

Efficient polymer-supported Sharpless alkene epoxidation catalyst

Laetitia Canali,^a Jaana K. Karjalainen,^a David C. Sherrington^a and Osmo Hormi^b

^a Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, UK G1 1XL

^b Department of Chemistry, University of Oulu, Oulu, Finland

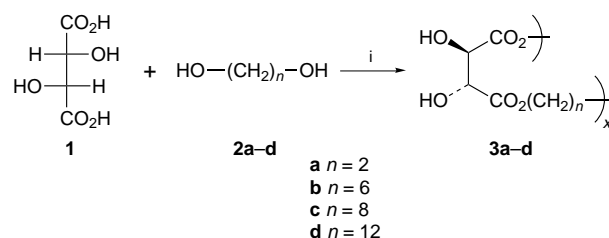
Linear poly(tartrate ester) ligands provide high chemical yields and enantiomeric excesses in the epoxidation of *trans*-hex-2-en-1-ol using Ti(OPr)₄-*tert*-butyl hydroperoxide.

The advantages of polymer-supported reactive species are now widely recognised by organic chemists, and increasing exploitation of these systems is occurring both in academic and industrial laboratories.¹ The effective immobilisation of asymmetric catalysts, reagents and auxiliaries is a particularly important methodological target, especially for metal complex-based catalysts. Progress in the area has been reviewed by Hodge² and Sherrington.¹ Unfortunately, more often than not the supported systems display levels of induction below those of the corresponding low molecular weight species. However, a notable exception is the Zn-catalysed asymmetric alkylation of aldehydes using ZnEt₂ with chiral amino alcohols, where polymer-supported analogues yield very high levels of enantiomeric excess (ee).^{3,4} Recently attention has focussed on a number of asymmetric alkene oxidation catalysts. Attempts to immobilise Jacobsen's asymmetric Mn^{III}-based alkene epoxidation catalyst⁵ have led to polymeric species which offer only relatively low ees in typical reactions.^{6,7} However, the results reported by Song *et al.*⁸ on the Sharpless asymmetric dihydroxylation of alkenes⁹ using catalytic levels of OsO₄ with K₃Fe(CN)₆-K₂CO₃ as secondary oxidant and polymeric alkaloids as the chiral ligand are remarkable, with essentially quantitative asymmetric induction coupled with high chemical yields.

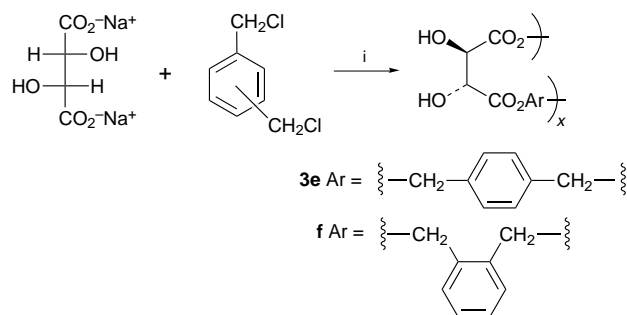
Interestingly, there are no reports of the successful immobilisation of the Sharpless Ti-tartrate ester-based asymmetric alkene epoxidation catalyst, despite this being a relatively long-standing and well used methodology.¹⁰ An early attempt to develop a polymer-supported system by Farrell *et al.*¹¹ employed a single tartrate ester unit bound to a polystyrene resin. However, the induction achieved (*ca.* 50–60% ee) was only modest. We now report on the synthesis of a group of poly(tartrate ester)s and their use with titanium tetraisopropoxide [Ti(OPr)₄] and *tert*-butyl hydroperoxide (tBHP) as the oxidant in epoxidising *trans*-hex-2-en-1-ol **4** in high chemical yield and good ee.

Poly(tartrate ester)s **3a–d** were synthesised from 1-(+)-tartaric acid **1** and diols **2** using a standard polycondensation procedure¹² (Scheme 1). Water and unreacted diol were

removed by distillation under high vacuum at the end of the reaction. The polymers were extracted with acetone in a Soxhlet apparatus and dried in a vacuum oven (50 °C) for *ca.* 15 h. Poly(tartrate ester)s **3e,f** were synthesised from 1-(+)-tartaric acid disodium salt dihydrate dissolved in water and α,α' -dichloroethylene dissolved in CHCl₃ by a phase transfer catalysed procedure¹³ using tetrabutylammonium bromide hydrate (TBAB) as the catalyst (Scheme 2). The results of polymerisations are shown in Table 1. All the polymers were soluble in Me₂SO and so crosslinking side-reactions involving the secondary OH group on the tartrate residue appear to be absent. The polymers also display a positive optical rotation, and while it is not possible to say that no racemisation of the tartrate residues occurs during polymerisation, the values of the observed



Scheme 1 Reagents and conditions: i, toluene-*p*-sulfonic acid (3 mass%), *ca.* 120 °C, 3 d



Scheme 2 Reagents and conditions: i, Bu₄NBr (20 mol%), H₂O, CHCl₃, reflux, 7 d

Table 1 Synthesis of polyesters **3** derived from 1-(+)-tartaric acid and diols

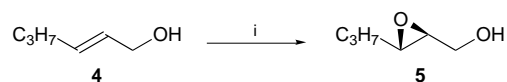
Polyester	Conversion (%)	[α] _D ^{25a}	ν_{max} /cm ⁻¹ (C=O, OH)	Elemental microanalysis (%)	
				Calculated	Found
3a	73	+13 ^b	1755, 3479	C, 40.92; H, 4.58	C, 39.2; H, 4.6
3b	68	+25	1755, 3479	C, 51.72; H, 6.94	C, 51.5; H, 6.5
3c	95	+17	1747, 3469	C, 55.37; H, 7.74	C, 56.4; H, 7.8
3d ^d	55	+4 ^e	1755, 3470	C, 60.74; H, 8.92	C, 61.0; H, 9.2
3e	45	+18	1748, 3430	C, 57.14; H, 4.80	C, 52.3; H, 5.1
3f	48	+15	1747, 3420	C, 57.14; H, 4.80	C, 56.3; H, 5.1

^a Concentrations: 0.2 g per 100 ml Me₂SO, Perkin-Elmer WM250. ^b Concentration: 0.4 g per 100 ml MeOH. ^c Washed with hexane. ^d $\overline{M}_w = ca.$ 4,200, $\overline{M}_w/\overline{M}_n = ca.$ 1.7, determined by GPC with polystyrene standards in THF. ^e Concentration: 0.8 g per 100 ml in CHCl₃.

Table 2 Epoxidation of *trans*-hex-2-en-1-ol with tBHP catalysed by 1-(+)-polyester **3** and Ti(OPrⁱ)₄

Ligand	Molar ratio 4 : Ti : tartrate	<i>T</i> /°C	Reaction time/h ^a	Epoxide yield (%) ^b	Isolated yield (%) ^c	Work-up ^d	Ee ^e (%)
DMT	100:5:6	-30	3	91 ^g	44	A	≥98 ^g
3a	100:17:20	-20	3	51	50	B	8
3b	100:17:20	-20	3	63	63	B	55
3c	100:5:10	-20	3	22	59	B	79
3c	100:17:20	-20	7	92	58	B	79
3d	100:12:12	-20	3	65	60	B	41
3d	100:5:10	-20	3	21	46	B	52
3d	100:10:30	-20	3	80	61	B	77
3d	100:17:20	-20	3	75	61	B	64
3e	100:17:20	-20	3	73	42	B	47
3f	100:17:20	-20	3	74	80	B	68

^a From addition of **4**. ^b From GC analysis after 3 h. ^c After additional 12 h in freezer, work-up and Kugelrohr distillation. ^d A = ferrous sulfate, tartaric acid (ref. 15); B = non-acidic aqueous workshop (ref. 15). ^e (2*S*,3*S*)-(-)-Propyloxiranemethanol determined *via* chiral HPLC (Chiralcel OB, hexane-PrⁱOH). ^f DMT = 1-(+)-dimethyl tartrate. ^g Chemical yield = 85%, ee = 94%; Sharpless using 1-(+)-diethyltartrate (ref. 15).



Scheme 3 Reagents and conditions: i, poly(tartrate ester) (10–30 mol%), Ti(OPrⁱ)₄ (5–17 mol%), Bu^tOOH (2 equiv.), 4 Å molecular sieves, CH₂Cl₂, -20 °C, 3 h

rotations are comparable with those reported¹⁴ for dimethyl 1-(+)-tartrate {[α]_D²² + 21 (*c* 2.5, H₂O)} and for diethyl 1-(+)-tartrate {[α]_D²⁰ + 8.5 (neat)}.

Polyesters **3a–f** were used as ligands in the epoxidation of **4** with Ti(OPrⁱ)₄-tBHP as shown in Scheme 3. Powdered activated 4 Å molecular sieves, polymeric ligand and Ti(OPrⁱ)₄ were first mixed in CH₂Cl₂ at -20 °C for 1 h, the tBHP was added and the mixture stirred for a further 1 h at -20 °C before **4** in CH₂Cl₂ was added. The reaction was then left to proceed for 3 h at *ca.* -20 °C, when the GC yield was determined. Each reaction mixture was then stored overnight in a freezer before work-up and isolation of pure **5** *via* Kugelrohr distillation. Enantiomeric excess was determined by chiral HPLC using a Chiralcel OB column and hexane-isopropyl alcohol (97.5:2.5) as eluent. The results are summarised in Table 2. Generally reactions are fast even at -20 °C with GC yields (3 h) in the range 20–90% depending upon the polymer ligand **3** used. In some instances isolated yields are higher than GC yields because the reactions continue in the freezer overnight. Isolated yields, however, are by no means optimised; pure **5** was isolated simply for optical rotation measurements and considerable scope remains for optimisation. Enantiomeric excesses generally fall in the range 40–80% with a significant dependence on the poly(tartrate ester) employed. Polymer (**3a**) is very poor, and polymer (**3c**) the most effective. The origin of the ‘polymer effect’ is not clear and may well involve a contribution from solubility and molecular weight variation, and from conformational factors. Polymers **3a** and **3b** are rather insoluble in CH₂Cl₂, as is **3c**. However, the latter does form a CH₂Cl₂ soluble complex with Ti(OPrⁱ)₄. This led us to prepare **3d** which is itself soluble in CH₂Cl₂; however, **3d** gave poorer levels of induction than **3c** under comparable conditions so that solubility alone is not the only factor. Solubility limitations have made molecular weight determination difficult, but two different batches of **3d** yielded $\bar{M}_w = 4150$ and 4210, with $\bar{M}_w/\bar{M}_n = 1.7$ (gel permeation chromatography; polystyrene standards in THF). Compound **3d** is therefore oligomeric rather than polymeric, and further work is underway to investigate this parameter. It seems most likely that the active species with simple dialkyl tartrate-Ti(OPrⁱ)₄ are rather complicated, possibly 2:2 complexes.¹⁶ The effectiveness of poly(tartrate ester)s

may well therefore depend also on the ability of these backbones to assume a conformation which allows maximum opportunity for the formation of such complexes. In this respect, in due course, investigation of poly(tartrate ester)s may well provide useful structural information on the active species themselves.

At the moment we are further optimising these reactions and pursuing the above structural aspects. We are also making crosslinked poly(tartrate ester) gels and immobilising linear poly(tartrate ester)s on supports such as poly(styrenedivinylbenzene) in an attempt to produce highly practical re-usable heterogeneous Sharpless epoxidation catalysts.

We acknowledge funding from the Neste Oy Foundation and the Finnish cultural Foundation. We also appreciate the molecular weight determinations carried out by RAPRA.

References

- D. C. Sherrington, ‘Polymer-supported Synthesis’, in *Chemistry of Waste Minimisation*, ed. J.H. Clark, Blackie, 1995, ch. 6, p. 141.
- P. Hodge, ‘Polymer-supported asymmetric organic synthesis’, in *Innovation and Perspectives in Solid Phase Synthesis*, ed. R. Epton, SPCC UK, 1990, p. 273.
- S. Itsuno, Y. Sakurai, K. Ito, T. Maruyama and J. M. M. Frechet, *J. Org. Chem.*, 1990, **55**, 304.
- P. Hodge, paper presented at SCI Meeting on Ion Exchange Resins as Catalysts, London, June 1994; also in *Macromolecules 1991*, ed. J. Kahovec, VSP, Utrecht, 1993, p. 441.
- E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Echer and Li Deng, *J. Am. Chem. Soc.*, 1991, **113**, 7063.
- B. B. De, B. B. Lohray, S. Sivaram and P. K. Dhal, *Tetrahedron: Asymmetry*, 1995, **6**, 2105.
- F. Minutolo, D. Pini and P. Salvadori, *Tetrahedron Lett.*, 1996, **37**, 335.
- C. E. Song, J. W. Yang, H. J. Ha and S.-G. Lee, *Tetrahedron: Asymmetry*, 1996, **7**, 645.
- R. A. Johnson and K. B. Sharpless, ‘Catalytic Asymmetric Dihydroxylation’, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, New York, 1993, p. 227.
- T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974.
- M. J. Farrall, M. Alexis and M. Trecarten, *Nouv. J. Chim.*, 1983, **7**, 449.
- D. Seebach, H.-O. Kalinowski, W. Langer, G. Grass and E. M. Wilka, *Org. Synth.*, 1983, **61**, 24.
- J. March, *Advanced Organic Chemistry*, Wiley, New York, 3rd ed., 1985, p. 353.
- Aldrich Handbook of Fine Chemicals*, 1994–1995.
- Y. Gao, R. M. Hanson, J. M. Klunder, S. Y. Ko, H. Masumune and K. B. Sharpless, *J. Am. Chem. Soc.*, 1987, **109**, 5765.
- M. G. Finn and K. B. Sharpless, *J. Am. Chem. Soc.*, 1991, **113**, 113.

Received, 10th October 1996; Com. 6/06954A