A Novel Configuration-Controlled Stereoselectivity in Enol Silylation of Ketones. Stereochemistry of Amine-Promoted Enol Silylation of Meso and Racemic α,α′-Dichloro Ketones and of Ketonization of the Resultant Enol Silyl Ethers

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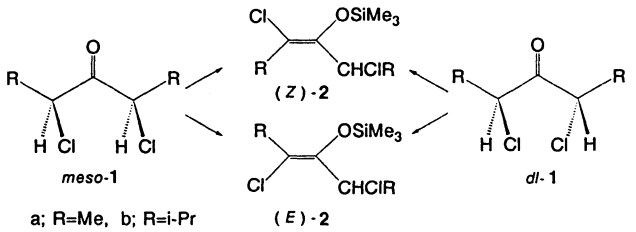
Stereochemistry in amine-promoted enol trimethylsilylation of *meso*- and *dl*-α,α′-dichloro ketones, RCHClCOCHClR (**1a**; R=Me and **1b**; R=*i*-Pr), and in ketonization of the resultant enol silyl ethers (**2a** and **2b**) has been studied. The Et_3N-promoted silylation of **1** in benzene shows a marked diastereoselectivity; the racemic isomer exhibits 84% and 98% (*E*)-selectivities for **1a** and **1b**, while the *meso* isomer, 97% and 98% (*Z*)-selectivities respectively. Both stereo- and diastereo-selectivities markedly depend upon solvent polarity and base strength. For example, both *meso*- and *dl*-**1a** showed small (*Z*)-selectivities in DMF. The diastereoselectivity markedly decreased with increasing base strength; both **1a** and **1b** exclusively gave the (*E*)-isomer of **2** irrespective of the configuration of the ketone when treated with lithium diisopropylamide in the presence of chlorotrimethylsilane at −78 °C. The ketonization of **2a** and **2b** was also diastereoselective in the direction opposite that observed in the forward reaction; the (*E*)-isomer predominantly gave the meso ketone (24% d.e.), while the (*Z*)-isomer, the racemic ketone (ca. 70% d.e.) upon protonation with concd hydrochloric acid in THF.

Chemistry of enol silyl ethers has received continuous synthetic interests.[1,2] A convenient and widely applicable method for preparation of enol silyl ethers is a treatment of ketones with triethylamine in the presence of chlorotrimethylsilane (TMS-Cl) in DMF developed by House and his co-workers.[3] This enol silylation is considered to be a thermodynamically controlled process. We have found during the course of study on 2-(trimethylsiloxy)allyl cations[4] that the enol silylation of 2,4-dichloro-3-pentanone (**1a**) by the House method gives an almost 1 : 1 mixture of (*E*)- and (*Z*)-2,4-dichloro-3-trimethylsiloxy-2-pentene (**2a**) starting with either *meso* (*meso*-**1a**) or racemic isomer (*dl*-**1a**), seemingly in agreement with the thermodynamic control of stereochemistry; however, we also found a high diastereoselectivity when the same enol silylation was carried out in weakly polar solvents. Thus, the Et_3N-promoted silylation of **1a** in ether gave predominantly (*Z*)-**2a** (94% diastereoisomeric excess (d.e.)) from the meso isomer, while (*E*)-**2a** (72% d.e.) from the racemic isomer (Scheme 1)[5]. The striking diastereoselectivity clearly indicates a kinetic control of the stereochemistry of this enol silylation.

The stereochemistry of the kinetic deprotonation of the carbonyl compounds is generally considered to be a function of two types of steric effects associated with groups at the α carbon a hydrogen of which is deprotonated; one is steric interactions between the largest group at the C_α and a carbonyl substituent, and the other between the group and an approaching base.[6–8] The two diastereomeric ketones like *meso*- and *dl*-**1a** must be subjected equally to these steric effects as long as the carbonyl substituent simply acts as steric bulk. Apparently, the diastereoselectivity in the Et_3N-promoted enol silylation of **1a** does not arise from these steric effects and provides a novel example of configuration-controlled stereoselection in deprotonation.



Scheme 1.

This paper deals with the stereochemistry of the amine-promoted enol trimethylsilylation of the *meso* and racemic isomers of **1a** and 3,5-dichloro-2,6-dimethyl-4-heptanone (**1b**) together with a reference compound, 3-chloro-2-butanone (**3**), and the stereochemistry of the ketonization of the resultant enol silyl ethers **2a** and **2b**.

Results and Discussion

The ketones, *meso*-**1a** (stereochemical purity 99.2%), *dl*-**1a** (98.5%), *meso*-**1b** (92.6%), and *dl*-**1b** (82.4%) were obtained by chlorination of 3-pentanone and 4-heptanone with sulfuryl chloride followed by fractionation. Stereochemical assignment of *meso*-**1a** and *dl*-**1a** has been determined by Claeson and Thalen.[9] Stereochemistry of the diastereoisomers of **1b** was deduced from the comparison with **1a**; of the two isomers, the lower-boiling one which appeared faster on GLC (Apiezon grease L) and was more abundant in a base-induced equilibration mixture was assigned to the racemic isomer. Stereochemistry of (*E*)-**2a** and (*Z*)-**2a** was confirmed previously by the spectral analysis and by chemical evidence that they were converted almost

stereospecifically to 2-chloro-2,4-dimethyl-8-oxabicyclo [3.2.1]oct-6-en-3-one on treatment with silver perchlorate in the presence of furan in nitromethane.[4] The stereochemistry of the silyl enol ether **2b** was deduced from the comparison of NMR and GLC data with those for **2a**; the (*E*)-isomer appeared faster on GLC (Apiezon grease L) and resonated at about 0.4 ppm lower field for the allylic proton of a CHClR group than the (*Z*)-isomer.

Diastereoselectivity in Enol Silylation. Amine-promoted enol trimethylsilylation of the ketone **1** was carried out by taking the ketone **1**, 2.2 equiv an amine, and 2.0 equiv TMS-Cl in a given solvent at about 0.25 mol dm^{-3} concentration for the ketone at 25 °C for most cases. The reaction was almost quantitative based on the consumed ketone. A representative reaction profile for the enol silylation is illustrated by Fig. 1 which deals with the Et_3N- promoted enol trimethylsilylation of *meso*-**1a** in ether at 25 °C. The enol silylation was accompanied by partial isomerization of the unchanged ketone as shown in Fig. 1; however, the isomerization did not reach the equilibrium even after 80% completion of the reaction indicating a faster rate of the enol silylation than that of the isomerization of the ketone. An equilibrated *meso*/*dl* ratio was 30/70 for **1a** at 25 °C and 41/59 for **1b** at 50 °C. As shown in Fig. 1, the (*Z*)-composition in the product **2a** slightly decreased as the reaction progressed. Since both the (*E*) and (*Z*)-isomers of **2a** did not isomerize to each other under the reaction conditions, the decrease in the (*Z*)-composition must result from the contamination of the starting ketone with the racemic isomer during the reaction. Extrapolation of the (*E*)/(*Z*) ratios to the zero conversion gives us a ratio of 3/97 which shows the stereoselectivity of the enol silylation of the pure *meso*-**1a** in ether. The reaction of the racemic isomer showed a similar reaction profile from which we determined the stereoselectivity of (*E*)/(*Z*)=86/14 for *dl*-**1a** by extrapolation of (*E*)/(*Z*) ratios observed at various reaction times to the zero conversion.

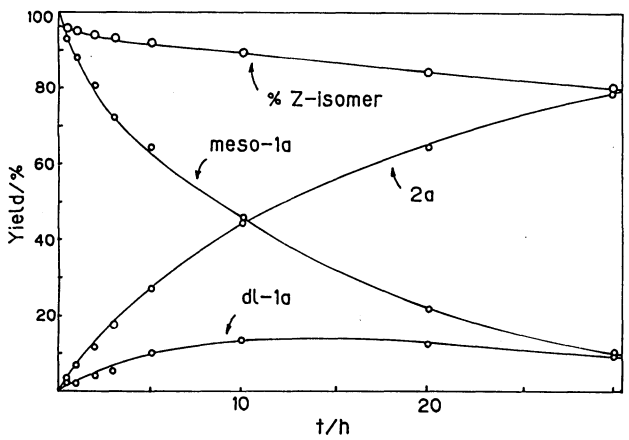
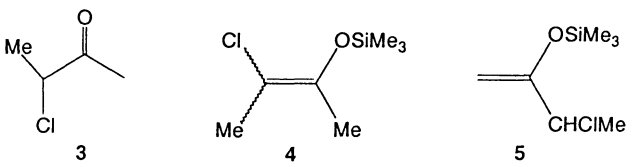


Fig. 1. Reaction profile for Et_3N-promoted enol trimethylsilylation of *meso*-**1a** in ether.

We define the diastereoselectivity (DSS) of the enol silylation as Eq. 1. The DSS is a stereochemical split between the reactions of the two diastereoisomeric ketones; a diastereospecific reaction shows 100% DSS, while a reaction in which the two diastereoisomeric ketones show the same stereochemical result exhibits 0% DSS.

$$\text{DSS (\%)}=[\%\ (Z)\ \text{from } \textit{meso}\text{-}\mathbf{1}] - [\%\ (Z)\ \text{from } \textit{dl}\text{-}\mathbf{1}] \quad (1)$$

Thus, the Et_3N-promoted enol silylation of **1a** in ether is characterized as a highly diastereoselective reaction with 83% DSS. These stereochemical results are interestingly compared with the observation that an Et_3N-promoted enol silylation of a reference compounds **3** in



ether gave 2-chloro-3-trimethylsiloxy-2-butene **4** as an almost 1 : 1 mixture of the (*E*)- and (*Z*)-isomers along with 3-chloro-2-trimethylsiloxy-1-butene **5**(**4**/**5**=45/55). Apparently, Me and Cl groups at the α-carbon act as almost equivalent substituents in the enol silylation in

Table 1. Stereochemistry in Et_3N-Promoted Enol Silylation of **1**[a]

Solvent	% (*Z*)-**2**[b] from *meso*-**1**	% (*Z*)-**2**[b] from *dl*-**1**	DSS/%[c]
2,4-Dichloro-3-pentanone (**1a**)			
Ether	97	14	83
C_6H_6	97	16	81
CH_2Cl_2	87	38	45
CH_3CN, 0°	66	49	17
CH_3CN, −40°	70	58	12
DMF	52	41	11
DMF, −60°	57	60	3
DMF/C_6H_6 (1 : 9)	88	22	66
DMF/C_6H_6 (1 : 1)		42	
3,5-Dichloro-2,6-dimethyl-4-heptanone (**1b**)			
C_6H_6, 50°	95[d], 98[f]	20[e], 2[f]	96[f]
DMF, 50°	65[d]	5[e]	60
3-Chloro-2-butanone (**3**)			
Ether	51		

a) All reactions were carried out by taking **1**, 2.2 equiv triethylamine, and 2.0 equiv chlorotrimethylsilane in a given solvent (0.25 mol dm^{-3} for **1**) at 25 °C except as noted. b) Extrapolated value to zero conversion. c) Diastereoselectivity defined as [% (*Z*) from *meso*-**1**] −[% (*Z*) from *dl*-**1**]. d) Using a 93/7 *meso* and racemic mixture. e) Using an 82/18 racemic and *meso* mixture. f) Estimated value after correction for the isomeric purity of the ketone.

Table 2. Effect of Base[a]

Base	Solvent	% (*Z*)-**2** from *meso*-**1**	% (*Z*)-**2** from *dl*-**1**
2,4-Dichloro-3-pentanone (**1a**)			
Et_3N	C_6H_6	97	16
n-Bu_3N	C_6H_6	92	15
DABCO	C_6H_6	94	16
DBU	C_6H_6	46	9
DBU[b]	Ether	34	5
Et_3N	DMF	52	41
n-Bu_3N	DMF	55	45
HMDS	DMF	40	42
DBU[b]	DMF	30	36
LDA[c,d]	THF	4	9
LDA[c,e]	THF	11	23
LDA[c,e]	THF/HMPA (2:1)	20	26
3,5-Dichloro-2,6-dimethyl-4-heptanone (**1b**)[f]			
Et_3N[g]	C_6H_6	95, 98[h]	20, 2[h]
LDA[c,d]	THF	<1	<1
3-Chloro-2-butanone (**3**)			
LDA[c,d]	THF	23	

a) At 25 °C; ketone : base : chlorotrimethylsilane=1 : 2.2 : 2.0 (mol) except as noted. b) At 0 °C. c) At −78 °C. d) Into a THF solution of LDA (1.2 equiv) and chlorotrimethylsilane (1.2 equiv) was added to the ketone. e) Chlorotrimethylsilane was added to an enolate solution prepared by addition of the ketone to a THF solution of LDA (1.2 equiv). f) Isomeric purity is 93% for the meso and 82% for the racemic ketones. g) At 50 °C. h) Estimated value after correction for the isomeric purity of the starting ketones.

Table 3. Effects of Base and Solvent on the Rate of Enol Silylation[a]

Base	Solvent	$t_{1/2}$[b] (% Isomerization[c]) *dl*-**1**	$t_{1/2}$[b] (% Isomerization[c]) *meso*-**1**
2,4-Dichloro-3-pentanone (**1a**)			
Et_3N	Ether	17 h (27)	14 h (44)
	C_6H_6	11 h (13)	5 h (34)
	CH_2Cl_2	1 h (67)[d]	24 m (91)[d]
	CH_3CN	22 m (73)[d]	18 m (67)[d]
	CH_3CN	3.5 h (<5)[e]	2.5 h (17)[e]
	DMF	3 m (23)[d]	12 m (13)[d]
	DMF	10 h (<5)[f,g]	12 h (<3)[f,g]
n-Bu_3N	C_6H_6	h)[h]	h)[h]
DABCO	C_6H_6	5 h	3 h
DBU	C_6H_6	<1 m (<5)	<1 m (<5)
n-Bu_3N	DMF	26 m	34 m
i-Bu_3N	DMF	i)[i] (100)	
HMDS	DMF	3.5 h (100)[j]	3.5 h (100)[j]
3,5-Dichloro-2,6-dimethyl-4-heptanone (**1b**)			
Et_3N	DMF	1.6 h[k]	4.5 h (10)[k]
	C_6H_6	46 h[k]	36 h (41)[k]

a) Using 0.25 mol dm^{-3} solutions at 25 °C; ketone : amine : chlorotrimethylsilane=1.0 : 2.2 : 2.0 (mol) except as noted. b) Time at which 50% of the ketone was converted into the silyl enol ether. c) Percent completion of equilibration of the initial isomer of the ketone after $t_{1/2}$. d) At 0 °C. e) At −40 °C. f) At −60 °C. g) Time at which 25% of the ketone was consumed. h) Very slow. i) About 0.6% completion of the reaction after 5 h. j) Isomerization of the ketone was completed within 20 min. k) At 50 °C.

ether when the carbonyl substituent is changed from a CHClMe group to a methyl group. Undoubtedly, the configuration of the carbonyl substituent plays the major role in controlling the stereochemistry of the enol silylation of **1a**.

In a similar procedure described above, the stereoselectivities of the enol silylation of **1a** and **lb** under various conditions were determined and the results are given in Tables 1 and 2. Table 3 shows the rates of the enol silylation determined semiquantitatively by measuring a time $t_{1/2}$ at which 50% of the ketone is converted into the enol silyl ether. Table 3 also includes the extent of the isomerization of the unchanged ketone at the time $t_{1/2}$; the % isomerization of the ketone was calculated as 100×(% *dl*-**1a**/70) for the reaction of *meso*-**1a**, 100×(% *meso*-**1a**/30) for *dl*-**1a**, 100×(% *dl*-**1b**/59) for *meso*-**1b**, and 100×(% *meso*-**1b**/41) for *dl*-**1b**.

Effects of Solvent. The rates of the enol silylation increased with increasing solvent polarity, as shown in Table 3. For example, DMF accelerated the Et_3N-promoted enol silylation of *dl*-**1a** by a factor of more than 340 relative to ether. In weakly polar solvents like ether and benzene, the *meso* ketone underwent the enol silylation slightly more rapidly than the racemic isomer, while the racemic ketone was slightly more reactive than the *meso* isomer in DMF.

Noteworthy is a striking dependence of the stereochemistry on solvent polarity, as shown in Tables 1 and 2. The diastereoselectivity dramatically decreases with increasing solvent polarity. For example, the Et_3N-promoted enol silylation of **1a** shows more than 80% DSS in ether and benzene but 45% in dichloromethane, 17% in acetonitrile, and almost no diastereoselectivity in DMF at −60 °C. The fact that the reaction in a benzene–DMF (9 : 1) mixture gave an intermediate diastereoselectivity (66% DSS) between the DSS's observed in each pure solvent suggests that the effect of solvent arises mainly from the polarity of the medium rather than specific interactions between the ketone and a solvent.

The diastereoselectivity was more pronounced for **lb** than for **1a**; the Et_3N-promoted enol silylation of **lb** was almost diastereospecific with 96% DSS in benzene and diastereoselective (60% DSS) even in DMF.

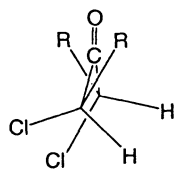
The decrease in the diastereoselectivity in polar solvents does not arise from the partial or complete isomerization of the starting ketone. The rate of the enol silylation was significantly faster than that of the isomerization of the ketone in DMF; in fact, the isomerization was negligibly small in the reaction of **1a** in DMF at −60 °C (Table 3).

Effect of Base. The effect of base is also striking. It

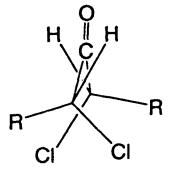
is clear from Table 2 that the replacement of triethylamine with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) caused a large rate acceleration but a marked reduction in the diastereoselectivity. It should be noted that whereas the enol silylation of *dl*-**1a** with DBU in benzene or ether was more (*E*)-selective (>82% d.e.) than that with triethylamine, the reaction of *meso*-**1a** with DBU also showed a significant (*E*)-selectivity (32% d.e. in ether) in contrast to the marked (*Z*)-selectivity (>94% d.e.) with triethylamine. A further dramatic change in the stereochemistry was observed with lithium diisopropylamide (LDA). Generation of lithium enolates of the ketones **1a** and **1b** by treatment with LDA in the presence of TMS-Cl at −78 °C resulted in the selective formation of (*E*)-**2** [>91% (*E*) for **1a** and 99% (*E*) for **1b**] irrespective of the configuration of the ketones. Obviously, the enol silylation with LDA was highly stereoselective but not diastereoselective at all. When the lithium enolate of **1a** was first prepared by addition of **1a** to a LDA solution in a 2:1 THF–hexamethylphosphoric triamide (HMPA) mixture at −78 °C and then quenched with TMS-Cl, moderate (*E*)-selectivities resulted, i. e., 74 and 80% (*E*) for *dl*-**1a** and *meso*-**1a** respectively, suggesting equilibration between the (*E*)- and (*Z*)-enolates under thermodynamic conditions.[10,11] It is worth stating that the enol silylation of **3** with LDA also showed a pronounced 77% (*E*)-selectivity.

Replacement of triethylamine with 1,4-diazabicyclo [2.2.2]octane (DABCO) and tributylamine did not cause significant change in the stereochemistry; however, the rate of the enol silylation markedly decreased with increasing steric bulk of the amines in the order DABCO>Et_3N≫*n*-Bu_3N>hexamethyldisilazane (HMDS)≫*i*-Bu_3N, as shown in Table 3. The enol silylation with the last two amines proceeded slowly as compared to the isomerization of the ketone. Triisobutylamine could not induce the enol silylation in benzene at all; even in DMF, *dl*-**1a** underwent only 0.6% enol silylation after 5 h at 25 °C, while the unchanged ketone reached a diastereomeric equilibrium within 1 h.

Mechanism. The predominant to exclusive formation of the lithium enolates of the (*E*)-configuration from **1** and **3** under kinetic controlled conditions suggests that these ketones take such a conformation about the groups at C_α that the chlorine is anti or anticlinal to the carbonyl group. This is reasonable since in α-chloro ketones, the chlorine prefers an antiperiplanar to anticlinal position in nonpolar solvents.[12–14] Table 4 shows favorable conformations for **1a** and **1b** calculated by MM2.[15] The calculation indicates that both the meso and racemic isomers of **1** take conformations in which the two chlorines are anticlinal to the carbonyl group, as illustrated by the structures **6** and **7**.



6 (*meso*)



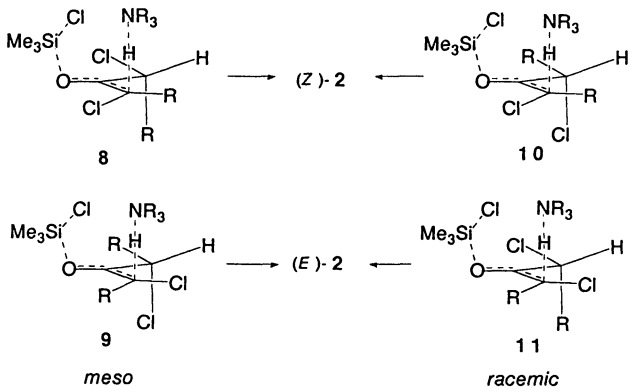
7 (*dl*)

The stereochemistry of the deprotonation of **1a** with LDA under thermodynamic conditions further suggests a pronounced thermodynamic stability of the (*E*)-enolate as compared to the (*Z*)-enolate. In view of these stereochemical observations, it can be said that the highly diastereoselective amine-promoted enol silylation of **1** does not proceed via the formation of a free enolate. This is compatible with the finding that triisobutylamine did not induce significantly the enol silylation despite the occurrence of the isomerization of the ketone which undoubtedly proceeds via an enolate intermediate.

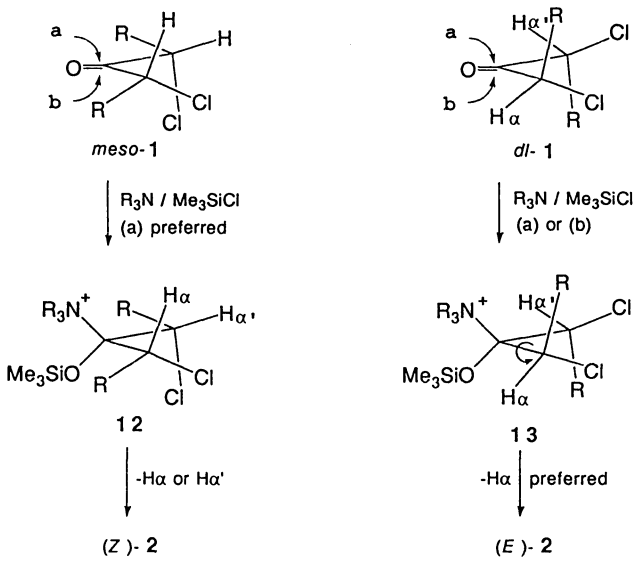
The precise origin for the diastereoselectivity is not clear at present but the following discussion is worth stating. One explanation is to assume the transition state in which the ketone interacts with the amine and TMS-Cl simultaneously. The electrophilic interaction of silicon with carbonyl group is well-known in hypervalent species.[16] Provided the amine approached a C_α-hydrogen, which is deprotonated, through the least hindered space made by the three groups at the C_α', we can draw four structures **8**—**11** as the transition states leading to (*E*)-**2** and (*Z*)-**2**, as shown in Scheme 2. On the steric ground, **8** is more favorable than **9**, whereas **11** is more favorable than **10** resulting in predominant (*E*)-selectivity from *dl*-**1** and (*Z*)-selectivity from *meso*-**1**.

Table 4. Stable Conformations for **1a** and **1b** Calculated by MM2

	Dihedral angles/degree			
	dl-**1a**	*meso*-**1a**	*dl*-**1b**	*meso*-**1b**
∠$ClC_\alpha C{=}O$	144.9	−106.6	128.4	−123.6
∠$HC_\alpha C{=}O$	30.0	136.6	15.7	122.4
∠$RC_\alpha C{=}O$	−88.6	15.7	−102.5	4.2
∠$O{=}CC_\alpha{'}Cl$	144.0	163.4	165.9	171.2
∠$O{=}CC_\alpha{'}H$	29.8	−82.5	53.9	−59.1
∠$O{=}CC_\alpha{'}R$	−89.4	35.9	−64.2	57.5



Scheme 2.



Scheme 3.

Table 5. Stereochemistry in Ketonization of **2**, **14**, and **15**

Reactant	Conditions[b]	% *dl*-**1**[a] from	
		(*E*)-**2**	(*Z*)-**2**
2a	Hexane, A	49	84
	C_6H_6, A	47	82
	Acetone, A	38	77
	THF, A	41	86
	THF, B	40	85
	THF, C	47	78
	THF, D	38	84
14	THF, D	36	80
15a	THF, E[c]	44	
2b	THF, D	38	86
15b	THF, E[c]	49	

a) The racemic and meso ketones (**1a** and **1b**) did not isomerize under the ketonization conditions presently employed. b) Ketonization was carried out at 25 °C using 0.3 mol dm^{-3} solutions of a given solvent containing 1% (vol) the following proton donors: A; methanol (15 h), B; water (15 h), C; acetic acid (15 h), and D; concd hydrochloric acid (4 h). c) E: Lithium enolate was quenched with concd hydrochloric acid at −78 °C.

However, the effects of solvent and base do not seem to be rationalized well by this scheme.

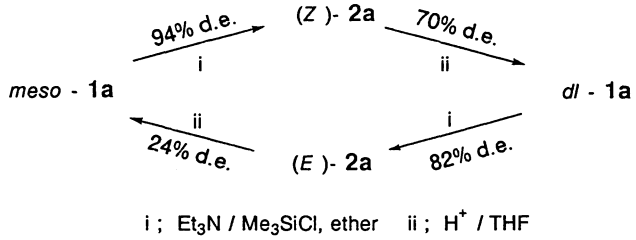
An alternative explanation involves an enol silylation via nucleophilic addition of the amine to the carbonyl group followed by an anti-β-elimination, as outlined by Scheme 3. The enolization of ketones via an addition-elimination mechanism has been demonstrated in the amine-promoted enolization of oxaloacetic acid.[17] If we assume the conformations **6** and **7** for *meso*-**1** and *dl*-**1** in weakly polar solvents like benzene, the stereoselectivity of the enol silylation would appear in the different steps for the two diastereoisomers. For *meso*-**1**, the stereoselectivity arises from the direction in which the amine adds to the carbonyl group via a path (a) or a path (b). The path (a) would be sterically more attainable than the path (b). A subsequent anti-β-elimination with a loss of a hydrogen either H_α or $H_{\alpha'}$, from the resultant adduct, probably a form of a silyl ether **12**, yields (**Z**)-**2**. On the other hand, the two addition pathways (a) and (b) are identical for *dl*-**1** and the stereochemistry of the enol silylation is controlled in the next elimination step; a loss of a hydrogen H_α from an adduct **13** gives (*E*)-**2**, while that of $H_{\alpha'}$, (*Z*)-**2**. The least motion favors the former elimination resulting in the predominant (*E*)-selectivity. The solvent effects and steric effect of the amines are compatible with this mechanism. Marked reduction in the stereoselectivity in polar solvents is ascribed to increasing contributions from conformers in which one or two α-chlorines are syn to synclinal to the carbonyl group.[12,13]

The effect of base strength, however, is puzzling. The stereochemistry of the DBU-promoted enol silylation of **1** is rather similar to that of lithium enolates than that of the Et_3N-promoted reaction, and a conventional deprotonation mechanism may be operative in part or dominantly.

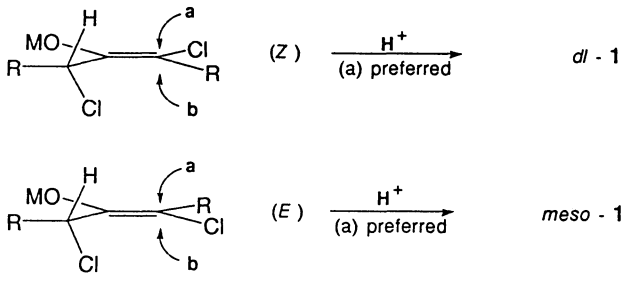
Diastereoselectivity in Ketonization. Interestingly, the ketonization of the enol silyl ethers **2** was also diastereoselective, as shown in Table 5. Noteworthy is the stereoselectivity opposite the forward enol silylation. Thus, (*E*)-**2a** preferentially gave *meso*-**1** (*meso*/*dl*=62/38), whereas (*Z*)-**2a** gave predominantly *dl*-**1a** (*meso*/*dl*=15/85) upon protonation with concd. hydrochloric acid in THF. The racemic and meso ketones were stable and did not undergo isomerization under the ketonization conditions listed in Table 5.

The combined stereochemical results of the Et_3N-promoted enol silylation of **1** and the ketonization of **2** shows a stereochemical cycle shown in Scheme **4** which provides an example formally against the microscopic reversibility.

The diastereoselectivity of the ketonization of **2** undoubtedly arises from the face-differentiation of the protonation to the double bond, whatever a real mechanism for the protonation of the enol silyl ethers would be.[18] It is instructive to note the observation that the stereoselectivity was little affected by the change in the allylic alkyl groups (**2a** vs. **2b**) and in the O-substituted groups including Me_3Si (**2a**), *t*-$BuMe_2Si$ (**14**), and Li (**15**). This observation suggests that the face-differentiation is caused mainly by the hydrogen and



Scheme 4.



2; M=Me_3Si, 14; M=t-$BuMe_2Si$, 15; M=Li

Scheme 5.

chlorine groups of the allylic carbon. Thus, it is reasonable to assume the transition states in which the allylic alkyl group, the largest group of the three allylic substituents, is located anti to the double bond, as shown in Scheme 5. The protonation would preferentially occur at the less hindered face of the double bond, i.e., the same side of the allylic hydrogen, in the product-forming step.

Experimental

IR spectra were recorded on a Hitachi R-215 spectrophotometer. NMR were recorded on a Hitachi R-20B spectrometer in carbon tetrachloride. GLC analysis was performed with a Yanagimoto G-8 and a Hitachi 163 gas chromatographs equipped with a glass column (6 mm×1.1 m) packed with 25% Apiezon grease L on Chamelite CK (Column A) and a glass column (6 mm×2 m) packed with 25% Apiezon grease L on Chamelite CK for the first half of the column and 15% Carbowax 20M on Chromosorb W for the rest half (Column B).

Preparation of (*E*)- and (*Z*)-trimethylsilyl enol ethers (**2a**) of 2,4-dichloro-3-pentanone (**1a**) was described previously;[4] a pure sample for each isomer was obtained by GLC. (*E*)-**2a**: NMR δ=0.29 (9H, s), 1.53 (3H, d, *J*=6.5 Hz), 2.01 (3H, s), 5.30 (1H, q, *J*=6.5 Hz). (*Z*)-**2a**: NMR δ=0.29 (9H, s), 1.57 (3H, d, *J*=6.5 Hz), 2.14 (3H, s), 4.87 (1H, q, *J*=6.5 Hz). The stereochemistry of the enol silyl ether **2a** was confirmed by an almost stereospecific conversion to 2-chloro-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one, a *trans*-isomer from (*E*)-**2a** and *cis*-isomer from (*Z*)-**2a**, accomplished by treatment with silver perchlorate in nitromethane in the presence of furan.[4]

Racemic and Meso 2,4-Dichloro-3-pentanone (*dl*-1a and *meso*-1a)[9] Into a stirred solution of 3-pentanone (60 g) in carbon tetrachloride (100 cm^3) was added sulfuryl chloride (205 g) at room temperature over a period of 2 h and the mixture was stirred for 3 h at ambient temperature. Usual workup followed by distillation under reduced pressure (15 Torr; 1 Torr=133.3 Pa) gave four fractions: I (10 g) bp 30—36 °C, II (15 g) bp 36—45 °C, III (31 g) bp 45—53 °C, and IV (10 g) bp 53—56 °C. The fractions I and II contained mainly α-chloro- and α,α'-dichloroketones; the fractions III and IV contained mainly 2,4-dichloro-3-pentanone. The fractions III and IV were fractionated through a 30 cm spinning band column to give 3.08 g of *dl*-**1a** (isomeric purity 98.5%), bp 40—40.5 °C (15 Torr) [lit,[9] bp 42.5 °C (15 Torr)] and 4.93 g of *meso*-**1a** (isomeric purity 99.2%), bp 57—58 °C (15 Torr) [lit,[9] bp 57.5—58 °C (15 Torr)]. The former ketone contained 0.2% 2,2-dichloro-3-pentanone, while the latter ketone contained 1.1% 2,2,4-trichloro-3-pentanone. GLC retention times (t_R) for *dl*-**1a** and *meso*-**1a** were 4.8 and 6.2 min respectively on Column A (110 °C).

Racemic and Meso 3,5-Dichloro-2,6-dimethyl-4-heptanone (*dl*-1b and *meso*-1b). In a similar procedure described above was chlorinated 2,6-dimethyl-4-heptanone (63 g) with sulfuryl chloride (30.0 g) and a crude oil obtained after usual workup was distilled to give four fractions: I (5.8 g) bp 65—70 °C (5 Torr), II (11.1 g) bp 70—74 °C (5 Torr), III (19.1 g) bp 74—90 °C (5 Torr), and IV (1.9 g) bp 90—95 °C (5 Torr). The fraction III, which was shown to be a mixture of mono-, α,α-di-, α,α'-di-, tri-, and tetra-chloro derivatives in the ratio 14:13:61:7:3, was fractionated through a 30 cm spinning band column to give eight fractions. A fraction (1.9 g) boiling at 51—52 °C (5 Torr) was an 82.4:17.6 mixture of *dl*-**1b** and *meso*-**1b** (Column A, 150 °C, t_R; 15.0 and 18.0 min, respectively) containing 1.5% α,α'-dichloro-isomer. A fraction (5.8 g) boiling at 57—58 °C (5 Torr) was a 7.4:92.6 mixture of the *dl*- and *meso*-isomers. A pure sample for each isomer was obtained by GLC. *dl*-**1b**: NMR δ=1.02 (6H, d, *J*=6.2Hz), 1.12 (6H, d, *J*=6.2 Hz), 2.0—2.8 (2H, m), 4.31 (2H, d, *J*=7.8 Hz). Found: C, 51.42; H, 7.75%. Calcd for $C_9H_{16}Cl_2O$: C, 51.20; H, 7.64%. *meso*-**1b**: NMR δ=1.06 (6H, d, *J*=6.2 Hz), 1.07 (6H, d, *J*=6.2 Hz), 2.36 (2H, m), 4.32 (2H, d, *J*=7.8 Hz). Found: C, 51.11; H, 7.60%. Calcd for $C_9H_{16}Cl_2O$: C, 51.20; H, 7.64%.

3,5-Dichloro-2,6-dimethyl-4-trimethylsiloxy-3-heptene (2b). A mixture of the ketone **1b** (2.16 g, *dl*/*meso*=26/74), chlorotrimethylsilane (3.2 g), and triethylamine (4.4 g) in DMF (18 cm^3) was heated at 60 °C for five days. Usual workup gave 1.94 g (67%) of the corresponding enol trimethylsilyl ether **2b** as a 1:1 mixture of (*E*)- and (*Z*)-stereoisomers (Column A/150 °C, t_R=24.4 and 28.4 min respectively); bp 61—63 °C (0.3 Torr); IR 1640, 1255, 845 cm^{-1}. A pure sample for each isomer was obtained by preparative GLC. (*E*)-**2b**: NMR δ=0.27 (9H, s), 0.83—1.16 (12H, complex), 1.5—2.5 (1H, m), 2.7—3.5 (1H, m), 4.76 (1H, d, *J*=9.6 Hz). (*Z*)-**2b**: 0.27 (9H, s), 0.83—1.18 (12H, complex), 1.5—2.5 (1H, m), 2.95 (1H, m), 4.32 (1H, d, *J*=9 Hz).

3-(*t*-Butyldimethylsiloxy)-2,4-dichloro-2-pentene (14). A mixture of **1a** (3.32 g, *dl*/*meso*=6/4), triethylamine (6 cm^3), and *t*-butyldimethylchlorosilane (3.23 g) in acetonitrile (10 cm^3) was heated at 70 °C for 4 h. Usual workup gave 2.98 g of **14** as a 2:1 (*E*) and (*Z*) stereoisomeric mixture, bp 74—77 °C (2 Torr). Pure sample for each isomer was obtained by GLC. (*E*)-**14**: IR 1645 cm^{-1}; NMR δ=0.18 (3H, s), 0.31 (3H, s), 1.00 (9H, s), 1.52 (3H, d, *J*=7.1 Hz), 2.03 (3H, s), 5.32 (1H, q, *J*=7.1 Hz). (*Z*)-**14**: IR 1650 cm^{-1}; NMR δ=0.26 (6H, s), 1.00 (9H, s), 1.58 (d, *J*=7.1 Hz), 2.15 (3H, s), 4.89 (1H, q, *J*=7.1 Hz).

Enol Silylation of 1. The amine-promoted enol silylation was carried out by taking the ketone **1**, 2.2 equiv an amine, and 2.0 equiv chlorotrimethylsilane in a given solvent at ca. 0.25 mol dm^{-3} concentration of the ketone at 25 °C for most cases. Ratios, **1**/**2**, *meso*-**1**/*dl*-**1**, and (*E*)-**2**/(*Z*)-**2**, were determined directly by GLC analysis (Column B, 130 °C) of the reaction mixture at appropriate time intervals.

Ketonization of 2. The ketonization of **2** was carried out using a 0.3 mol dm^{-3} solution in a given solvent containing 1% (vol) proton donor-including acetic acid, methanol, water, and concd hydrochloric acid. The *dl*-**1**/*meso*-**1** ratio was deter-

mined directly by GLC analysis (Column B, 130 °C) at appropriate time intervals.

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