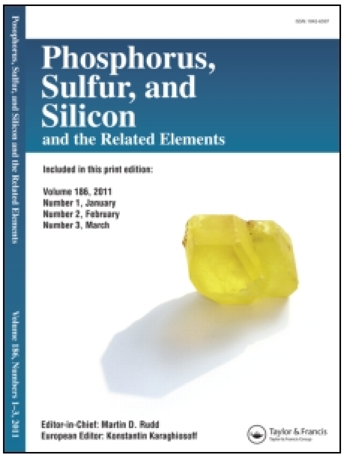

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Asymmetric Synthesis of Enantiopure α-Sulfenyl Dithioacetals and α-Sulfenyl Aldehydes

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ASYMMETRIC SYNTHESIS OF ENANTIOPURE α-SULFENYL DITHIOACETALS AND α-SULFENYL ALDEHYDES

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Abstract The BF_3•Et_2O promoted thiolytic cleavage of the diastereomeric oxazolidines **(1'*R*)-2** and **(1'*S*)-2** has been studied. The thioacetalisations took place with concomitant thioetherification at the carbinol centres, giving rise to the α-sulfenyl dithioacetals (α-SDTA's) **(*S*)-3** and **(*R*)-3** respectively. Selective manipulation of the latter compounds was also achieved. Thus, oxidative hydrolysis gave the corresponding α-sulfenyl aldehydes which were shown to be enantiopure.

INTRODUCTION

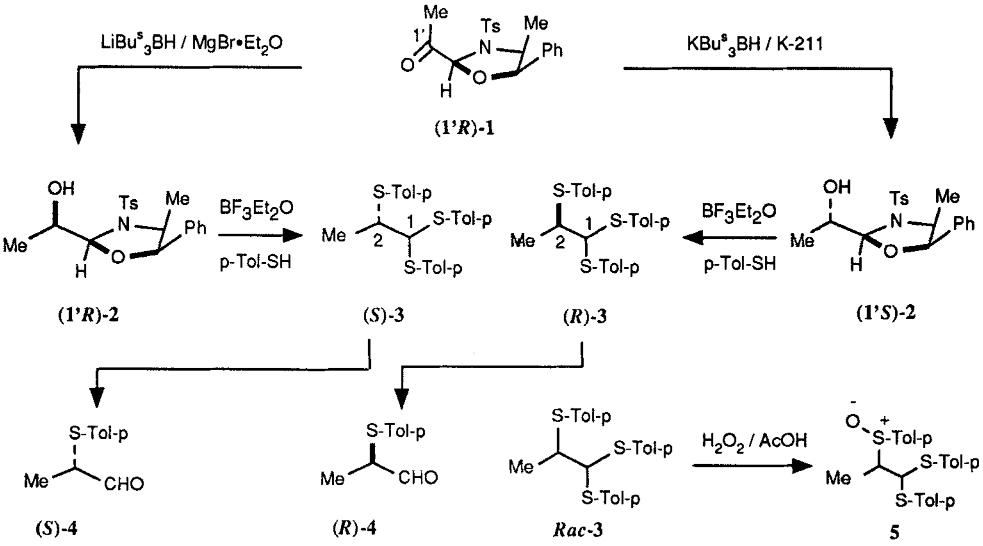
In our ongoing studies on the use of nor-ephedrine in asymmetric synthesis, we recently discovered that tri-*s*-butyl borohydride addition to methyl ketone **1** could be directed to either the *Si* or the *Re* carbonyl π-face with virtually complete selectivity under "chelating" or "naked" conditions (scheme).[1] The thiolytic removal of the nor-ephedrine moiety from **(1'*R*)-2** and **(1'*S*)-2** was next investigated.

MECHANISTIC STUDY OF THE THIOLYSIS

In striking contrast with our previous results,[2] separate treatment of the carbinols **(1'*R*)-2** and **(1'*S*)-2** with p-thiocresol and BF_3•Et_2O in CH_2Cl_2 gave the α-sulfenyl dithioacetals (α-SDTA's) **(*S*)-3** and **(*R*)-3** respectively.

The mechanism of this multiple transformation is believed to involve the following steps in chronological order: *a]* a rate determining thioacetalisation; *b]* an acid promoted thiiranium ion[3] formation (*via* intramolecular displacement at C-2); *c]* a regioselective interception at C-1 of the thiiranium ions by a third thiol molecule.

Additional experiments proved that the postulated dithioacetal intermediate is converted to the α-SDTA under the same reaction conditions. Conversely, re-equilibration of the latter compounds to the parent thiiranium ions via internal displacement at C-2 is not possible. It thence follows that the α-SDTA's **3** are generated from **2** with net inversion of stereochemistry. Moreover, they are not expected to racemise during the reaction.



SELECTIVE MANIPULATION OF THE α-SDTA's

Treatment of (*S*)-**3** and (*R*)-**3** with $(CF_3CO_2)PhI$ in $MeCN/H_2O$[4] afforded the α-sulfenyl aldehydes[5] (*S*)-**4** and (*R*)-**4** which were shown to be enantiopure.[6] On the other hand, oxidation of ***Rac*-3** with H_2O_2 in AcOH gave sulfoxide **5** as a single diastereoisomer. Thus, depending on the oxidating system, either the dithioacetal or the thioethereal sulfur atom in **3** could be conveniently selected.

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6. To the best of our knowledge this method represents the first asymmetric synthesis of enolisable enantiopure α-sulfenyl aldehydes. See for example: J-H. Youn, R. Herrmann, I. Ugi, *Synthesis*, 159. (1987).