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Communications

Reaction of Thioallylic Carbanion with R-Glyceraldehyde¹

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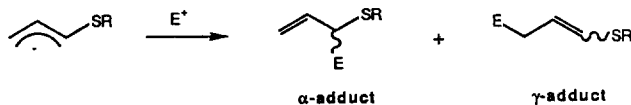
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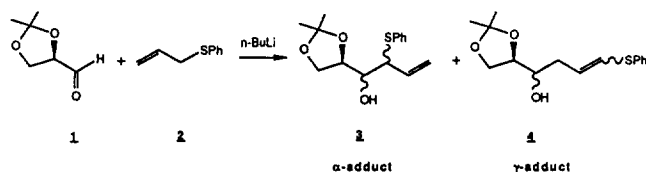
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Thioallylic carbonions have been recognized as an increasingly important tool in synthetic chemistry.

In general, the basic problem in synthetic utility of thioallylic carbonions is regioselectivity, i.e., control of the relative abundance of α -and/or γ -adducts as indicated below.²



Based on our interest in using thioallylic anions in organic synthesis, enhanced level of stereo and regioselection in addition reaction to a chiral aldehyde has been observed. Treatment of the acetonide of R-glyceraldehyde **1**³ with allyl phenyl sulfide **2** and *n*-BuLi in THF followed by addition of saturated aqueous ammonium carbonate (30 min, -78°C) afforded a 1:4 mixture of two regioisomeric products in 57% combined yield. High regioselectivity has been realized in this reaction.



Unfortunately, attempts to improve the regioselectivity for γ -adduct under a variety of Lewis acid conditions were unsuccessful. The reactions under Lewis acid proceeded

Table 1. Reaction of **1** with **2** and regioselectivity

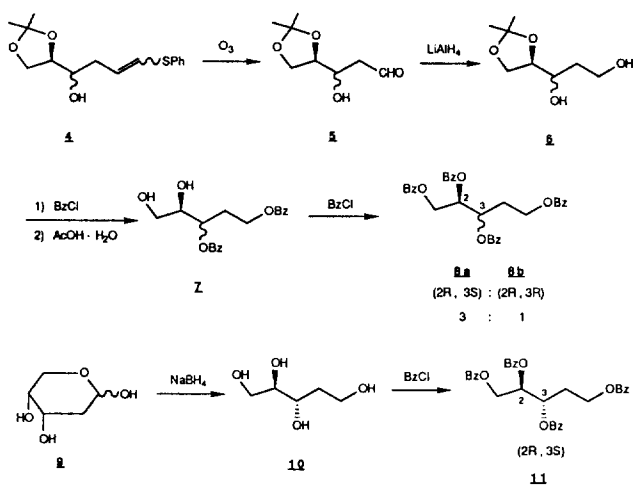
Entry	Lewis acid	α -product (3), %	γ -product (4), %	Total Yield (%)
1	none	20	80	57
2	CuI	27	73	74
3	ZnCl ₂	40	60	60
4	AlEt ₃	91	9	65
5	Ti(O- <i>i</i> Pr) ₄	94	6	50

In all cases, the ratios and yields are determined by column chromatography.

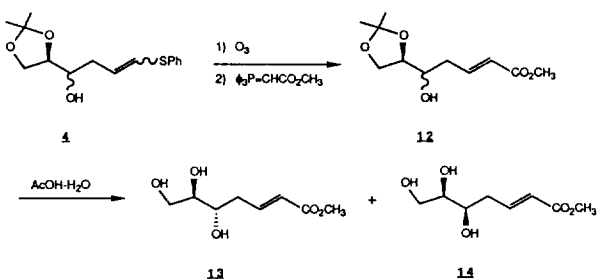
through preferential α -attack, presumably owing to the "ate" complex of sulfur stabilized allyl carbanion⁴. The results are summarized in Table 1.

The configuration of the hydroxy group of γ -adduct **4** was ascertained as follows: Ozonolysis and reduction with lithium aluminum hydride afforded diol **6** in 69% yield, which was reacted with benzoyl chloride and pyridine to dibenzoylated compound. Treatment of dibenzoylated compound with 80% acetic acid at room temperature gave **7** (92%), which was converted to tetrabenzoylated compound **8** in 94% yield. The tetrabenzoylated compound **8** was separated and two diastereomers were identified (ratio=3:1) by HPLC and 200MHz NMR. The major isomer was assigned structure **8a** on the basis of comparison with an authentic tetrabenzoate, which was prepared in two steps (NaBH₄ and benzylation) from the 2-deoxy-D-ribose. The minor isomer **8b** was presumed to be a diastereoisomer derived from the reaction of **1** and **2**.

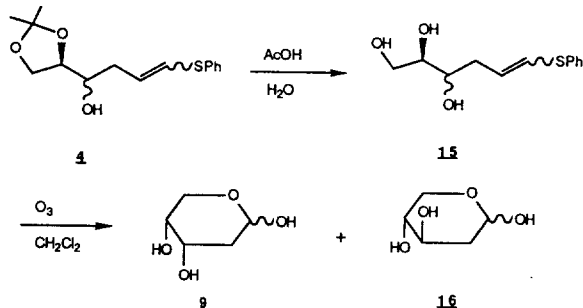
Since the absolute configuration of **11** is shown in Scheme 1, the relative and absolute configuration of **8a** is established unequivocally. The predominant product is the one predicted by application of Felkin's model⁵ for asymmetric induction and by assuming the alkoxy group to be the "large" group. The Cram cyclic model⁶ for asymmetric induction is not followed. The stereochemistry of addition of lithium enolates derived from esters and ketone to chiral aldehydes has been investigated.⁷ Our result is in well agreement with their observation. The mixture **4** was inseparable by column chromatography and thus, separation was postponed to a later stage of the synthesis. Ozonolysis of **4** afforded aldehyde **5**, which was treated with excess carbomethoxymethylenetri-



Scheme 1



Scheme 2



Scheme 3

phenylphosphorane to give ester 12 in 57% yield.

Deprotection of 12 with 80% acetic acid provided a 3:1 mixture of 13 and its diastereoisomer 14 in 93% yield, respectively (Scheme 2). The facile transformation of 13 to LTA₄ has been earlier described by the Rokach group.⁸

Also, the mixture 4 was treated with 80% acetic acid to give triol 15 in 93% yield. Ozonolysis of 15 afforded a 3:1 mixture of 9 and 16 in 57% yield (Scheme III).

A Typical procedure for the reaction of 1 with 2 is as follows;

To a stirred solution of allyl phenyl sulfide 2 (4.85g, 32.3mmol) in dry THF(60ml) at -78°C was slowly added n-butyllithium (22ml, 1.6M) under a nitrogen atmosphere. Lewis acids (35.0 mmol) were added slowly and stirred for 30 mins. [R]-2,3-O-isopropylidene glyceraldehyde 1 (4.20g, 32.3 mmol) was introduced by syringe. The reaction mixture was

stirred for 30 min and immediately quenched with sat. ammonium carbonate (50ml). The mixture was poured into water (50ml). The aqueous layer was extracted with ether (3×60ml), and the combined organic solution were washed with brine, dried and concentrated. The residue was purified by column chromatography. The products were identified by IR, ¹H-NMR, and MS, respectively. Isolated product ratio and yields are shown in Table 1.

In this study, the reaction of thioallylic carbonion with R-glyceraldehyde occurs efficiently and with high regio- and stereoselectivity. The potential synthetic utility of the title reaction was demonstrated by the conversion of 4 to 13 and 9. Work is being done to establish the generality and to increase the regio- and stereoselectivity of the title reaction.

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