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Preliminary communication

CHEMISTRY OF THE MAIN GROUP METALS: A STEREOSELECTIVE SYNTHESIS OF ALLYL VINYL THIOETHERS FOR THE THIO—CLAISEN REACTION

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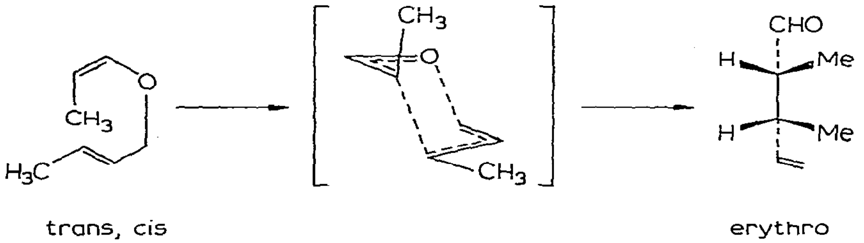
Summary

A stereoselective route to allyl vinyl thioethers has been developed which relies on the reaction of vinylalanates with allyl thiosulfonates.

The Claisen rearrangement, the [3,3]-sigmatropic rearrangement of 3-oxa-1,5-diene intermediates to γ,δ-unsaturated carbonyl compounds, has, since its discovery in 1912, come to enjoy considerable use as a tool for the construction of complex natural products [1]. Much of the utility of this process stems from the observation that this rearrangement reaction proceeds through a highly ordered chair-like transition state leading to unsaturated carbonyl compounds of fixed olefin geometry [2].



By starting with crotyl propenyl ethers of known olefin geometry, Schmid has shown that as a further consequence of the stringent geometry of this rearrangement, either *threo-* or *erythro*-2,3-dimethyl-4-pentenals can be derived [3]. Relatively little attention has, however, been focused on use of the Claisen reaction as a method for establishing the relative stereochemistry about two contiguous carbon centers joined by a newly formed carbon—carbon single bond. To exploit this sigmatropic rearrangement in this manner demands that a stereoselective method for the synthesis of terminally substituted allyl vinyl ethers be available.

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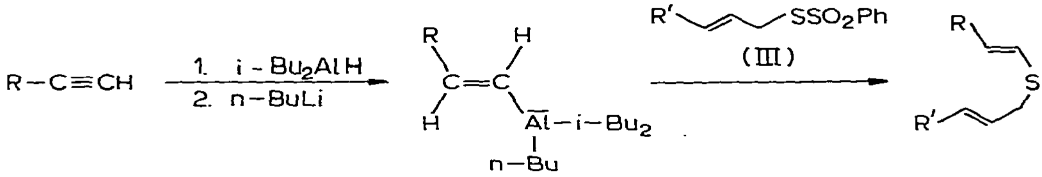
Ireland has provided one elegant solution to this problem through his variant of the Claisen process [4]. This methodology relies on the stereoselective generation of ester enolates as the mechanism for controlling stereochemistry of the vinyl moiety, the stereochemistry of the allyl portion being fixed in advance. Either the *Z*- or *E*-enolate can be generated with high selectivity by simply varying the solvent system employed, thus providing either the *threo*- or *erythro*-γ,δ-unsaturated acid upon rearrangement.

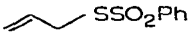
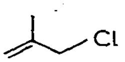
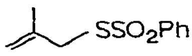
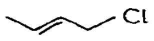
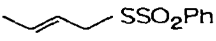
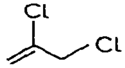
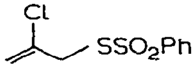
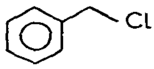
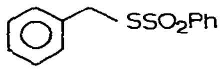
In this paper we present another method for the stereoselective generation of 3-hetero-1,5-dienes for the Claisen process. This method provides a route to allyl vinyl sulfides, compounds which have previously been shown by Yamamoto to readily undergo the thio-Claisen rearrangement when refluxed in a mixture of dimethoxyethane and water [5]. We had envisaged that these allyl vinyl thioethers could be conveniently synthesized by the reaction of a vinylalanate (II) with an allyl thiosulfonate (III). Since the ate complexes II are conveniently prepared by the hydroalumination of an alkyne, a process which has previously been shown to proceed in a highly stereoselective *cis*-fashion [6] and since retention of configuration at the vinyl carbon is generally observed on electrophilic cleavage of the carbon–aluminum bond [7], this overall scheme would provide a route to allyl vinyl thioethers of *E*-stereochemistry about the vinyl moiety.



(I) (II) (IV)

TABLE 1

PREPARATION OF ALLYL THIOSULFONATES III

Entry	Allyl halide [a]	Thiosulfonate [b]	Isolated yield (%) [c]
1			79
2			63
3			57
4			72
5			82

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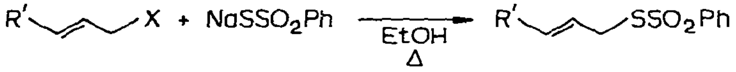
[a] The allyl halides were distilled prior to use. [b] Structures of all compounds reported herein were confirmed by IR, NMR and mass spectral analysis. [c] Yields have not been optimized.

The requisite allyl thiosulfonates (III) can be prepared in good yield by reaction of an allyl halide (bromide or chloride) with sodium benzenethiosulfonate (VI) (from sodium sulfide and benzenesulfonyl chloride) in ethanol at 50°C [8]. The thiosulfonates III were obtained in 60—80% yield after chromatographic purification on silica gel with 10% ethyl acetate/hexane as eluent (Table 1).



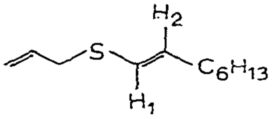
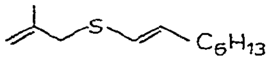
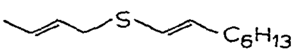
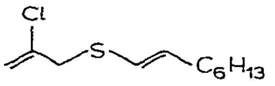
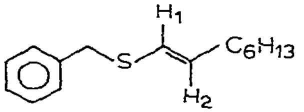
(V) (VI) (III)

The reaction of these thiosulfonates (III) with the vinylalanate (II) prepared from 1-octyne by the method of Zweifel was tested [7]. The thiosulfonate was added as a toluene solution to II ($R = C_6H_{13}$) in heptane at −70°C. After addition was complete, the reaction mixture was slowly warmed to room temperature over a 90 min period. The now white mixture was quenched with moist sodium sulfate and the nonpolar products were extracted with ether (2×). The ethereal extracts were combined, dried ($MgSO_4$) and concentrated by rotary evaporation to furnish a yellow oil. The isolated crude product was chromatographed on silica gel (1% ethyl acetate/hexane) to afford the desired thioether (50—64%) which was homogeneous by TLC and ^1H NMR analysis (Table 2).

Convincing evidence that thioether formation had, as anticipated, proceeded with retention of configuration at the vinyl carbon was obtained by examination

TABLE 2

REACTION OF ALLYL THIOSULFONATES (III) WITH THE VINYLALANATE DERIVED FROM 1-OCTYNE

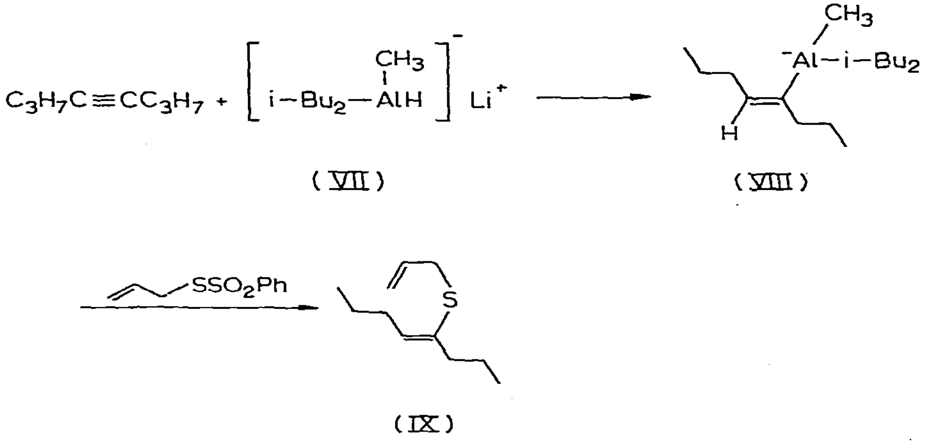
Entry	Thiosulfonate (entry number from Table 1)	Product	Yield (%)[a]
6	1		64
7	2		52
8	3		65
9	4		55
10	5		56

[a] Yields have not been optimized.

of the 250 MHz ^{1}H NMR spectra of the thioethers prepared from allyl- and benzyl-thiosulfonate (entry 6 and 10, respectively). Coupling constants ($J(H^1,H^2)$) of 14.9 and 15.2 Hz were observed for the protons of the vinyl groups in the respective thioethers, values clearly indicative of *trans* stereochemistry [9].

By starting with an allyl halide of defined olefin geometry, this sequence permits ready access to thioethers of fixed stereochemistry about both the vinyl and allyl moieties (e.g., entry 8).

Since the hydroalumination reaction of symmetrical internal alkynes with Li-diisobutylmethylaluminum hydride results in *trans* addition [10], the reaction of the vinylalanate derived by this process with an allylthiosulfonate provides a strategy for preparing a thioether of *Z*-stereochemistry about the vinyl moiety. This scheme was used to prepare thioether (IX) from 4-octyne (51% yield).



The method outlined herein should thus serve as a general route to stereodefined thioethers for the thio-Claisen process. Work is presently in progress to assay the reactivity of other vinylmetallics with allyl thiosulfonates so as to enhance the versatility of this scheme as well as to improve the overall yields. The stereoselectivity of the thio-Claisen process will also be subjected to experimental scrutiny.

Acknowledgements

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