# Stereochemistry of Silyl Ketene Acetals of Some 8-Phenylmenthyl Arylacetates

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Trimethylsilyl ketene acetals derived from 8-phenylmenthyl phenyl-, *p*-fluorophenyl, and *p*-(trifluoromethyl)phenylacetates, methyl phenylacetate, and isopropyl phenylacetate have been studied. It was shown that it is not possible, under kinetic conditions, to form exclusively the desired *E*-isomer and that the thermodynamic *Z*-isomer is also obtained as the major product under reaction conditions which can be considered kinetic. The results could be rationalized using the Ireland's and Dauben's models on the basis of the changes in the acidity of the proton to be abstracted and the strength of the base. Dimethyl-*tert*-butylsilyl ketene acetals have also been studied. It appeared that reaction of TBDMSCl onto the Li-enolates favored the *E*-isomer. We proposed that, at the temperature (above −20 °C) at which the reaction occurs, the *E*-*Z* equilibrium between the Li-enolates starts to play a role, and therefore the silyl ketene acetals *E*/*Z* ratios are kinetically controlled but by the second step (reaction of the reagent onto the Li-enolate).

During work on asymmetric synthesis of various bioactive compounds, we became interested in using the (−)-8-phenylmenthol as a recoverable chiral auxiliary.[1,2] When part of dicarbonyl derivatives, the Corey's chiral auxiliary[3] usually leads to high diastereoselectivity[4] (>90%); however, methylation of the 8-phenylmenthyl phenylacetate **1a** led to no selectivity even when the lithium enolate was generated at −78 °C from kinetically selective bases such as LDA or LTMP.[5] These results prompted us to study the stereochemistry of the silyl ketene acetals of **1a**. We report here our results concerning the effect of the enolizing base and silylating agent on the silyl ketene acetal (*E*/*Z*) ratios obtained for 8-phenylmenthyl arylacetates **1a–c** and for isopropyl phenylacetate (**3**), Scheme 1. Methyl phenylacetate (**5**), although already known, has been restudied for comparison.

## Results and Discussion

**Structures of Silyl Ketene Acetals: $^1$H NMR.** In the case of the trialkyl ketene acetals **6**(Me) and **6**(tBu) the chemical shifts of the *E*- and *Z*-α-vinylic protons ($H_v$), *E*- and *Z*-*Me*$_3$Si, *Me*$_2$Si, and t*Bu*Si were found to be almost identical to those given in the literature,[6,7] Table 1.

Stereochemistries of (*E*)-**6**(tBu) and (*Z*)-**6**(tBu) have been determined using the NOESY technique, as shown on Scheme 2. It thus appeared that changing from $SiMe_3$ to $SiMe_2tBu$ did not invert the (*E*)-$H_v$ and (*Z*)-$H_v$ chemical shifts.

Stereochemistries of (*E*)-**4**(Me) and (*Z*)-**4**(Me) were deduced from the known (*E*)-**6**(Me) and (*Z*)-**6**(Me)[6] using the α-vinylic protons and considering that the modifications introduced on passing from **6**(Me) to **4**(Me) were too small to be able to invert the (*E*)-$H_v$ and (*Z*)-$H_v$ chemical shifts.

In the case of the chiral silyl acetals **2a**(Me), **2a**(tBu), **2b**(Me), and **2c**(Me) the (*E*)- and (*Z*)-$H_1$ protons (which appear as characteristic double triplets) displayed a large nonequivalence of ~0.4 ppm. Assignment of the two $H_1$ signals to the *E* and *Z* geometry was carried out, using the NOESY technique, on the 45/55 *E*/*Z* mixture of the trimethylsilyl ketene acetal **2b**(Me) (where the α-vinylic protons, $H_v$, had the largest nonequivalence between the two isomers). As shown in Scheme 3, stereochemistries of (*E*)-**2b**(Me) and (*Z*)-**2b**(Me) were determined using the NOE between $SiMe_3$ ($\delta$ = 0.37) and $H_v$ ($\delta$ = 4.63) for the *E* isomer, and $SiMe_3$ ($\delta$ = 0.32) and $H_{arom}$ ($\delta$ = 7.51) for the *Z* isomer. Most importantly, the presence of a NOE in the *Z* isomer between $H_1$ (dt, $\delta$ = 4.06) and $H_v$ (s, $\delta$ = 4.70) allowed unambiguous correlation of the $H_v$ signal with the more suitable $H_1$ signal, indicating also that conformation $Z_2$ might be significantly populated.[8]

*E* and *Z* stereochemistries of silyl ketene acetals **2a**(Me), **2a**(tBu), and **2c**(Me) were then deduced from that of **2b**(Me) using the $H_1$ signal, Table 1, and considering that the structure modifications were not enough to invert the $H_1$ chemical shifts. One must notice that, whereas in silyl ketene acetals **4**(Me), **6**(Me), and **6**(tBu) the α-vinylic protons ($H_v$) appear at lower field in the $^1$H NMR spectrum of the *E*-isomers ($\delta H_v(E) - \delta H_v(Z)$ = +0.08 to +0.16 ppm) as expected from literature results,[6,7,9] in the silyl ketene acetals derived from (−)-8-phenylmenthol, **2b**(Me), and **2a**(tBu), they appear at higher field ($\delta H_v(E) - \delta H_v(Z)$ = −0.07 and −0.06 ppm).

It is also worth noticing that the absence of shielding of the α-vinylic protons in ketene acetals **2a–c** ($\delta$ = 4.60–4.73), as compared to **4** and **6** ($\delta$ = 4.62–4.78), suggests that the phenyl ring might be trans to the chain, in opposition to the corresponding esters with a 0.6 ppm shielding of protons $CH_2Ph$ in **1a** as compared to the $CH_2Ph$ in **3**.

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(3) Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 6908.

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(8) MMX calculations of **2b**(Me) using PCMODEL-3 showed that conformation $Z_2$ was indeed only about 1 kcal higher than conformation $Z_1$.

(9) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

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**Scheme 1**

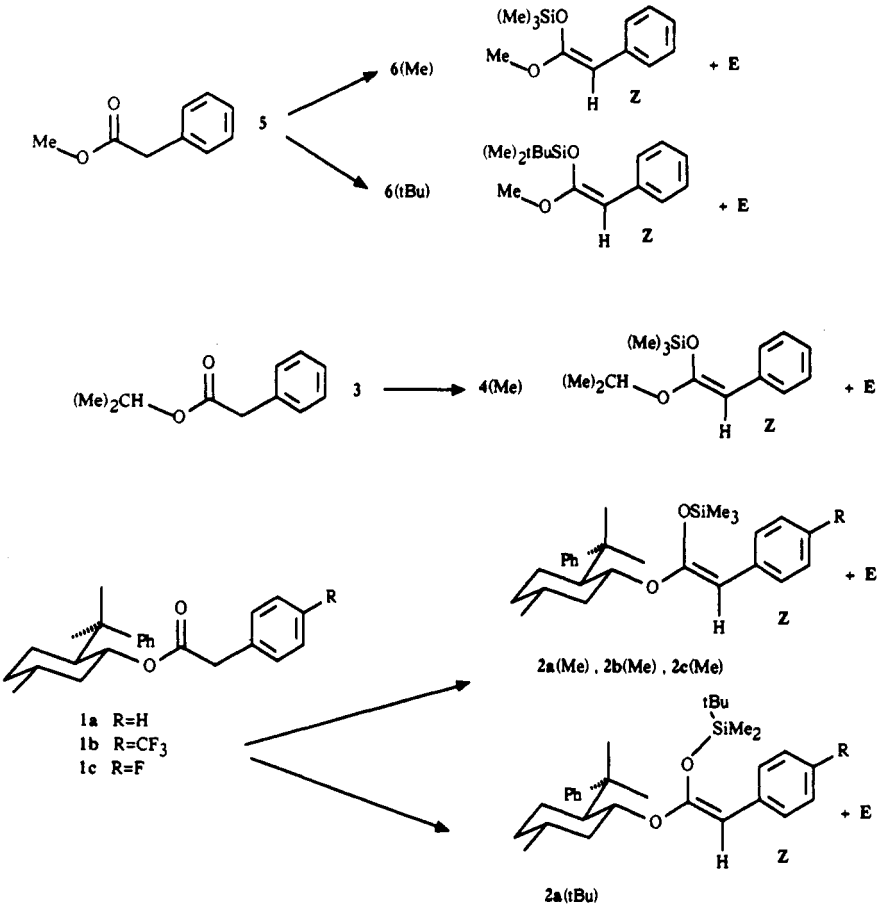



**Table 1. Chemical Shifts (δ, $CDCl_3$/TMS) of Silyl Ketene Acetals**

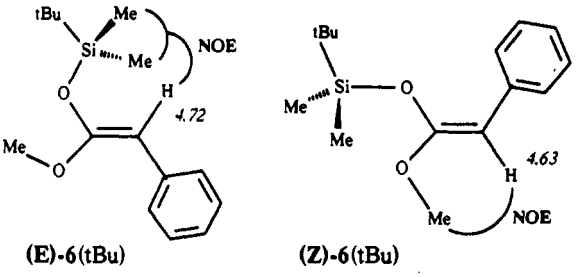
| | | δ $H_v$ ($\Delta\delta^a$) | δ $H_1$ ($\Delta\delta^a$) | δ $SiMe_3$ ($\Delta\delta^a$) | δ $SiC(Me)_3$ ($\Delta\delta^a$) |
|---|---|---|---|---|---|
| **2a**(Me) | **E** | 4.73(0) | 4.42 (+0.40) | 0.37 (+0.05) | |
| | **Z** | 4.73 | 4.02 | 0.32 | |
| **2b**(Me) | **E** | 4.63 (−0.07) | 4.43 (+0.37) | 0.37 (+0.05) | |
| | **Z** | 4.70 | 4.06 | 0.32 | |
| **2c**(Me) | **E** | 4.61 (−0.03) | 4.36 (+0.38) | 0.32 (+0.05) | |
| | **Z** | 4.64 | 3.98 | 0.27 | |
| **2a**(tBu) | **E** | 4.65 (−0.06) | 4.47 (+0.44) | | 1.01 (+0.02) |
| | **Z** | 4.71 | 4.03 | | 0.99 |
| 4(Me) | **E** | 4.78 (+0.16) | 4.65 (+0.24)[f] | 0.36 (+0.01) | |
| | **Z** | 4.62 | 4.41 | 0.35 | |
| 6(Me) | **E** | 4.71 (+0.08)[b] | | 0.36 (+0.04)[c] | |
| | **Z** | 4.63[b] | | 0.32[c] | |
| 6(tBu) | **E** | 4.72 (+0.09)[d] | | | 1.03 (+0.03)[e] |
| | **Z** | 4.63[d] | | | 1.00[e] |

[a] $\Delta\delta = \delta(E) - \delta(Z)$. [b] Reference 7, $H_v$: $\delta(E) = 4.69$, $\delta(Z) = 4.60$, $\Delta\delta = +0.09$. [c] Reference 7, $Si(Me)_3$: $\delta(E) = 0.33$, $\delta(Z) = 0.30$. [d] Reference 8, $H_v$: $\delta(E) = 4.72$, $\delta(Z) = 4.60$, $\Delta\delta = +0.12$. [e] Reference 8, $SiC(Me)_3$: $\delta(E) = 1.02$, $\delta(Z) = 1.00$; and $Si(Me)_2$: $\delta(E) = 0.30$; $\delta(Z) = 0.23$. [f] $H_1$ = $Me_2CHO$.

## Results

Because it reacts at −78 °C without HMPA,[6,10] TMSCl can be considered as a good trapping agent of lithium enolates and can be expected to lead to *E*/*Z* ratios representative of the *E*/*Z* ratios of the lithium enolates generated at −78 °C. Whereas TBDMSCl, which requires higher temperature (−20 °C) or added HMPA,[6,7] can be expected to lead to modified *E*/*Z* ratios.[11] As we wanted to compare the *E*/*Z* ratios of the silyl ketene acetal **2a**(Me) with the results of MeI methylation of the corresponding lithium enolate, the trapping was conducted as a two-step procedure at −78 °C (the alkylation temperature) and not as an internal quench (although this last method is known to lead to higher selectivities[10]), and the lithium enolates were generated with just a slight excess of base (although it has been pointed out that *E*/*Z* equilibration is slow only when a 2-fold excess of base is used[12]). Besides, because we observed (using NMR and the $H_1$ signal) that the *E* isomer of trimethylsilyl ketene acetal **2b**(Me) was hydrolyzed into the starting ester **1b** (probably by traces of humidity of undried NMR $CDCl_3$) faster than the *Z* isomer, Table 2, we decided to avoid the usual aqueous workup of the reaction and to analyze immediately the crude mixtures of the reactions after vacuum concentration (1 mmHg) and using specially dried $CDCl_3$.

**Scheme 2. NOESY of Ketene Acetal 6(tBu)**




(10) Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.

(11) We observed that when the Li-enolate of **1a**, generated at −78 °C with BuLi, was trapped with TBDMSCl at −30 °C (2 h) and then the reaction quenched at −30 °C with $H_2O$, the starting ester **1a** was the only compound recovered, and according to literature results (refs 6, 7, and 9), the aqueous workup could not be responsible for this result.

(12) (a) Fataftah, Z. A.; Kopka, I. E.; Rathke, M. W. *J. Am. Chem. Soc.* **1980**, *102*, 3959–60. (b) Beutelman, H. P.; Xie, L.; Saunders, W. H. *J. Org. Chem.* **1989**, *54*, 1703.

**Scheme 3. NOESY of Ketene Acetal 2b(Me)**

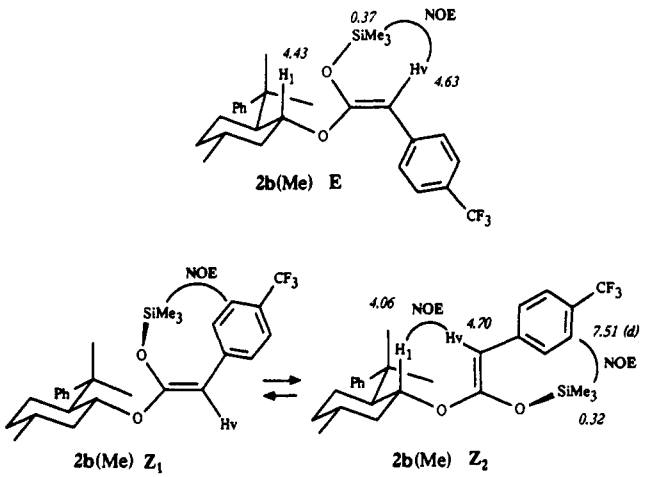



**Table 2. Decomposition of Ketene Acetal 2b(Me) inside the NMR Tube**

| | ratio, % | |
|---|---|---|
| t (h) | 1b/E/Z | E/Z |
| 1 | 20/36/44 | 45/55 |
| 12 | 28/29/43 | 40/60 |
| 36 | 66/10/24 | 29/71 |

**Table 3. E/Z Ratios of Trimethylsilyl Ketene Acetals 2a(Me), 2b(Me), 2c(Me), 4(Me), and 6(Me) Obtained from Esters 1a–c, 3, and 5**

| ester | ketene | base | solvent | E/Z | $t_1$ (min) | yield, % |
|---|---|---|---|---|---|---|
| 1a | 2a(Me) | LDA | THF | 81/19 | 30 | 91[a] |
| | | BuLi | THF | 30/70 | 30 | 78[a] |
| | | tBuLi | THF | 50/50 | 30 | 70[a] |
| 1b | 2b(Me) | LDA | THF | 45/55 | 30 | 80[a] |
| 1c | 2c(Me) | LDA | THF | 80/20 | 30 | 88[a] |
| 3 | 4(Me) | LDA | THF | 80/20 | 30 | 90[a] |
| | | BuLi | RHF | 32/68 | 30 | 65[b] |
| 5 | 6(Me) | LDA | THF | 79/21 | 30 | 75[a] |
| | | LDA | THF | 74/26 | 60 | 73[a] |
| | | BuLi | THF | 10/90 | 30 | 30[c] |

[a] % conversion; the complement to 100% is the corresponding starting ester. [b] The complements to 100% are 5% ester, 20% ketone, and 10% keto enolate. [c] The complements to 100% are 45% ester, 10% ketone and 15% keto enolate.

The effects of the base and aromatic substituent on the *E*/*Z* ratios of trimethylsilyl ketene acetals are gathered in Table 3.

Fuji's results (*E*/*Z* = 81/19[6]) were correctly reproduced when phenylacetate **5** was deprotonated with LDA at −78 °C (Table 3, line 8). When LDA was used as base (a) the *E* isomer was the major product (Table 3, lines 1, 6, and 8), although the regioselectivity is poor (60%); (b) the *E*/*Z* ratios did not change with the nature of the R ester substituent (compare lines 1, 6, and 8, Table 3) as already observed for alkyl propionate[13] and alkyl butanoate.[7] When fluorine was introduced in the para position, no effect was observed on the *E*/*Z* ratio (ketene acetal **2c**(Me); Table 3, line 5), but when a trifluoromethyl group was introduced in the para position (**2b**(Me)) the percentage of (*E*)-isomer decreased (Table 3, line 4).

The *Z* isomer of trimethylsilyl ketene acetal **2a**(Me) became the major product from ester **1a** when BuLi was used as base but a 45/55 *E*/*Z* mixture was obtained when tBuLi was used as base (Table 3, lines 2 and 3). It must be noticed that no ketone and/or corresponding silyl enolate were observed from ester **1a** when BuLi was used as base, although about 30% of esters **3** and **5** were converted into the corresponding ketones in the same conditions (Table 3, compare line 2 with lines 7 and 10 and comments b and c at the bottom of Table 3).

**Table 4. E/Z ratios of Dimethyl-*tert*-butylsilyl Ketene Acetals 2a(tBu) Obtained from 2a and 4a**

| ester | ketene | base | E/Z | yield, % |
|---|---|---|---|---|
| 1a | 2a(tBu) | LDA | 95/5 | 84[a] |
| | | BuLi | 82/18 | 61[a] |
| | | tBuLi | 90/10 | 73[a] |
| 5 | 6(tBu) | LDA | 96/4 | 50[a] |

[a] % conversion, the complement to 100% is the starting ester.

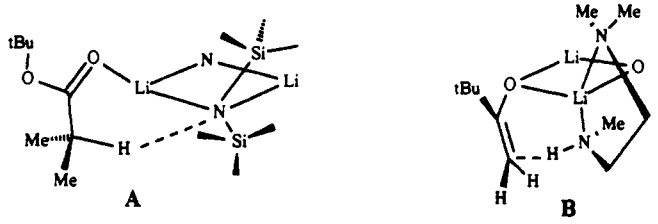



**Figure 1.**

When TBDMSCl was reacted with the lithium enolates of esters **1a** and **5** (−30 °C to rt) the (*E*)-isomer was significantly favored (compare Table 3 lines 1–3 and 8 with Table 4).

## Discussion

Since the early works of Zook[13] and House,[14] there is increasing experimental evidence for the involvement of aggregated species in enolate formation[15] and/or enolate reaction.[16] As suggested by Williard,[17] the two Li complexes, **A**[18] and **B**,[19] provide models for pre- and post-deprotonations (Figure 1). A close examination of these structures shows indeed that they are quite close to Ireland's[8] and Dauben's[20] models: (a) in **A**, the carbonyl oxygen is complexed to the lithium and the available protons directed toward one of the $NR_2$ fragments (in a satisfying $S_N2$-like direction to disrupt the N–Li bond); (b) in **B**, the N–H bond is directed toward the $CH_2$ $\pi$-orbital with a nonlinear C–H–N angle.

We will thus use the Ireland's model and extend it to alkyllithium bases, keeping in mind that BuLi has been shown to be a dimer–tetramer mixture in THF[21a,b] while tBuLi has been shown to be a monomer in THF.[21c]

The obtention (with LDA as base) of 79–81% of the (*E*)-isomer in the case of phenylacetates (**1a**, **3**, and **5**), instead of the 95% (*E*)-isomer obtained with alicyclic esters,[5,7,9,10,22] could be understood (using Ireland's model) on the basis that in phenylacetates (for stereoelectronic

(13) Zook, H. D.; Russo, T. J. *J. Am. Chem. Soc.* **1960**, *82*, 1258.
(14) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.
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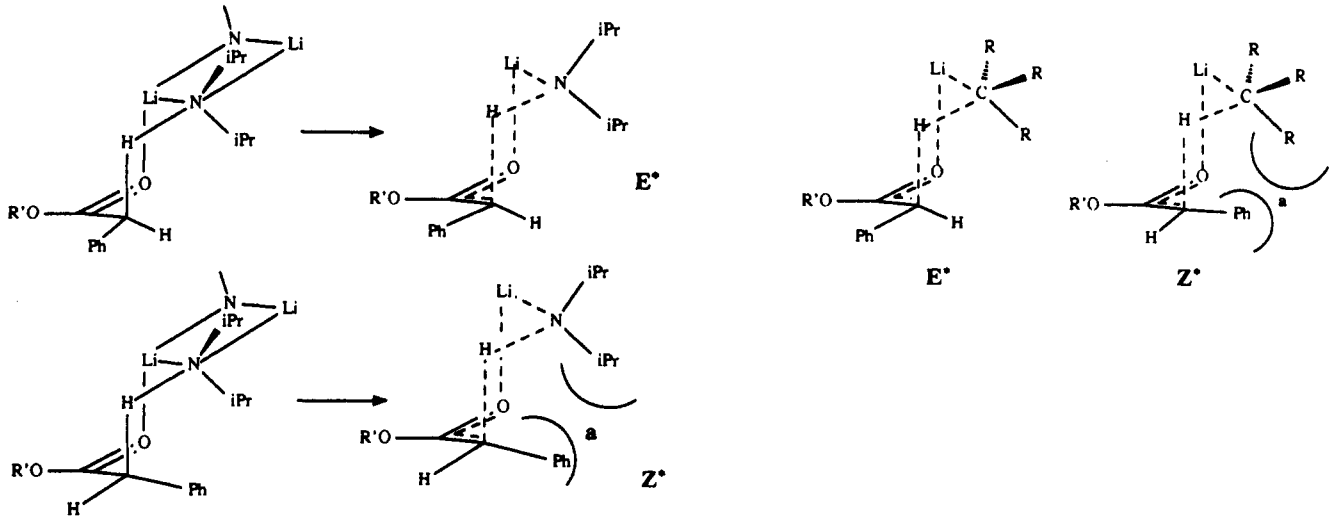
(17) Williard, P. G.; Salvino, J. M. *J. Org. Chem.* **1993**, *58*, 1–3.
(18) Williard, P. G.; Liu, Q. Y. *J. Am. Chem. Soc.* **1992**, *114*, 348–50.
(19) Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373.
(20) Moreland, D. W.; Dauben, W. G. *J. Am. Chem. Soc.* **1985**, *107*, 2264–2273. As pointed out by Dauben, it must be kept in mind that, at least in the early stage of the approach, the base-side is an aggregate.
(21) (a) Seebach, D.; Hässig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, *66*, 308. (b) Bauer, W.; Clark, T.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1987**, *109*, 970. (c) Bauer, W.; Winchester, W. R.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371.
(22) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. A.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

**Scheme 4. Ireland's Model and Extension of Ireland's Model to Alkyllithium**




reasons, $\pi$(Ph)–$\sigma$($CH_2$) interactions) the $CH_2$ protons are more acidic which make the transition state more reactant-like with looser C–H–N and O–Li–N interactions thus decreasing the a-interaction and stabilizing the *Z*-transition state versus the *E*-transition state, Scheme 4.

The increase in percentage of (*Z*)-isomer on passing to BuLi[23a] as base could be rationalized in the same way. Considering that butyllithium is a stronger base (and a dimer in THF[21a,b] like LDA) one could understand that the transition state is still more reactant-like thus increasing the stability and the percentage of the *Z*-transition state through a decrease of the a-interaction, Scheme 4.

When tBuLi was used as base, a 1/1 ratio[23b] was observed. Although tBuLi is a monomer in THF,[21c] its much larger size might explain the destabilization of the *Z*-transition state (and thus the decrease in percentage of (*Z*)-isomer) through an increase of the a-interaction, Scheme 4.

The variations of *E*/*Z* ratios with $CF_3$-substitution[23c] (starting ester **1b**) could be rationalized using the known $\sigma$- and $\pi$-electron-withdrawing ability[24a,b] of this substituent. Since the $CH_2$ protons are more acidic in **1b** (than in **1a**), the transition states will be more reactant-like with smaller a-interaction, and larger amount of the (*Z*)-isomer will be formed.

It appeared also that introduction of a fluorine in the para position has no effect on the *E*/*Z* ratio. It is known that fluorine interacts with a phenyl by withdrawing $\sigma$ electrons and donating $\pi$ electrons[24a,b] and therefore does not change the acidity of the $CH_2$ protons.

The results obtained with TBDMSCl could be rationalized by postulating that the less-hindered *E*-transition state reacts faster with the large TBDMSCl than the *Z*-transition state while *E* and *Z* exchange faster than the reactions occur (on both *E* and *Z*) in the reaction conditions ($t > -20$ °C).

## Conclusion

Under the conditions used (the alkylation conditions), it was not possible to form exclusively the (*E*)-trimethylsilyl ketene acetals of 8-phenylmenthyl arylacetates **1a–c** (Table 3); one can therefore expect a low diastereoselectivity upon alkylation of the corresponding Li-enolates.[25]

Nontheless, the results could be rationalized using the Ireland's and Dauben's models on the bases of the changes in the acidity of the proton to be abstracted and the strength of the base.

Although the (*Z*)-trimethylsilyl ketene acetal can be considered as the "thermodynamic" isomer,[5,7,26] it was formed as the major compound even under reaction conditions which can be considered kinetic, that is, using a strong base (BuLi) where the reverse reaction is not possible and at low temperature (–78 °C) where the exchanges (*Z*/*E*) are slow, *cf.* Table 3).

TBDMSCl favored the (*E*)-isomer (compared to TMSCl); here one can think that, at the temperature (–20 °C) at which the reaction starts to occur, the *E*/*Z* equilibrium between the Li-enolates starts also to play a role and therefore the silyl ketene acetals *E*/*Z* ratios are controlled by the second step (reaction of TBDMSCl onto the Li-enolate).

## Experimental Section

All starting materials were commercially available research-grade chemicals and used without further purification. THF is refluxed over Na/benzophenone. Trimethylsilyl chloride from Aldrich was distilled under argon prior to use. Dimethyl-*tert*-butylsilyl chloride and methyl and isopropyl phenylacetate were purchased from Aldrich and used without further purification. All reactions were run under argon. (–)-8-Phenylmenthol (optically pure and free from the other isomer, $[\alpha]_D = -26.2°$ ($c$ = 2,

(23) (a) If 13% of the 22% of ester **1a** observed with BuLi had been formed exclusively from the (*E*)-isomer because of solvent humidity, which is an extreme possibility since we have seen that the (*Z*)-isomer is also converted into the starting ester by humidity (Table 2), one would get 91% yield (as with LDA) but with a 39/61 *E*/*Z* ratio. Therefore, there is still a decrease in the percentage of (*E*)-isomer on passing from LDA to BuLi. (b) The same holds for tBuLi. For a 91% yield one would get a 61/39 *E*/*Z* ratio and the trend is not inverted by the yield correction: an increase of the *E*-percentage is still observed on passing from BuLi to tBuLi. (c) In the case of ketene acetal **2b**(Me) and LDA, a 91% yield and exclusive conversion of the (*E*)-isomer into the starting ester would give a 52/48 *E*/*Z* ratio, which does not change the trend observed without correction.

(24) (a) Rabalais, J. W. *Principles of Ultraviolet Photoelectron Spectroscopy*; John Wiley & Sons: New York, 1977; Chapter 10. (b) Hehre, W. J.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 1496.

(25) Although Li-enolates are usually dimeric in THF (*cf.* refs 13–18), aggregates are not envisaged here because only O-silylation has been observed.

(26) We have found using MMX calculations and PCMODEL-3 that (*Z*)-**6**(Me) was indeed about 1 kcal lower than (*E*)-**6**(Me).

EtOH) has been prepared from (+)-pulegone (from Aldrich, distilled before use) and purified according to a modified Corey's method.[27,28] $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker AC 200 instrument, assignments of para-C(H) were based on the intensity ratios ortho/para and meta/para (~1.9). IR spectra were recorded on a Perkin-Elmer 1310 instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. TLC plates silica gel 60 $F_{254}$ have been used, and the spots were detected using UV and vanillin solution. Flash column chromatographies were carried out with Merck silica gel 60.

**8-Phenylmenthyl Arylacetates 1a–c.** To a well-stirred solution of (−)-8-phenylmenthol (1.07 mmol) in THF (0.5 mL) were successively added dicyclohexylcarbodiimide (1.07 mmol), 4-(dimethylamino)pyridine (0.10 mmol), and the desired arylacetic acid (0.97 mmol) in THF (0.25 mL), and the mixture was refluxed for 3 h. After cooling to room temperature, the white solid was filtered out and washed with $Et_2O$ (3 × 2 mL). The combined organic layers were successively washed with water (3 × 5 mL), 5% acetic acid (3 × 5 mL), water (3 × 5 mL), and brine (1 × 5 mL) and dried over $MgSO_4$. After concentration, the colorless liquid was purified by flash chromatography (8/2 hexane/diethyl ether).

**8-Phenylmenthyl Phenylacetate (1a)**: colorless oil (85%); IR (neat) 1720 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.31 (5H, m), 7.25 (2H, m), 7.15 (3H, m), 4.82 (1H, td, 2 $J$ = 10 Hz, 5 Hz), 2.98 (2H, bs), 2.10–0.81 [17H, among which 2.04 (1H, td, $J$ = 11, 4 Hz), 1.30 (3H, s), 1.21 (3H, s), 0.85 (3H, d, $J$ = 6.5 Hz)]; $^{13}C$ NMR (50.3 MHz, $CDCl_3$) δ 170.91, 151.92 and 134.34, 129.44, 128.51, 128.17 and 125.62, 126.98 and 125.29, 74.62, 50.46, 41.68 and 41.35, 39.79, 34.73, 31.43, 28.68, 26.66, 24.57 and 22.01. Anal. Calcd for $C_{24}H_{30}O_2$: C, 82.29; H, 8.57. Found: C, 82.48; H, 8.48.

**8-Phenylmenthyl *p*-(trifluoromethyl)phenylacetate (1b)**: pale yellow oil (90%); IR (neat) 1710 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.57 (2H, d, $^3J$ = 8 Hz), 7.40–7.37 (4H, m), 7.24 (3H, m), 4.94 (1H, td, $J$ = 11 Hz, 4.5 Hz), 3.02 (2H, bs), 2.25–0.51 [17H, among which 2.14 (1H, td, $J$ = 12, 4 Hz), 1.34 (3H, s), 1.23 (3H, s), 0.90 (3H, d, $J$ = 7 Hz)]; $^{13}C$ NMR (50.3 MHz, $CDCl_3$) δ 169.92, 152.05 and 138.39, 129.21 (q, $J$ = 33 Hz), 129.81, 128.13, 125.53 and 125.40, 124.40 (q, $J$ = 253 Hz), 74.78, 50.33, 41.63, 40.78, 39.62, 34.63, 31.38, 29.27, 26.48, 23.64 and 21.85. Anal. Calcd for $C_{25}H_{29}F_3O_2$: C, 71.75; H, 6.98. Found: C, 71.56; H, 7.11.

**8-Phenylmenthyl *p*-fluorophenylacetate (1c)**: colorless oil (90%); IR (neat) 1720 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.31 (4H, two lines), 7.17 (1H, m), 7.0 (4H, m, ~$(AB)_2X$ system, $J$ ~ 9 Hz, $J$ ~ 5 Hz), 4.81 (1H, td, $J$ = 11, 4.5 Hz), 2.91 (2H, s), 2.10–0.79 [17H, among which 2.04 (1H, td, $J$ = 11, 4.5 Hz), 1.29 (3H, s), 1.20 (3H, s), 0.85 (3H, d, $J$ = 6.5 Hz)]; $^{13}C$ NMR (50.3 MHz, $CDCl_3$) δ 170.6, 161.9 (d, $J$ = 246 Hz), 151.9, 131.0 (d, $J$ = 10 Hz), 130.0 (d, $J$ = 3 Hz), 128.1, 125.5, 125.2, 115.2 (d, $J$ = 20 Hz), 74.6, 50.4, 41.7, 40.3, 39.7, 34.7, 31.4, 28.9, 26.6, 24.1, 21.9. Anal. Calcd for $C_{24}H_{29}FO_2$: C, 78.23; H, 7.93. Found: C, 78.45; H, 7.82.

**Isopropyl phenylacetate (3)**: $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.30 (5H, m), 5.02 (1H, sept, $J$ = 6.5 Hz), 3.59 (2H, s), 1.23 (6H, d, $J$ = 6.5 Hz).

**Reactions with Lithium Diisopropylamide (LDA).** To a solution of diisopropylamine (0.82 mmol) in 2.0 mL of anhydrous THF at −78 °C was added dropwise a 1.5 M solution of BuLi in hexane and the solution was stirred for 30 min at −78 °C. A solution of the desired ester (0.66 mmol) in 0.5 mL of anhydrous THF was then added slowly, and the solution stirred 30 min at −78 °C. After addition of trimethylsilyl chloride (0.5 mL), or of a solution of *tert*-butyldimethylsilyl chloride (1.5 mmol) in THF (0.5 mL), stirring was maintained at −78 °C for 3 h. The temperature was then allowed to reach 25 °C and the solvent was rapidly evaporated under reduced pressure (1 mmHg). The residue was dissolved in $CDCl_3$ (dried on molecular sieves 4 Å) and the solution filtered into an NMR tube under argon.

**Reactions with Alkyllithiums.** To a solution of the corresponding ester (0.66 mmol) in anhydrous THF (2.0 mL), at −78 °C, was added dropwise a solution of BuLi 1.5 M in hexane or $^t$BuLi 1.7 M in pentane (0.82 mmol). After 30 min at −78 °C, trimethylsilyl chloride (0.5 mL), or a solution of *tert*-butyldimethylsilyl chloride (1.5 mmol) in THF (0.5 mL), was added and the operations were continued as above.

**2a**(Me): $E/Z$ = 81/19; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.5–6.95 (10H, m, E + Z, $H_{arom}$), 4.73 (1H, s, $E$ + $Z$), 4.42 (1H, td, $J$ = 11, 4 Hz, $E$, 81%), 4.02 (1H, td, $J$ = 11, 4 Hz, $Z$, 19%), 2.1–0.8 [17H, among which 1.55 (3H, s, $Z$), 1.50 (3H, s, $Z$), 1.47 (3H, s, $E$), 1.35 (3H, s, $E$), 0.85 (3H, d, $J$ = 7 Hz, $E$)], 0.37 (9H, s, $E$, 81%), 0.32 (9H, s, $Z$, 19%).

**2a**(tBu): $E/Z$ = 82/18; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.5–6.95 (10H, m, $E$ + $Z$), 4.71 (1H, s, $Z$, 18%), 4.65 (1H, s, $E$, 82%), 4.47 (1H, td, $J$ = 11, 4 Hz, $E$, 82%), 4.03 (1H, td, $J$ = 11, 4 Hz, $Z$, 19%), 2.1-0.75 [26H, among which 1.55 (3H, s, $E$), 1.45 (3H, s, $E$), 1.01 (9H, s, $E$), 0.99 (9H, s, $Z$)], 0.37 (3H, s, $E$, 82%), 0.32 (3H, s, $E$, 82%), 0.25 (3H, s, $Z$, 18%), 0.21 (3H, s, $Z$, 18%).

**2b**(Me): $E/Z$ = 45/55; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.55–7.01 (9H, m, $E$ + $Z$), 4.70 (1H, s, $Z$, 55%), 4.63 (1H, s, $E$, 45%), 4.43 (1H, td, $J$ = 11, 4Hz, $E$, 45%), 4.06 (1H, td, $J$ = 11, 4Hz, $Z$, 55%), 2.25–0.75 [17H, among which 1.52, 1.50, 1.49, and 1.44 (4 singlets for $E$ and $Z$), 0.85 (2 doublets for $E$ and $Z$)], 0.37 (9H, s, $E$, 45%), 0.32 (9H, s, $Z$, 55%).

**2c**(Me): $E/Z$ = 80/20; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.4–7.1 (7H, m, $E$ + $Z$), 6.87 (2H, 2 slightly overlapped t, $J$ = 8 Hz, $E$ + $Z$), 4.64 (1H, s, $Z$, 20%), 4.61 (1H, s, $E$, 80%), 4.36 (1H, td, $J$ = 11, 4 Hz, $E$, 80%), 3.98 (1H, td, $J$ = 11, 4 Hz, $Z$, 20%), 2.1–0.8 [17H, among which 1.50 and 1.45 (2 singlets, $Z$), 1.42 and 1.34 (2 singlets, $E$), 0.84 (3H, d, $J$ = 7 Hz, $Z$), 0.80 (3H, d, $J$ = 7 Hz, $E$)], 0.32 (9H, s, $E$, 80%), 0.27 (9H, s, $Z$, 20%).

**4**(Me): $E/Z$ = 80/20; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.5 (2H, m, $E$ + $Z$), 7.25 (2H, m, $E$ + $Z$), 7.05 (1H, m, $E$ + $Z$), 4.78 (1H, s, $E$, 80%), 4.65 (1H, sept, $J$ = 6.5 Hz, $E$, 80%), 4.62 (1H, s, $Z$, 20%), 4.41 (1H, sept, $J$ = 6.5 Hz, $Z$, 20%), 1.35 (6H, d, $J$ = 6.5 Hz, $Z$, 20%), 1.32 (6H, d, $J$ = 6.5 Hz, $E$, 80%), 0.31 (9H, s, $E$, 80%), 0.30 (9H, s, $Z$, 20%).

**6**(Me): $E/Z$ = 74/26; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.45 (2H, m, $E$ + $Z$), 7.30 (2H, m, $E$ + $Z$), 7.10 (1H, t, $E$ + $Z$), 4.71 (1H, s, $E$, 74%), 4.63 (1H, s, $Z$, 26%), 3.70 (3H, s, $E$, 74%), 3.68 (3H, s, $Z$, 26%), 0.36 (9H, s, $E$, 74%), 0.32 (9H, s, $Z$, 26%).

**6**(tBu): $E/Z$ = 57/43; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.4 (2H, m, $E$ + $Z$), 7.25 (2H, m, $E$ + $Z$), 7.0 (1H, t, $E$ + $Z$), 4.72 (1H, s, $E$, 57%), 4.63 (1H, s, $Z$, 43%), 3.70 (3H, s, $E$, 57%), 3.65 (3H, s, $Z$, 43%), 1.03 (9H, s, $E$, 57%), 1.00 (9H, s, $Z$, 43%), 0.30 (6H, s, $E$, 57%), 0.23 (6H, s, $Z$, 43%).

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