Myxochelins B, C, D, E and F: A New Structural Principle for Powerful Siderophores Imitating Nature☆

Horst-Dieter Ambrosi[a], Vera Hartmann[b], Daniel Pistorius[b], Rolf Reissbrodt[c] and Wolfram Trowitzsch-Kienast*[b]

AnalytiCon AG[a],
Gustav-Meyer-Allee 25, D-13355 Berlin, Germany.

Technische Fachhochschule Berlin, Fachbereich 3, Chemie- und Biotechnik[b],
Luxemburgerstr. 10, D-13353 Berlin, Germany
Fax: (internat.) + 49-30/4505-2014,
E-mail: kienast@tfh-berlin.de

Robert-Koch-Institut, Experimental Bacteriology[c],
Burgstr. 37, D-38855 Wernigerode, Germany

Received February 14, 1997

Keywords: Siderophores / DHB ligands / Chiral recognition / Mycobacteria / Antivirals

The synthesis of the natural siderophore myxochelin B (**1**$_S$) and its enantiomer **1**$_R$ is described. **1**$_S$ and **1**$_R$ served as precursors for the synthesis of new *hexa*dentate siderophores, the myxochelins C (**7**$_S$) and C$_R$ (**7**$_R$), D (**14**$_S$) and D$_R$ (**14**$_R$), E (**19**$_S$) and (*RS*)-F (**26**$_{R,S}$), with 2,3-dihydroxybenzoate (DHB) ligands and the simple backbones of asymmetric 1,2,*n*-triamino-*n*-alkanes. For the myxochelins C, D, E and F *n* is 6 (from lysine), 5 (from ornithin), 4 (from asparagine amide) and 7 [from (±)-2-aminopimelic acid], respectively. The additional amino functions in the starting compounds were provided by dehydration of the corresponding primary amides, and subsequent reduction of the nitriles by cobalt boride in methanol. All new siderophores supply bacteria with ferric ions with an efficiency which depends on their chain length and stereochemistry. They show significant activity against the cytomegalo virus.

Compounds which are able to supply microorganisms or plants with the ferric ions which are essential are designated as siderophores. They are produced by plants and most of the microorganisms living in the soil, as well as being produced in higher animals, e.g. enterobacteria[1]. These siderophores are applied to the medical treatment of patients who suffer from an excess of iron: e.g. thalassemiae. They are also in use as, and are discussed as being, antiviral and antiparasitic agents. When fed to the hosts the parasites are no longer able to acquire the ferric ions necessary for their survival. Due to the similar ionic radii of ferric and aluminium ions, the siderophores have been postulated as active agents in the prevention of Alzheimer's desease, due to their ability to interfere with the transport of aluminium ions into the brain[2]. The suppression of the immuno response, as well as some influence on the radical processes during the Fenton's reaction observed at inflammatory processes[1], have also been discussed.

In the course of a screening program with myxobacteria we isolated (in addition to the saframycin Mx 1 produced by the myxobacteria strain *Myxococcus xanthus Mx x48*) the *tetradentate* 2,3-dihydroxybenzoyl (DHB) siderophore myxochelin B (**1**$_S$)[3], which has a 1,2,6-triaminohexane skeleton in which the N^2 and N^6 positions are amidated with DHB groups.

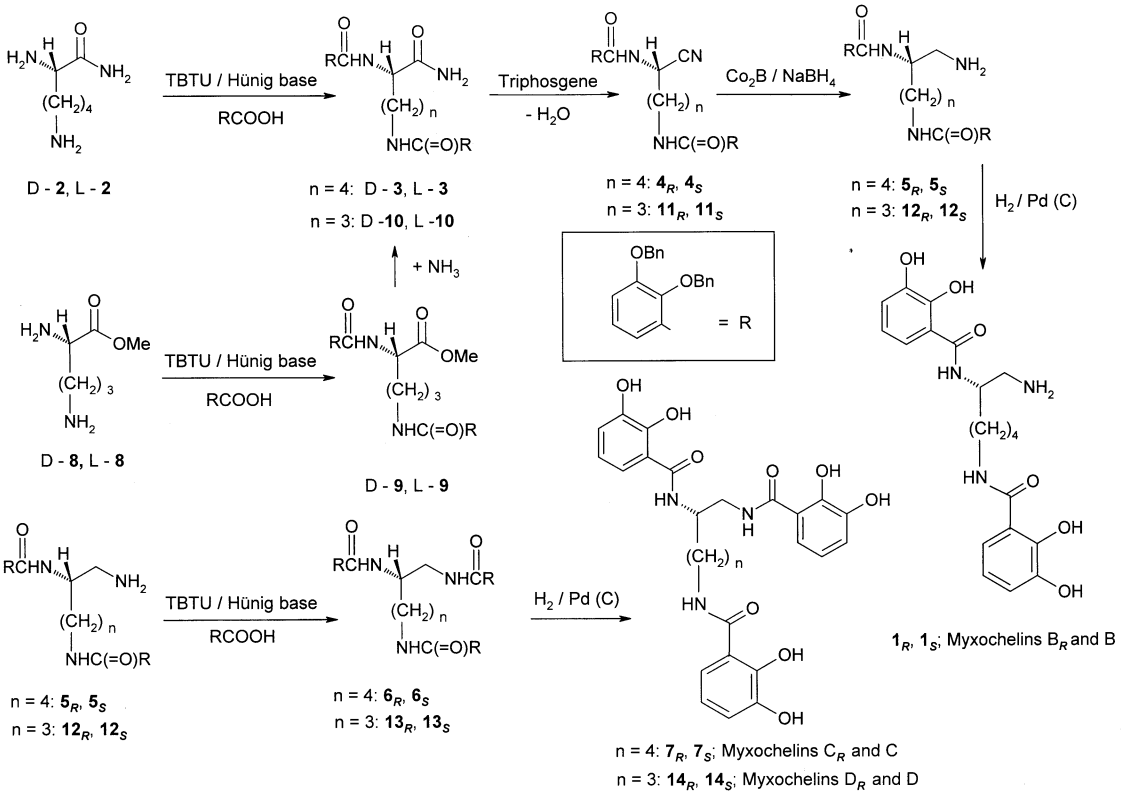
The Synthesis of Myxochelins B, B$_R$,C and C$_R$

The initial steps for the total synthesis of myxochelin B from L-lysinamide [(+)-L-**2**] are shown in Scheme 1, in which all compounds are presented in their *S* configuration. Condensation of lysine (+)-L-**2** with two equiv. of the benzyl-protected 2,3-dihydroxybenzoic acid (2,3-bis-*O*-Bn-DHBA)[4], and employing TBTU and Hünig's base, yielded (−)-L-**3**. Treatment of (−)-**3** with triphosgene eliminated one molecule of water, so yielding the nitrile (−)-**4**$_S$. Nitrile (−)-**4** could selectively be reduced to the amine (−)-**5**$_S$ by a mixture of sodium tetrahydridoborate/cobalt boride (from $CoCl_2$ and $NaBH_4$)[5]. The amine **5**$_S$ was deprotected to yield the myxochelin B (**1**$_S$) with $[\alpha]_d^{20} = -8.5$, $c = 0.6$ in 6 N HCl. Starting with the enantiomer D-**2** ($[\alpha]_D = -17.5$) the same sequence of reactions delivered (+)-**1**$_R$ with $[\alpha]_D = +8.0$ ($c = 1.0$, 6 N HCl). Natural **1** had $[\alpha]_D^{20} = -10$[6] ($c = 1$, 6 N HCl) as the mixed phosphate salt and hence exhibits the *S* configuration.

With the tetra-*O*-benzyl-protected amine (−)-**5**$_S$ we had a compound to hand which could be transformed into a variety of derivatives, among them the most active siderophore [(+)-**7**$_S$], equipped with a third DHB group as a *hexa*dentate siderophore. We named **7**$_S$ because of its relationship to the natural compound myxochelin C. The amidation of (−)-**5**$_S$ with 2,3-bis-*O*-Bn-DHBA succeeded, with good yields, by using either the DCC/HOBT or the TBTU/Hünig's base method [TBTU = *O*-(benzotriazol-1-yl)-*N,N,N′,N′*-tetramethyluronium tetrafluoroborate] to give the hexabenzyl-protected triamide (+)-**6**$_S$, from which myxochelin C, (+)-**7**$_S$, was liberated by dehydrogenation. As it is well known[7] that bacteria synthesize transport proteins for the process of active transport through the bac-

  1434−193X/98/0303−0541 $ 17.50+.50/0

Scheme 1. The syntheses of myxochelins B, B_R, C, C_R, D and D_R



terial membrane we were interested in whether or not certain bacteria use both forms of the stereoisomers; therefore we also synthesized the isomer (−)-7_R, myxochelin C_R.

Dehydrogenation of Z-D-Lys-(Z)-NH_2 yielded D-**2**, from which the synthesis of myxochelin C_R, following the same reaction path, succeeded as smoothly as for the *S* isomer.

The Synthesis of Myxochelins D, D_R, E and F

In order to investigate the effects of the carbon-chain length (between C-2 and C-*n*) on biological activity, we synthesized homologs with shorter chains (three and two $-CH_2-$ groups) and one possessing five CH_2 groups. The synthesis of myxochelins D started with H-L-Orn-OMe [(+)-L-**8**], and with its D isomer (−)-D-**8**. (+)-L-**8** was first condensed with two equiv. of the benzyl-protected 2,3-dihydroxybenzoic acid to give the diamide (−)-**9**. Attack on (−)-L-**9** by ammonia led to the primary amide (−)-L-**10**. Dehydration of (−)-**10** yielded the nitrile (−)-11_S which was reduced to the amine (−)-12_S. The second coupling reaction with the protected DHB acid resulted in the fully protected myxochelin D, (+)-13_S. Without any optimization of the six reaction steps, deprotection gave, in moderate overall yield (28%), the myxochelin D, (+)-14_S. When starting with the optical enantiomer (−)-D-**8**, we could isolate the myxochelin D_R, (−)-14_R in almost the same yield.

H-L-Asn-NH_2 was used as the starting material for the synthesis of the shortest possible chiral homolog in this series, myxochelin E. First the free amino function was amidated with 2,3-bis-*O*-Bn-DHBA to give the primary diamide (+)-L-**15**, followed by dehydration of both amide groups to the dinitrile (−)-16_S. No side reaction was observed on the reduction to diamine 17_S in methanol. Cyclization took place when aprotic solvents were used to reduce dinitriles of similar chain length[8]. The amidation to triamide (−)-18_S led, after dehydrogenation, to the desired target molecule (−)-19_S.

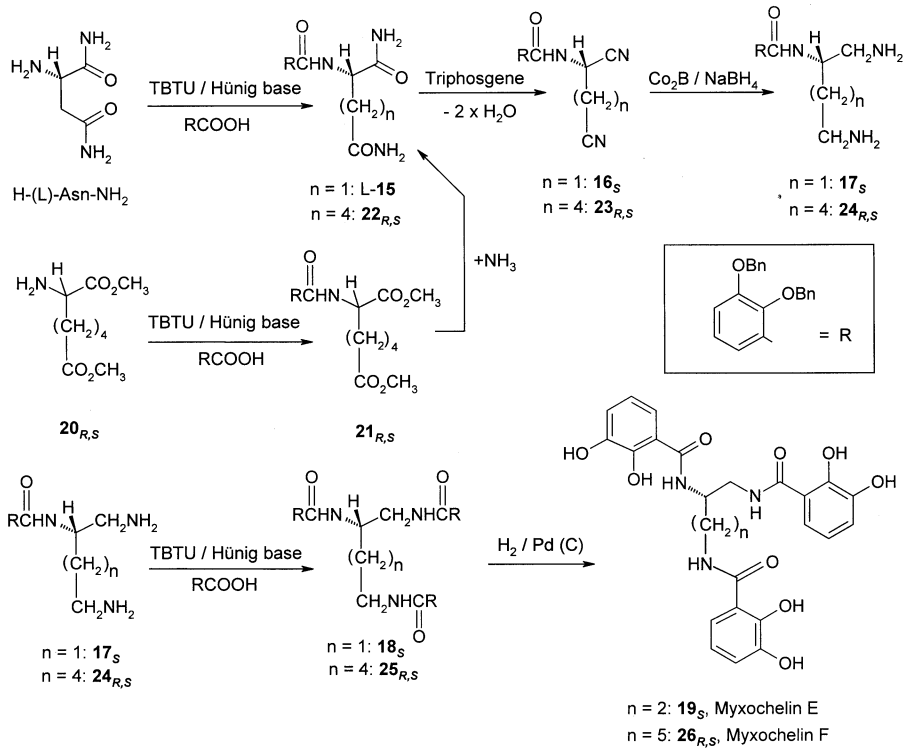
A similar reaction sequence led to the racemic homolog with five CH_2 groups, myxochelin F, starting with racemic 2-aminopimelic acid. The first 2,3-bis-*O*-Bn-DHBA group was introduced after esterification of $20_{R,S}$ to yield $21_{R,S}$. The following steps were as described for myxochelin E. The diamide $22_{R,S}$ was followed by the dinitrile $23_{R,S}$, and reduction furnished the diamine $24_{R,S}$. This was then transformed into the hexa-*O*-Bn-protected amide $25_{R,S}$, which, after dehydrogenation to $26_{R,S}$ generated myxochelin F.

Encouraged by the unexpectedly strong efficiency of myxochelin B_R as a siderophore for *mycobacteria* we looked for another tetradentate cheline with higher lipophilicity, and chose the nitriles of myxochelins D and D_R (27_S and 27_R), which could be easily obtained by dehydrogenation of the corresponding tetra-*O*-benzyl-protected compounds.

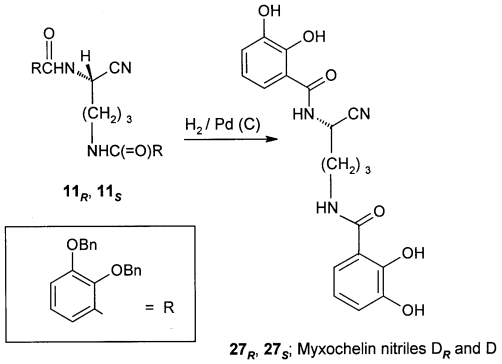
The reaction time was reduced to 30 min, to minimize the possibility of excessive reduction by attack of the nitrile function. This was assured by TLC monitoring and the ninhydrin reaction test.

The structures of all compounds were investigated by MS, IR-, ^{1}H- and ^{13}C-NMR spectroscopy (see Experimental Section). For the homolog derivatives the optical ro-

Scheme 2. The syntheses of myxochelins E and F



Scheme 3. The syntheses of the myxochelin-nitriles of D and D_R



tation values increase the shorter the carbon chains are, which may produce stronger chirally disturbed chromophores. TLC shows a decrease in the R_f values with shorter carbon chains, which points to an increase in polarity.

Biological Activity

The efficiency of all compounds to supply bacteria with ferric ions (enterobacteria, morganella and mycobacteria were all tested) is summarized in Tables 1−4. The indicator strains were grown on agar plates in a medium which was deficient in ferric ions, i.e. the ferric ions were held in bipyridyl complexes, which can not pass the bacterial membranes and hence are useless for the microorganisms tested. Paper discs moistened with the siderophore solution were added on top of the agar plates. Growth zones around the discs, which correspond to the efficiencies of the compounds, were measured in mm and show logarithmical relationships as described by Reissbrodt et al.[9].

In general, the observed responses of the various bacteria to the chain lengths and to the stereochemistry of the siderophores differ quite widely. Table 1 summarizes the effects of the enantiomeric myxochelins C on enterobacteria.

That they strongly react to different stereochemistry is best illustrated by *S. typhimurium* TA 2700 and *P. aeruginosa* 6609, which only can be fed with the *S* isomers. This behavior could be used to probe the stereochemical purity of our compounds, which were not otherwise checked. The *E. coli* strain IR 112 can use only the *R* isomer of myxochelin C. To some extent this stereodifferentiation was also observed for the series of *mycobacteria* tested (see Table 2.)

Table 3 documents the finding that *S. thyphimurium* is less efficiently fed with ferric ions by siderophores with shorter chains, while Table 4 shows that the reverse case holds for *mycobacteria*, where we observed a 27-mm growth-zone for myxochelin E. The same table also documents the large growth zone for the tetradentate $\mathbf{1}_R$. Except for $\mathbf{19}_S$, all chelines efficiently supply *Morganella morganii*, with the best values obtained for the tetradentate nitriles **27.**

It should be mentioned that our new myxochelins are also quite active as antiviral agents in the cytomegalo system.[10]

Is Myxochelin C also a Secondary Metabolite?

Myxochelin B ($\mathbf{1}_S$) was purified as a cationic species (CM-Sephadex) in the course of the isolation of the antitumor-active saframycins Mx 1 and Mx 2[11] from *Myxo-*

Table 1. Cross-feeding tests of myxochelins 7_S and 7_R (5 µg siderophore/disc, growth zones in mm)

myxochelin	*S.typhimurium* enb-7	*S.typhimurium* TA2700	*S.stanleyville* 207/81	*E.coli* AB2847	*E.coli* IR 112	*E.coli* LG1522	*K.pneumoniae* KN4401	*Y.enterocolitica* H5030	*P.aeruginosa* 6609
iron related marker	ent class II	ent class I	wild	aroB	tonB	fepA iuc	ent iuc	aroA	pvd
7_S	32	33	-	30	-	(+)	33	16	34
7_R	25	-	-	13	20	-	25	-	-

Table 2. Cross-feeding tests of myxochelins 7_S and 7_R – *Mycobacteria spp.* (5 µg/disc, growth zones in mm)

myxochelin	*M. smegmatis 987*	*M. smegmatis mutant 10*	*M. fortuitum*	*M. chelonae*
7_S	23	13	27	25
7_R	15	0	17	12

Table 3. Cross-feeding tests of myxochelin homologs and nitriles (5 µg/disc, growth zones in mm)

myxochelin	*S. typhimurium* enb-7	*S. typhimurium* SR 1001	*S. enteritidis* P 125109	*S. stanleyville* 207/81 75µM[a]	*S. stanleyville* 207/81 200 µM[a]	*E. coli* AB2847
1	22	0	n.d.	n.d.	n.d.	n.d.
$\mathbf{14}_S$	18	0	14	22	0	0
$\mathbf{14}_R$	17	0	15w	19	0	0
$\mathbf{19}_S$	15	0	14w	n.d.	n.d.	0
$\mathbf{26}_{R,S}$	0	0	n.d.	n.d.	n.d.	n.d.
$\mathbf{27}_S$	8	0	n.d.	n.d.	n.d.	n.d.
$\mathbf{27}_R$	12	0	n.d.	n.d.	n.d.	n.d.

[a] Checked in VB medium with 75 µM bipyridyl (medium iron-limited) and 200 µM bipyridyl ("high-affinity" iron limitation); w: faint growth zone.

Table 4. Cross-feeding tests of myxochelin homologs and nitriles (5 µg/disc, growth zones in mm)

myxochelin	*Y. enterocolitica* H5030	*M. morganii* SBK 3	*P. aeruginosa* PAO 6609	*M. smegmatis* SG 987
$\mathbf{1}_S$	0	24	14	8
$\mathbf{1}_R$	19	34	20	22
$\mathbf{14}_S$	21	30	0	18/23[b]
$\mathbf{14}_R$	20	18	0	20/23[b]
$\mathbf{19}_S$	8	0	0	22/27[b]
$\mathbf{26}_{R,S}$	18	32	17	20
$\mathbf{27}_S$	13	35	19	20
$\mathbf{27}_R$	17	38	27	20

[b] Read after 24 h at 37°C as usual and after further 3 days at room temperature.

coccus xanthus Mx x48. Myxochelin C, which can also be found as a natural product, is, apart from the third DHB group, identical to $\mathbf{1}_S$, but lacks its basic properties. Cochromatography on TLC of a freshly prepared XAD extract of *Myxococcus xanthus* Mx x48 with myxochelins C and B delivered, after spraying with ferric chloride solution, only one blue spot, identical to that of the ferric complex of $\mathbf{1}_S$.

Further studies regarding the structures of the metal complexes by NMR, MS and Mößbauer experiments, as well as computational studies of possible structures[12], are in progress and will be published elsewhere. The capabilities of the best of our siderophores to be used as growth factors for certain bacteria, especially for *mycobacteria*, are also under study. Some of our new compounds now are tested as "Trojan horses" to smuggle antibiotics into *mycobacteria* and others species.

Financial support of this work by the *Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie* (WIP program, H.-D. A.) and by the research commission of the *Polytechnical Highschool Berlin* (W. T.-K.) is gratefully acknowledged, as is the research-dependent, part-time exemption from teaching. Mrs. *G. Cramer* was of great help as a technical assistant and Mrs. *R. Dambowski* managed the elemental analysis; both are from the WIP group of Dr. *Ambrosi*. Dr. *V. Wray*, GBF Braunschweig, took the first NMR spectra of myxochelin C. The NMR and MS spectra were provided by the staff of the Institute of Angewandte Chemie (ACA) Berlin-Adlershof, in particular Drs. *B. Costisella* and *Bartoszek*. Dr. *H. Irschik*, GBF Braunschweig, provided the fermentation extract of *Myxococcus xanthus* Mx x48. We are very grateful to all these people who were involved.

Experimental Section

TLC: Silica 60 F_{254} on alumina foil, 0.2 mm thickness (Merck), detection at λ = 254 nm. – Flash chromatography: Silica-gel column, dimension d = 30 mm, l = 400, V = 280 cm^3, p = 250 kPa, special eluents are given in the text. – Optical rotation: Perkin-Elmer-241 Polarimeter, solvents are given. – ^{1}H- and ^{13}C-NMR spectra: Varian Gemini 300, or the Varian UNITYplus-300 or -500 with tetramethylsilane as the inner standard. – Mass spectra: GC/MS-System HP 5985 in the FAB, ESI and CI mode. – IR spectra: Specord 75 (Carl Zeiss, Jena). – Elemental analysis: C,H,N: Elementar-Analyser-mod 1106 (Carlo Erba); Cl: gravimetrically.

Synthesis of Myxochelins B, B_R, C and C_R

(–)-2,3-Dibenzyloxybenzoyl-L-Lys(2,3-dibenzyloxybenzoyl)-NH_2 [(–)-L-**3**]: 3.06 g (9.15 mmol) of 2,3-dibenzyloxybenzoic acid, prepared according to the literature[4], and 2.77 g (20.5 mmol) of HOBt were dissolved in 10 ml of dry dimethylformamide (DMF) and kept at 0°C. After the addition of 0.95 g (4.6 mmol) of DCC the solution was stirred for 1 h while cooled with ice, and then for an additional 1 h at room temp. A suspension of 0.5 g (2.3 mmol) of L-lysinamide hydrochloride (Bachem, Swiss), dissolved in 3 ml of THF and 1 ml of triethylamine, was added to this solution, and the stirring continued for 12 h. The DMF was evaporated in vacuo and 15 ml of ethyl acetate added. The organic layer was washed with a 1 M $NaHCO_3$ aqueous solution, acetic acid (1%) and again

with 1 M $NaHCO_3$. After drying with sodium sulfate, the organic layer was concentrated in vacuo yielding 1.63 g of raw material. Flash chromatography on silica gel dichloromethane/methanol (1.5%) furnished 1.01 g (57%) of (−)-L-**3** (TLC: R_f = 0.60, ethyl acetate) with m.p. 120°C. On TLC (−)-**3** reacts with ninhydrin only after heating to give a typical brownish spot, while the starting material gives rise to a purple spot without heating. − $[\alpha]_D^{25}$ = −1.1 (*c* = 0.45, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3371 cm^{-1} (NH), 3032 (arom. CH), 2930 (aliph. CH), 1651 (amide-I), 1526 (amide-II). − ^1H NMR (300 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 7.4 Hz, 1 H, N^2−H), 7.90 (t, *J* = 5.4 Hz, 1 H, N^6−H), 7.67 (m, 4 H, 2 × benzoyl-4-H and 2 × benzoyl-6-H), 7.30 (m, 20 H, arom. H), 7.15 (m, 2 H, 2 × benzoyl-5-H), 6.37 (s, 1 H, prim. amide-H_a), 5.30 (s, 1 H, prim. amide-H_b), 5.16 (m, 8 H, O−CH_2−phe), 4.42 (dd, J_1 = 7.5 Hz, J_2 = 7.6 Hz, 1 H, 2-H), 3.16 (dd, J_1 = 6.6 Hz, J_2 = 5.4 Hz, 2 H, 6-CH_2−), 1.74 (m, 1 H, 3-CH_a−), 1.34 (m, 2 H, 4-CH_2−), 1.21 (m, 3 H, 3-CH_b−, 5-CH_2−). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 22.8 (t, C-4), 28.7 (t, C-3), 30.6 (t, C-5), 39.0 (t, C-6), 53.0 (d, C-2), 71.2, 71.3, 76.2, 76.3 (t, O−CH_2−phe), 116.9, 117.4 (d, arom. =CH−), 123.0, 123.3 (d, arom. =CH−), 124.4, 124.4 (d, arom. =CH−), 126.7, 127.3 (s, quat. arom. C); 127.7−128.9 (d, 20 × arom. =*C*H−), 136.2, 136.4 (s, quat. arom. C), 146.8, 146.9 (s, quat. arom. =*C*−O−), 151.7, 151.7 (s, quat. arom. =*C*−O), 165.0, 165.6 (s, sec. amide−*C*=O), 173.7 (s, prim. amide−*C*=O). − $C_{48}H_{47}N_3O_7$ (777.3): calcd. C 74.16, H 6.10 , N 5.41; found C 73.98, H 5.99, N 4.34.

(−)-(2S)-2,6-Bis[(2,3-dibenzyloxybenzoyl)amino]hexanenitrile [(−)-$\mathbf{4}_S$]: 1.85 g (2.38 mmol) of (−)-**3** was dissolved in 30 ml of dichloromethane and 0.57 ml (7.14 mmol) of pyridine added. After stirring for 5 min, 352 mg (1.18 mmol) of triphosgene was added carefully under a hood and the stirring continued for 30 min. The solvents were then evaporated in vacuo and the resulting oil was dissolved in CH_2Cl_2, which was extracted with dil. HCl and then with water. The organic layer was concentrated in vacuo. From this crude material, 1.39 g (77%) of (−)-**4** (TLC on silica gel, ethyl acetate, R_f = 0.65) was isolated using flash chromatography on silica gel[dichloromethane/methanol (1.5%) as the solvent]. In addition 0.3 g (16%) of the unreacted (−)-**3** (TLC, ethyl acetate, R_f = 0.60) was recovered. − $[\alpha]_D^{20}$ = −19 (*c* = 1, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3367 cm^{-1} (NH), 3031 (arom. CH), 2927 (CH), 2230 (CN), 1661 (amide-I), 1520 (amide-II). − ^1H NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 7.9, 1 H, N^2−H), 7.91 (t, *J* = 5.4 Hz, 1 H, N^6−H), 7.75−7.10 (m, 26 H, arom. =C*H*−), 5.20−5.0 (m, 8 H, 4 × −O−CH_2−phe), 4.78 (dd, J_1 = 7.4 Hz, J_2 = 5.2 Hz, 1 H, 2-H), 3.15 (q, *J* = 6.7 Hz, 2 H, 6-CH_2−), 1.35 (m, 2 H, 3-CH_2−), 1.18 (m, 4 H, 4-, 5-CH_2−). − ^{13}C NMR (75.4, $CDCl_3$): δ = 22.7 (t, C-4), 28.4 (t, C-5), 32.1 (t, C-3), 39.0 (t, C-6), 40.3 (d, C-2), 71.3, 71.4, 76.4, 76.6 (t, O−*C*H_2−phe), 117.0, 117.9 (d, arom. =*C*H−), 118.4 (s, −*C*N), 123.3, 123.5, 124.4, 124.5 (d, arom. =*C*H−), 125.3, 127.1 (s, quat. arom. C), 127.6, 127.7, 128.4, 128.7, 128.8, 129.0 (d, 20 × arom. =*C*H−), 135.9, 135.9, 136.2, 136.4 (s, quat. arom. C), 141.1, 146.8 (s, quat. arom. =*C*−O−), 151.6, 151.7 (s, quat. arom. =*C*−O−), 164.5, 165.0 (s, sec. amide-*C*=O). − $C_{48}H_{45}N_3O_6$ (759.9): calcd. C 75.87, H 5.97, N 5.53; found C 75.18, H 5.63, N 5.36.

(−)-(2S)-2,6-Bis[(2,3-dibenzyloxybenzoyl)amino]-1-aminohexane [(−)-$\mathbf{5}_S$]: 670 mg (0.88 mmol) of (−)-**4** was dissolved in 10 ml of THF and 40 ml of methanol. 114 mg (0.88 mmol) of Co_2B, which was prepared from 260 mg of $CoCl_2$ and 190 mg of $NaBH_4$ using the protocol of Heinzman and Ganem[5], was added, with an additional 333 mg (8.8 mmol) of $NaBH_4$. The reaction mixture was stirred for 12 h. To destroy the Co−B complex, 60 ml of 5% hydrochloric acid was added (pH = 1.5−2.5) and the resulting rose-red solution kept at pH = 12 by the addition of ammonia. Chloroform was used for extraction. The end point of the extraction was determined by spraying a TLC spot with ninhydrin. The extract was dried with sodium sulfate and concentrated in vacuo. 320 mg (48%) of a highly viscous oil was isolated after flash chromatography on silica gel with chloroform/methanol (10%). − $[\alpha]_D^{20}$ = −24 (*c* = 1, chloroform). − ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 9.1 Hz, 1 H, N^2−H), 7.81 (t, *J* = 5.5 Hz, 1 H, N^6−H), 7.61−7.02 (m, 26 H, arom. =C*H*−), 5.11−4.99 (m, 8 H, 4 × −O−CH_2−phe), 3.87 (br., m, 1 H, 2-H), 3.10 (quint, *J* = 5.2 Hz, 2 H, 6-CH_2−), 2.60 (m, 1 H, 1-CH_a−), 2.39 (m, 1 H, 1-CH_b−), 1.90 (br., 2 H, N^1−H_2), 1.10−0.98 (m, 6 H, 3-, 4-, 5-CH_2−). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 23.3 (t, C-4), 29.1 (t, C-5), 31.7 (t, C-3), 39.3, 39.3 (t, C-1, C-6), 45.7 (d, C-2), 71.2, 71.3 (t, −O−*C*H_2−phe), 76.1, 76.3 (t, −O−*C*H_2−phe), 116.8, 117.0, 123.2, 123.3, 124.3, 124.4 (all d, arom. =*C*H−), 127.4, 127.6 (s, quat. arom. *C*), 127.6, 128.2, 128.4, 128.6, 128.7, (all d, 20 × arom. =*C*H−), 136.3, 136.35, 136.4, 136.5 (s, quat. arom. *C*), 146.7, 146.8 (s, quat. arom. =*C*−O), 151.5, 151.6 (s, quat. arom. =*C*−O), 165.0, 165.4 (s, sec. amide−*C*=O). − $C_{48}H_{49}N_3O_6$ (763.9): calcd. C 75.47, H 6.46, N 5.50; found C 75.35, H 6.42, N 5.24.

(−)-(2S)-2,6-Bis[(2,3-dihydroxybenzoyl)amino]-1-aminohexane [(−)-$\mathbf{1}_S$, Myxochelin B]: 43 mg (0.056 mmol) of (−)-**5** was dissolved in 10 ml of methanol and, after addition of 30 mg of Pd/C (5%), dehydrogenated for 6 h at room temp. and normal pressure. After that time, no starting material was observable by TLC (1-butanol/acetic acid/water = 4:1:1) but, by spraying with a 1% methanolic ferric chloride solution, a deep blue spot appeared immediately at R_f = 0.3. Purification of (−)-**1** was achieved by filtration of the solution through Kieselgur and evaporation of the solvent in vacuo resulting in 22 mg of (−)-$\mathbf{1}_S$ (100%). − $[\alpha]_D^{20}$ = −8.5 (*c* = 0.5, 6 N HCl), natural myxochelin B (as a mixed phosphate salt) had $[\alpha]_D^{20}$ = −10[6] (*c* = 1, 6 N HCl). − $C_{20}H_{25}N_3O_6$ (403.44): calcd. C 59.54, H 6.25, N 10.41; found C 59.19, H 6.20, N 9.81. − All the spectroscopic properties of (−)-**1** were identical with those of natural myxochelin B: ^1H NMR (300 MHz, [D_6]DMSO): δ = 7.33 (dd, J_1 = 1.5 Hz, J_2 = 8.1 Hz, 1 H, benzoyl-6-H), 7.19 (dd, J_1 = 1.5 Hz, J_2 = 8.1 Hz, 1 H, benzoyl-6-H), 6.98 (dd, J_1 = 1.5 Hz, J_2 = 7.8 Hz, 1 H, benzoyl-4-H), 6.95 (dd, J_1 = 1.5 Hz, J_2 = 7.8 Hz, 1 H, benzoyl-4-H), 6.76 (t, *J* = 8.0 Hz, 1 H, benzoyl-5-H), 6.72 (t, *J* = 8.0 Hz, 1 H, benzoyl-5-H), 4.41 (m, 1 H, 2-H), 3.22 (dd, J_1 = 3.9 Hz, J_2 = 13.0 Hz, 1 H, 1-H_a), 3.07 (dd, J_1 = 9.8 Hz, J_2 = 13.0 Hz, 1 H, 1-H_b), 3.43 (t, *J* = 6.8 Hz, 2 H, 6-H_2), 1.77 (t, *J* = 9.0 Hz, 2 H, 5-H_2), 1.7 (m, 2 H, 3-H_2), 1.56 (m, 2 H, 4-H_2). − ^{13}C NMR (75.9 MHz, [D_6]DMSO): δ = 22.9 (t, C-4), 28.7 (t, C-5), 31.3 (t, C-3), 38.6 (t, C-6), 44.0 (t, C-1), 48.7 (d, C-2), 115.7 (s, benzoyl-C-1), 115.7 (s, benzoyl-C-1), 153.6 (s, benzoyl-C-2), 151.6 (s, benzoyl-C-2), 147.6 (s, benzoyl-C-3), 147.0 (s, benzoyl-C-3), 118.4 (d, benzoyl-C-4), 117.8 (d, benzoyl-C-4), 117.2 (d, benzoyl-C-5), 116.0 (d, benzoyl-C-5), 115.8 (d, benzoyl-C-6), 114.1 (d, benzoyl-C-6), 169.3 (s, sec. amide-*C*=O), 169.9 (s, sec. amide-*C*=O). − (+)-FAB MS: *m/z* (%) = 404 [M + H^+]$^+$ (100).

(+)-(2S)-1,2,6-Tris[(2,3-dibenzyloxybenzoyl)amino]hexane [(+)-$\mathbf{6}_S$]: 800 mg (ca. 1 mmol) of (−)-**5** was dissolved in 50 ml of dichloromethane. 338 mg (1mmol) of TBTU, 352 mg (1 mmol) of 2,3-dibenzyloxybenzoic acid and 0.366 ml (2 mmol) of Hünig base were added. After stirring for 72 h, the solution was diluted with further 50 ml of dichloromethane, followed by extraction of the organic layer with 5% hydrochloric acid, satd. sodium hydrogen carbonate and finally with satd. brine. The organic layer was dried with sodium sulfate and concentrated in vacuo. 780 mg of the raw material was isolated, which was chromatographed using flash chromatography on silica gel with *n*-hexane/ethyl acetate = 1:1 to yield 450 mg (41%) of pure (+)-**6** as a viscous oil. − $[\alpha]_D^{20}$ = +1.3

(c = 0.6, chloroform), $[\alpha]_D^{20}$ = +7.7 (c = 0.6, acetone). − IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1} (NH), 3034 (arom. CH), 2939 (CH), 1662 (amide-I), 1526 (amide-II). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92 (t, J = 6.1 Hz, 1 H, sec. amide-NH), 7.75 (t, J = 5.2 Hz, 1 H, sec. amide-NH), 7.75 (d, J = 8.2 Hz, 1 H, N^1−H), 7.64−7.01 (m, 39 H, arom. =C*H*−), 5.07−4.88 (m, 12 H, −O−CH_2−phe), 3.92 (m, 1 H, 2-H), 3.26 (m, 1 H, 1-H_a), 3.17 (m, 1 H, 1-H_b), 3.04 (dt, J_1 = 6.4 Hz, J_2 = 5.8 Hz, 2 H, 6-CH_2−), 1.10−0.95 (m, 6 H, 3-, 4-, 5-CH_2-). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 23.4 (t, C-4), 29.0 (t, C-5), 31.9 (t, C-3), 39.4 (t, C-6), 43.4 (t, C-1), 49.7 (d, C-2), 71.3, 71.35, 71.4 (t, O−*C*H_2−phe), 116.9, 117.1, 117.15 (d, arom. =CH−), 123.3, 123.4, 123.5 (d, arom. =CH−), 124.1, 124.2, 124.3 (d, arom. =CH−), 127.1, 127.6, 127.8 (s, quat. arom. =C−), 127.6, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 128.65, 128.7, (d, 30 × arom. =CH−), 136.38, 136.43, 136.48 (s, quat. arom. =C−), 146.7, 146.8, 146.9 (s, quat. arom. =C−O−), 151.6, 151.70, 151.74 (s, quat. arom. =C−O−), 165.1, 165.6, 165.7 (sec. amide−C=O). − (+)-ESI MS: *m/z* (%) = 1080 (15) [M + H^+]$^+$, 1102 (100) [M + Na^+]$^+$. − $C_{69}H_{65}N_3O_9$ (1089.3): calcd. C 76.71, H 6.06, N 3.89; found C 76.15, H 6.05, N 3.76.

(+)-(2S)-1,2,6-Tris[(2,3-dihydroxybenzoyl)amino]hexane [(+)-**7**$_S$, Myxochelin C]: 614 mg of (+)-**6** (0.57 mmol) was dissolved in 10 ml of THF and 100 ml of methanol. After addition of 200 mg of Pd/C (10%), dehydrogenation took place for 6 h at room temp. and normal pressure. The slightly blue solution was filtered through Kieselgur and the residue concentrated in vacuo. For the separation of any metal complex, especially traces of iron complexes which are problematic when running NMR spectra, the crude material [307 mg (100%)] was again dissolved in a few ml of dichloromethane/methanol (10%). The solvent mixture had been ensured to be metal-free by using a small chelex-100 column. The siderophore solution was loaded on a small silica-gel column, which had also been washed with the same solvent, and was eluted with three bed volumes. Any complexes (dark blue) remained on the top of the column. After evaporation of the solvent, 250 mg (81%) of (+)-**7** crystallized in plates, m. p. 115°C (TLC: R_f = 0.30, dichloromethane/methanol/glacial acid = 94:5:1). − $[\alpha]_D^{20}$ = +9.1 (c = 0.35, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3649 cm^{-1} (CH), 33669 (OH), 2937 (CH), 1637 (amide-I), 1585 (aryl), 1526 (amide-II). − ^{1}H NMR (600 MHz, $CDCl_3$ + 5% CD_3OD): δ = 7.25 (m, 3 H, 3 × 6-H of benzoyl groups), 6.90 and 6.25 (m, 6 H, 3 × 5-H, 3 × 4-H of benzoyl groups), 4.40 (m, 1 H, 2-H), 3.65 (m, 1 H, 1-H_a), 3.59 (m, 1 H, 1-H_b), 3.43 (m, 2 H, 6-CH_2), 1.9−1.5 (m, 6 H, 3-, 4-, 5-CH_2). − ^{13}C NMR (125.0 MHz, $CDCl_3$ + 5% CD_3OD): δ = 22.9 (t, C-4), 28.6 (t, C-5), 31.3 (t, C-3), 38.8 (t, C-6), 43.4 (t, C-1), 49.9 (d, C-2), 114.6, 114.7, 114.8 (s, quat. benzoyl-C-1), 117.2, 117.3, 117.4, 118.3, 118.5, 118.7 (d, 3 × benzoyl-C-4, 3 × benzoyl-C-5), 145.3 (s, 3 × quat. arom. O−*C*=), 148.3 (s, 3 × quat. arom. O−*C*=), 169.9 (s, 3 × sec. amide-*C*=O). − (−)-FAB MS: *m/z* (%) = 538 (100) [M − H]$^-$. − (+)-ESI MS: *m/z* (%) = 562 (100) [M + Na^+]$^+$. − HR MS: $C_{27}H_{28}N_3O_9$ calcd. 538.1826, found 538.1879. − $C_{27}H_{29}N_3O_9$ (539.6): calcd. C 60.10, H 5.42, N 7.79; found C 59.88, H 5.52, N 7.34.

(+)-H-(D)-Lys-NH_2 × 2 HCl [(+)-D-**2**]: (+)-**2** was synthesized by dehydrogenation of Z-(D)-Lys(Z)-NH_2 (m.p.155°C, $[\alpha]_D^{20}$ = −0.8, c = 1, dimethyl formamide). 2.5 g of Z-(D)-Lys(Z)-NH_2 (6 mmol) was dissolved in 10 ml of THF and 50 ml of methanol. After addition of 500 mg of Pd/C (10%), the mixture was hydrogenated for 5 h at room temp. and normal pressure. The product was filtered through Kieselgur, which was then itself was washed with 35 ml of 5% HCl. Both filtrates were combined and concentrated in vacuo. 1.2 g (92%) of a viscous, yellow oil was recovered, which slowly crystallized, m.p. 215°C, TLC: *n*-butanol/glacial acid/water = 4:2:3, R_f = 0.30. − $[\alpha]_D^{20}$ = −14.5 (c = 1, H_2O). − ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 8.30 and 8.20 (s, br., each 2 H, −NH_2), 8.1 (s, 1 H, O=C−NH_a), 7.52 (s, 1 H, O=C−NH_b), 3.71 (t, J = 6.1 Hz, 1 H, 2-H), 2.72 (m, 2 H, 6-CH_2), 1.76, 1.58, 1.36 (m, 6 H, 3-, 4-, 5-CH_2). − ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 21.1 (t, C-4), 26.2 (t, C-5), 30.1 (t, C-3), 38.2 (t, C-6), 51.8 (d, C-2), 170.4 (s, C-1). − $C_6H_{17}Cl_2N_3O$ (218.1): calcd. C 33.04, H 7.86, Cl 32.51, N 19.08; found C 32.89, H 7.75, Cl 32.37, N 18.87.

(+)-2,3-Dibenzyloxybenzoyl-D-Lys(2,3-dibenzyloxybenzoyl)-NH_2 [(+)-D-**3**]: From the reaction with 0.5 g (2.3 mmol) of (+)-**2**, 1.53 g (4.6 mmol) of 2,3-dibenzyloxybenzoic acid, 1.47 g (4.6 mmol) of TBTU and 2.34 ml (13.8 mmol) of Hünig base, as described for the synthesis of (−)-**3**, appoximately 1.51 g (84%) of (+)-**3** was recovered. − $[\alpha]_D^{20}$ = +9.2 (c = 0.5, acetone). − $C_{48}H_{47}N_3O_7$ (777.3): calcd. C 74.16, H 6.10, N 5.41, found C 73.76, H 5.99, N 4.34.

(+)-(2R)-2,6-Bis[(2,3-dibenzyloxybenzoyl)amino]hexanenitrile, [(+)-**4**$_R$]: 0.98 g (1.19 mmol) of (+)-D-**3** was dissolved in 15 ml of dichloromethane, and 0.29 ml of pyridine was added. The dehydration was achieved as described for (−)-**4**$_S$. After flash chromatography 670 mg of (+)-**4**$_R$ could be isolated (74%), TLC: R_f = 0.36, ethyl acetate/*n*-hexane = 1:1. − $[\alpha]_D^{20}$ = +18.5 (c = 1, chloroform). − $C_{48}H_{45}N_3O_6$ (759.9): calcd. C 75.87, H 5.97, N 5.53; found C 75.18, H 5.82, N 4.16.

(+)-(2R)-2,6-Bis[(2,3-dibenzyloxybenzoyl)amino]-1-aminohexane [(+)-**5**$_R$]: 130 mg (1 mmol) of $CoCl_2$ was stirred with 190 mg (5 mmol) of sodium tetrahydridoborate in 10 ml of methanol for 10 min. The black precipitate of Co_2B was filtered, washed with small portions of methanol, and immediately added to the reaction vessel. 670 mg of (+)-**4**$_R$ (0.88 mmol) and 333 mg (8.8 mmol) of sodium tetrahydridoborate were dissolved in 10 ml of THF and 40 ml of methanol. 114 mg (0.88 mmol) of Co_2B was added and the mixture cooled using an ice bath. After 12 h, a further 333 mg of sodium tetrahydridoborate and 400 mg of Co_2B were added. After 3 h, all the starting material had reacted. The mixture was worked up as described for (−)-**5**. Using flash chromatography 360 mg (54%) of pure (+)-**5**$_R$ could be recovered. − $[\alpha]_D^{20}$ = +23.3 (c = 0.5, chloroform). − $C_{48}H_{49}N_3O_6$ (763.9): calcd. C 75.47, H 6.46, N 5.50; found C 74.84, H 6.42, N 5.31.

(+)-(2R)-2,6-Bis[(2,3-dihydroxybenzoyl)amino]-1-aminohexane [(+)-**1**$_R$, Myxochelin B$_R$]: 120 mg (0.16 mmol) of (+)-**5**$_R$ was dehydrogenated with 65 mg of Pd/C (5%) for 2 h at room temp. and normal pressure yielding, after the workup, 60 mg (95%) of myxochelin B$_R$. − $[\alpha]_D^{20}$ = +8.3 (c = 0.5, 6 N HCl).

(−)-(2R)-1,2,6-Tris[(2,3-dibenzyloxybenzoyl)amino]hexane [(−)-**6**$_R$]: 790 mg (1.034 mmol) of (+)-**5**$_R$ was dissolved in 50 ml of dichloromethane and, after the addition of 332 mg (1.034 mmol) of TBTU, 346 mg (1.034 mmol) of 2,3-dibenzyloxybenzoic acid and 0.36 ml of Hünig base, the reaction mixture was stirred for 48 h. The workup procedure was as for the synthesis of (+)-**6**$_S$, and after flash chromatography 942 mg (84%) of (−)-**6**$_R$ was isolated. − $[\alpha]_D^{20}$ = −1.8 (c = 0.5, chloroform), $[\alpha]_D^{20}$= −7.7 (c = 0.6, acetone). − $C_{69}H_{65}N_3O_9$ (1080.3): calcd. C 76.15, H 6.06, N 3.89; found C 75.86, H 6.05, N 3.76.

(−)-(2R)-1,2,6-Tris[(2,3-dihydroxybenzoyl)amino]hexane [(−)-**7**$_R$, Myxochelin C$_R$]: 614 mg (0.57 mmol) of (−)-**6**$_R$ was dissolved in 10 ml of THF and 100 ml of methanol. Dehydrogenation took place after the addition of 200 mg of Pd/C (5%) for 6 h at room temp. and normal pressure. 307 mg (100%) of **(−)-7**$_R$ was isolated after a workup as described for the synthesis of myxochelin C. − $[\alpha]_D^{20}$ = −9.8 (c = 1.2, CH_3OH). − $C_{27}H_{29}N_3O_9$ (539.6): calcd. C 60.10, H 5.42, N 7.79; found C 59.73, H 5.72, N 7.03.

Synthesis of Myxochelins D_R and D

H-(D)-Orn-OMe × 2 HCl [(−)-D-**8**]: 5.0 g (29.66 mmol) of H-(D)-Orn(H)-OH, ($[\alpha]_D^{24}$ = −22.2, *c* = 1, 6 N HCl) was dissolved in 50 ml of freshly dried methanol. For 30 min gaseous HCl was bubbled through this solution while cooling with an ice/sodium chloride mixture. After standing for 2 d at room temp., the solvent was evaporated in vacuo. The precipitating dihydrochloride was washed with diethyl ether to remove unreacted starting materials. 5.9 g (91%) of (−)-D-**8** was isolated, m.p.192°C (TLC: R_f = 0.32, *n*-butanol/water/glacial acid = 4:1:1). − $[\alpha]_D^{24}$ = −22.4 (*c* = 1, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1} (NH_3^+), 1735 (ester CO). − ^1H NMR (301.9 MHz, CD_3OD): δ = 8.83 (br., 3 H, NH_3^+), 8.30 (br., 3 H, NH_3^+), 4.03 (m, 1 H, 2-H), 3.76 (s, 3 H, O−CH_3), 2.78 (m, 2 H, 5-H_2), 1.90 (m, 2 H, 3-H_2), 1.77 (m, 2 H, 4-H_2). − ^{13}C NMR (75.9 MHz, [D_6]DMSO): δ = 22.6 (t, C-4), 27.1 (t, C-3), 37.9 (t, C-5), 51.3 (d, C-2), 52.8 (q, O−*C*H_3), 169.7 (s, *C*=O). − (+)-CI MS: *m/z* (%) = 147 (100) [M + H^+ − 2 × HCl]$^+$. − $C_6H_{16}Cl_2N_2O_2$ (219.1): calcd. C 32.89, H 7.36, N 12.78; found C 32.66, H 7.51, N 12.75.

(+)-2,3-Dibenzyloxybenzoyl-D-Orn(2,3-dibenzyloxybenzoyl)-OCH_3 [(+)-D-**9**]: 1.0 g (4.56 mmol) of (−)-D-**8** was dissolved in 40 ml of dichloromethane (dried over molecular sieve 3μ). As described for the corresponding Lys derivative, 3.05 g (9.12 mmol) of 2,3-dibenzyloxybenzoic acid, 2.93 g (9.12 mmol) of TBTU, and 4.69 ml (27.4 mmol) of Hünig base were added. The reaction mixture was stirred for 5 d at room temp. The mixture was extracted with 30 ml of 5% HCl , followed by 20 ml of satd. sodium bicarbonate solution and than with satd. brine. The resulting organic phase was dried with magnesium sulfate and concentrated in vacuo. The crude extract (4.17 g) was purified by flash chromatography using ethyl acetate/*n*-hexane = 1:1 as the solvent, yielding 2.12 g (60%) of (+)-D-**9** as a pale yellow viscous oil (TLC: R_f = 0.76, ethyl acetate). − $[\alpha]_D^{24}$ = +9.3 (*c* = 1, chloroform). − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1} (NH), 3055 and 3022 (arom. =CH-), 2930, 2910 and 2860 (CH), 1635 (amide-I), 1570 (amide-II). − ^1H NMR (499.8 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 7.6 Hz, 1 H, 2-NH), 7.83 (t, *J* = 5.5 Hz, 1 H, 6-NH), 7.48−7.18 (m, 26 H, arom. =CH-), 5.17−5.02 (m, 8 H, 4 × O−CH_2−phe), 4.58 (ddd, J_1 = 5.5 Hz, J_2 = 7.6 Hz, J_3 = 3.1 Hz, 1 H, 2-H), 3.67 (s, 3 H, O−CH_3), 3.13 (dt, J_1 = 7.0 Hz, J_2 = 13.1 Hz, 2 H, 5-H_2), 1.63, 1.35, (m, each 2 H, 3-, 4-H_2). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 25.6 (t, C-4), 29.5 (t, C-3), 39.1 (t, C-5), 52.2 (d, C-2), 52.5 (q, O−*C*H_3), 71.3, 71.4, 76.1, 76.4 (t, O−*C*H_2−phe), 116.9, 117.3, 123.3, 123.4, 124.3, 124.3 (d, arom. =*C*−H), benzoyl), 126.5, 127.3 (s, quat. arom. =C−, benzoyl), 127.6−128.7 (d, 20 × arom. =CH−, phe), 136.3, 136.4 (s, quat. arom. C, phe), 146.7, 147.0 (s, arom. =*C*−O), 151.6, 151.7 (s, arom. =*C*−O), 164.9, 164.9 (sec. amide-*C*=O), 172.4 (ester-*C*=O). − (+)-CI MS: *m/z* (%) = 779.2 (100) [M + H^+]$^+$. − (+)-FAB MS: *m/z* (%) = 780 (100) [M + H^+]$^+$. − $C_{48}H_{46}N_2O_8$ (778.9): calcd. C 73.81, H 5.80, N 3.66; found: C 73.51, H 6.89, N 3.33.

(−)-2,3-Dibenzyloxybenzoyl-L-Orn(2,3-dibenzyloxybenzoyl)-OCH_3 [(−)-L-**9**]: The L-enantiomer was produced starting with 820 mg (3.74 mmol) of L-Orn-OCH_3 × 2 HCl, 2.5 g (7.48 mmol) of 2,3-dibenzyloxybenzoic acid, 2.401 g (7.48 mmol) of TBTU and 3.84 ml (22.44 mmol) of Hünig base. From the workup procedure 2.15 g (74%) of (−)-**10** resulted as a highly viscous oil. − $[\alpha]_D^{24}$ = −10.0 (*c* = 1, chloroform). − $C_{48}H_{46}N_2O_8$ (778.9): calcd. C 73.81, H 5.80, N 3.66; found C 73.69, H 5.96, N 3.37.

(+)-2,3-Dibenzyloxybenzoyl-D-Orn(2,3-dibenzyloxybenzoyl)-NH_2 [(+)-D-**10**]: In a two-neck bottle 2.12 g (2.72 mmol) of (+)-D-**9** was dissolved in 10 ml of THF and 90 ml of dry methanol. While cooling with ice, ammonia was bubbled through the solution for 2 h. The volume of the mixture was approximately doubled. This solution was quickly placed into an autoclave, which was kept closed and at room temp. for 3 d. Then the vent was opened carefully and the solution concentrated in vacuo. 1.62 g (78%) of crystalline (+)-D-**10** , m.p. 122−126°C, was isolated after flash chromatography using ethyl acetate/*n*-hexane = 1:1 as the eluent (TLC: R_f = 0.49, ethyl acetate). − $[\alpha]_D^{24}$ = +27.5 (*c* = 1, chloroform). − IR (KBr): $\tilde{\nu}$ = 3460 cm^{-1} (NH), 3055 (arom. CH), 2930, 2910 (aliph. CH), 1635 (amide-I), 1570 (arom. C=C), 1515 (amide-II). − ^1H NMR (499.8 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 7.9 Hz, 1 H, 2-NH), 7.94 (t, *J* = 5.6 Hz, 1 H, 5-NH), 7.48−7.12 (m, 26 H, arom. =CH−), 6.63 (s, 1 H, amide-NH_a), 5.20 (s, 1 H, amide-NH_b), 5.17−5.02 (m, 8 H, −O−CH_2−phe), 4.69 (m, 1 H, 2-H), 3.01 (m, 2 H, 5-CH_2−), 1.66, 1.35 (m, 4 H, 3-, 4-CH_2−). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 26.0 (t, C-4), 29.5 (t, C-3), 38.3 (t, C-5), 51.9 (d, C-2), 71.3, 71.4, 76.2, 76.4 (t, −O−*C*H_2−phe), 117.1, 117.4, 123.1, 123.2, 124.3, 124.4 (d, arom. =CH-, benzoyl), 126.8, 127.2 (s, arom. =C-, benzoyl), 127.7−129.0 (d, 20 arom. = CH−, phe), 136.2, 136.3, 136.3, 136.4 (s, quat. arom. =C−, phe), 146.8, 147.0, 151.2, 151.8 (s, quat. arom. =C−O−, benzoic acid), 165.4, 165.6 (s, sec. amide−*C*=O), 173.9 (s, prim. amide−*C*=O). − (+)-FAB MS: *m/z* (%) = 764 (100)[M + H^+]$^+$. − $C_{47}H_{45}N_3O_7$ (763.9): calcd. C 73.90, H 5.94, N 5.50; found C 73.69, H 5.76, N 5.00

(−)-2,3-Dibenzyloxybenzoyl-L-Orn(2,3-dibenzyloxybenzoyl)-NH_2 [(−)-L-**10**]: As desribed for (+)-**10** 2.15 g (2.76 mmol) of (−)-**9** was used for the synthesis of the enantiomer. After chromatography, 1.75 g (83%) of (−)-L-**10** as crystals, m.p. 125−127°C, was isolated. − $[\alpha]_D^{24}$ = −28.9 (*c* = 1, chloroform). − $C_{47}H_{45}N_3O_7$ (763.9): calcd. C 73.90, H 5.94, N 5.50; found C 73.66, H 5.98, N 5.25.

(+)-(2R)-2,5-Bis[(2,3-dibenzyloxybenzoyl)amino]-pentanenitrile [(+)-$\mathbf{11}_R$]: 1.494 g (1.96 mmol) of (+)-D-**10** was dissolved in 100 ml of dichloromethane, and 0.332 ml (4.11 mmol) of pyridine and 233 mg (0.786 mmol) of triphosgene were added. After 30 min, all the starting material had reacted and the mixture was extracted with 5% HCl, followed by satd. sodium bicarbonate and finally satd. brine. The organic layer was dried with magnesium sulfate and concentrated in vacuo. The purification of the desired product was done by flash chromatography with ethyl acetate/*n*-hexane = 65:85 as the eluent. 1.058 g of crystalline (+)-$\mathbf{11}_R$ could be isolated (73%), m.p. 134−136°C, TLC: R_f = 0.2, ethyl acetate/*n*-hexane = 65:85. − $[\alpha]_D^{24}$ = +16.9 (*c* = 1, in chloroform). − IR (KBr): $\tilde{\nu}$ = 3065 cm^{-1}, 3015 (arom. CH), 2925, 2900, 2855 (aliph. CH), 2230 (CN), 1630 (amide-I), 1570 (aryl), 1525 (amide-II). − ^1H NMR (301.9 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 8.1 Hz, 1 H, 2-NH-), 7.81 (t, br., 1 H, 5-NH), 7.48−7.13 (m, 26 H, arom. =CH-), 5.16, 5.15, 5.08, 5.06 (m, 8 H, 4 × -O−CH_2−phe), 4.77 (m, 1 H, 2-H), 3.13 (m, 2 H, 5-H_2), 1.28 (m, 4 H, 3- and 4-H_2). − ^{13}C NMR (75.9 MHz, $CDCl_3$): δ = 25.4 (t, C-4), 29.9 (t, C-3), 38.5 (t, C-5), 40.2 (d, C-2), 71.3, 71.4, 76.5, 76.7 (t, -O−*C*H_2−phe), 117.1, 117.9 (d, arom. =*C*H-, benzoic acid), 118.2 (-*C*N), 123.3, 123.4, 124.4, 124.5 (d, arom. =*C*H-, benzoyl), 125.2, 126.9 (s, quat. arom.=*C*-, benzoyl), 127.6−129.0 (d, 20 × arom. =*C*H-, phe), 135.8, 136.1, 136.3, 136.4 (s, quat. arom. =*C*-, phe), 146.9, 147.1, 151.5, 151.6 (s, quat. arom. =*C*−O-Bn), 164.4, 165.0 (s, sec. amide C=O). − (+)-CI MS: *m/z* (%) = 746 (100) [M + H^+]$^+$. − $C_{47}H_{43}N_3O_6$ (745.9): calcd. C 75.68, H 5.81, N 5.63; found C 75.70, H 5.90, N 5.42.

(−)-(2S)-2,5-Bis[(2,3-dibenzyloxybenzoyl)amino]pentanenitrile [(−)-$\mathbf{11}_S$]: Starting with 2.11 g (2.76 mmol) of (−)-L-10 in 200 ml

of dichloromethane, 0.47 ml (5.8 mmol) of pyridine and 329 mg (1.11 mmol) of triphosgene, 1.72 g of (−)-**11**$_S$ (84%) was isolated as described above, m.p. 134−136°C. − $[\alpha]_D^{24}$ = −18.4 (*c* = 0.7, chloroform). − $C_{47}H_{43}N_3O_6$ (745.9): calcd. C 75.68, H 5.81, N 5.63; found C 75.66, H 5.80, N 5.36.

(+)-(2R)-1-Amino-2,5-bis[(2,3-dibenzyloxybenzoyl)amino]-pentane [(+)-**12**$_R$]: 0.5 g (0.67 mmol) of (+)-**12** was dissolved in 15 ml of THF and 25 ml of methanol. Three separate quarters of 652 mg of Co_2B, prepared as for (−)-**5**, were added to this solution. To one portion, during heavy stirring, 3.3 g of sodium tetrahydridoborate was slowly added. After 1 h (and after checking by TLC), the remaining quarter of Co_2B (218 mg) was added; 30 min later all the starting material had reacted. After the workup as described for (−)-**5** and after flash chromatography, 373 mg (74%) of (+)-**12**$_R$ was isolated as a viscous oil, TLC: R_f = 0.32, chloroform/methanol = 10:1. − $[\alpha]_D^{24}$ = +15.8 (*c* = 1, chloroform). − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1} (NH), 3060, 3025 (arom. CH), 2925, 2860 (CH), 1650 (amide-I), 1570 (aryl), 1525 (amide-II). − ^{1}H NMR (301.9 MHz, $CDCl_3$): δ = 7.91 (m, 2 H, 2- and 5-NH), 7.48−7.13 (m, 26 H, arom. =CH−), 3.93 (m, 1 H, 2-H), 3.18 (m, 2 H, 5-H_2), 2.60 (m, 1 H, 1-H_a), 2.38 (m, 1 H, 1-H_b), 1.27, 0.98 (m, 4 H, 3-, 4-H_2). − ^{13}C NMR (75.9 MHz, $CDCl_3$): δ = 26.0 (t, C-4), 30.0 (t, C-3), 39.4 (t, C-5), 45.7 (t, C-1), 51.5 (d, C-2), 71.2, 71.3, 76.2, 76.3 (t, −O−*C*H_2−phe), 116.9, 117.1, 123.3, 123.4, 124.3, 124.4 (d, arom. =CH−, benzoyl), 126.8, 127.3 (s, quat. arom. =C−, benzoyl), 127.6−128.7 (d, 20 arom. =C−, phe), 136.3, 136.3, 136.4, 136.5 (s, quat. arom. =C−, phe), 146.7, 146.9, 151.6, 151.7 (s, arom. =C−O−Bn), 165.0, 165.4 (sec. amide−C=O). − (+)-ESI MS: *m*/*z* (%) = 750.4 (100) $[M + H^+]^+$. − $C_{47}H_{47}N_3O_6$ (749.9): calcd. C 75.28, H 6.32, N 5.60; found C 74.88, H 6.23, N 5.38.

(−)-(2S)-1-Amino-2,5-bis[(2,3-dibenzyloxybenzoyl)amino]-pentane, [(−)-**12**$_S$]: The synthesis of the enantiomer followed exactly the same protocol as that described above. We isolated 385 mg (76%) of (−)-**12**$_S$ as a viscous oil. − $[\alpha]_D^{24}$ = −16.3 (*c* = 1, chloroform). − $C_{47}H_{47}N_3O_6$ (749.9): calcd. C 75.28, H 6.32, N 5.60; found C 74.91, H 6.44, N 5.36.

(−)-(2R)-1,2,5-Tris[(2,3-dibenzyloxybenzoyl)amino]pentane [(−)-**13**$_R$]: 360 mg (0.48 mmol) of (+)-**12**$_R$ and 160 mg 0.478 mmol) of 2,3-dibenzyloxybenzoic acid reacted together with 154 mg (0.48 mmol) of TBTU and 165 µl (0.963 mmol) of Hünig base as described for the synthesis of (−)-**6**$_R$. After the workup and flash chromatography with ethyl acetate/*n*-hexane (3:1) 430 mg (84%) of (−)-**13**$_R$ was isolated as an oil, TLC: R_f = 0.40, ethyl acetate/*n*-hexane = 3:1. − $[\alpha]_D^{24}$ = −1.9 (*c* = 0.8, chloroform). − IR (KBr): $\tilde{\nu}$ = 3355 cm^{-1} (NH), 3000 (arom. CH), 2920, 2860 (aliph. CH), 1630 (amide-I), 1515 (amide-II). − ^{1}H NMR (301.9 MHz, $CDCl_3$): δ = 7.94 (t, br., 1 H, 1-NH), 7.79 (m, 2 H, 2- and 5-NH), 7.48−7.06 (m, 39 H, arom. =CH−), 5.15−4.96 (m, 12 H, 6 × −O−CH_2−phe), 3.96 (m, 1 H, 2-H), 3.23 (m, 2 H, 1-H_2), 1.18, 0.88 (m, 4 H, 3- and 4-CH_2−). − ^{13}C NMR (75.9 MHz, $CDCl_3$): δ = 25.8 (t, C-4), 29.7 (t, C-3), 39.4 (t, C-5), 43.3 (t, C-1), 49.6 (d, C-2), 71.3, 71.3, 71.3, 75.8, 76.1, 76.3 (t, −O−*C*H_2−phe), 116.9, 117.0, 117.1, 123.2, 123.3, 123.4, 124.1, 124.2, 124.3 (d, arom. =*C*H−, benzoyl), 126.9, 126.9, 127.6 (s, quat. arom. C, benzoyl), 127.6−128.7 (d, 30 × arom. C, phe), 136.3, 136.3, 136.4, 136.4, 136.5, 136.5 (s, quat. arom. C, phe), 146.6, 146.7, 146.9, 151.6, 151.7, 151.7 (s, quat. arom. =*C*−O−, benzoyl), 164.9, 165.0, 165.6 (s, sec. amide−*C*=O). − (+)-ESI MS: *m*/*z* (%) = 1066.6 (100) $[M^+]^+$. − $C_{68}H_{63}N_3O_9$ (1066.3): calcd. C 76.60, H 5.96, N 3.94; found C 76.58, H 5.92, N 3.78.

(+)-(2S)-1,2,5-Tris[(2,3-dibenzyloxybenzoyl)amino]pentane [(+)-**13**$_S$]: To synthesize the enantiomer, 400 mg (0.533 mmol) of (−)-**12**$_S$, 179 mg (0.533 mmol) of 2,3-dibenzyloxybenzoic acid, 172 mg (0.533 mmol) of TBTU and 185 µl (1.08 mmol) of Hünig base were used under the conditions described above. Flash chromatography yielded 445 mg (78%) of (+)-**13**$_S$, TLC: R_f = 0.4, ethyl acetate/*n*-hexane = 3:1 .− $[\alpha]_D^{24}$ = +1.5 (*c* = 0.8, chloroform). − $C_{68}H_{63}N_3O_9$ (1066.3): calcd. C 76.60, H 5.96, N 3.94; found C 76.42, H 5.86, N 3.78.

(−)-(2R)-1,2,5-Tris[(2,3-dihydroxybenzoyl)amino]pentane [(−)-**14**$_R$, Myxochelin D$_R$]: 260 mg of (−)-**13**$_R$ (0.244 mmol) was dissolved in 5 ml of THF and 20 ml of methanol. After addition of 50 mg of Pd/C (5%), the triamide was hydrogenated for 5 h at room temp. and at 1 atm. The reaction mixture was filtered through Kieselgur and concentrated in vacuo. The workup procedure followed that for (+)-**7**. 112 mg (86%) was isolated, TLC: R_f = 0.42, dichloromethane/methanol = 5:1. − $[\alpha]_D^{24}$ =−8.2 (*c* = 1, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1} (br., NH, OH), 2925 (CH), 1630 (amide-I), 1580 (aryl), 1530 (amide-II). − ^{1}H NMR (300.1 MHz, CD_3OD): δ = 8.80−8.60 [m, residual signals (br.), 3 H, N^1−H, N^2−H, N^5−H], 7.25−7.20 (m, 3 H, benzoic acid), 6.91−6.86 (m, 3 H, benzoic acid), 6.65−6.60 (m, 3 H, benzoic acid), 4.39 (m, 1 H, 2-H), 3.60 (m, 1 H, 1-H_a), 3.52 (m, 1 H, 1-H_b), 3.0 (m, 2 H, 5-H_2), 1.75 (m, 2 H, 3-H_2), 1.26 (m, 2 H, 4-H_2). − ^{13}C NMR (75.4 MHz, CD_3OD): δ = 17.6 (t, C-4), 21.0 (t, C-3), 30.6 (t, C-5), 34.9 (t, C-1), 41.4 (d, C-2), 107.7, 107.8, 109.1, 109.3, 109.4, 109.5, 109.6, 109.8, 110.0 (d, 12 × arom. C, benzoic acid), 138.4, 138.4, 138.6, 142.0, 142.1, 142.6 (s, 6 × quat. arom. =*C*−O), 162.3, 162.6, 162.7 (s, quat. sec. amide−*C*=O). − (−)-ESI MS: *m*/*z* (%) = 524 (100) $[M - H^+]^-$ − $C_{26}H_{27}N_3O_9$ (525.5): calcd. C 59.42, H 5.18, N 8.00; found C 59.19, H 5.11, N 7.77.

(+)-(2S)-1,2,5-Tris[(2,3-dihydroxybenzoyl)amino]pentane [(+)-**14**$_S$, Myxochelin D]: Under similar conditions as those described for the synthesis of myxochelin D$_R$, 117 mg (92%) of myxochelin D [(+)-**15**] could be recovered, starting from 257 mg (0.241 mmol) of (+)-**13** (92%). − $[\alpha]_D^{24}$ = +6.9 (*c* = 1, CH_3OH). − $C_{26}H_{27}N_3O_9$ (525.5): calcd. C 59.42, H 5.18, N 8.00; found C 59.30, H 5.12, N 7.71.

Synthesis of Myxochelin E

2,3-Dibenzyloxybenzoyl-L-Asn-NH$_2$ [(+)-L-**15**]: 500 mg (2.98 mmol) of (L)-H-Asn-NH_2 × HCl (Bachem, m.p. 224−226°C, $[\alpha]_D^{24}$ = +14.5, *c* = 1.0, CH_3OH) was dissolved in 30 ml of dichloromethane and 20 ml of acetonitrile. After the addition of 998 mg (2.98 mmol) of 2,3-dibenzyloxybenzoic acid, 958 mg (2.98 mmol) of TBTU and 1.54 ml (8.94 mmol) of Hünig base, the mixture was stirred for 5 d. The reaction mixture was concentrated in vacuo and again dissolved in 40 ml of ethyl acetate, washed with 5% HCl, followed by sodium bicarbonate and finally satd. brine. The organic layer was dried with sodium sulfate and concentrated to half of its volume. 1.0 g (75%) of (+)-L-**15** crystallized on standing overnight in the refrigerator, TLC: R_f = 0.46, dichloromethane/methanol = 9:1, m.p. 170−173°C. − $[\alpha]_D^{24}$ = +18.7 (*c* = 1, THF). − IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1}, 3170 (NH, NH_2), 3055, 3020 (arom. CH), 2930, 2860 (aliph. CH), 1660 (amide-I); 1570 (aryl), 1515 (amide-II). − ^{1}H NMR (499.8 MHz, [D_6]DMSO): δ = 8.65 (d, *J* = 7.6 Hz, 1 H, N^2−H), 7.50−7.06 (m, 15 H, 13 × arom. =CH−, 2 × prim. NH−), 7.05 (s, 1 H, NH−), 6.90 (s, 1 H, NH−), 5.19 (s, 2 H, −O−CH_2−phe), 5.04 (AB system, q, 2 H, J_1 = 10.3 Hz, J_2 = 23.5 Hz, O−CH_2−phe), 4.69 (ddd, J_1 = 6.7 Hz, J_2 = 7.6 Hz, J_3 = 5.8 Hz, 1 H, 2-H), 2.50 (ddd, J_1 = 5.8 Hz, J_2 = 6.7 Hz, J_3 = 15.3, 2 H, 3-H_2. − ^{13}C NMR (75.9 MHz, [D_6]DMSO): δ = 37.1 (t, C-3), 49.8 (d, C-2), 70.2, 74.9 (t, O−*C*H_2−phe), 116.4, 121.4, 123.9 (d, arom. =*C*H−, benzoic acid), 127.9, 128.3, 128.7, 128.8 [d (10 ×), arom. =*C*H−, phe and s, 1 ×, quat. arom. C, benzoyl], 136.4,

136.5 (s, quat. arom. *C*, phe), 145.5, 151.5 (s, arom. =*C*−O−Bn), 164.4 (s, sec. amide−*C*=O), 171.5, 172.5 (prim. amide−*C*=O). − (+)-FAB MS: *m/z* (%) = 448 (85) $[M + H^+]^+$, 470 (100) $[M + Na^+]^+$. − $C_{25}H_{25}N_3O_5$ (447.5): calcd. C 67.10, H 5.63, N 9.39; found C 66.94, H 5.68, N 9.20.

(−)-(2S)-2-[(2,3-Dibenzyloxybenzoyl)amino]butane-1,4-dinitrile [(−)-**16**$_S$]: Dehydration was achieved as for the nitrile syntheses described above. From 1.0 g (2.23 mmol) of (+)−**15** in 100 ml of dichloromethane, 0.76 ml (9.4 mmol) of pyridine and 663 mg (2.23 mmol) of triphosgene 690 mg (75%) of (−)-**16**$_S$ was isolated as crystals, m.p. 168−169°C, TLC: R_f = 0.89, in ethyl acetate, R_f = 0.52, in ethyl acetate/*n*-hexane = 1:1. − $[\alpha]_D^{24}$ = −6.3 (*c* = 1, chloroform). − IR (KBr): $\tilde{\nu}$ = 3420 cm^{-1}, 3290 (NH), 3030, 3015 (arom. CH), 2920, 2860 (aliph. CH), 2235 (CN), 1655 (amide-I), 1565 (aryl), 1505 (amide-II). − ^{1}H NMR (301.9 MHz, $CDCl_3$): δ = 8.75 (d, *J* = 8.1 Hz, 1 H, 2-NH), 7.72 (dd, J_1 = 1.9 Hz, J_2 = 7.1 Hz, 1 H, benzoyl-6-H), 7.50−7.40 (m, 20 H, phenyl), 7.25 (dd, J_1 = 1.3 Hz, J_2 = 7.5 Hz, 1 H, benzoyl-4-H), 7.18 (dd, J_1 = 8.1 Hz, J_2 = 7.1 Hz, 1 H, benzoyl-5-H), 5.26−5.17 (m, 4 H, O−CH_2−phe), 5.07 (dt, J_1 = 6.7 Hz, J_2 = 8.1 Hz, 1 H, 2-H), 2.65 (d, *J* = 6.7 Hz, 2 H, 3-H_2). − ^{13}C NMR (75.9 MHz, $CDCl_3$): δ = 22.2 (t, C-3), 37.4 (d, C-2), 71.5, 76.9 (t, O−*C*H_2−phe), 114.3, 115.5 (s, CN), 118.5, 123.3, 124.6 (d, arom. =*C*H−, benzoyl-C-4, C-5, C-6), 124.2 (s, benzoyl-C-1), 127.2−129.2 (d, 10 × arom. =*C*H−, phenyl), 135.8, 136.0 (s, quat. arom. C, phenyl-C-1), 147.3, 151.5 (s, quat. arom. =*C*−O−Bn), 164.7 (s, sec. amide−*C*=O). − (+)-CI MS (NH_3): *m/z* (%) = 412 (40) $[M + H^+]^+$, 385 (87) $[M - CN]^+$, 91 (100) $[C_7H_7]^+$. − $C_{25}H_{21}N_3O_3$ (411.5): calcd. C 72.97, H 5.14, N 10.21; found C 73.18, H 5.24, N 10.74.

(2S)-1,4-Diamino-2-[(2,3-dibenzyloxybenzoyl)amino]butane (**17**$_S$): 2.3 g of the Co_2B mixture [prepared as described for the synthesis of (−)-**5**] was added to a solution of 690 mg (1.68 mmol) of (−)-**16** in 15 ml of THF and 20 ml of methanol. Under vigorous stirring 2.0 g of sodium tetrahydridoborate was added slowly, but in one portion. After about 1 h, an additional portion of 700 mg of Co_2B was added. After the usual workup procedure, 555 mg (79%) of **17**$_S$ was isolated as a dark-colored oil, which was not stable and was therefore used without purification in the next step.

(−)-(2S)-1,2,4-Tris[(2,3-dibenzyloxybenzoyl)amino]butane [(−)-**18**$_S$]: 555 mg (1.32 mmol) of diamine-**17**, 885 mg (2.64 mmol) of 2,3-dibenzyloxybenzoic acid, 850 mg (2.64 mmol) of TBTU and 906 µl (5.29 mmol) of Hünig base was dissolved in 15 ml of THF and 25 ml of methanol and this mixture was stirred for 5 d. After the workup as described for the other triamides and after flash-chromatography (ethyl acetate/*n*-hexane = 3:1), 670 mg (48%) of (−)-**18**$_S$ as a highly viscous oil was collected, TLC: R_f = 0.48, ethyl acetate/*n*-hexane = 3:1, R_f = 0.90, in dichloromethane/methanol = 5:1. − $[\alpha]_D^{20}$ = −23 (*c* = 1, in chloroform). − IR (KBr): $\tilde{\nu}$ = 3350 cm^{-1} (NH), 3055, 3015 (arom. CH), 2920, 2860 (aliph. CH), 1655 (amide-I), 1565 (aryl), 1515 (amide-II). − ^{1}H NMR (301.9 MHz, $CDCl_3$): δ = 7.88−7.83 (m, 3 H, 1-NH, 2-NH, 4-NH), 7.63−7.05 (m, 39 H, 3 × benzoyl, 6 × phenyl), 5.13−4.93 (m, 12 H, O−CH_2−phe), 4.05 (m, 1 H, 2-H), 3.33 (m, 1 H, 1-H_a), 3.19 (m, 2 H, 4-H_2), 2.95 (m, 1 H, 1-H_b), 1.59 (m, 2 H, 3-H_2). − ^{13}C NMR (75.9 MHz, $CDCl_3$): δ = 32.2 (t, C-3), 36.4 (t, C-4), 43.3 (t, C-1), 47.7 d, C-2), 71.2, 71.3, 71.3 (t, O−CH_2−phe), 116.8, 117.0, 117.1, 123.0, 123.2, 123.3, 124.0, 124.1, 124.1 (d, benzoyl-C-4, C-5, C-6), 127.1, 127.5, 127.5 (s, arom. C, benzoyl-C-1), 127.6−128.8 (d, 30 × arom. C, phenyl), 136.2, 136.4, 136.5 , 136.5 (s, 6 × quat. arom. C, phenyl), 146.7, 146.7, 146.8 (s, quat. arom. =*C*−O−), 151.5, 151.6, 151.7 (s, quat. arom. =*C*−O−), 165.2, 165.3, 165.7 (s, sec. amide−*C*=O). − (+)-ESI MS: *m/z* (%) = 1074.6 (100) $[M + Na^+]^+$, 1052.5 (30) $[M + H^+]^+$. − $C_{67}H_{61}N_3O_9$ (1052.2): calcd. C 76.48, H 5.84, N 3.99; found C 76.19, H 5.79, N 3.72.

(−)-(2S)-1,2,4-Tris[(2,3-dihydroxybenzoyl)amino]butane [(−)-**19**$_S$, Myxochelin E]: 330 mg (0.31 mmol) of (−)-**18**$_S$ was dehydrogenated and yielded after the workup 142 mg (89%) of (−)-**19**$_S$ as a highly viscous oil. − $[\alpha]_D^{20}$ = −54.5 (*c* = 0.5, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1} (NH, OH, br.), 2930 (CH), 1630 (amide-I), 1580 (aryl), 1530 (amide-II). − ^{1}H NMR (301.9 MHz, CD_3OD): δ = 8.68 (t, *J* = 5.7 Hz, 1 H, 4-NH), 8.59 (t, *J* = 5.8 Hz, 1 H, 1-NH), 8.43 (d, *J* = 8.2 Hz, 1 H, 2-NH), 7.33 (dd, J_1 = 7.8 Hz, J_2 = 1.3 Hz, 1 H, benzoyl-6-H), 7.26 (dd, J_1 = 7.1 Hz, J_2 = 1.4 Hz, 1 H, benzoyl-6-H), 7.24 (dd, J_1 = 7.3 Hz, J_2 = 1.3 Hz, 1 H, benzoyl-6-H), 6.91 (m, 3 H, 3 × benzoyl-4-H), 6.80 (m, 3 H, 3 × benzoyl-5-H), 4.44 (ddd, J_1 = 4.4 Hz, J_2 = 9.5 Hz, J_3 = 8.1 Hz, 1 H, 2-H), 3.64 (m, 1 H, 4-H_2), 3.60 (m, 1 H, 1-H_a), 3.31 (m, 1 H, 1-H_b, covered by methanol signal), 2.04 (m, 1 H, 3-H_a), 1.93 (m, 1 H, 3-H_b). − ^{13}C NMR (75.9 MHz, CD_3OD): δ = 32.9 (t, C-3), 37.6 (t, C-4), 44.2 (t, C-1), 50.2 (d, C-2), 116.7, 116.8, 116.8 (s, quat. arom. C, benzoyl-C-1), 118.7, 118.8, 118.9, 119.6, 119.6, 119.7, 119.7, 119.8, 119.8 (d, arom. =*C*H−, benzoyl), 147.3, 147.3, 147.4 (s, quat. arom. =*C*−O− , benzoyl-C-2 or C-3), 150.2, 150.3, 150.3 (s, quat. arom. =*C*−O−, benzoyl-C-2 or C-3), 171.6, 172.0, 172.1 (s, sec. amide−*C*=O). − (+)-ESI MS: *m/z* (%) = 534.1 (100) $[M + Na^+]^+$. − $C_{25}H_{25}N_3O_9$ (511.5): calcd. C 58.74, H 4.93, N 8.22; found C 58.62, H 4.80, N 7.91.

Synthesis of Myxochelin F

Dimethyl (2R,2S)-2-Aminoheptane-1,7-dioate Hydrochloride (**20**$_{R,S}$): 5.0 g (28.5 mmol) of D,L-2-aminoheptanedioic acid (Bachem, Swiss), were suspended in approximately 100 ml of dry methanol. HCl gas was introduced until the solution became clear. Stirring was continued for 12 h, and the solution was concentrated in vacuo. Flash chromatography on silica with *n*-hexane/ethyl acetate = 7:3 yielded 4.78 g (70%) of **20**$_{R,S}$. − ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 8.7 (s, br. 3 H, NH_3), 3.91 (q, *J* = 5.5 Hz, 1 H, 2-H), 3.69 (s, 3 H, CH_3−O), 3.54 (s, 3 H, CH_3−O), 2.26 (t, *J* = 7.1 Hz, 2 H, 6-H_2), 1.77 (m, 2 H, 5-H_2), 1.37 (m, 4 H, 3- and 4-H_2). − ^{13}C NMR (75.4 MHz, [D_6]DMSO): δ = 23.7 (t, C-4), 23.9 (t, C-3), 29.6 (t, C-5), 33.0 (t, C-6), 51.4 (d, C-2), 51.9 and 52.9 (q, O−*C*H_3), 170.2 (−*C*=O), 173.5 (−*C*=O). − APCI MS: *m/z* (%) = 520 (50) $[M + H]^+$, 542 (6) $[M + Na]^+$, 317 (100). − $C_9H_{18}ClNO_4$ (239.5): calcd. C 45.09, H 7.52, Cl 14.82, N 5.85; found C 45.07, H 7.66, Cl 15.28, N 5.64.

Dimethyl (2R,2S)-2-[(2,3-Dibenzyloxybenzoyl)amino]heptane-1,7-dioate (**21**$_{R,S}$): 1.5 g (4.5 mmol) of 2,3-dibenzyloxybenzoic acid was dissolved in 50 ml of dichloromethane, and 1.08 g (4.5 mmol) of **20**$_{R,S}$, 1.44 g (4.5 mmol) of TBTU and 1.74 g (13.5 mmol) of Hünig base was added. Stirring was continued for 72 h. For the workup the organic layer was washed with 50 ml of 5% HCl, then with satd. sodium bicarbonate solution and finally with satd. brine. After drying with $MgSO_4$, the organic layer was concentrated in vacuo. Flash chromatography furnished with *n*-hexane/ethyl acetate = 1:1 as the eluent 630 mg (27%) of **21**$_{R,S}$ as a clear oil. − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1}, (NH), 2925 (CH), 1730 (ester CO), 1655 (amide-I), 1560 (amide-II). − APCI MS: *m/z* (%) = 520 (50) $[M + H]^+$, 542 (6) $[M + Na]^+$, 317 (100). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, *J* = 7.5 Hz, 1 H, NH), 7.75−7.15 (m, 13 H, 2 × phenyl and benzoyl), 5.16 (s, 2 H, −O−CH_2−phe), 5.15 (d, *J* = 10.5 Hz, 2 H, −O−CH_2−phe), 4.66 (dt, J_1 = 7.5 Hz, J_2 = 5.5 Hz, 1 H, 2-H), 3.71 (s, 3 H, CH_3−O−), 3.63 (s, 3 H, CH_3−O−), 2.18 (t, *J* = 7.3 Hz, 2 H, 6-H_2), 1.72 (m, 1 H, 3-H_a), 1.53 (m, 1 H, 3-H_b), 1.51 (m, 2 H, 5-H_2), 1.23 (m, 2 H, 4-H_2). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 24.5 (t, C-4), 25.1 (t, C-5), 31.7 (t, C-3), 33.7

(t, C-6), 51.6 (d, C-2), 52.3 and 52.6 (q, O−CH_3), 71.4 and 76.3 (t, O−CH_2), 117.4, 123.5, 124.7 (d, arom. =C−H), 126.8 (s, arom. =C−H), 128.0, 128.7, 128.9, 129.0 (each d, arom. =C−H), 128.5 and 128.8 (s, arom. =C−H), 136.5 and 136.6 (s, arom. =C−H), 147.2 and 152.0 (s, arom. =C−O), 165.2 (s, amide CO), 173.0 and 174.0 (ester CO). − $C_{30}H_{33}NO_7$ (519.6): calcd. C 69.35, H 6.40, N 2.70; found C 68.70, H 6.31, N 3.01.

(2R,2S)-2-[(2,3-Dibenzyloxybenzoyl)amino]heptane-1,7-dioic Acid Diamide (**22**$_{R,S}$): 630 mg (1.2 mmol) of **21**$_{R,S}$ was dissolved in 150 ml of methanol, the solution was cooled to −5°C. During 3 h gaseous NH_3 was bubbled through the cooled solution. While still cold, the solution was put into an autoclave which was kept closed and at room temp. for 3 d. After opening the bottle carefully, the reaction mixture was concentrated in vacuo and 470 mg (80%) of crystalline **22** recovered, m.p. 200−203°C. − IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1} (NH), 3180 and 3250 (NH_2), 2850, 2930, 3020, 3050 (CH), 1640 and 1650 (amide-I), 1520 (amide-II). − CI MS (NH_3): *m/z* (%) = 490 (22) $[M + H]^+$, 472 (18) $[M - H_2O + H]^+$, 455 (55), 365 (100), 337 (56), 275 (81), 247 (48), 11 (76). − ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.44 (d, J = 7.9 Hz, 1 H, N^2-H), 7.59−7.16 (m, 15 H, 2 × phenyl, benzoyl, −NH_2), 7.12 (s, 1 H, amide NH_a), 6.67 (s, 1 H, amide NH_b), 5.21 (s, 2 H, −O−CH_2−phe), 5.04 (d, J = 10.5 Hz, 2 H, −O−CH_2−phe), 4.41 (dt, J_1 = 7.8 Hz, J_2 = 5.3 Hz, 1 H, 2-H), 1.96 (t, J = 7.2 Hz, 2 H, 6-H_2), 1.64 (m, 1 H, 3-H_a), 1.48 (m, 1 H, 3-H_b), 1.42 (m, 2 H, 5-H_2), 1.22 (m, 2 H, 4-H_2). − ^{13}C NMR (75.4 MHz, [D_6]DMSO): δ = 24.8 (t, C-4), 24.9 (t, C-5), 32.3 (t, C-3), 34.9 (t, C-6), 52.6 (d, C-2), 70.4 and 75.1 (t, −O−CH_2−), 116.6, 121.6, 124.3 (d, arom. =C−H), 128.2, 128.2, 128.6, 128.8 (d, arom. =C−H), 136.7 and 136.8 (s, quat. arom. =C−), 145.8 and 151.8 (s, quat. arom. =C−O), 164.5 (s, sec. amide-CO), 173.6 and 174.3 (prim. amide-CO). − $C_{28}H_{31}N_3O_5$ (489.58): calcd. C 69.69, H 6.38, N 8.58; found C 69.50, H 6.29, N 8.48.

(2R,2S)-2-[(2,3-Dibenzyloxybenzoyl)amino]heptane-1,7-dinitrile (**23**$_{R,S}$): 450 mg (0.92 mmol) of **22**$_{R,S}$, 0.3 ml (3.68 mmol) of pyridine and 200 mg (0.62 mmol) of triphosgene in 80 ml of dichloromethane was stirred for 1 h at room temp. The organic layer was extracted with 5% HCl and with satd. brine. The organic layer was dried with $MgSO_4$ and concentrated in vacuo; 350 mg (84%) of oily, pure **23** was isolated. − IR (KBr): $\tilde{\nu}$ = 3330 cm^{-1} (−CH), 2870, 2925, 3020, 3055 (−CH), 2235 (−CN), 1650 (amide-I), 1570 (amide-II). − CI MS (NH_3): *m/z* (%) = 454 (100) $[M + H]^+$, 471 (8) $[M + NH_4]^+$, 427 (39) $[M - CN + H]^+$, 337 (89) $[M - CN - benzyl + H^+]^+$. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.44 (d, J = 7.7 Hz, 1 H, NH), 7.77−7.15 (m, 13 H, 2 × phe, benzoyl), 5.19 (s, 2 H, −O−CH_2−phe), 5.16 (d, J = 10.7 Hz, 2 H, −O−CH_2−phe), 4.91 (q, J = 7.8 Hz, 1 H, 2-H), 2.24 (t, J = 7.1 Hz, 2 H, 6-H_2), 1.55 (m, 2 H, 5-H_2), 1.43 (m, 4 H, 3-, 4-H_2). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 16.9 (t, C-4), 24.5 (t, C-5), 24.7 (t, C-3), 31.8 (t, C-6), 40.1 (d, C-2), 71.5 and 76.8 (t, −O−CH_2−), 118.4 and 119.3 (s, −CN), 118.2, 123.7 and 124.8 (d, arom. =C−H), 125.2, 128.7, 128.7 (s, quat. arom. C), 129.0, 129.2, 129.3 (6 C, d, arom. C), 136.3 and 136.4 (s, arom. C), 147.4 and 151.9 (s, arom. =C−O), 164.8 (sec. amide CO). − $C_{28}H_{27}N_3O_3$ (453.5): calcd. C 74.15, H 6.00, N 9.26; found C 73.66, H 6.10, N 9.20.

(2R,2S)-1,7-Diamino-2-[(2,3-dibenzyloxybenzoyl)amino]-heptane (**24**$_{R,S}$): 300 mg (0.66 mmol) of **23** and 200 mg of Co_2B with 0.5 g of $NaBH_4$ were dissolved in 10 ml of THF and 40 ml of methanol and stirred for 2 h. To this mixture was added 5% HCl (pH = 2−3), to destroy the boride complex, and then ammonia to maintain the mixture at pH = 12. The mixture was extracted several times with 30 ml of chloroform until a spot of the extract on a TLC plate no longer reacted with ninhydrin. The chloroform solution was dried with $MgSO_4$ and concentrated in vacuo. 324 mg of oily diamine **24** was isolated as raw material, which was used for the next reaction without purification.

(2R,2S)-1,2,7-Tris[(2,3-dibenzyloxybenzoyl)amino]heptane (**25**$_{R,S}$): 417 mg (1.23 mmol) of TBTU, 0.43 g (1.23 mmol) of 2,3-dibenzyloxybenzoic acid and 0.44 ml (2.6 mmol) of Hünig base in 50 ml of dichloromethane were added to 300 mg of **24**. Stirring was continued for 72 h. The workup procedure was as described for **22**$_{R,S}$. After flash chromatography (n-hexane/ethyl acetate = 1:1 as the eluent), 311 mg (43% from **23**$_{R,S}$) of **25**$_{R,S}$ was isolated. − IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1} (NH), 2850, 2915, 3020, 3055 (CH), 1630 (amide-I), 1565 (amide-II). − ESI MS: *m/z* (%) = 1094.4 (100) $[M + H]^+$, 1116.5 (65) $[M + Na]^+$, 1132.4 (36) $[M + K]^+$. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (t, J = 6.9 Hz, 1 H, amide NH), 7.87 (t, J = 6.7 Hz, 1 H, sec. amide-NH), 7.85 (d, J = 7 Hz, 1 H, sec. amide N^2−H),7.75−7.09 (m, 39 H, 6 × phe, 3 × benzoyl groups), 5.15−4.93 (m, 12 H, 4 × −O−CH_2−phe), 4.03 (m, 1 H, 2-H), 3.36 (dt, J_1 = 14.1 Hz, J_2 = 5.2 Hz, 1 H, 1-H_a), 3.26 (q, J = 6.5 Hz, 1 H, 1-H_b), 3.17 (q, J = 6.0 Hz, 2 H, 6-H_2), 1.60 (m, 2 H, 5-H_2), 1.02 (m, 4 H, 3-, 4-H_2). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 25.7 (t, C-5), 26.9 (t, C-4), 29.2 (t, C-6), 32.3 (t, C-3), 39.7 (t, C-7), 43.5 (t, C-1), 49.9 (d, C-2), 71.4, 71.4, 71.4, 75.9, 76.2, 76.5 (t, −O−CH_2−phe), 117.0, 117.1, 117.2 (d, arom. =CH−), 123.4, 123.6, 123.7 and 124.4, 124.5, 124.6 (d, arom. =CH−), 127.2, 127.7, 128.0 (s, quat. arom. =C−), 127.8, 127.9, 127.9, 128.5, 128.5, 128.7, 128.7, 128.8, 128.80, 128.85, 128.85, 128.90, 128.90, 128.93, 128.93 (all d, arom. =CH−), 136.57, 136.6, 136.6, 136.63, 136.7, 136.7, (s, quat. arom. =CH−), 146.9, 147.0, 147.1 (s, quat. =C−O), 151.9, 152.0, 152.0 (s, quat. =C−O), 165.2, 165.4, 165.9 (s, sec. amide CO).− $C_{70}H_{67}N_3O_9$ (1094.3): calcd. C 76.83, H 6.17, N 3.84; found C 76.91, H 6.23, N 4.19.

(2R,2S)-1,2,7-Tris[(2,3-dihydroxybenzoyl)amino]heptane [**26**$_{R,S}$, Myxochelin F]: 113 mg (0.1 mmol) of **25**$_{R,S}$ was dissolved in 20 ml of THF and 30 ml of methanol. 40 mg of Pd/C (5%) was added and hydrogenation was continued for 3 h. After filtration through Kieselgur, the solution was concentrated in vacuo and 50 mg (87%) of **26**$_{R,S}$ was isolated. − ESI MS: *m/z* (%) = 576 (100) $[M + Na]^+$. − ^{13}C NMR (100.6 MHz, CD_3OD): δ = 26.9 (t, C-4), 27.8 (t, C-5), 30.3 (t, C-6), 33.1 (t, C-3), 40.4 (t, C-7), 44.6 (t, C-1), 51.2 (d, C-2), 116.9, 116.9, 117.0 (s, quat. arom. =CH−), 118.7, 118.9, 119.0, 119.6, 119.7, 119.7 (all d, arom. =CH−), 147.3, 147.3, 147.4 (s, arom. =C−O−), 150.2, 150.2, 150.3 (s, arom. =C−O−), 171.5, 171.8, 172.0 (s, amide CO). − $C_{28}H_{31}N_3O_9$ (553.6): calcd. C 60.75, H 5.64, N 7.59; found C 60.30, H 5.73, N 7.27.

(+)-(2R)-2,5-Bis[(2,3-dihydroxybenzoyl)amino]pentanenitrile [(+)-**27**$_R$, Myxochelin D_R Nitrile]: 50 mg (67 μmol) of (+)-**11**$_R$ was dehydrogenated under standard conditions, but for only 30 min. It was verified by TLC that no ninhydrin-positive product appeared during that reaction time. After filtration and evaporation of the solvents, 25 mg (97%) of (+)-**27**$_R$ could be recovered. − $[\alpha]_D^{20}$ = +17.4 (c = 1, CH_3OH). − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1} (NH,OH), 2930 (CH), 2230 (CN), 1640 (amide-I), 1590 (C=C arom.), 1530 (amide-II). − ^{1}H NMR (499.8 MHz, CD_3OD): δ = 8.30 (br. t, residual signal, partly exchanged, 1 H, 5-NH), 7.9 (br. d, residual signal, partly exchanged, 1 H, 2-NH), 6.46 (dd, J_1 = 8.2 Hz, J_2 = 1.2 Hz, 1 H, benzoic acid, 1 × 6-H), 6.41 (dd, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1 H, benzoic acid, 1 × 6-H), 6.17 (dd, J_1 = 7.8 HZ, J_2 = 1.2 Hz, 1 H, benzoic acid, 1 × 4-H), 6.13 (dd, J_1 = 7.7 Hz, J_2 = 1.1 Hz, 1 H, benzoic acid, 1 × 4-H), 5.95 (dd, J_1 = 8.2 Hz, J_2 = 8.1 Hz, 1 H, benzoic acid, 1 × 5-H), 5.91 (dd, J_1 = 8.1 Hz, J_2 = 7.8 Hz, 1 H, benzoic acid, 1 × 5-H), 4.32 (dd, J_1 = 7.8 Hz, J_2 = 7.3 Hz, 1 H, 2-H), 2.67 (dd, J_1 = 7.0 Hz, J_2 = 6.6 Hz, 2 H, 5-H_2),

1.25 (nonett, J_1 = 15.5 Hz, J_2 = 7.8 Hz, J_3 = 7.7 Hz, 2 H, 3-H_2), 1.02 (quint, J_1 = 14.8 Hz, J_2 = 7.4 Hz, 2 H, 4-H_2). – ^{13}C NMR (125.7 MHz, CD_3OD): δ = 26.8 (t, C-4), 30.9 (t, C-3), 39.3 (t, C-5), 41.5 (d, C-2), 116.1, 116.7 (s, benzoic acid, 2 × C-1), 118.6, 119.1, 119.6, 119.7, 119.9, 120.4 (d, benzoic acid, 6 × =*C*H–), 119.8 (s, –*C*N), 147.3, 147.4, 150.2, 150.3 (s, benzoic acid, 2 × C-2 and C-3), 171.1, 171.7 (s, sec. amide *C*=O). – $C_{19}H_{19}N_3O_6$ (385.4): calcd. C 59.36, H 4.72, N 10.93; found C 59.10, H 4.84, N 10.52.

(–)-(2S)-2,5-Bis[(2,3-dihydroxybenzoyl)amino]pentanenitrile [(–)-**27**$_S$, Myxochelin D Nitrile]: When the same procedure was used with 50 mg (67 μmol) of (–)-**11**$_S$, 24 mg (93%) of (–)-**27**$_S$ could be isolated. – $[\alpha]_D^{20}$ = –15.5 (*c* = 1, CH_3OH). – $C_{19}H_{19}N_3O_9$ (385.4): calcd. – C 59.36, H 4.72, N 10.93; found C 59.33, H 4.79, N 10.67.

Growth Promotion Tests: The growth promotion of the myxochelins was checked by means of bioassays using different gram-negative bacteria as siderophore indicator strains, as well as strains of mycobacteria and of morganella as listed in the Tables 1–4. The strains of *Salmonella typhimurium* and *stanleyville*, of *E. coli* and of *Klebsiella pneumonia*, *Yersinia enterocolitica* and *Pseudomonas aeruginosa* tested are characterized by special iron-related markers. These strains are blocked in the production of high-affinity siderophores, e.g. enterobactin, aerobactin, yersiniabactin, pyoverdin, pyochelin, and mycobactin for the *mycobacteria*. These strains possess the ferrisiderophore uptake and utilization systems in their entirety or in part. The indicator strains were seeded in iron-deprived nutrient media, e.g. tris-succinate medium or Vogel-Bonner medium containing non-utilizable artificial iron chelators as α,α′-bipyridyl or ethylenediamine-di-(*o*-hydroxyphenylacetic acid), EDDHA. The efficacy of the bioassay media was controlled by siderophores and intermediates of the biosynthesis pathway.

The siderophore to be tested was applicated as loaded filter-paper discs (5 μg/disc) on the surface of the bioassay plate, incubated at 30°C or 37°C overnight and read. A growth zone around the loaded filter paper disc means a positive reaction.[9]

☆ Dedicated to Prof. Dr. *Hans Brockmann* on the occasion of his 60th birthday.

[1] W. Rabsch, R. Reissbrodt, *BIOforum* **1992**, *15*, 10–15.
[2] P. Park, *New Scientist* **1991**, *18*, 1752.
[3] W. Trowitzsch-Kienast, B. Kunze, H. Irschik, V. Wray, H. Reichenbach, G. Höfle, *9. DECHEMA-Jahrestagung der Biotechnologen,* Berlin, **1991**, Referateband p. 382.
[4] F. Kanai, K. Isshiki, H. Nagawana, T. Takeuchi, H. Umezawa, *J. Antibiot.* **1985**, *37*, 3987.
[5] S. W. Heinzman, B. Ganem, *J. Amer. Chem. Soc.* **1982**, *104*, 6801–6802.
[6] W. Trowitzsch-Kienast et al., unpublished.
[7] D. E. Crowley, Y. C. Wang, C. P. P. Reid, P. J. Szaniszlo, *Plant and Soil* **1991**, *130*, 179–198.
[8] H. U. Sieveking, W. Lüttke, *Angew. Chem*. **1969**, *81*, 431–432; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 457-458.
[9] R. Reissbrodt, L. Heinisch, U. Möllmann, W. Rabsch, H. Ulbricht, *BioMetals* **1993**, *6* 155–162.
[10] Dr. K.-U. Bindseil, Fa. AnalytiCon AG, Berlin, H. W. Doerr, J. Cinatl, H. Rabenau, M. Scholz, J. W. Goethe-Universität, Frankfurt a. M., Institut für Medizinische Virologie, to be published.
[11] W. Trowitzsch-Kienast, H. Irschik, H. Reichenbach, V. Wray, G. Höfle, *Liebigs. Ann. Chem.* **1988**, 475–481.
[12] M. Meyer, W. Trowitzsch-Kienast, *J. Mol. Struct. (Theochem)* **1997**, *418*, 93–98.

[97028]