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# TADDOLs – from Enantioselective Catalysis to Dendritic Cross Linkers to Cholesteric Liquid Crystals

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When we and others realized in the early eighties [1] that organotitanium compounds $(R'O)_3TiR$ react much more selectively with electrophiles than their conventional Mg and Li counterparts, we immediately searched for suitable chiral alkoxides which would render these reagents enantioselective. One of the first novel alkoxides tested successfully was obtained by addition of excess PhMgBr to the commercial acetonide of tartrate ester, see Fig. 1 (Aryl = Ph, $R^1 = R^2 = Me$, X = O, Y = Z = OH). The formidable systematic name was abbreviated as TADDOL, and, over the years, it turned out (i) that this compound could be widely modified by using various aldehydes, ketones, aryl Grignard derivatives, cyclic $C_2$-symmetrical dicarboxylates for its preparation, (ii) that substitution of the OH groups by other functionalities in the diarylmethanol moieties was feasible, see Fig. 1.

Far beyond the original purpose, TADDOL derivatives emerged as most general chiral auxiliaries in the broadest sense: compounds with the help of which 'chirality can be introduced', *i.e.* enantiopure products (EPC) [4] (or phases) can be prepared (generated) from achiral or racemic precursors, by catalytic, stoichiometric, or even excessive use of the auxiliary which may be the reagent itself, or which may be covalently or non-covalently attached to a reactant. A list of uses is collected in Fig. 2.

Most recently, we have started using immobilized TADDOL derivatives, with excellent results [10–13]. Most remarkably, TADDOLs with dendritic arms (à la Fréchet) and 8 or 16 peripheral styryl groups, when embedded as cross-linkers in polystyrene, provide a material of unique properties: swelling of the polymer beads is maintained over 20 cycles of application (polymer-bound Ti-TADDOLate for catalytic enantioselective additions of $Et_2Zn$ to PhCHO); the catalytic sites are accessible under diffusion control, and essentially no difference in enantioselectivity or rate is detectable between the monomeric (homogeneous reaction) and the dendritically incorporated polymer-bound TADDOLate (heterogeneous conditions), see Fig. 3. Preliminary results with BINOL and Salen ligands which have been incorporated into polystyrene as modified, cross-linking styryl derivatives suggest that the effect observed with TADDOLs is a general one [14].

Another effect – most surprising to us – was encountered with controlled-pore-glass (CPG) grafted TADDOLates [13]: The TADDOL was grafted to the surface of microporous silicagel (surface area 350 $m^2/g$), and the material silylated (hydrophobization), as shown in Fig. 4. In the first run, the enantioselectivity of our standard reaction ($Et_2Zn$ + PhCHO, mediated by the derived Ti-TADDOLate) was essentially identical to that observed in homogeneous solution (*ca.* 98:2); but, after ten runs it had dropped to 92:8. We dared to wash the material with HCl/$H_2O$/$Me_2CO$, to find that – after washing with distilled water, rigorous drying, and reloading with titanate – the reactivity and enantioselectivity were restored, a process which could be carried out repeatedly!

A comparison of TADDOL with BINOL reveals intriguing similarities in structure and reactivity, but also intrinsic differences. The ease of TADDOL preparation and modification is

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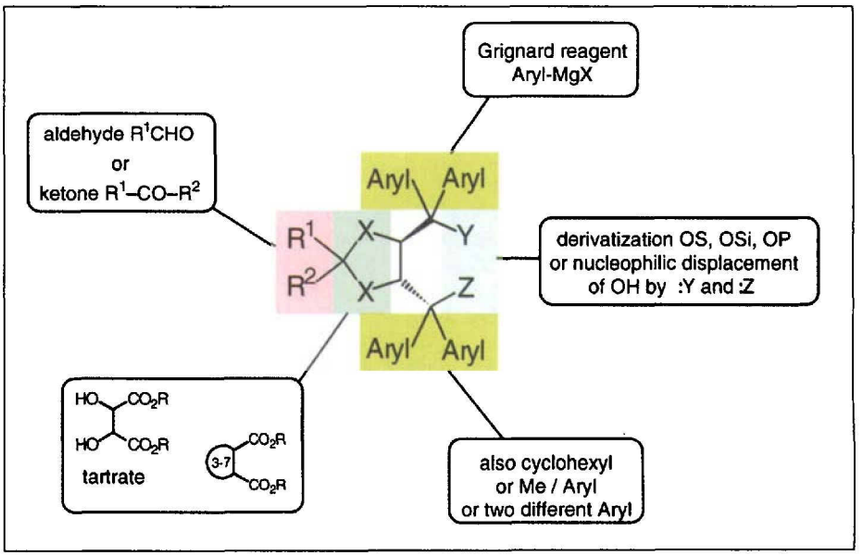


Fig. 1. TADDOL derivatives and analogues from $C_2$-symmetrical dicarboxylates, aldehydes or ketones, Grignard reagents, and heteroatomic chlorides or nucleophiles [2] [3].

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## What are TADDOL derivatives good for ?

- chiral additives in liquid crystals (nematic ⟶ cholesteric phases)
- enantiomer separation (hydrogen bonding, clathrate formation) resolution by crystallization, NMR shift reagents
- solid-state reactions, including photochemistry
- ligands and ligand components on metal centers for stoichiometric and catalytic (homogeneous and heterogeneous) stereoselective reactions

Li Mg Al Si Cu Zn Ce Ti Zr Mo Rh Pd Pt

- nucleophilic 1,2- and 1,4- additions
- [2+1], [2+2], [3+2], [4+2] cycloadditions
- metatheses
- allylations
- iodolactonizations
- ene reactions

- stoichiometric chiral reagents (*cf.* protonations, oxidations)

Fig. 2. Uses of TADDOLs for 'introducing chirality' – in liquid crystals [5], for resolutions [6], in NMR analyses [7], in solid-state reactions (including photochemical processes) [6], as ligands on metals for reactions involving Lewis acidic [8] and other organometallic centers [2][9], and as stoichiometric reagents.

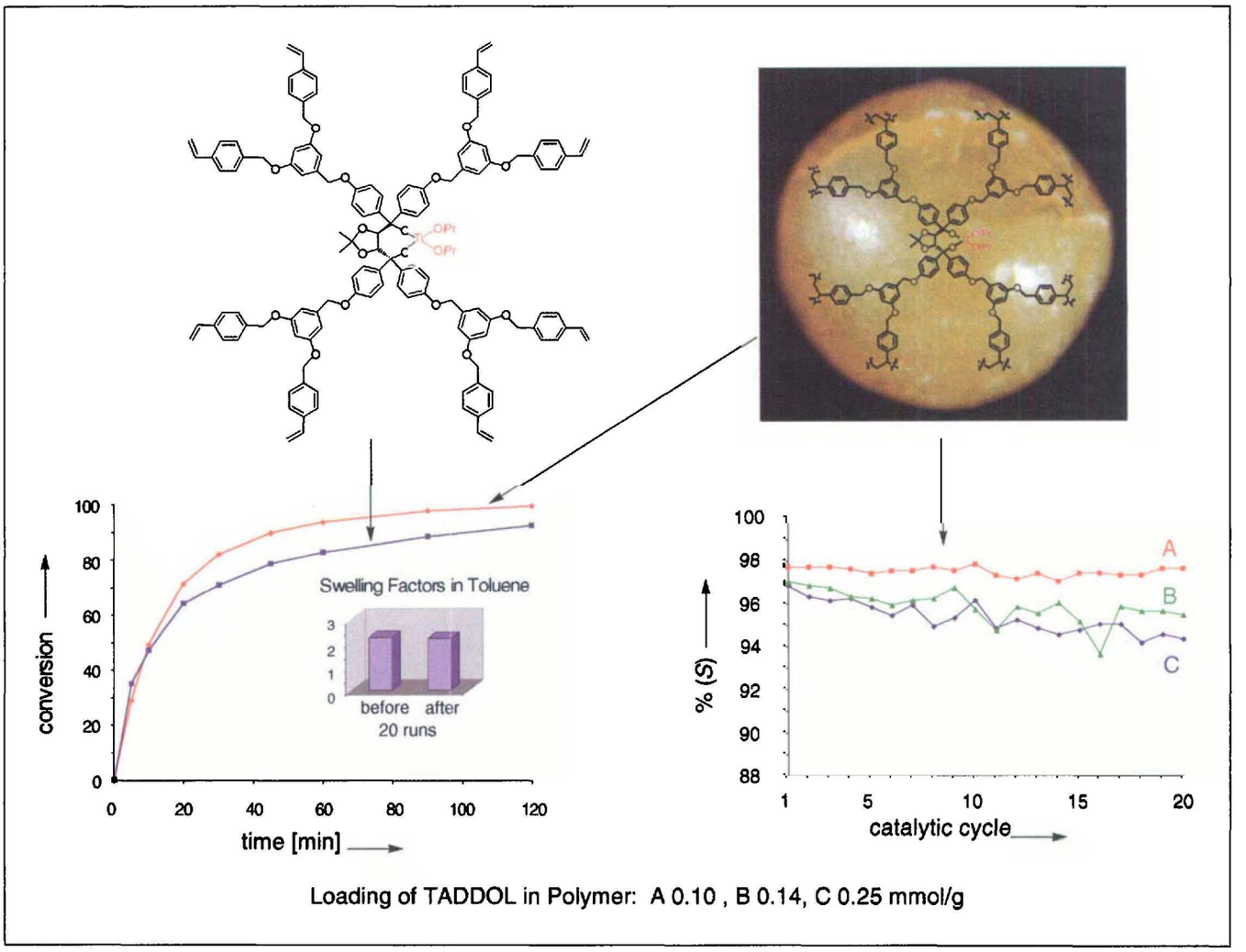


Fig. 3. Comparison of dendritic Ti-TADDOLate in homogeneous solution and embedded in polystyrene by cross-linking suspension polymerization for the standard test reaction $Et_2Zn$ + PhCHO [11].

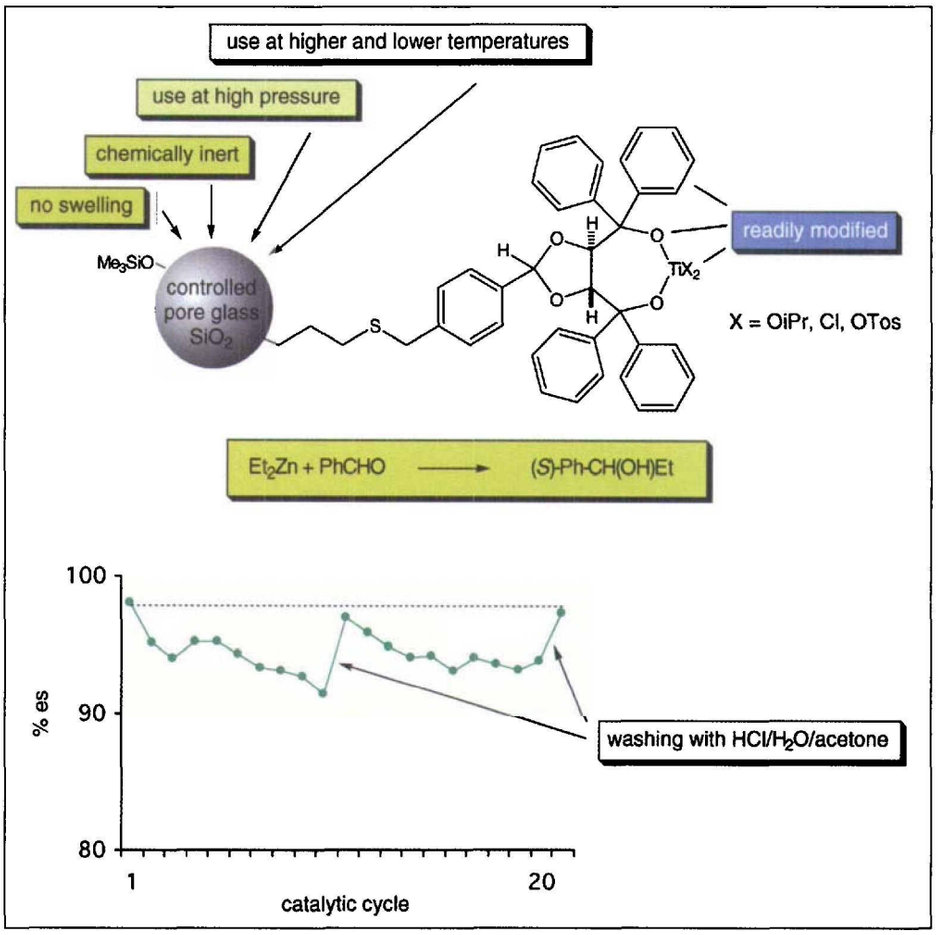


Fig. 4. $SiO_2$-bound Ti-TADDOLate may be washed in multiple applications for the standard test reaction, with restoration of activity (not shown here) and enantioselectivity [13]. Obviously, the SiOH-protecting groups ($Me_3SiO$) are not lost in the washing process (without them, the reaction does not work at all!).

unrivalled by BINOL. On the other hand, the phenolic OH groups of BINOL have a $pK_a$ of *ca.* 10 to successfully complex metal ions such as the lanthanides even in aqueous and other protic media [15], while TADDOL is a much less acidic aliphatic diol, so that it is doomed to fail as ligand for these ions. Various avenues to the synthesis of 'acidic' TADDOL derivatives are being pursued in our laboratory.

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