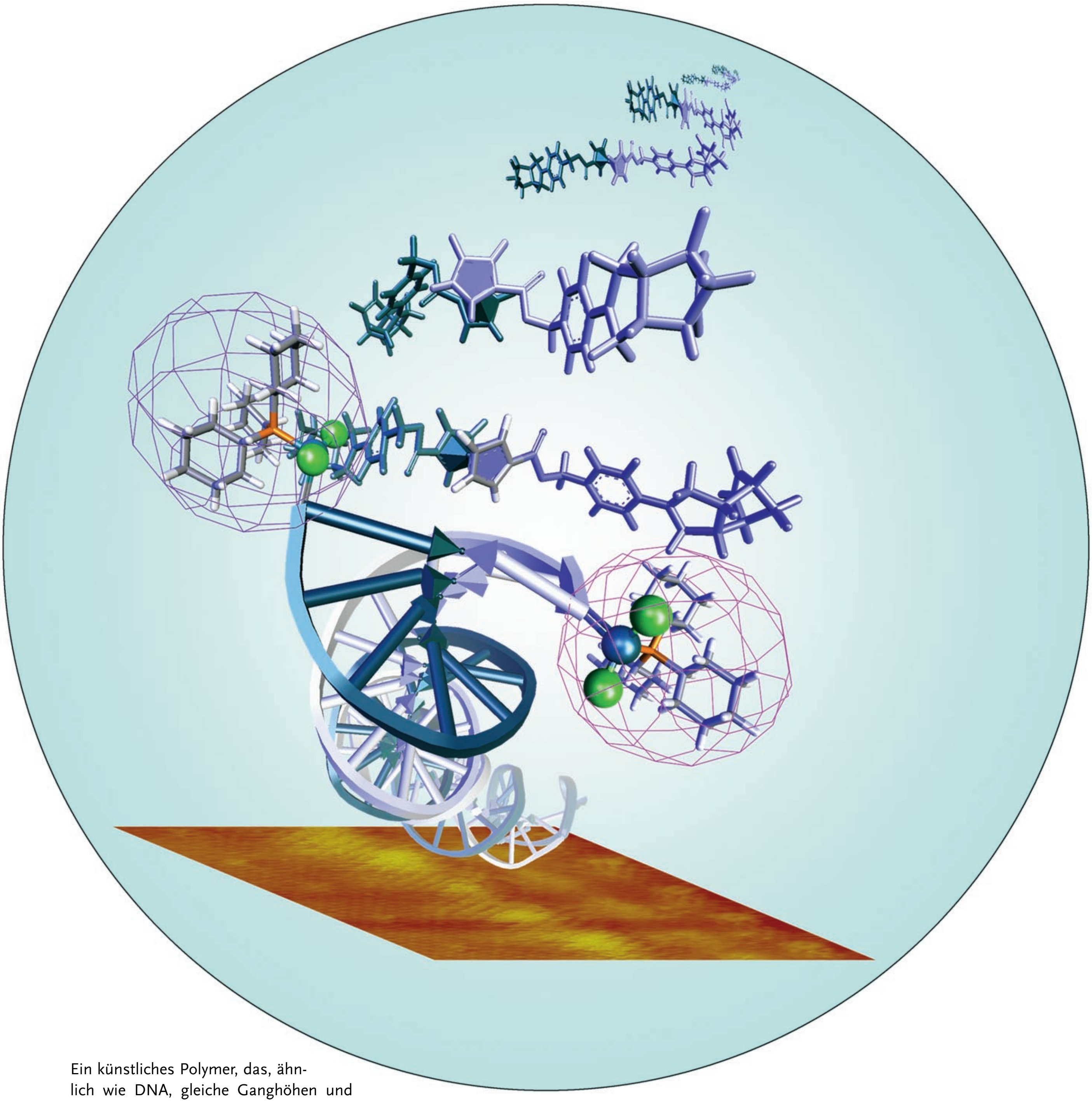
Zuschriften

DOI: 10.1002/ange.200503406



Ein künstliches Polymer, das, ähnlich wie DNA, gleiche Ganghöhen und Zahl an Monomereinheiten pro Windung aufweist, wurde durch Ringöffnungsmetathesepolymerisation erhalten und mit Rastertunnelmikroskopie untersucht. Als Monomer diente ein Bisnorbornenderivat mit starrer Ferrocenbrücke. Einzelheiten zur Synthese, experimentellen Charakterisierung und Modellierung finden Sie in der folgenden Zuschrift von T.-Y. Luh et al.

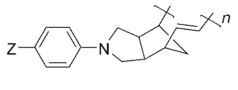
DNA-like Polymers

DOI: 10.1002/ange.200503406

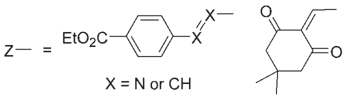
Molecular Architecture towards Helical Double-Stranded Polymers**

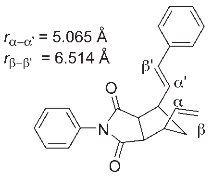
*Hui-Chun Yang, Shu-Yi Lin, Hsiao-Ching Yang,
Cheng-Lan Lin, Lun Tsai, Shou-Ling Huang,
I. Wen-Peter Chen, Chun-hsien Chen, Bih-Yaw Jin, and
Tien-Yau Luh**

Biopolymers provide unique structural features and fascinating chemical and biological properties that artificial polymers are still far from matching. In DNA, the linking base pairs are perpendicular to the deoxyribose phosphate backbones and π–π stacking between base-pair layers is characteristic of the double-helical structure. Much effort has focused on the helical double-stranded oligomers in which the two single chains are chelated to metal ions,[1] complexed through hydrogen bonding,[2] π–π stacked,[3] or form inclusion complexes.[4] Ladderlike organic polymers that have two strands connected by covalent dative or ionic bonds have been briefly explored.[5] The synthesis of polymers structurally comparable to those of DNA remains a challenge. Herein we report the molecular architecture of the first helical double-stranded polymer. Our design involves a suitable monomer that contains two polymerizable groups linked by a rigid spacer. The control of the orientation of the linkers during polymerization is indispensable for the synthesis of double-stranded polymers.



1





2

It has been shown that polymers **1**, obtained from ring-opening metathesis polymerization (ROMP) of norbornenes with rigid pendant groups by using the Grubbs I catalyst,[6] exhibit second-order nonlinear optical hyperpolarizability that is molecular-weight dependent.[7] Such a relationship implies that these polymers may adopt a brushlike structure with relatively uniform stereochemistry and conformation. The spacing of each monomeric unit in **1** was 5–6 Å as revealed by the X-ray crystal structure of **2**.[7b] It is envisaged that the introduction of another norbornene moiety at the end of this pendant group may furnish a useful entry for double-stranded polymers.

The bisnorbornene derivative, **3**, was synthesized according to Scheme 1. The ferrocene moiety was incorporated as part of the linker as it has a certain rigidity but is somewhat flexible. It is interesting to note that the closest Fe–Fe interatomic distances in single-crystal ferrocene and its derivatives range from 5.5 to 5.9 Å.[8] This spacing occupied by the ferrocene moiety appears to be within the limit of span for the vinylcyclopentane monomeric unit in polynorbornenes. Moreover the benzylic moiety and the ester linkage in **3** provide additional flexibility in this linker. Treatment of **3** with 10 mol% of the Grubbs I catalyst afforded, in 90% yield, **4**, which is soluble in $CHCl_3$, CH_2Cl_2, and THF. The ^{13}C NMR spectrum of **4** matched nicely that of **3** and the signals of **4** are relatively sharp, which is consistent with it having a double-stranded structure. Temperature-dependent ^1H NMR spectra of **4** in CD_2Cl_2 suggest that the polymer is very fluxional and the barrier for this conformational equilibrium is very low. The UV absorption for **4** is at $\lambda_{max} = 261$ nm ($\varepsilon = 45.9\ g^{-1}cm^2$), which is blue-shifted in comparison with that of **3** ($\lambda_{max} = 267$ nm; $\varepsilon = 55.8\ g^{-1}cm^2$). In addition, a decrease in ε for **4** suggests that there might be some kind of interaction between the linking chromophores.[9]

Treatment of **3** with 10% NaOH in a mixture of MeOH/$CHCl_3$ at room temperature afforded **5** and **6** in essentially quantitative yield. Under the same conditions, methanolysis of **4** gave the corresponding single-stranded polymer, **7a** ($\bar{M}_n = 7330\ g\,mol^{-1}$, PDI = 1.46; $\bar{M}_n$ is the number-average molecular weight, PDI is the polydispersity index) in 89% yield in addition to **5** in 66% yield. Polymer **7b** ($\bar{M}_n = 3540\ g\,mol^{-1}$, PDI = 1.28) was also obtained from the reaction of **6** with the Grubbs I catalyst in 89% yield. It is interesting to note that **7a** showed the same spectroscopic properties as **7b**. These results imply that **4** has a molecular weight of $\bar{M}_n = 21\,000\ g\,mol^{-1}$ and on average about 29 repetitive units. More-detailed experimental methods and spectroscopic properties are found in the Supporting Information.

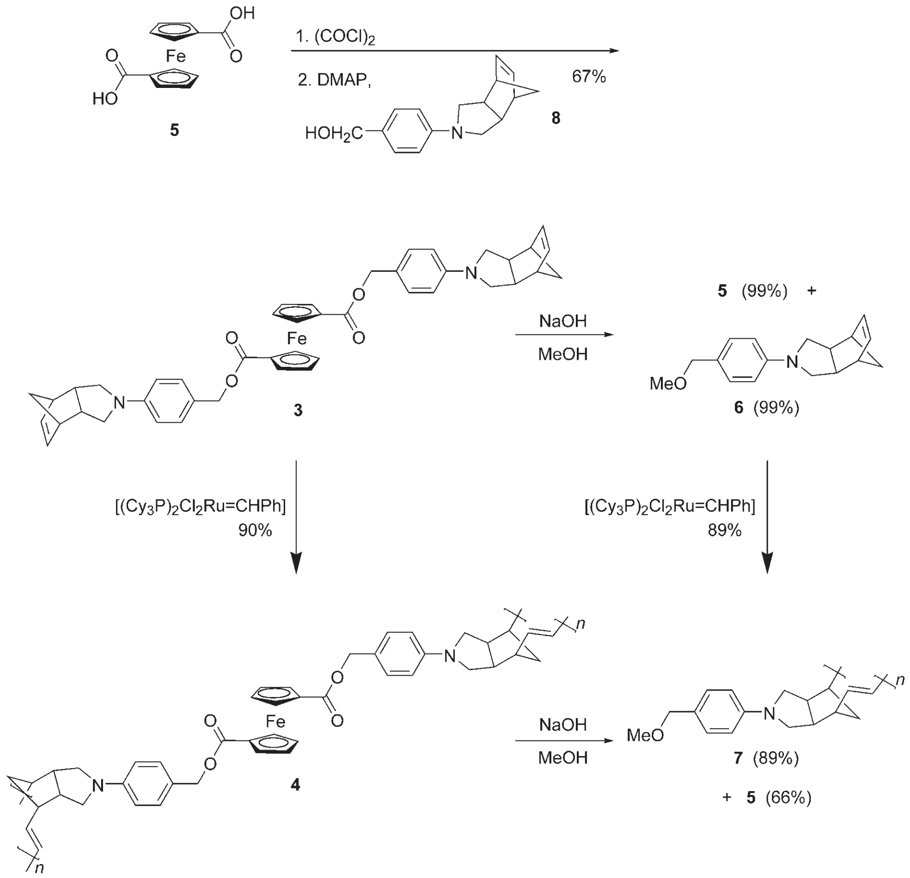
Both **3** and **4** exhibit reversible redox peaks that correspond to the ferrocene moiety. The formal potentials of **3** and **4** were 385 and 439 mV (versus Fc/Fc$^+$), respectively. There was an additional redox pair with a formal potential of 506 mV for **3** arising from the *para*-substituted aniline moiety. This oxidation was not observed with **4**. Presumably the peak

---

[*] H.-C. Yang, Dr. H.-C. Yang, Dr. C.-L. Lin, L. Tsai, S.-L. Huang,
Prof. B.-Y. Jin, Prof. T.-Y. Luh
Department of Chemistry
National Taiwan University
Taipei 106 (Taiwan)
Fax: (+886) 2-2364-4971
E-mail: tyluh@ntu.edu.tw
H.-C. Yang, Prof. T.-Y. Luh
Institute of Polymer Science and Engineering
National Taiwan University
Taipei 106 (Taiwan)
Dr. S.-Y. Lin, I. W.-P. Chen, Prof. C.-H. Chen
Department of Chemistry
National Tsing Hua University
Hsinchu 300 (Taiwan)
Dr. C.-L. Lin
Institute of Chemistry
Academia Sinica
Nangang, Taipei 115 (Taiwan)

[**] This work was funded by the National Science Council of the Republic of China.

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



Scheme 1. Synthetic routes of molecules used in this work. DMAP = 4-dimethylaminopyridine.

might merge with the oxidation of the ferrocene moiety in the polymer.

Scanning tunneling microscopy (STM) was employed to characterize the structure of **4**. Helical, supercoil, and ladder structures were observed (Figure 1). The length of these features in Figure 1 is longer than what was estimated based on the average molecular weight. It seems likely that weak adsorbate–substrate interactions may result in only those that have large molecular weights or exhibit strongly lateral attractions were imaged. Figure 1a shows a helical structure **A** on a flat graphite substrate (highly ordered pyrolytic graphite, HOPG). The lengths of the stripes range from 1.2 to 2.4 nm and are shorter for bright stripes (crossover regions) and longer for dim stripes. The average spacing between stripes is 0.45 ± 0.04 nm, the average pitch length is 5.2 ± 0.2 nm, and each pitch consists of twelve or thirteen monomeric units.

For the supercoil structure **B** (Figure 1b) the average spacing per turn, the apparent height, and the nominal width are about 7.1, 3.2, and 3.0 nm, respectively, which is consistent with the structure being a hollow coil. Attempts to observe molecularly resolved images for supercoils were unsuccessful. Presumably, half of the coil per turn is not in contact with the graphite substrate, which results in enhanced thermal motion and makes imaging difficult.

The ladder structures **C** shown in Figure 1c display an apparent uniform width throughout and exhibit parallel lines or bright spots, for example, going from the upper right to the lower left corner in Figure 1c. Vertical to these parallel lines are fine rows; together these lines and rows create a ladderlike image. The width of these ladders ranges from 2.2 to 2.4 nm and the spacing between the rows falls between 0.45 and 0.55 nm, which is consistent with the proposed ladder structure although the ferrocene diester, benzene ring, and the backbone moieties cannot be unambiguously identified at this stage.

The observation of three different images of **4** on HOPG appears to be consistent with the fluxional behavior of **4** as revealed by the variable-temperature NMR spectroscopy study. Molecular-mechanics calculations were carried out to

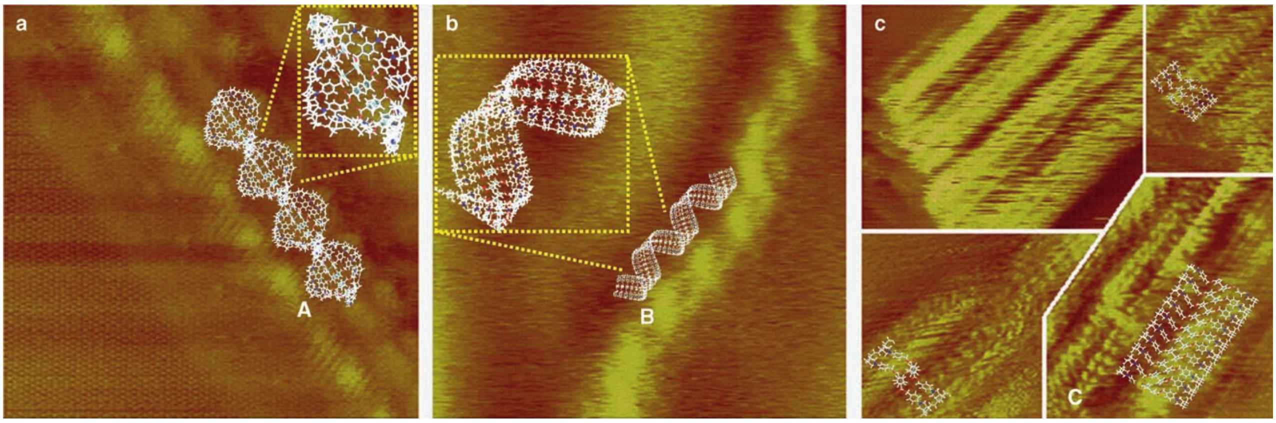


Figure 1. STM images of **4** on HOPG at a flat terrace rather than at a step edge or domain boundaries.[10] The values in parentheses are the corresponding imaging sizes and conditions: a) helical structure (16.8 × 16.8 nm, $E_{bias} = 0.19$ V, $i_{tunneling} = 200$ pA); b) supercoil (58 × 58 nm, $E_{bias} = 0.19$ V, $i_{tunneling} = 20$ pA); c) ladder (clockwise from the upper left one: 35 × 28 nm, 5.0 × 6.5 nm, 7.0 × 7.4 nm, 7.2 × 5.3 nm; $E_{bias} = 0.24$ V, $i_{tunneling} = 20$ pA). E_{bias} is the applied bias potential, $i_{tunneling}$ is the tunneling current.

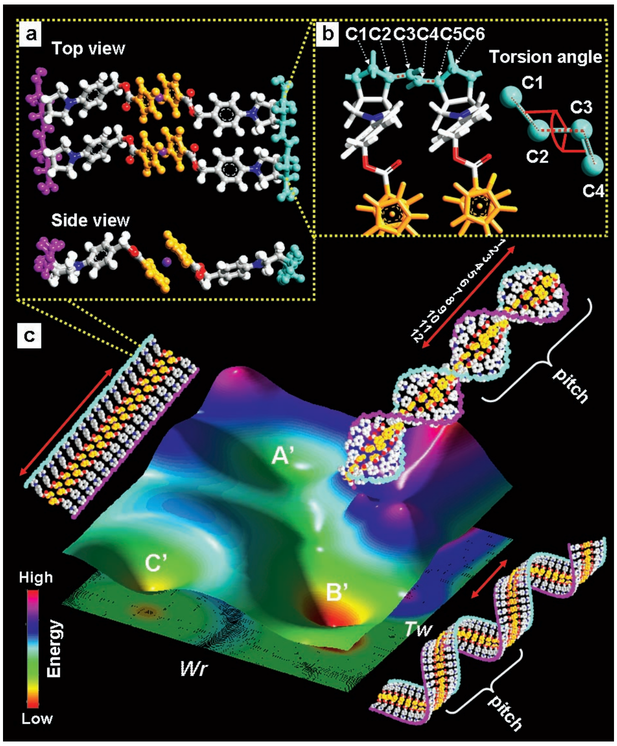


Figure 2. Schematic representation of the molecular modeling. a) Structures of monomer and isotactic dimer. b) Definition of torsion angles on backbone (C1-C2-C3-C4 and C3-C4-C5-C6) related to conformational transition. c) The potential-energy surface based on the simulated energies of three local structures: **A**′ (helical), **B**′ (supercoil), **C**′ (ladder), and transition-energy for interconversions. The two geometrical characteristics, twisting number (*Tw*) and writhing number (*Wr*), define the topology of the secondary structures.

simulate the structures of **4** (with different molecular weights) and **3** by using a modified version of universal force field found in molecular-modeling programs.[11] The 3D topologies of the secondary structures of **4** were established by varying both the conformation of **3** and the tacticity of the backbone of **4**. The two carboxy groups on the cyclopentadienyl moieties in **3** were *anti* relative to the ferrocene moiety and this zigzag structure (Figure 2a) was used as a basis for estimating the secondary structure of **4**. The double bonds in **4** were all *trans* according to the NMR results. With these constraints and extensive exploration of the potential surface by combining geometrical optimization and molecular simulation, we conclude that **4** is more stable in the isotactic than in the syndiotactic form. To account for the STM results described above, three major secondary structures of **4** in the isotactic form were obtained: double-stranded helix **A**′, supercoil **B**′, and ladder **C**′. Local structure **A**′ (Figure 2c) had a diameter of 2.2 nm and 12 monomeric units in a pitch. These data closely matched the results from the STM image of **A**. Structure **B**′ appeared to be more flexible, and the modeled supercoil with 25 monomeric units per pitch had a diameter of 3.1 nm, which is consistent with the experimental structure, **B** (Figure 1b).

Figure 2c shows a schematic map based on the simulated energies of three local structures, **A**′, **B**′, and **C**′. The supercoil form, **B**′, was the most stable whereas the helical structure, **A**′, had the highest energy among these three structures. The most important feature of these structures is the strong coupling between the dihedral angles in the backbone and the space occupied by the linkers. The shear-induced twist–writhe transition (Figure 2c) results in the translation from one form to another.[12] It is interesting to note that a slight change in torsion angles may provoke such a profound influence on the secondary structure. The detailed calculations are described in the Supporting Information.

In summary, we have described an unprecedented synthesis of a DNA-like double-stranded polymer obtained by ROMP of a bisnorbornene derivative. The polymer structurally resembles DNA by having a comparable width, a similar number of monomeric units per pitch, five-membered rings in the polymeric frame, perpendicular linkers to the backbones, and similar spacing between neighboring monomeric units. The fluxional behavior of the polymer and its ability to dissociate hydrolytically into two single-stranded polymers make it further resemble DNA molecules. The oxidation-labile ferrocene linkers in this polymer are aligned coherently along the polymer axis. Insight into the structural features of such a polymer might pave the way to tailor other polymers that simulate biological systems.

Received: September 27, 2005

Keywords: helical structures · metathesis · molecular modeling · ring-opening polymerization · scanning probe microscopy

---

[1] a) J.-M. Lehn, A. Rigault, J. Siegel, J. Harrowfield, B. Chevrier, D. Moras, *Proc. Natl. Acad. Sci. USA* **1987**, *84*, 2565–2569; b) U. Koert, M. M. Harding, J.-M. Lehn, *Nature* **1990**, *346*, 339–342; c) E. C. Constable, *Pure Appl. Chem.* **1996**, *68*, 253–260; d) C. R. Woods, M. Benaglia, F. Cozzi, J. S. Siegel, *Angew. Chem.* **1996**, *108*, 1977–1980; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1830–1833; e) C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005–2062; f) A. Williams, *Chem. Eur. J.* **1997**, *3*, 15–19; g) M. Albrecht, *Chem. Rev.* **2001**, *101*, 3457–3497; h) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes, J. S. Moore, *Chem. Rev.* **2001**, *101*, 3893–4011, and references therein; i) A. Orita, T. Nakano, D.-L. An, K. Tanikawa, K. Wakamatsu, J. Otera, *J. Am. Chem. Soc.* **2004**, *126*, 10389–10396.

[2] a) J. Sánchez-Quesada, C. Steel, P. Prados, J. de Mendoza, *J. Am. Chem. Soc.* **1996**, *118*, 277–278; b) B. Gong, Y. Yan, H. Zeng, E. Skrzypczak-Jankunn, Y. W. Kim, J. Zhu, H. Ickes, *J. Am. Chem. Soc.* **1999**, *121*, 5607–5608; c) V. Berl, I. Huc, R. G. Khoury, M. J. Krische, J.-M. Lehn, *Nature* **2000**, *407*, 720–723; d) A. P. Bisson, F. J. Carver, D. S. Eggleston, R. C. Haltiwanger, C. A. Hunter, D. L. Livingstone, J. F. Mccabe, C. Rotger, A. E. Rowan, *J. Am. Chem. Soc.* **2000**, *122*, 8856–8868; e) P. S. Corbin, S. C. Zimmerman, *J. Am. Chem. Soc.* **2000**, *122*, 3779–3780; f) H. Zeng, R. S. Miller, R. A. Flowers II, B. Gong, *J. Am. Chem. Soc.* **2000**, *122*, 2635–2644; g) P. S. Corbin, S. C. Zimmerman, *J. Am. Chem. Soc.* **2000**, *122*, 3779–3780; h) J. S. Nowick, D. M. Chung, K. Maitra, S. Maitra, K. D. Stigers, Y. Sun, *J. Am. Chem. Soc.* **2000**, *122*, 7654–7661; i) V. Berl, I. Huc, R. G. Khoury, J.-M. Lehn, *Chem. Eur. J.* **2001**, *7*, 2810–2820; j) I. Huc, *Eur. J. Org. Chem.* **2004**, 17–29; k) M. Albrecht, *Angew. Chem.* **2005**, *117*, 6606–6609; *Angew. Chem. Int. Ed.* **2005**, *44*, 6448–6451; l) H. Gong, M. J.

Krische, *J. Am. Chem. Soc.* **2005**, *127*, 1719 – 1725; m) Y. Tanaka, H. Katagiri, Y. Furusho, E. Yashima, *Angew. Chem.* **2005**, *117*, 3925 – 3938; *Angew. Chem. Int. Ed.* **2005**, *44*, 3867 – 3870.

[3] G. J. Gabriel, B. L. Iverson, *J. Am. Chem. Soc.* **2002**, *124*, 15174 – 15175.

[4] a) A. Harada, J. Li, M. Kamachi, *Nature* **1994**, *370*, 126 – 128; b) A. P. Bisson, C. A. Hunter, *Chem. Commun.* **1996**, 1723 – 1724.

[5] a) S. Nagahama, A. Matsumoto, *J. Am. Chem. Soc.* **2001**, *123*, 12176 – 12181; b) T. E. O. Screen, J. R. G. Thorne, R. G. Denning, D. G. Bucknall, H. L. Anderson, *J. Am. Chem. Soc.* **2002**, *124*, 9712 – 9713; c) H. Tang, J. Sun, J. Jiang, X, Zhou, T. Hu, P. Xie, R. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 10482 – 10488; d) M. M. Green, J.-W. Park, T. Sato, A. Teramoto, S. Lifson, R. L. B. Selinger, J. V. Selinger, *Angew. Chem.* **1999**, *111*, 3328 – 3345; *Angew. Chem. Int. Ed.* **1999**, *38*, 3138 – 3154; e) T. Nakano, Y. Okamoto, *Chem. Rev.* **2001**, *101*, 4013 – 4038; f) J. J. L. M. Cornelissen, A. E. Rowan, R. J. M. Nolte, N. A. J. M. Sommerdijk, *Chem. Rev.* **2001**, *101*, 4039 – 4070; g) L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071 – 4097; h) E. Yashima, K. Maeda, T. Nishimura, *Chem. Eur. J.* **2004**, *10*, 42 – 51.

[6] a) P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100 – 110; b) J. G. Hamilton in *Handbook of Metathesis, Vol. 3* (Ed.: R. H. Grubbs), Wiley-VCH, Weinheim, **2003**, pp. 143 – 179.

[7] a) J. A. Sattigeri, C.-W. Shiau, C.-C. Hsu, F.-F. Yeh, S. Liou, B.-Y. Jin, T.-Y. Luh, *J. Am. Chem. Soc.* **1999**, *121*, 1607 – 1608; b) W.-Y. Lin, M. G. Murugesh, S. Sudhakar, H.-C. Yang, H.-C. Tai, C.-S. Chang, Y.-H. Liu, Y. Wang, Y. I.-W. P. Chen, C.-h. Chen, T.-Y. Luh, *Chem. Eur. J.* **2006**, *12*, 324 – 330.

[8] J. D. Dunitz, L. E. Orgel, A. Rich, *Acta Crystallogr.* **1956**, *9*, 373 – 375;

[9] a) D. M. Shin, I. S. Lee, Y. K. Chung, *Eur. J. Inorg. Chem.* **2003**, 2311 – 2317; b) A. Dirksen, U. Hahn, F. Schwanke, M. Nieger, J. N. H. Reek, F. Vögtle, L. D. Cola, *Chem. Eur. J.* **2004**, *10*, 2036 – 2047.

[10] C. R. Clemmer, T. P. Beebe, Jr., *Science* **1991**, *251*, 640 – 642.

[11] a) D. Frenkel, B. Smit, *Understanding Molecular Simulation: From Algorithms to Applications*, Academic Press, New York, **1996**; b) A. R. Leach, *Molecular Modeling. Principles and Applications*, Longman, Essex, **1997**; c) A. K. Rappé, C. J. Casewit, K. S. Colwell, W. A. Goddard III, W. M. Skiff, *J. Am. Chem. Soc.* **1992**, *114*, 10024 – 10035; d) C. J. Casewit, K. S. Colwell, A. K. Rappé, *J. Am. Chem. Soc.* **1992**, *114*, 10035 – 10046; e) A. K. Rappé, C. J. Casewit, *Molecular Mechanics Across Chemistry*, University Science Books, Sausalito, **1997**; f) J. A. McCammon, S. C. Harvey, *Dynamics of Proteins and Nucleic Acids*, Cambridge University Press, Cambridge, **1988**.

[12] a) F. B. Fuller, *Proc. Natl. Acad. Sci. USA* **1971**, *68*, 815 – 819; b) M. D. Frank-Kamenetskii, *Unraveling DNA*, VCH, Weinheim, **1995**.