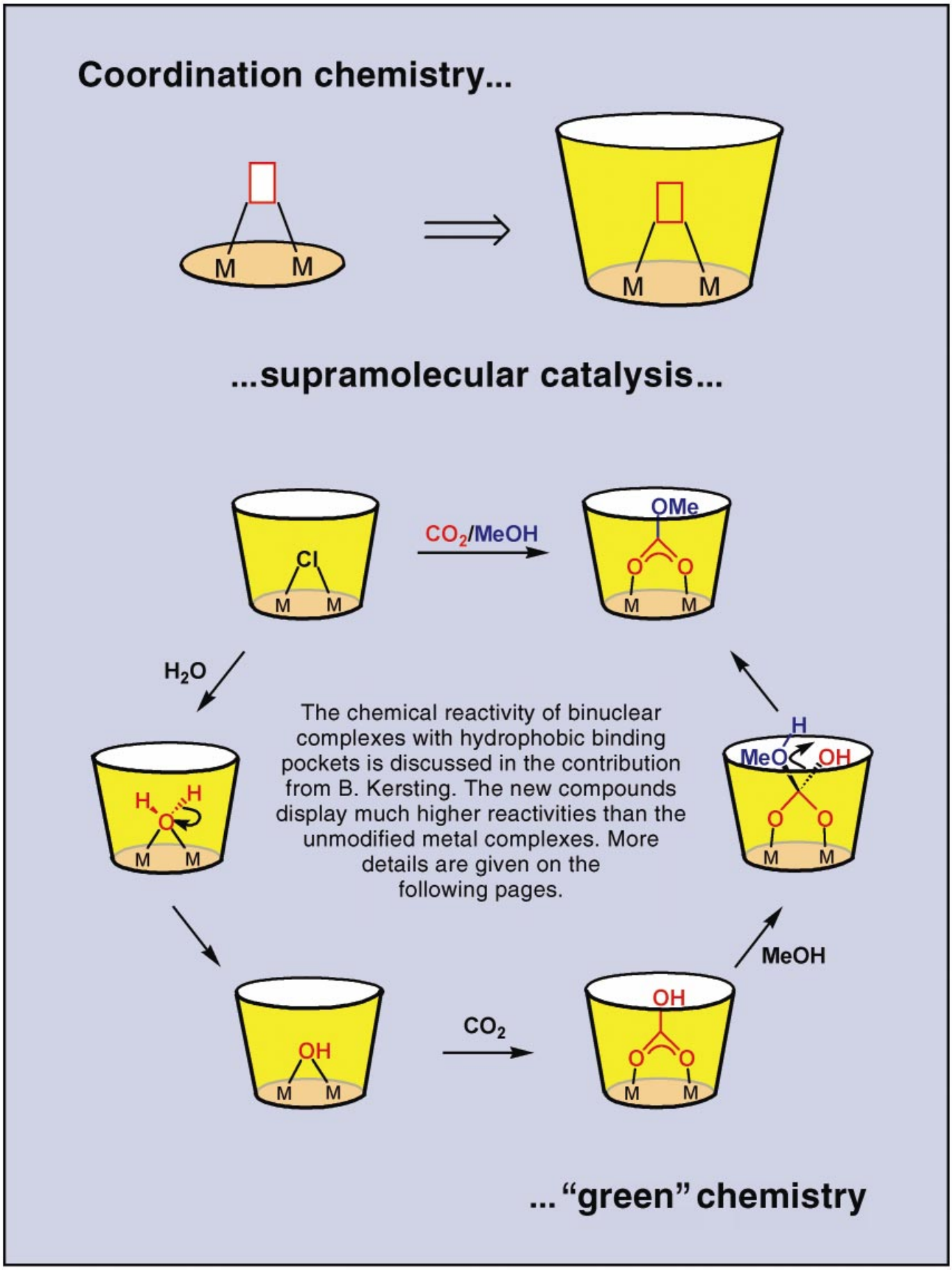
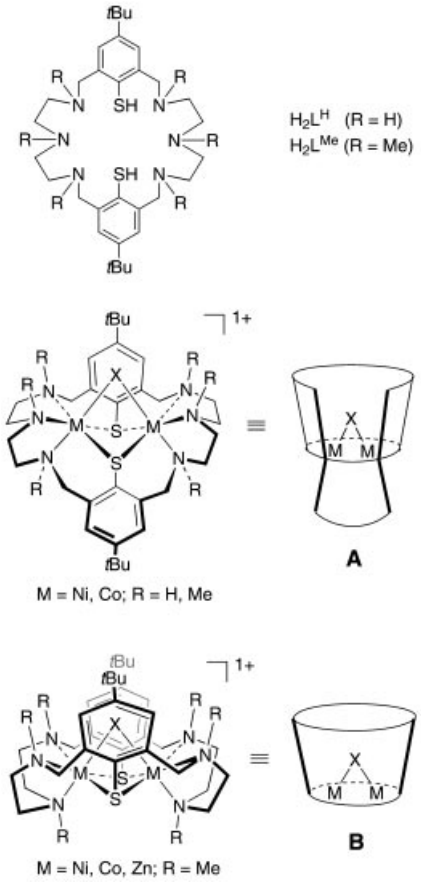


 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 2001 1433-7851/01/4021-3987 $ 17.50+.50/0

Carbon Dioxide Fixation by Binuclear Complexes with Hydrophobic Binding Pockets**

Berthold Kersting*

Metal complexes with hydrophobic binding pockets currently attract much interest, because of their unusual chemical reactivities. Most compounds are mononuclear species and have been used for the stabilization of reactive intermediates,[1] for selective organic transformations,[2] or as catalysts for reactions which depend on the reaction medium.[3] Some complexes have also been designed to mimic the hydrophobic binding site of metalloproteins.[4] These observations led us to study binuclear complexes of peralkylated amine – thiophenol macrocycles hoping to generate a hydrophobic cavity about a free coordination site. We report here the synthesis and structures of binuclear Ni^{II}, Co^{II}, and Zn^{II} complexes of the permethylated macrocycle $(L^{Me})^{2-}$ (see Scheme 1) and demonstrate their remarkable ability in the fixation and transformation of carbon dioxide.



Scheme 1. Structures of the ligands and schematic representation of the structures of the corresponding metal complexes **A** and **B** (X = binding site of the complexes).

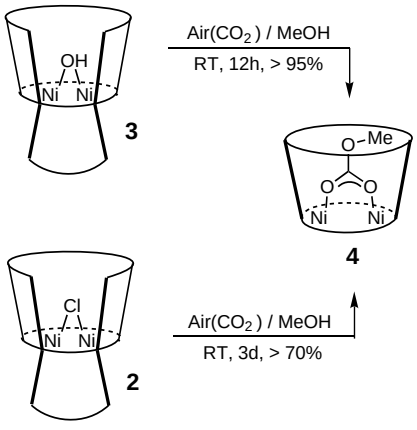
It has already been demonstrated that utilization of the permethylated ligand $(L^{Me})^{2-}$ in place of $(L^{H})^{2-}$ drastically alters the ease of substitution of the bridging ligands in binuclear nickel complexes of the type **A** (Scheme 1).[5] Thus, the hydroxo-bridged complex **3** (Table 1), which represents the starting point of this investigation, can be prepared in high yields by reaction of the μ-Cl species **2** with sodium hydroxide in MeOH.

Table 1. Synthesized complexes, their structure type, and selected spectroscopic data.[a]

Complex	Structure type (d(M···M) [Å])	$\nu(RCO_2^-)$ [cm^{-1}]
$[(L^{H})Ni^{II}_2(\mu\text{-Cl})]^+$ **1**	**A** (3.098)[5]	
$[(L^{Me})Ni^{II}_2(\mu\text{-Cl})]^+$ **2**	**A** (3.201)[5]	
$[(L^{Me})Ni^{II}_2(\mu\text{-OH})]^+$ **3**	**A** (3.037)[5]	
$[(L^{Me})Ni^{II}_2(\mu\text{-}O_2COMe)]^+$ **4**	**B** (3.491)[6]	1633, 1332
$[(L^{Me})Ni^{II}_2(\mu\text{-}OH_2)]^{2+}$ **5**	not known[8]	
$[(L^{Me})Ni^{II}_2(\mu\text{-}O_2COH)]^+$ **6**	**B** (3.471)[6]	1675, 1378
$[(L^{Me})Ni^{II}_2\{\mu\text{-}O_2P(OH)_2\}]^+$ **8**	**B** (3.569)[6]	1200, 1130
$[(L^{Me})Ni^{II}_2(\mu\text{-}O_2COEt)]^+$ **9**	**B** (3.485)[6]	1641, 1316
$[(L^{Me})Ni^{II}_2(\mu\text{-}O_2COR)]^+$ **10**[b]	**B** (3.490)[6]	1642, 1313
$[(L^{Me})Co^{II}_2(\mu\text{-Cl})]^+$ **11**	**A** (3.180)[6]	
$[(L^{Me})Co^{II}_2(\mu\text{-}O_2COMe)]^+$ **12**	**B** (3.452)[6]	1630, 1336
$[(L^{Me})Co^{II}_2(\mu\text{-}O_2COEt)]^+$ **13**	**B** (3.467)[6]	1634, 1319
$[(L^{Me})Zn^{II}_2(\mu\text{-}O_2CH)]^+$ **14a**	**B**[c]	
$[(L^{Me})Zn^{II}_2(\mu\text{-}O_2CMe)]^+$ **14b**	**B** (3.427)[6]	1585, 1428
$[(L^{Me})Zn^{II}_2(\mu\text{-}O_2CPh)]^+$ **14c**	**B**[c]	
$[(L^{Me})Ni^{II}_2(\mu\text{-}O_2CMe)]^+$ **15**	**B** (3.483)[6]	1588, 1426

[a] The complexes were isolated as ClO_4^- or BPh_4^- salts. [b] R = CH_2CH_2OH. [c] The experimentally determined structures of **14b** and **15** suggest that complexes **14a** and **14c** adopt the form **B**.

We have now found that complex **3** fixes carbon dioxide from air in the form of the methyl carbonate complex **4** in nearly quantitative yields [Eq. (1)]. The product was identified by IR spectroscopy (Table 1) and by X-ray crystal structure analysis.[6] Surprisingly, exposure of a solution of the μ-Cl complex **2** in MeOH to air also gives **4** in high yields [Eq. (2)]. Complex **1**, on the other hand, was found to be unreactive, which is presumably due to the more hydrophilic



[*] Dr. B. Kersting
Institut für Anorganische und Analytische Chemie
Universität Freiburg
Albertstrasse 21, 79104 Freiburg (Germany)
Fax: (+49) 761-203-5987
E-mail: kerstber@sun2.ruf.uni-freiburg.de

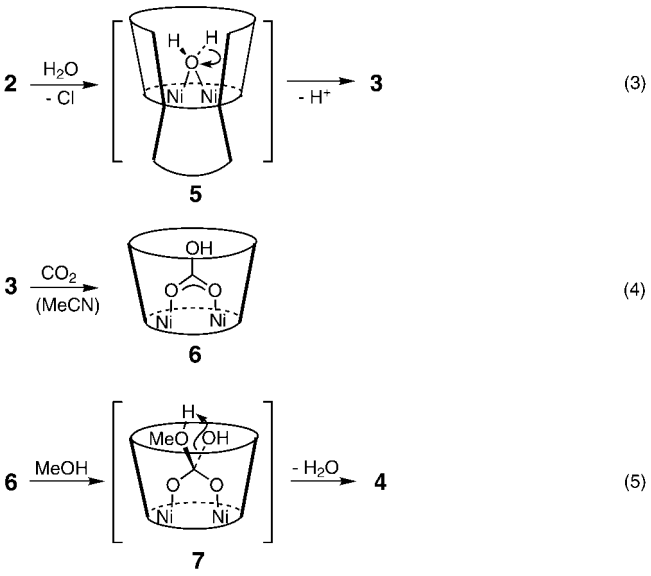
[**] This work was supported by the Deutsche Forschungsgemeinschaft (Project No. KE 585/3-1). The author thanks Prof. Dr. H. Vahrenkamp for his support of this work.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 2001 1433-7851/01/4021-3988 $ 17.50+.50/0

environment at the binding site. Note that the amine functions in **2** are methylated, precluding the possibility of hydrogen bonding.

In general, the fixation of carbon dioxide is only possible in a basic reaction medium, where a nucleophilic M–OH or M–OR unit attacks the electrophilic carbon atom of the CO_2 molecule.[7] The reaction in Equation (2) proceeds under neutral to slightly acidic conditions and is thus rather unusual. A proposed mechanism for the formation of **4** is given in Equations (3) – (5).



(3)

(4)

(5)

The μ-aqua complex $[(L^{Me})Ni_2(\mu\text{-}OH_2)]^{2+}$ (**5**) can be formulated as the first intermediate [Eq. (3)].[8] The aqua ligand is activated by two Lewis-acidic Ni^{II} centers, and this should favor its deprotonation to give the known μ-OH complex **3**. The production of HCl during the formation of **4** was ascertained readily by pH indicator paper. We reasoned that a bicarbonate complex was the next intermediate and sought to trap this species by carrying out the reaction in Equation (4) in MeCN as solvent. The tetraphenylborate salt of complex **6** crystallized in a form suitable for X-ray structure analysis. In the solid state the HCO_3^- group bridges the two Ni^{II} centers in a symmetric fashion. Note that the structure of complex **6** is of the type **B**, which features a much more pronounced bowl-shaped binding pocket than in complexes of the type **A**. The methanolysis reaction in Equation (5) can then be considered as the final reaction step. This was confirmed by the experiment. The smooth conversion of **6** into **4** suggests that the two metal ions activate the carboxyl carbon atom of the HCO_3^- ligand such that it is more susceptible for nucleophilic attack by the solvent.

Substitution reactions at carboxyl carbon atoms proceed via tetrahedral intermediates. In the case of **6**, the intermediate is the monomethyl orthocarbonate complex **7**, which is reversibly formed by attack of MeOH on the carbonyl group. Elimination of water then leads to the product. If this reaction proceeds in the coordination sphere of complex **6**, its binding pocket must be large enough to accomodate an orthocarbonate group. This was supported by the coordination of a $H_2PO_4^-$ ion in complex $[(L^{Me})Ni_2\{\mu\text{-}O_2P(OH)_2\}]^+$ (**8**), which was prepared according to Equation (6). The $H_2PO_4^-$ group can be regarded as a substitute for the orthocarbonate group (Figure 1). Further support is provided by the different

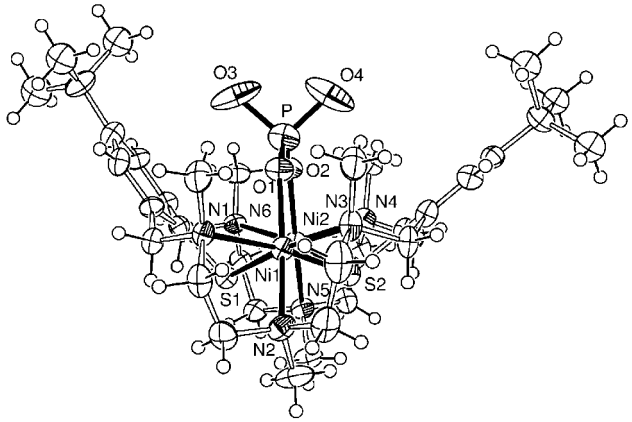
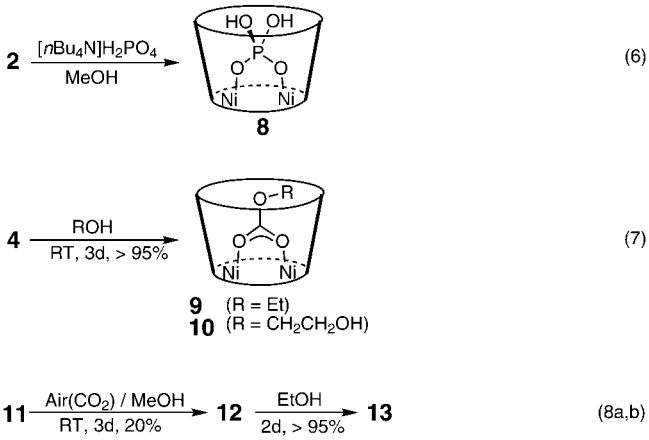


Figure 1. Molecular structure of the $H_2PO_4^-$ complex **8**.

reactivity of **4** towards primary, secondary, and tertiary alcohols. In the case of primary alcohols such as ethanol or ethylene glycol the formation of the corresponding products **9** and **10**, respectively, was observed [Eq. (7)]. In the case of



(6)

(7)

(8a,b)

secondary (*i*PrOH) or tertiary alcohols (*t*BuOH) no reaction occurred. This is presumably due to the limited space in the binding pocket, which allows the formation of an alkyl orthocarbonate of a primary alcohol but not of a higher one.

Further experiments have shown that the chemical reactivity of the cobalt(II) complex **11** (Table 1) is very similar to that of **3**. Thus the preparation of the methyl and ethyl carbonate complexes **12** and **13** can be accomplished by treatment of the monocation **11** with the corresponding alcohol in the presence of air or by transesterification of the alkyl carbonate species [Eq. (8a,b)]. These results indicate that the chemical reactivity is based on the Lewis acidity of the complexes and not restricted to a specific metal d^n electronic configuration.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 2001 1433-7851/01/4021-3989 $ 17.50+.50/0

Hydrophobic effects may also be responsible for the enhanced chemical reactivity of complexes **2** and **3**. The hydrophobicity of a binding cavity can be probed by determining the binding constants of different guests.[9] For this purpose the relative stability constants (K_{rel}) of the formiato, acetato, and benzoato-bridged zinc complexes **14a–c** were determined. The stability constants increase in the order **14a** < **14b** < **14c** and differ by two orders of magnitude ($K_{rel} = 0.1/1.0/5.0$). Thus the larger the organic residue R of the carboxylate anion ($RCOO^-$) the larger the binding constant. The observed trend is indicative of hydrophobic effects between the substituents of the carboxylate ion and the ligand matrix of the complex.

The synthesis of novel binuclear complexes with hydrophobic binding pockets has been described. The complexes show enhanced chemical reactivity towards the activation and transformation of small molecules such as CO_2. We are currently probing the possibility whether the Lewis acidity can be increased by changing the metal oxidation state and whether variation of the alkyl residues allows fine tuning of the size of the binding pocket.

Received: July 5, 2001 [Z17426]

[1] C. Wieser-Jeunesse, D. Matt, A. De Cian, *Angew. Chem.* **1998**, *110*, 3027–3030; *Angew. Chem. Int. Ed.* **1998**, *37*, 2861–2864.

[2] a) M. T. Reetz, S. R. Waldvogel, *Angew. Chem.* **1997**, *109*, 870–873; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 865–867; b) T. Ooi, Y. Kondo, K. Maruoka, *Angew. Chem.* **1998**, *110*, 3213–3215; *Angew. Chem. Int. Ed.* **1998**, *37*, 3039–3041.

[3] S. Hecht, J. M. J. Fréchet, *Angew. Chem.* **2001**, *113*, 76–94; *Angew. Chem. Int. Ed.* **2001**, *40*, 74–91.

[4] a) M. Ruf, H. Vahrenkamp, *Inorg. Chem.* **1996**, *35*, 6571–6578; b) N. Kitajima, W. B. Tolman, *Prog. Inorg. Chem.* **1995**, *43*, 419–531; c) S. Blanchard, L. Le Clainche, M.-N. Rager, B. Chansou, J.-P. Tuchagues, A. F. Duprat, Y. Le Mest, O. Reinaud, *Angew. Chem.* **1998**, *110*, 2861–2864; *Angew. Chem. Int. Ed.* **1998**, *37*, 2732–2735.

[5] B. Kersting, G. Steinfeld, *Chem. Commun.* **2001**, 1376–1377.

[6] For details of the crystal structure determinations see Supporting Information. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-166700–166709. 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).

[7] F. A. Cotton, G. Wilkinson, C. A. Murillo, M. Bochmann, *Advanced Inorganic Chemistry*, 6th ed., Wiley, New York, **1999**, p. 1225.

[8] The coordination of neutral substrates is possible as shown by the successful preparation of the μ-pyridazine complex $[(L^{Me})Ni_2(\mu\text{-pydz})]^{2+}$; B. Kersting, G. Steinfeld, unpublished results.

[9] D. B. Smithrud, E. M. Sanford, I. Chao, S. B. Ferguson, D. R. Carcanague, J. D. Evanseck, K. N. Houk, F. Diederich, *Pure. Appl. Chem.* **1990**, *62*, 2227–2236.

Functionalized DNA: A New Replicable Biopolymer**

Oliver Thum, Stefan Jäger, and Michael Famulok*

During the past decade a number of methods have been developed that allow the isolation of biopolymers with tailored functionalities from highly diverse libraries of polypeptides or nucleic acids.[1] Polypeptide-based libraries require coding strategies such as phage-,[2] ribosome-,[3] or mRNA-display[4] that ensure an unmistakable combination of genotype and phenotype. Only then it is possible to identify a few molecules with the desired activities from mixtures of up to 10^{14} individual molecules.

In contrast, functional nucleic acids such as aptamers[5] and ribozymes[6] have the advantage that they carry along—at all times—the blueprint for their own replication, thereby making special encoding strategies for their detection and optimization obsolete. A potential disadvantage compared to polypeptides, however, is the low diversity of chemical functionalities provided by the four natural nucleotides. Expanding their functional-group repertoire will certainly further enhance their catalytic and binding properties.

Therefore, efforts currently concentrate on developing approaches that combine the advantages of the direct enzymatic amplification of nucleic acids with the chemical diversity of polypeptides by adding protein-like functionalities to the nucleobases of DNA. For example, DNA molecules containing functionalized residues were enzymatically synthesized from natural DNA templates[7] and used for in vitro selection.[8] Although the incorporation of four modified nucleotides bearing fluorescent dyes or alkynyl chains was recently reported,[9] the ultimate goal of substituting all four nucleobases with different functionalized residues within a single oligonucleotide and the subsequent use of the resulting polymer as a template for enzymatic replication has not been achieved to date. Nucleic acids that are highly functionalized in this way would represent a novel class of enzymatically replicable biopolymers that, from a chemical point of view, bridge the gap between proteins and nucleic acids, and might exhibit interesting new properties.[10]

Here we describe the first enzymatic synthesis of oligodeoxynucleotides, in which all four natural nucleobases are substituted by different synthetic residues which bring a broad range of additional chemical functionalities, and the conditions that are required for the enzymatic replication of the new oligodeoxynucleotides. Modifications were designed to include important amino acid side-chains such as carboxylic acid, alkylamino, guanidine, and hydrophobic residues. We

[*] Prof. Dr. M. Famulok, Dipl.-Chem. O. Thum, Dipl.-Chem. S. Jäger
Kekulé-Institut für Organische Chemie und Biochemie
Universität Bonn
Gerhard-Domagk-Strasse 1, 53121 Bonn (Germany)
Fax: (+49) 228-735388
E-mail: m.famulok@uni-bonn.de

[**] We thank Dr. Andreas Marx, University of Bonn, for helpful advice and discussions. This work was supported by the Fonds der Chemischen Industrie, the Karl-Ziegler Stiftung, and the Deutsche Forschungsgemeinschaft.

 © WILEY-VCH Verlag GmbH, D-69451 Weinheim, 2001 1433-7851/01/4021-3990 $ 17.50+.50/0