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Efficient Transfer of Chelating Amides into Different Types of Esters and Lactones

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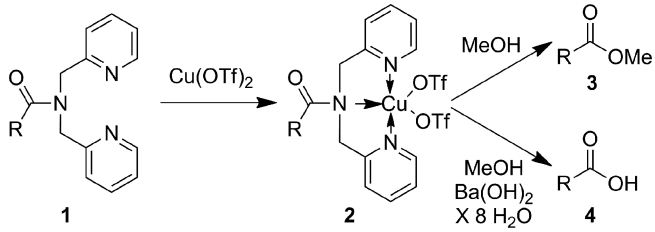
We describe a general and versatile approach for the conversion of carboxylic acid amides into their corresponding esters despite the fact that the former are thermodynamically more stable. The transformations are mediated by the coordination of Cu^{I} by a chelating entity. The resulting weakening of the amide bond allows for nucleophilic attack by alcoholic hydroxyl functions. The principle is demonstrated for a wide variety of transformations, leading to different kinds of esters and lactones.

Introduction

In 1970, Houghton and Puttner published a seminal work on chelating amides,[1] which served us as a basis for the development of a new protection scheme for carboxylic acids.[2] The approach is based on a mild conversion of a carboxamide into a methyl ester by using Cu^{2+} salts in methanol. The protection of carboxylic acids with bispicolylamine (bpa) as chelating entity fulfilled almost all criteria for an ideal protecting group for carboxylic acids. The protection was easily performed starting from the carboxylic acid and bispicolylamine by applying a commonly used activating agent such as *N*,*N*,*N*′,*N*′-tetramethyl-*O*-(benzotriazol-1-yl)uronium tetrafluoroborate (TBTU).[3] The resulting amide **1** turned out to be very robust and could be applied in combination with a wide variety of reaction conditions. Moreover, the transformation into its methyl ester or the free acid is possible under mild reaction conditions involving the amide nitrogen in an unusual complexation to Cu^{2+} as in **2**. The involvement of the amide nitrogen in the complexation to Cu^{2+} leads to an enhancement of the electrophilicity on the carbonyl C-atom, rendering it amenable for a nucleophilic attack by MeOH.[4] The transformation into the free acid was achieved in the presence of $Ba(OH)_2 \cdot 8H_2O$ followed by acidic workup (Scheme 1). Attempts to achieve the direct transfer of **2** into the free acid in aqueous systems was unsuccessful. We had demonstrated the principle for aromatic and aliphatic acids as well as for amino acids.[5] The only disadvantages of the initially reported bpa-based relay protection scheme were the relatively long reaction times and the use of the rather expensive $Cu(OTf)_2$, which had to be applied in equimolar amounts. Hence, this could become an issue on a large-scale synthesis. These disadvantages were solved by replacing bpa with chelator amine **5**, which we have named dmepa [*N*-(**dim**ethylamino**e**thyl)**p**icolyl**a**mine]. Here, the methanolysis of the pertinent amide with $CuCl_2$ was far superior to that with $Cu(OTf)_2$ and was finished after less than one hour.[6] Recently, we have extended the system with the tetradentate amine **6** derived from *N*,*N*′-**b**is(**p**icolyl)-*N*-propyl**e**thylene**di**amine (bped, **6**, Figure 1).



Scheme 1. Principle of the solvolysis reaction of bpa-derived amides.

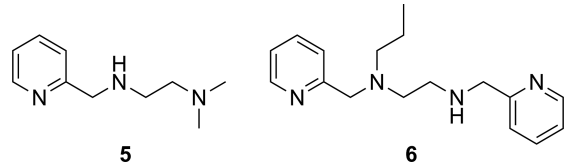


Figure 1. Structures of chelating amines **5** (dmepa) and **6** (bped).

Surprisingly, methanolysis of the corresponding amides of amine **6** was fastest with $Zn(OTf)_2$. From the rate of methanolysis with different salts, we surmised that even an orthogonal hydrolysis of amides carrying either bpa, **5** or **6** should be feasible. To verify this assumption, we synthesised a trisamide that incorporated the three different chela-

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tors embedded into the same chemical environment so that differences in the rate of methanolysis could be directly attributed to the individual chelating protecting group.

Methanolysis reactions using first $FeCl_3$, then $Zn(OTf)_2$ and then $CuCl_2$ yielded finally the desired tris methyl ester. The individual cleavage processes occurred with complete selectivity.[6] All activities concerning chelating amides published so far have focused on methanolysis reactions employing MeOH as a nucleophile. In the present work we aimed to establish a general method for the transformation of chelating amides into esters. Such an approach could be regarded as a change of paradigm in synthetic organic chemistry. Due to the higher thermodynamic stability of amides with respect to esters, which is in the order of 30 kJ/mol, this transformation is generally only possible the other way round.

As a consequence, nonenzymatic solvolytic reactions of carboxamides are only possible if special criteria are met that lead to a pyramidalisation of the nitrogen, thereby preventing amide resonance and simultaneously enhancing the electrophilicity on the carbon, rendering it susceptible to nucleophilic attack. This leads to a concomitant increase of the basicity of the nitrogen. Prominent examples for such twisted amides (Figure 2) revealing these properties are illustrated by structures **7**–**9**,[7] as well as by the medium-bridged lactams of basic type **10**.[8] Furthermore, the amide resonance can also be prevented in sterically demanding amides such as in **11**[9] or in amides in which a combination of steric demand together with an electron-withdrawing substituent on the α-carbon as in **12** can be applied. For the last example, an interesting mechanism involving a ketene intermediate has been postulated.[10] The transfer of amides into esters can also be facilitated, if a byproduct can be trapped to form a thermodynamic sink that compensates for the difference in thermodynamic stability between amides and esters and even rendering the reaction irreversible. Such an approach was recently demonstrated for the transformation of amides of type **13** into *n*Bu esters **14**, with the initially formed amino ethanol being trapped as oxazolidinone **15** (Scheme 2). The reaction is also entropically favoured.[11]

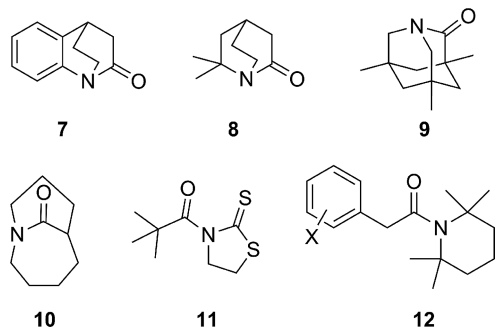
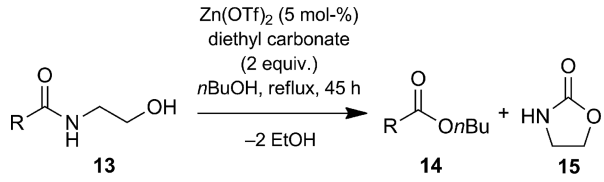


Figure 2. Reactive amides.

Unfortunately, as far as the synthetic utility of twisted or nonplanar amides is concerned, only the bridged medium-sized lactams of type **10** might have the potential to be applied, for example, to the synthesis of natural products. As mentioned earlier, the advantage of using chelating amides as relay protecting groups is the mild cleavage conditions; this is achieved through complexation to a metal ion with the unusual involvement of the free electron pair of the amide nitrogen followed by nucleophilic attack of methanol.[12] In contrast to the structurally fixed examples of twisted amides shown in Figure 2, we induced the reaction by complexation, and the resulting pyramidalisation is then the prerequisite for the methanolysis, which proceeds possibly by a methoxide as nucleophile.[4] In addition, the cleavage process yields bpa-metal complex, which is thermodynamically more stable than amide complex **2**. For these reasons, these amide systems represent a combination of the pyramidalisation of the nitrogen together with a thermodynamically relevant stable side product. Prior to this work, we had applied these favourable properties for the development of linker systems for solid-phase chemistry.[13] Taking all aspects together, we surmised that our systems might be generally prone to a transformation into esters or might even have the potential to transform amide-protected hydroxy carboxylic acids into lactones. With respect to the chelating protection scheme, such a technique would significantly widen the scope of application. This would allow amides to be transferred after synthetic operations into different kinds of esters, which would allow for specific orthogonal deprotections or further manipulations such as allyl esters in Tsuji–Trost reactions.[14] As a further option, the still protected amide could possibly be transformed directly into lactones.



Scheme 2. Transfer of amide **13** into *n*-butyl ester **14** with concomitant transfer of aminoethanol into cyclic urethane **15**.

Results and Discussion

The rates of methanolysis of the bpa-amide of benzoic acid **1a** (R = C_6H_5) after the application of $Cu(OTf)_2$, $CuCl_2$, CuCl, $Cu(OAc)_2$ and $FeCl_3$ are depicted in Figure 3. As can be deduced from the plots, the rate of transformation into methyl ester **16a** increased in the order: $CuCl_2 < Cu(OTf)_2 < FeCl_3 < Cu(OAc)_2 < CuCl$, with the last being far superior as activating agent. When switching to EtOH as nucleophile and using the same metal salts for activation, the formation of the corresponding ethyl ester **20a** dropped significantly when $CuCl_2$, $Cu(OTf)_2$, $Cu(OAc)_2$ or $FeCl_3$ were employed. In contrast, we realised to our delight that CuCl still mediated a fast, efficient and mild transfer to the ethyl ester **17a** in less than 2 h at room temp. The reason for this unexpected behaviour of CuCl is a topic of ongoing research (Figure 4).

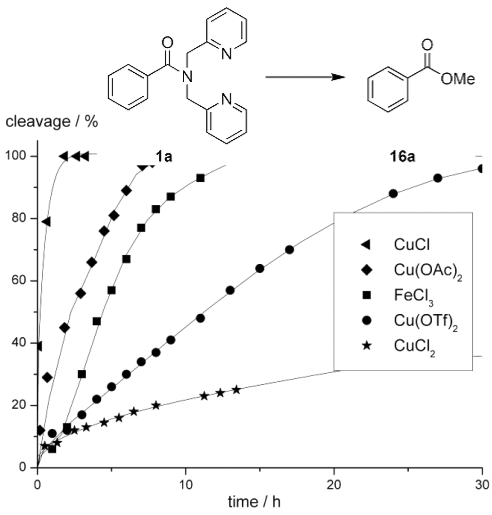


Figure 3. Rate of methanolysis for amide **1a** using various metal salts.

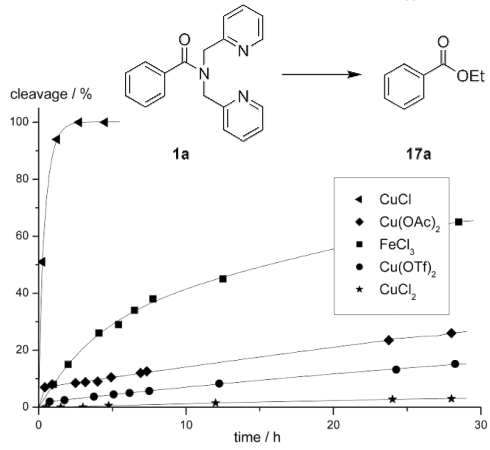
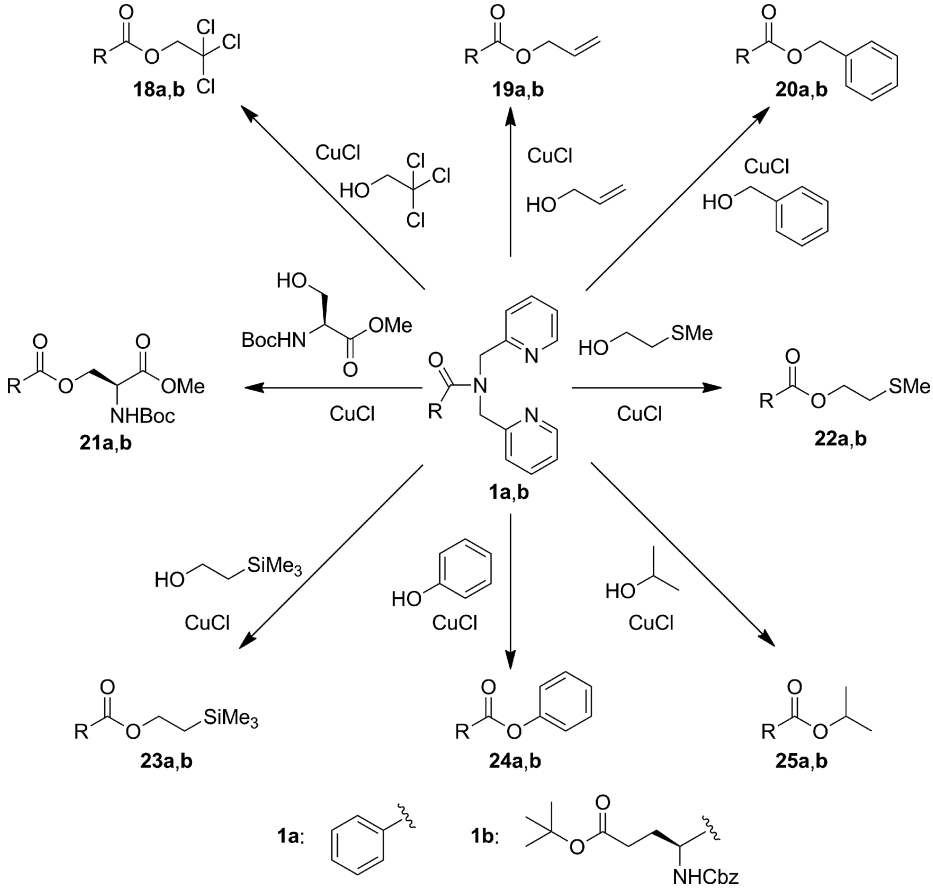


Figure 4. Rate of ethanolysis for amide **1a** using various metal salts.

Despite the fact that CuCl is only poorly soluble in the applied mixture of MeCN and EtOH, the rate of transformation was nevertheless highly dependent on the stoichiometry, which might be due to an enhanced surface area. For this reason, we carried out all the following experiments with 5 equiv. CuCl. The intriguing results in the ethanolysis experiments prompted us to test amide **1a** with an array of different alcohols, leading to esters **18a**–**25a** (Scheme 3). Thus, we dissolved amide **1a** in a 1:1 mixture of MeCN and the alcohol, then solid CuCl was added and the progress of the reaction was followed by HPLC. As illustrated in Figure 5, most reactions were complete after approximately 1 h at room temp. Slightly longer reaction times were required for the formation of esters **22a** and **23a**.



Scheme 3. Array of esters **18a**,**b**–**25a**,**b** obtained from the bpa-derived amide **1a** (aromatic) and **1b** (aliphatic).

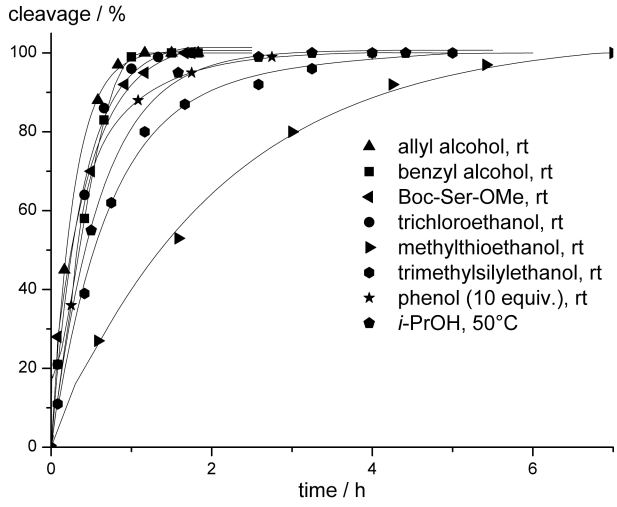


Figure 5. Transformation of bpa-derivative **1a** into esters **18a**–**25a** by using a range of alcohols.

The same positive result was obtained with phenol (**24a**) as nucleophile. With 2-propanol as sterically more demanding secondary alcohol, the transformation into isopropyl ester **25a** at room temp. was relatively slow but could be improved significantly by elevating the reaction temperature to 50 °C and/or by adding DIPEA so that it was also complete after approximately 3 h. Recently, we were able to demonstrate that the approach is not restricted to aromatic amides and that we also observed the formation of methyl esters when aliphatic amides were used.[5,6] To demonstrate that it is possible to synthesise various esters from aliphatic amides, we prepared esters **18b**–**25b** by applying a range of alcohols. The quantitative transformation of aliphatic amide **1b** into esters **18b**–**25b** required only slightly longer reaction times (Figure 6). In most cases, we obtained the esters in a quantitative manner when the reaction was conducted at room temp. Only in the case of methylthioethanol was the reaction carried out at an elevated temperature of approximately 50 °C, which led then to a conversion of approximately 80%.

In the experiments outlined above, the alcoholysis reactions were carried out with a relatively large excess of the alcohol. Nevertheless, the results encouraged us to investigate the possibility of synthesising lactones in an intramolecular manner. For this purpose, hydroxy amide **26b**, which had been prepared through coupling of benzoyl propionic acid with bpa followed by reduction with $NaBH_4$, was used as a benchmark substrate to establish optimal conditions especially concerning the use of metal salts. The formation of the pertinent phenyl lactone **26c** was monitored by HPLC. It turned out that **26b** could be successfully transformed into the phenyl lactone **26c** by using $CuCl_2$ (1.1 equiv.), Cu^ICl (5 equiv.) or $Cu(OAc)_2$ (1.1 equiv.) in MeCN in high yields, and the reaction was already complete after 1 h. In contrast, the presence of $Cu(OTf)_2$ and $Zn(OTf)_2$ led to slow formation of the lactone ($< 5\%$ after 6 h) but the reaction rate could be significantly enhanced by adding DIPEA (1.1 equiv.; Figure 7). In summary, the use of Cu^ICl turned out to be superior compared with the use of other metal salts. For this reason substrates **26b**–**34b** were also transformed into their corresponding γ-, δ- and ε-lactones by using 5 equiv. Cu^ICl. The products were isolated after short column chromatography on a preparative scale and in decent yields (Table 1). The formation of medium-sized lactones was not successful and we were not able to prepare macro lactones. Corresponding dmepa- and bped-analogues had also been successfully synthesised and transformed into lactones but because the results obtained with the bpa derivatives were more convincing, the dmepa- and bped-conversions were not elaborated in more detail.

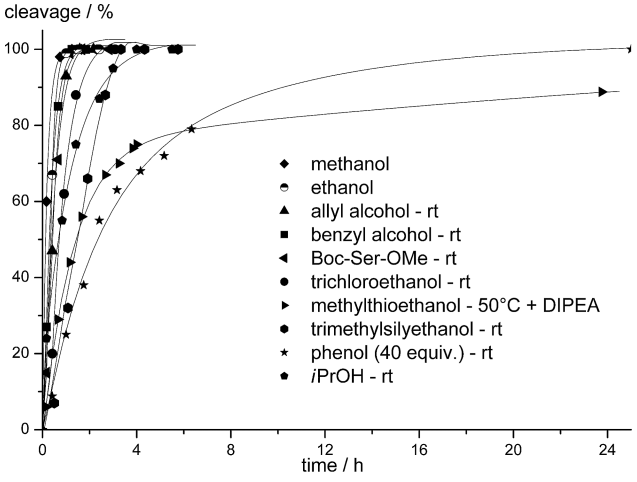


Figure 6. Transformation of bpa-derivative **1b** into esters **18b**–**25b** by using various alcohols.

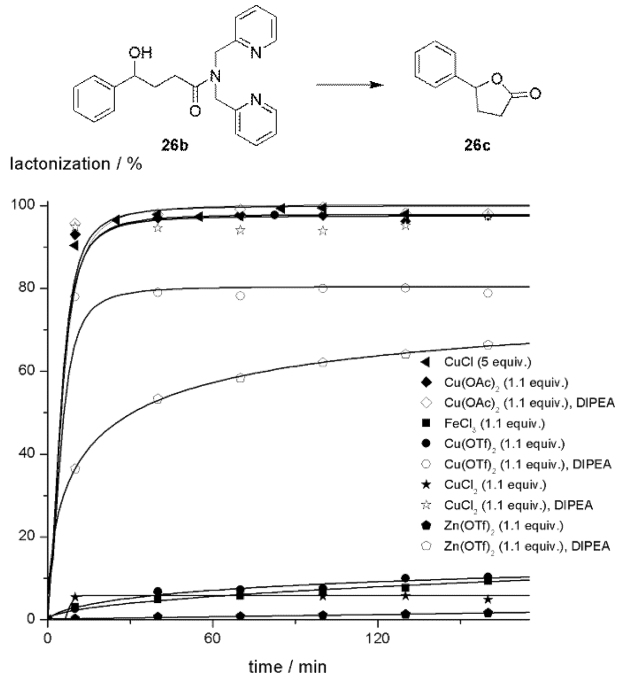
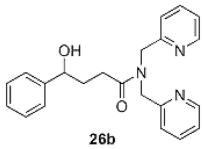
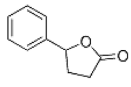
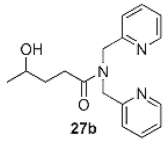
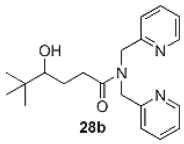
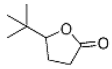
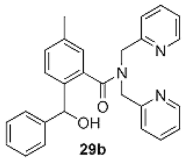
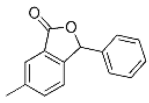
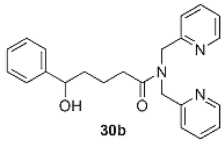
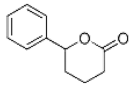
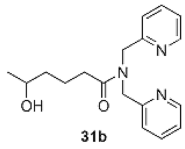
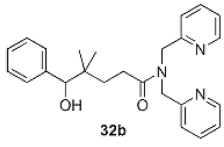
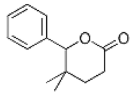
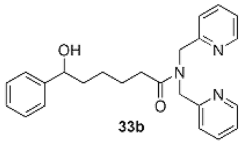
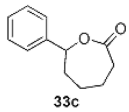
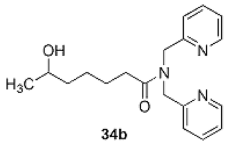


Figure 7. Transformation of hydroxy amide **26b** into lactone **26c** under various reaction conditions.

Table 1. Array of different lactones **26c**–**34c** synthesised from hydroxy-amide precursors **26b**–**34b**.

Precursor	Lactone	Yield[a,b]
 **26b**	 **26c**	98%
 **27b**	 **27c**	71%
 **28b**	 **28c**	75%
 **29b**	 **29c**	94%
 **30b**	 **30c**	88%
 **31b**	 **31c**	64%
 **32b**	 **32c**	83%
 **33b**	 **33c**	79%
 **34b**	 **34c**	68%

[a] CuCl (5 equiv.), MeCN, room temp., 6 h. [b] Isolated yield after column chromatography.

Conclusions

We have described a synthetically useful approach for the transformation of carboxamides into the corresponding esters. The unusual principle enables for this transfer to take place under very mild conditions despite of the fact that carboxamides are thermodynamically more stable than the resulting esters. This reaction can otherwise only be mediated by enzymes. The principle was demonstrated for bpa-derived chelating amides, which are prone to undergo nucleophilic attack by hydroxy functions after addition of $Cu^{I}Cl$, leading to esters or lactones, respectively. The results should be of high value in synthetic organic chemistry.

Experimental Section

General: ^{1}H NMR spectra were recorded with a Bruker AM 400 (400 MHz) or a Varian Mercury VX 300 (300 MHz) spectrometer as solutions in $CDCl_3$, [D_4]MeOH or [D_6]DMSO. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS, δ = 0 ppm) and are referenced to $CHCl_3$ (δ = 7.26 ppm), MeOH (δ = 3.31 ppm) or DMSO (δ = 2.50 ppm) as internal standard. All coupling constants are absolute values and J values are expressed in Hertz [Hz]. The description of signals include: s = singlet, br. s = broad singlet, d = doublet, t = triplets, m = multiplet, m_c = centred mutiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, dt = doublet of triplets, td = triplet of doublet. The spectra were analysed according to first order. ^{13}C NMR spectra were recorded with a Bruker AM 400 (100 MHz) or a Bruker Avance DRX (125 MHz) spectrometer as solutions in $CDCl_3$, MeOH or DMSO. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS, δ = 0 ppm) and are referenced to $CHCl_3$ (δ = 77.0 ppm), MeOH (δ = 49.0 ppm) or DMSO (δ =39.5 ppm) as internal standard. MS (EI, electron impact mass spectrometry), MS (CI, chemical ionization mass spectrometry) and GC/MS (EI or CI) were recorded with an TSQ 700 spectrometer. MS (ESI, electrospray ionisation mass spectrometry) or MS (APCI, atmospheric pressure chemical ionisation mass spectrometry) were measured with an LCQ Advantage or Exactive. HRMS spectra were recorded with a Thermo Exactive with Orbitrap-Analysator spectrometer. The molecular fragments are quoted as the relation between mass and charge (m/z), the intensities as a percentage value relative to the intensity of the base signal (100%). The molecular ion contains the abbreviation [M^+]. Analytical thin-layer chromatography (TLC) was carried out on Merck silica gel coated aluminium plates (silica gel 60, F254), detected under UV-light at 254 nm. Solvent mixtures are understood as volume/volume. Solvents, reagents and chemicals were purchased from Acros, ABCR, Alfa Aesar, Merck or Sigma–Aldrich. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride prior to use. Anhydrous toluene and THF were distilled from sodium using benzophenone as indicator in case of THF. All other solvents, reagents and chemicals were used as purchased. All reactions involving moisture-sensitive reactants were executed under an argon atmosphere, using oven-dried and/or flame-dried glassware. Purification by column chromatography was performed by using freshly distilled solvents CH_2Cl_2, cyclohexane (CH), EtOAc (EE) and MeOH (p.A. quality). The solid phase consisted of either silica gel (Kieselgel 60, Fa. Merck, size 40–63 μm) or basic aluminium oxide (activity 1, Fa. Machery–Nagel). HPLC-measurements were performed with an Agilent 1100 Series and column from Waters

(μBondapak C_{18}; 3.9 mm × 150 mm). Samples for the HPLC measurements were taken with Hamilton syringes (Terumo Micro Syringe MS50 and Hamilton GASTIGHT 250 μL). The mobile phase was mixtures of MeCN/H_2O. Phenol was used as internal standard.

Acylation with TBTU and the Carboxylic Acid; General Procedure A: The carboxylic acid (1.0 equiv. or 1.4 equiv.) and TBTU (1.0 equiv. or 1.4 equiv.) were suspended in CH_2Cl_2 and *N*,*N*-diisopropylethylamine (DIPEA; 6.0 equiv.) was added. After 10 min, the secondary amine (1.0 equiv.) was added. After stirring overnight at room temp., the mixture was washed with water (2 times) and dried with Na_2SO_4. The organic solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica gel; CH_2Cl_2/MeOH, 98:2→85:15 or aluminium oxide with CH/EE mixtures).

Esterification with DCC; General Procedure B: The carboxylic acid (1.0 equiv.) and 4-(*N*,*N*-dimethylamino)pyridine (DMAP; 0.1 equiv.) were dissolved in CH_2Cl_2 and ROH (3.0 equiv.). After 30 min stirring at room temp., the reaction was cooled to 0 °C and *N*,*N*′-dicyclohexylcarbodiimide (DCC; 1.0 equiv.) was added in one portion. After stirring at room temp. overnight, urea was filtered off using a kieselguhr plug. The organic solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica gel; CH_2Cl_2).

Reduction of Keto Functions in Keto Amides; General Procedure C: The keto amide was solved in a mixture of MeOH/Et_2O (1:1 ratio; p.A. grade). $NaBH_4$ (2.0 equiv.) was dissolved in a little water and added to the keto amide derivative. The whole reaction mixture was stirred at room temperature overnight. A half-saturated solution of $NaHCO_3$ was then added and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic phases were dried with Na_2SO_4 and the solvent was removed under reduced pressure. The hydroxy amides **26b**–**34b** were isolated after column chromatography (silica gel; CH_2Cl_2→CH_2Cl_2/MeOH, 90:10).

Esterification Using Cu^ICl; General Procedure D: Amide **1a/b** was solved in a mixture of MeCN and the pertinent alcohol [1:1 ratio (v/v); exception: phenol, 10 equiv. for **1a**, 40 equiv. for **1b**] and solid Cu^ICl (5 equiv.) was added. The resulting suspension was stirred and the progress of the reaction was monitored by HPLC (UV detection at 254 nm for aromatic esters **16a**–**25a**; detection at 210 nm for aliphatic esters **16b**–**25b**; independently synthesised esters were used to obtain calibration lines).

Lactonisation Using Cu^ICl in MeCN; General Procedure E: A 10 mM solution of the hydroxy amide **26b**–**34b** in MeCN was stirred for 5 min. Solid Cu^ICl was then added in one portion and the suspension was stirred for 6 h at room temp. After removing a large part of the solvent, the residue was purified by filtration through a small layer of silica gel using CH_2Cl_2 as eluent. Evaporation of the solvent gave lactones **26c**–**34c** (for yields, see Table 1).

Benz-bis[(2-pyridyl)methyl]amine (1a): Synthesised according to General Procedure A. The resulting dark oil was purified by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2→95:5). The resulting yellow gum (0.97 g, 3.20 mmol, 80%) crystallised overnight, m.p. 58–59 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.70 (s, 2 H, CH_2Py), 4.90 (s, 2 H, CH_2Py), 7.19 (m, 3 H, ArH), 7.32–7.45 (m, 4 H, ArH), 7.52–7.56 (m, 2 H, ArH), 7.62–7.72 (m, 2 H, ArH), 8.50–8.59 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.5, 54.6, 121.4, 122.4, 122.5, 127.0, 128.5, 129.8, 136.0, 136.8, 149.4, 149.9, 156.8, 157.2, 172.6 ppm. MS (CI, NH_3): *m*/*z* (%) = 304.1 (100) $[M + H]^+$. HRMS (CI, NH_3): *m*/*z* calcd. for $C_{19}H_{17}N_3O$ $[M + H]^+$ 304.13716; found 304.13720. $C_{19}H_{17}N_3O$ (303.36): calcd. C 75.23, H 5.65, N 13.85; found C 75.06, H 5.62, N 13.81.

Bispicolyl Amide γ-*tert*-Butyl Z-L-Glutamate (1b): Z-Glu(O*t*Bu)-OH was converted into the pertinent bispicolyl amide **1b** according to General Procedure A. After purification by column chromatography (silica gel; CH_2Cl_2→CH_2Cl_2/MeOH, 96:4), amide **1b** (0.89 g, 1.72 mmol, 87%) was obtained as a pale-yellow gum. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, C(CH_3)$_3$], 2.09–2.19 (m, 2 H, CH_2CH$_2$), 2.27 (m_c, 2 H, CH$_2$CH_2), 4.60 (m, 1 H, α-C*H*), 4.78–4.91 (m, 4 H, 2 × CH_2Py), 5.03–5.11 (m, 2 H, CH_2Ph), 5.70 (d, *J* = 8.7 Hz, 1 H, N*H*CO$_2$), 7.12–7.38 (m, 9 H, ArH), 7.58 (dt, *J* = 11.5, 1.9 Hz, 1 H, ArH), 7.59–7.65 (m, 1 H, ArH), 8.48 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.52–8.53 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2, 28.7, 29.4, 29.5, 31.2, 38.7, 50.8, 51.4, 52.8, 66.9, 80.7, 121.8, 122.4, 122.5, 122.8, 128.1, 128.2, 128.6, 136.6, 136.9, 149.4, 149.9, 156.1, 157.0, 172.4, 172.9 ppm. MS (+ APCI): *m*/*z* (%) = 519.3 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{29}H_{35}N_4O_5$ $[M + H]^+$ 519.26075; found 519.26000.

Methyl Benzoate (16a):[15] Synthesised according to General Procedure B. Purification by column chromatography (silica gel, CH_2Cl_2) gave **16a** (0.52 g, 3.82 mmol, 95%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, OCH_3), 7.40–7.45 (m, 2 H, ArH), 7.52–7.56 (m, 1 H, ArH), 8.02–8.05 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.1, 128.3, 129.6, 130.2, 132.9, 167.1 ppm. MS (GC/MS-EI): *m*/*z* (%) = 105.1 (100) $[M - OCH_3]^+$, 136.1 (53) $[M^+]$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_8H_9O_2$ $[M + H]^+$ 137.06025; found 137.06020.

5-*tert*-Butyl 1-Methyl 2-{[(Benzyloxy)carbonyl]amino}pentanedioate (16b):[16] Synthesised according to the General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **16b** (0.47 g, 1.34 mmol, 97%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, C(CH_3)$_3$], 1.95 (m_c, 1 H, NHCHC*H*CH$_2$), 2.09–2.20 (m, 1 H, NHCHC*H*CH$_2$), 2.21–2.39 (m, 2 H, CH_2COO*t*Bu), 3.74 (s, 3 H, OCH_3), 4.39 (m_c, 1 H, NHC*H*), 5.10 (s, 2 H, CH_2Ph), 5.42 (m_c, 1 H, N*H*), 7.28–7.38 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.7, 28.1, 31.5, 52.5, 53.6, 67.1, 80.9, 128.1, 128.2, 128.6, 136.3, 156.0, 172.0, 172.5 ppm. MS (+ ESI): *m*/*z* (%) = 374.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{18}H_{25}NO_6Na$ $[M + Na]^+$ 374.15796; found 374.15790.

Ethyl Benzoate (17a):[17] Synthesised according to the General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **17a** (0.56 g, 3.73 mmol, 90%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 3 H, OCH$_2$CH_3), 4.37 (q, *J* = 7.1 Hz, 2 H, OCH_2CH$_3$), 7.40–7.45 (m, 2 H, ArH), 7.51–7.56 (m, 1 H, ArH), 8.03–8.06 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 60.9, 128.3, 129.6, 130.6, 132.8, 166.6 ppm. MS (+ APCI): *m*/*z* (%) = 151.0 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_9H_{11}O_2$ $[M + H]^+$ 151.07590; found 151.07600.

5-*tert*-Butyl 1-Ethyl 2-{[(Benzyloxy)carbonyl]amino}pentanedioate (17b):[18] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **17b** (0.47 g, 1.29 mmol, 93%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H, CH$_2$CH_3), 1.43 [s, 9 H, C(CH_3)$_3$], 1.94 (m_c, 1 H, NHCHC*H*CH$_2$), 2.09–2.20 (m, 1 H, NHCHC*H*CH$_2$), 2.23–2.39 (m, 2 H, CH_2COO*t*Bu), 4.19 (q, *J* = 7.1 Hz, 2 H, CH_2CH$_3$), 4.36 (m_c, 1 H, NHC*H*), 5.10 (s, 2 H, CH_2Ph), 5.39 (m_c, 1 H, N*H*), 7.27–7.36 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 27.8, 28.1, 31.5, 53.6, 61.6, 67.1, 80.8, 128.1, 128.2, 128.6, 136.4, 156.0, 172.0 ppm. MS (+ ESI): *m*/*z* (%) = 388.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH):

m/*z* calcd. for $C_{19}H_{27}NO_6Na$ [M + Na]$^+$ 388.17361; found 388.17330.

2,2,2-Trichloroethyl Benzoate (18a):[19] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **18a** (0.79 g, 3.12 mmol, 76%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.97 (s, 2 H, CH_2), 7.46–7.52 (m, 2 H, ArH), 7.60–7.65 (m, 1 H, ArH), 8.12–8.16 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 74.5, 76.4, 95.1, 128.7, 128.8, 130.1, 133.9 ppm. MS (GC/MS-CI, NH_3): *m*/*z* (%) = 105.1 (100) [M – OCH_2CCl_3]$^+$, 254.0 (20) [M + H]$^+$. $C_9H_7Cl_3O_2$ (253.51): calcd. C 42.64, H 2.78; found C 42.46, H 2.73.

5-*tert*-Butyl 1-(2,2,2-Trichloroethyl) 2-{[(Benzyloxy)carbonyl]-amino}pentanedioate (18b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **18b** (0.57 g, 1.22 mmol, 88%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, C(CH_3)$_3$], 1.94–2.11 (m, 1 H, NHCHCHCH$_2$), 2.16–2.32 (m, 1 H, NHCHCHCH$_2$), 2.33–2.46 (m, 2 H, CH_2COO*t*Bu), 4.52 (m$_c$, 1 H, NHCH), 4.67 (d, *J* = 11.8 Hz, 1 H, OCHCCl$_3$), 4.90 (d, *J* = 11.8 Hz, 1 H, OCHCCl$_3$), 5.11 (s, 2 H, CH_2Ph), 5.49 (m$_c$, 1 H, NH), 7.27–7.39 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.1, 28.1, 31.5, 53.7, 67.3, 74.4, 81.1, 94.5, 128.2, 128.3, 128.6, 136.2, 156.1, 170.7, 172.0 ppm. MS (+ APCI): *m*/*z* (%) = 468.1 (100) [M + H]$^+$. MS (– APCI): *m*/*z* (%) = 504.0 (100) [M + Cl]$^–$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{19}H_{25}NO_6Cl_3$ [M + H]$^+$ 468.07475; found 468.07480. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{19}H_{24}NO_6Cl_4$ [M + Cl]$^–$ 502.03577; found 502.03620.

Allyl Benzoate (19a):[19] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **19a** (0.60 g, 3.70 mmol, 90%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.81–4.84 (m, 2 H, OCH_2CHCH$_2$), 5.26–5.44 (m, 2 H, OCH$_2$CHCH_2), 5.99–6.09 (m, 1 H, OCH$_2$CHCH$_2$), 7.41–7.46 (m, 2 H, ArH), 7.52–7.57 (m, 1 H, ArH), 8.05–8.08 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.5, 118.2, 128.4, 129.7, 130.2, 132.2, 133.0, 166.3 ppm. MS (GC/MS-EI): *m*/*z* (%) = 105.1 (100) [M – O-allyl]$^+$, 162.1 (14) [M$^+$]. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{10}H_{11}O_2$ [M + H]$^+$ 163.07590; found 163.07610.

5-*tert*-Butyl 1-Prop-2-en-1-yl 2-{[(Benzyloxy)carbonyl]amino}-pentanedioate (19b): Synthesised according to general procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **19b** (0.51 g, 1.35 mmol, 97%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 [s, 9 H, C(CH_3)$_3$], 1.95 (m$_c$, 1 H, NHCHCHCH$_2$), 2.09–2.22 (m, 1 H, NHCHCHCH$_2$), 2.23–2.40 (m, 2 H, CH_2COO*t*Bu), 4.41 (m$_c$, 1 H, NHCH), 4.63 (d, *J* = 5.4 Hz, 2 H, OCH_2CHCH$_2$), 5.10 (s, 2 H, CH_2Ph), 5.25 (dd, *J* = 10.4, 1.1 Hz, 1 H, OCH$_2$CHCH), 5.32 (dd, *J* = 10.4, 1.1 Hz, 1 H, OCH$_2$CHCH), 5.41 (m$_c$, 1 H, NH), 5.83–5.95 (m, 1 H, OCH$_2$CHCH$_2$), 7.27–7.37 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.8, 28.2, 31.6, 53.7, 66.2, 67.2, 80.9, 119.1, 128.2, 128.3, 128.6, 131.6, 136.4, 156.1, 171.8, 172.1 ppm. MS (+ ESI): *m*/*z* (%) = 400.2 (100) [M + Na]$^+$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{20}H_{27}NO_6Na$ [M + Na]$^+$ 400.17361; found 400.17350.

Benzyl Benzoate (20a):[19] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **20a** (0.71 g, 3.35 mmol, 82%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.37 (s, 2 H, CH_2), 7.31–7.47 (m, 7 H, ArH), 7.52–7.57 (m, 1 H, ArH), 8.06–8.10 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7, 25.5, 35.0, 55.8, 66.7, 128.2, 128.3, 128.4, 128.6, 129.8, 130.2, 133.1, 136.1 ppm. MS (+ APCI): *m*/*z* (%) = 230.1 (100) [M + NH_4]$^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{14}H_{16}NO_2$ [M + NH_4]$^+$ 230.11810; found 230.11820. $C_{14}H_{12}O_2$ (212.25): calcd. C 79.23, H 5.70; found C 78.70, H 5.80.

1-Benzyl 5-*tert*-Butyl 2-{[(Benzyloxy)carbonyl]amino}pentanedioate (20b):[20] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **20b** (0.52 g, 1.22 mmol, 87%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 [s, 9 H, C(CH_3)$_3$], 1.87–2.05 (m, 1 H, NHCHCHCH$_2$), 2.06–2.21 (m, 1 H, NHCHCHCH$_2$), 2.22–2.40 (m, 2 H, CH_2COO*t*Bu), 4.44 (m$_c$, 1 H, NHCH), 5.10 (s, 2 H, NHCOOCH_2Ph), 5.17 (s, 2 H, CHCOOCH_2Ph), 5.43 (m$_c$, 1 H, NH), 7.27–7.41 (m, 10 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.6, 28.1, 31.4, 53.6, 67.1, 67.3, 80.9, 128.2, 128.3, 128.5, 128.6, 128.7, 135.3, 136.2, 140.5, 156.0, 171.9, 172.0 ppm. MS (+ APCI): *m*/*z* (%) = 428.2 (100) [M + H]$^+$. MS (– APCI): *m*/*z* (%) = 462.2 (100) [M + Cl]$^–$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{24}H_{30}NO_6$ [M + H]$^+$ 428.20731; found 428.20730. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{24}H_{29}NO_6Cl$ [M + Cl]$^–$ 462.16834; found 462.16860. HRMS (– APCI, MeOH) *m*/*z* [(M – H)$^–$]: Calcd. for $C_{24}H_{28}NO_6$: 426.19166, found 426.19190.

2-(*tert*-Butoxycarbonylamino)-2-(methoxycarbonylethyl) Benzoate (21a): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **21a** (0.50 g, 1.55 mmol, 38%) as a white solid, m.p. 130–132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 [s, 9 H, C(CH_3)$_3$], 3.80 (s, 3 H, OCH_3), 4.56–4.68 (m, 2 H, OCH_2CH), 4.69–5.46 (m, 1 H, OCH$_2$CH), 7.40–7.48 (m, 2 H, ArH), 7.58–7.60 (m, 1 H, ArH), 7.97–8.03 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.9, 28.3, 34.0, 52.9, 53.1, 65.0, 80.5, 128.5, 129.5, 129.8, 133.4, 155.2, 166.1, 170.4 ppm. MS (+ APCI): *m*/*z* (%) = 341.1 (100) [M + NH_4]$^+$. HRMS (+ APCI, MeOH/NH_4^+): *m*/*z* calcd. for $C_{16}H_{25}N_2O_6$ [M + NH_4]$^+$ 341.17126; found 341.17110. $C_{16}H_{21}NO_6$ (323.35): calcd. C 59.43, H 6.55, N 4.33; found C 58.96, H 6.67, N 4.20.

1-[2-(*tert*-Butoxycarbonylamino)-3-methoxy-3-oxopropyl] 5-*tert*-Butyl 2-[(Benzyloxycarbonyl)amino]pentanedioate (21b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **21b** (0.57 g, 1.06 mmol, 76%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, C(CH_3)$_3$], 1.45 [s, 9 H, NHCOOC(CH_3)$_3$], 1.88–2.07 (m, 1 H, NHCHCHCH$_2$), 2.07–2.23 (m, 1 H, NHCHCHCH$_2$), 2.25–2.40 (m, 2 H, CH_2COO*t*Bu), 3.76 (s, 3 H, OCH_3), 4.28–4.45 (m, 2 H, NHCH, NHCH), 4.45–4.62 (m, 2 H, NHCHCH_2OOCCH), 5.11 (m$_c$, 2 H, CH_2Ph), 5.45 (m$_c$, 1 H, NHCHCH$_2$CH$_2$), 5.56 (m, 1 H, NHCHCH$_2$O), 7.27–7.40 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2, 28.1, 28.4, 31.3, 52.9, 53.7, 65.2, 67.2, 80.5, 81.2, 128.2, 128.3, 128.6, 136.2, 140.5, 155.4, 156.0, 170.0, 171.5, 172.1 ppm. MS (+ APCI): *m*/*z* (%) = 539.3 (100) [M + H]$^+$. MS (– APCI): *m*/*z* (%) = 573.2 (100) [M + Cl]$^–$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{26}H_{39}N_2O_{10}$ [M + H]$^+$ 539.26047; found 539.26040. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{26}H_{38}N_2O_{10}Cl$ [M + Cl]$^–$ 573.22150; found 573.22150.

2-Methylsulfanylethyl Benzoate (22a): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **22a** (0.79 g, 4.03 mmol, 90%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, SCH_3), 2.86 (t, *J* = 6.8 Hz, 2 H, CH_2SCH$_3$), 4.49 (t, *J* = 6.8 Hz, 2 H, CH_2CH$_2$SCH$_3$), 7.41–7.46 (m, 2 H, ArH), 7.53–7.58 (m, 1 H, ArH), 8.03–8.07 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.9, 32.7, 63.6, 128.4, 129.6, 130.1, 133.1, 166.4 ppm. MS (GC/MS-CI, NH_3): *m*/*z* (%) = 214.2 (100) [M + NH_4]$^+$, 197.1

(67) $[M + H]^+$. $C_{10}H_{12}O_2S$ (196.26): calcd. C 61.20, H 6.16, S 16.34; found C 61.24, H 6.12, S 16.18.

5-*tert*-Butyl 1-[2-(Methylsulfanyl)ethyl] 2-{[(Benzyloxy)carbonyl]-amino}pentanedioate (22b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) gave **22b** (0.39 g, 0.95 mmol, 80%) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, $C(CH_3)_3$], 1.96 (m_c, 1 H, NHCHC*H*CH_2), 2.14 (s, 3 H, SCH_3), 2.15–2.22 (m, 1 H, NHCHC*H*CH_2), 2.25–2.41 (m, 2 H, CH_2COO*t*Bu), 2.72 (t, J = 6.4 Hz, 2 H, CH_2SCH_3), 4.30 (t, J = 6.4 Hz, 2 H, $CH_2CH_2SCH_3$), 4.39 (m_c, 1 H, NHC*H*), 5.11 (s, 2 H, CH_2Ph), 5.41 (m_c, 1 H, N*H*), 7.29–7.38 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8, 27.6, 28.3, 31.5, 32.4, 53.7, 63.9, 67.1, 80.9, 128.1, 128.2, 128.3, 128.6, 136.3, 156.0, 171.9, 172.0 ppm. MS (+ ESI): *m*/*z* (%) = 434.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{20}H_{29}NO_6NaS$ $[M + Na]^+$ 434.16133; found 434.16110.

2-(Trimethylsilanyl)ethyl Benzoate (23a): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) gave **23a** (0.70 g, 3.15 mmol, 88%) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.09 [s, 9 H, $Si(CH_3)_3$], 1.11–1.16 [m, 2 H, $CH_2Si(CH_3)_3$], 4.39–4.45 [m, 2 H, $CH_2CH_2Si(CH_3)_3$], 7.40–7.45 (m, 2 H, ArH), 7.51–7.56 (m, 1 H, ArH), 8.02–8.06 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 1.3, 17.5, 63.3, 128.4, 129.6, 130.8, 132.8, 166.9 ppm. MS (GC/MS-CI, NH_3): *m*/*z* (%) = 195.1 (100) $[M + NH_4 - (CH_3)_3]^+$, 240.2 (52) $[M + NH_4]^+$. $C_{12}H_{18}O_2Si$ (222.36): calcd. C 64.82, H 8.16; found C 64.48, H 8.09.

5-*tert*-Butyl 1-[2-(Trimethylsilyl)ethyl] 2-{[(Benzyloxy)carbonyl]-amino}pentanedioate (23b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel, CH_2Cl_2/MeOH, 98:2) gave **23b** (0.31 g, 0.71 mmol, 95%) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.05 [s, 9 H, $Si(CH_3)_3$], 1.00 [t, J = 8.4 Hz, 2 H, $CH_2Si(CH_3)_3$], 1.43 [s, 9 H, $C(CH_3)_3$], 1.94 (m_c, 1 H, NHCHC*H*CH_2), 2.15 (m_c, 1 H, NHCHC*H*CH_2), 2.22–2.34 (m, 2 H, CH_2COO*t*Bu), 4.22 [m_c, 2 H, $CH_2CH_2Si(CH_3)_3$], 4.35 (m_c, 1 H, NHC*H*), 5.10 (s, 2 H, CH_2Ph), 5.39 (m_c, 1 H, N*H*), 7.28–7.36 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –1.4, 17.5, 27.9, 28.2, 31.6, 53.8, 64.1, 67.1, 80.9, 128.1, 128.2, 128.3, 128.6, 136.5, 156.0, 172.1, 172.2 ppm. MS (+ ESI): *m*/*z* (%) = 460.2 (100) $[M + Na]^+$; HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{22}H_{35}NO_6NaSi$ $[M + Na]^+$ 460.21314; found 460.21310.

Phenyl Benzoate (24a):[21] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) to give **24a** (0.61 g, 3.07 mmol, 75%) as a white solid, m.p. 68–70 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.23 (m, 2 H, ArH), 7.24–7.28 (m, 1 H, ArH), 7.39–7.44 (m, 2 H, ArH), 7.47–7.52 (m, 2 H, ArH), 7.59–7.64 (m, 1 H, ArH), 8.18–8.22 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 121.7, 125.9, 128.6, 129.5, 129.6, 130.2, 133.6, 151.0, 165.2 ppm. MS (+ APCI): *m*/*z* (%) = 199.0 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{13}H_{11}O_2$ $[M + H]^+$ 199.07590; found 199.07580. $C_{13}H_{10}O_2$ (198.22): calcd. C 78.77, H 5.08; found C 78.79, H 5.02.

1-*tert*-Butyl Phenyl 4-{[(Benzyloxy)carbonyl]amino}pentanedioate (24b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2/MeOH, 98:2) to give **24b** (0.35 g, 0.85 mmol, 72%) as a white solid, m.p. 68–70 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.45 [s, 9 H, $C(CH_3)_3$], 2.13 (m_c, 1 H, NHCHC*H*CH_2), 2.26–2.36 (m, 1 H, NHCHC*H*CH_2), 2.36–2.51 (m, 2 H, CH_2COO*t*Bu), 4.63 (m_c, 1 H, NHC*H*), 5.14 (s, 2 H, CH_2Ph), 5.51 (m_c, 1 H, N*H*), 7.10 (m_c, 2 H, ArH), 7.22–7.26 (m, 1 H, ArH), 7.29–7.41 (m, 7 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.6, 28.1, 31.6, 53.9, 67.2, 77.3, 81.1, 121.4, 126.2, 128.2, 128.3, 128.6, 129.6, 136.3, 150.5, 156.1, 170.8, 172.0 ppm. MS (+ ESI): *m*/*z* (%) = 436.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{23}H_{27}NO_6Na$ $[M + Na]^+$ 436.17361; found 436.17340.

Isopropyl Benzoate (25a):[22] Synthesised according to General Procedure B. Purification by column chromatography (silica gel; CH_2Cl_2) to give **25a** (0.59 g, 3.60 mmol, 88%) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 5.25 [sept, J = 6.3 Hz, 1 H, $OCH(CH_3)_2$], 7.40–7.45 (m, 2 H, ArH), 7.51–7.56 (m, 1 H, ArH), 8.02–8.06 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 68.4, 128.3, 129.6, 131.0, 132.7, 166.2 ppm. MS (GC/MS-EI): *m*/*z* (%) = 105.1 (100) $[M - OCH(CH_3)_2]^+$, 164.1 (32) $[M^+]$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{10}H_{13}O_2$ $[M + H]^+$ 165.09155; found 165.09180.

5-*tert*-Butyl 1-Propan-2-yl 2-(Benzyloxycarbonylamino)pentanedioate (25b): Synthesised according to General Procedure B. Purification by column chromatography (silica gel, CH_2Cl_2/MeOH, 98:2) gave **25b** (0.36 g, 0.95 mmol, 80%) as a colourless liquid. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.21–1.27 [m, 6 H, $CH(CH_3)_2$], 1.43 [s, 9 H, $C(CH_3)_3$], 1.86–1.98 (m, 1 H, NHCHC*H*CH_2), 2.13 (m_c, 1 H, NHCHC*H*CH_2), 2.21–2.39 (m, 2 H, CH_2COO*t*Bu), 4.33 (m_c, 1 H, NHC*H*), 5.04 [sept, J = 6.3 Hz, 1 H, $CH(CH_3)_2$], 5.10 (s, 2 H, CH_2Ph), 5.40 (m_c, 1 H, N*H*), 7.28–7.37 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 27.9, 28.1, 31.5, 53.7, 67.0, 69.4, 80.8, 128.1, 128.2, 128.6, 136.4, 156.0, 171.5, 172.1 ppm. MS (+ ESI): *m*/*z* (%) = 402.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for $C_{20}H_{29}NO_6Na$ $[M + Na]^+$ 402.18926; found 402.18890.

4-Oxo-4-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)butyramide (26a): Benzoyl propionic acid was coupled with bpa in the presence of TBTU and DIPEA as described in General Procedure A. The resulting amide **26a** (0.56 g, 1.56 mmol, 89%) was isolated after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 96:4). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.93 (t, J = 6.4 Hz, 2 H, $NCOCH_2CH_2$), 3.41 (t, J = 6.4 Hz, 2 H, $NCOCH_2CH_2$), 4.78 (s, 2 H, CH_2Py), 4.82 (s, 2 H, CH_2Py), 7.14 (ddd, J = 7.6, 4.9, 1.2 Hz, 1 H, ArH), 7.18 (ddd, J = 7.6, 4.9, 1.2 Hz, 1 H, ArH), 7.31 (m_c, 2 H, ArH), 7.41–7.47 (m, 2 H, ArH), 7.51–7.56 (m, 2 H, ArH), 7.62 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.69 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.98–8.02 (m, 2 H, ArH), 8.48 (m_c, 1 H, ArH), 8.56 (m_c, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.6, 34.1, 51.9, 53.2, 120.9, 122.3, 122.4, 128.1, 128.7, 133.0, 136.9, 149.2, 149.9, 156.8, 157.4, 172.8, 199.2 ppm. MS (CI, NH_3): *m*/*z* (%) = 360.2 (100) $[M + H]^+$. HRMS (CI, NH_3): *m*/*z* calcd. for $C_{22}H_{22}N_3O_2$ $[M + H]^+$ 360.17120; found 360.17100.

4-Hydroxy-4-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)butyramide (26b): Keto amide **26a** was reduced as described in General Procedure C. The resulting amide **26b** (0.47 g, 1.30 mmol, 81%) was obtained as a colourless oil after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.03–2.12 (m, 1 H, C*H*), 2.20–2.28 (m, 1 H, C*H*), 2.56–2.63 (m, 1 H, C*H*), 2.79–2.86 (m, 1 H, C*H*), 4.63–4.70 (m, 2 H, CH_2Py), 4.77–4.86 (m, 3 H, CH_2Py, C*H*OH), 7.14–7.25 (m, 4 H, ArH), 7.28–7.38 (m, 5 H, ArH), 7.61–7.67 (m, 2 H, ArH), 8.49 (ddd, J = 4.9, 1.7, 0.9 Hz, 1 H, ArH), 8.55 (ddd, J = 4.9, 1.7, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5, 34.6, 51.5, 53.3, 73.1, 121.8, 122.5, 122.9, 122.9, 125.8, 127.2, 128.4, 137.0, 137.2, 145.0, 149.1, 150.0, 156.3, 157.3, 174.6 ppm. MS (+ ESI): *m*/*z* (%) = 384.2 (100) $[M + Na]^+$. MS (– ESI): *m*/*z* (%) = 360.2 (100) $[M - H]^-$. HRMS (+ ESI, MeOH): *m*/*z* calcd. for

$C_{22}H_{23}N_3O_2Na$ $[M + Na]^+$ 384.16880; found 384.16830. HRMS (– ESI, MeOH): *m*/*z* calcd. for $C_{22}H_{22}N_3O_2$ $[M - H]^-$ 360.17120; found 360.17180.

5-Phenyldihydro-2(3*H*)-furanone (26c):[23] The bpa precursor **26b** was transformed into the pertinent lactone **26c** according to General Procedure E. Evaporation of the solvent gave lactone **26c** (59.6 mg, 0.37 mmol, 98%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13–2.25 (m, 1 H, C*H*), 2.60–2.74 (m, 3 H, CH_2, C*H*), 5.49–5.52 (m, 1 H, C*H*Ph), 7.31–7.41 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.9, 30.9, 81.2, 125.2, 128.4, 128.7, 139.3, 176.8 ppm. MS (+ APCI): *m*/*z* (%) = 163.1 (100) $[M + H]^+$. MS (– APCI): *m*/*z* (%) = 177.1 (100) $[M + O - H]^-$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{10}H_{11}O_2$ $[M + H]^+$ 163.07590; found 163.07610. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{10}H_9O_3$ $[M + O - H]^-$ 177.05517; found 177.05520.

4-Oxo-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (27a): Levulinic acid was coupled with bpa in the presence of TBTU and DIPEA as described in General Procedure A. The resulting amide **27a** (0.55 g, 1.85 mmol, 81%) was isolated after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 96:4). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.18 (s, 3 H, CH_3), 2.69–2.73 (m, 2 H, CH_2), 2.79–2.82 (m, 2 H, CH_2), 4.72 (s, 4 H, 2 × CH_2Py), 7.09–7.17 (m, 2 H, ArH), 7.23–7.26 (m, 2 H, ArH), 7.58 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.64 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.45 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.52 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.1, 29.9, 38.1, 51.5, 53.0, 120.9, 122.2, 122.2, 122.4, 136.7, 136.8, 149.0, 149.7, 156.5, 157.3, 172.6, 207.6 ppm. MS (+ APCI): *m*/*z* (%) = 298.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{17}H_{20}N_3O_2$ $[M + H]^+$ 298.15555; found 298.15590.

4-Hydroxy-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (27b): Compound **27a** was reduced according to General Procedure C. The pertinent hydroxy amide **27b** (0.49 g, 1.64 mmol, 79%) was obtained as a colourless oil after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.74 (dddd, *J* = 14.2, 8.9, 6.7, 5.3 Hz, 1 H, C*H*), 1.94 (dddd, *J* = 14.1, 8.6, 5.5, 3.1 Hz, 1 H, C*H*), 2.54 (ddd, *J* = 15.9, 6.7, 5.5 Hz, C*H*), 2.82 (ddd, *J* = 16.0, 8.6, 5.4 Hz, 1 H, C*H*), 3.84 (tdd, *J* = 15.3, 9.3, 3.1 Hz, 1 H, C*H*), 4.61–4.67 (m, 2 H, CH_2Py), 4.78–4.83 (m, 2 H, CH_2Py), 7.11–7.14 (m, 1 H, ArH), 7.16–7.20 (m, 2 H, ArH), 7.26–7.28 (m, 1 H, ArH), 7.58 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.63 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.46 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.54 (ddd, *J* = 4.7, 1.8, 1.1 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.5, 29.3, 34.2, 51.3, 53.1, 68.8, 121.7, 122.3, 122.6, 122.7, 136.7, 137.0, 149.0, 149.8, 156.3, 157.3, 174.3 ppm. MS (+ APCI): *m*/*z* (%) = 300.2 (100) $[M + H]^+$. MS (– APCI): *m*/*z* (%) = 334.1 (100) $[(M + Cl]^-$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{17}H_{22}N_3O_2$ $[M + H]^+$ 300.17120; found 300.17130.

5-Methyloxolan-2-one (27c):[24] The bpa precursor **27b** was transformed into the pertinent lactone **27c** according to General Procedure E. Evaporation of the solvent gave lactone **27c** (30.0 mg, 0.30 mmol, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.83 (m, 1 H, C*H*), 2.35 (m, 1 H, C*H*), 2.54 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 29.2, 29.8, 77.4, 177.3 ppm. MS (+ APCI): *m*/*z* (%) = 101.1 (100) $[M + H]^+$. HRMS (+ APCI, CH_2Cl_2): *m*/*z* calcd. for $C_5H_9O_2$ $[M + H]^+$ 101.06025; found 101.06030.

5,5-Dimethyl-4-oxohexanoic Acid:[25] The β-keto carboxylic acid was prepared according to a reported procedure in two steps from α-bromo-pinacolone and dimethyl malonate. The resulting 5,5-dimethyl-4-hexanoic acid (0.14 g, 0.89 mmol, 15% over two steps; Lit. 38%[26]) was obtained as white needles, m.p. 66–67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 [s, 9 H, C(CH_3)$_3$], 2.62 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.81 (t, *J* = 6.4 Hz, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.6, 28.1, 31.5, 44.1, 178.6, 214.1 ppm. MS (– APCI): *m*/*z* (%) = 157.1 (100) $[M - H]^-$. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_8H_{13}O_3$ $[M - H]^-$ 157.08647; found 157.08680.

5,5-Dimethyl-4-oxo-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (28a): Pivaloyl propionic acid was coupled with bpa in the presence of TBTU and DIPEA as described in General Procedure A. The resulting amide **28a** (0.18 g, 0.53 mmol, 73%) was isolated as an almost colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.17 [s, 9 H, C(CH_3)$_3$], 2.71 (t, *J* = 6.3 Hz, 2 H, CH_2), 2.92 (t, *J* = 6.3 Hz, 2 H, CH_2), 4.76 (s, 4 H, 2 × CH_2Py), 7.11–7.18 (m, 2 H, ArH), 7.25–7.28 (m, 2 H, ArH), 7.60 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.66 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.47 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1 H, ArH), 8.54 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5, 26.6, 27.1, 32.0, 43.9, 51.5, 53.1, 53.4, 120.9, 122.2, 122.2, 122.4, 136.8, 136.9, 149.1, 149.8, 156.7, 157.4, 173.0 ppm. MS (+ APCI): *m*/*z* (%) = 340.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{20}H_{26}N_3O_2$ $[M + H]^+$ 340.20250; found 340.20230.

4-Hydroxy-5,5-dimethyl-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (28b): The β-keto amide **28a** was reduced according to General Procedure C. The pertinent β-hydroxy amide **28b** (0.13 g, 0.38 mmol, 94%) was obtained as a colourless gum after purification by column chromatography (silica ge; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 [s, 9 H, C(CH_3)$_3$], 1.72 (dddd, *J* = 14.0, 10.9, 7.0, 5.1 Hz, 1 H, C*H*CH_2CONR$_2$), 1.96 (dddd, *J* = 13.9, 8.4, 5.4, 2.3 Hz, 1 H, C*H*CH_2CONR$_2$), 2.58 (ddd, *J* = 15.9, 7.0, 5.3 Hz, 1 H, CH$_2$C*H*CONR$_2$), 2.82 (ddd, *J* = 15.9, 8.4, 5.1 Hz, 1 H, CH$_2$C*H*CONR$_2$), 3.21 (dd, *J* = 10.9, 2.2 Hz, 1 H, C*H*), 3.73 (br. s, 1 H, O*H*), 4.62–4.71 (m, 2 H, CH_2Py), 4.79–4.85 (m, 2 H, CH_2Py), 7.13–7.21 (m, 3 H, ArH), 7.28–7.30 (m, 1 H, ArH), 7.60 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.65 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.48 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.54–8.56 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 26.8, 30.3, 35.0, 51.2, 53.2, 63.7, 78.8, 121.7, 122.3, 122.7, 136.8, 137.0, 149.1, 149.9, 156.5, 157.4, 174.9 ppm. MS (– APCI): *m*/*z* (%) = 376.2 (100) $[M + Cl]^-$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{20}H_{28}N_3O_2$ $[M + H]^+$ 342.21815; found 342.21840. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{20}H_{27}N_3O_2Cl$ $[M + Cl]^-$ 376.17918; found 376.17980.

5-*tert*-Butyl-4,5-dihydro-2(3*H*)-furan (28c):[26,27] The bpa precursor **28b** was transformed into the pertinent lactone **28c** according to General Procedure E. Evaporation of the solvent led to lactone **28c** (35.2 mg, 0.25 mmol, 75%) as a colourless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 [s, 9 H, C(CH_3)$_3$], 1.92–2.02 (m, 1 H, C*H*), 2.08–2.16 (m, 1 H, C*H*), 2.47–2.59 (m, 2 H, CH_2), 4.19 (dd, *J* = 8.8, 6.9 Hz, 1 H, C*H*t*B*u) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.1, 25.1, 29.5, 34.0, 88.4, 177.5 ppm. MS (+ APCI): *m*/*z* (%) = 143.1 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_8H_{15}O_2$ $[M + H]^+$ 143.10720; found 143.10730. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_8H_{18}NO_2$ $[M + NH_4]^+$ 160.13375; found 160.13380.

2-Benzoyl-4-methyl-*N*,*N*-bis(pyridin-2-ylmethyl)benzamide (29a): 2-Benzoyl-5-methylbenzoic acid was coupled with bpa in the presence of TBTU and DIPEA as described in General Procedure A. The resulting amide **29a** (0.89 g, 2.11 mmol, 85%) was isolated as a yel-

low gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 96:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 4.67 (s, 2 H, CH_2Py), 4.86 (s, 2 H, CH_2Py), 7.11–7.16 (m, 2 H, ArH), 7.23–7.25 (m, 2 H, ArH), 7.27–7.31 (m, 1 H, ArH), 7.37–7.44 (m, 2 H, ArH), 7.47–7.50 (m, 2 H, ArH), 7.60–7.66 (m, 3 H, ArH), 7.74–7.77 (m, 2 H, ArH), 8.45 (ddd, J = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.53 (ddd, J = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 50.3, 54.2, 122.0, 122.1, 122.3, 122.6, 127.6, 128.3, 129.5, 130.3, 134.5, 136.6, 136.8, 137.1, 137.9, 144.0, 148.8, 149.6, 156.4, 157.0, 171.4 ppm. MS (+ APCI): m/z (%) = 422.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_{27}H_{24}N_3O_2$ $[M + H]^+$ 422.18685; found 422.18690.

2-[Hydroxy(phenyl)methyl]-4-methyl-*N*,*N*-bis(pyridin-2-ylmethyl)-benzamide (29b): Compound **29a** was reduced according to General Procedure C. The resulting hydroxy amide **29b** (0.79 g, 1.87 mmol, 88%) was obtained as a pale-yellow gum after purification with column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 4.53 (s, 2 H, CH_2Py), 4.87 (s, 2 H, CH_2Py), 6.21 (s, 1 H, CH), 7.12–7.47 (m, 12 H, ArH), 7.61–7.68 (m, 2 H, ArH), 8.49–8.51 (m, 1 H, ArH), 8.56–8.57 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 54.6, 82.8, 122.2, 122.4, 122.9, 125.7, 126.5, 127.1, 128.8, 129.4, 129.5, 129.7, 133.5, 134.3, 136.6, 137.1, 143.3, 149.1, 149.4, 149.9 ppm. MS (+ ESI, MeOH): m/z (%) = 446.2 (100) $[M + Na]^+$. HRMS (+ APCI): m/z calcd. for $C_{27}H_{25}N_3O_2Na$ $[M + Na]^+$ 446.18445; found 446.18410.

6-Methyl-3-phenyl-1,3-dihydro-2-benzofuran-1-one (29c):[28] The bpa precursor **29b** was transformed into the pertinent lactone **29c** according to General Procedure E. Evaporation of the solvent led to lactone **29c** (49.8 mg, 0.22 mmol, 94%) as a white solid, m.p. 126–127 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 6.37 (s, 1 H, ArCHPh), 7.14–7.19 (m, 4 H, ArH), 7.30–7.33 (m, 1 H, ArH), 7.52–7.56 (m, 1 H, ArH), 7.63 (ddd, J = 7.5, 7.5, 1.2 Hz, 1 H, ArH), 7.94–7.96 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 82.7, 122.8, 125.5, 125.7, 127.0, 129.2, 129.6, 133.4, 134.2, 139.3, 149.8, 170.5 ppm. MS (+ ESI): m/z (%) = 247.1 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): m/z calcd. for $C_{15}H_{12}O_2Na$ $[M + Na]^+$ 247.07350; found 247.07360.

5-Oxo-5-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (30a): Benzoyl butyric acid was coupled with bpa according to General Procedure A. The resulting keto amide **30a** (0.96 g, 2.57 mmol, 84%) was obtained as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 94:6). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (tt, J = 10.4, 7.0 Hz, 2 H, $CH_2CH_2CH_2$), 2.61 (t, J = 7.0 Hz, 2 H, $CH_2CH_2CH_2$), 3.09 (t, J = 7.0 Hz, 2 H, $CH_2CH_2CH_2$), 4.73 (s, 2 H, CH_2Py), 4.79 (s, 2 H, CH_2Py), 7.13–7.19 (m, 3 H, ArH), 7.31–7.34 (m, 1 H, ArH), 7.42–7.47 (m, 2 H, ArH), 7.53–7.66 (m, 3 H, ArH), 7.94–7.97 (m, 2 H, ArH), 8.48–8.51 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8, 32.1, 37.7, 51.2, 53.0, 120.9, 122.3, 122.4, 122.7, 128.1, 128.5, 133.0, 136.8, 136.9, 149.8, 156.6, 157.3, 173.5, 200.0 ppm. MS (+ APCI): m/z (%) = 374.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_{23}H_{24}N_3O_2$ $[M + H]^+$ 374.18685; found 374.18660.

5-Hydroxy-5-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (30b): Compound **30a** was reduced according to General Procedure C. The pertinent hydroxy amide (0.69 g, 1.84 mmol, 82%) was isolated as a colourless gum after purification with column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70–1.87 (m, 4 H, 2 × CH_2), 2.46–2.62 (m, br. s, 3 H, CH_2, OH), 4.66–4.82 (m, 5 H, 2 × CH_2Py, CHOH), 7.14–7.34 (m, 9 H, ArH), 7.60–7.67 (m, 2 H, ArH), 8.47 (ddd, J = 4.9, 1.8, 1.0 Hz, 1 H, ArH), 8.54 (ddd, J = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 32.6, 38.6, 38.7, 51.3, 53.1, 73.6, 120.9, 122.3, 122.5, 122.7, 125.8, 127.2, 128.3, 136.9, 136.9, 144.9, 148.9, 149.8, 156.7, 157.3, 174.1 ppm. MS (+ ESI): m/z (%) = 398.2 (100) $[M + Na]^+$. MS (– ESI): m/z (%) = 374.2 (100) $[M – H]^–$. HRMS (+ ESI, MeOH): m/z calcd. for $C_{23}H_{25}N_3O_2Na$ $[M + Na]^+$ 398.18445; found 398.18390. HRMS (– ESI, MeOH): m/z calcd. for $C_{23}H_{24}N_3O_2$ $[M – H]^–$ 374.18685; found 374.18720.

6-Phenyloxan-2-one (30c):[24] The γ-lactone **30c** was synthesised from bpa precursor **30b** according to General Procedure E. The lactone (35.5 mg, 0.20 mmol, 88%) was isolated as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.82–1.92 (m, 1 H, CH), 1.95–2.02 (m, 2 H, CH_2), 2.13–2.20 (m, 1 H, CH), 2.53–2.61 (m, 1 H, CH), 2.67–2.75 (m, 1 H, CH), 5.35 (dd, J = 10.4, 3.4 Hz, 1 H, CHPh), 7.30–7.40 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 29.4, 30.4, 81.6, 125.6, 128.2, 128.5, 139.7, 171.3 ppm. MS (+ APCI): m/z (%) = 177.1 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_{11}H_{13}O_2$ $[M + H]^+$ 177.09155; found 177.09160.

5-Oxo-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (31a): 4-Acetyl butyric acid was coupled with bpa according to General Procedure A. The pertinent keto amide **31a** (0.72 g, 0.23 mmol, 96%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.91 (tt, J = 7.1, 7.1 Hz, 2 H, $CH_2CH_2CH_2$), 2.07 (s, 3 H, CH_3), 2.46 (t, J = 7.1 Hz, 2 H, $CH_2CH_2CH_2$), 2.49 (t, J = 7.1 Hz, 2 H, $CH_2CH_2CH_2$), 4.66 (s, 2 H, CH_2Py), 4.72 (s, 2 H, CH_2Py), 7.09–7.15 (m, 3 H, ArH), 7.23–7.25 (m, 1 H, ArH), 7.56–7.62 (m, 2 H, ArH), 8.44 (ddd, J = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.51 (ddd, J = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 29.7, 31.9, 38.5, 42.6, 51.2, 52.9, 120.8, 122.1, 122.4, 136.6, 136.7, 149.0, 149.8, 156.6, 157.4, 173.2, 208.4 ppm. MS (+ ESI): m/z (%) = 334.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): m/z calcd. for $C_{18}H_{21}N_3O_2Na$ $[M + Na]^+$ 334.15315; found 334.15330.

5-Hydroxy-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (31b): Compound **31a** was reduced according to General Procedure C. The pertinent hydroxy amide **31b** (0.49 g, 1.57 mmol, 72%) was isolated as a colourless gum after purification with column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (d, J = 6.2 Hz, 3 H, CH_3), 1.42–1.50 (m, 2 H, CH_2), 1.71–1.88 (m, 2 H, CH_2), 2.49 (t, J = 7.1 Hz, 2 H, CH_2), 3.76 (qt, J = 12.4, 6.2 Hz, 1 H, CHOH), 4.70–4.80 (m, 4 H, 2 × CH_2Py), 7.12–7.19 (m, 3 H, ArH), 7.27–7.29 (m, 1 H, ArH), 7.60 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.63 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.47 (ddd, J = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.54 (ddd, J = 4.8, 1.8, 1.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 23.4, 32.7, 38.8, 51.4, 53.1, 67.0, 120.9, 122.2, 122.5, 122.5, 136.7, 136.8, 149.1, 149.8, 156.7, 157.4, 174.1 ppm. MS (+ ESI): m/z (%) = 336.2 (100) $[M + Na]^+$. HRMS (+ ESI, MeOH): m/z calcd. for $C_{18}H_{23}N_3O_2Na$ $[M + Na]^+$ 336.16880; found 336.16910. HRMS (– ESI, MeOH): m/z calcd. for $C_{18}H_{22}N_3O_2$ $[M – H]^–$ 312.17120; found 312.17130.

6-Methyloxan-2-one (31c):[24] The bpa precursor **31b** was transformed into the pertinent lactone **31c** according to General Procedure E. Evaporation of the solvent led to lactone **31c** (18.3 mg, 0.16 mmol, 64%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (d, J = 6.3 Hz, 3 H, CH_3), 1.47–1.56 (m, 1 H, CH), 1.78–1.94 (m, 3 H, CH_2, CH), 2.38–2.46 (m, 1 H, CH), 2.52–2.60 (m, 1 H, CH), 4.43 (m_c, 1 H, CHCH$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 21.6, 29.2, 29.6, 38.6, 76.8, 171.7 ppm. MS

(+ APCI): *m*/*z* (%) = 132.1 (100) $[M + NH_4]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_6H_{14}NO_2$ $[M + NH_4]^+$ 132.10245; found 132.10240. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_6H_{11}O_2$ $[M + H]^+$ 115.07590; found 115.07580.

4,4-Dimethyl-5-oxo-5-phenylpentanoic Acid:[29] Ethyl 4,4-dimethyl-5-oxo-5-phenylpentanoate was synthesised from isobutyrophenone and ethyl 3-bromopropionate in the presence of NaH. The crude ethyl ester was then heated to reflux in a solution of sodium hydroxide in MeOH (35 mL) and water (5 mL). After cooling to room temperature, the mixture was diluted in water and washed with CH. The aqueous phase was acidified with 2 N HCl, extracted with CH_2Cl_2 (3× 60 mL) and the combined organic phases were dried with Na_2SO_4. The resulting carboxylic acid (1.29 g, 5.84 mmol, 58% over two steps) was obtained as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 6 H, 2×CH_3), 2.08–2.12 (m, 2 H, CH_2), 2.31–2.36 (m, 2 H, CH_2), 7.38–7.42 (m, 2 H, ArH), 7.44–7.48 (m, 1 H, ArH), 7.65–7.68 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.8, 29.8, 35.2, 47.0, 127.6, 128.2, 131.1, 138.5, 179.4, 208.1 ppm. MS (+ APCI): *m*/*z* (%) = 221.1 (100) $[M + H]^+$. MS (– APCI): *m*/*z* (%) = 255.1 (100) $[M + Cl]^-$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{13}H_{17}O_3$ $[M + H]^+$ 221.11777; found 221.11780. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{13}H_{16}O_3Cl$ $[M + Cl]^+$ 255.07880; found 255.07890.

4,4-Dimethyl-5-oxo-5-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (32a): 4,4-Dimethyl-5-oxo-5-phenylpentanoic acid **32** was coupled with bpa according to General Procedure A. The pertinent keto amide **32a** (0.66 g, 1.65 mmol, 85%) was isolated as a colourless gum after purification with column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 6 H, 2×CH_3), 2.18–2.22 (m, 2 H, CH_2), 2.41–2.45 (m, 2 H, CH_2), 4.64 (s, 2 H, CH_2Py), 4.74 (s, 2 H, CH_2Py), 7.07–7.67 (m, 8 H, ArH), 7.53–7.69 (m, 3 H, ArH), 8.48 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.51 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 28.9, 36.0, 38.6, 47.2, 51.4, 53.0, 120.9, 122.3, 122.4, 122.6, 127.6, 128.1, 131.0, 136.7, 136.8, 138.7, 149.0, 149.8, 156.6, 157.5, 173.6, 208.5 ppm. MS (+ ESI): *m*/*z* (%) = 402.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{25}H_{28}N_3O_2$ $[M + H]^+$ 402.21815; found 402.21800.

5-Hydroxy-4,4-dimethyl-5-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)pentanamide (32b): Compound **32a** was reduced according to General Procedure C. The pertinent hydroxy amide **32b** (0.49 g, 1.22 mmol, 88%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 6 H, 2×CH_3), 2.16–2.22 (m, 2 H, CH_2), 2.40–2.44 (m, 2 H, CH_2), 4.63 (s, 2 H, CH_2Py), 4.73 (s, 2 H, CH_2Py), 7.06–7.45 (m, 9 H, ArH), 7.58–7.64 (m, 2 H, ArH), 8.47 (ddd, *J* = 4.9, 1.7, 0.9 Hz, 1 H, ArH), 8.49–8.51 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 28.9, 36.0, 38.6, 47.2, 51.5, 53.0, 120.9, 122.2, 122.4, 122.6, 127.6, 128.1, 131.0, 136.7, 138.7, 149.0, 149.8, 156.6, 157.5, 173.6, 208.5 ppm. MS (+ APCI): *m*/*z* (%) = 404.2 (100) $[M + H]^+$. MS (– APCI): *m*/*z* (%) = 438.2 (100) $[M + Cl]^-$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{25}H_{30}N_3O_2$ $[M + H]^+$ 404.23380; found 404.23380. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{25}H_{29}N_3O_2Cl$ $[M + Cl]^-$ 438.19483; found 438.19500.

5,5-Dimethyl-6-phenyloxan-2-one (32c):[30] The bpa precursor **32b** was transformed into the pertinent lactone **32c** according to General Procedure E. Evaporation of the solvent gave lactone **32c** (24.8 mg, 0.12 mmol, 83%) as a white solid, m.p. 100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 1.69–1.78 (m, 1 H, C*H*), 1.83–1.94 (m, 1 H, C*H*), 2.68–2.73 (m, 2 H, CH_2), 5.08 (s, 1 H, C*H*), 7.23–7.38 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 26.8, 27.5, 33.3, 34.3, 89.1, 127.5, 127.8, 128.2, 136.3, 171.3 ppm. MS (+ APCI): *m*/*z* (%) = 222.1 (100) $[M + NH_4]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{13}H_{20}NO_2$ $[M + NH_4]^+$ 222.14940; found 222.14950. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{13}H_{17}O_2$ $[M + H]^+$ 205.12285; found 205.12300.

6-Oxo-6-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (33a): Benzoyl pentanoic acid was coupled with bpa according to General Procedure A. The pertinent keto amide **33a** (0.66 g, 1.71 mmol, 93%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.75–1.80 (m, 4 H, CH_2CH_2), 2.51 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.97 (t, *J* = 7.0 Hz, 2 H, CH_2), 4.71 (s, 2 H, CH_2Py), 4.78 (s, 2 H, CH_2Py), 7.13–7.18 (m, 3 H, ArH), 7.29–7.31 (m, 1 H, ArH), 7.42–7.46 (m, 2 H, ArH), 7.52–7.56 (m, 1 H, ArH), 7.60–7.66 (m, 2 H, ArH), 7.91–7.94 (m, 2 H, ArH), 8.48–8.49 (m, 1 H, ArH), 8.54–8.55 (m, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.9, 24.8, 32.9, 38.3, 51.4, 53.1, 120.7, 122.3, 122.4, 122.5, 128.0, 128.5, 132.9, 136.7, 136.8, 137.0, 149.1, 149.9, 156.8, 157.5, 173.6, 200.1 ppm. MS (+ APCI): *m*/*z* (%) = 410.2 (100) $[M + Na]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{24}H_{25}N_3O_2Na$ $[M + Na]^+$ 410.18445; found 410.18400.

6-Hydroxy-6-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide (33b): 6-Oxo-6-phenyl-*N*,*N*-bis(pyridin-2-ylmethyl)hexanamide **33a** was reduced according to General Procedure C. The pertinent hydroxy amide **33b** (0.49 g, 1.26 mmol, 85%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.49 (m, 2 H, CH_2), 1.61–1.82 (m, 4 H, 2×CH_2), 2.41 (t, *J* = 7.4 Hz, 2 H, CH_2CONR$_2$), 2.71 (br. s, 1 H, O*H*), 4.63–4.67 (m, 1 H, C*H*OH), 4.67 (s, 2 H, CH_2Py), 4.74 (s, 2 H, CH_2Py), 7.10–7.17 (m, 3 H, ArH), 7.20–7.31 (m, 6 H, ArH), 7.57–7.64 (m, 2 H, ArH), 8.44 (ddd, *J* = 4.9, 1.8, 0.9 Hz, ArH), 8.51 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.8, 25.4, 32.9, 38.7, 51.4, 53.1, 74.0, 120.6, 122.2, 122.4, 122.5, 125.8, 127.3, 128.3, 136.7, 136.8, 145.0, 149.0, 149.8, 156.8, 157.4, 173.9 ppm. MS (+ APCI): *m*/*z* (%) = 390.2 (100) $[M + H]^+$. MS (– APCI): *m*/*z* (%) = 424.2 (100) $[M + Cl]^-$. HRMS (+ APCI): *m*/*z* calcd. for $C_{24}H_{28}N_3O_2$ $[M + H]^+$ 390.21815; found 390.21820. HRMS (– APCI, MeOH): *m*/*z* calcd. for $C_{24}H_{27}N_3O_2Cl$ $[M + Cl]^-$ 424.17918; found 424.17990.

7-Phenyloxepan-2-one (33c):[31,32] The bpa precursor **33b** was transformed into the pertinent lactone **33c** according to General Procedure E. Evaporation of the solvent led to lactone **33c** (27.3 mg, 0.14 mmol, 79%) as a white solid, m.p. 68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66–1.82 (m, 2 H, CH_2), 1.97–2.15 (m, 4 H, CH_2CH_2), 2.75–2.78 (m, 2 H, CH_2), 5.29 (d, *J* = 9.6 Hz, 1 H, C*H*Ph), 7.28–7.40 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.8, 28.6, 34.9, 37.4, 82.1, 125.8, 128.1, 128.5, 140.8, 174.8 ppm. MS (+ APCI): *m*/*z* (%) = 191.1 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): *m*/*z* calcd. for $C_{12}H_{15}O_2$ $[M + H]^+$ 191.10720; found 191.10720.

6-Oxo-*N*,*N*-bis(pyridin-2-ylmethyl)heptanamide (34a): Acetyl pentanoic acid was coupled with bpa according to General Procedure A. The pertinent keto amide **34a** (0.71 g, 2.18 mmol, 84%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51–1.59 (m, 2 H, CH_2), 1.61–1.68 (m, 2 H, CH_2), 2.07 (m, 3 H, CH_3), 2.39 (t, *J* = 7.1 Hz, 2 H, CH_2), 2.43 (t, *J* = 7.2 Hz, 2 H, CH_2), 4.67 (s, 2 H, CH_2Py), 4.73 (s, 2 H, CH_2Py), 7.10–7.17 (m, 3 H, ArH), 7.24–7.28 (m, 1 H, ArH), 7.58 (ddd, *J* = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.61 (ddd, *J* = 7.7, 7.7,

1.8 Hz, 1 H, ArH), 8.45 (ddd, J = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.52 (ddd, J = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.3, 24.5, 29.7, 32.7, 38.5, 43.4, 51.4, 53.0, 120.7, 122.2, 122.4, 122.4, 136.6, 136.7, 149.0, 149.8, 156.7, 157.4, 173.5, 208.6 ppm. MS (+ APCI): m/z (%) = 326.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_{19}H_{24}N_3O_2$ $[M + H]^+$ 326.18685; found 326.18680.

6-Hydroxy-*N*,*N*-bis(pyridin-2-ylmethyl)heptanamide (34b): Compound **34a** was reduced according to General Procedure C. The pertinent hydroxy amide **34b** (0.43 g, 1.31 mmol, 87%) was isolated as a colourless gum after purification by column chromatography (silica gel; $CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH, 90:10). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (d, J = 6.2 Hz, 3 H, CH_3), 1.31–1.45 (m, 4 H, 2 × CH_2), 1.59–1.75 (m, 2 H, CH_2), 2.00 (br. s, 1 H, OH), 3.73–3.81 (m, 1 H, CHOH), 4.70 (s, 2 H, CH_2Py), 4.75 (s, 2 H, CH_2Py), 7.11–7.18 (m, 3 H, ArH), 7.27–7.29 (m, 1 H, ArH), 7.59 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 7.62 (ddd, J = 7.7, 7.7, 1.8 Hz, 1 H, ArH), 8.46 (ddd, J = 4.9, 1.8, 0.9 Hz, 1 H, ArH), 8.54 (ddd, J = 4.8, 1.8, 0.9 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4, 24.8, 25.3, 32.9, 38.9, 51.4, 53.1, 67.5, 120.7, 122.2, 122.4, 122.5, 136.7, 136.8, 149.1, 149.8, 156.9, 157.5, 173.9 ppm. MS (+ APCI): m/z (%) = 328.2 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_{19}H_{26}N_3O_2$ $[M + H]^+$ 328.20250; found 328.20230.

7-Methyloxepan-2-on (34c):[33] The bpa precursor **34b** was transformed into the pertinent lactone **34c** according to General Procedure E. Evaporation of the solvent led to lactone **34c** (27.2 mg, 0.21 mmol, 68%) as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (d, J = 6.4 Hz, 3 H, CH_3), 1.54–1.69 (m, 3 H, CH, CH_2), 1.85–1.96 (m, 3 H, CH, CH_2), 2.55–2.69 (m, 2 H, CH_2), 4.43 (m_c, 1 H, CHOCO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 22.9, 28.3, 35.0, 36.2, 76.8, 175.5 ppm. MS (+ APCI): m/z (%) = 129.1 (100) $[M + H]^+$. HRMS (+ APCI, MeOH): m/z calcd. for $C_7H_{13}O_2$ $[M + H]^+$ 129.09155; found 129.09150.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra.

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