Hanyu, E. Takezawa, S. Sakaguchi, Y. Ishii, *Tetrahedron Lett.* **1998**, *39*, 5557; f) K. P. Peterson, R. C. Larock, *J. Org. Chem.* **1998**, *63*, 3185.

[4] a) I. E. Markó, P. R. Giles, M. Tsukazaki, S. Brown, C. J. Urch, *Science* **1996**, *274*, 2044; b) I. E. Markó, M. Tsukazaki, P. R. Giles, S. M. Brown, C. J. Urch, *Angew. Chem.* **1997**, *109*, 2297; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2208; c) I. E. Markó, A. Gautier, I. Chellé-Regnaut, P. R. Giles, M. Tsukazaki, C. J. Urch, S. M. Brown, *J. Org. Chem.* **1998**, *63*, 7576.

[5] I. E. Markó, P. R. Giles, M. Tsukazaki, I. Chellé-Regnaut, C. J. Urch, S. M. Brown, *J. Am. Chem. Soc.* **1997**, *119*, 12661.

[6] For an independent report on the TPAP-catalyzed aerobic oxidation of alcohols, see: a) R. Lenz, S. V. Ley, *J. Chem. Soc. Perkin Trans. 1* **1997**, 3291; b) B. Hinzen, R. Lenz, S. V. Ley, *Synthesis* **1998**, 977. c) For an excellent review on ruthenium-catalyzed reactions, see: T. Naota, H. Takaya, S.-I. Murahashi, *Chem. Rev.* **1998**, *98*, 2599.

[7] a) H. C. Clarck, H. Kurosawa, *J. Chem. Soc. Chem. Commun.* **1972**, 150; b) M. Kraus, *Collect. Czech. Chem. Commun.* **1972**, *37*, 460; c) Y. Lin, X. Zhu, Y. Zhou, *J. Organomet. Chem.* **1992**, *429*, 269; d) T. Karlen, A. Ludi, *Helv. Chim. Acta* **1992**, *75*, 1604; e) D. V. McGrath, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1991**, *113*, 3611; f) S. H. Bergens, B. Bosnich, *J. Am. Chem. Soc.* **1991**, *113*, 958; g) W. Smadja, G. Ville, C. Georgoulis, *J. Chem. Soc. Chem. Commun.* **1980**, 594; h) M. Dedieu, Y.-L. Pascal, *C. R. Acad. Sci. Ser. C* **1976**, *282*, 65; i) W. Strohmeier, L. Weigelt, *J. Organomet. Chem.* **1975**, *86*, C17; j) Y. Sasson, G. L. Rempel, *Tetrahedron Lett.* **1974**, 4133; k) B. M. Trost, R. J. Kulawiec, *J. Am. Chem. Soc.* **1993**, *115*, 2027; l) B. M. Trost, R. J. Kulawiec, *Tetrahedron Lett.* **1991**, *32*, 3039; m) J.-E. Bäckvall, U. Andreasson, *Tetrahedron Lett.* **1993**, *34*, 5459.

[8] For example, the Trost ruthenium catalyst is ineffective for the isomerization of geraniol (**1**) into citronellal (**2**).[7k]

[9] In general, a greater amount of 2-undecanone (**5**; 30–45%) is produced in these reactions. The difference between the theoretical and the experimental quantities of **5** relates to the reoxidation of the Ru^{III} catalyst into a Ru^{V} species by the adventitious presence of O_2. The subsequent reduction of the Ru^{V} complex back to the active, low-valent Ru^{III} derivative necessarily requires the further consumption of the sacrificial alcohol **4**. See also: S.-I. Murahashi, T. Naota, N. Hirai, *J. Org. Chem.* **1993**, *58*, 7318.

[10] That a ruthenium alkoxide **7** is an intermediate in this process is clearly revealed by the complete lack of reactivity of the trimethylsilyl ether derived from **6**.

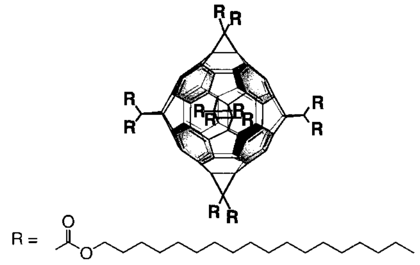
[11] The [1,4] addition of ruthenium hydrides to enones is well-documented; see for example: Y. Ishii, K. Osakada, T. Ikariya, M. Saburi, S. Yoshikawa, *J. Org. Chem.* **1986**, *51*, 2034. For a similar mechanism involving the [1,4]-hydride addition to conjugated iminium intermediates, see, for example: S.-I. Inoue, H. Takaya, K. Tani, S. Otsuka, T. Sato, R. Noyori, *J. Am. Chem. Soc.* **1990**, *112*, 4897.

[12] Beside being a by-product of the oxidation of **4**, 2-undecanone also appears to act as a ligand for the low-valent ruthenium catalyst.

Nanospheres from Polymerized Lipofullerenes[**]

Michael Hetzer, Hauke Clausen-Schaumann, Sibylle Bayerl, Thomas M. Bayerl,[*] Xavier Camps, Otto Vostrowsky, and Andreas Hirsch[*]

We have shown recently that dipalmitoylphosphatidylcholine (DPPC) self assembles to multilamellar vesicles (MLVs) in an aqueous medium with a high content of lipophilic hexakisadduct of C_{60}, such as **1**, while the incorporated lipofullerene forms rodlike fullerene nanoaggregates within the lecithin bilayers.[1, 2] These intercalated lipofullerene structures are several μm long, have diameters up to 30 nm, and significantly change the micromechanical properties of these composite membrane systems. As an example, an increase of the bending stiffness of the bilayers is observed, and at the same time decoupled lateral diffusion of lipids and lipofullerenes within the double layer has been found.[1–3] In this connection it was of interest as to whether the self assembling of lipofullerenes within these supramolecular structures can be used for the formation of stable nanoarchitectures based on fullerenes.



1

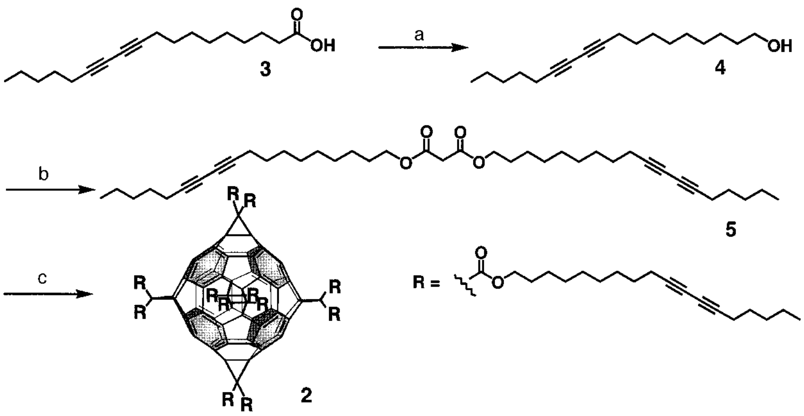
Herein we report on the synthesis of filled and hollow nanospheres formed upon polymerization of lipofullerenes intercalated into such MLVs. Butadiyne groups have been chosen as polymerizable structural elements within the lipophilic chains. They should allow a covalent linkage between the lipofullerene molecules[7] through a 1,4-addition inside the aggregates upon UV irradiation.[4-6] It is known that membranes built up from lipids with butadiyne units can be polymerized photochemically and give rise to the formation of an oligodiacetylene network.[8] The T_h symmetrical hexakisadduct **2**, which is hyperfunctionalized by its twelve octadecadiynyl side chains, served as the monomeric lipofullerene element. This hyperfunctionality ensures the formation of a perfect network in three dimensions. To synthe-

---

[*] Prof. Dr. T. M. Bayerl, Dr. M. Hetzer,
Dipl.Phys. H. Clausen-Schaumann, Dr. S. Bayerl
Physikalisches Institut EP-5 der Universität
D-97074 Würzburg (Germany)
Fax: (+49) 931-7840759
E-mail: bayerl@physik.uni-wuerzburg.de

Prof. Dr. A. Hirsch, Dr. X. Camps, Dr. O. Vostrowsky
Institut für Organische Chemie der Universität Erlangen-Nürnberg
D-91054 Erlangen (Germany)
Fax: (+49) 9131-8526864
E-mail: andreas.hirsch@organik.uni-erlangen.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft.



Scheme 1. Synthesis of the polymerizable lipofullerene hexakisadduct **2**. a) $LiAlH_4$, diethyl ether; b) $ClCOCH_2COCl$/pyridine, CH_2Cl_2; c) C_{60}, DMA, CBr_4, DBU, toluene.

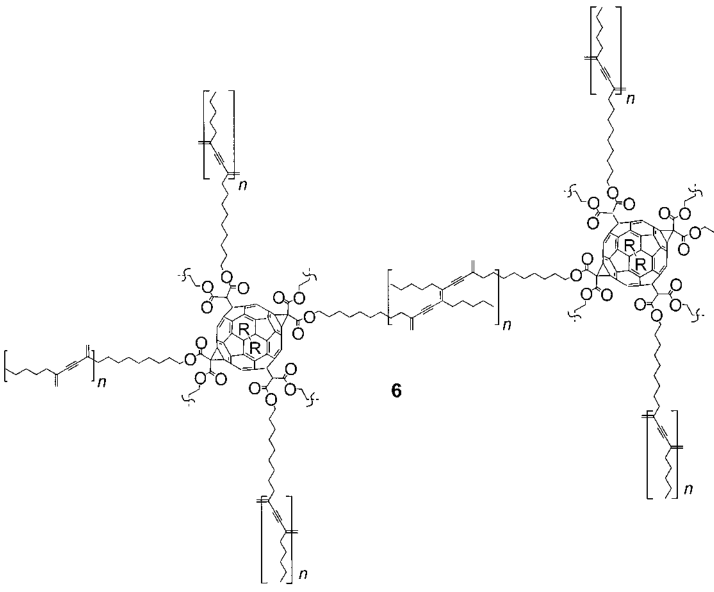
size **2** (Scheme 1), 10,12-octadecadiynoic acid (**3**) was reduced and the corresponding alcohol **4** formed. The latter was then treated with malonyl dichloride to give dioctadecadiynyl malonate (**5**). The T_h symmetrical hexakisadduct **2** was obtained from ester **5** by template activation[9] with dimethylanthracene (DMA) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and subsequent exhaustive cyclopropanation[10, 11] of **2** (Scheme 1), and characterized (Table 1).

To investigate the photochemical networkability of **2** a film coating of the neat monomer on a glass plate was irradiated (300 W lamp) for two days. While the yellow monomer **2** melts at 42 °C, the shiny red-brownish and insoluble photolysis product **6** did not exhibit any phase transition up to 280 °C. The ^{13}C solid-state NMR analysis (MAS) as well as the IR spectra of **6** revealed newly formed endiyne units ($\delta = 90-140$; $\tilde{\nu} = 2230$ (C≡C), 1600 cm^{-1} (C=C)) as well as intact butadiyne funtions ($\delta = 65, 77$). This means, that for steric reasons only two, or very few, monomeric elements might cross-link together by formation of short endiyne units.

Table 1. ^1H NMR, ^{13}C NMR, IR, UV, and MS data of **2**.

^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.90$ (t, 36H, $J = 7$ Hz, CH_3), 1.35–1.55 (m, 216H, CH_2), 1.68 (tt, 24H, $J_1 = J_2 = 7$ Hz, CH_2), 2.24 (t, 48H, $J = 7$ Hz, $CH_2C{\equiv}C$), 4.24 (t, 24H, $J = 7$ Hz, CH_2O); ^{13}C NMR (100.5 MHz, $CDCl_3$): $\delta = 13.84$ (CH_3), 19.09, 19.13, 22.09, 25.74, 27.98, 28.31, 28.36, 28.78, 28.99, 29.13, 29.31, 30.92 (CH_2), 45.33 (methanobridge), 65.23, 65.26 (sp-*C*), 66.92 (CH_2O), 69.06 (C_{60} sp^3-*C*), 77.43, 77.48, (sp *C*), 141.15, 145.81 (C_{60} sp^2-*C*), 163.92 (*C*=O); IR (KBr): $\tilde{\nu} = 2930.8$, 2856.4, 2256.1, 2155.5, 1746.3, 1465.1, 1264.4, 1215.8, 1080.2, 715.7, 529.3 cm^{-1}; UV (CH_2Cl_2): $\lambda_{max} = 270.5$, 280.5, 318.0, 336.0, 383.0 nm; MS (α-cyano-*p*-hydroxycinnamic acid (CCA), MALDI): *m/z*: 4267 [M^+]

To achieve a matrix controlled polymerization **2** was intercalated into multilamellar phospholipid vesicles. Subsequent deuterium solid-state NMR (^2H NMR) and freeze fracture electron microscopy analyses revealed that **2** exhibited the same tendency for self aggregation as was observed with the analogous saturated and nonpolymerizable, lipofullerenes.[1, 2] An aqueous dispersion of multilamellar DPPC vesicles containing 15 mol% of **2** was subjected to UV irradiation (8 W, 256 nm) for 12 h at 50 °C (fluid lipid phase[1, 2]) in a quartz-glass cuvette. In control experiments with neat DPPC–MLVs no indication of thermal degradation or irradiation damage of the DPPC was observed by differential scanning calorimetry (DSC) under the experimental conditions applied. In contrast the polymerizable lipofullerene–DPPC system showed significant changes after the UV treatment with respect to the dynamic properties of the lipids. Figure 1 shows the deuterium NMR spectra of the lipofullerene–DPPC system (chain perdeuterated DPPC) prior and after polymerization under fluid bilayer conditions. The change of the signal line shape is explained by an



6

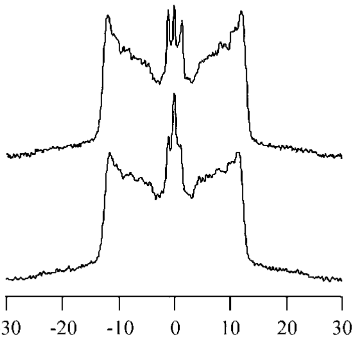


Figure 1. ^2H NMR spectra of perdeuterated multilamellar DPPC vesicles [D_{62}]DPPC containing 15 mol% lipofullerene **2** prior (top) and after UV irradiation (bottom) at 50 °C.

enhancement of the membrane bending modulus.[1] Furthermore, the polymerization is manifested in a significant reduction of the ^{2}H NMR transverse relaxation time t_2 of the perdeuterated DPPC chains by more than 10%. This reduction in t_2 of the lipid chains can be explained by the presence of rigid structures in their immediate vicinity. Relaxation control experiments revealed that the polymerization was finished after an irridiation period of 12 h and that analogously treated neat DPPC–MLVs did not exhibit any reduction in t_2.

An investigation of the fluid phase samples by freeze fracture electron microscopy showed that the rodlike structures at the MLV surface observed prior to polymerization (Figure 2a) had vanished. Instead, perfectly spherical objects made up from polymerized lipofullerenes with diameters ranging from 100 nm up to several µm were obtained (Figure 2b). The smaller spheres with diameters of less than 150 nm were hollow and transparent, and the replica background below them was visible through the objects. The larger beads were filled and their centers inpenetrable to the electron beam. The DPPC was removed after polymerization by extraction with organic solvent. As a consequence vacuum dried nanospheres were accessible to inspection by transmission electron microscopy (TEM) in the absence of the freeze fracture replica (Figure 2c). Atomic force microscopy (AFM) analysis of single C_{60} balls sticking out from the bead surface revealed a medium C_{60}–C_{60} distance of 16 nm (Figure 3). An average surface coarseness of 0.9 nm with maximum hight amplitudes of 1.5 nm was determined after a computational smoothing of the surfaces. The filled beads seem to exhibit an unusually high strength and did not reveal any mechanical damage inspite of the considerable forces they were subjected to (one to two orders of magnitudes greater than the 1 nN chosen for the AFM in Figure 3). The fact that no edge darkening was observed in the transmission electron micrographs of the transparent small hollow spheres indicates that the wall thickness of the beads is below the resolution limit of the microscope used (namely, below 10 nm).

The polymerization presented here can be seen as a special kind of emulsion polymerization, where the monomer in an aqueous solution is polymerized in the presence of a detergent.[12] From the fact that the formation of round and three-dimensional spheres is observed from the fluid MLV phase, where only a quasi-two-dimensional lateral mobility of the monomeric elements should be allowed, it can be concluded that the vesicles serve an essential template function during polymerization.

Interestingly, **2** can also be polymerized to spheric polymers in the absence of DPPC, however, only in very low yields and in addition to amorphous material. Originally performed as a control experiment, a solution of 5 mg mL^{-1} of **2** in decane was irradiated (80 W, 256 nm) at room temperature. The formation of a shiny brownish precipitate at the vessel walls and additionally a colloidal suspension of small spherical objects within the solution was observed after only 30 min. In this case, however, no hollow spheres were found. To our knowledge, this is the first case reported for an isotropic polymerization, and is likely made possible by the shape and the hyperfunctionality of the highly symmetrical monomer **2**.

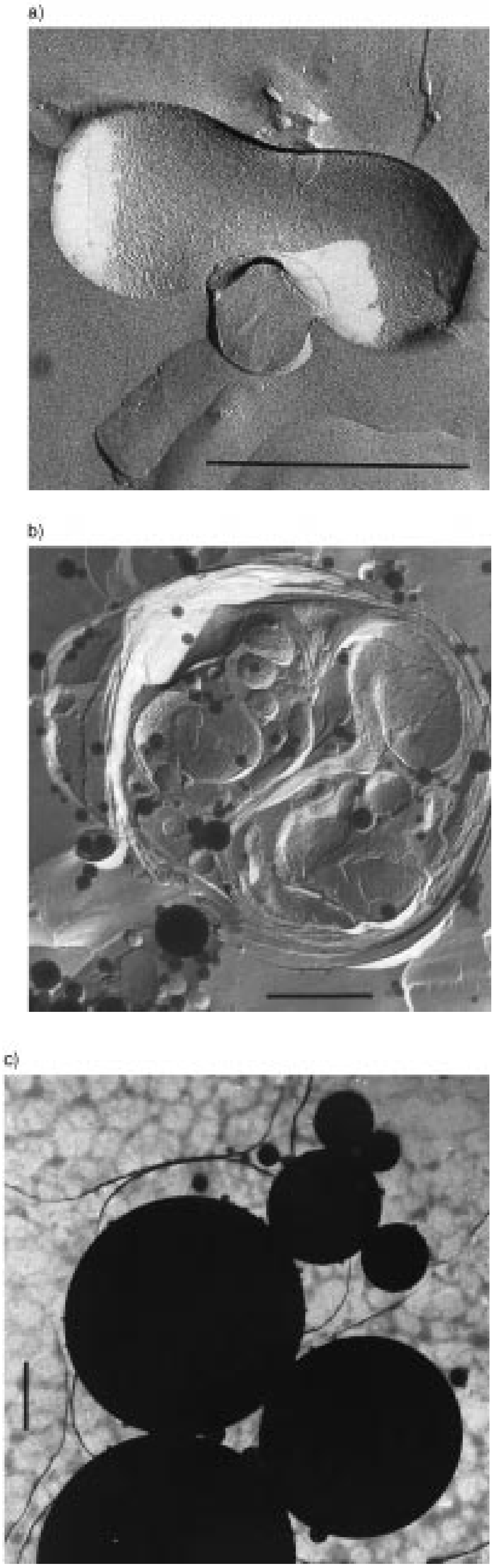


Figure 2. TEM pictures of 15 mol% lipofullerenes **2** in DPCC multilamellar vesicles a) prior and b) after UV-initiated polymerization. c) Lipofullerene polymerspheres after extraction of DPPC and subsequent vaccuum drying. The bar corresponds to 1 µm.

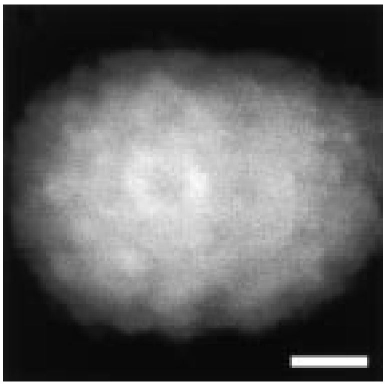


Figure 3. AFM picture of a lipofullerene polymersphere after extraction of the DPPC. The bar corresponds to 50 nm.

Only a small part of the twelve groups available for networking is used up for polymerization because of steric reasons. The remaining unreacted endiyne functions at the beads surface cause a dendritic isotropic polymer growth to an isotropic 3D network by diffusion control of the monomers in solution. Thus, it acts like a "living polymer" filling the space available. The polymerization in solution can to some extent be compared with that in the MLVs. In both cases a medium is available for the diffusion control: the solvent decane or the fluid lipid bilayer. The reason for the formation of the small hollow spheres upon vesicle polymerization can be found in the stability of small vesicles. Only lateral diffusion is allowed as a consequence of their shape and small volumes, and hence an anisotropic and quasi-two-dimensional polymerization to hollow spheres is enabled. With the same arguments, the formation of concentrically filled "onionlike" balls could be expected from the bigger multilamellar vesicles. However, it seems more reasonable that the single lamellae do not withstand the polymerization pressure and a rupture of the membrane might occur. Diffusion of the monomers is now enabled from outside (and inside) of the membrane layer and results in the formation of compactly filled three-dimensional polymer spheres.

Experimental Section

Synthesis of lipofullerene monomeric element **2**: 10,12-Octadecadiyn-1-ol (**4**) is obtained quantitatively from $LiAlH_4$ reduction of commercially available 10,12-octadecadiynoic acid (**3**) in diethyl ether. The subsequent acylation with malonyl dichloride/pyridine in CH_2Cl_2 gives rise to the formation of di-10,12-octadecadiynyl malonate (**5**, yield 63%). The following template-assisted cyclopropanation[9–11] of C_{60} (108 mg, 0.15 mmol), DMA (310 mg, 1.50 mmol), **4** (894 mg, 1.50 mmol), CBr_4 (497 mg, 1.50 mmol), and DBU (0.448 mL, 3 mmol) in 70 mL toluene gave, after column (SiO_2; hexane/CH_2Cl_2 1/1) and preparative HPLC chromatography (grom-Sil 100Si, NPI, 5 μL, 20 mL min^{-1} CH_2Cl_2/heptane 7/3), 1,2:18,36:22,23:27,45:31,32:55,56-hexakis{[di(10,12-octadecadiynyloxycarbonyl)]-methano}-1,2,18,36,22,23,27,45,31,32,55,56-dodecahydro-[60]fullerene **2** (166 mg, 26%).

The preparation of the MLV samples for freeze fracture electron microscopy as well as the TEM studies were carried out according to the technique described in reference [1]. Triafol hole foils were used after removal of the lipids and directly inserted into the electron beam for the TEM recordings of the polymer spheres. The dried polymer spheres were deposited in the holes of the foils.

The AFM measurements (Nanoscope IIIa, Digital Instruments, Mannheim, Germany) were carried out in the contact mode on mica plates in 1-propanol at 15°C after removal of the lipids with CH_2Cl_2. Recording parameters: constant force (< 1 nN), silicium nitride cantilever (30 mN m^{-1}), 6.8 lines per sec, 90° scanning angle.

The ^2H NMR experiments were carried out as described in reference [1]. For the determination of the transverse relaxation time t_2 the pulse distance in the quadrupole echo sequence was varied between 30 and 120 μs, a half logarithmical recording of the echo intensity over the double pulse distance gave $(t_2)^{-1}$ as the slope of a straight line.

Received: February 26, 1999 [Z13087IE]
German version: *Angew. Chem.* **1999**, *111*, 2103–2106

Keywords: atomic force microscopy · fullerenes · lipofullerenes · polymerizations · vesicles

---

[1] M. Hetzer, S. Bayerl, X. Camps, O. Vostrowsky, A. Hirsch, T. M. Bayerl, *Adv. Mater.* **1997**, 913–917.

[2] M. Hetzer, S. Bayerl, T. M. Bayerl, X. Camps, O. Vostrowsky, A. Hirsch in *Molecular Nanostructures* (Eds.: H. Kuzmany, J. Fink, M. Mehring, S. Roth), World Scientific, **1997**, pp. 528–532.

[3] M. Hetzer, T. Gutberlet, M. F. Brown, X. Camps, O. Vostrowsky, H. Schönberger, A. Hirsch, T. M. Bayerl, *J. Phys. Chem. A* **1999**, *103*, 637–642.

[4] a) G. Wegner, *Z. Naturforsch. B* **1969**, *24*, 824–832; b) G. Wegner, *Chimia* **1974**, *28*, 475–484; c) G. Wegner, *Angew. Chem.* **1974**, *93*, 352–371; *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 361–381.

[5] K. Takeda, G. Wegner, *Makromol. Chem.* **1972**, *160*, 349–353.

[6] *Modern Acetylene Chemistry* (Eds.: P. Stang, F. Diederich), VCH, Weinheim **1995**.

[7] Contrary to the classical topologically controlled polymerization of butadiynes[4–6] no preorganization appears in this case, which allows the formation of a long-chain polydiacetylene backbone.

[8] *Phospholipids Handbook*, (Ed.: G. Cevc), Marcel Dekker, New York, **1993**.

[9] I. Lamparth, C. Mössmer, A. Hirsch, *Angew. Chem.* **1995**, *107*, 1755–1757; *Angew. Chem. Int. Ed. Engl.* **1995**, *35*, 1607–1609.

[10] A. Hirsch, I. Lamparth, H. R. Karfunkel, *Angew. Chem.* **1994**, *106*, 453–455; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 437–438.

[11] F. Djojo, A. Herzog, I. Lamparth, F. Hampel, A. Hirsch, *Chem. Eur. J.* **1996**, *2*, 1537–1547.

[12] M. S. El-Aasser, E. D. Sudol in *Emulsion Polymerization and Emulsion Polymers* (Eds.: P. A. Lovell, M. S. El-Aasser), Wiley, Chichester, **1997**, pp. 37–55.