[27] J. Kapp, K. Schade, A. M. El-Nahasa, P. von R. Schleyer, *Angew. Chem.* **1996**, *108*, 2373; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2236.

[28] Crystal data for **3** ($C_{15}H_{37}P_3Si_4$): $M_r = 422.7$, monoclinic, space group $P21/c$ (no. 14), $a = 9.887(3)$, $b = 20.310(3)$, $c = 14.129(2)$ Å, $\beta = 108.21(2)^\circ$, $V = 2695.1$ Å^3, $Z = 4$. $Mo_{(K\alpha)}$ radiation, data collection with an Enraf-Nonius CAD4 diffractometer. Of 4727 reflections measured, 2127 were observed ($I > 2\sigma(I)$). $R = 0.083$, $wR2 = 0.182$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-101 105. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Facile Synthesis of Cyclic Tetrapeptides from Nonactivated Peptide Esters on Metal Centers**

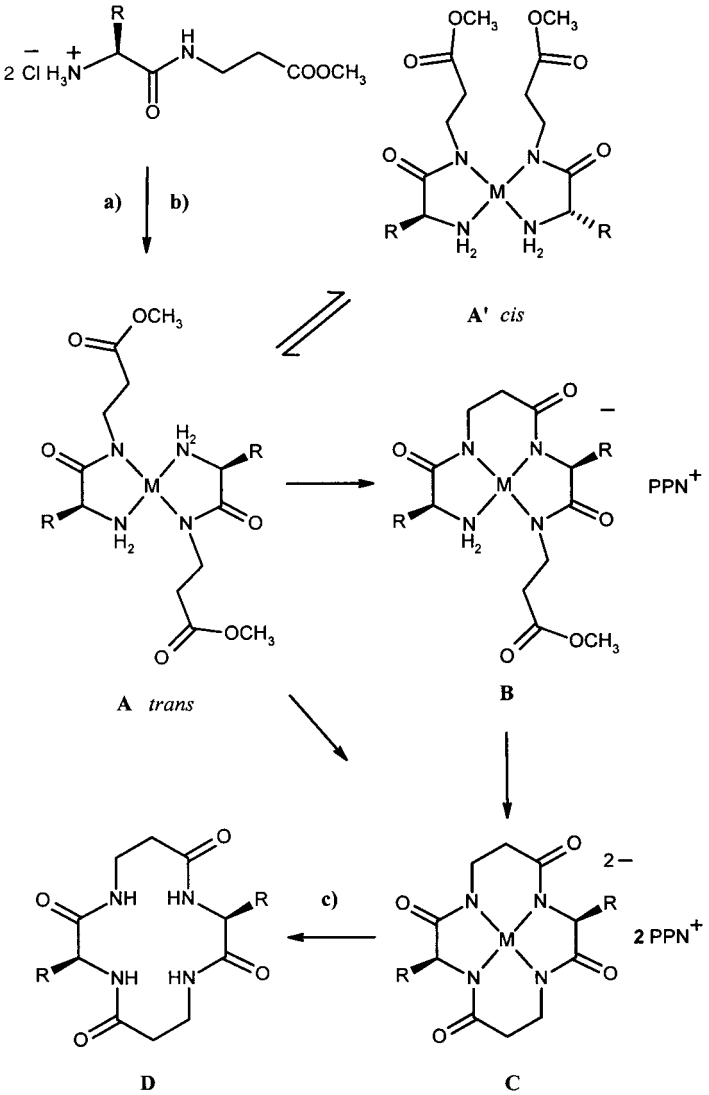
Katharina Haas, Werner Ponikwar, Heinrich Nöth, and Wolfgang Beck*

Dedicated to Professor Dieter Seebach on the occasion of his 60th birthday

The search for a comprehensive understanding of the structure–activity relationship for conformationally rigid peptides has led to a greater interest in cyclic peptides.[1, 2] Synthetic cyclopeptides are interesting target molecules owing to their biological activity, their model character for conformational analyses, and their potential as drugs, among other things.[3] Synthetic analogues of hormones[4] show the link between reduced peptide flexibility due to cyclization and increased receptor specificity in a particularly impressive fashion. As the metabolic degradation of peptides begins preferably at the C or N terminals,[1] cyclic peptides are expected to have a longer biological availability than their linear analogues. Cyclic tetrapeptides with biological activity are also found in nature.[5]

Present methods for the cyclization of peptides generally require a completely protected peptide precursor, which is cyclized in solution or at a solid phase by using a coupling agent, as well as a strongly activated acyl component. In order to avoid intermolecular oligomerizations, the cyclization of small peptides, in particular (e.g., tetrapeptides), must be performed under high dilution conditions.[6]

In the course of our continuing studies into the formation of oligopeptides at metal centers,[7] we have found a facile, metal-mediated synthesis of 12-, 14-, 16-, and 18-membered cyclic tetrapeptides or macrolactams from readily accessible nonactivated dipeptide ester precursors. The reaction of Ni^{II}, Pd^{II}, and Cu^{II} salts with two equivalents of dipeptide ester in methanol in the presence of NaOMe as base results in dianionic complexes, which can be isolated by precipitation with suitable cations (e.g., Ca^{2+}, Cs^+, $PPN^+ = (Ph_3PNPPh_3)^+$ (**1**–**11**, see Scheme 2). The cyclization of the dipeptides coordinated to the metal probably occurs as shown in Scheme 1. The crucial step is the same as that assumed for the oligomerization of peptides at metal centers,[7, 8] namely



Scheme 1. Postulated mechanism of the metal-supported synthesis of C_2-symmetrical cyclic tetrapeptides, exemplified for a 14-membered ring. a) $Na_2[PdCl_4]$, $NiCl_2 \cdot 6H_2O$ or $CuCl_2 \cdot 2H_2O$, 6 NaOMe, MeOH, 24 h, 65 °C; b) [PPN]Cl, H_2O; c) HCl/MeOH (saturated), room temperature, 15 min.

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[**] Metal Complexes of Biologically Relevant Ligands, Part 99. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We wish to thank Prof. W. Steglich and Dr. W. Spahl, München, for obtaining the mass spectra. Part 98: A. Böhm, B. Schreiner, N. Steiner, R. Urban, K. Sünkel, K. Polborn, W. Beck, *Z. Naturforsch.*, in press.

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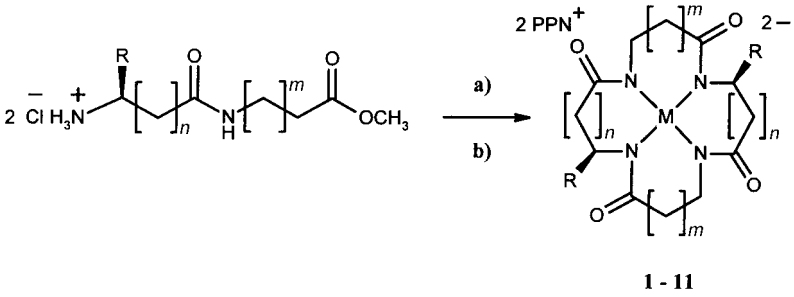
the nucleophilic attack of a coordinated terminal amino group on the carbonyl group of the neighboring *trans*-coordinated dipeptide ester in **A**. It is not clear whether the cyclization in the planar complex is a concerted process, as the hypothetical monoanionic intermediate **B** was not isolated. The prerequisite for such a double head-to-tail condensation is that in the initial step the dipeptide esters coordinate to the metal in a *trans* fashion. It can be assumed that the neutral *trans*-bis(dipeptide ester) complex **A** is in equilibrium with the corresponding *cis* complex **A′** and that during the reaction an isomerization to the *trans* compound takes place.[9] Several neutral *trans*-bis(dipeptide ester) complexes **A** with M = Pd were isolated and the complex *trans*-[Pd(Gly-β-Ala($-H^+$)-OMe)$_2$] was characterized by X-ray structure analysis.[10] The liberation of the tetrapeptide **D** from complex **C** can be achieved nearly quantitatively by using saturated methanolic HCl, and this was exemplified for **8** (see Experimental Section).

In order to determine the limitations of this method, we allowed dipeptide esters of α-, β-, γ-, and δ-amino acids to react with Pd^{II}, Ni^{II}, and Cu^{II} as templates (Scheme 2, Table 1).



Scheme 2. Synthesis of the C_2-symmetrical cyclotetrapeptide complexes **1**–**11**. a) $Na_2[PdCl_4]$, $NiCl_2 \cdot 6H_2O$ or $CuCl_2 \cdot 2H_2O$, 6 NaOMe, MeOH, 24 h, 65 °C; b) [PPN]Cl, H_2O.

The X-ray crystal structure analysis[11] of $\mathbf{1} \cdot 8H_2O \cdot 3CH_3CN$ shows that the cyclic tetrapeptide is bound to the metal through the four deprotonated amide nitrogen atoms. The palladium center and the N atoms lie in a plane (sum of the angles around the Pd atom is 360°) (Figure 1). The anions in **1** form layers in the crystal lattice, in which the carbonyl groups are linked by hydrogen bonds to the water molecules that are arranged between the anions (Figure 2). The acetonitrile molecules similarly fill the space between the PPN cations.

Table 1. C_2-symmetrical cyclotetrapeptide complexes prepared according to Scheme 2.

Compound	M	*n*	*m*	R	Number of atoms in the ring
1	Pd	0	1	H	14
2	Pd	0	1	CH_3	14
3	Pd	0	1	CH_2OH	14
4	Pd	0	2	H	16
5	Pd	0	3	H	18
6	Pd	1	1	H	16
7	Ni	0	0	CH_3	12
8	Ni	0	1	H	14
9	Ni	0	1	CH_3	14
10	Ni	0	1	$CH(CH_3)_2$	14
11	Cu	0	1	H	14

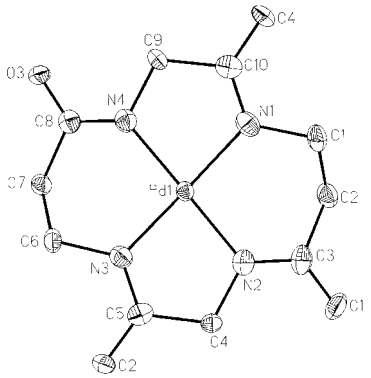


Figure 1. Molecular structure of an anion in the crystal of **1**. Selected bond lengths [Å] and angles [°]: Pd1 – N1 1.974(4), Pd1 – N2 1.994(4), Pd1 – N3 1.971(4), Pd1 – N4 1.991(4), N1 – C1 1.484(6), N1 – C10 1.291(7), C1 – C2 1.513(8), C2 – C3 1.569(8), C3 – O1 1.266(7); N1-Pd1-N2 97.9(2), N2-Pd1-N3 83.2(2), N3-Pd1-N4 96.2(2), N4-Pd1-N1 82.7(2).

The orange-colored Ni^{II} complexes **8**–**10** are diamagnetic, which indicates a planar arrangement of the nitrogen atoms around the metal center. The results of the cyclizations can be correlated with the ionic radii of the metals: for instance, the condensation of dipeptide esters of α-amino acids to a 12-membered cyclic tetrapeptide occurs only at Ni^{II} (ionic radius 63 pm), while the larger 16- and 18-membered cyclopeptides are only formed at the "larger" template[12] Pd^{II} (ionic radius 78 pm). All compounds listed in Table 1 have been characterized by elemental analyses, IR, ^1H, and ^{13}C NMR spectroscopy, as well as by mass spectrometry (Table 2). The Na salt of the complex anion of **11** had already earlier been directly obtained from cyclo(β-alanylglycyl-β-alanylglycyl).[13] Cyclic β-tetrapeptides such as that in **6** have been reported by Seebach et al.[14]

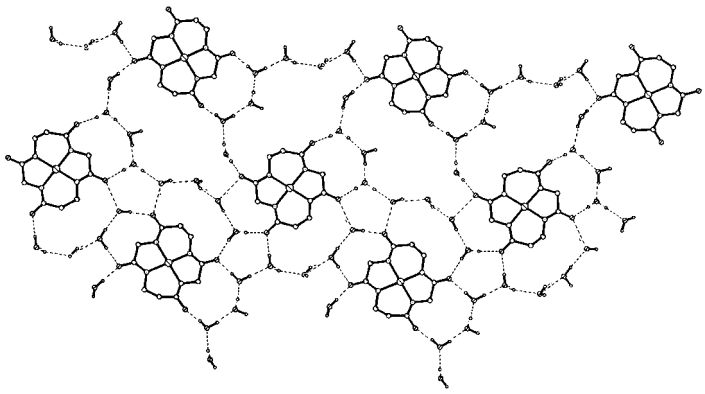


Figure 2. Segment of the layer structure formed by the anions of **1**.

Tetrapeptide esters can be employed instead of two dipeptide esters. This leads to complexes such as **12**, which must form via the open-chain intermediate **E** (Scheme 3).

The synthesis of cyclotetrapeptides described herein represents a facile procedure that requires neither a protecting group nor an activated group or a coupling reagent. It can be performed as a one-pot process. High dilution of the reaction

Table 2. Spectroscopic data for **1**–**11** and **12**.[a]

1: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.64-7.34$ [m, 60 H, PPN^+], 3.87 [s, 4 H, Gly], 3.12 [ψ-t, $^3J = 5.66$ Hz, 4 H, NCH_2CH_2CO], 2.17 [ψ-t, $^3J = 5.66$ Hz, 4 H, NCH_2CH_2CO]; ^{13}C-NMR (100 MHz, CD_3OD): $\delta = 179.70$, 173,56 [C=O], 58.31 [Gly], 43.40, 42.15 [β-Ala]; IR (KBr): $\tilde{\nu} = 1568.7$ (vs), 1548.1 cm^{-1}(vs) [amide-I] ; MS (– FIB): *m/z* (%): 358 (100) [M^{2-}H], 896 (8) [$M^{2-}PPN^+$]; yield 78 %

2: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.72-7.50$ [m, 60 H, PPN^+], 4.28 [q, $^3J = 6.87$ Hz, 2 H, $CH(CH_3)$], 3.52 [ABCD system, ddd, $^2J_{AB} = 13.36$ Hz, $^3J_{AC} = {}^3J_{AD} = 3.95$ Hz, 2 H, $NCH_AH_BCH_CH_DCO$], 2.85 [ddd, $^2J_{AB} = 13.36$ Hz, $^3J_{BC} = 12.35$ Hz, $^3J_{BD} = 2.60$ Hz, 2 H, H_B], 2.36 [ddd, $^2J_{CD} = 15.79$ Hz, $^3J_{BC} = 12.35$ Hz, $^3J_{AC} = 3.95$ Hz, 2 H, H_C], 2.20 [ddd, $^2J_{CD} = 15.79$ Hz, $^3J_{AD} = 3.95$ Hz, $^3J_{BD} = 2.60$ Hz, 2 H, H_D], 1.35 [d, $^3J = 6.87$ Hz, 6 H, $CH(CH_3)$]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 182.81$, 173.09 [C=O], 63.94 [$CH(CH_3)$], 43.27 [CH_2], 20.87 [$CH(CH_3)$]; IR (KBr): $\tilde{\nu} = 1562.2$ (vs), 1548.4 cm^{-1}(vs) [amide-I]; MS (– ESI): *m/z* (%): 387 (100) [M^{2-}H], 926 (23) [$M^{2-}PPN^+$]; yield 72 %

3: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.72-7.50$ [m, 60 H, PPN^+], 4.46 [dd, $^3J = 7.51$ Hz, $^3J = 3.25$ Hz, 2 H, $CHCH_2OH$], 3.95 [dd, $^2J = 10.23$ Hz, $^3J = 3.25$ Hz, 2 H, $CHHCHOH$], 3.72 [dd, $^2J = 10.23$ Hz, $^3J = 7.51$ Hz, 2 H, $CHHCHOH$], 3.54 [ddd, $^2J_{AB} = 12.36$ Hz, $^3J_{AC} = {}^3J_{AD} = 4.13$ Hz, 2 H, H_A], 2.91 [ddd, $^2J_{AB} = 13.57$ Hz, $^3J_{BC} = 12.36$ Hz, $^3J_{BD} = 1.01$ Hz, 2 H, H_B], 2.39 [ddd, $^2J_{CD} = 15.12$ Hz, $^3J_{BC} = 12.36$ Hz, $^3J_{AC} = 4.13$ Hz, 2 H, H_C], 2.24 [ABCD system, ddd, $^2J_{CD} = 15.12$ Hz, $^3J_{AD} = 4.13$ Hz, $^3J_{BD} = 1.01$ Hz, 2 H, $NCH_AH_BCH_CH_DCO$], 1.15 and 1.16 [2s, 1.2 H, OH]; ^{13}C NMR (68 MHz, CD_3OD): $\delta = 175.45$, 178.98 [C=O], 70.91 [$CHCH_2OH$], 69.15 [$CHCH_2OH$], 43.11, 42.83 [CH_2CH_2]; IR (KBr): $\tilde{\nu} = 3429.6$ (vs, br.) [OH], 1570.6 (vs), 1541.9 cm^{-1} (vs) [amide-I]; MS (– ESI): *m/z* (%): 419 (100) [M^{2-}H], 956 (22) [$M^{2-}PPN^+$]; yield 62 %

4: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.74-7.53$ [m, 60 H, PPN^+], 4.02 [s, 4 H, CH_2], 3.17 [ψ-t, $^3J = 6.44$ Hz, 4 H, $NCH_2CH_2CH_2CO$], 2.52 [ψ-t, $^3J = 6.44$ Hz, 4 H, $NCH_2CH_2CH_2CO$], 1.70 [ψ-quint., $^3J = 6.44$ Hz, 4 H, $NCH_2CH_2CH_2CO$]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 180.81$, 177.90 [C=O], 57.674 [CH_2], 45.34 [$NC^1H_2C^2H_2C^3H_2CO$], 36.93 [C^3], 27.88 [C^2]; IR (KBr): $\tilde{\nu} = 1565.7$ (vs), 1536.3 cm^{-1} (vs) [amide-I]; MS (– ESI): *m/z* (%): 387 (100) [M^{2-}H], 925 (15) [$M^{2-}PPN^+$]; yield 48 %

5: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.72-7.49$ [m, 60 H, PPN^+], 3.36 [s, 4 H, CH_2], 2.85 [ψ-t, $^3J = 7.30$ Hz, 4 H, $NCH_2CH_2CH_2CH_2CO$], 2.17 [ψ-t, $^3J = 7.30$ Hz, 4 H, $NCH_2CH_2CH_2CH_2CO$], 1.57 [ψ-quint., $^3J = 7.30$ Hz, 4 H, $NCH_2CH_2CH_2CH_2CO$], 1.51–1.43 [m, 4 H, $NCH_2CH_2CH_2CH_2CO$]; ^{13}C NMR (68 MHz, CD_3OD): $\delta = 183.07$, 181.74 [C=O], 49.97 [CH_2], 46.86 [$NC^1H_2C^2H_2C^3H_2C^4H_2CO$], 39.19 [$C^4$], 31.57 [$C^2$], 25.51 [$C^3$]; IR (KBr): $\tilde{\nu} = 1578.6$ (vs), 1564.2 cm^{-1} (vs) [amide-I]; yield 17 %

6: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.72-7.50$ [m, 60 H , PPN^+], 2.98 [m, 8 H, CH_2CH_2], 2.52 [m, 8 H, CH_2CH_2]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 175.44$ [C=O], 42.80, 41.27 [CH_2CH_2]; IR (KBr): $\tilde{\nu} = 1547.5$ cm^{-1} [amide-I]; MS (– ESI): *m/z* (%): 387 (100) [M^{2-}H], 926 (5) [$M^{2-}PPN^+$]; yield 78 %

7: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.71-7.50$ [m, 60 H, PPN^+], 4.18 [q, br., $^3J = 7$ Hz, 2 H, $CH(CH_3)$], 3.38 [d, br., $^2J = 12$ Hz, 2 H, HCH], 3.10 [d, br., $^2J = 12$ Hz, 2 H, HCH], 1.38 [d, $^3J = 7$ Hz, 6 H, $CH(CH_3)$]; IR (KBr): $\tilde{\nu} = 1580.3$ (vs), 1586.6 cm^{-1} (vs) [amide-I]; yield 21 %

8: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.73-7.51$ [m, 60 H, PPN^+], 3.59 [s, 4 H, CH_2], 2.83 [ψ-t, $^3J = 5.89$ Hz, 4 H, NCH_2CH_2CO], 2.05 [ψ-t, $^3J = 5.89$ Hz, 4 H, NCH_2CH_2CO]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 179.65$, 175.13 [C=O], 56.11 [CH_2], 40.60, 38.90 [CH_2CH_2]; IR (KBr): $\tilde{\nu} = 1568.0$ (vs), 1540.2 cm^{-1} (vs) [amide-I]; MS (– ESI): *m/z* (%): 311 (100) [M^{2-}H], 848 (19) [$M^{2-}PPN^+$]; yield 96 %

9: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.92-7.51$ [m, 60 H, PPN^+], 3.69 [q, $^3J = 6.90$ Hz, $CH(CH_3)$], 3.22 [ABCD-system, ddd, br., $^2J_{AB} = 12.73$ Hz, $^3J_{AC} = {}^3J_{AD} = 3.48$ Hz, 1 H, $NCH_AH_BCH_CH_DCO$], 2.33 [ψ-t, br., $^2J_{AB} = {}^3J_{BC} = 12.73$ Hz, $^3J_{BD}$ not resolved, 1 H, H_B], 2.23 [ddd, $^2J_{CD} = 15.27$ Hz, $^3J_{AC} = 4.15$ Hz, $^3J_{BC} = 12.73$ Hz, 1 H, H_C], 1.96 [ddd, br., $^2J_{CD} = 15.27$ Hz, $^3J_{BD} = 2.51$ Hz, 1 H, H_D], 1.19 [d, $^3J = 6.90$ Hz, 3 H, $CH(CH_3)$]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 183.28$, 175.10 [C=O], 60.77, [$CH(CH_3)$], 40.66, 39.93 [CH_2CH_2], 21.06 [$CH(CH_3)$]; IR (KBr): $\tilde{\nu} = 1562.5$ (vs), 1541.0 cm^{-1} (vs) [amide-I]; yield 94 %

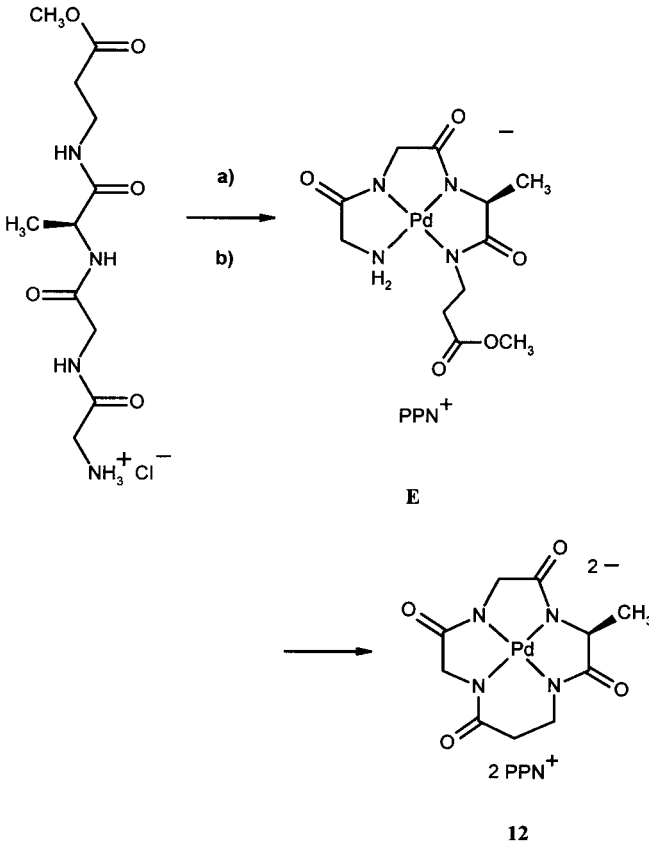
Table 2 (continued)

10: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.75-7.43$ [m, 60 H, PPN^+], 4.07 [d, $^3J = 3.06$ Hz, 2 H, $CHCH(CH_3)_2$], 3.22–3.19 [m, 2 H, $NHCHCH_2CO$], 2.34–2.26 [m, 4 H, $NHCHCH_2CO$, $CHCH(CH_3)_2$], 2.09–1.97 [m, 4 H, NCH_2CH_2CO], 1.33 and 1.17 [2d, $^3J = 6.89$ Hz, 6 H, $CHCH(CH_3)_2$]; ^{13}C NMR (68 MHz, CD_3OD): $\delta = 181.45$, 175.28 [C=O], 68.86 [$CHCH(CH_3)_2$], 40.53, 40.41 [CH_2CH_2], 34.34 [$CHCH(CH_3)_2$], 20.98, 20.16 [$CHCH(CH_3)_2$]; IR (KBr): $\tilde{\nu} = 1564.1$ (vs), 1541.1 cm^{-1} (vs) [amide-I]; MS (– FAB/mNBA): *m/z* (%):395 (100) [M^{2-}H], 932 (1) [$M^{2-}PPN^+$]; yield 86 %

11: IR (KBr): $\tilde{\nu} =$ 1575.3 (vs), 1542.7 cm^{-1} (vs) [amide-I]; MS (– FAB, mNBA): *m/z* (%): 316 (100) [M^{2-}H], 853 (3) [$M^{2-}PPN^+$]; yield 37 %

12: ^{1}H NMR (400 MHz, CD_3OD): $\delta = 7.63-7.44$ [m, 60 H, PPN^+], 3.85 [q, $^3J = 6.43$ Hz, 1 H, $CH(CH_3)$], 3.76 [d, $^2J = 18.4$ Hz, 1 H, CH_2], 3.69 [d, $^2J = 18.4$ Hz, 1 H, CH_2], 3.34–3.21 [m, 4 H, CH_2CH_2 and CH_2], 2.19 [t, $^3J = 6.42$ Hz, 2 H, CH_2CH_2]; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 186.32$, 181.66, 180.82, 178.65 [C=O], 55.70, 60.01 [2 Gly], 51.32 [$CH(CH_3)$], 46.58, 41.33 [CH_2CH_2], 20.12 [$CH(CH_3)$]; IR (KBr) $\tilde{\nu} = 1603.0$ (sh), 1587.4 (vs), 1566.7 cm^{-1} (vs) [amide-I]; yield 45 %

[a] CD_3OD as internal standard, ^{13}C NMR shifts of the anion.



Scheme 3. Metal-supported cyclization of a tetrapeptide ester to form **12**. a) $Na_2[PdCl_4]$, 5 NaOMe, MeOH, 24 h, 65 °C; b) [PPN]Cl, H_2O.

mixture is also not necessary. We are currently investigating the extension of this method to other metal ions. Furthermore longer peptide chains will be studied to determine whether they can also be cyclized by using a template-supported reaction.

Experimental Section

The peptide ester hydrochlorides were prepared according to standard methods.[15]

General method for the preparation of **1**–**12**: Dipeptide ester hydrochloride (2 mmol) or tetrapeptide ester hydrochloride (1 mmol) and metal

  1433-7851/98/3708-1088 $ 17.50+.50/0

salt ($Na_2[PdCl_4]$, $NiCl_2 \cdot 6H_2O$ or $CuCl_2 \cdot 2H_2O$) (1 mmol) were dissolved in methanol (40 mL). A methanolic sodium methanolate solution (6 or 5 mmol, respectively) was added dropwise. The mixture was then heated to 65 °C for 24 h, after which [PPN]Cl (2 mmol) was added. Upon the addition of water, the products **1**–**12** were obtained as crystalline solids.

Liberation of the cyclotetrapeptide from **8**: HCl gas was passed through a solution of **8** (2 mmol) in absolute MeOH (2 mL) at room temperature. After 15 min, the cyclic peptide precipitated, was washed three times with as little as possible absolute MeOH and subsequently dried. ^{1}H NMR (400 MHz, $CF_3COOD/CDCl_3$ 8/2): $\delta =$ 4.08 (s, 4H, Gly), 3.69 (t, $^3J =$ 5.28 Hz, 4H, CH_2CH_2), 2.70 (t, $^3J =$ 5.28 Hz, 4H, CH_2CH_2); IR (KBr): $\tilde{\nu} =$ 3329.3 (vs), 1646.1 (vs), 1548.0 cm^{-1} (vs); MS (EI): *m*/*z* (%): 256 (100) [M^+].

Received: September 17, 1997 [Z10937IE]
German version: *Angew. Chem.*, **1998**, *110*, 1200–1203

Keywords: copper · cyclopeptides · nickel · palladium · peptides

[1] H. Kessler, *Angew. Chem.* **1982**, *94*, 509–520; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 512–523.
[2] U. Schmidt, *Nachr. Chem. Tech. Lab.* **1989**, *37*, 1034–1043.
[3] R. Haubner, D. Finsinger, H. Kessler, *Angew. Chem.* **1997**, *109*, 1440–1456; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1374–1389; C. M. Deber, V. Madison, E. R. Blout, *Acc. Chem. Res.* **1976**, *9*, 106–112.
[4] K. D. Kopple, *J. Pharm. Sci.* **1972**, *61*, 1345–1356; V. J. Hruby, *Life Sci.* **1982**, *31*, 189–199; F. Al-Obedi, A. M. del L. Castrucci, M. E. Hadley, V. J. Hruby, *J. Med. Chem.* **1989**, *32*, 2555–2561.
[5] a) D. Seebach, O. Bezençon, B. Jaun, T. Pietzonka, J. L. Matthews, F. N. M. Kühnle, W. B. Schweizer, *Helv. Chim. Acta* **1996**, *79*, 588–608; b) R. E. Shute, M. Kawai, D. A. Rich, *Tetrahedron* **1988**, *44*, 685–693; c) U. Schmidt, *Pure Appl. Chem.* **1986**, *58*, 295–304; U. Schmidt, J. Langner, *J. Peptide Res.* **1997**, *49*, 67, and references therein.
[6] a) E. R. Blout, *Biopolymers* **1981**, *20*, 1901–1902; N. J. Manesis, M. Goodmann, *J. Org. Chem.* **1987**, *52*, 5331–5341; b) J. S. McMurray, *Tetrahedron Lett.* **1991**, *32*, 2040–2048; c) U. Schmidt, A. Lieberknecht, H. Gressner, J. Talbiersky, *J. Org. Chem.* **1982**, *47*, 3261–3264; d) L. A. Carpino, A. El-Faham, F. Albericio, *Tetrahedron Lett.* **1994**, *35*, 2279–2282; S. A. Kabee, N. A. Solé, C. R. Johnson, D. Hudson, G. Barang, F. Albericio, *ibid.* **1993**, *34*, 1549–1552; e) W. F. De Grado, E. T. Kaiser, *J. Org. Chem.* **1980**, *45*, 1295–1300; *ibid.* **1982**, *47*, 3258–3261; G. Ösapay, A. Profit, J. W. Taylor, *Tetrahedron Lett.* **1990**, *31*, 6121–6124; G. Ösapay, J. W. Taylor, *J. Am. Chem. Soc.* **1990**, *112*, 6046–6051; M. Xu, N. Nishino, H. Mihara, T. Fujimoto, N. Izumiya, *Chem. Lett.* **1992**, 191–194; N. Nishino, M. Xu, H. Mihara, T. Fujimoto, *Tetrahedron Lett.* **1992**, *33*, 1479–1482.
[7] W. Beck, R. Krämer, *Angew. Chem.* **1991**, *103*, 1492–1493; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1467–1469; R. Krämer, M. Maurus, K. Polborn, K. Sünkel, C. Robl, W. Beck, *Chem. Eur. J.* **1996**, *2*, 1518–1526.
[8] M. Wagatsuma, S. Terashima, S. Yamada, *Tetrahedron* **1973**, *29*, 1497–1502.
[9] See for example: P. Comba, T. W. Hambley, G. A. Lawrance, L. L. Martin, P. Renold, K. Varnagy, *J. Chem. Soc. Dalton Trans.* **1991**, 277–283.
[10] K. Haas, E.-M. Ehrenstorfer-Schäfers, K. Polborn, W. Beck, unpublished results.
[11] Single crystals of $\mathbf{1} \cdot 8H_2O \cdot 3CH_3CN$ in the form of large colorless prisms were obtained by slowly cooling a saturated solution of **1** in acetonitrile. Monoclinic, space group $P2_1/n$, $Z = 4$. $M_r = 1703.0$, crystal dimensions $0.3 \times 0.23 \times 0.2$ mm^3. The crystals were covered with perfluoroether oil, mounted on a glass fiber and centered at -80 °C; all reflections in the range $2\theta =$ 2–58° were measured by using a Siemens P4 diffractometer equipped with a CCD area detector. $a =$ 17.0397(3), $b = 19.2297(3)$, $c = 26.5244(4)$ Å, $\beta = 102.14(1)°$, $V =$ 8497(1) Å^3, $F(000) =$ 3560, $\mu = 0.36$ mm^{-1}; R(int) = 0.0819, 15916 symmetry-independent reflections, 10598 observed with $I > 4\sigma(I)$; refinement: 1078 variables, $R = 0.068$, $R_w = 0.119$, GOF = 1.112, largest residual electron density: 0.74 e Å^{-3}; all calculations using the program SHELXL-97. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-100954. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
[12] N. F. Curtis, *Coord. Chem. Rev.* **1968**, *3*, 3–47; D. S. C. Black, A. J. Hartshorn, *ibid.* **1972**, *9*, 219–274; J. J. Christensen, D. J. Eatough, R. M. Izatt, *ibid.* **1974**, *74*, 351–384; D. H. Busch, N. A. Stephenson, *ibid.* **1990**, *100*, 119–154; P. Comba, N. F. Curtis, G. A. Lawrance, A. M. Sargeson, B. W. Skelton, A. H. White, *Inorg. Chem.* **1986**, *25*, 4260–4267.
[13] J. S. Rybka, D. W. Margerum, *Inorg. Chem.* **1980**, *19*, 2784–2790; *ibid.* **1981**, *20*, 1453–1458.
[14] D. Seebach, J. L. Matthews, A. Meden, T. Wessels, C. Baerlocher, L. B. McCusker, *Helv. Chim. Acta* **1997**, *80*, 173–182.
[15] M. Bodanszky, *Principles of Peptide Synthesis*, 2nd ed., Springer, Berlin, **1994**; V. Dourtoglou, B. Gross, *Synthesis* **1984**, 572–574.

The $[Ag\{Se_2C_2(CN)_2\}(Se_6)]^{3-}$, $[Sb\{Se_2C_2(CN)_2\}_2]^{3-}$, and $[As(Se)_3(CH_2CN)]^{2-}$ Anions: Facile Formation of the Maleonitrilediselenolate (mns) Ligand, $[Se_2C_2(CN)_2]^{2-}$**

Donna M. Smith, Thomas E. Albrecht-Schmitt, and James A. Ibers*

Dedicated to Professor Achim Müller on the occasion of his 60th birthday

Despite numerous reports[1, 2] of complexes containing the maleonitriledithiolate (mnt) ligand, $[Ni\{Se_2C_2(CN)_2\}_2]^{2-}$ is the only reported example of a complex containing the Se analogue maleonitrilediselenolate (mns).[3] Its synthesis involves several steps as well as the use of CSe_2 and dicyanoacetylene, both difficult reagents to synthesize and use.[3] We report here facile syntheses of the complexes **1** and **2**, which

$[K([2.2.2]cryptand)]_3[Ag\{Se_2C_2(CN)_2\}(Se_6)]$ (**1**)

$[K([2.2.2]cryptand)]_3[Sb\{Se_2C_2(CN)_2\}_2] \cdot 2CH_3CN$ (**2**)

$[K([2.2.2]cryptand)]_2[As(Se)_3(CH_2CN)]$ (**3**)

contain the mns ligand, and the synthesis of **3**, as its formation is suggestive of possible mechanisms for the formation of **1** and **2**.

Reaction of $[\{IrCl(cod)\}_2]$ (cod = (*Z*,*Z*)-1,5-cyclooctadiene), $AgBF_4$, and $[K([2.2.2]cryptand)]_2[Se_n]$ ($n = 3, 5, 6$) in liquid ammonia followed by extraction of the residue with CH_3CN results in the formation of **1**. The anion in **1** (Figure 1)

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[**] This research was sponsored by the U.S. National Science Foundation (grants CHE 95-31232 and DMR 91-14934).