arom.). ^1H NMR (250 MHz, $CDCl_3$), isomer 1: δ = 1.20–1.33 (m, 2 H, cPr-H), 1.61 (dd, ^2J = 10, ^3J = 10 Hz, 1 H, cPr-H), 2.12–2.32 (m, 2 H, 1′′-H), 3.65 (m_c, 2 H, 2′′-H), 3.70 (s, 3 H, OCH_3), 4.57 (s, 2 H, OCH_2Ph), 7.25–7.45 (m, 5 H, Ph-H). Isomer 2: δ = 1.48 (dd, ^2J = 7, ^3J = 10 Hz, 1 H, cPr-H), 1.72–2.04 (m, 4 H, cPr-H, 1′-H), 3.65 (m_c, 2 H, 2′-H), 3.75 (s, 3 H, OCH_3), 4.57 (s, 2 H, OCH_2Ph), 7.25–7.45 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT), isomer 1: δ = 11.6 (–, cPr-C), 20.3 (+, cPr-C), 31.6 (–, C-1′), 52.8 (+, OCH_3), 68.8 (–, C-2′), 72.9 (–, OCH_2Ph), 115.3 (C_{quat}, C-2), 127.49 (+, Ph-C), 127.53 (+, Ph-C), 128.3 (+, Ph-C), 138.3 (C_{quat}, Ph-C), 143.8 (C_{quat}, cPr-C), 162.4 (C_{quat}, COO) ppm. Isomer 2: δ = 15.6 (–, cPr-C), 16.1 (+, cPr-C), 31.5 (–, C-1′), 52.8 (+, OCH_3), 69.3 (–, C-2′), 73.0 (–, OCH_2Ph), 114.6 (C_{quat}, C-2), 127.49 (+, Ph-C), 127.53 (+, Ph-C), 128.3 (+, Ph-C), 143.3 (C_{quat}, cPr-C), 162.7 (C_{quat}, COO) ppm. MS (70 eV): *m/z* (%) = 280 (< 1) [M^+], 245 (1) [M^+ – Cl], 189 (2) [M^+ – CH_2Ph], 91 (100) [CH_2Ph^+]. $C_{15}H_{17}ClO_3$ (280.8): calcd. C 64.17, H 6.10; found C 63.24, H 5.97.

Methyl 2-[(2′-Benzyloxymethyl)cyclopropylidene]-2-chloroacetate (7b): Compound **10b** (60.3 g, 185 mmol) was converted by the same method as described above for **10a** to yield **7b** (35.4 g, 55%) as a 1:1.5 mixture of diastereoisomers as a slightly yellow oil. IR (film): $\tilde{\nu}$ = 3060 cm^{-1}, 3030, 2960, 2870, 1780, 1730 (C=O), 1450, 1430, 1370, 1270, 1200, 1150, 1100, 1070, 1040, 1010, 910, 760, 740, 700. ^1H NMR (270 MHz, $CDCl_3$), isomer 1: δ = 1.37 (dd, 1 H, 3′-H), 1.62 (dd, 1 H, 3′-H), 2.26 (m_c, 1 H, 2′-H), 3.07 (dd, 1 H, 1′′-H), 3.69 (s, 3 H, OCH_3), 3.89 (dd, 1 H, 1′′-H), 4.45 (AB system, 2 H, OCH_2Ph), 7.25 (m_c, 5 H, Ar-H) ppm. Isomer 2: δ = 1.56 (dd, 1 H, 3′-H), 1.83 (dd, 1 H, 3′-H), 2.08 (m_c, 1 H, 2′-H), 3.24 (dd, 1 H, 1′′-H), 3.71 (dd, 1 H, 1′′-H), 3.75 (s, 3 H, OCH_3), 4.48 (AB system, 2 H, OCH_2Ph), 7.25 (m_c, 5 H, Ar-H) ppm. MS (70 eV): *m/z* (%) = 234 (0.2) [M^+ – MeOH], 231 (0.1) [M^+ – Cl], 213 (1.0), 160 (6.2) [M^+ – CClCOOMe], 145 (2.0), 125 (1.1), 107 (1.4), 91 (100) [CH_2Ph^+], 77 (3.5) 65 (11), 59 (2.3) [$COOMe^+$], 51 (5.0). ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT), isomer 1: δ = 10.8 (–, cPr-C), 22.1 (+, cPr-C), 52.8 (+, OCH_3), 69.6 (–, C-1′′), 72.7 (–, O*C*H_2Ph), 115.9 (C_{quat}, cPr-C), 127.5 (+, Ph-C), 127.6 (+, Ph-C), 128.5 (+, Ph-C), 137.9 (C_{quat}, Ph-C), 140.2 (C_{quat}, C-2), 162.5 (C_{quat}, COO) ppm. Isomer 2: δ = 14.5 (–, cPr-C), 18.3 (+, cPr-C), 52.8 (+, OCH_3), 69.5 (–, C-1′′), 72.7 (–, O*C*H_2Ph), 115.5 (C_{quat}, cPr-C), 127.5 (+, Ph-C), 127.6 (+, Ph-C), 128.5 (+, Ph-C), 137.9 (C_{quat}, Ph-C), 140.1 (C_{quat}, C-2), 162.3 (C_{quat}, COO) ppm. Further spectroscopic data were identical with those reported.[12b]

Compound 11a: To a solution of **7a** (11.98 g, 42.7 mmol) in anhydrous MeOH (100 mL) was added under a nitrogen atmosphere *N*,*N*-dibenzylamine (8.42 g, 42.7 mmol), and the mixture was stirred at room temperature for 16 h. The solvent was evaporated under reduced pressure and the residue purified by column chromatography on silica gel (300 g) eluting with light petroleum/Et_2O, 9:1 (R_f = 0.19), to yield **11a** (15.71 g, 77%) as a 1:1.6 mixture

of two diastereoisomers as a slightly yellow oil. IR (film): $\tilde{\nu}$ = 3029 cm^{-1}, 2926, 2850, 1758 (C=O), 1732 (C=O), 745, 698. ^1H NMR (250 MHz, $CDCl_3$), isomer 1: δ = 0.49 (dd, ^2J = 6, ^3J = 6 Hz, 1 H, cPr-H), 1.05–2.35 (m, 4 H, cPr-H, 1′′-H), 3.44–3.63 (m, 2 H, 2′′-H), 3.75 (s, 3 H, OCH_3), 3.91 (s, 4 H, NCH_2Ph), 4.21 (s, 1 H, 2-H), 4.49 (s, 2 H, OCH_2Ph), 7.08–7.43 (m, 15 H, Ph-H). Isomer 2: δ = 0.88 (dd, ^2J = 5, ^3J = 5 Hz, 1 H, cPr-H), 1.05–2.35 (m, 4 H, cPr-H, 1′′-H), 3.44–3.63 (m, 2 H, 2′′-H), 3.74 (s, 3 H, OCH_3), 3.96 (s, 4 H, NCH_2Ph), 4.50 (s, 2 H, OCH_2Ph), 4.71 (s, 1 H, 2-H), 7.08–7.43 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT), isomer 1: δ = 23.6 (–, cPr-C), 29.2 (+, cPr-C), 29.4 (–, C-1′′), 51.1 (C_{quat}, cPr-C), 52.8 (+, OCH_3), 56.6 (–, NCH_2Ph), 62.1 (+, C-2), 69.8 (–, C-2′′), 72.8 (–, OCH_2Ph), 126.5 (+, Ph-C), 126.6 (+, Ph-C), 127.6 (+, Ph-C), 128.3 (+, Ph-C), 128.7 (+, Ph-C), 128.8 (+, Ph-C), 138.4 (C_{quat}, Ph-C), 139.7 (C_{quat}, Ph-C), 169.1 (C_{quat}, COO). Isomer 2: δ = 23.2 (–, cPr-C), 26.0 (+, cPr-C), 29.5 (–, C-1′′), 50.4 (C_{quat}, cPr-C), 52.9 (+, OCH_3), 56.6 (–, NCH_2Ph), 64.3 (+, C-2), 69.8 (–, C-2′′), 72.9 (–, OCH_2Ph), 126.5 (+, Ph-C), 126.6 (+, Ph-C), 127.6 (+, Ph-C), 128.3 (+, Ph-C), 128.7 (+, Ph-C), 128.8 (+, Ph-C), 138.4 (C_{quat}, Ph-C), 139.0 (C_{quat}, Ph-C), 169.5 (C_{quat}, COO) ppm. MS (70 eV): *m*/*z* (%) = 442 (<1) [M^+ – Cl], 386 (<1) [M^+ – CH_2Ph], 91 (100) [CH_2Ph^+]. $C_{29}H_{32}ClNO_3$ (478.0): calcd. C 72.87, H 6.75; found C 72.53, H 6.84.

Compound 11b: Compound **7b** (5.88 g, 22.0 mmol) was converted by the same method as described above for **7a** to yield **11b** (8.07 g, 79%, light petroleum/Et_2O, 10:1, R_f = 0.18) in a 1:2.3 mixture of diastereoisomers as a slightly yellow oil. IR (film): $\tilde{\nu}$ = 3028 cm^{-1}, 2951, 2855, 1756 (C=O), 1734 (C=O), 1454, 1272, 746 (C–$H_{arom.}$), 698 (C–$H_{arom.}$). ^1H NMR (250 MHz, $CDCl_3$), isomer 1: δ = 1.24 (dd, ^2J = 5.7, ^3J = 5.7 Hz, 1 H, cPr-H), 1.45 (dd, ^2J = 5.7, ^3J = 9.7 Hz, 1 H, cPr-H), 1.59–1.80 (m, 1 H, cPr-H), 3.51–3.85 (m, 2 H, 1′′-H), 3.75 (s, 3 H, OCH_3), 3.94 (br. s, 4 H, NCH_2Ph), 4.41 (s, 1 H, 2-H), 4.51 (s, 2 H, OCH_2Ph), 7.10–7.48 (m, 15 H, Ph-H) ppm. Isomer 2: δ = 0.79 (dd, ^2J = 5.7, ^3J = 5.7 Hz, 1 H, cPr-H), 1.20 (dd, ^2J = 5.7, ^3J = 9.7 Hz, 1 H, cPr-H), 1.59–1.80 (m, 1 H, cPr-H), 3.51–3.85 (m, 2 H, 1′′-H), 3.73 (s, 3 H, OCH_3), 3.99 (br. s, 4 H, NCH_2Ph), 4.49 (s, 2 H, OCH_2Ph), 4.86 (s, 1 H, 2-H), 7.10–7.48 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT), isomer 1: δ = 21.4 (–, cPr-C), 27.6 (+, cPr-C), 50.1 (C_{quat}, cPr-C), 52.8 (+, OCH_3), 56.6 (–, NCH_2Ph), 63.9 (+, C-2), 68.0 (–, C-1′′), 72.8 (–, OCH_2Ph), 126.5 (+, Ph-C), 127.5 (+, Ph-C), 127.8 (+, Ph-C), 128.2 (+, Ph-C), 128.4 (+, Ph-C), 128.7 (+, Ph-C), 138.0 (C_{quat}, Ph-C), 139.7 (C_{quat}, Ph-C), 169.2 (C_{quat}, COO). Isomer 2: δ = 22.3 (–, cPr-C), 30.9 (+, cPr-C), 51.1 (C_{quat}, cPr-C), 52.8 (+, OCH_3), 56.5 (–, NCH_2Ph), 61.3 (+, C-2), 68.3 (–, C-1′′), 72.6 (–, OCH_2Ph), 126.5 (+, Ph-C), 127.5 (+, Ph-C), 127.8 (+, Ph-C), 128.2 (+, Ph-C), 128.4 (+, Ph-C), 128.7 (+, Ph-C), 138.2 (C_{quat}, Ph-C), 139.5 (C_{quat}, Ph-C), 169.0 (C_{quat}, COO) ppm. MS (70 eV): *m*/*z* (%) = 428 (9) [M^+ – Cl], 372 (<1) [M^+ – CH_2Ph], 91 (100) [CH_2Ph^+]. $C_{28}H_{30}ClNO_3$ (464.0): calcd. C 72.48, H 6.52; found C 72.58, H 6.57.

Compound 12a: A solution of **11a** (13.31 g, 27.84 mmol) in THF (400 mL) was treated with water (10 mL) and freshly prepared zinc/copper couple[19] (30 g). The reaction mixture was stirred for 12 h, filtered through Celite, and the solvent evaporated under reduced pressure. The residue was dissolved in Et_2O (300 mL), the solution washed with saturated Na_2CO_3 solution (200 mL) and dried with $MgSO_4$. Purification by column chromatography on silica gel (250 g), eluting with light petroleum/Et_2O/NEt_3, 9:1:0.01, yielded **12a** (7.64 g, 62%) as a slightly yellow oil. IR (film): $\tilde{\nu}$ = 3029 cm^{-1}, 2850, 1736 (C=O), 1267, 734, 697. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.38 (dd, *J* = 4, *J* = 5 Hz, 1 H, cPr-H), 0.85 (m_c, 1 H, cPr-H), 0.78–0.97 (m, 1 H, cPr-H), 1.21–1.42 (m, 1 H, 1′′-H), 1.42–1.60 (m, 1 H, 1′′-H), 2.30 (d, ^2J = 15 Hz, 1 H, 2-H), 2.93 (d, ^2J = 15 Hz, 1 H, 2-H), 3.25 (t, ^3J = 7 Hz, 2 H, 2′′-H), 3.71 (d, ^2J = 14 Hz, 2 H, NCH_2Ph), 3.77 (s, 3 H, OCH_3), 3.85 (d, ^2J = 14 Hz, 2 H, NCH_2Ph), 4.44 (s, 2 H, OCH_2Ph), 7.15–7.58 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.6 MHz, $CDCl_3$, DEPT): δ = 20.0 (–, cPr-C), 25.4 (+, cPr-C), 29.8 (–, C-1′′), 32.9 (–, C-2), 44.8 (C_{quat}, cPr-C), 51.5 (+, OCH_3), 56.2 (–, NCH_2Ph), 69.8 (–, C-2′′), 72.7 (–, OCH_2Ph), 126.6 (+, Ph-C), 127.4 (+, Ph-C), 127.5 (+, Ph-C), 127.9 (+, Ph-C), 128.2 (+, Ph-C), 128.9 (+, Ph-C), 138.5 (C_{quat}, Ph-C), 140.1 (C_{quat}, Ph-C), 173.7 (C_{quat}, COO) ppm. MS (70 eV): *m*/*z* (%) = 352 (<1) [M^+ – CH_2Ph], 107 (9) [OCH_2Ph^+], 91 (100) [CH_2Ph^+]. $C_{29}H_{33}NO_3$: calcd. 443.2460 (correct mass).

Compound 12b: A solution of **11b** (10.10 g, 21.77 mmol) in THF (500 mL) was treated with water (8 mL) and freshly prepared zinc/copper couple[19] (25 g). The reaction mixture was stirred for 12 h, filtered through Celite, and the solvent evaporated under reduced pressure. The residue was taken up in Et_2O (250 mL), the solution washed with saturated NaCl solution (150 mL) and dried with $MgSO_4$. Purification by column chromatography on silica gel (200 g), eluting with light petroleum/Et_2O/NEt_3, 9:1:0.01, yielded **12b** (5.88 g, 63%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3028 cm^{-1}, 2851, 1739 (ester), 1453, 1209 (OCH_2Ph), 1075 (OCH_2Ph), 699. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.58 (dd, ^2J = 5, ^3J = 6 Hz, 1 H, cPr-H), 0.91 (dd, ^2J = 5, ^3J = 10 Hz, 1 H, cPr-H), 1.32 (m_c, 1 H, cPr-H), 2.39 (d, ^2J = 15 Hz, 1 H, 2-H), 2.91 (d, ^2J = 15 Hz, 1 H, 2-H), 3.36 (m_c, 2 H, 1′′-H), 3.74 (s, 3 H, OCH_3), 3.77 (d, ^2J = 13 Hz, 2 H, NCH_2Ph), 3.87 (d, ^2J = 13 Hz, 2 H, NCH_2Ph), 4.46 (s, 2 H, OCH_2Ph), 7.12–7.45 (m, 15 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.5 (–, cPr-C), 26.9 (+, cPr-C), 33.2 (–, C-2), 45.1 (C_{quat}, cPr-C), 51.7 (+, OCH_3), 56.1 (–, NCH_2Ph), 69.8 (–, C-1′′), 72.5 (–, OCH_2Ph), 126.7 (+, Ph-C), 127.4 (+, Ph-C), 127.5 (+, Ph-C), 127.9 (+, Ph-C), 128.3 (+, Ph-C), 128.9 (+, Ph-C), 138.5 (C_{quat}, Ph-C), 140.0 (C_{quat}, Ph-C), 173.6 (C_{quat}, COO) ppm. MS (70 eV): *m*/*z* (%) = 429 (3) [M^+], 398 (4) [M^+ – OCH_3], 356 (2) [M^+ – CH_2COOCH_3], 338 (94) [M^+ – CH_2Ph], 91 (100) [CH_2Ph^+]. $C_{28}H_{31}NO_3$ (429.6): calcd. C 78.29, H 7.27, N 3.26; found C 78.32, H 7.35, N 3.23.

Compound 13a. From 12a: Hydrogen was purged through a solution of **12a** (3.53 g, 7.96 mmol) and palladium on charcoal (10%, 600 mg) in MeOH (50 mL). The solution was stirred under hydrogen at ambient pressure for 3 d. The catalyst was filtered off through a plug of Celite, and the filtrate concentrated under reduced pressure. Minor impurities were removed by a second filtration through a short layer of silica gel eluting with methanol. Evaporation of the solvent yielded **13a** (1.11 g, 81%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3365 cm^{-1} (N–H), 1744 (C=O), 1001 (C–OH). ^1H NMR (250 MHz, D_2O): δ = 0.33 (dd, ^2J = 6, ^3J = 6 Hz, 1 H, cPr-H), 0.86 (dd, ^2J = 6, ^3J = 10 Hz, 1 H, cPr-H), 0.93–1.09 (m, 1 H, cPr-H), 1.20–1.37 (m, 1 H, 1′-H), 1.50–1.70 (m, 1 H, 1′′-H), 2.56 (m_c, 2 H, 2-H), 3.52 (t, ^3J = 7 Hz, 2 H, 2′′-H), 3.63 (s, 3 H, OCH_3) ppm. ^{13}C NMR (125.7 MHz, D_2O): δ = 17.1 (–, cPr-C), 20.8 (+, cPr-C), 31.1 (–), 34.1 (–), 37.7 (C_{quat}, cPr-C), 52.6 (+, OCH_3), 61.5 (–, C-2′′), 174.7 (C_{quat}, COO) ppm. MS (70 eV): *m*/*z* (%) = 172 (4) [M^+ – H], 142 (82) [M^+ – OCH_3], 128 (100) [M^+ – EtO]. $C_8H_{15}NO_3$: calcd. 173.1051 (correct mass).

Compound 13b. From 12b: Hydrogen was purged through a solution of **12b** (4.81 g, 11.2 mmol) and palladium on charcoal (10%, 2.0 g) in MeOH (80 mL). The solution was stirred under hydrogen at ambient pressure for 4 d. The catalyst was filtered off through a plug of Celite, and the filtrate concentrated under reduced pressure. Minor impurities were removed by a second filtration through a short layer of silica gel eluting with methanol. Evaporation of the

solvent yielded **13b** (1.44 g, 81%) as a colorless oil. From Compound **11b**: Hydrogen was purged through a solution of **11b** (4.60 g, 9.91 mmol) and palladium on charcoal (10%, 2.5 g) in MeOH (80 mL). The solution was stirred under hydrogen at ambient pressure for 14 d. Work-up as described above yielded **13b** (1.54 g, 98%) as a viscous oil. IR (film): $\tilde{\nu}$ = 3358 cm^{-1} (N–H), 2889, 1734 (C=O), 1604 (NH_2), 1020 (C–OH). ^1H NMR (250 MHz, D_2O): δ = 0.73 (dd, ^2J = 7, ^3J = 7 Hz, 1 H, cPr-H), 1.17 (dd, ^2J = 7, ^3J = 10 Hz, 1 H, cPr-H), 1.44–1.62 (m, 1 H, cPr-H), 2.69 (d, ^2J = 18 Hz, 1 H, 2-H), 2.84 (d, ^2J = 18 Hz, 1 H, 2-H), 3.35 (dd, J = 7, J = 12 Hz, 1 H, 1′-H), 3.56 (dd, J = 7, J = 12 Hz, 1 H, 1′-H), 3.60 (s, 3 H, OCH_3) ppm. **13b·HCl:** ^{13}C NMR (75.5 MHz, D_2O): δ = 15.3 (–), 24.5 (+), 35.6 (C_{quat}), 36.0 (–), 54.0 (+), 61.3 (–), 174.3 (C_{quat}, C=O) ppm. MS (70 eV): *m/z* (%) = 159 (3) [M^+], 142 (43) [M^+ – OH], 128 (19) [M^+ – OCH_3], 59 (100) [$COOMe^+$].

Compound 14a: To a vigorously stirred suspension of **13a** (750 mg, 4.33 mmol) in saturated Na_2CO_3 solution (30 mL) was added at –5 °C within 20 min benzyl chloroformate (960 mg, 5.63 mmol, 50% solution in toluene), and stirring was continued for 5 h at the same temperature. After extraction with EtOAc (3 × 75 mL), drying over $MgSO_4$ and evaporation of the solvent, the residue was purified by column chromatography on silica gel (40 g), eluting with Et_2O, to yield **14a** (1.04 g, 78%) as a colorless oil (R_f = 0.35). IR (film): $\tilde{\nu}$ = 3368 cm^{-1} (N–H), 1732 (C=O), 1700 (C=O), 1514, 1257 (O–CH_2Ph), 734, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.40 (dd, ^2J = 6, ^3J = 6 Hz, 1 H, cPr-H), 1.01 (m_c, 1 H, cPr-H), 1.10–1.30 (m, 2 H, cPr-H, 1′′-H), 1.89–2.02 (m, 1 H, 1′′-H), 2.16 (d, ^2J = 17 Hz, 1 H, 2-H), 3.03 (d, ^2J = 17 Hz, 1 H, 2-H), 3.67 (s, 3 H, OCH_3), 3.75 (t, ^3J = 4 Hz, 2 H, 2′′-H), 5.02 (d, ^2J = 12 Hz, 1 H, CH_2Ph), 5.10 (d, ^2J = 12 Hz, 1 H, CH_2Ph), 5.92 (s, 1 H, NH), 7.24–7.40 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.0 (–, cPr-C), 24.4 (+, cPr-C), 32.1 (–, C-1′′), 33.6 (C_{quat}, cPr-C), 37.4 (–, C-2), 51.5 (+, OCH_3), 61.9 (–, C-2′′), 66.9 (–, OCH_2Ph), 128.0 (+, Ph-C), 128.1 (+, Ph-C), 128.4 (+, Ph-C), 136.0 (C_{quat}, Ph-C), 157.1 (C_{quat}, NCO), 172.6 (C_{quat}, OCO) ppm. MS (70 eV): *m/z* (%) = 307 (<1) [M^+], 276 (<1) [M^+ – OCH_3], 172 (8) [M^+ – OC-OCH_2Ph], 91 (100) [CH_2Ph^+]. $C_{16}H_{21}NO_5$: calcd. 307.1419 (correct mass).

Compound 14b: To a vigorously stirred suspension of **13b** (1.02 g, 6.41 mmol) in saturated Na_2SO_3 solution (35 mL) was added at –5 °C within 30 min benzyl chloroformate (1.21 g, 7.09 mmol, 50% solution in toluene), and stirring was continued for 4 h at the same temperature. After extraction with EtOAc (3 × 100 mL), drying over $MgSO_4$ and evaporation of the solvent, the residue was purified by column chromatography on silica gel (150 g), eluting with Et_2O, to yield **14b** (0.91 g, 48%) as a colorless oil (R_f = 0.28). IR (film): $\tilde{\nu}$ = 3357 cm^{-1} (N–H), 2953, 1718 (C=O), 1499, 1249, 734 (C–$H_{arom.}$), 698 (C–$H_{arom.}$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.58 (dd, ^2J = 6.3, ^3J = 6.3 Hz, 1 H, cPr-H), 1.11 (dd, ^2J = 6.3, ^3J = 9.4 Hz, 1 H, cPr-H), 1.49 (dddd, ^3J = 9.4, ^3J = 6.3, ^3J = 10.6, ^3J = 4.0 Hz, 1 H, cPr-H), 2.52 (d, ^2J = 17.0 Hz, 1 H, 2-H), 2.94 (d, ^2J = 17.0 Hz, 1 H, 2-H), 3.17 (dd, ^3J = 10.6, ^2J = 11.3 Hz, 1 H, 1′′-H), 3.50 (s, 1 H, OH), 3.66 (s, 3 H, OCH_3), 3.93 (dd, ^3J = 4.0, ^2J = 11.3 Hz, 1 H, 1′′-H), 5.07 (s, 2 H, CH_2Ph), 5.90 (s, 1 H, NH), 7.32 (m_c, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.5 (–, cPr-C), 28.8 (+, cPr-C), 34.1 (C_{quat}, cPr-C), 36.7 (–, C-2), 52.0 (+, OCH_3), 62.3 (–, C-1′′), 66.7 (–, CH_2Ph), 128.0 (+, Ph-C), 128.1 (+, Ph-C), 128.4 (+, Ph-C), 136.2 (C_{quat}, Ph-C), 156.1 (C_{quat}, NCO), 173.5 (C_{quat}, OCO) ppm. MS (70 eV): *m/z* (%) = 143 (7) [M^+ – NHZ], 91 (73) [CH_2Ph^+], 59 (93) [$COOMe^+$]. $C_{15}H_{19}NO_5$ (293.3): calcd. C 61.42, H 6.53, N 4.78; found C 61.38, H 6.48, N 4.78.

Compound 15a: To a solution of **14a** (558 mg, 1.82 mmol), triphenylphosphane (477 mg, 1.82 mmol) and phthalimide (268 mg, 1.82 mmol) in anhydrous THF (15 mL) was added DEAD (317 mg, 1.82 mmol), and the mixture was stirred at ambient temperature overnight. The solvent was evaporated under reduced pressure, and the residue purified by column chromatography on silica gel (70 g), eluting with dichloromethane/EtOAc, 85:15, to yield **15a** (521 mg, 66%) as a colorless oil (R_f = 0.32). IR (film): $\tilde{\nu}$ = 3359 cm^{-1}, 2951, 1772 (C=O), 1713 (C=O), 1396, 721, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.44 (dd, ^2J = 6, ^3J = 6 Hz, 1 H, cPr-H), 1.00–1.36 (m, 2 H, cPr-H), 1.48–1.71 (m, 1 H, 1′′-H), 1.75–1.92 (m, 1 H, 1′′-H), 2.72 (s, 2 H, 2-H), 3.59 (s, 3 H, OCH_3), 3.85 (m_c, 2 H, 2′′-H), 5.04 (s, 2 H, OCH_2Ph), 5.61 (s, 1 H, NH), 7.23–7.44 (m, 5 H, Ph-H), 7.65–7.91 (m, 4 H, Phth-H) ppm. MS (70 eV): *m/z* (%) = 436 (<1) [M^+], 405 (5) [M^+ – OCH_3], 345 (8) [M^+ – CH_2Ph], 301 (92) [M^+ – $OCOCH_2Ph$], 160 (70) [$PhthNCH_2^+$], 91 (100) [CH_2Ph^+]. $C_{24}H_{24}N_2O_6$: calcd. 436.1634 (correct mass).

Compound 15b: To a solution of **14b** (745 mg, 2.54 mmol), triphenylphosphane (666 mg, 2.54 mmol) and phthalimide (374 mg, 2.54 mmol) in anhydrous THF (15 mL) was added DEAD (317 mg, 1.82 mmol), and the mixture was stirred at ambient temperature overnight. The solvent was evaporated under reduced pressure, and the residue purified by column chromatography on silica gel (100 g), eluting with dichloromethane/EtOAc, 9:1, to yield **15b** (724 mg, 67%) as a colorless oil (R_f = 0.42). IR (film): $\tilde{\nu}$ = 3361 cm^{-1} (N–H), 2953, 1772 (C=O), 1712 (C=O), 1391, 1240, 733 (C–$H_{arom.}$), 698 (C–$H_{arom.}$). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.73 (dd, ^2J = 6.5, ^3J = 6.5 Hz, 1 H, cPr-H), 1.17 (m_c, 1 H, cPr-H), 1.70–1.90 (m, 1 H, cPr-H), 2.50 (d, ^2J = 17.9 Hz, 1 H, 2-H), 2.99 (d, ^2J = 17.9 Hz, 1 H, 2-H), 3.55 (s, 3 H, OCH_3), 3.55–3.71 (m, 2 H, 1′′-H), 5.00 (s, 2 H, CH_2Ph), 5.60 (s, 1 H, NH), 7.12–7.42 (m, 5 H, Ph-H), 7.61–7.92 (m, 4 H, Phth-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.5 (–, cPr-C), 24.4 (+, cPr-C), 34.2 (C_{quat}, cPr-C), 36.9 (–, C-2), 37.8 (–, C-1′′), 51.7 (+, OCH_3), 66.5 (–, OCH_2Ph), 123.2 (+, Phth-C), 128.0 (+, Ph-C), 128.0 (+, Ph-C), 128.4 (+, Ph-C), 132.7 (C_{quat}, Phth-C), 133.9 (+, Phth-C), 136.3 (C_{quat}, Ph-C), 168.2 (C_{quat}, NCO), 172.3 (C_{quat}, OCO) ppm. MS (70 eV): *m/z* (%) = 422 (<1) [M^+], 331 (11) [M^+ – CH_2Ph], 287 (35) [M^+ – $OCOCH_2Ph$], 91 (100) [CH_2Ph^+]. $C_{23}H_{22}N_2O_6$: calcd. 422.1477 (correct mass).

Compound 16a: To a solution of **15a** (352 mg, 0.81 mmol) in a 1:1 mixture of MeOH and dichloromethane (10 mL) was added at ambient temperature hydrazine hydrate (122 mg, 2.43 mmol), and the mixture was stirred for 24 h. Then a mixture of glacial acid and MeOH (1:4, 10 mL) was added with stirring for 5 min at room temperature. The mixture was cooled down to –20 °C for 5 h. The resulting precipitate was filtered off and dissolved in EtOAc (30 mL). The organic phase was washed with saturated $NaHCO_3$ (3 × 25 mL), dried with $MgSO_4$ and the solvent evaporated under reduced pressure. Purification by column chromatography on silica gel (20 g), eluting with Et_2O/MeOH/Et_3N 6:4:1, yielded **16a** (95 mg, 38%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3362 cm^{-1}, 2953, 1734 (C=O), 732, 698. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.41 (dd, ^2J = 5.6, ^3J = 5.6 Hz, 1 H, cPr-H), 1.02–1.14 (m, 2 H, 1′′-H), 1.45–1.60 (m, 1 H, cPr-H), 1.68–1.90 (m, 1 H, cPr–H), 2.46 (d, ^2J = 17.1 Hz, 1 H, 2-H), 2.78 (d, ^2J = 17.1 Hz, 1 H, 2-H), 2.82–3.10 (m, 2 H, 2′′-H), 3.63 (s, 3 H, OCH_3), 5.01 (s, 2 H, OCH_2Ph), 6.04 (br. s, 3 H, NH_2, NH), 7.20–7.43 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.8 (–, cPr-C), 23.5 (+, cPr-C), 29.8 (–, C-1′′), 33.6 (C_{quat}, cPr-C), 36.7 (–, C-2), 40.3 (–, C-2′′), 51.6 (+, OCH_3), 66.5 (–, OCH_2Ph), 127.9 (+, Ph-C), 128.0 (+, Ph-C), 128.4 (+, Ph-C), 136.1 (C_{quat}, Ph-C), 156.4 (C_{quat}, NCO), 172.4 (C_{quat}, OCO) ppm.

Compound 17: Compound **15b** (600 mg, 1.42 mmol) was converted by the same method as described above for compound **15a** yielding **17** (315 mg, 85%) as a slightly yellow oil. IR (film): $\tilde{\nu}$ = 3436 cm^{-1}, 1710 (C=O), 1653 (C=O), 1521, 1456, 1416, 1057. ^1H NMR (250 MHz, CD_3OD): δ = 0.66–0.82 (m, 2 H, cPr-H), 1.24–1.39 (m, 1 H, cPr-H), 2.63 (d, ^2J = 16 Hz, 1 H, 2-H), 2.76 (d, ^2J = 16 Hz, 1 H, 2-H), 3.23 (d, ^2J = 13 Hz, 1 H, 5-H), 3.64 (d, ^2J = 13 Hz, 1 H, 5-H), 4.94 (s, 2 H, CH_2Ph), 7.09–7.31 (m, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, CD_3OD, DEPT): δ = 12.7 (–, cPr-C), 19.2 (+, cPr-C), 32.0 (C_{quat}, cPr-C), 37.2 (–), 40.2 (–), 61.4 (–, CH_2Ph), 128.7 (+, Ph-C), 128.9 (+, Ph-C), 129.4 (+, Ph-C), 138.0 (C_{quat}, Ph-C), 158.2 (C_{quat}, NCO), 173.5 (C_{quat}, OCO) ppm.

Compound 18: Hydrogen was slowly (1–2 bubbles/s) purged through a solution of **17** (50 mg, 0.19 mmol) and a tiny amount of Pd/C (10% Pd, 50% H_2O) in MeOH for 1 h. The catalyst was filtered off through a plug of Celite, and the filtrate treated with a few drops of hydrogen chloride solution (4.5 M in Et_2O). Evaporation under reduced pressure yielded **18** (31 mg, 99%) as a slightly yellow oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.07 (m_c, 1 H, cPr-H), 1.26 (m_c, 1 H, cPr-H), 1.89 (m_c, 1 H, cPr-H), 2.95 (d, J = 17 Hz, 1 H, 2-H), 3.05 (d, J = 17 Hz, 1 H, 2-H), 3.49 (d, J = 13 Hz, 1 H, 5-H), 3.85 (d, J = 13 Hz, 1 H, 5-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.47 (–, cPr-C), 16.28 (+, C-4), 33.40 (C_{quat}, C-3), 34.98 (–, C-2*), 40.02 (–, C-5*), 171.40 (C_{quat}, C-1) ppm. $C_6H_{10}N_2O$ (amine): calcd. 126.0793 (correct mass).

Compound 19a: To a solution of **14a** (1.60 g, 5.21 mmol) in dichloromethane (40 mL) was added at 0 °C NEt_3 (1.02 g, 10.1 mmol) and methanesulfonyl chloride (1.19 g, 10.4 mmol), and the mixture was stirred at the same temperature for 2 h. The solvent was evaporated under reduced pressure, the residue dissolved in EtOAc (50 mL), the solution washed with saturated $NaHCO_3$ solution, dried with Na_2SO_4 and evaporated under reduced pressure to yield **19a** (2.01 g, quant.) as a slightly yellow solid, m.p. 90 °C (decomp.). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.48 (m_c, 1 H, cPr-H), 1.05–1.20 (m, 2 H, cPr-H), 1.65–1.90 (m, 2 H, 1′′-H), 2.52 (d, 1 H, 2-H), 2.60 (d, 1 H, 2-H), 2.99 (s, 3 H, SCH_3), 3.65 (s, 3 H, OCH_3), 4.35 (m_c, 2 H, 2′′-H), 5.02 (s, 2 H, CH_2Ph), 5.68 (s, 1 H, NH), 7.30 (m_c, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.93 (–, cPr-C), 22.09 (+, cPr-C), 29.22 (–, C-1′′), 33.41 (C_{quat}, cPr-C), 36.60 (–, C-2), 37.10 (+, SCH_3), 51.64 (+, OCH_3), 66.34 (–, OCH_2), 69.30 (–, OCH_2), 127.83 (+, Ph-C), 127.98 (+, Ph-C), 128.37 (+, Ph-C), 136.22 (C_{quat}, Ph-C), 155.71 (C_{quat}, NCO), 172.08 (C_{quat}, CO_2Me) ppm. MS (70 eV): m/z (%) = 385 (<1) [M^+], 294 (8) [M^+ – Bn], 250 (40) [M^+ – OCOBn], 91 (100) [Bn^+]. $C_{17}H_{23}NO_7S$ (385.4): calcd. C 52.98, H 6.01; found C 53.08, H 6.00.

Compound 19b: To a solution of **14b** (540 mg, 1.84 mmol) in dichloromethane (35 mL) was added at 0 °C NEt_3 (317 mg, 3.13 mmol) and methanesulfonyl chloride (380 mg, 3.32 mmol), and the mixture was stirred at the same temperature for 2 h. The solvent was evaporated under reduced pressure, the residue dissolved in EtOAc (50 mL), washed with saturated $NaHCO_3$ solution, dried with Na_2SO_4 and evaporated under reduced pressure to yield **19b** (659 mg, 96%) as a colorless solid, m.p. 87 °C (decomp.). IR (KBr): $\tilde{\nu}$ = 3354 cm^{-1}, 1722 (C=O), 1685 (C=O), 1507 (δ_{NH}), 1363. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.81 (dd, J_1 = 6, J_2 = 6 Hz, 1 H, cPr-H), 1.31 (m_c, 1 H, cPr-H), 1.63 (m_c, 1 H, cPr-H), 2.61 (d, J = 17 Hz, 1 H, 2-H), 2.77 (d, J = 17 Hz, 1 H, 2-H), 3.05 (s, 3 H, SCH_3), 3.69 (s, 3 H, OCH_3), 4.24 (m_c, 2 H, 1′′-H), 5.06 (s, 2 H, OCH_2Ph), 5.66 (s, 1 H, NH), 7.33 (m_c, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.73 (–, cPr-C), 23.99 (+, cPr-C), 34.41 (C_{quat}, cPr-C), 36.87 (–, C-2), 37.90 (+, SCH_3), 51.91 (+, OCH_3), 66.71 (–, OCH_2), 69.42 (–, OCH_2), 128.04 (+, Ph-C), 128.19 (+, Ph-C), 128.53 (+, Ph-C), 136.12 (C_{quat}, Ph-C), 155.60 (C_{quat}, NCO), 171.81 (C_{quat}, CO_2Me) ppm. FAB-MS (glycerine): m/z (%) = 372 [M + H^+]. $C_{16}H_{21}NO_7S$ (371.4): calcd. C 51.74, H 5.70; found C 51.84, H 5.76.

Compound 20a: To a solution of **19a** (2.01 g, 5.21 mmol) in anhydrous DMF (10 mL) was added at room temperature sodium azide (1.69 g, 26.0 mmol), and the mixture was stirred for 4 d. The solvent was evaporated under reduced pressure and the residue dissolved in EtOAc (100 mL). The organic phase was washed with water, dried with Na_2SO_4, and the solvent evaporated under reduced pressure. Purification by column chromatography on silica gel, eluting with light petroleum/Et_2O, 1:1 → Et_2O, yielded **20a** (1.54 g, 89%) as a colorless oil. IR (film): $\tilde{\nu}$ = 3357 cm^{-1}, 2952, 2099 (N≡N), 1737 (C=O), 1501 (δ_{NH}), 1241, 1100, 738, 699. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.48 (m_c, 1 H, cPr-H), 1.05–1.26 (m, 2 H, cPr-H), 1.49 (m_c, 1 H, 1′′-H), 1.75 (m_c, 1 H, 1′′-H), 2.54 (d, ^2J = 17 Hz, 1 H, 2-H), 2.69 (d, ^2J = 17 Hz, 1 H, 2-H), 3.42 (m_c, 2 H, 2′′-H), 3.68 (s, 3 H, OCH_3), 5.05 (s, 2 H, CH_2Ph), 5.60 (br. s, 1 H, NH), 7.33 (m_c, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.27 (–, cPr-C), 23.24 (+, cPr-C), 29.16 (–, C-1′′), 33.49 (C_{quat}, cPr-C), 36.64 (–, C-2), 50.81 (–, C-2′′), 51.78 (+, OCH_3), 66.50 (–, CH_2Ph), 128.04 (+, 4 C, Ph-C), 128.48 (+, Ph-C), 136.19 (C_{quat}, Ph-C), 155.79 (C_{quat}, NCO), 172.31 (C_{quat}, CO_2Me) ppm. MS (DCI, NH_3): m/z (%) = 350 (100) [M + NH_4^+], 333 (10) [M + H^+]. $C_{16}H_{20}N_4O_4$ (332.4): calcd. C 57.82, H 6.07; found C 57.54, H 5.87.

Compound 20b: To a solution of **14b** (520 mg, 1.77 mmol) and triphenylphosphane (511 mg, 1.95 mmol) in anhydrous benzene was added a solution of hydrazoic acid in benzene (2.07 mL, 1.95 mmol, 0.94 M) avoiding intensive light. A solution of DIAD (394 mg, 1.95 mmol) in benzene (2 mL) was added dropwise, and the mixture was stirred for 15 min. The solvent was evaporated and the residue purified by column chromatography on silica gel, eluting with light petroleum/Et_2O, 1:1 → Et_2O (R_f [Et_2O] = 0.60). A mixture of compound **20b** along with the hydrazine derivative of the coupling reagent (638 mg, ratio 1.2:1) was obtained, yield ca. 74% of **20b**. This mixture was used for the following transformation to compound **23** without further purification. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.68 (m_c, 1 H, cPr-H), 1.10–1.30 (m, 1 H, cPr-H), 1.47 (m_c, 1 H, cPr-H), 2.64 (br. s, 2 H, 2-H), 3.28 (m_c, 2 H, 1′′-H), 3.66 (s, 3 H, OCH_3), 5.04 (br. s, 2 H, OCH_2Ph), 5.74 (br. s, 1 H, NH), 7.31 (m_c, 5 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.72 (–, cPr-C), 24.12 (+, cPr-C), 33.49 (C_{quat}, cPr-C), 36.80 (–, C-2), 50.91 (–, C-1′′), 51.78 (+, OCH_3), 66.56 (–, OCH_2Ph), 128.00 (+, Ph-C), 128.06 (+, Ph-C), 128.41 (+, Ph-C), 136.12 (C_{quat}, Ph-C), 155.65 (C_{quat}, NCO), 171.97 (C_{quat}, COO) ppm. MS (DCI, NH_3): m/z (%) = 654 (3) [2 M + NH_4^+], 336 (100) [M + NH_4^+], 319 (15) [M + H^+].

Compound 21: To a solution of **20a** (1.51 g, 4.54 mmol) in THF (5 mL) was added at room temperature triphenylphosphane (1.19 g, 4.54 mmol) and water (82 μL, 4.5 mmol), and the mixture was stirred for 24 h. The solvent was evaporated under reduced pressure. The residue of crude **16a** was taken up in a 1:1 mixture of light petroleum/Et_2O and the mixture in a flask was immersed in an ultrasound bath to precipitate triphenylphosphane oxide. The phosphane oxide was filtered off, washed with an additional 100 mL of the solvent mixture, and the filtrate was concentrated in vacuo. The residue was dissolved in DMF (15 mL) and *N*,*N*′-(dibenzyloxycarbonyl)thiourea-*S*-methyl ether (1.63 g, 4.55 mmol), $HgCl_2$ (1.23 g, 4.53 mmol) and NEt_3 (0.92 g, 9.09 mmol) were added, and the mixture was stirred at ambient temperature for 2 h. The reaction mixture was filtered through Celite, and the Celite

washed with Et_2O (150 mL). The filtrate was washed with water (100 mL) and dried with $MgSO_4$. Purification by column chromatography on silica gel, eluting with Et_2O yielded **21** (1.82 g, 65%) as a colorless oil. ^1H NMR (250 MHz, $CDCl_3$): δ = 0.48 (m_c, 1 H, cPr-H), 1.11 (m_c, 2 H, cPr-H), 1.63 (m_c, 2 H, 1′′-H), 2.52 (d, ^2J = 17.3 Hz, 1 H, 2-H), 2.74 (d, ^2J = 17.3 Hz, 1 H, 2-H), 3.40–3.80 (m, 2 H, 2′′-H), 3.66 (s, 3 H, OCH_3), 5.05–5.20 (m, 6 H, CH_2Ph), 5.69 (s, 1 H, NH), 7.2–7.4 (m, 15 H, Ph-H), 8.61 (br. s, 1 H, NH), 11.75 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.2 (–, cPr-C), 23.6 (+, cPr-C), 28.8 (–, C-1′′), 33.2 (C_{quat}, cPr-C), 36.7 (–, C-2), 40.5 (–, C-6), 51.6 (+, OCH_3), 66.4 (–, OCH_2), 67.0 (–, OCH_2), 67.9 (–, OCH_2), 127.7–128.6 (+, 15 C, Ph-C), 134.5 (C_{quat}, Ph-C), 136.2 (C_{quat}, Ph-C), 136.7 (C_{quat}, Ph-C), 153.5 (C_{quat}, NCO), 155.8 (C_{quat}, 2 C, NCO), 163.6 (C_{quat}, NCN), 172.4 (C_{quat}, COO) ppm. $C_{33}H_{36}N_4O_8$ (616.7): calcd. C 64.27, H 5.88; found C 64.57, H 6.07.

Compound 23: To a solution of an aliquot of the above described crude **20b** (344 mg, max. 194 mg **20b**) in THF (1 mL) was added at room temperature triphenylphosphane (176 mg, 0.67 mmol) and water (12 µL, 0.67 mmol), and the mixture stirred for 24 h. The solvent was evaporated under reduced pressure. The residue of crude **16b** was dissolved in MeOH (10 mL), *N*-(benzyloxycarbonyl) succinimide (228 mg, 0.92 mmol) and NEt_3 (135 mg, 1.33 mmol) were added, and the mixture stirred at room temperature for 1 h. The solvent was evaporated, and the residue taken up in Et_2O (30 mL), the solution washed with saturated Na_2CO_3 solution and dried with Na_2SO_4. Purification by column chromatography on silica gel, eluting with light petroleum/Et_2O, 1:2, yielded **23** (90 mg, 35%) as a colorless oil (R_f = 0.21). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.60 (m_c, 1 H, cPr-H), 1.13 (m_c, 1 H, cPr-H), 1.33 (m_c, 1 H, cPr-H), 2.4–2.8 (m, 3 H, 2-H, 1′′-H), 3.65 (s, 3 H, OCH_3), 3.65–3.80 (m, 1 H, 1′′-H), 5.06 (s, 2 H, OCH_2), 5.11 (s, 2 H, OCH_2), 5.80 (s, 1 H, NH), 5.92 (br. s, 1 H, NH), 7.2–7.4 (m, 10 H, Ph-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.90 (–, cPr-C), 24.81 (+, cPr-C), 33.28 (C_{quat}, cPr-C), 36.30 (–, C-2), 41.45 (–, C-1′′), 51.76 (+, OCH_3), 66.37 (–, OCH_2), 66.57 (–, OCH_2), 127.85 (+, Ph-C), 127.91 (+, Ph-C), 127.97 (+, Ph-C), 128.05 (+, Ph-C), 128.31 (+, Ph-C), 128.39 (+, Ph-C), 136.00 (C_{quat}, Ph-C), 136.65 (C_{quat}, Ph-C), 156.14 (C_{quat}, 2 C, NCO), 172.49 (C_{quat}, C-1) ppm. MS (DCI, NH_3), *m/z* (%):871 (1), 444 (199) [M + NH_4^+], 427 (15) [M + H^+].

3,4,5,6-Tetrahydro-5-{*N*-methyl-*N*-[(*E*)-β-3′,4′-methanohomoarginyl]amino}-2-(ureido)pyrimidin-4-one Dihydrochloride (2): To a solution of **21** (300 mg, 0.486 mmol) in dioxane (6 mL) was added 2 N NaOH solution (5 mL), and the mixture was stirred for 1 h, then water (50 mL) was added, and the mixture extracted with EtOAc (50 mL). The pH value of the aqueous phase was adjusted to 5.4 using a glass electrode by dropwise addition of 1 M hydrochloric acid, the solution was then extracted with dichloromethane (3 × 50 mL), the organic phase washed with saturated $(NH_4)_2CO_3$ solution (30 mL), dried with $MgSO_4$, and the solvent evaporated under reduced pressure to yield crude **4**-Z_3 (292 mg). ^1H NMR (250 MHz, $CDCl_3$): δ = 0.46 (m_c, 1 H, cPr-H), 1.09 (m_c, 2 H, cPr-H), 1.61 (m_c, 2 H, 1′′-H), 2.53 (d, ^2J = 17 Hz, 1 H, 2-H), 2.75 (d, ^2J = 17 Hz, 1 H, 2-H), 3.4–3.8 (m, 2 H, 2′′-H), 5.05–5.20 (m, 6 H, CH_2Ph), 5.83 (s, 1 H, NH), 7.2–7.5 (m, 15 H, Ph-H), 8.60 (s, 1 H, NH), 8.97 (s, 1 H, NH), 11–12 (br. s, 1 H, COOH) ppm. FAB-MS (glycerine matrix): *m/z* (%) = 625 (20) [M + Na^+], 603 (45) [M + H^+]. An aliquot of the crude **4**-Z_3 (157 mg, max. 261 µmol) was dissolved in anhydrous DMF (4 mL) and treated with the dihydropyrimidinone derivative **22** (48 mg, 0.26 mmol), HATU (198 mg, 0.52 mmol) and Hünig's base (67 mg, 0.52 mmol). The mixture was stirred for 1 d with exclusion of light, the solvent was evaporated, the residue dissolved in dichloromethane (100 mL), and the organic phase washed with 2 N HCl (100 mL). Evaporation and drying under reduced pressure yielded **2**-Z_3 (187 mg, max. 93%) as a 1:1 mixture of two diastereoisomers as a colorless powder. ^1H NMR (250 MHz, [D_6]DMSO): δ = 0.43 (br. s, 1 H, cPr-H), 0.87 (br. s, 2 H, cPr-H), 1.55 (br. s, 2 H, 2′-H), 2.87 (s, 3 H, NCH_3), 3.2–3.8 (m, 6 H, 5′-H, 6′-H, 6-H), 4.90–5.20 (m, 7 H, CH_2Ph, 5-H) 7.2–7.7 (m, 19 H, Ph-H, NH), 8.55 (br. s, 1 H), 10.50 (br. s, 1 H), 11.60 (br. s, 1 H) ppm. MS (ESI$^+$): calcd. for ($C_{38}H_{43}N_9O_9$ + H): 770.8; found [M + H]: 770.3.

Hydrogen was slowly (1–2 bubbles/s) purged through a suspension of an aliquot of **2**-Z_3 (72 mg, 94 µmol) and $PdCl_2$ (17 mg, 96 µmol) in MeOH for 4.5 h, palladium black was filtered off through a plug of Celite, and the solvent evaporated under reduced pressure to yield the dihydrochloride of **2** (43 mg, quant.) as a mixture of two diastereoisomers. ^1H NMR (250 MHz, D_2O): δ = 0.88 (m, 1 H), 0.93 (m, 1 H), 1.05 (m, 1 H), 1.12 (m, 2 H), 2.81–3.02 (m, 5 H), 3.07 (m. 2 H), 3.92 (m, 2 H), 4.95 (m, 1 H) ppm. ^{13}C NMR (75.5 MHz, D_2O, 35 °C, APT): δ = 14.6 (–, cPr-C), 18.7 (+, C-4′), 26.4 (–, C-5′), 33.5 (–, C-2′), 34.1 (–, C-3′), 34.4 and 35.2 (+, NMe), 38.3 (–, C-6), 39.9 (–, C-6′), 53.6 and 54.4 (+, C-5), 151.9 (–, guanidino-C), 154.3 (–, C-2), 156.4 (–, ureido-C), 166.5 (–, C-1′), 172.1 and 172.4 (–, C-4) ppm. MS (ESI$^+$): calcd. for ($C_{14}H_{25}N_9O_3$ + H) 368.4; found [M + H] 368.2.

3,4,5,6-Tetrahydro-5-{*N*-methyl-*N*-[(*E*)-β-3′,4′-methanoornithinyl]amino}-2-(ureido)pyrimidin-4-one Dihydrochloride (3): To a solution of **23** (80.0 mg, 0.188 mmol) in dioxane (3 mL) was added 2 N NaOH solution (2 mL), and the mixture was stirred for 1.5 h, then pH 5.00 buffer solution (citric acid/NaOH, 30 mL) was added, and the pH value of the aqueous phase adjusted to pH 4.9 using a glass electrode by dropwise addition of 2 N HCl (2 mL). The aqueous phase was extracted with dichloromethane (2 × 30 mL), washed with saturated $(NH_4)_2CO_3$ solution (30 mL), dried with $MgSO_4$, and the solvent evaporated under reduced pressure. The residue was dissolved in anhydrous DMF (6 mL), to the solution was added **22** (35.0 mg, 0.189 mmol), HATU (143 mg, 0.376 mmol) and Hünig's base (50 mg, 0.387 mmol), and the mixture was stirred overnight with exclusion of light. The solvent was evaporated under reduced pressure, the residue taken up in dichloromethane (50 mL) and the flask immersed in an ultrasound bath until the residue had completely dissolved. The solution was washed with 1 N HCl (50 mL) and then saturated NaCl solution (50 mL). The solvent was concentrated, a small amount of light petroleum added and the mixture cooled to –18 °C. Upon cautious shaking a colorless solid precipitated. This was filtered off to yield 133 mg of crude **3**-Z_2·2HCl (impurified by side products stemming from the coupling reagent). An aliquot of this crude product (100 mg, max. 0.14 mmol) was dissolved in MeOH (10 mL), $PdCl_2$ (24 mg) was added and hydrogen (2–3 bubbles/s) purged through the mixture for 5 h. Palladium black was filtered off through a plug of Celite, and the solvent evaporated under reduced pressure. A thin layer of light petroleum was added, and the vial shaken carefully. The precipitating solid was filtered off to yield compound **3** (36 mg, 66%) as its hygroscopic dihydrochloride salt as a mixture of two diastereoisomers. ^1H NMR (250 MHz, D_2O): δ = 0.83 (m_c, 1 H, cPr-H), 1.31 (m_c, 1 H, cPr-H), 1.61 (m_c, 1 H, cPr-H), 2.73–3.22 (m, 7 H), 3.80–3.93 (m, 2 H), 5.05 (m_c, 1 H) ppm. ^{13}C NMR (62.9 MHz, D_2O, DEPT): δ = 13.99 (–, cPr-C), 18.24 and 18.32 (+, C-4′), 33.91 and 34.07 (–, C-2′), 34.23 and 34.29 (C_{quat}, C-3′), 34.35 and 35.31 (+, NCH_3), 38.01 (–, C-5′*), 38.15 (–, C-6*), 53.58 and 54.63 (+, C-5), 151.75 (C_{quat}), 154.30 (C_{quat}), 166.45 and 166.52 (C_{quat}, C-1′), 171.76 and 171.81 (C_{quat}, C-4) ppm. MS (ESI$^+$): calcd. for ($C_{12}H_{21}N_7O_3$ + Na) = 334.3; found [M + Na] = 334.2.

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