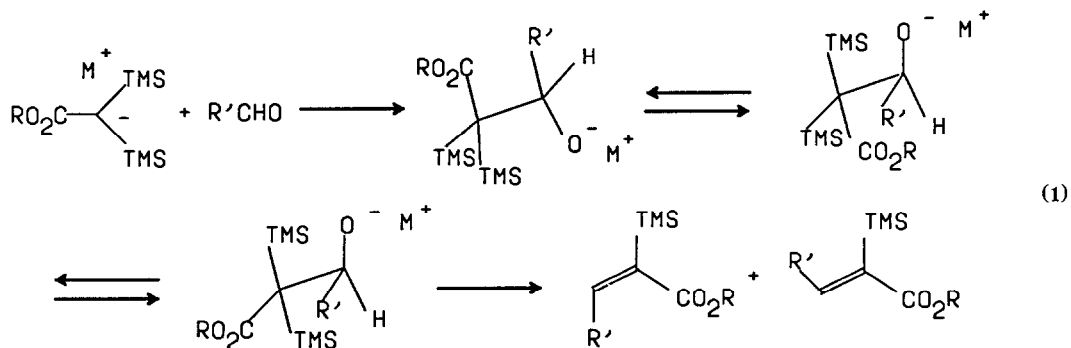


COUNTERION EFFECTS ON GEOMETRIC CONTROL IN THE PETERSON
 REACTION OF BISTRIMETHYLSILYL ESTERS: SYNTHETIC
 SCOPE AND MECHANISTIC IMPLICATIONS

Robert K. Boeckman Jr.* and Richard L. Chinn
 Department of Chemistry
 University of Rochester, Rochester New York 14627

Summary: An interesting and useful level of geometric control can be realized in the reaction of enolates derived from bistrimethylsilyl acetates and aldehydes leading to α -trimethylsilyl esters and derived compounds depending upon the cation employed. Mechanistic experiments are described which suggest that chelation may play a role in the origin of the observed selectivities.

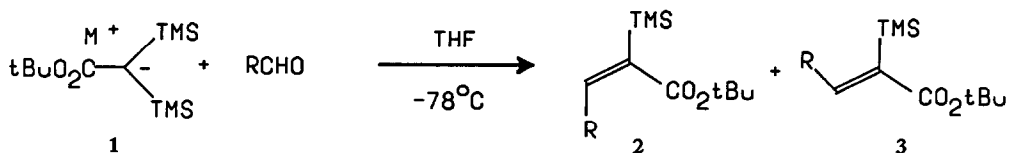
The Peterson reaction has become a widely utilized synthetic method for the production of a variety of substituted olefins.¹ Studies by Hudrlík and others have established that the elimination step is stereospecific occurring SYN or ANTI depending on the reaction conditions.² In connection with other work ongoing in these laboratories, we required a method for the preparation of trimethylsilyl (TMS) substituted dienes with specific control over olefin geometry. Thus, we were attracted to the potential for use of bis-silylated esters in the Peterson reaction. Rathke and others have investigated the use of silylated esters,³ and Rathke has extended the process to disilylated esters, although the potential for geometric control was not established.⁴ We reasoned that in this case the geometric outcome would be determined at the stage of elimination since the aldol step can produce only a single diastereomer (Eqn. 1). Control of olefin geometry could conceivably arise by modifying the selectivity of the elimination step, a process known to be cation dependent.⁵ We therefore undertook the studies described below



to establish whether synthetically useful levels of control could be realized based upon this hypothesis.

The reaction of various metal enolates of *t*-butyl bistrimethylsilylacetate (1) with aldehydes was investigated and the results are outlined in Table 1. For example, treatment of the lithium enolate of 1, prepared as described

previously,^{4,6} with isobutyraldehyde at -78°C afforded the expected α,β -unsaturated esters **2** and **3** ($\text{R} = \text{iPr}$) in a ratio of 6.5:1 (E:Z) in 78% yield. The assignment of geometry was made by analogy with other substituted acrylates, and confirmed by NOE studies.^{7,8} When the potassium enolate (prepared by use of KDA⁹) is utilized,

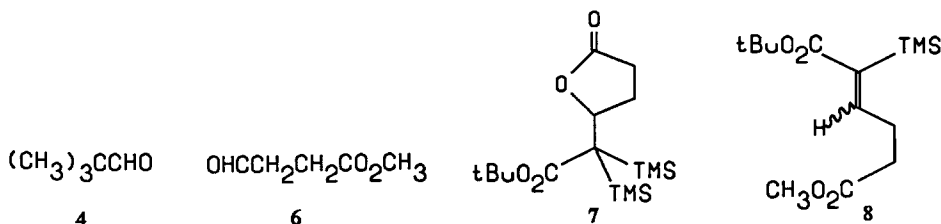
Table 1^a

Entry	R	Metal	Products (2:3) ^b	Yield(%) ^c
1	Et	K	1:1	78
2	Et	Li	2:1	91
3	Et	Mg	1:2	94
4	Et	Et_2Al	1.2:1	75
5	iPr	K	>100:1	82
6	iPr	Li	6.5:1	82
7	iPr	Mg	1:3.5	82
8	iPr	Et_2Al	1:4	82
9	Ph	K	17:1	91
10	Ph	Li	9.4:1	88
11	Ph	Mg	3.4:1	83
12	Ph	Et_2Al	1:2.5	84
13	tBu	K	>100:1	84
14	tBu	Li	>100:1	51
15	tBu	Mg	30:1	93
16	tBu	Et_2Al	1:9	81

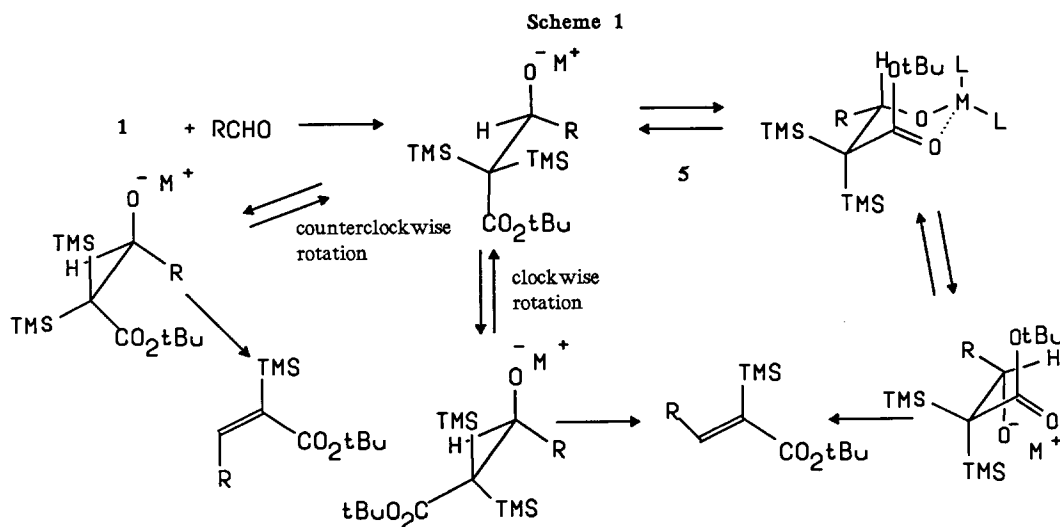
a) All new compounds exhibited spectral data consistent with the assigned structures and provided acceptable combustion analytical or exact mass analytical data. b) Product ratios were determined by NMR and confirmed where possible by capillary gas chromatography. c) Refers to isolated yields of chromatographically pure products.

the selectivity for the E isomer is usually quite significant (>15:1). Therefore, there appears to be an inherent preference for the thermodynamically more stable E isomer when the metal-carbon bond becomes more ionic.¹⁰ However, when relatively covalent metal enolates such as Mg or Al (prepared from the Li enolate by reaction with $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ or Et_2AlCl) are utilized, the selectivity is shifted markedly toward the corresponding Z isomer. Superimposed upon the counterion effects appears to be the effect of steric bulk in the aldehyde which generally reinforces the effects which arise from changes in the counterion. For unhindered cases (Entries 1-4), low and variable levels of selectivity are obtained. For aldehydes bearing α substitution or α,α disubstitution, useful levels of selectivity for E are obtained with Li and K, while moderate to good levels of selectivity for Z are seen for Al (and in some cases Mg). In the most dramatic case, pivalaldehyde (**4**) (Entries 13-16), a 900-fold change is observed (from >100:1 E to 9:1 Z).

One possible mechanistic rationale for the observed results is given in Scheme 1. The observed selectivity must arise from the preferential elimination of one of the two diastereotopic TMS groups in the initial β -alkoxy ester intermediate **5**. Considering the Newman projection of this intermediate in the non-chelated form, elimination can occur from this species by a 60° rotation in two directions to the accepted syn-coplanar elimination geometry,²



which leads to the E and Z isomers respectively. The preferred direction should be that which minimizes the nonbonded interactions which develop with the group R. The more sterically demanding is R, the greater the should be the observed selectivity. Some equilibrium concentration of the analogous chelated form undoubtedly exists in all cases. Consideration of the chelated form of **5** reveals that only one of the two diastereotopic TMS groups lies 60° from the required syn-coplanar elimination geometry. If one then assumes a least motion pathway, preferential elimination from the chelated form of intermediate **5** should occur to afford preferentially the Z isomer.



Thus, the observed data in Table 1 suggests that elimination occurs largely (if not exclusively) from a nonchelated form of **5** for $\text{M}=\text{K}$, and that as the metal-oxygen bond becomes more covalent and chelation tendency increases, the elimination occurs preferentially from the chelated form of **5**. For $\text{M}=\text{Li}$, elimination is still largely from the nonchelated form. For $\text{M}=\text{Mg}$ and Al , elimination appears to occur largely from the chelated form of **5** leading to preferential formation of the Z isomer. The sensitivity to steric bulk of aldehyde alkyl group R is also generally consistent with this model which predicts increasing selectivity as the steric bulk of R increases.

We have attempted to test this mechanistic model by trapping the intermediate addition product in order to directly observe the elimination step. However under all conditions utilized, independent of the counterion,

elimination is very rapid at -78°C . For example, condensation of **1** (M=Li or Mg) with aldehyde **6** did not afford the expected lactone **7** but rather the diesters **8** (~1:1/E:Z) in 50-55% yield.^{1,1} The esters **8** must have arisen by direct elimination since nucleophile initiated anti elimination from **7** would have afforded corresponding the mono acid. Less than 5% of acidic products were obtained. These results also appear to preclude reversible formation of **5** in either the open or chelated forms. However, some indirect evidence for the role of chelation has been obtained by addition of HMPA or 15-crown-5 to the reaction medium. The HMPA or 15-crown-5 should by solvation of the counter ion reduce the tendency of **5** to exist in the chelated form, which for M=Mg and Al should shift the ratio of isomers toward the E isomer. When **1**(M=Mg) is condensed with isobutyraldehyde at -78°C in the presence of 2.1 equiv of HMPA or 2.1 equiv of 15-crown-5, the ratio shifts from 1:3 (E:Z) to 1.5-2.5:1. When this experiment is repeated for **1**(M=Li) using HMPA, the ratio remains unchanged at 6.5:1 (E:Z).

Thus, significant levels of selectivity appear to be realizable by judicious choice of counterion in the Peterson reaction of bis-silylated esters with aldehydes. This methodology provides access in a synthetically useful process to the thermodynamically less stable isomers of certain TMS substituted esters and related derivatives.

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- Typical Experimental Procedure: To a stirred solution of LDA (0.42mL of a 1M solution in THF) at -78°C was added a solution of **1**(0.42 mmol) in 0.5 mL of THF over 1 min. After 1h, isobutyraldehyde (0.42 mmol) was added and the mixture was stirred for 10 min at -78°C then warmed to rt and held for 1h. The reaction mixture was quenched with 0.2N HCl (0.4 mL) and the products isolated by pentane extraction.
- NOE experiments were performed at 400MHz, on the E and Z isomers for R=tBu. Irradiation of the trimethylsilyl group resulted in a 20.5% enhancement of the vinyl proton signal at 5.66 δ for the E isomer **2**, and no enhancement of the corresponding vinyl proton signal for **3** at 6.77 δ . The remainder of the isomers were assigned by analogy to the tBu case in which the Z isomer always possessed the lower field vinyl proton resonance in accord with other substituted acrylate derivatives and the assignment confirmed by NOE for R=Ph.
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- We did not obtain experimental data on the relative stabilities of the E and Z isomers in our studies, however, the E isomer is usually obtained exclusively under equilibrating conditions, for example see ref 8.
- For an example of the trapping of a intermediate alkoxide in this manner see: Boeckman, Jr., R. K.; Bruza, K. J. Tetrahedron **1981**, 37, 3997. Examples of trapping of the intermediate alkoxide using aldehyde **6** at -78°C have been observed by Professor R. H. Schlessinger, we thank him for sharing these results with us prior to publication.

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