with an anion-exchange resin. Pentasodium polytriphosphate was a product of Sigma Chemical Co. The sodium salts of ATP and ADP were obtained from Boehringer Mannheim. All other chemicals used were high-purity commercial products.

Methods. (A) NMR Kinetic Analysis. ^{31}P NMR spectra were recorded at 121.42 MHz on a Varian XL300. Chemical shifts in ppm are relative (+, downfield) to an external reference of 85% H_3PO_4. Probe temperature was regulated by a variable-temperature accessory. The use of low decoupler power for heteronuclear decoupling at the reported concentrations of reagents and salts in 5-mm NMR tubes did not result in apparent temperature variations.

The solution pH was recorded at 22 or 25 °C with a Radiometer pH meter; adjustments to the desired pH of 0.5-mL samples containing the ligand and substrate were made with ~5 M NaOH or HCl. Kinetic studies were performed by following the time-dependent change in the integrals from the resolved ^{31}P NMR signals of P_α, P_β, and P_γ of ATP and peaks for inorganic phosphate and the phosphoryl derivatives of the macrocycles **1**-**4**. Calibration curves were employed when the integral ratios were not equal because of variations in the ^{31}P relaxation times. By this method of analysis, the calculated standard deviation for the observed rates was 6%.

In a typical experiment, a 0.5-mL solution containing 0.010 or 0.030 M ATP and the polyamine as its hexahydrochloride or hexahydrobromide salt (0.010, 0.015, or 0.030 M) in 10% D_2O/H_2O was placed in the NMR probe in a 5-mm tube at the temperature indicated. By the use of an automated program, an adequate number of acquisitions were accumulated for each sequential spectrum over a period of several half-lives.

(B) HPLC Kinetic Analysis. A Waters Model 501 high-performance liquid chromatograph together with Waters Model 481 absorbance detector and Model 740 data analyzer was used in these studies. Samples were injected on a silica column containing amine groups (Waters Bondpak-NH_2) which, in the reverse phase of operation, gives an ion-exchange-based separation. The mobile phase was a mixture of 15% acetonitrile and 85% 0.05 M ammonium phosphate at pH 4.5.

Aqueous solutions of the substrates, macrocycles, and inhibitor if present in concentrations of 1 μM or more each of substrates at 70 °C with pH adjusted as described in the NMR studies were used. Samples were analyzed by first quenching 20-μL aliquots of the reaction mixture by addition to 40 μL of the mobile phase adjusted to pH 10.5 prior to injection. Resolution of AMP, ADP, ATP, and ATP analogues afforded integral values used in the determination of the concentrations of the individual adenine-containing species at each time point. Analysis was based on multiple samples accumulated over several half-lives with the exception of the studies using excess ATP, where initial velocities were obtained from multiple samples taken during the initial phase of the reaction.

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Stereodifferentiating Complexation of Diastereomeric Cyclic Depsipeptides by Alkali Ions

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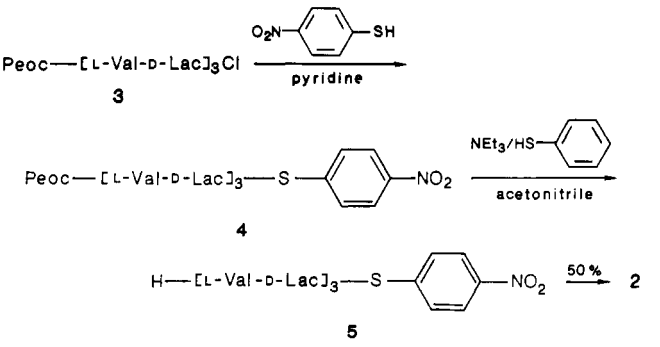
Abstract: The all-L-configurated cyclohexadepsipeptide cyclo[L-Val-L-Lac]$_3$ (**1**) and its diastereomer cyclo[L-Val-D-Lac]$_3$ (**2**) surprisingly show completely different complexing abilities toward alkali cations. As is demonstrated by ^1H and ^7Li NMR spectroscopy, **1** does not form complexes with alkali ions. In contrast, the diastereomer **2** shows marked complex formation with Li^+, Na^+, and K^+ ions. This yes-no diastereoselectivity of alkali ions toward the diastereomeric cyclodepsipeptides **1** and **2** may be of general interest for understanding selective biological ion transport and actions of ion-mediated biological catalysis.

Complexation of chiral molecules plays a decisive role in biological processes, e.g., in the construction of enzyme active sites or in the selective ion transport via chiral carriers or channels. Cyclic depsipeptides consisting of alternating sequences of α-amino acids and α-hydroxy acids, e.g., valinomycin[1] and the enniatines,[2] show strong antibiotic effects, which obviously are closely related to their complexing abilities toward cations.[3] The complexing properties of these antibiotics and of their synthetic analogues depend upon ring size and structure of the constituents and are also sensitive to configurational changes.[4]

We here report on a yes-no decision in the complexation of alkali ions by diastereomeric cyclohexadepsipeptides consisting of either L-valine and L-lactic acid (c-LL) **1** or L-valine and D-lactic acid (c-LD) **2**.

cyclo[L-Val-L-Lac]$_3$ **1** cyclo[L-Val-D-Lac]$_3$ **2**

Scheme I

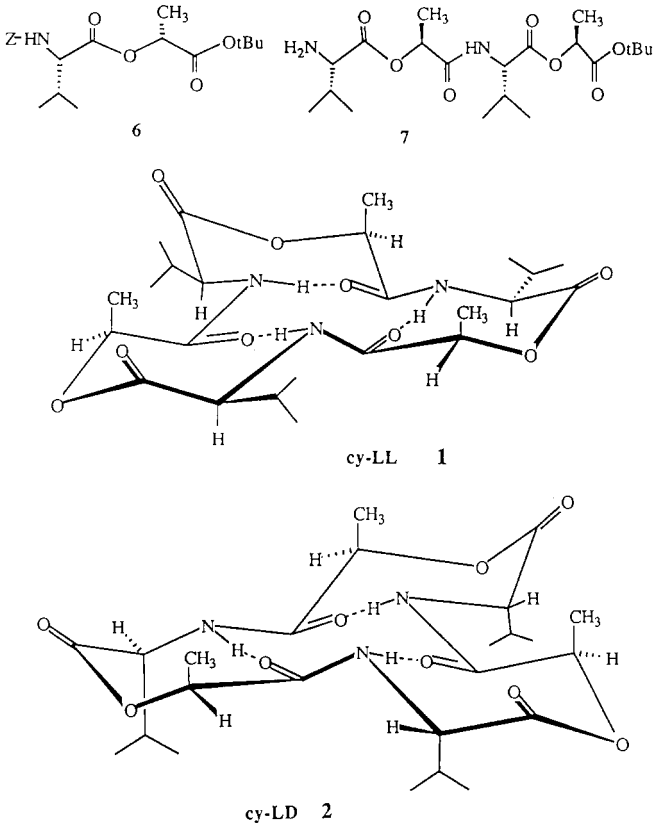


The synthesis of the formerly unaccessible all-L-configurated cyclodepsipeptide **1** with exclusively non-N-methylated amino acid residues was accomplished by applying the *N*-(2-phosphonio)-ethoxycarbonyl- (Peoc-) protected linear depsipeptide chlorides.[5] Analogously, the D-lactic acid containing diastereomer **2** can more easily be cyclized starting from the Peoc-hexadepsipeptide chloride **3**. It is reacted first with *p*-nitrothiophenol in pyridine. The

(1) Brockmann, H.; Schmidt-Kastner, G. *Chem. Ber.* **1955**, *88*, 57.
(2) Plattner, P. A.; Nager, U.; Boller, A. *Helv. Chim. Acta* **1948**, *31*, 594.
(3) Shemyakin, M. M.; Ovchinnikov, Y. A.; Ivanov, V. T.; Kiriushkin, A. A.; Shdanov, G. L.; Ryabova, I. D. *Experientia* **1963**, *19*, 566.
(4) For a review, see: Ovchinnikov, Y. A.; Ivanov, V. T. In *International Review of Science: Organic Chemistry, Series 2*; Rydon, H. N., Ed.; Butterworth: London, 1976; Vol. 6, p 219.
(5) Kunz, H.; Lerchen, H.-G. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 808.

0002-7863/89/1511-6335$01.50/0

Chart I



formed thioester **4** is then N-deblocked by using triethylamine/thiophenol in acetonitrile (Scheme I).

Under the conditions applied, the liberated hexadepsipeptide thioester **5** cyclizes to give **2** in good yield. The L,L- and the L,D-diastereomeric cyclodepsipeptides are characterized by correct elemental analyses and FAB- and FD-MS [m/e = 514 (M^+ + 1)]. Both **1** and **2** give simple 400-MHz ^{1}H NMR spectra in $CDCl_3$ displaying only one signal for each type of proton: the amide and the methine groups of lactic acid and of valine and their side-chain protons. The 100-MHz ^{13}C NMR spectra of **1** and **2** also show only one signal for each type of carbon atom. Interestingly, with the exception of the disappeared NH signals the NMR spectra of **1** and **2** are almost unchanged in deuteriomethanol. This clearly suggests that both **1** and **2** adopt conformations with C_3 symmetry in $CDCl_3$ and in methanol-d_4. The downfield location of the NH doublet (c-LL **1**, δ = 7.15; c-LD **2**, δ = 6.72), the small temperature dependence of their chemical shifts, and the amide I band for associated amides in the IR spectra ($\bar{\nu}$ = 1650 cm^{-1}) are proofs of stable intramolecular hydrogen bonds in **1** and **2**. Differences in the chemical shifts of the methine proton signals of **1** and **2** relative to the corresponding signals of open-chain depsipeptides, e.g., **6** and **7**,[5] suggest that **1** and **2** prefer conformations in chloroform and methanol, which are schematically depicted in Chart I.

In both c-LL **1** and c-LD **2** three equivalent hydrogen bonds build up a central "ring" to which three lactone "rings" ($\bar{\nu}$ = 1755 cm^{-1}) are "annelated". The ^{1}H NMR spectrum of **1** shows a downfield shift of the lactic acid methine signal (δ = 5.24) relative to the corresponding signals of **6** (δ = 4.90) and **7** (δ = 4.92), whereas the valine methine signal is slightly shifted upfield (**1**, δ = 4.25; **6**, δ = 4.35; **7**, δ = 4.58). Therefore, we conclude that the lactic methyl groups are located in quasi-axial position and the valine isopropyl groups are quasi-equatorial. This conclusion is also supported by a strong NOE between the lactic methine proton and the valine methyl groups.

For the diastereomer c-LD **2** the ^{1}H NMR spectrum reveals almost identical chemical shifts for the D-lactic methine signals (δ = 5.25) while the valine methine signal is shifted downfield (δ = 4.46). In its case we find an NOE between the lactic and

Table I. ^{7}Li Chemical Shift of Lithium Iodide in 0.4 mL of Methanol-d_4 in the Presence of Cyclodepsipeptides **1** or **2**

entry	LiI, mg	cyclodepsipeptide, mg	molar ratio	δ/Hz
1	1.8		1:0	0
2	1.5	c-LL **1** 5.7	1:1	0.5
3	1.8	c-LD **2** 3.5	2:1	6.84
4	1.8	c-LD **2** 6.9	1:1	11.23
5	1.8	c-LD **2** 13.8	1:2	17.09
6	1.8	c-LD **2** 20.7	1:3	21.48

Table II. ^{1}H Chemical Shift of Methine Signals of Cyclodepsipeptides **1** and **2**[a] As a Function of Added Alkali Ion Concentration

entry	cyclodepsipeptide	alkali salt	molar ratio	OCH δ, ppm	OCH J, Hz	NCH δ, ppm	NCH J, Hz
1	c-LL **1**		1:0	5.24	6.9	4.25	7.9
2	c-LL **1**	LiCl	1:4	5.25	6.9	4.24	8.0
3	c-LL **1**	KSCN	1:3	5.24	6.9	4.26	8.0
4	cy-LD **2**		1:0	5.25	6.8	4.39	5.4
5	cy-LD **2**	LiCl	2:1	5.24	6.8	4.34	5.6
6	cy-LD **2**	LiCl	1:1	5.23	6.8	4.30	5.8
7	cy-LD **2**	LiCl	1:3	5.21	6.9	4.23	6.1
8	cy-LD **2**	NaBr	2:1	5.15	6.9	4.19	6.3
9	cy-LD **2**	NaBr	1:1	5.14	7.0	4.14	6.4
10	cy-LD **2**	NaBr	1:2	5.12	7.0	4.12	6.5
11	cy-LD **2**	NaBr	1:3	5.12	7.0	4.12	6.5
12	cy-LD **2**	KSCN	2:1	5.17	6.9	4.26	6.1
13	cy-LD **2**	KSCN	1:1	5.13	6.9	4.21	6.3
14	cy-LD **2**	KSCN	1:3	5.09	6.9	4.18	6.4

[a] Concentration ~0.01 M in methanol-d_4.

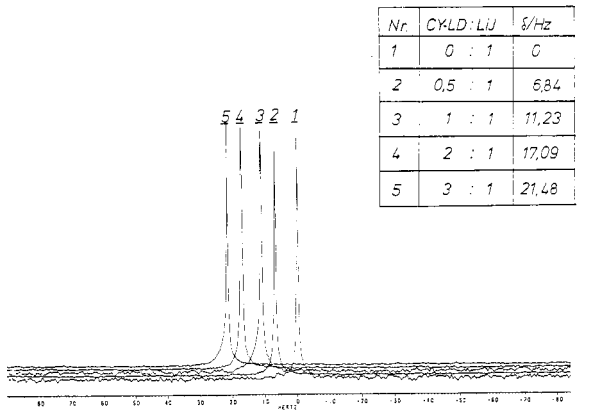


Figure 1. ^{7}Li Chemical shift of lithium iodide in the presence of increasing concentrations of the cyclodepsipeptide **2** in CD_3OD.

the valine methine protons, both located in quasi-equatorial positions. That means, the side-chain alkyl groups prefer quasi-axial positions, thus, avoiding peri-interactions with the neighboring annelated lactone ring.

The complexing behavior of the diastereomeric depsipeptides is investigated by ^{1}H and ^{7}Li NMR spectroscopy in methanol-d_4. The ^{7}Li signal of lithium iodide shifts less than 0.5 Hz downfield after addition of equivalent amounts of c-LL **1** (see Table I). Also, the 400-MHz ^{1}H NMR spectrum of **1** shows no changes after addition of lithium or potassium salts (see Table II). It has to be concluded that **1** does not form complexes with these alkali ions. In contrast, the diastereomer c-LD **2** exhibits marked complexing abilities toward alkali ions. Addition of **2** to a solution of lithium iodide in methanol-d_4 results in a clear downfield shift of the ^{7}Li signal. Surprisingly, up to a ligand to lithium ratio of 3:1 (the solubility of **2** is limiting) the shift is almost porportional to the concentration of the ligand (see Table I and Figure 1). However, even with excess of the salt only one Li signal can be observed. Analogously to similar effects described for cryptands,[6,7]

(6) Cahen, Y. M.; Dye, J. L.; Popov, A. J. *J. Phys. Chem.* **1975**, *79*, 1292.

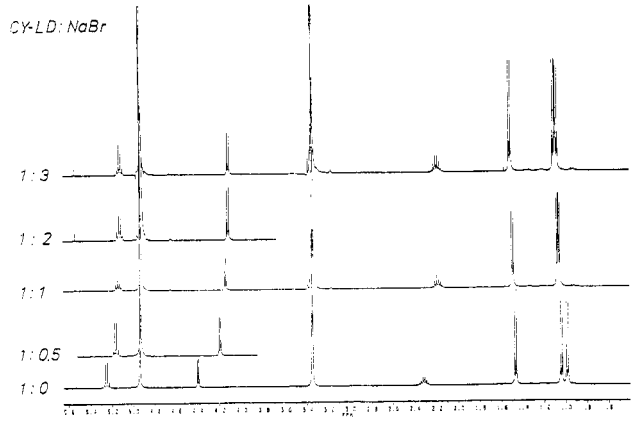


Figure 2. ^{1}H NMR spectrum of the cyclodepsipeptide **2** in CD_3OD in the presence of sodium bromide.

this feature suggests that **2** forms only weak complexes with Li^+, which undergo fast exchange of ions. With equimolar amounts of **2** a downfield shift of ~11 Hz is observed (entry 4). The same amount of **1** exhibits no effect (entry 2).

The fast ion exchange is also substantiated by the sharp ^{1}H NMR signals of c-LD **2** after addition of alkali salts. Obviously, the average C_3 symmetry of **2** is retained in the complexes. The signals shift in dependence of increasing salt concentration, indicating an enhanced complex formation. This is most effective for the methine signals of the lactic and valine units (see Table II and Figure 2).

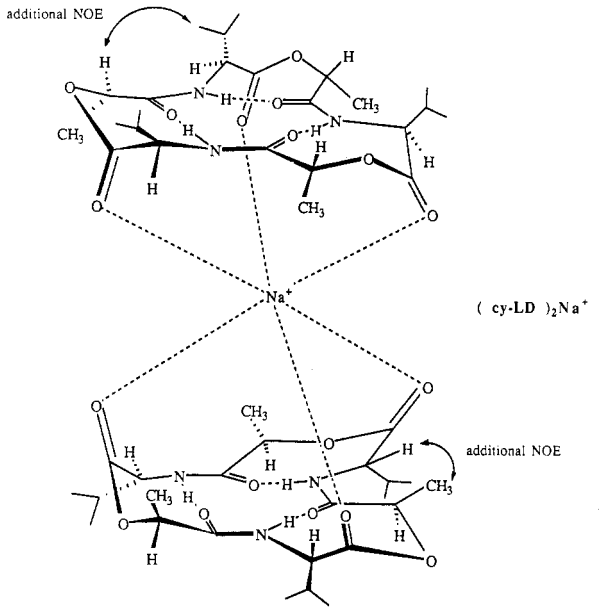
The results quoted in Table II illustrate the fundamental difference in the behavior of **1** and **2**. The LD diastereomer **2** obviously forms the most stable complexes with sodium ions (entries 8–11). The highfield shift of the valine methine signal is of particular significance. In the case of the sodium complex, this shift is already achieved to a great extent at a molar ratio of Na^+:c-LD = 1:2 (entry 8 vs 4), suggesting a preferred sandwichlike 1:2 complex. Of course, a parallel existence of 1:1 complexes cannot be excluded on the basis of the data available.

Potassium ions have a similar but weaker effect. The weakest complex is formed with the lithium ion. The spectroscopic data of the complex formation can be explained by the assumption that the ions approach c-LD **2** from the "methyl" face. Addition of either lithium, sodium, or potassium salt to the solution of c-LD **2** in methanol-d_4 causes a slight downfield shift of the amide carbonyl signal in the 100-MHz ^{13}C NMR spectra of ~1.2 ppm, showing a weak participation of these groups in the complex formation. Since the metal salts and their complexes of **2** are insoluble in chloroform and other aprotic solvents, the influence of the complex formation on the central N–H hydrogen bonds cannot be investigated. The sodium and potassium complexes are mainly enforced by the interaction of the ion with the ester carbonyl oxygens (see Chart II).

In these complexes the conformation of c-LD obviously is changed and the ester carbonyl groups are pulled to a quasi-axial position. Thus, their deshielding effect on the valine methine protons is markedly lowered (see Table II). Another consequence is that the lactic methyl groups are pushed in a more equatorial position. This can be demonstrated by NOE measurements on the sodium complex that show additional NOEs between the α-CH of lactic acid and the valine isopropyl protons on the one hand and the α-CH of valine and the methyl group of lactic acid on the other. Obviously, the movement of the lactic acid methyl group to the quasi-equatorial position is only possible for the c-LD diastereomer **2**. In the case of the LL diastereomer **1** the analogous conformational change is strongly hindered by the peri interactions of the methyl and the isopropyl groups, which cannot occupy quasi-equatorial positions at the same time. After all, the changed conformations of c-LD **2** in its complexes must also have C_3 symmetry, as is demonstrated by the sharp single signals for each type

(7) Lehn, J. M. *Acc. Chem. Res.* **1978**, *11*, 49.

Chart II



of proton or carbon in their NMR spectra.

The contrary complexing behavior of the diastereomeric cyclodepsipeptides **1** and **2** illustrates that simple alkali ions of radial symmetry can selectively differentiate between diastereomeric structures of biological relevance, an effect that may be of fundamental importance in biological selectivity.

Experimental Section

NMR spectra were run at 400 (^{1}H) and 100.6 MHz (^{13}C). Linear depsipeptides are prepared according to or in analogy to earlier descriptions.[5,8,9]

***N*-(Triphenylphosphonioethoxycarbonyl)-L-valyl-L-lactoyl-L-valyl-L-lactoyl-L-valyl-L-lactic acid chloride (Peoc-[L-Val-L-Lac]$_3$-OH)**: mp 135 °C; $[\alpha]^{22}_D$ = −60.3° (*c* 0.75, MeOH). Anal. Calcd for (monohydrate) $C_{45}H_{61}N_3O_{13}PCl$: C, 58.85; H, 6.70; N, 4.57. Found: C, 58.62; H, 6.94; N, 4.85.

***N*-(Triphenylphosphonioethoxycarbonyl)-L-valyl-D-lactoyl-L-valyl-D-lactoyl-L-valyl-D-lactic acid] chloride (Peoc-[L-Val-D-Lac]$_3$-OH)**: mp 135 °C dec; $[\alpha]^{22}_D$ = −12.9° (*c* 1.3, $CHCl_3$). Anal. Calcd for (dihydrate) $C_{45}H_{63}N_3O_{14}PCl$: C, 57.71; H, 6.79; N, 4.49. Found: C, 57.96 H, 7.09; N, 4.21.

***N*-(Triphenylphosphonioethoxycarbonyl)hexadepsipeptide-4-nitrophenyl Esters (4 and Its L,L Diastereomer). General Procedure.** Under a nitrogen atmosphere, the Peoc-hexadepsipeptide (counterion is chloride, see above) (5 mmol) in dry dichloromethane (30 mL) is reacted with 1.27 g (10 mmol) of oxalic acid dichloride for 30 min. The solvent and excess excess oxalic acid chloride are removed in vacuo. To the remaining *N*-(triphenylphosphonioethoxycarbonyl)hexadepsipeptide chloride **3** or its L,L diastereomer respectively dissolved in dry dichloromethane (100 mL) are added 0.5 g (6 mmol) of pyridine and 0.93 g (6 mmol) of 4-nitrothiophenol at −20 °C. After being stirred for 15 h at room temperature, the solution is extracted twice with 10 mL of 0.5 N HCl with 10 mL of water and dried over sodium sulfate. Removal of the solvent affords a yellowish oil, which can be obtained as an amorphous precipitate from chloroform (60 mL) by addition of ether (300 mL) and petroleum ether (300 mL). The thioester **4** and its L,L diastereomer may contain ~5% of the starting Peoc-hexadepsipeptide. The sensitive compounds are immediately used for the cyclization reactions.

***N*-Triphenylphosphonioethoxycarbonyl)-L-valyl-L-lactoyl-L-valyl-L-lactoyl-L-valyl-L-lactic acid-4-nitrophenyl-thioester chloride**: yield 86%; ^{1}H NMR δ 8.2, 7.5 (2 m, 4 H, 4-nitrophenyl); 7.7 (m, 17 H, C_6H_5-P, Peoc, 2 NH); 7.3 (d, J = 9 Hz, 1 H, NH); 5.4–4.8 (m, 3 H, OCH); 4.4–3.2 (m, 7 H, NCH, CH_2CH_2, Peoc); 2.5–2.0 (m, 3 H, β-CH, Val); 1.4 (m, 9 H, CH_3, Lac); 0.9 (m, 18 H, CH_3, Val).

(8) Lerchen, H.-G. Ph.D. Thesis, Universität Mainz, West Germany, 1987. Details of the syntheses of linear depsipeptides will be dealt with in a separate paper.

(9) Selective deprotections of Peoc-desipeptides and activation of Peoc-amino acids and -hydroxy acids have earlier been described: Kunz, H.; Bechtolsheimer, H.-H. *Liebigs Ann. Chem.* **1982**, 2068; *Synthesis* **1982**, 303.

N-Triphenylphosphonioethoxycarbonyl)-L-valyl-D-lactoyl-L-valyl-D-lactoyl-L-valyl-D-lactic acid-4-nitrophenyl-thioester chloride 4: yield 87%; ^{1}H NMR: δ 8.2, 7.55 (2 m, 4 H, 4-nitrophenyl); 7.7 (m, 16 H, C_6H_5-P, Peoc, NH); 7.62, 7.32 (2 d, J = 9 Hz, NH); 5.4–5.0 (m, 3 H, OCH); 4.7–3.8 (m, 7 H, NC H, CH_2CH_2, Peoc); 2.35 (m, 2 H, 2 β-CH, Val); 2.11 (m, 1 H, β-H, Val); 1.45 (m, 9 H, CH_3, Lac); 0.95 (m, 18 H, CH_3, Val).

Cyclohexadepsipeptides—General Cyclization Procedure. A solution of 4.15 g (4 mmol) of the Peoc-hexadepsipeptide-4-nitrophenylthio ester (**4** or its all-L diastereomer) in acetonitrile (100 mL) is added dropwise to a mixture of 3.2 g (32 mmol) of triethylamine, 5.7 g (52 mmol) of thiophenol, and 4 L of acetonitrile. The solution is stirred for 4 weeks. After removal of the solvent, the remaining oily residue is eluted from 100 g of silica gel (Kieselgel 60, E. Merck, Darmstadt, West Germany), first with chloroform (800 mL), then with ethyl acetate (800 mL), and finally with methanol (400 mL). Concentration of the ethyl acetate eluate affords the crude cyclohexadepsipeptide. The purification is carried out as follows:

Cyclo-L-lactoyl-L-valyl-L-lactoyl-L-valyl-L-lactoyl-L-valine (cyclo[L-Val-L-Lac]$_3$ = c-LL 1). The crude product is purified by flash chromatography on silica gel (60 g, 230–400 mesh, E. Merck, Darmstadt, West Germany) with chloroform/ethyl acetate (4:1, v/v). Detection of the cyclic depsipeptide is carried out by analytical HPLC. The desired c-LL is eluted from silica gel (5 μm) with heptane/acetone (6:4, v/v) and a flow of 2 mL/min after a retention time of 2.52 min. Concentration of the corresponding fractions and recrystallization of the remaining residue from dichloromethane/pentane affords the desired all-L-configurated cyclodepsipeptide c-LL: yield 500 mg (24%); mp 95 °C; $[\alpha]^{22}_D$ = −100.0° (c 0.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.16 (d, J = 7.5 Hz, 3 H, NH); 5.20 (q, J = 6.9 Hz, 3 H, OCH); 4.27 (dd, J = 7.5 Hz, 3 H, NCH); 2.14 (d sept, 6.7, 7.5 Hz, 3 H, β-CH, Val); 1.51 (d, J = 6.9 Hz, 9 H, CH_3, Lac); 0.99, 0.96 (2 d, J = 6.7 Hz, 18 H, CH_3, Val); ^{13}C NMR. δ 171.0 (N—C=O); 168.5 (O—C=O); 71.0 (CH, Lac); 59.1 (α-CH, Val); 30.4 (β-CH, Val); 19.0, 18.4, 18.0 (CH_3); FAB-MS, m/z 514 (M^+ + 1, 100). Anal. Calcd for $C_{24}H_{39}N_3O_9$: C, 59.12; H, 7.66; N, 8.18. Found: C, 56.27; H, 7.51; N, 7.98.

A side product (retention time, 2.46 min) is isolated with less than 5% total yield. It is a nonsymmetrical cyclohexadepsipeptide diastereomer, as is indicated by FAB-MS [m/z = 514 (M^+ + 1)] and by ^{1}H NMR: ^{1}H NMR (CD_2Cl_4) δ 7.63 (d, J = 9 Hz, NH); 6.62 (d, J = 7.7 Hz, NH); 6.56 (d, J = 4.8 Hz, NH); 5.19 (q, J = 6.9 Hz, OCH); 5.10 (q, J = 7.2 Hz, OCH); 5.09 (q, J = 7.2 Hz, OCH); 4.39 (dd, J = 2 × 9 Hz, N-CH); 4.18 (dd, J = 2 × 7.7 Hz, NCH); 3.99 (dd, J = 4.8, 7.8 Hz, NCH); 2.0 (m, 3 H, β-CH, Val); 1.48 (d, J = 6.9 Hz, CH_3, Lac); 1.42 (d, J = 7.2 Hz, CH_3, Lac); 1.40 (d, J = 7.2 Hz, CH_3, Lac); 0.95–0.79 (m, 18 H, CH_3, Val). This side product is not a different conformer but a diastereomer, as is indicated by temperature-dependent NMR (T, 353 K).

Cyclo-D-lactoyl-L-valyl-D-lactoyl-D-valyl-D-lactoyl-L-valine (cyclo[L-Val-D-Lac]$_3$ = c-LD 2). The crude product is purified by flash chromatography on silica gel (70 g, 230–400 mesh) with a mixture of chloroform/ethyl acetate (2:1, v/v) and finally with pure ethyl acetate. The detection is performed by analytical HPLC (RP 18, methanol/water 7:3 v/v, flow 0.8 mL/min.) The desired cyclodepsipeptide **2** is eluted with a retention time of 2.29 min. Concentration of the corresponding fractions and recrystallization of the remaining residue from dichloromethane/pentane affords the pure c-LD (1.02 g, 50%): mp 198 °C; $[\alpha]^{22}_D$ = −66.2° (c 0.17, chloroform); ^{1}H NMR ($CDCl_3$) δ 6.72 (d, J = 8.4 Hz, 3 H, NH); 5.21 (q, J = 6.8 Hz, 3 H, OCH); 4.46 (dd, J = 8.4, 5.0 Hz, 3 H, NCH); 2.27 (d sept, J = 5.0, 6.9 Hz, 3 H, β-CH, Val); 1.43 (d, J = 6.8 Hz, 9 H, CH_3, Lac); 0.97, 0.93 (2 d, J = 6.9 Hz, 18 H, CH_3, Val); ^{13}C NMR δ 170.5 (N—C=O); 170.0 (O—C=O); 71.3 (CH, Lac); 57.7 (α-CH, Val); 30.5 (β-CH, Val); 19.2, 17.9, 17.0 (CH_3); FAB-MS, 514 (M^+ + 1, 100). Anal. Calcd for $C_{24}H_{39}N_3O_9$: C, 56.12; H, 7.66; N, 8.18. Found: C, 55.82; H, 7.66; N, 8.13.

Table III. ^{13}C NMR Chemical Shifts of c-LD in Dependence of the Alkali Ion Concentration

group	c-LD	c-LD/ LiCl (1:5)	c-LD/ NaBr (1:3)	c-LD/ KSCN (1:3)
N—C=O	173.4	174.3	174.1	174.1
O—C=O	171.5	171.1	173.9	173.8
O—CH	72.3	70.9	72.2	72.3
N—CH	59.2	60.5	60.2	59.9
β-CH	31.4	30.7	30.4	30.7
CH_3-Lac	19.8	19.4	19.5	19.6
CH_3-Val	18.4	19.4	19.5	19.4
	17.4	18.4	18.1	18.1

Investigation of Complex Formation of the Cyclodepsipeptide c-LL 1. The all-L-configurated c-LL (20 mg, 0.039 mmol) is dissolved in methanol-d_4. LiCl (20 mg, 4.7 mmol) or KSCN (50 mg, 5.1 mmol) is added. Changes of chemical shifts are recorded by ^{1}H and ^{13}C NMR spectroscopy. The resulting most significant changes in chemical shifts are summarized in Table II, entries 1–3.

Investigation of Li$^+$ Complex Formation of c-LL 1 and c-LD 2 by ^{7}Li NMR Spectroscopy. Lithium iodide (1.8 mg, 0.014 mmol) is dissolved in methanol-d_4 (0.4 mL). Different equivalents of c-LL **1** or c-LD **2** are added as is quoted in Table I. The resulting ^{7}Li chemical shifts are summarized in Table I.

Investigation of Complex Formation of c-LD 2 with Alkali Ions by Means of ^{1}H and ^{13}C NMR Spectroscopy. Three standard solutions are prepared Solution I, 20 mg (0.04 mmol) of c-LD/2 mL of methanol-d_4; solution II, 0.25 mmol of alkali salt/5 mL of methanol-d_4; solution III, 0.5 mmol of alkali salt/5 mL of methanol-d_4. Alkali salts are LiCl, NaBr, or KSCN. In order to obtain the desired molar ratios of c-LD and the alkali ions, the solutions are combined in the following manner:

c-LD	alkali ion	I, mL	II, mL	III, mL
1	0.5	0.5	0.1	
1	1	0.5	0.2	
1	2	0.5	0.2	0.1
1	3	0.5	0.2	0.2

Chemical shifts of the α-CH proton signals and the coupling constants in dependence of the ligand/ion ratio are summarized in Table II, entries 4–14. The changes in ^{13}C NMR chemical shifts are shown in Table III.

Registry No. 1, 92269-64-2; **2**, 121249-37-4; **3**, 121250-44-0; **3** (all-L diastereomer), 92269-70-0; **4**, 121249-38-5; **4** (all-L diastereomer), 121249-40-9; Peoc-[L-Val-L-Lac]$_3$-OH·Cl$^-$, 121176-43-0; Peoc-[L-Val-D-Lac]$_3$-OH·Cl$^-$, 121249-39-6; Li, 7439-93-2; K, 7440-09-7; Na, 7440-23-5; ^{7}Li, 13982-05-3.

Supplementary Material Available: ^{7}Li NMR spectra of cyclodepsipeptide **1** and ^{1}H NMR spectra of cyclodepsipeptide **2** (3 pages). Ordering information is given on any current masthead page.