

138. Dendritic Styryl TADDOLs as Novel Polymer Cross-Linkers: First Application in an Enantioselective Et_2Zn Addition Mediated by a Polymer-Incorporated Titanate

Preliminary Communication

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TADDOLs ($\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanols) with dendritic branches attached to the aryl groups and with 8 or 16 peripheral styryl double bonds have been synthesized (**4** and **5**). With these compounds, dendritic molecules were employed for the first time as cross-linkers in a polymerization. The resulting polystyrene was loaded with titanate ($\text{Ti}(\text{OCHMe}_2)_4$) to generate polymer beads incorporating Ti-TADDOLate centers (Figs. 1 and 2) for enantioselective catalysis (Et_2Zn addition to PhCHO). Compared with conventionally polymer-attached, insoluble Ti-TADDOLates (cf. **3**), the new materials have a much higher catalytic activity, rather close to that of soluble analogs (Fig. 3).

TADDOLs ($\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanols) have been shown to be useful ligands in metal complexes for stoichiometric and catalytic enantioselective transformations²⁾. Due to their preparation from tartrate, the original TADDOLs of C_2 - (**1**) and C_1 -symmetry (**2**) are readily modified; we have recently demonstrated that a styryl-substituted TADDOL can be incorporated in a cross-linked (divinylbenzene) polystyrene, and that the corresponding titanate **3** can, for instance, be used for highly enantioselective nucleophilic additions to aldehydes [2]. Of course, the insoluble titanate **3** was catalyzing the reactions studied less efficiently than the monomers derived from **1** or **2** (*vide infra*) [3]. We, therefore, decided to prepare dendritically substituted TADDOLs, with peripheral styryl groups, such as **4** and **5**. To the best of our knowledge³⁾ there has been no report in the literature of the use of a dendrimer as cross-linker in a polymerization. Also, we are not aware of any work (outside of our own group) in which a chiral, catalytically active site has been placed in the core of a dendrimer. It is important to emphasize that only dendrimers of low generation number can possibly serve as carriers of ligands for catalysis: the densely packed surfaces of high-generation dendrimers (with critical size) prevent catalytic activity, both, at the surface (crowding!) and

¹⁾ Part of the projected Ph. D. thesis of P.B.R., and of the Master's thesis of H. S., ETH-Zürich, 1997.

²⁾ For short review articles, see [1].

³⁾ Besides a distyryl-TADDOL [2], a distyryl salen has been used as a cross-linker in a polymerization [4]. There are, of course, myriads of chiral ligands which were polymer bound or copolymerized for immobilization, see ref. in [2], and two recent articles on soluble [5] and insoluble [6] polymers containing quinine-type ligands for dihydroxylations.

in the cavities (hindered access!)⁴). We hoped that, due to the conformationally flexible dendritic spacers between the chiral ligand and the polymer backbone(s), the cross-linked, insoluble polymers obtained from compounds **4** or **5**, and styrene would have readily accessible TADDOL moieties, and thus provide catalytic activity comparable to that of soluble analogs.

The synthesis of the novel cross-linkers starts with the reaction of {[4-(*tert*-butyl)dimethylsilyloxy]phenyl} magnesium bromide with the commercial acetonide of (*R,R*)-diethyl tartrate to give diol **6** (80%) which was deprotected (Bu_4NF) to yield the hexol **7** (87%) and etherified at the phenolic positions by the corresponding benzylic branch bromides to furnish ⁵) 60–70% of the desired first- and second-generation dendrimers **4** and **5**, respectively. The branches were obtained by *Fréchet's* convergent methodology [8] from 4-vinylbenzyl chloride and 3,5-dihydroxybenzoate⁶). For comparison purposes (*vide infra*), we have also prepared the dendrimer **8** lacking the vinyl groups⁷) present in **4**.

The styryl TADDOLs **4** and **5** were copolymerized with styrene, following the suspension procedure detailed in [2]. The size of the beads (100–600 μm) obtained decreased with increasing ratio styrene/styryl-TADDOL (6:1–48:1). Treatment of the thoroughly dried beads with $\text{Ti}(\text{OCHMe}_2)_4$ in toluene (azeotropic removal of Me_2CHOH) gave the Ti-loaded particles (accompanied by a color change, see *Fig. 1*). A schematic presentation of polymer **9a** (from **4**) is given in *Fig. 2*; **9b** (from **5**) has an analogous composition, with 16 rather than 8 attachments to the polystyrene backbone.

The new polymer-incorporated Ti-TADDOLates were tested for the catalysis of Et_2Zn addition to PhCHO under the usual conditions [2] [10]. The results, including those of a comparison with soluble Ti-TADDOLates, are shown in the *Table*: *i*) the dendritically cross-linked Ti-TADDOLate polymers **9** give rise to almost the same enantioselectivity as the simple polymer-bound analog **3**. *ii*) With 0.2 equiv. of Ti-TADDOLates, the enantioselectivities obtained under homogeneous (er up to 99:1) and heterogeneous (er up to 98:2) conditions are comparable. *iii*) The selectivity seems to increase with decreasing TADDOLate content in the dendritic polymers **9**. *iv*) The polymer **9b** prepared with the second-generation dendrimer **5** does not appear to give better results than the one from first-generation **4**.

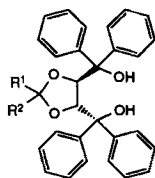
In *Fig. 3*, we show the rates of Et_2Zn -to-PhCHO additions at -25° with the different catalysts. While the polymer-bound Ti-TADDOLate **3** is considerably slower (4.5 h to 90% conversion) [3] than the soluble analogs from **2** (10 min), and from **8** (12 min), the novel dendritically incorporated Ti-TADDOLate **9a** is in fact much faster (40 min) than **3**. Thus, our expectation that dendritic cross-linking ligands for catalytic applications of organometallic complexes would render polymer-incorporated active sites, which are more easily accessible, was actually met!

⁴) For large dendrimers with chiral building blocks on the surface, see the papers on 'dendritic boxes' and on dendrimers as chiral catalysts – a critical note' [7].

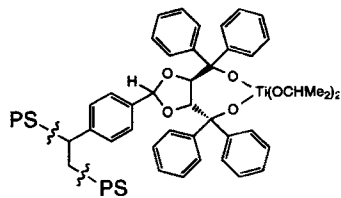
⁵) We were surprised to observe formation of side products containing five branches (one on a tertiary C-atom of the TADDOL unit!).

⁶) See also our previous syntheses of chiral dendrimers with *Fréchet* branches [9].

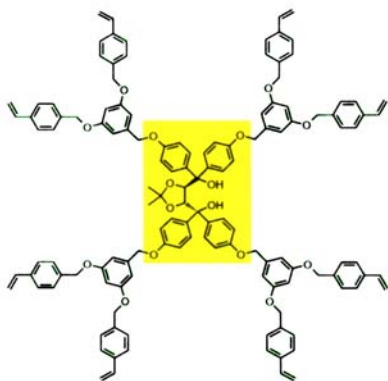
⁷) In spite of the propensity for spontaneous polymerization (especially in solution), the compounds containing styryl groups, as described here, can be handled with due care; they were purified (by chromatography or recrystallization) and fully characterized (including by elemental analyses).



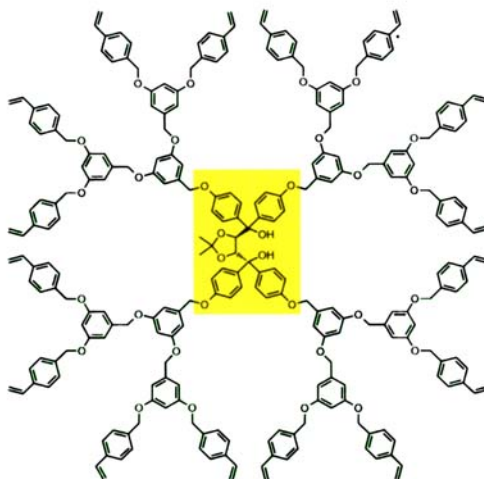
1 (R¹ = R² = Me)
2 (R¹ = Ph, R² = H)



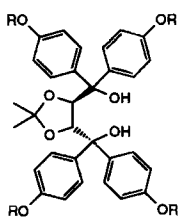
3 (PS = polystyrene chain)



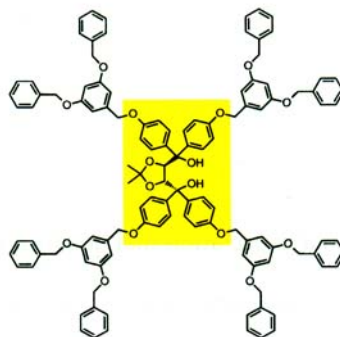
4 (m.p. 63-65°)



5 (m.p. 68-70°)



6 (R = TBDMS)
7 (R = H)



8 (m.p. 72-73°)

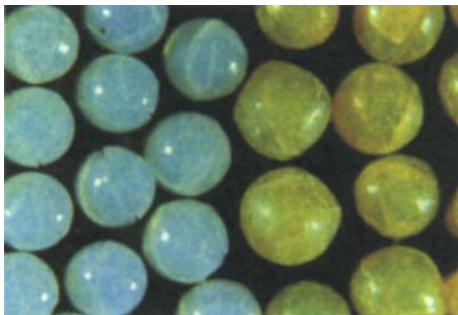


Fig. 1. Polymer beads (diameter ca. 600 μm) formed by suspension polymerization of the dendritic styryl TADDOL **4** and styrene before (left) and after (right) titanate loading. The particles shown were obtained by fractional sieving of a bead population from styrene/17% **4**.

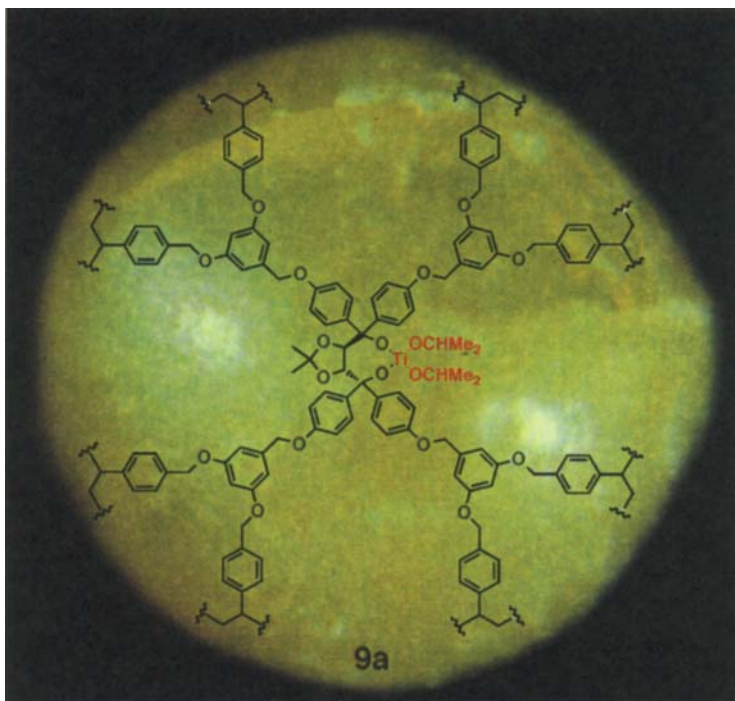
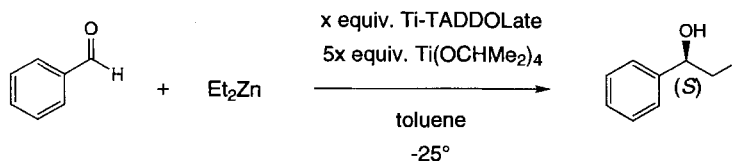


Fig. 2. Schematic presentation of the diisopropoxy-Ti-TADDOLate **9a** derived from the cross-linked suspension copolymer obtained from **4** and styrene (ratio 1:20), after treatment with $\text{Ti}(\text{OCHMe}_2)_4$ (with removal of 2 equiv. of HOCHMe_2)

Multiple use of the new materials and applications in other reactions, together with all experimental details, will be described in a forthcoming full paper.

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Table. *Enantioselective Formation of (S)-1-Phenylpropan-1-ol by Ti-TADDOLate-Catalyzed Et₂Zn Addition to PhCHO*. The percentages given in square brackets for the polymer-bound Ti-TADDOLates are the mol-% amounts of the dendritic TADDOLs used in the copolymerization with styrene.



Ti-TADDOLate (x equiv.)	PhCHO [mmol]	Et ₂ Zn [mmol]	Conversion after 20 h [%]	Enantiomer ratio (er) of product
<i>Homogeneous</i>				
from 2 (0.2)	11	20	quant.	99:1
from 8 (0.2)	4	7.2	quant.	97:3
<i>Heterogeneous</i>				
3 (0.2) ^a)	11	20	quant.	98:2
9a [17% 4] (0.02)	10	18	68	59:41
9b [13% 5] (0.02)	10	18	53	51:49
9a [6% 4] (0.05)	4	7.2	41	76:24
9a [5% 4] (0.05)	4	7.2	53	83:17
9b [3% 5] (0.05)	10	18	23	76:24
9a [5% 4] (0.20)	4	7.2	quant.	94:6
9b [2% 5] (0.20)	3	5.4	quant.	93:7

^a) Taken from [2].

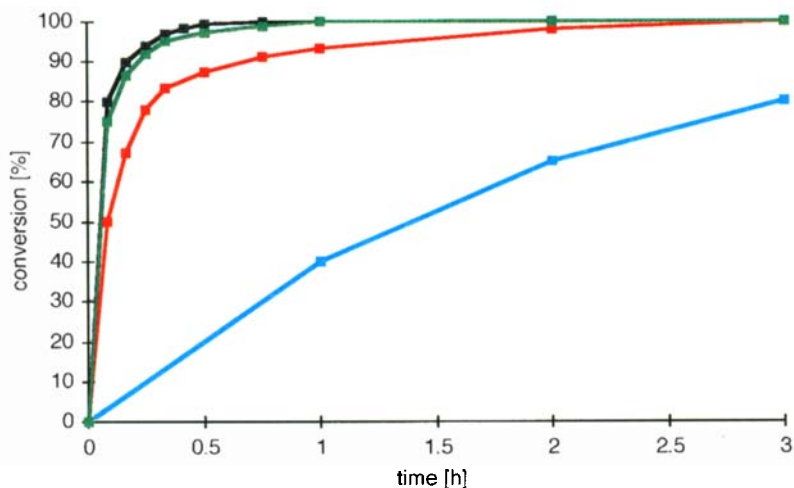


Fig. 3. *Reaction rates of the addition of Et₂Zn to PhCHO*. Catalysis by the soluble Ti-TADDOLates from **2** (black) and from the dendritic compound **8** (green). Catalysis by the polymer-bound non-dendritic Ti-TADDOLate **3** (blue) and **9a** (red). Ti-TADDOLate/Ti(OCHMe₂)₄ ratio is in all cases 1:5. Enantioselectivities with Ti-TADDOLates from **2** (er 99:1), **8** (er 97:3) with **3** (er 98:2), and with **9a** (er 94:6).

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