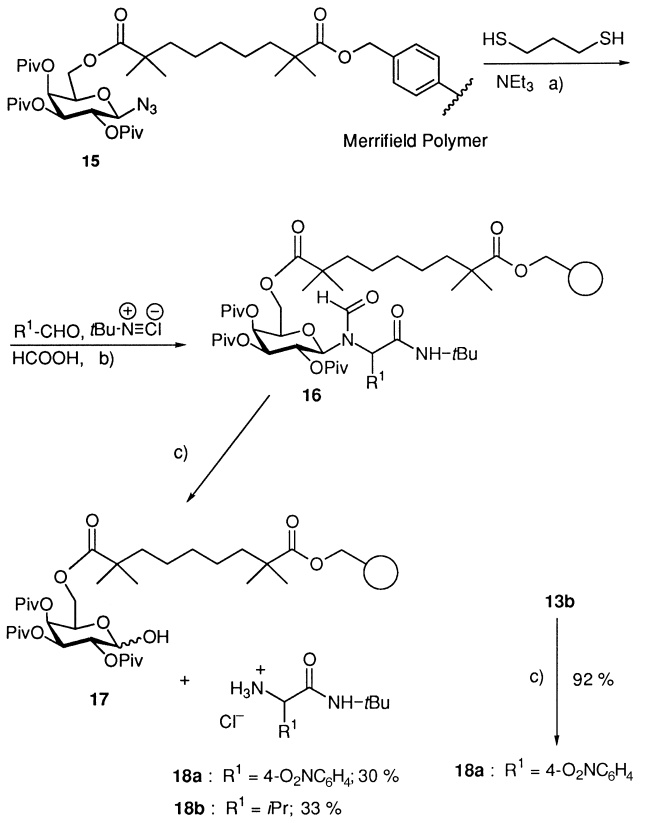


Scheme 4. a) DMF, 2 d, room temperature; b) $ZnCl_2 \cdot Et_2O$, THF, $-40\,^{\circ}C \rightarrow 0\,^{\circ}C$, 24 h; c) $CH_2Cl_2$/HCl (saturated) in MeOH (3:1), 12 h, then a little $H_2O$.

The potential of this stereodifferentiating synthesis on solid phase becomes evident, if one keeps in mind that the corresponding L-amino acid derivatives are available by analogous use of the D-arabinopyranosylamine,[15] that combinatorial reactions with phosphites give $\alpha$-aminophosphonic acid derivatives,[16] those with silyl ketene acetals yield $\beta$-amino acid derivatives[17] or with silyl dienol ethers furnish mono- and bicyclic chiral nitrogen heterocycles.[18, 19] Thus, the stereodifferentiating effect of solid-phase-linked glycosylamines of type **11** provides a versatile combinatorial access to chiral products of diverse structure.

Received: August 25, 1999
Revised: January 4, 2000 [Z13922]

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## Ring-Opening Metathesis Polymerization: Access to a New Class of Functionalized, Monolithic Stationary Phases for Liquid Chromatography

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Monolithic separation media for liquid chromatograpy were described as early as the 1960s and 1970s.[1, 2] The introduction of compressed, continuous supports by Hjertén et al. initiated an intense research activity in this field of materials science.[3, 4] Compared to classical, packed columns, continuous stationary phases offer a series of advantages. On one hand, the time-consuming procedures of particle syn-

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  0570-0833/00/3908-1433 $ 17.50+.50/0 

thesis and column packing are no longer necessary. On the other hand, lowered back pressures ($< 5$ MPa), high flow rates (up to 10 mm s$^{-1}$), and a significantly enhanced mass transfer have to be mentioned. Finally, dead volumes are eliminated. Consequently, monolithic separation media allow fast separations with comparably high resolutions. Additionally, capillary end frits that have to be used with packed columns in capillary liquid chromatography (CLC) and capillary electrochromatography (CEC) are no longer required. So far, a variety of functionalized and nonfunctionalized monolithic columns based on either organic or inorganic polymers are available. Interestingly, almost all rods based on organic polymers have been prepared by radical polymerization.[5, 6] Starting from polystyrene and glycidyl methacrylate, acrylate, or acrylamides, only a "simple" functionalization such as the generation of amino, alcohol, phenol, sulfonic acid, or carboxylate groups may be accomplished in a controlled way. We already combined ring-opening metathesis polymerization (ROMP)[7] with grafting and precipitation techniques for the synthesis of functionalized separation media.[8–11] A general advantage of ROMP is the possibility to use functional monomers. This and the controlled ("living") polymerization allow a highly reproducible functionalization.

Owing to the broad applicability of ROMP and the high definition of the resulting materials, we investigated to which extent this polymerization technique might be applied to the preparation of functionalized monolithic separation media.[12] The following steps describe the new concept for the synthesis of functionalized monoliths (Figure 1): 1) generation of a continuous matrix by ring-opening metathesis copolymerization of suitable monomers and a cross-linker in the presence of porogenic solvents within the separation device (column); 2) consecutive in situ derivatization with a suitable ROMP-active monomer. Through the use of ROMP, this in situ derivatization is made possible for the first time. Because of the living character of this polymerization technique, the majority of the initiator remains active. The fraction of the initiator that is covalently bound to the surface of the rod is accessible and may be used for further derivatization. Thus, pumping solutions of a ROMP-active monomer over the column allows grafting of the monomer onto the surface of the monolith.

Nonfunctionalized rods were prepared, and the influence of the stoichiometry of the reactants, porogenic solvents, and the initiator on the microstructure of the monolith was determined. Among the possible combinations of monomers and cross-linkers—for example, norbornene (NBE), norbornadiene, dicyclopentadiene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphthalene (Q1), and 1,4a,5,8,8a,9,9a,10,10a-decahydro-1,4,5,8,9,10-trimethanoanthracene, various Grubbs catalysts of the general formula $[Cl_2(PR_3)_2Ru(=CHPh)]$[13] (R = cyclohexyl (Cy), phenyl) as well as different porogenic solvents—the copolymerization of NBE with Q1 in the presence of two porogenic solvents, 2-propanol and toluene, with $[Cl_2(PCy_3)_2Ru(=CHPh)]$ was found to be the best. Investigations by electron microscopy revealed that the resulting rods consist of spherical, agglomerated microglobules (Figure 2). Under adequate polymerization conditions, the diameters of the microglobules may be varied within

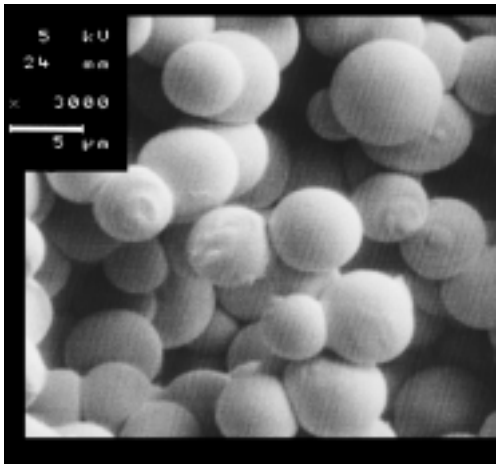



Figure 2. SEM image of the microstructure of monolith **VIII**.

0.6 – 30 μm, and comparably narrow particle size distributions (±20%) are achieved. As a consequence of the structural homogeneity the new materials possess excellent chromatographic properties. This was illustrated by the separation of bioactive proteins by reverse-phase chromatography (Figure 3) on a nonfunctionalized monolith.

The broad applicability of in situ functionalization was demonstrated by the derivatization of monoliths with a series of ROMP active monomers **1** – **7**. The extent of functionalization was checked in a qualitative way by FT-IR spectroscopy

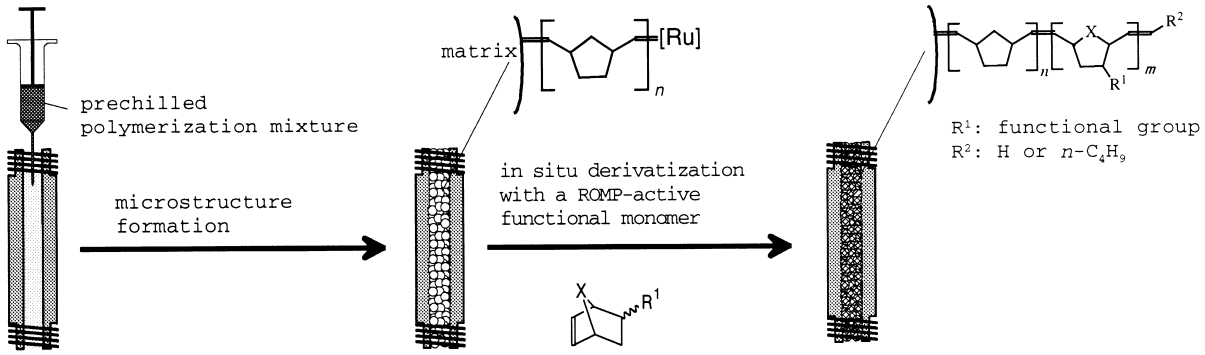



Figure 1. Preparation and in situ derivatization of continuous separation media by ring-opening methathesis polymerization. [Ru] = $[RuCl_2(PCy_3)_x]$ ($x = 1$, 2).

  0570-0833/00/3908-1434 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2000**, *39*, No. 8

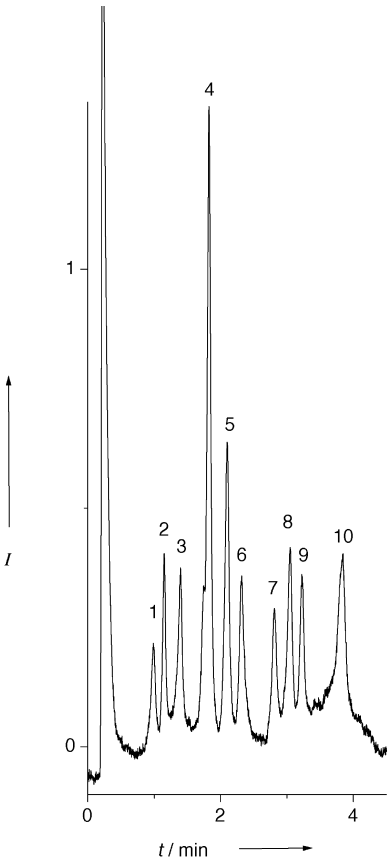
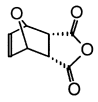
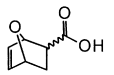
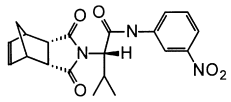
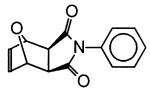
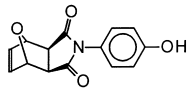
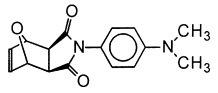
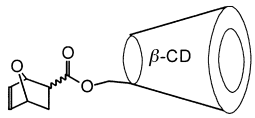



Figure 3. Protein separation by reversed-phase chromatography on monolith **VIII**. Column: $3 \times 50$ mm. Conditions: flow rate 6 mm s$^{-1}$; room temperature; mobile phases: A: acetonitrile (ACN) + 0.1 % trifluoroacetic acid (TFA), B: water + 0.1 % TFA; gradient: 0–0.5 min: 21 →36 % A, 0.5–3 min: →40 % A, 3–6 min: →55 % A; UV (218 nm). Analytes: 1) ribonuclease A, 2) insulin, 3) cytochrome C, 4) lysozyme, 5) $\beta$-lactoglobulin A, 6) transferrin, 7) myoglobin, 8) $\alpha$-chymotrypsinogen A, 9) catalase, 10) ovalbumin. $V$=1 μL; $c$ = 50 (1–3, 5–8), 100 (4, 9), 200 μg mL$^{-1}$ (10).

and in a quantitative way by acid–base titration (**I**, **II**) and elemental analysis (**III**–**VII**). The relevant IR signals of the corresponding monoliths as well as the amount of functional graft polymer are summarized in Table 1. The successful derivatization with the cyclodextrin (CD) derivative **7** was shown indirectly by a chiral separation. According to the demands on continuous supports, the enantioselective separation of proglumide was accomplished on monolith **VII** within 2.5 min (Figure 4).

In summary, the new continuous rods presented here differ from other continuous separation media as follows:[14] 1) They possess a new poly(cyclopentadiylvinylen) backbone, 2) they offer the possibility of functionalization through use of a large variety of functional groups including chiral selectors, and 3) they possess a homogeneous microstructure that may be tailored. Despite the ease of oxidation of this backbone, these materials are completely air-stable. To the best of our knowledge, no continuous stationary phases that have a comparable homogeneous-spherical microstructure and allow an in situ derivatization have been reported so far. Thus, in addition to the applications listed here, the reported concept possesses enormous potential in the synthesis of separation media for microapplications such as CLC and CEC.

Table 1. IR signals and capacities of functionalized continuous media for monoliths **I**–**VIII**, $\sigma = 90$ m$^2$, $\varepsilon_p = 49$ %, $\varepsilon_z = 8$ %.

| Monolith | Functional monomer | | IR signals $\tilde{\nu}$ [cm$^{-1}$] | Assignment | Capacity [mmol g$^{-1}$] |
|---|---|---|---|---|---|
| **I** |  | **1** | 1872, 1794 | C=O st | 0.2[a] |
| **II** |  | **2** | 3460 (br.)<br>1717 | COO–H st<br>C=O st | 0.14[a] |
| **III** |  | **3** | 1773, 1692<br>1541, 1522 | C=O st<br>C–C$_{arom.}$ | 0.03[b] |
| **IV** |  | **4** | 1771, 1700<br>1570, 1510<br>710 | C=O st<br>C–C$_{arom.}$<br>C–H$_{arom.}$ ($\delta$, oop) | 0.22[b] |
| **V** |  | **5** | 3436 (br.)<br>1783, 1725<br>1560, 1501<br>802 | O–H st<br>C=O st<br>C–C$_{arom.}$<br>C–H$_{arom.}$ ($\delta$, oop) | 0.06[b] |
| **VI** |  | **6** | 1783, 1719<br>1615, 1522<br>814 | C=O st<br>C–C$_{arom.}$<br>C–H$_{arom.}$ ($\delta$, oop) | 0.26[b] |
| **VII** |  | **7** | 3373<br>1746 | O–H st<br>C=O st | n.d.[c] |
| **VIII** | | – | – | – | – |

[a] Determined by acid–base titration. [b] Determined by elemental analysis (nitrogen analysis). [c] n.d. = not determined.

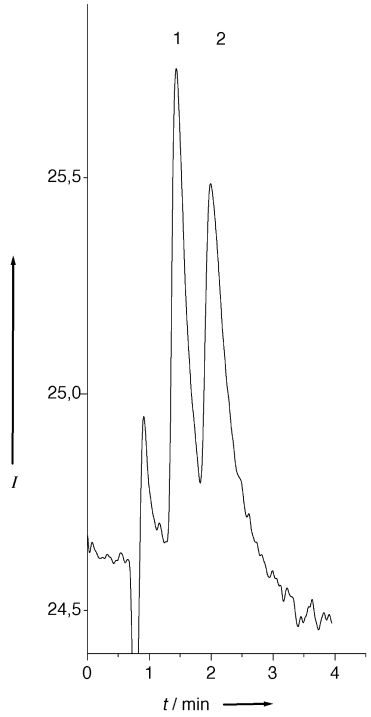



Figure 4. Enantioselective separation of proglumide on monolith **VII**. Column: $3 \times 150$ mm. Conditions: flow rate 6 mm s$^{-1}$; 0 °C; $V$ = 4 μL; $c$ = 20 μg mL$^{-1}$; mobile phase: ACN/MeOH/TFA/triethylamine 99.75/0.25/0.25/0.075 (v/v/v/v); UV (254 nm).

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*Experimental Section*

All experiments were carried out under argon using standard Schlenk techniques. Degassed and dry solvents were used throughout. Borosilicate columns (3 × 50 mm, 3 × 150 mm) silanized with bicyclo[2.2.1]hept-5-en-2-yltrichlorosilane were used. Monoliths **I**–**VIII** were prepared as follows: Solution A (chilled to −20 °C, NBE/Q1/2-propanol 25/25/40 (in wt %)) and solution B (toluene/$[Cl_2(PCy_3)_2Ru(=CHPh)]$ 9.995/0.005 (in wt %))[13] were mixed and rapidly transferred to the prechilled borosilicate column. Polymerization was allowed to proceed at 0 °C for 30 min and then at room temperature overnight. The initiator was cleaved off by passing 1-hexene/toluene (10/90) over the column. For functionalization of monoliths **I**–**VII**, 1 h after polymerization was started the column was purged with toluene to remove unchanged initiator. An aliquot (1 mL) of a 10% solution of monomer **1**–**7** in toluene or dimethylformamide was passed over the column. The HPLC columns were sealed and kept at 60 °C overnight. The catalyst was removed as described above. The total amount of ruthenium that remained within the monolith was determined by atom absorption spectroscopy (AAS) to be less than 10 $\mu g^{-1}$. Use of the stoichiometry described here allows the preparation of monoliths whose microstructure consists of microglobules that are 4 ± 1 μm. Nevertheless, the microstructure may be varied within 0.5–30 μm by changing the stoichiometry of the reactants and the porogenic solvents. For scanning electron micrtoscopy (SEM), samples were sputtered with Au/Pd under high vacuum. The specific surface ($\sigma$), the pore porosity ($\varepsilon_p$), and the interparticle porosity ($\varepsilon_z$) were determined by inverse gel permeation chromatography (GPC).[15] The in situ derivatization did not cause any significant changes in these values.

Received: September 30, 1999 [Z14085]


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# Optimized Two-Dimensional NLO Chromophores with a Threefold Symmetry Axis**

J. Jens Wolff,* Fred Siegler, Ralf Matschiner, and Rüdiger Wortmann*

*Dedicated to Professor Dieter Hellwinkel on the occasion of his 65th birthday*

The design of nonlinear optical (NLO) chromophores without dipole moment is a current area of research in molecular nonlinear optics.[1] Such molecules can be used for processes such as frequency doubling, frequency mixing, parametric oscillation, and electrooptical modulation. This seems to be in contradiction to the traditional opinion that efficient NLO chromophores should be designed as dipolar π systems substituted with one donor and one acceptor—like the prototype *p*-nitroaniline (*p*NA). However, in contrast to one-dimensional (1D) chromophores of the *p*NA type, nondipolar NLO chromophores with multiple donor–acceptor substitution generally show several significant tensor elements of the second-order polarizability ($\beta$). New NLO processes where electrical fields of different polarizations can be efficiently coupled with each other only become possible through two- and three-dimensional (2D and 3D) chromophores. So far, however, effective strategies for the optimization of such nondipolar chromophores have not been found. Thus, it is still uncertain whether they are really superior to their dipolar analogues with respect to the general efficiency–transparency problem—as has been stated several times.[2] For example, in planar, conjugated chromophores with a threefold symmetry axis, several efficient donor and acceptor groups have to be coupled to a central π system without great steric hindrance. Here we describe the most active 2D chromophores found so far and present the first systematic comparison between 2D chromophores of symmetry $D_{3h}$ and analogous 1D chromophores of symmetry $C_{2v}$.

Four 1,3,5-triazine derivatives with the donor groups 4-*N*,*N*-diethylaminophenyl and 4-*N*,*N*-diethylaminophenylethynyl (**1**, **2**, **5**, **6**) were synthesized by nucleophilic aromatic substitutions of cyanuric fluoride (Scheme 1). As representatives of the second new class of compounds, 1,3,5-tricyanobenzenes **3**, **4**, **7**, and **8** with single and triple substitution were obtained starting from 1,3,5-tricyano-2,4,6-trichlorobenzene. All UV/Vis spectra are shown in Figure 1.

These two structural types were chosen after a careful analysis[1a] of the nondipolar NLO chromophores published so

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[**] The authors would like to thank the Volkswagenstiftung and the Fonds der Chemischen Industrie for generous financial supports of this work.

  0570-0833/00/3908-1436 $ 17.50+.50/0 