Unexpected asymmetric epoxidation reactions catalysed by polyleucine-based systems

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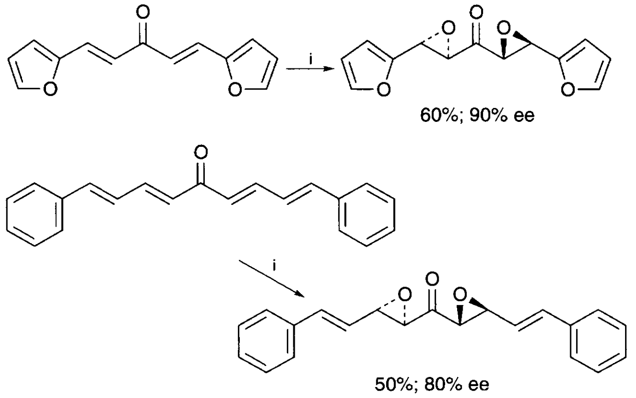
Polyleucine-based systems have been shown to catalyse the asymmetric epoxidation of a variety of enones, an enynone, selected enediones and an unsaturated ketoester.

The Juliá–Colonna asymmetric epoxidation reaction using polyleucine as the catalyst[1] has attracted world-wide attention.[2] Initially the reaction was believed to be limited to chalcones, but we indicated in an earlier paper that the substrate range included dienes and tetraenes (Scheme 1).[3] Moreover the preparation of the catalyst needed painstaking work and, despite due care, the quality of the material was often variable. Recently we found a reliable method for the preparation of effective catalyst.[4]

Given the improved access to the catalyst we were anxious to explore further the range of asymmetric epoxidations catalysed by the polyleucine derivatives. Some of our recent results are reported in Table 1.

The substituents R^1 and R^2 need not be aromatic. Entries 1 and 2 show that a *tert*-butyl group can be accommodated adjacent to the ketone moiety. The ensuing oxidation reaction is quite fast and the yields and enantiomeric excesses (ees) are good or excellent. If one of the methyl groups in the *tert*-butyl unit is exchanged for hydrogen or a methoxy group, the epoxidation reaction is prolonged and the optical purities of the products are modest (entries 3 and 4). In contrast, a cyclopropyl group is tolerated adjacent to the carbonyl group or at the β-position. Yields are in the range 61–85% and the ees are good to excellent (entries 5–9). Finally, an alkyne unit next to the carbonyl group has been shown to act as a benign fixture (entry 10).

The difference in pattern of reactivity of the *tert*-butyl compound R^1 = Ph; R^2 = Bu^t featured in entry 1 and the isopropyl compound R^1 = Ph; R^2 = Pr^i described in entry 4 was examined further by running the PLL-catalysed oxidation reaction on a mixture of the two compounds. The *tert*-butyl compound was oxidized at the usual rate proving that the isopropyl compound was not interfering with the 'active site' of the catalyst.

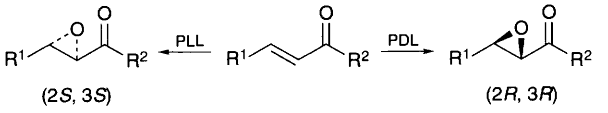


Scheme 1 *Reagents and conditions*: i, Poly-(L)-leucine, H_2O_2, NaOH, H_2O, CH_2Cl_2

The enone **1** was oxidized with moderate stereoselectivity using DAP-PLL[4] (Scheme 2). The absolute configuration of the product has not been established. This is the first example of an α-substituted β-unsubstituted enone undergoing asymmetric oxidation with any degree of efficiency using this methodology.

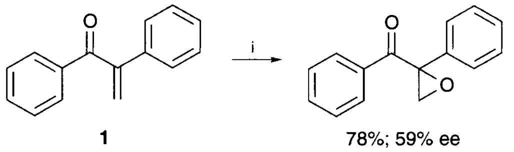
The fact that the α-substituted enones can undergo asymmetric epoxidation is endorsed by the conversion of the

Table 1 Oxidation of some enones using polyleucine-based catalysts

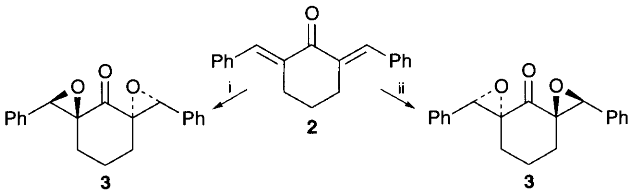


					Product	
Entry	R^1	R^2	Reaction conditions	*t*/h	Yield (%)	Enantiomeric excess (%)
1	Ph	Bu^t	*a*	18	92	>98
2	Ph	Bu^t	*b*	18	90	>86
3	Ph	CMe_2OMe	*a*	84	70	63
4	Ph	CMe_2H	*a*	168	60	62
5	Ph	cyclopropyl	*a*	18	85	77
6	2-naphthyl	cyclopropyl	*b*	29	61	90
7	PhCH=CH	cyclopropyl	*a*	42	73	74
8	PhCH=CH	cyclopropyl	*c*	19	52	98
9	cyclopropyl	2-naphthyl	*a*	28	73	⩾98
10	Ph	$C{\equiv}CPh_2$	*d*	96	57	90

[a] Poly-(L)-leucine (PLL), NaOH, H_2O_2, H_2O, CH_2Cl_2. [b] Poly-(D)-leucine (PDL), NaOH, H_2O_2, H_2O, CH_2Cl_2. [c] Poly-(L)-leucine (PLL), $NaBO_3$, H_2O, NaOH, CH_2Cl_2, aliquat 336. [d] Immobilised poly-(L)-leucine,[5] NaOH, H_2O_2, toluene.

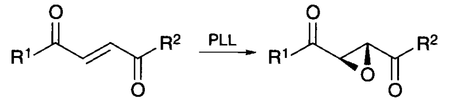


Scheme 2 *Reagents and conditions*: i, DAP-PLL, NaOH, H_2O_2, H_2O, PhMe, aliquat 336, 17 h



Scheme 3 *Reagents and conditions*: i, PDL, NaOH, H_2O_2, H_2O, CH_2Cl_2, 7 d

Table 2 Oxidation of some enediones and unsaturated ketoesters



Entry	R¹	R²	Reaction conditions	Product	
				Yield (%)	Enantiomeric excess (%)
1	Ph	Ph	*a*	76	76
2	Ph	*p*-Cl C_6H_4	*b*	60	89
3	Ph	Bu^t	*a*	79	82
4	Bu^t	Bu^t	*c*	>95	>95
5	Ph	OBu^t	*c*	66	≥95

[a] Poly-(L)-leucine (PLL), H_2O_2, NaOH, H_2O, CH_2Cl_2. [b] Poly-(L)-leucine (PLL), $NaBO_3$, H_2O, NaOH, CH_2Cl_2. [c] Immobilised poly-(L)-leucine (PLL),[5] NaOH, H_2O_2, toluene.

cyclohexanone derivative **2** into the bis-epoxide **3** of good optically purity (Scheme 3) albeit in a slow reaction.

Finally, enediketones and unsaturated ketoesters are oxidized efficiently, often with high selectivity, using these catalysts (Table 2).

Thus aryl (entries 1,2) and *tert*-butyl (entries 3,4) groups can be tolerated at the termini of the enedione moiety. Other substituents have not been investigated to date. Similarly, the *tert*-butyl ester described in entry 5 was oxidized in reasonable (unoptimized) yield and excellent ee. Other unsaturated ketoesters and diesters are under investigation.

In conclusion we believe that the asymmetric epoxidation reaction, based on the catalyst introduced in the seminal work by Julia and Colonna[1] may be applied to a wide range of α,β-unsaturated carbonyl and dicarbonyl compounds.

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Footnote

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