The Construction of Polymeric [2×2] Metal Grids utilizing Supramolecular Initiators

Richard Hoogenboom, Daan Wouters and Ulrich S. Schubert*
Laboratory of Macromolecular Chemistry and Nanoscience,
Eindhoven University of Technology and Dutch Polymer Institute,
PO Box 513, 5600 MB Eindhoven, The Netherlands
Fax: 31-(0)40-247-4186, e-mail: u.s.schubert@tue.nl; www.schubert-group.com.

Functionalized 3,6-bis(2-pyridyl)-pyridazine ligands were synthesized by inverse electron-demand Diels-Alder reactions between 3,6-bis(2-pyridyl)-tetrazine and various (functional) alkynes. A hydroxy-functionalized ligand was subsequently utilized as co-initiator for the controlled ring-opening-polymerization of L-lactide. Detailed investigations of the resulting poly(L-lactide) macroligands revealed the successful incorporation of the metal coordinating ligand into the polymer chains. Moreover, complexation of both the hydroxy-functionalized ligand and the macroligands into (polymeric) [2×2] grids was proven by UV-vis spectroscopic investigations. In addition, the presence of defined metallo-supramolecular polymeric [2×2] grids was confirmed by AFM measurements.
Key words: Supramolecular chemistry, metal coordination, 3,6-bis(2-pyridyl)-pyridazine, supramolecular initiator, polylactide, grid-like architectures

1. INTRODUCTION

The introduction of supramolecular interactions into defined polymer structures seems to be a promising approach for the construction of novel (responsive) materials and nanomaterials with new mechanical and physical properties.[1,2] The most commonly used types of supramolecular interactions are hydrogen bonding, metal–ligand interactions and ionic interactions, whereby the first two are highly directional and thus preferable for the directed self-assembly of (macro)molecules. We choose to use metal-coordinating units because the self-assembly can be easily tuned from very labile to inert by varying the metal ion.[3] Metal coordinating units can be introduced into macromolecules via functional monomers,[4,5] end group[6] or side group[7] functionalization and via functional initiators.[8,9] For the synthesis of polymers with exactly one metal coordinating ligand, the end-group functionalization and functional initiator approach are best suitable, whereby the use of functional initiators provides easier isolation of the products.
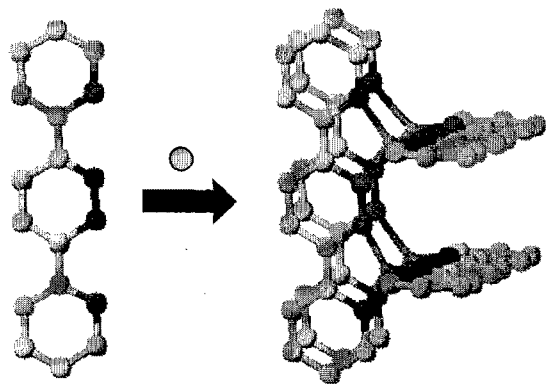

Figure 1: Self-assembly of 3,6-bis(2-pyridyl)pyridazine with copper(I) or silver(I) ions into [2×2] grids.
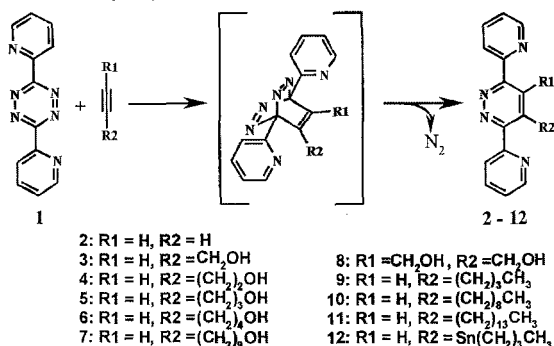
This functional initiator approach has been applied mainly with bipyridine and terpyridine functionalized initiators for controlled radical polymerizations,[10] living cationic ring-opening- polymerization of 2-oxazolines[8,9,11] and the controlled polymerization of lactides and lactones.[8,12,13] To extend this approach to larger self-assembled architectures, grid forming metal coordinating units can be used, which self-assemble with four or more entities together upon addition of metal ions. A synthetically easily accessible grid-forming ligand is 3,6-bis(2-pyridyl)-pyridazine, which self-assembles into [2×2] grids upon addition of copper(I) or silver(I) ions as depicted in Figure 1.[14]

In this contribution, the synthesis of various functionalized 3,6-bis(2-pyridyl)-pyridazine ligands is described (see ref. [15] for more detailed information). In addition, we discuss the utilization of one of those ligands as supramolecular co-initiator for the controlled ring-opening polymerization of L-lactide and subsequent investigations of the complexation of those macroligands (see also ref. [16]).

2. SYNTHESIS OF FUNCTIONAL LIGANDS

4,5-Substituted 3,6-bis(2-pyridyl)-pyridazines can be synthesized from the corresponding 3,6-bis(2-pyridyl)-tetrazine with alkenes and alkynes by an inverse electron demand Diels-Alder reaction. The synthesis of this tetrazine and its application in such cycloaddition reactions was first reported by Butte and Case.[17]

Scheme 1 depicts the investigated inverse type Diels-Alder reactions between 3,6-bis(2-pyridyl)-tetrazine 1 and various alkynes, which resulted in substituted 3,6-bis(2-pyridyl)-pyridazines 2-12 after elimination of a nitrogen molecule. The progress of the reactions could be followed visually, because the intense violet color of the tetrazine disappeared.

Scheme 1: Schematic representation of the inverse electron demand Diels-Alder reaction between 3,6-bis(2-pyridyl)-tetrazine **1** and various alkynes.

2: R1 = H, R2 = H
3: R1 = H, R2 = CH₂OH
4: R1 = H, R2 = (CH₂)₂OH
5: R1 = H, R2 = (CH₂)₃OH
6: R1 = H, R2 = (CH₂)₄OH
7: R1 = H, R2 = (CH₂)₆OH

8: R1 = CH₂OH, R2 = CH₂OH
9: R1 = H, R2 = (CH₂)₃CH₃
10: R1 = H, R2 = (CH₂)₈CH₃
11: R1 = H, R2 = (CH₂)₁₃CH₃
12: R1 = H, R2 = Sn(CH₂)₃CH₃

The cycloadditions of electron rich hydroxy-functional alkynes and the tributylstannyl acetylene could be performed in refluxing toluene, whereas the cyclo-additions of the unsubstituted alkynes needed more stringent conditions and were done in refluxing DMF (synthetic details are given in ref. [15]). Single crystals suitable for X-ray analysis were obtained for 3,6-bis(2-pyridyl)-bishydroxymethylpyridazine **8**. The observed molecular structure (ORTEP-plot depicted in the right inset of Figure 2) revealed the presence of hydrogen bonding between the hydroxyl groups and the nitrogen atoms of the outer pyridyl rings causing a torsion angle of 43.5 ° between the inner and the outer rings. The presence of those hydrogen bonds in solid state was also shown with IR spectroscopy (hydroxyl stretch vibration at 3200 cm⁻¹). Furthermore, the occurrence of hydrogen bonding in (deuterated) chloroform solution was proven with nuclear Overhauser effect NMR spectroscopy (NOESY), which demonstrated the through space coupling of the hydroxyl protons with the protons next to the nitrogen atoms of the pyridyl rings.

The complexation of functionalized 3,6-bis(2-pyridyl)-pyridazines was studied utilizing the bishydroxy functionalized compound **8**, because the conformation of this compound is stabilized by intramolecular hydrogen bonding. Thus, if this compound would be capable of flipping the outer rings for the self-assembly in supramolecular grids, the other (non-stabilized) functional ligands will also be able to do so.
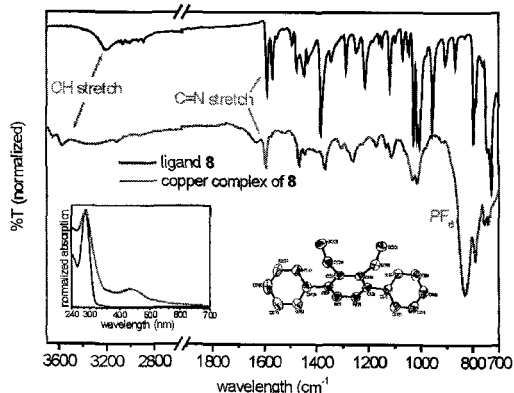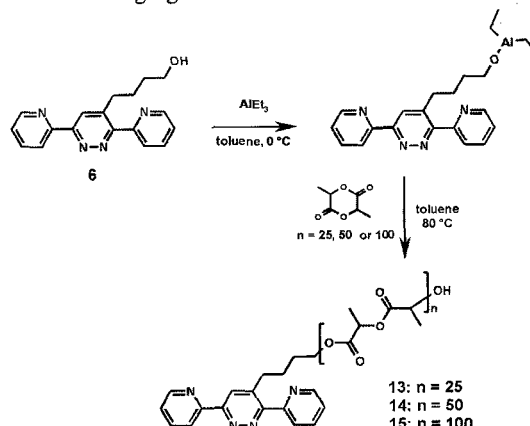

Figure 2: IR spectra of ligand **8** and the corresponding copper(I) complex together with the UV-vis spectra (left inset) and an ORTEP-plot (50% probability) of ligand **8** (right inset).

Scheme 2: Synthesis of poly(L-lactide) macroligands **13-15** utilizing ligand **6** as co-initiator.

n = 25, 50 or 100

13: n = 25
14: n = 50
15: n = 100

The self-assembly process was performed by adding ligand **8** (in dichloromethane) to a dichloromethane solution of tetrakis(acetonitrile)copper(I) hexafluoro-phosphate (both colorless solutions) resulting in instantaneous precipitation of the brown copper(I) grid complex. ¹H-NMR spectroscopy revealed broader signals and switching of the positions of the H3 and H6 protons of the pyridyl rings, which is indicative of complexation. IR spectroscopy showed a shift in C=N stretch vibration plus the disappearance of hydrogen bonding (Figure 2) and ESI-QTOF-MS revealed the existence of complete [2×2] grids together with many fragments. UV-vis spectroscopy clearly showed the appearance of the typical metal to ligand charge transfer band (MLCT) at 436 nm (Figure 2, left inset) that was also described for the formation of copper(I) grids with the unsubstituted 3,6-bis(2-pyridyl)-pyridazine.

3. MACROLIGAND SYNTHESIS

Poly(L-lactide) macroligands **13-15** were synthesized by utilizing the monohydroxy functionalized 3,6-bis(2-pyridyl)-4-hydroxybutylpyridazine **6** as co-initiator for the controlled ring-opening polymerization of L-lactide.[18,19] By the addition of one equivalent triethyl aluminum to ligand **6**, an aluminum alkoxide initiator was generated in situ. Different amounts of L-lactide were added to this initiating species resulting in polymers **13-15** (Scheme 2). ¹H-NMR spectroscopic investigations of the polymers, after precipitation in methanol, clearly revealed the incorporation of the ligands into the polymer backbones.
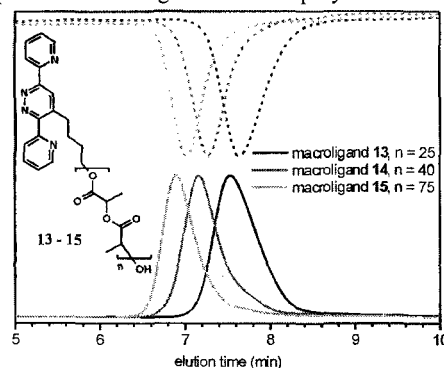

macroligand 13, n = 25
macroligand 14, n = 40
macroligand 15, n = 75

13 - 15

Figure 3: GPC traces of macroligands **13-15** obtained with RI-detector (dotted lines) and UV-detector (254 nm, solid lines) utilizing chloroform as eluent.

Table 1: Molecular weight data for the synthesized macroligands **13-15**.

	Macroligand 13	Macroligand 14	Macroligand 15
$M_{n,th}$	3900	7500	14700
$M_{n, NMR}$	3840	6800	11100
$M_{n,GPC\ UV}$	4900	9600	15600
$PDI_{GPC,UV}$	1.20	1.21	1.20
$M_{n,GPC\ RI}$	5500	10700	17300
$PDI_{GPC,RI}$	1.18	1.22	1.18
$M_{n,MALDI}$	3000	5000	8700
PDI_{MALDI}	1.12	1.11	1.06

Gel permeation chromatography (GPC) of the polymeric ligands (Figure 3) demonstrated narrow polydispersities around 1.20, which is indicative for controlled polymerizations. Moreover, the polymers were detected with both RI- and UV-detector, which proves the incorporation of the ligand into the polymers since the poly(L-lactide) backbone has no UV absorption at 254 nm. The molecular weights obtained from GPC are about 1.5 times higher than the molecular weights calculated from the NMR integrals (Table 1). This discrepancy is due to the calculation of molecular weights from GPC against polystyrene standards, which are likely to have a different hydrodynamic volume than poly(L-lactide)s. Moreover, the molecular weight of macroligand **15** is lower than the theoretical molecular weight, which is probably due to insufficient reaction time and thus incomplete reaction. MALDI-TOFMS characterization revealed well-resolved signals, whereby the mass peaks corresponded exactly to the masses calculated for single polymer chains containing a 3,6-bis(2-pyridyl)-pyridazine unit. The molecular weights obtained from MALDI-TOFMS are lower than those from ¹H-NMR spectroscopy and GPC (Table 1), which is likely due to underestimation of the high-mass poly(lactide) chains because of their lower ionization probability.

4. MACROLIGAND COMPLEXATION STUDIES

The complexation of the macroligands with copper(I) ions into polymeric [2×2] grids was studied by UV-vis spectroscopic investigations. A stock solution of tetrakis(acetonitrile)copper(I) hexafluorophosphate in dichloromethane was titrated into solutions containing macroligands **13-15**.[20] During the titration the color of the solutions changed from colorless to brownish indicating the spontaneous self-assembly of the macroligands with copper(I) ions. The titrations were followed by measuring an UV-vis spectrum after each addition of copper(I) ions as depicted in Figure 4 for macroligand **15**. Upon titration of copper(I) ions to polymeric ligand **15** an absorption band appears at 467 nm. After the addition of approximately 1 equivalent of copper(I) ions,[21] this absorption bands shifts to 437 nm, which is similar to the MLCT band of the copper(I) grid from the non-polymerized ligand **6**. Figure 5 shows the absorption at 437 nm and the change in absorption maximum against equivalents of copper(I) ions added for all three macroligands **13-15** as it was obtained from the UV-vis titrations.
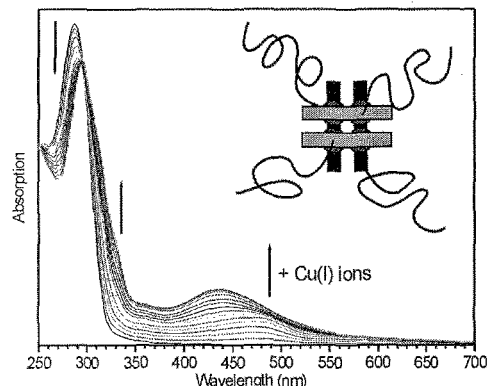

Figure 4: UV-vis titration of macroligand **15** with Cu(I) ions in dichloromethane. Each titration step represents the addition of 0.16 equivalents of copper(I) ions relative to the macroligand. The inset shows a schematic representation of the polymeric [2×2] grid-like complex.

For macroligands **13** and **14**, the absorption at 437 nm increased linearly until the addition of one equivalent of copper(I) salt after which the absorption leveled off, demonstrating the formation of complete copper(I) grids. For macroligand **15** also a linear increase in absorption at 437 nm is observed. However, the increase continues until the addition of two equivalents of copper(I) ions and the final absorption is only half the absorption that was obtained for the other two macroligands. Moreover, the absorption maximum of the polymeric grid-like complexes shifted from 467 nm to 437 nm. This shift is not completely understood, but it might result from a transition from complexes with two ligands and one copper(I) ion into complete polymeric [2×2] grid-like complexes. The shift in absorption maximum occurs at different equivalents of added copper(I) salt for the different macroligands, whereby it is evident that the transition occurs at higher amounts of added copper(I) ions for higher molecular weight macroligands. This indicates that the longer the polymer chains onto the ligand are the more difficult it becomes to form complete grids due to increased shielding of the metal-coordinating ligand by the larger polymers and/or decreased diffusion of copper(I) ions to the ligands. For macroligand **15**, the influence of the large polymer chains is so strong that not all macroligands form complete polymeric [2×2] grids resulting in a lower final absorption at 437 nm.
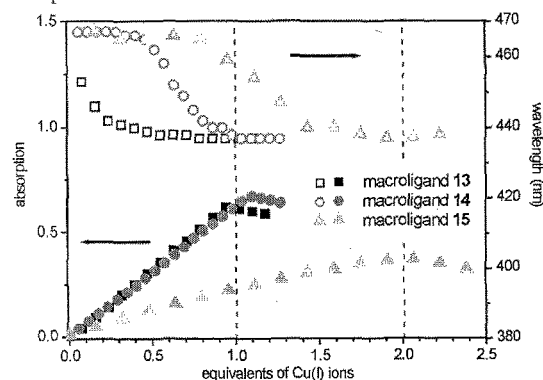

Figure 5: Increase in absorption at 437 nm (closed symbols) and absorption maximum shift (open symbols) upon addition of copper(I) ions.
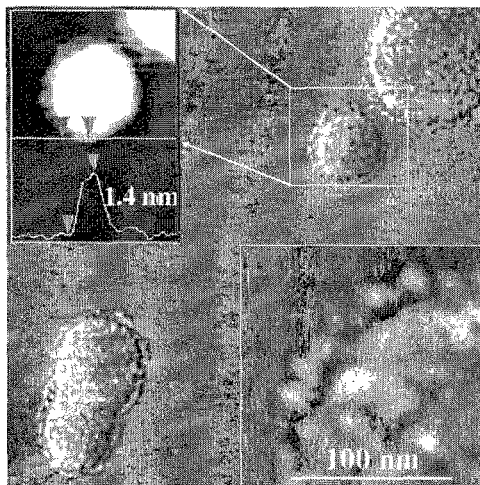
Figure 6: AFM phase image of polymeric [2×2] grids from macroligand **13** (image size 1.33 μm).

Polymeric [2×2] grid-like metal complexes from macroligand **13** were additionally investigated with atomic force microscopy (AFM).[22] Clusters of single spherical particles surrounded by a corona of single isolated particles were observed as depicted in Figure 6. The top-left inset displays a line scan over a single particle showing their height of 1.4 nm. An enlarged quarter of a large cluster of single spherical particles is depicted in the bottom-right inset of the phase image. The single particles in the corona have a diameter of 13-15 nm (not corrected for tip shape). The size and the height of the single particles imply that they consist of individual polymeric [2×2] grids, whereby the poly(*L*-lactide) chains are flattened on the surface. Moreover, AFM investigations of the free macroligand **13** did not show any special features indicating that the observed species are indeed resulting from the complexation.

5. CONCLUSIONS

Novel functionalized 3,6-bis(2-pyridyl)pyridazines were prepared by the inverse electron demand Diels-Alder reaction with various alkynes. The potentials of those ligands were demonstrated by the successful formation of a copper(I) [2×2] grid-like metal complex.

A monohydroxy functional ligand was subsequently used as co-initiator for the controlled polymerization of *L*-lactide) resulting in well-defined poly(*L*-lactide) macroligands. The successful incorporation of the ligand into the polymers was demonstrated using ¹H-NMR spectroscopy and GPC. Complexation studies of those macroligands with copper(I) ions were performed by UV-vis spectroscopic titrations. The smaller macroligands **13** and **14** could be completely converted into polymeric grid, but the longer polymer chains of macroligand **15** prohibited the formation of solely polymeric [2×2] grids. AFM investigations on the polymeric copper(I) grid from macroligand **13** showed the presence of clusters of polymeric grids surrounded by a corona of discrete polymeric grids.

Further studies on structure, properties and stability of these polymeric [2×2] grids are ongoing. Moreover, such systems might lead to novel smart materials.

REFERENCES AND NOTES

[1] L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.*, **101**, 4071-4097 (2001).

[2] U. S. Schubert, C. Eschbaumer, *Angew Chem.*, **114**, 3016-3050 (2002); *Angew. Chem. Int. Ed.*, **41**, 2892-2926 (2002).

[3] B. G. G. Lohmeijer, U. S. Schubert, *J. Polym. Sci.: Part A: Polym. Chem.*, **41**, 1413-1427 (2003).

[4] U. S. Schubert, H. Hofmeier, *Macromol. Rapid. Commun.*, **23**, 561-566 (2002).

[5] A. Lavalette, J. Hamblin, A. Marsh, D. M. Haddleton, M. J. Hannon, *Chem. Commun.*, 3040-3041 (2002).

[6] B. G. G. Lohmeijer, U. S. Schubert, *Angew. Chem.*, **114**, 3980-3984 (2002); *Angew. Chem. Int. Ed.*, **41**, 3825-3829 (2002).

[7] Y. Chujo, K. Sada, T. Saegusa, *Macromolecules*, **26**, 6315-6319 (1993).

[8] U. S. Schubert, M. Heller, *Chem. Eur. J.*, **7**, 5252-5259 (2001).

[9] J. J. S. Lamba, C. L. Fraser, *J. Am. Chem. Soc.*, **119**, 1801-1802 (1997).

[10] W. Wu, J. E. Collins, J. E. McAlvin, R. W. Cutts, C. L. Fraser, *Macromolecules*, **34**, 2812-2821 (2001).

[11] G. Hochwimmer, O. Nuyken, U. S. Schubert, *Macromol. Rapid Commun.*, **19**, 309-313 (1998).

[12] M. Heller, U. S. Schubert, *Macromol. Symp.*, **177**, 87-96 (2002).

[13] P. S. Corbin, M. P. Webb, J. E. McAlvin, C. L. Fraser, *Biomacromolecules*, **2**, 223-232 (2001).

[14] M.-T. Youinou, N. Rahmouni, J. Fischer, J. A. Osborn, *Angew. Chem.*, **104**, 771-773 (1992); *Angew. Chem. Int. Ed.*, **31**, 775-778 (1992).

[15] R. Hoogenboom, G. Kickelbick, U. S. Schubert, *Eur. J. Org. Chem.*, in press (2003).

[16] R. Hoogenboom, D. Wouters, U. S. Schubert, *Macromolecules*, **36**, 4743-4749 (2003).

[17] W. A. Butte, F. H. Case, *J. Org. Chem.*, **26**, 4690-4692 (1961).

[18] H. R. Kricheldorf, T. Mang, J. M. Jonté, *Macromolecules*, , **17**, 2173-2181 (1984).

[19] H. R. Kricheldorf, I. Kreiser-Saunders, *Macromol. Symp.*, **171**, 85-102 (1996).

[20] Titrations were performed at a polymer concentration of 0.50 mg/mL (macroligand **13**), 1.0 mg/mL (**14**) or 2.0 mg/mL (**15**) in dichloromethane.

[21] Equivalents are given with regard to the ligand molecules. The concentration of ligand molecules is calculated from the $M_{n,NMR}$.

[22] A solution of the polymeric grids (0.05 mg/mL) was dropcast onto mica and imagined utilizing tapping mode AFM.