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Synthesis of Highly Functionalized Macrocycles by the Peripheral Functionalization of Macrocyclic Diimines

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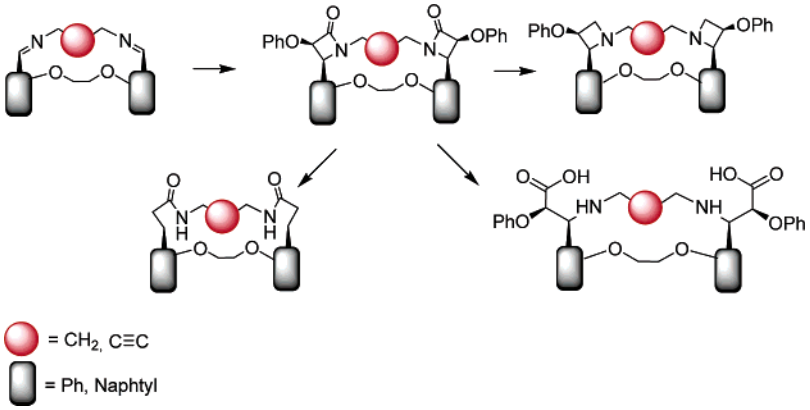

The easily available macrocyclic diimines **4**−**7** can be stereoselectively transformed to macrocyclic bis-*β*-amino acids **13**−**17**, macrocyclic bisazetidines **18**−**20**, and macrocyclic bisamides **21** and **22** by means of the corresponding bis-*β*-lactam scaffolds **8**−**12**. These key intermediates are available through standard Staudinger reaction and obtained as the *cis-cis* diastereomers, exclusively. An interesting relation between the proximity of the reactive C=N bonds and the selectivity in the formation of the bis-*β*-lactams **8**−**12** is observed. Thus, diimine **4** leads to low selectivities, producing a 1:1 mixture of *cis-syn-cis* and *cis-anti-cis* diastereomers, while diimines **5**−**7** having the diimine sites more separated lead almost exclusively to the *cis-anti-cis* diastereomers. The stereochemistry of all the products was unambiguously assigned by X-ray diffraction analysis of compounds *cis-syn-cis* **8** and *cis-anti-cis* **12-Co_2CO_6** complex.

Introduction

Despite the plethora of synthesis of compounds having the *β*-lactam ring[1] and the number of transformations in which the 2-azetidinone ring is involved,[2] the scarce use of these compounds in the functionalization of macrocycles is surprising. Romo[3] and Wasserman[4] have elegantly employed the 2-azetidinone ring as a macrolactamization agent. Hegedus reported the synthesis of cyclams and biscyclams[5] starting from azacarbapenams and bisazacarbapenams, respectively. Otherwise, the building of one or more *β*-lactam rings in a preformed macrocyclic imine or polyimine to further manipulate the four-

† To whom inquires regarding the X-ray determination of the structures of compound **8** and compound **12-$Co_2(CO)_6$** should be addressed.

(1) See: (a) Gómez-Gallego, M.; Mancheño, M. J.; Sierra, M. A. *Tetrahedron* **2000**, *56*, 5743. Selected reviews in the synthesis and biology of *β*-lactams: (b) Dürckheimer, W.; Blumbach, J.; Lattrell, R.; Scheunemann, K. H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 180. (c) *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, 1992.

(2) In fact, the term *β-lactam synthon approach* was coined for these methodologies. See: (a) Hatanaka, N.; Abe, R.; Ojima, I. *Chem. Lett.* **1982**, 445. Reviews: (b) Ojima, I. *Adv. Asymmetry Synth.***1995**, *1*, 95−146. (c) Manhas, M. S.; Wagle, D. R.; Chiang, J.; Bose, A. K. *Heterocycles* **1988**, *27*, 1755−1802. (d) Palomo, C.; Aizpurua, J. M.; Ganboa, I.; Oiarbide, M. *Pure Appl. Chem.* **2000**, *72*, 1763.

(3) Romo, D.; Rzasa, R. M.; Shea, H. A.; Park, K.; Langenhan, J. M.; Sun, L.; Akhiezer, A.; Liu, J. O. *J. Am. Chem. Soc.* **1998**, *120*, 12237.

(4) Wasserman, H. H.; Matsuyama, H.; Robinson, R. P. *Tetrahedron* **2002**, *58*, 7177 and references therein.

(5) (a) Achmatowicz, M.; Hegedus, L. S.; David, S. *J. Org. Chem.* **2003**, *68*, 7661. (b) Hegedus, L. S.; Sundermann, M. J.; Dorhout, P. K. *Inorg. Chem.* **2003**, *42*, 4346. (c) Wynn, T.; Hegedus, L. S. *J. Am. Chem. Soc.* **2000**, *122*, 5034. (d) Gil, J. M.; David, S.; Reiff, A. L.; Hegedus, L. S. *Inorg. Chem.* **2005**, *44*, 585 and references therein.

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membered ring and to produce differently functionalized macrocycles is unknown.[6]

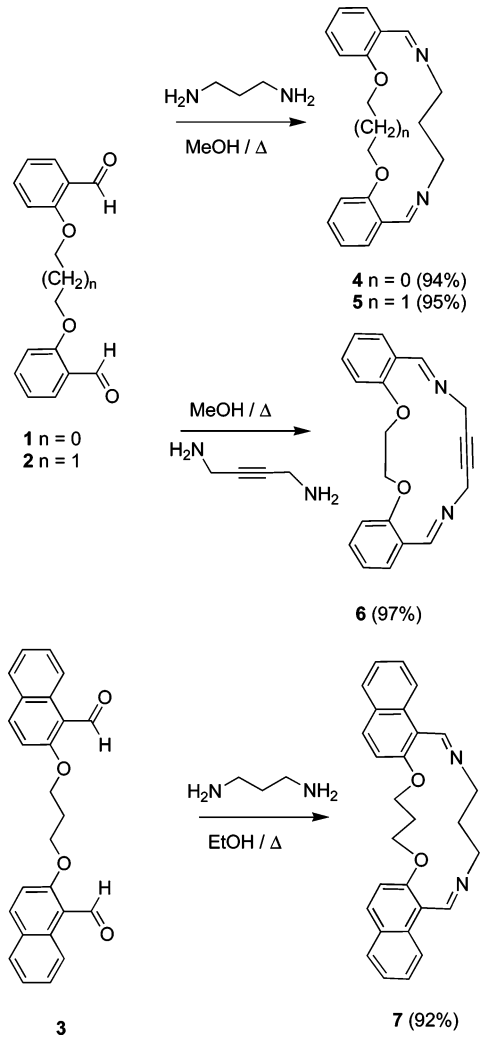
Macrocyclic polyimines have been prepared in the context of metal chelating cavities,[7] and they are very attractive scaffolds to construct macrocyclic bisazetidinones that can be further elaborated to macrocyclic polyamino acids, macrocyclic amides, and macrocyclic azetidines within the diversity oriented synthesis (DOS) concept.[8] Reported in this paper is the implementation of this idea.

Results and Discussion

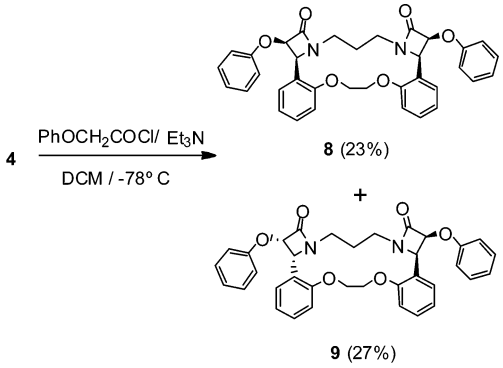
Dialdehydes **1**−**3**[9] were condensed with 1,3-diaminopropane and 1,4-diamino-2-butyne in nearly quantitative yields in boiling MeOH or EtOH to form the macrocyclic imines **4**−**7** used in this work (Scheme 1). The reaction conditions have been tuned up to avoid the formation of dimers or oligomers as byproducts.[10] Diimine **4** was reacted with phenoxyacetyl chloride in dry CH_2Cl_2 at −78 °C in the presence of Et_3N. After heating to room temperature and quenching with MeOH/H_2O, a 1:1 mixture of two bis-β-lactam derivatives (78% yield) was obtained. The mixture was separated by column chromatography to yield compounds **8** and **9**, isolated in 23 and 27% yields, respectively (Scheme 2). Both compounds have a *cis-cis* stereochemistry in the β-lactam ring as deduced from the coupling constants of H3−H4 and H3′−H4′ protons ($J_{3,4}$ = 4.5 and 4.4 Hz for compounds **8** and **9**, respectively).[11] Therefore, the reaction yielded both the *cis-syn-cis* **8** and the *cis-anti-cis* **9** isomers. No trace amounts of any of the remaining isomers having one or both rings in a *trans*-stereochemistry were detected. A single crystal of *cis-syn-cis* **8** was submitted to X-ray diffraction analysis thus unambiguously establishing this relative stereochemistry.

Having unambiguously characterized compound **8** as the *cis-syn-cis* isomer, the *cis-anti-cis* stereochemistry was assigned to compound **9**. Reactions of imines **5**−**7** and phenoxyacetyl chloride under the conditions discussed above yielded products **10**, **11**, and **12** in 78, 45, and 74%, respectively. Compounds **10**−**12** were isolated as single diastereomers. Traces (<10%) of the other *cis-cis* diastereomers were observed in the crude reaction mixture, but they could not be isolated. All compounds **10**−**12** have the signal corresponding to the β-lactam H4 shielded (4.88, 4.88, and 5.38 ppm, respectively) compared to that of the minor isomers (5.34, 5.36, and 5.58 ppm, respectively[12]). This shielding was also observed in compound **9** (δ_{H4} = 5.17) compared to compound **8** (δ_{H4} = 5.41) from which the

SCHEME 1



SCHEME 2



(6) The formation of some macrocyclic bis-β-lactams in very low yields has been reported for the preparation of 4,7-fused β-lactam synthesis. See: Brooks, G.; Hunt, E. *J. Chem. Soc., Perkin Trans. 1* **1983**, 115.

(7) (a) Armstrong, L. G.; Lindoy, L. F. *Inorg. Chem.* **1975**, *14*, 1322. (b) Armstrong, L. G.; Grimsley, P. G.; Lindoy, L. F.; Lip, H. C.; Norris, V. A.; Smith, R. J. *Inorg. Chem.* **1978**, *17*, 2350. (c) Lindoy, L. F.; Lip, H. C.; Power, L. F.; Rea, J. H. *Inorg. Chem.* **1976**, *15*, 1724. (d) Anderegg, G.; Ekstrom, A.; Lindoy, L. F.; Smith, R. J. *J. Am. Chem. Soc.* **1980**, *102*, 2670. (e) Baldwin, D.; Duckworth, P. A.; Erickson, G. R.; Lindoy, L. F.; McPartlin, M.; Mockler, G. M.; Moody, W. E.; Tasker, P. A. *Aust. J. Chem.* **1987**, *40*, 1861. (f) Adam, K. R.; Leong, A. J.; Lindoy, L. F.; Lip, H. C.; Skelton, B.; White, A. H. *J. Am. Chem.* Soc. **1983**, *105*, 4645. (g) Miyokawa, K.; Hirashima, H.; Masuda, I. *Tetrahedron* **1985**, *41*, 1891. (h) Leoni, P.; Grilli, E.; Pasquali, M.; Tomassini, M. *J. Chem. Soc., Dalton Trans.* **1985**, 2561. (i) Martell, A. E.; Hancock, R. D. *Chem. Rev.* **1989**, *89*, 1875.

(8) Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46.

(9) Simion, C.; Simion, A.; Mitoma, Y.; Nagashima, S.; Kawaji, T.; Hasimoto, I.; Tashiro, M. *Heterocycles* **2000**, *53*, 2459.

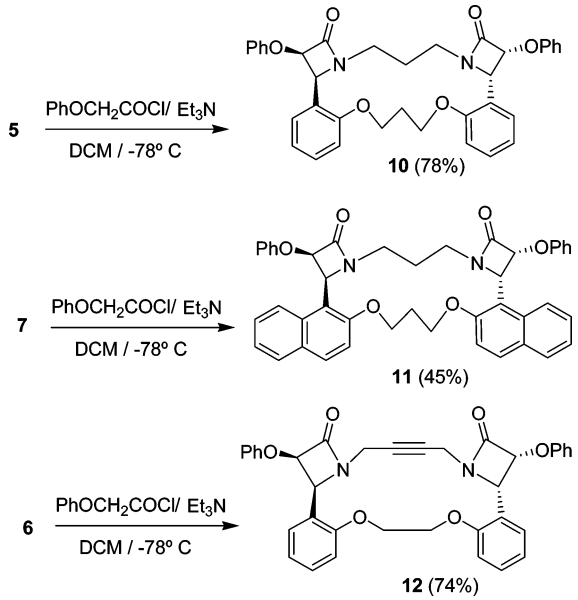
(10) The formation of dimers and oligomers as undesired byproducts in the synthesis of macrocyclic diimines depends not only on the reaction conditions employed but also on the size and conformational flexibility of the molecules involved. See for example: Simion, A.; Simion, C.; Kanda, T.; Nagashima, S.; Mitoma, T.; Yamada, T.; Mimura, K.; Tashiro, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2071 and ref 7a.

(11) The most usual method for the determination of the relative stereochemistry of 2-azetidinones is ^{1}H NMR. The $J_{3,4}$ *cis* value is ca. 4.5−6 Hz, while $J_{3,4}$ *trans* is ca. 2−2.5 Hz. See for example: (a) Manhas, M. S.; Ghosh, M.; Bose, A. K. *J. Org. Chem.* **1990**, 55, 575. (b) Sharma, A. K.; Mazumdar, S. N.; Mahajan, M. P. *J. Org. Chem.* **1996**, *61*, 5506. (c) Alcázar, R.; Ramírez, P.; Vicente, R.; Mancheño, M. J.; Sierra, M. A.; Gómez-Gallego, M. *Heterocycles* **2001**, *55*, 511.

(12) Data measured in ^{1}H NMR spectra of the mixtures enriched in these minor isomers.

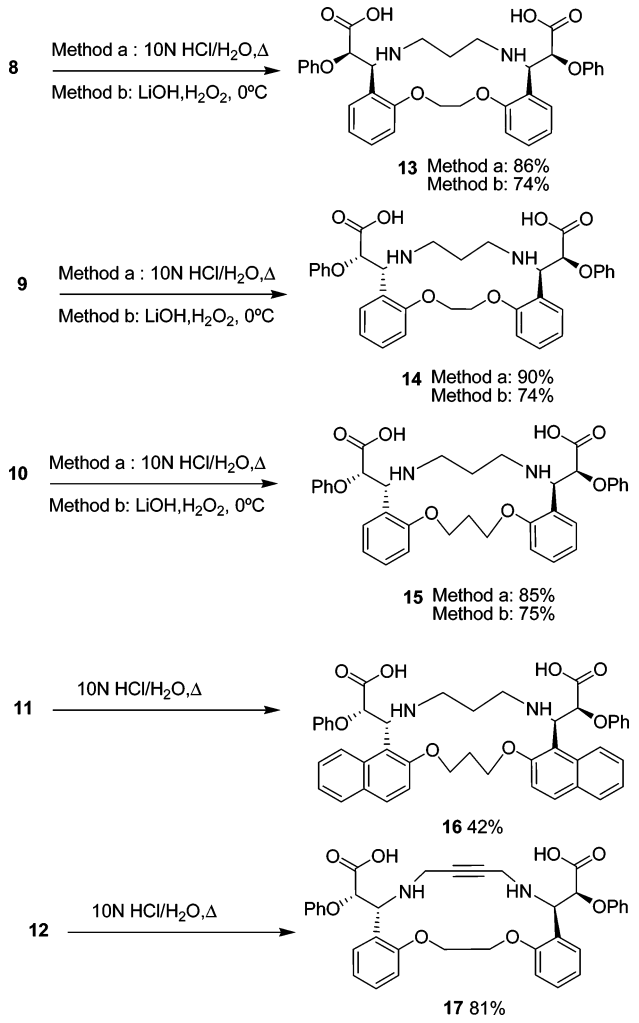
relative stereochemistry was unambiguously ascertained by X-ray analysis. Therefore, the *cis-anti-cis* stereochemistry was assigned to products **10**−**12** (Scheme 3).[13] Definitive confirmation of the stereochemical assignment for these compounds was achieved by preparing the $Co_2(CO)_6$ complex derived from **12**. Compound **12·Co$_2$(CO)$_6$** produced crystals suitable for X-ray diffraction analysis that unambiguously confirmed the *cis-anti-cis* stereochemistry of this product and, by analogy, the validity of the stereochemical assignment made for compounds **9**−**11**.

SCHEME 3



The stereochemistry observed in the double Staudinger reaction leading to compounds **8**−**12** deserves some comments. It is known that cyclic imines prefer to form the *trans*-β-lactams due to the fixed *Z*-configuration of the imine C═N bond imposed by the cyclic structure.[14] This is not the case for macrocyclic imines **4**−**7** that have *E*-configuration[15] and follow the usual pattern observed for open-chain imines[16] giving only the *cis*-β-lactams. More intriguing is the observed selectivity during the formation of the bis-β-lactam system. Except for diimine **4**, which forms the equimolecular amount of *cis-syn-cis* and *cis-anti-cis* isomers, imines **5**−**7** have a clear bias for the formation of *cis-anti-cis* isomers. These facts suggest a direct influence of one of the emerging four-membered rings on the torquoselectivity[17] of the second ring closure but only when both centers are not too close to each other as in compound **4**, in which the tether between the O−Ar groups is a CH_2-CH_2 chain (compare the stereochemistry of the reaction products derived from compounds **4** and **5** or **7**). The formation of 1:1

SCHEME 4



syn/anti diastereomeric mixtures has been also reported in the synthesis of acyclic *cis*-bis-β-lactams linked by an ethylene bridge.[18] The origin of the selectivity in the formation of β-lactams and the influence of several factors (structural, electronic, reaction conditions) is still a subject of debate.[14b] The diastereoselectivity reported in this paper may be due to a better stabilization of the intermediate zwitterions and could be topologically demanding. While this effect has been observed previously in peripheral functionalization,[19] it has not been rationalized. A theoretical model to reflect this effect is being developed in our laboratories and will be reported in due time.

With an efficient and stereoselective entry to macrocyclic bis-β-lactams ascertained, the use of these compounds as scaffolds to obtain functionalized macrocycles was explored next. The hydrolysis of compounds **8**−**12** to the novel macrocyclic bis-β-amino acids **13**−**17** was carried out by boiling compounds **8**−**12** in 10 N HCl. The amino acids were obtained as hydrochlorides in good to excellent yields with retention of the stereochemistry of the starting bis-β-lactam. The use of Evans' conditions (LiOH, H_2O_2 at 0 °C)[20] in compounds **8**−**10** also formed bisamino acids **13**−**15** in good yields (Scheme 4).

(13) Preliminary MM studies carried out with compounds **8** and **9** show that the rigidity imposed in the macrocycle by the embedding of two β-lactam ring places the aromatic ring of one four-membered ring close to the other in the *cis-anti-cis* isomer. This effect is not seen in the *cis-syn-cis* isomer.

(14) Jiao, L.; Liang, Y.; Xu, J. *J. Am. Chem. Soc.* **2006**, *128*, 6060 and references therein.

(15) The *E*-configuration of the cyclic diimines derived from dialdehydes **1**−**3** has been reported. See: References 7h and 10.

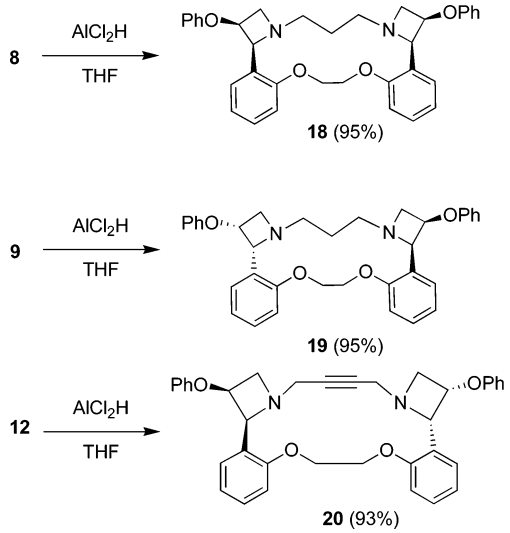
(16) (a) Dumas, S.; Hegedus, L. S. *J. Org. Chem.* **1994**, *59*, 4967. (b) Hegedus, L. S.; Montgomery, J.; Narukawa, Y.; Sanustad, D. C. *J. Am. Chem. Soc.* **1991**, *113*, 5784.

(17) Cossio, F. P.; Arrieta, A.; Lecea, B.; Ugaldby, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 2085 and references therein.

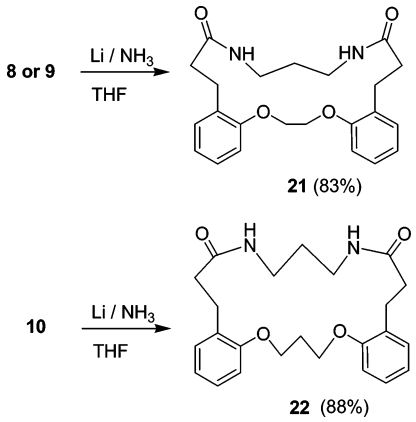
(18) Karupaiyan, K.; Puranik, V. G.; Deshmukh, A. R. A. S.; Bhawal, B. M. *Tetrahedron* **2000**, *56*, 8555.

(19) (a) Still, W. C.; Romero, A. G. *J. Am. Chem. Soc.* **1986**, *108*, 2105. (b) Schreiber, S. L.; Sammakia, T.; Hulin, B.; Schulte, G. *J. Am. Chem. Soc.* **1986**, *108*, 2106.

SCHEME 5



SCHEME 6



The amide C═O group of compounds **8**, **9**, and **12** was reduced to form the corresponding bisazetidines **18**−**20**[21] in the presence of $AlCl_2H$ in very high yields.[22] Compounds **18**−**20** were obtained as single stereoisomers and retain the stereochemistry of the starting 2-azetidinones (Scheme 5). It should be noted that *cis*-*syn*-*cis* bis-*β*-lactam **8** and its derivatives **13** and **18** are meso-forms, while the *cis*-*anti*-*cis* bis-*β*-lactams **9**−**12** and their derivatives **14**−**20** are racemic mixtures. This may be of interest if an enantioselective route to these compounds will be developed.

To finally demonstrate the versatility of macrocyclic bis-*β*-lactams **8**−**12** to produce functionalized macrocycles, compounds **8**−**10** were submitted to reaction with Li/NH_3. Under these conditions, macrocycles **21** and **22** were produced in high yields. It is worthy to note that together with the fragmentation of the N1−C4 bond breakage the phenoxy group is also reductively removed.

In conclusion, easily available macrocyclic imines can be stereoselectively transformed to macrocyclic bis-*β*-amino acids, macrocyclic bisazetidines, and macrocyclic bisamides by means of the corresponding bis-*β*-lactam scaffolds. These key intermediates are available through standard Staudinger reaction. Efforts to extend this approach to the peripheral functionalization of bigger macrocycles and to use the obtained products as chelating agents are being currently pursued in our laboratories.

Experimental Section

General procedures have been previously reported.[23] Dialdehydes **1** and **2** were obtained following the reported procedure.[9] Diimines **4**−**7** were prepared following a modification of the literature procedure.[7a,10]

Synthesis of Dialdehyde 3: K_2CO_3 (30 g, 0.2 mol) was suspended in butanone (75 mL) in a two-neck round flask equipped with a reflux condenser and magnetic stirring bar. A solution of 2-hydroxynaphthalene-1-carbaldehyde (4 g, 0.023 mol) in butanone (40 mL) was added dropwise, and the solution became dark green. The mixture was purged with argon and stirred under reflux for 1.30 h. Then, NaI (80 mg, 05. mol) and a solution of 1,3-dibromopropane (2.42 g, 0.012 mol) in butanone (20 mL) was added. The mixture was stirred under reflux under argon for 48 h. After reaching room temperature, the crude reaction mixture was filtered through Celite, then 100 mL of distilled water was added to the organic layer that was subsequently extracted with dichloromethane (3 × 100 mL). The organic extracts were dried over $MgSO_4$, filtered, and evaporated to dryness at reduced pressure. The resulting solid was recrystallized in EtOH to yield 1.38 g (30%) of a pale brown solid: mp 193−196 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.95 (s, 2H), 9.24 (d, J = 8.7 Hz, 2H), 8.06 (d, J = 9.2 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 7.65−7.59 (m, 2H), 7.45−7.42 (m, 2H), 7.29 (d, J = 9.2 Hz, 2H), 4.50 (t, J = 5.9 Hz, 4H), 2.50 (q, J = 5.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.5, 163.0, 137.7, 131.5, 129.9, 128.6, 128.2, 124.9, 124.8, 116.8, 113.2, 65.6, 29.5; IR (KBr) ν_{max} 3442, 2935, 2887, 1670,1591, 1512, 1245, 1151, 1058 cm^{-1}. Anal. Calcd for $C_{25}H_{20}O_4$: C, 78.11; H, 5.24. Found: C, 78.32; H, 5.41.

General Procedure for the Synthesis of *β*-Lactams (8−12): A solution of phenoxyacetyl chloride in dry CH_2Cl_2 was purged with argon and cooled at −78 °C. Then, a solution of triethylamine in dry CH_2Cl_2 was added dropwise. The mixture was stirred for 30 min, and a solution of the corresponding diimine in dry CH_2Cl_2 was added dropwise by means of a syringe pump for 2 h. The reaction mixture was stirred at room temperature for the periods specified in each case, quenched with MeOH and water, and extracted with CH_2Cl_2. The organic layer was washed with 0.5 M HCl (to remove the excess of triethylamine) and brine, and then dried with $MgSO_4$. The desiccant was removed by filtration and the solvent evaporated at reduced pressure. The crude solid was suspended in Et_2O, filtered, and dried.

Synthesis of *β*-Lactams 8 and 9: Following the general procedure, phenoxyacetyl chloride (1.77 g, 10.4 mmol) in dry CH_2Cl_2 (20 mL), triethylamine (2.11 g, 20.8 mmol) in dry CH_2Cl_2 (10 mL), and diimine **4** (1.07 g, 3.5 mmol) in dry CH_2Cl_2 (10 mL) were reacted for 16 h. The reaction yielded 1.58 g (78%) of a 1:1 mixture of isomers **8** and **9**. The isomers were separated by flash chromatography in hexane/AcOEt 7:3 affording 465 mg (23%) of **8** and 550 mg (27%) of **9**. The structure of **8** was confirmed by X-ray diffraction. ***β*-Lactam 8:** white crystals; mp 215−217 °C (CH_2Cl_2/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, J_1 =

(20) Evans, D. A.; Britton, T. C.; Ellman, J. A. *Tetrahedron Lett.* **1987**, *28*, 6141.

(21) Polyamines having the azetidine ring embedded in a macrocyclic structure are interesting ligands for metal ions since the four-membered ring imposes strong conformational restrictions from which some unusual characteristics may emerge. See: Harrowfield, J.; Kim, J. Y.; Kim, Y.; Lee, Y. H.; Thuéry, P. *Polyhedron* **2005**, *24*, 1569 and the pertinent references therein.

(22) Ojima, I.; Zhao, M.; Yamato, T.; Nakahashi, K.; Yamashita, M.; Abe, R. *J. Org. Chem.* **1991**, *56*, 5263.

(23) Ramírez-López, P.; Gómez-Gallego, M.; Mancheño, M. J.; Sierra, M. A.; Bilurbina, M.; Ricart, S. *J. Org. Chem.* **2003**, *68*, 3538.
Simion, C.; Simion, A.; Mitoma, Y.; Nagashima, S.; Kawaji, T.; Hasimoto, I.; Tashiro, M. *Heterocycles* **2000**, *53*, 2459.

7.6 Hz, J_2 = 1.6 Hz, 2H), 7.27−7.11 (m, 6H), 6.96−6.75 (m, 10H), 5.57 (d, J = 4.5 Hz, 2H), 5.41 (d, J = 4.5 Hz, 2H), 4.55−4.41 (m, 4H), 3.48−3.30 (m, 2H), 3.10−2.96 (m, 2H), 1.70−1.47 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.1, 157.0, 156.3, 130.5, 129.7, 129.2, 121.9, 121.4, 120.8, 115.4, 111.5, 81.2, 65.6, 54.6, 38.1, 24.4; IR (KBr) ν_{max} 3446, 1757, 1598, 1492, 1409, 1290, 1236, 1060, cm^{-1}. ESI-MS: 577.0 [M + H]$^+$. Anal. Calcd for $C_{35}H_{32}N_2O_6$: C, 72.90; H, 5.59. Found: C, 73.21; H, 5.74. ***β*-Lactam 9:** white crystals; mp 217−220 °C (CH_2Cl_2/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (dd, J_1 = 7.7 Hz, J_2 = 1.4 Hz, 2H), 7.26 (dt, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 2H), 7.09 (t, J = 7.7 Hz, 4H), 7.00 (t, J = 7.4 Hz, 2H), 6.90−6.81 (m, 4H), 6.67 (d, J = 8.1 Hz, 4H), 5.36 (d, J = 4.4 Hz, 2H), 5.16 (d, J = 4.4 Hz, 2H), 4.48−4.38 (m, 4H), 3.70−3.61 (m, 2H), 2.86−2.76 (m, 2H), 1.77−1.71 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.9, 157.3, 156.7, 129.7, 129.1, 128.9, 121.8, 121.0, 120.7, 115.3, 112.1, 81.4, 67.7, 53.87, 36.6, 23.2; IR (KBr) ν_{max} 3447, 1756 1598, 1494, 1409, 1292, 1235, 1053 cm^{-1}. ESI-MS: 577.0 [M + H]$^+$. Anal. Calcd for $C_{35}H_{32}N_2O_6$: C, 72.90; H, 5.59. Found: C, 72.54; H, 5.71.

Synthesis of *β*-Lactam 10: Following the general procedure, phenoxyacetyl chloride (2.25 g, 13.2 mmol) in CH_2Cl_2 (20 mL), triethylamine (2.67 g, 26.4 mmol) in CH_2Cl_2 (10 mL), and diimine **5** (1.42 mg, 4.4 mmol) in CH_2Cl_2 (10 mL) were reacted for 15 h. The crude reaction yielded 2.04 g (78%) of *β*-lactam **10** as white crystals: mp 225−228 °C (CH_2Cl_2/MeOH 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (dd, J_1 = 7.5 Hz, J_2 = 1.6 Hz, 2H), 7.21 (dt, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 2H), 7.08 (t, J = 7.5 Hz, 4H), 6.99 (t, J = 7.5 Hz, 2H), 6.88−6.74 (m, 4H), 6.60 (d, J = 8.0 Hz, 4H), 5.42 (d, J = 4.3 Hz, 2H), 4.88 (d, J = 4.3 Hz), 4.30−4.25 (m, 2H), 4.03−3.99 (m, 2H), 3.80−3.66 (m, 2H), 2.82−2.73 (m, 2H), 2.41−2.31 (m, 2H), 1.84−1.74 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 156.9, 156.5, 129.8, 128.7, 128.5, 121.7, 121.0, 120.4, 115.3, 111.8, 81.4, 66.6, 53.6, 35.8, 28.7, 22.9; IR (KBr) ν_{max} 3486, 2925, 1751, 1598, 1589, 1490, 1404, 1290, 1232, 1087 cm^{-1}. ESI-MS: 591.1 [M + H]$^+$. Anal. Calcd for $C_{36}H_{34}N_2O_6$: C, 73.20; H, 5.80. Found: C, 73.42; H, 5.66.

Synthesis of *β*-Lactam 11: Following the general procedure, phenoxyacetyl chloride (725 mg, 4.26 mmol) in CH_2Cl_2 (15 mL), triethylamine (860 mg, 8.5 mmol) in CH_2Cl_2 (10 mL), and diimine **7** (600 mg, 1.42 mmol) in CH_2Cl_2 (5 mL) were reacted for 20 h. The crude reaction mixture was purified by flash chromatography in hexane/AcOEt (1:1) to yield 450 mg (45%) of *β*-lactam **11** as white crystals: mp 135−138 °C (CH_2Cl_2/MeOH 3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 9.0 Hz, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.48 (t, J = 7.1 Hz, 2H), 7.36 (t, J = 7.1 Hz, 2H), 7.28 (d, J = 9.0 Hz, 2H), 7.03 (t, J = 7.6 Hz, 4H), 6.80 (t, J = 7.1 Hz, 2H), 6.60 (d, J = 8.2 Hz, 4H), 6.11 (d, J = 4.6 Hz, 2H), 5.28 (d, J = 4.6 Hz, 2H), 4.59−4.48 (m, 2H), 4.46−4.35 (m, 2H), 3.59−3.48 (m, 2H), 2.66−2.53 (m, 4H), 1.81−1.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7, 156.8, 156.1, 133.5, 131.9, 129.8, 129.6, 128.8, 128.6, 127.2, 124.7, 124.0, 121.6, 115.0, 114.2, 113.5, 82.8, 67.1, 54.6, 37.6, 29.6, 23.7; IR (KBr) ν_{max} 3431, 1755, 1669, 1596, 1494, 1240, 1058, 1037 cm^{-1}. Anal. Calcd for $C_{44}H_{38}N_2O_6$: C, 76.50; H, 5.54. Found: C, 76.72; H, 5.66.

Synthesis of *β*-Lactam 12: Following the general procedure, phenoxyacetyl chloride (1.79 g, 10.5 mmol) in CH_2Cl_2 (15 mL), triethylamine (2.13 g, 21.1 mmol) in CH_2Cl_2, and diimine **6** (1.12 g, 3.52 mmol) in CH_2Cl_2 (15 mL) were reacted for 18 h. The crude solid product was dispersed in 100 mL of diethyl ether, filtered, and dried under vacuum to afford 1.53 g (74%) of pure *β*-lactam **12** as white crystals: mp 266−268 °C (CH_2Cl_2/MeOH 3:1); ^{1}H NMR (300 MHz, CDCl) δ 7.37−7.26 (m, 4H), 7.14−7.00 (m, 6H), 6.91−6.79 (m, 4H), 6.71 (d, J = 7.9 Hz, 4H), 5.65 (d, J = 4.6 Hz, 2H), 5.39 (d, J = 4.6 Hz, 2H), 4.64 (d, J = 17.1 Hz, 2H), 4.38 (d, J = 7.3 Hz, 2H), 4.24 (d, J = 7.3 Hz, 2H), 3.56 (d, J = 17.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 156.73, 156.70, 129.6, 128.8, 128.0, 121.8, 120.8, 120.7, 115.4, 110.6, 82.3, 77.1, 66.4, 53.7, 29.4; IR (KBr) ν_{max} 1770, 1596, 1492, 1400, 1292, 1230, 1091, 1064 cm^{-1}. Anal. Calcd for $C_{36}H_{30}N_2O_6$: C, 73.71; H, 5.15. Found: C, 73.94; H, 5.33.

Synthesis of 12·$Co_2(CO)_6$ Complex: In a flame-dried round-bottom flask equipped with a magnetic stirring bar and in an argon atmosphere, a solution of *β*-lactam **12** (100 mg, 0.17 mmol) in dry and degassed CH_2Cl_2 (10 mL) was stirred with $Co(CO)_6$ (87 mg, 0.26 mmol) for 3 h. The crude product was filtered through Celite, and the solvent was evaporated at reduced pressure. The reaction yields 140 mg (94%) of a purple solid. The cobalt complex was recrystallized in MeOH/CH_2Cl_2 (1:1) to produce suitable crystals that were analyzed by NMR and X-ray: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.37 (d, J = 7.3 Hz, 2H), 7.31−7.23 (m, 2H), 7.12 (t, J = 7.8 Hz, 4H), 6.98 (t, J = 7.3 Hz, 2H), 6.88 (t, J = 7.3 Hz, 2H), 6.83−6.71 (m, 6H), 5.56 (d, J = 4.3 Hz, 2H), 5.43 (d, J = 4.3 Hz, 2H), 5.23 (d, J_2 = 16.3 Hz, 2H), 4.45 (s, 4H), 3.98 (d, J_2 = 16.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8, 166.3, 156.9, 156.7, 130.4, 130.1, 129.0, 121.9, 120.9, 120.3, 115.5, 110.9, 90.0, 82.2, 65.7, 58.1, 43.0.

General Procedure for the Synthesis of *β*-Amino acids 13−17: In a round-bottom flask equipped with a magnetic stirring bar and a reflux condenser, a suspension of the corresponding *β*-lactam in 10 M HCl was refluxed for 24−48 h. The crude product was extracted with CH_2Cl_2, and the aqueous layer was dried and the solvent removed at reduced pressure. The solid obtained was washed with CH_2Cl_2. The amino acids were obtained as hydrochlorides.

Synthesis of *β*-Amino acid 13: A suspension of *β*-lactam **8** (400 mg, 0.68 mmol) in 10 M HCl (25 mL) was refluxed for 24 h. *β*-Amino acid **13** (350 mg, 86%) was obtained as a pale pink solid: ^{1}H NMR (300 MHz, DMSO-d_6, 65 °C) δ 7.79 (d, J = 7.5 Hz, 2H), 7.42−7.28 (m, 2H), 7.27−7.14 (m, 4H), 7.11−6.89 (m, 10H), 5.33 (d, J = 8.2 Hz, 2H), 5.10 (d, J = 8.2 Hz, 2H), 4.56−4.49 (m, 2H), 4.39−4.29 (m, 2H), 2.94−2.82 (m, 2H), 2.64−2.52 (m, 2H), 2.20−2.09 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 170.7, 158.2, 157.8, 133.6, 130,9, 124.1, 123.1, 118.4, 117.2, 116.9, 113.5, 78.5, 67.4, 55.0, 43.0, 22.4; IR (KBr) ν_{max} 3411, 2939, 1735, 1589, 1496, 1224, 1180, 1053 cm^{-1}. ESI-MS: 613.7 [M + H]$^+$. Anal. Calcd for $C_{35}H_{38}N_2O_8Cl_2$: C, 61.32; H, 5.59; Cl, 10.34; N, 4.09. Found: C, 61.18; H, 5.42.

Synthesis of *β*-Amino acid 14: A suspension of *β*-lactam **9** (100 mg, 0.17 mmol) in 10 M HCl (15 mL) was refluxed for 24 h. *β*-Amino acid **14** (95 mg, 90%) was obtained as a pale pink solid: ^{1}H NMR (500 MHz, DMSO-d_6, 65 °C) δ 7.73 (d, J = 7.1 Hz, 2H), 7.37 (t, J = 7.8 Hz, 2H), 7.22 (t, J = 7.8 Hz, 4H), 7.10 (d, J = 8.3 Hz, 2H), 7.02−6.89 (m, 8H), 5.35 (d, J = 8.7 Hz, 2H), 5.01 (d, J = 8.7 Hz, 2H), 4.38 (s, 4H), 3.06−2.97 (m, 2H), 2.92−2.86 (m, 2H), 2.18−2.12 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6, 65 °C) δ 168.0, 156.2, 156.1, 131.0, 129.8, 128.9, 121.8, 120.5, 118.1, 115.7, 111.7, 77.2, 66.4, 53.7, 42.5, 20.5; IR (KBr) ν_{max} 3412, 2941, 1734, 1586, 1495, 1224, 1177, 1054 cm^{-1}. Anal. Calcd for $C_{35}H_{38}N_2O_8Cl_2$: C, 61.32; H, 5.59; Cl, 10.34; N, 4.09. Found: C, 61.60; H, 5.37.

Synthesis of *β*-Amino acid 15: A suspension of *β*-lactam **10** (250 mg, 0.42 mmol) in 10 M HCl (25 mL) was refluxed for 72 h. *β*-Amino acid **15** (220 mg, 85%) was obtained as a pale pink solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.75 (d, J = 7.8 Hz, 2H), 7.38−7.26 (m, 2H), 7.22 (t, J = 7.9 Hz, 4H), 7.12 (d, J = 8.2 Hz, 2H), 7.06−6.88 (m, 4H), 6.84 (d, J = 8.2 Hz, 4H), 5.08 (d, J = 8.1 Hz, 2H), 5.01 (d, J = 8.1 Hz, 2H), 4.36−4.28 (m, 2H), 4.08−3.99 (m, 2H), 2.87−2.78 (m, 2H), 2.69−2.58 (m, 2H), 2.19−2.10 (m, 2H), 1.94−1.82 (m, 2H); ^{13}C NMR (75 MHz, CD_3OD) δ 170.4, 158.9, 158.0, 133.5, 130.8, 130.2, 124.0, 123.4, 119.4, 117.1, 116.0, 78.9, 68.8, 54.7, 43.2, 30.2, 20.3; IR (KBr) ν_{max} 3421, 2939, 1733, 1589, 1494, 1226, 1180, 1055 cm^{-1}. Anal. Calcd for $C_{35}H_{38}N_2O_8Cl_2$: C, 61.80; H, 5.76; Cl, 10.13; N, 4.00. Found: C, 61.58; H, 5.77.

Synthesis of *β*-Amino acid 16: A suspension of *β*-lactam **11** (80 mg, 0.11 mmol) in 6 M HCl (15 mL) was refluxed for 24 h. *β*-Amino acid **16** (38 mg, 42%) was obtained as a pale brown solid: ^{1}H NMR (300 MHz, CD_3OD) δ 8.17 (d, J = 8.9 Hz, 2H),

7.62 (d, $J = 7.8$ Hz, 2H), 7.53 (t, $J = 7.2$ Hz, 2H), 7.40−7.30 (m, 10H), 7.07 (t, $J = 7.2$ Hz, 2H), 6.88 (d, $J = 8.2$ Hz, 4H), 5.25 (d, $J = 9.2$ Hz, 2H), 5.12 (d, $J = 9.2$ Hz, 2H), 4.91−4.84 (m, 2H), 4.62−4.51 (m, 2H), 3.00−2.88 (m, 4H), 2.70−2.57 (m, 2H), 1.86−1.76 (m, 2H); ^{13}C NMR (50 Hz, CD_3OD) δ 168.4, 159.2, 157.6, 134.6, 132.9, 131.0, 130.6, 130.1, 128.8, 124.7, 123.2, 122.4, 116.7, 116.4, 116.2, 80.6, 71.6, 64.5, 58.9, 30.9, 30.4; IR (KBr) ν_{max} 3425, 2933, 1735, 1587, 1495, 1231, 1118, 1057 cm^{-1}. Anal. Calcd for $C_{44}H_{44}N_2O_8Cl_2$: C, 66.08; H, 5.55; Cl, 8.87; N, 3.50. Found: C, 66.35; H, 5.28.

Synthesis of β-Amino acid 17: A suspension of β-lactam **12** (100 mg, 0.17 mmol) in 6 M HCl (15 mL) was refluxed for 24 h. β-Amino acid **17** (81 mg, 81%) was obtained as a pale pink solid: ^{1}H NMR (300 MHz, DMSO-d_6, 65 °C) δ 8.20−7.69 (m, 8H), 7.34 (t, $J = 7.2$ Hz, 2H), 7.18 (t, $J = 8.0$ Hz, 4H), 7.06−6.85 (m, 10H), 5.30 (d, $J = 7.8$ Hz, 2H), 5.09 (d, $J = 7.8$ Hz, 2H), 4.32 (d, $J = 8.1$ Hz, 2H), 4.19 (d, $J = 8.1$ Hz, 2H), 3.93 (d, $J = 16.0$ Hz, 2H), 3.51 (d, $J = 16.0$ Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6, 65 °C) δ 168.2, 156.4, 156.3, 130.5, 128.9, 128.7, 121.7, 120.4, 115.5, 111.7, 78.7, 77.7, 66.4, 53.8, 34.5; IR (KBr) ν_{max} 3421, 2927, 1728, 1589, 1496, 1220, 1122, 1064 cm^{-1}. Anal. Calcd for $C_{36}H_{36}N_2O_8Cl_2$: C, 62.16; H, 5.22; Cl, 10.19; N, 4.03. Found: C, 62.34; H, 4.96.

General Procedure for the Hydrolysis with LiOH/H_2O_2: In a round-bottom flask equipped with a magnetic stirring bar, a solution (or suspension) of the corresponding β-lactam in THF/H_2O (3:1) was cooled to 0 °C with an ice bath prior to the addition of H_2O_2 (30%). Then, LiOH·H_2O was added to the mixture at 0 °C. The system was left to reach room temperature, and the reaction was stirred until complete disappearance of the starting β-lactam (followed by TLC in $CHCl_3$/MeOH (1:1)). The reaction was quenched with a 1.5 M solution of Na_2SO_3. The crude mixture was extracted with CH_2Cl_2, and the aqueous layer was evaporated at reduced pressure. The solid obtained was purified by flash chromatography in $CHCl_3$/MeOH.

Reaction of β-Lactam 8 with LiOH/H_2O_2: Following the general procedure, from β-lactam **8** (250 mg, 0.44 mmol), 30% H_2O_2 (534 mg, 5.2 mmol), and LiOH·H_2O (80 mg, 1.6 mmol). After 6 h at room temperature, the reaction was quenched, extracted, and the residue purified by flash chromatography ($CHCl_3$/MeOH, 2:1) to yield 200 mg (74%) of β-amino acid **13** as a white powder.

Reaction of β-Lactam 9 with LiOH/H_2O_2: Following the general procedure, from β-lactam **9** (250 mg, 0.44 mmol), 30% H_2O_2 (534 mg, 5.2 mmol), and LiOH·H_2O (80 mg, 1.6 mmol). After 6 h at room temperature, the reaction was quenched, extracted, and the residue purified by flash chromatography ($CHCl_3$/MeOH, 2:1) to yield β-amino acid **14** (200 mg, 74%) as white powder.

Reaction of β-Lactam 10 with LiOH/H_2O_2: Following the general procedure, from a suspension of β-lactam **10** (250 mg, 0.42 mmol), 30% H_2O_2 (534 mg, 5.2 mmol), and LiOH·H_2O (80 mg, 1.6 mmol). After 6 h at room temperature, the reaction was quenched, extracted, and the residue purified by flash chromatography ($CHCl_3$/MeOH, 2:1) to yield β-amino acid **15** (200 mg, 75%) as a white powder.

General Procedure for the Synthesis of Azetidines (18−20): To a suspension of $LiAlH_4$ in dry THF in a flame-dried round-bottom flask equipped with a magnetic stirring bar under argon and at 0 °C was transferred a solution $AlCl_3$ in dry THF via cannula. The mixture was stirred for 30 min at room temperature to form the alane. Then, the suspension was cannulated over a solution of the β-lactam in dry THF at 0 °C. The reaction was stirred for 20 min at room temperature, then quenched with ice and extracted with diethyl ether (3 × 10 mL). The organic layer was washed with brine and dried with $MgSO_4$. The solvent was evaporated under reduced pressure to yield pure azetidines.

Synthesis of Azetidine 18: Following the general procedure from 20.2 mg (0.53 mmol) of $LiAlH_4$, 70 mg (0.53 mmol) of $AlCl_3$, and 50 mg (0.086 mmol) of β-lactam **8**. After 20 min of vigorous stirring, the reaction was quenched and extracted to afford 45 mg (95%) of azetidine **18** as brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.96 (dd, $J = 7.4$, 1.6 Hz, 2H), 7.19 (dt, $J = 8.0$, 1.6 Hz, 2H), 7.09 (t, $J = 7.6$ Hz, 4H), 7.00−6.87 (m, 4H), 6.77 (t, $J = 7.6$ Hz, 2H), 6.53 (dd, $J_1 = 8.1$ Hz, $J_2 = 0.9$ Hz, 4H), 4.71 (dt, $J_1 = 6.4$ Hz, $J_2 = 2.0$ Hz, 2H), 4.59 (d, $J = 8.0$ Hz, 2H), 4.45−4.36 (m, 4H), 3.66 (d, $J = 9.4$ Hz, 2H), 3.14 (dd, $J_1 = 9.4$ Hz, $J_2 = 6.4$ Hz, 2H), 2.66−2.54 (m, 2H), 2.43−2.33 (m, 2H), 1−14−1.01 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 157.4, 155.7, 133.3, 128.8, 128.1, 126.3, 120.4, 120.2, 114.8, 110.7, 70.4, 67.0, 62.0, 58.8, 56.4, 29.6; IR (KBr) ν_{max} 3031, 2922, 1598, 1587, 1487, 1452, 1222, 1109, 1055, 1026 cm^{-1}. Anal. Calcd for $C_{35}H_{36}N_2O_4$: C, 76.62; H, 6.61. Found: C, 76.75; H, 6.79.

Synthesis of Azetidine 19: Following the general procedure, from 16 mg (0.43 mmol) of $LiAlH_4$, 56 mg (0.43 mmol) of $AlCl_3$, and 40 mg (0.069 mmol) of β-lactam **9**. After 20 min of vigorous stirring, the reaction was quenched and extracted to afford 32 mg (95%) of azetidine **19** as brown oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (dd, $J = 7.6$, 1.6 Hz, 2H), 7.23−7.07 (m, 6H), 7.00−6.77 (m, 6H), 6.67 (d, $J = 8.1$ Hz, 2H), 5.44 (d, $J = 6.1$ Hz, 2H), 5.12 (dt, $J_1 = 6.1$ Hz, $J_2 = 3.0$ Hz, 2H), 4.48−4.40 (m, 4H), 3.75−3.64 (m, 4H), 2.79−2.58 (m, 4H), 1.26−1.18 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 154.4, 132.1, 128.9, 128.1, 120.5, 120.3, 120.1, 114.8, 110.4, 70.6, 64.4, 62.4, 59.0, 53.2, 29.6; IR (KBr) ν_{max} 3032, 2922, 1598, 1586, 1485, 1452, 1223, 1110, 1054, 1026 cm^{-1}. Anal. Calcd for $C_{35}H_{36}N_2O_4$: C, 76.62; H, 6.61. Found: C, 76.80; H, 6.34.

Synthesis of Azetidine 20: Following the general procedure from 40 mg (1.02 mmol) of $LiAlH_4$, 136 mg (1.02 mmol) of $AlCl_3$, and 100 mg (0.17 mmol) of β-lactam **12**. After 20 min of vigorous stirring, the reaction was quenched and extracted to afford 260 mg (93%) of azetidine **20** as brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.81 (d, $J = 6.8$ Hz, 2H), 7.31−7.22 (m, 2H), 7.11−7.04 (m, 6H), 6.81−6.76 (m, 4H), 6.61 (d, $J = 7.9$ Hz, 4H), 5.44 (d, $J = 5.6$ Hz, 2H), 4.91 (t, $J = 5.4$ Hz, 2H), 4.34−4.22 (m, 4H), 3.79−3.71 (m, 2H), 3.61 (d, $J = 5.4$ Hz, 4H), 3.36 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 157.4, 156.0, 129.2, 128.8, 128.2, 125.1, 120.7, 120.5, 115.2, 109.7, 79.5, 71.8, 66.0, 62.2, 53.4, 41.7; IR (KBr) ν_{max} 3028, 2929, 1598, 1589, 1487, 1452, 1257, 1230, 1099, 1072 cm^{-1}. Anal. Calcd for $C_{36}H_{34}N_2O_4$: C, 71.40; H, 6.13. Found: C, 71.48; H, 6.17.

General Procedure for the Reactions with Li/NH_3: In a three-neck round-bottom flask equipped with an NH_3 condenser and magnetic stirring bar at −78 °C, Na was introduced, and a NH_3 (gas) was injected in the system until 10−20 mL of liquid NH_3 condensed over the Na (the solution turns dark blue). Then, a solution of the β-lactam in dry THF/^{t}BuOH was added dropwise via syringe. The mixture was stirred for 5−10 min and quenched with solid NH_4Cl until complete disappearance of the blue color. The crude mixture was kept at room temperature until the NH_3 was evaporated. Then, water was added, and the solution was extracted with CH_2Cl_2. The organic layer was washed with water and brine, dried over $MgSO_4$, filtered, and the solvent evaporated at reduced pressure. The crude products were purified by flash chromatography in hexane/AcOEt (6:4).

Reaction of β-Lactam 8 with Li/NH_3: About 20 mL of NH_3 was condensed over 10 mg of Na (1.2 mmol). A solution of β-lactam **8** (65 mg, 0.12 mmol) in dry THF (5 mL) with a few drops of ^{t}BuOH was added dropwise to the solution. After 10 min stirring, the reaction was quenched, extracted, and the crude product purified by flash chromatography to yield 40 mg (83%) of macrocycle **21** as pale brown oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.20−7.14 (m, 4H), 6.90 (t, $J = 6.2$ Hz, 4H), 5.84 (br s, 2H), 4.38 (s, 4H), 3.22 (dd, $J = 6$, 11.3 Hz, 4H), 2.96 (t, $J = 7.5$ Hz, 4H), 2.44 (t, $J = 7.5$ Hz, 4H), 1.60−1.52 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.9, 156.2, 130.1, 129.3, 127.5, 121.0, 111.3, 66.6, 38.4, 36.6, 29.6, 26.5; IR (KBr) ν_{max} 3300, 2923, 1751,1647, 1598, 1550, 1490, 1238, 1132, 1058 cm^{-1}. Anal. Calcd for $C_{23}H_{28}N_2O_4$: C, 69.67; H, 7.12; N, 7.07. Found: C, 69.95; H, 7.28.

Reaction of β-Lactam 10 with Li/NH_3: About 50 mL of NH_3 was condensed over 20 mg of Na (2.4 mmol). β-Lactam **10** (100 mg, 0.17 mmol) was added over the NH_3 solution with a few drops of ^{t}BuOH. After 10 min stirring, the reaction was quenched, extracted, and the crude purified by flash chromatography to yield 70 mg (88%) of macrocycle **22** as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18−7.14 (m, 4H), 6.89 (d, J = 7.8 Hz, 2H), 6.79 (dt, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 2H), 4.27 (t, J = 5.7 Hz, 4H), 4.06 (br s, 2H), 2.98−2.92 (m, 4H), 2.90−2.83 (m, 4H), 2.37 (q, J = 6.0 Hz, 2H) 2.07−2.02 (m, 4H), 1.35−1.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 156.3, 131.4, 128.7, 127.8, 120.1, 110.6, 62.6, 38.2, 36.8, 29.6, 28.1, 26.1; IR (KBr) ν_{max} 3298, 2925, 1753, 1650, 1596, 1548, 1490, 1236, 1128, 1055 cm^{-1}. Anal. Calcd for $C_{24}H_{30}N_2O_4$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.08; H, 7.64.

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Supporting Information Available: Full experimental and characterization data for imines **4**−**7**, data for the X-ray characterization of compounds **8** and **12·Co$_2$(CO)$_6$**, and copies of ^{1}H and ^{13}C NMR spectra of compounds **4**−**22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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