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Stereoselective Epoxidation of bis-Sulfinyl Alkenes and Application to the Asymmetric Synthesis of α -Substituted Carboxylic Acids

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Stereoselective Epoxidation of bis-Sulfinyl Alkenes and Application to the Asymmetric Synthesis of α -Substituted Carboxylic Acids

Varinder K. Aggarwal,^{a*} Julia M. Worrall,^a and Rikki Alexander.^b

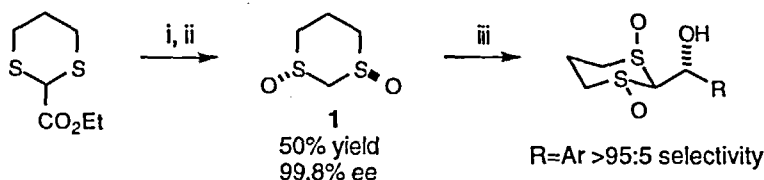
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Ketene thioacetals **3** can be easily prepared in optically pure form and react diastereoselectively with metal peroxides. The resulting bis-sulfinyl oxiranes can be converted in a single step to α -substituted acids.

INTRODUCTION

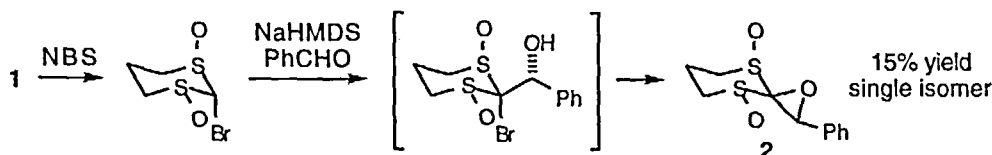
1,3-dithiane-1,3-dioxide **1** can be prepared in optically pure form via Modena oxidation of 1,3-dithiane-2-ethylcarboxylate.¹ It has been found to be effective as a diastereoselective carbonyl anion equivalent in reactions with aldehydes (scheme 1).²



Scheme 1 Reagents: i, (R,R)-DET, $\text{Ti}(\text{OiPr})_4$, PhCMe_2OOH , CH_2Cl_2 ; ii, NaOH , H_2O ; iii, NaHMDS , RCHO , THF, py

RESULTS AND DISCUSSION

We initially envisaged expanding on this chemistry by using 2-halo-1,3-dithiane-1,3-dioxide as a carbonyl anion equivalent in Darzens type reactions, providing access to spirocyclic epoxides **2**. Diastereoselective addition to aldehydes was achieved^{3,4} but the ring closure step proved problematic, giving low overall yields of epoxides.



Excellent diastereoselectivities in epoxidations of electron deficient alkenes have been achieved by Jackson, using metal peroxides as nucleophilic oxidants.⁵ We decided to apply his conditions to the oxidation of the ketene thioacetals **3**, prepared by aldol condensation of **1** with aldehydes. This was found to be a successful, highly diastereoselective alternative route to **2** (table 1). A more general route to the ketene thioacetals **3** was developed using Wadsworth-Emmons type reactions of phosphonate **5** with aldehydes. Subjection of dithiane phosphonate **4** to the Modena asymmetric oxidation conditions afforded the dioxide **5** in high enantiomeric excess (scheme 2).

Scheme 2 Oxidation route to the target epoxides

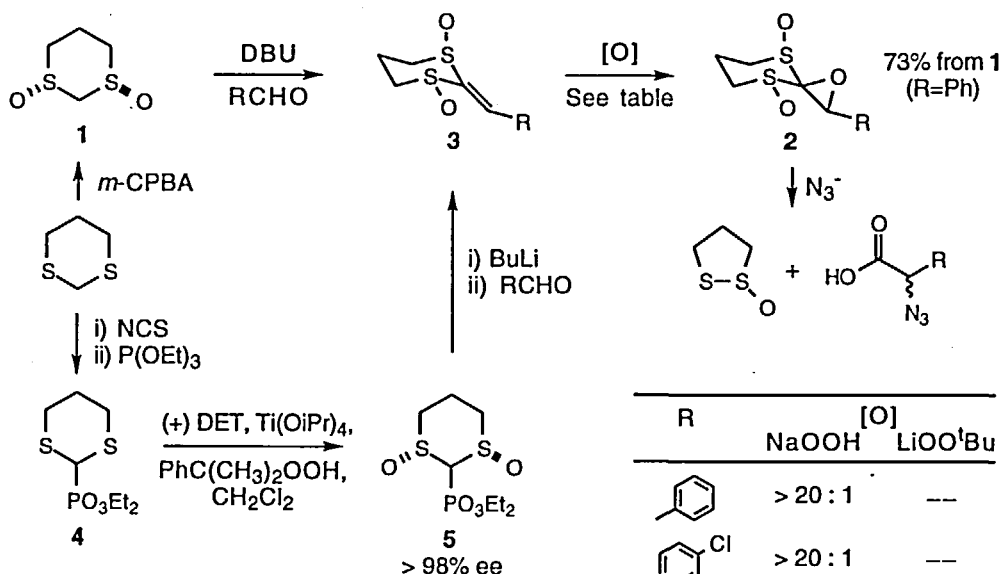


Table 1 Diastereoselective nucleophilic epoxidation of ketene thioacetals **3**

The masked carboxylic acid functionality α - to the newly formed stereocentre was revealed by nucleophilic opening of the epoxide.

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