dous opportunities for synthetic planning. The reaction works well with secondary and tertiary derivatives, but is less efficient with primary substrates (for example, **1g**) because the corresponding primary radical has a similar stability to the ethyl radical used to generate it. Both the monochloro and dichlorovinyl groups are immediate precursors of an acetylide anion by exposure to a simple base or butyllithium, respectively, in the Corey–Fuchs reaction.[13] This is illustrated by the quantitative conversion of **4k** into alkyne **5** (Table 2). The dichlorovinyl motif also serves as a source of chloroalkynes by exposure to base.[14] Chloroalkynes and both the monochloro- and dichlorovinyl derivatives are substrates for various transition metal induced couplings.[1] Moreover, ongoing preliminary studies seem to indicate that the vinyl sulfone reagent can be substituted in various other ways to provide a convergent, flexible strategy for the rapid assembly of complex structures.

Experimental Section

Typical procedures are as follows:

Procedure A: A solution of iodide **1a**, **b** (1 mmol) and ethyl vinyl sulfone **2a** (3 mmol) in degassed chlorobenzene (2 mL) was heated under reflux and treated portionwise with di-*tert*-butyl peroxide (3 to 4 drops) over 12–16 h. The solvent was evaporated under reduced pressure and the crude residue was purified by column chromatography on silica gel to furnish the desired products **4a**, **b**.

Procedure B: A solution of iodide or xanthate **1b–j** (1 mmol) and ethyl vinyl sulfone **2b**, **c** (3 mmol) in degassed heptane/chlorobenzene (6/1, 2 mL) was heated under reflux and treated portionwise by lauroyl peroxide (0.12–0.3 mmol) over 5–12 h. The solvent was evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel to give the desired products **4c–k**. With **2b** as sulfone, prior treatment for a few minutes with aqueous ammonia (to destroy excess sulfone) can sometimes simplify purification.

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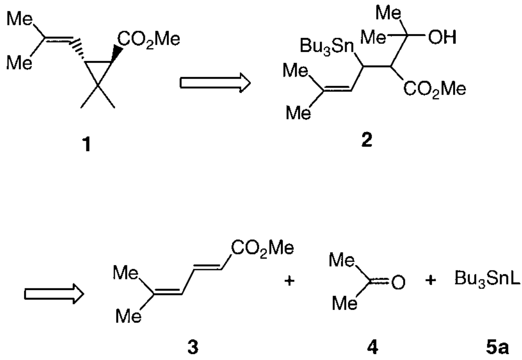
Metal-Mediated, Completely Diastereofacial Conjugate Addition of Trialkylstannylmetal Reagents to γ-Alkoxy-α,β-Unsaturated Esters[**]

Alain Krief,[*] Laurent Provins, and Willy Dumont

*Dedicated to Professor L. Ghosez
on the occasion of his 65th birthday*

A few years ago, we disclosed an efficient "three-component" synthesis of *trans*-methyl chrysanthemate **1** which allows the construction of the cyclopropane ring by insertion of the isopropylidene moiety arising from acetone **4** (Scheme 1).[1] We wanted to extend this strategy to the



Scheme 1. Synthesis of (1*R*)-*trans*-methyl chrysanthemate from a dienoic ester, acetone, and tributylstannyllithium.

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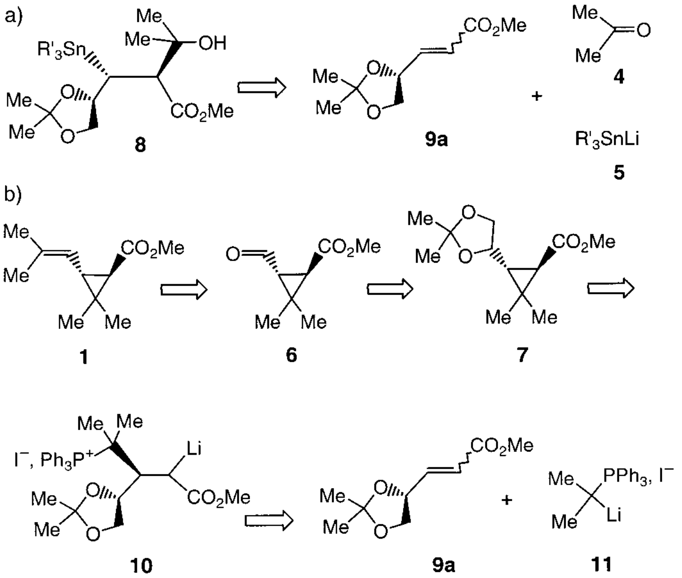
synthesis of the optically active (1*R*)-*trans* enantiomer, which is part of pyrethrin I, a natural product extracted from *Chrysanthemum cinerariaefolium* and a valuable insecticide.[2] We chose the α,β-unsaturated ester **9a** derived from D-glyceraldehyde as the starting material and a synthetic strategy (Scheme 2a) completely different from that described by Mulzer and Kappert for the synthesis of the same product (Scheme 2b) from the same unsaturated ester **9a**.[3]



Scheme 2. Synthetic strategies for (1*R*)-*trans*-methyl chrysanthemate.

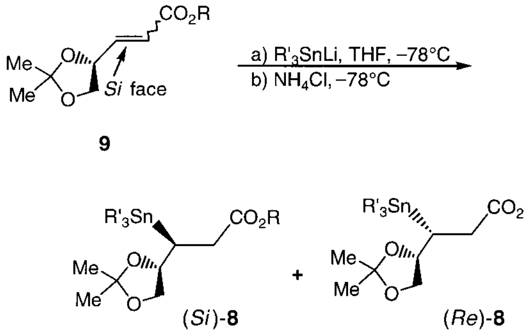
Conjugate addition of the stannyl moiety to the α,β-unsaturated esters **9** was identified as one of the crucial steps of the process, since the absolute stereochemistry of chrysanthemic acid is fixed at this stage by the face of attack of the γ-alkoxy-α,β-unsaturated ester. From the mechanism of the 1,3-elimination reaction we knew that the tributyltin moiety should be introduced at the *Re* face.[1]

To our knowledge, only tributyltin hydride has been treated with (*E*)-**9** under radical conditions ($n\mathrm{Bu_3SnH}$, AIBN cat., hexane, reflux).[4] This reaction does not suit our needs well i) since it requires a further metalation/hydroxyalkylation step to produce **8**, ii) due to the quite poor *de* previously reported for the resulting mixture of stereoisomers (58 % yield, *Re*/*Si* 58/42, *de* 16 %),[4] and iii) because we found that application of the same reaction to the *Z* stereoisomer did not lead to a much better diastereoselectivity (70 % yield, *Re*/*Si* 63/37, *de* 23 %). We therefore planned to introduce the stannyl moiety by means of its organometallic derivatives and to trap the resulting enolate with acetone.

Conjugate addition of various organometallic compounds to γ-alkoxy-α,β-unsaturated esters bearing an asymmetric center in the γ position was extensively studied in the past decade. This is the case for alkyl- and aryllithium compounds,[5] organocuprates,[6] phosphorus[3, 7] and sulfur ylides,[7] α-metallonitroalkanes,[8a] α-lithiosulfones,[8b] and lithium dialkylamides.[9] However, in most cases, the face of attack cannot be predicted accurately and depends not only on the reagent[5, 10, 11] but also upon the *E* or *Z* stereochemistry of the double bond.[7, 11]

We report here our preliminary results on the addition of metal stannyl compounds, especially the tri-*n*-butylstannyl derivative **5a**, to the esters (*Z*)- and (*E*)-**9**. We quenched the resulting enolates with water to enable us to compare our results with those reported for tri-*n*-butyltin hydride.[4]

We found that tri-*n*-butylstannyllithium[12] reacts quite efficiently with methyl esters (*Z*)- and (*E*)-**9a** to provide, in both cases after hydrolysis, compounds that arise from attack on the *Si* face (Scheme 3; Table 1, entries 1 and 2). The reaction is completely face selective for (*Z*)-**9a** (entry 1) but occurs with poorer diastereoselectivity for (*E*)-**9a** (entry 2). An even lower diastereoselectivity was observed for the *tert*-butyl ester (*E*)-**9b** (entry 3). For the *Z* stereoisomer, the reaction is completely diastereoselective regardless of the nature of the groups attached to the ester and of the tin reagent (entries d and e).



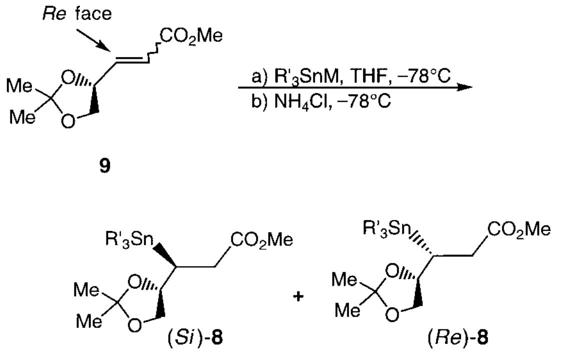
Scheme 3. Addition of stannyllithium reagents to **9**.

Table 1. Addition of stannyllithium reagents to **9**.

Entry	9	R	R′	Yield of **8** [%]	(*Si*)-**8**/(*Re*)-**8**
1	(*Z*)-**9a**	Me	*n*Bu	58	100/0
2	(*E*)-**9a**	Me	*n*Bu	50	74/26
3	(*E*)-**9b**	*t*Bu	*n*Bu	64	58/42
4	(*Z*)-**9b**	*t*Bu	*n*Bu	64	100/0
5	(*Z*)-**9a**	Me	Me	74	100/0

These results are surprising since stannyllithium compounds react at the opposite face to that attacked by alkyllithium reagents.[5] Furthermore, although these results are quite good, the required (*Re*)-**8** stereoisomer cannot be obtained as a single stereoisomer by this reaction. One solution would have been to use the enantiomeric ester (*Z*)-**9a**, but this is not readily obtained. Given the known difference in selectivity between alkyllithium reagents and related cuprates, we decided to study the reactivity of stannylcuprates.

Stannylcuprates were efficiently prepared by transmetalation of tin hydrides with higher order alkylcuprates.[13] They reacted mainly at the *Re* face of the γ-alkoxyester **9a**, that is, the opposite face to that attacked by the related lithium compounds (Scheme 4; Table 2, entries 1 and 2). Again, there was no difference between the trimethyl- and the tri-*n*-butylstannyl derivatives (cf. entries 3 and 1), and much higher



Scheme 4. Addition of stannylcuprate and stannylzincate reagents to **9**.

Table 2. Addition of stannylcuprate and stannylzincate reagents to **9**.

Entry	**9a**	R'_3SnM	Yield of **8** [%]	(*Si*)-**8**/(*Re*)-**8**
1	*Z*	$n\mathrm{Bu_3Sn(Bu)Cu(CN)Li_2}$	37	10/90
2	*E*	$n\mathrm{Bu_3Sn(Bu)Cu(CN)Li_2}$	84	43/57
3	*Z*	$\mathrm{Me_3Sn(Bu)Cu(CN)Li_2}$	71	11/89
4	*Z*	$n\mathrm{Bu_3Sn(Et_2)ZnLi}$	84	0/100
5	*E*	$n\mathrm{Bu_3Sn(Et_2)ZnLi}$	73	10/90
6	*Z*	$\mathrm{Me_3Sn(Et_2)ZnLi}$	77	0/100

diastereoselectivity was obtained with the *Z* stereoisomer (entries 1 and 2).

The diastereoselection in favor of (*Re*)-**8**, although very good, did not reach the standard attained for the synthesis of its stereoisomer (*Si*)-**8** from the same starting material and stannyllithium compounds, but since the counterion proved to have a dramatic effect on the stereochemical outcome of this reaction, we decided to replace lithium by zinc. To our knowledge, stannylzincates are unknown. However, their silyl analogues[14] were prepared from silyllithium compounds and diethylzinc and offered advantages over the related silyllithium and silylcuprate reagents.

We prepared stannylzincates by a procedure analogous to that reported for the synthesis of their silyl analogues[14] and found that they add to ester (*Z*)-**9a** like stannylcuprates but with complete stereocontrol in favor of the *Re* adducts (*Re*)-**8** (Scheme 4; Table 2, entry 4). These reagents also reacted at the *Re* face of (*E*)-**9a** and, although the stereoselection was not as high as with (*Z*)-**9a**, it provides an unusually high stereocontrol (Table 2, entry 5; cf. Table 2, entry 2 and Table 1, entry 2).

We have shown that the synthesis of the β-stannylesters (*Si*)-**8** and (*Re*)-**8** can be achieved in a completely stereoselective fashion from (trialkyltin)metal reagents and the γ-alkoxy-α,β-unsaturated ester **9a** given the appropriate choice of stereoisomer (*Z*) and counterion (Li or $\mathrm{LiZnEt_2}$, respectively). The stannylmetal reagents give far superior stereocontrol than radical-induced reactions of tin hydride.

These results could be explained in terms of an appropriate model such as the degenerate nonchelated Felkin–Anh or chelated Cram model. However, we feel that it is not worthwile to do so, since there is at present no adequate universal model which allows the stereochemical outcome of the reactions of γ-alkoxy α,β-unsaturated esters bearing a chiral γ-carbon to be predicted.

A configurational dichotomy that depends on reaction conditions, especially the counterion, was previously observed in conjugate addition reactions,[15] but not with the extremes reported here. Work is in progress to understand the reasons for such behavior and to generalize the reactions reported here.

Experimental Section

Lithium tri-*n*-butylstannyldiethylzincate was prepared by dropwise addition of a solution of tributylstannyllithium in THF/hexanes to a solution of diethylzinc (1 M in hexane) at 0°C. The yellow solution was then stirred for an additional 0.4 h at this temperature before use. Tributylstannyllithium was prepared[12] by addition of *n*-butyllithium (1.6 M in hexane) to hexa-*n*-butyldistannane in anhydrous THF at 0°C.

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