

Asymmetric epoxidation of some arylalkenyl sulfones using a modified Juliá–Colonna procedure

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Received 23 February 2004; revised 21 April 2004; accepted 30 April 2004

Abstract—A modified procedure for performing the Juliá–Colonna epoxidation reaction effects the oxidation of some vinyl sulfones to generate the corresponding epoxides **5–8** in good to excellent optical purity.

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1. Introduction and background information

The employment of amino acids and low molecular weight peptides as catalysts in asymmetric syntheses is a subject of considerable current interest.¹ One of the first transformations to be investigated was the asymmetric epoxidation of α,β -unsaturated ketones using aqueous sodium hydroxide with 30% hydrogen peroxide and a polyamino acid as the catalyst, a transformation discovered by Juliá and Colonna.² The first documented reaction mixture consisted of *three phases*, namely the aqueous phase, an organic solvent such as hexane or toluene and the insoluble polyamino acid such as polyalanine or polyleucine.

The reaction has been developed and improved in recent years in a variety of ways; some of the noteworthy developments are as follows:

- production of the catalyst on a large scale³ and the commercial availability of the polyamino acids;⁴
- modification of the protocol to allow the use of other oxidants, such as percarbonate⁵ and urea hydrogen peroxide (UHP),⁶ under nonaqueous *two-phase* conditions with consequent reduction in the amount of catalyst required (from ca. 20 to 5 mol%) and also

reaction times (from ca. 16 to 1 h for chalcone oxidation);

- production of immobilised catalyst⁷ (aiding recovery and recycling) and homogeneous catalyst⁸ (for use in membrane reactors⁹);
- substantial expansion of the range of α,β -unsaturated ketones undergoing epoxidation, giving ready access to a wide range of intermediates useful for the production of an impressive portfolio of natural products¹⁰ and biologically active compounds.¹¹

Recent work in the Bayer (Leverkeusen) laboratories has resulted in yet another significant improvement in the operation of the Juliá–Colonna reaction. Thus Geller et al.¹² have shown that modification of the original *triphasic* conditions through inclusion of a phase transfer catalyst (PTC) in the mixture gave rise to a much faster reaction. Most significantly, the amount of catalyst required was greatly reduced, 0.5 mol% of poly-(*L*)-leucine being required for oxidation of chalcone over 1.5 h.

Contemporaneous work in the Liverpool laboratories had shown that, in the *two-phase* system, mixing UHP and poly-(*L*)-leucine in an organic solvent resulted in rapid transfer of peroxide into the polyamino acid gel.¹³ This observation led us to speculate and then investigate whether a polyamino acid could abstract hydrogen peroxide from aqueous solution as used in the cheaper *three-phase* system and, if so, whether the resulting

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Table 1. Epoxides produced from the modified Juliá–Colonna procedure

Entry	Epoxide formed	Literature reference	Reaction time (h)	Conversion % (isolated yield)	Optical purity of epoxide ee (%)
1	1	1	6	100 (80)	95
2	2	14	3	66 (51)	>95
3	3	15	3	56 (51)	>95
4	4	6	3	80 (60)	>95
5	5	16	6	— (66)	91
6	6	—	6	65 (49)	94
7	7	—	6	— (61)	95
8	8	—	18	89 (76)	70

material could be utilised to perform Juliá–Colonna oxidations.

2. Results and discussion

Poly-(*L*)-leucine (insoluble, 0.1 mol%) was stirred with aqueous sodium hydroxide (5 M, 2.0 equiv), hydrogen peroxide (30%, 1.8 equiv), *tetra*-butylammonium hydrogensulfate (1.5 mol%) and toluene. After 3 h, the aqueous phase was removed to leave a biphasic system (toluene and gel-like polyamino acid containing peroxide) to which chalcone was added. After 6 h, the epoxidation reaction was complete and (*2R,3S*)-chalcone epoxide **1** (Table 1, entry 1) was isolated in 95% ee. The reaction has been conducted on a 5 g scale.

The reaction was applied to benzylidene acetone (entry 2) to afford the bis-epoxide **2** and the *meso*-isomer (de 92%). Of greater interest was that the hydroxide-sensitive esters ethyl 3-oxo-3-phenylbut-2-enoate¹⁴ and methyl 6-oxo-6-phenylhex-2,4-dienoate¹⁵ afforded the epoxides **3** and **4** (Table 1, entries 3 and 4) in high yields and excellent enantiomeric excesses. Such esters were found to give baseline materials under the oxidation conditions recommended by the Bayer scientists.

Attempts have been made previously to oxidize phenyl styrylsulfone under Juliá–Colonna conditions, with very limited success.¹⁶ Gratifyingly, slight modification of the new conditions¹⁷ provided a protocol better suited to the oxidation of vinyl sulfones as illustrated by the last four entries in Table 1. Thus phenylstyryl sulfone was oxidized in standard fashion to afford the crystalline epoxide **5**, in 91% ee.¹⁸ The corresponding *para*-bromostyryl sulfone and phenyl(3-pyridyl) vinyl sulfone gave the epoxides **6** and **7** in similar optical purities. Perhaps of greatest significance, *para*-tolyl vinyl sulfone was oxidised relatively slowly, but cleanly to afford the novel epoxide **8**. The optical purity of the product is moderate (70% ee) but the transformation has not been optimised.

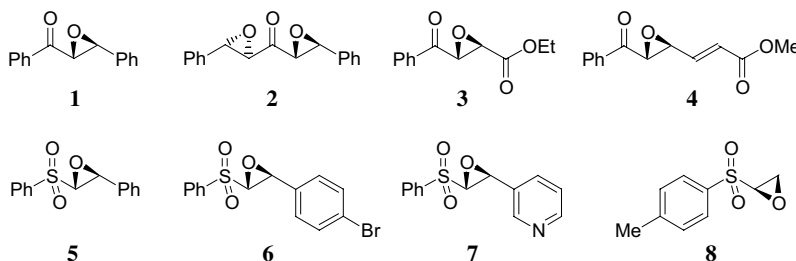
In summary, this communication highlights the fact that, surprisingly, poly-leucine sequesters peroxide from aqueous solution. The resultant polyamino acid/peroxide-containing gel efficiently oxidizes a selection of, α,β -unsaturated ketones and, notably, transforms a small range of arylvinyl sulfones to furnish the corresponding optically active epoxides having good to excellent optical purity. Thus this latest modification of the Juliá–Colonna oxidation system represents the simplest, cheapest and fastest way to effect the asymmetric epoxidation of a wide range of substrates, including unsaturated ketoesters and vinyl sulfones.

Acknowledgements

The Royal Society is thanked for provision of a Developing World Study Visit (to S.S.).

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18. The absolute configurations of the epoxysulfones are tentative, having been assigned on the basis of the equivalent epoxidation reactions on unsaturated ketones.