of a mixture containing 25%[19] of A produced by photolysis of **1** in *benzene* at room temperature showed two sharp resonances at δ 0.23 and 0.30 with relative intensities of 3:2, in addition to two peaks at δ 0.19 and 0.31 assignable, respectively, to Me_3Si and Me_2Si protons of **1.**

The silacyclopropene A in solution seems to be relatively stable at room temperature. When a reaction mixture containing 44%[19] of A and 22% of unchanged **1** was allowed to stand for 8 h at room temperature, only 6.6% of A was decomposed to give mainly a nonvolatile product. We are continuing this investigation to stabilize intermediate A.

Acknowledgment. The cost of this research was defrayed in part by a Grant-in-Aid for Scientific Research by the Ministry of Education and Toray Science and Technology Grants to which the author's thanks are due. They also express their appreciation to Toshiba Silicon Co., Ltd., and Shin-etsu Chemical Co., Ltd., for a gift of organochlorosilanes.

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(8) Protodesilylation of **2** by dry hydrogen chloride in dry ethyl ether gave 2,2,5,5-tetramethyl-4-phenyl-1-oxa-2-silacyclo-3-pentene and 2-methyl-3-phenyl-1,3-butadiene in 31 and 33% yield, respectively, indicating that the two silyl groups are attached to the same carbon atom.
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(10) Photolysis of **1** in the presence of diethylmethylsilane gave 1,1-diethyl-1,2,2-trimethyldisilane and **4** in 4 and 12% yield, respectively.
(11) One of the referees has raised a question as to the absence of a silyl enol ether which might be expected to form from H–O addition of the enol form of acetone across the silicon–carbon double bond, as observed by Sommer and his co-workers.[12] We have established that, unlike the thermally generated Si=C intermediates,[12] photochemical ones from either vinyldisilanes[6] and aryldisilanes[20] in the presence of an enolizable ketone such as acetone, cyclohexanone, and acetophenone never afford silyl enol ethers.
(12) C. M. Golino, R. D. Bush, D. N. Roark, and L. H. Sommer, *J. Organomet. Chem.*, **66,** 29 (1974).
(13) Yields reported here are based on unrecovered **1,** with its conversion being always approximately 70–80%.
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(15) Compound **8:** NMR (CCl_4) δ −0.05 (CH_3–SiMe, s, 6 H), 0.17 (CH_3–$SiMe_2$, s, 9 H), 3.30 (CH_3–O, s, 3 H), 7.18 (ring protons, broad s, 5 H), 7.65 (vinylic proton, s, 1 H).
(16) Compound **9:** NMR (CCl_4) δ 0.16 (CH_3–Si, s, 15 H), 3.14 (CH_3–O, s, 3 H). 6.44 (vinylic proton, s, 1 H), 6.8–7.3 (ring protons, m, 5 H).
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(19) The amount of the 1-silacyclopropene is taken to be equal to the sum of yields of methoxysilanes **6** and **7** formed by methanolysis of the photoproduct.
(20) M. Ishikawa, T. Fuchikami, and M. Kumada, manuscript in preparation.

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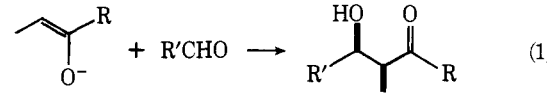
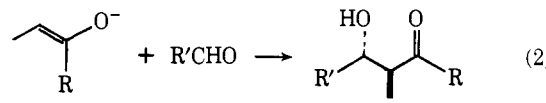
Stereoselection in the Aldol Condensation

Sir:

Dubois and co-workers have shown that the aldol condensation is subject to kinetic stereoselection, with (*Z*)-enolates giving predominantly the *erythro* aldol (eq 1), and (*E*)-enolates leading preferentially to the *threo* isomer (eq 2).[1] House and co-workers found that the use of preformed lithium enolates in the presence of chelating divalent cations such as Zn^{2+} and Mg^{2+} leads to product mixtures rich in the more stable *threo* aldol, regardless of enolate geometry.[2] We have examined the use of preformed lithium enolates and find that, under the proper conditions, *complete kinetic stereoselection* may be achieved.



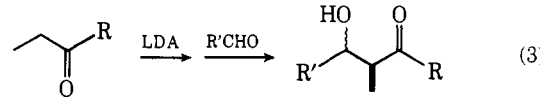
(1)



(2)

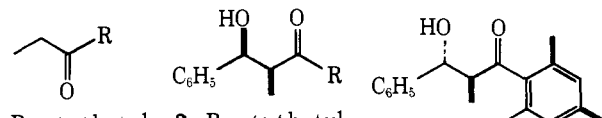
Reactions are carried out by preforming the enolate at −72 °C in THF or ether by addition of the ketone to a 1 M solution of lithium diisopropylamide (LDA).[3] After 15 min, the aldehyde is added in one portion to the rapidly stirring enolate solution. The reaction mixture is quenched by the addition of saturated aqueous NH_4Cl 5 s after addition of the aldehyde. After separation of the layers, the aqueous layer is extracted with ether and the combined organic layers are dried (anhydrous $MgSO_4$) and evaporated to afford the aldol in good yield. Further purification is achieved by distillation and/or recrystallization of the crude product. Diastereomer ratios were determined from the carbinol resonances in the ^1H NMR spectra of the crude aldol product, using the well-established fact that $J_{threo} > J_{erythro}$.[2] In cases where both diastereomeric aldols are not produced in the condensation, the kinetic aldol was equilibrated so that both stereoisomers were in hand.

Our results may be summarized as follows: In aldol condensations of the type typified by eq 1 and 2, complete kinetic stereoselection is observed, with the (*Z*)-enolate giving the *erythro* aldol and the (*E*)-enolate giving the *threo* aldol when R is bulky (*tert*-butyl, 1-adamantyl, mesityl, trimethylsilyl). When R is smaller (ethyl, isopropyl, phenyl, methoxy, *tert*-butoxy, diisopropylamino), stereoselectivity diminishes or disappears.



(3)

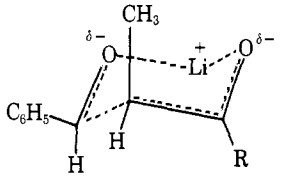
An example is provided by the condensation of ethyl *tert*-butyl ketone (**1,** 100% (*Z*)-enolate) with benzaldehyde to yield *erythro* aldol **2.** The crude aldol product in this reaction, obtained in quantitative yield, shows no measurable amount of *threo* aldol. Pure aldol **2** (mp 55–56 °C) is obtained in 78% yield after distillation (bp 105°/0.3 Torr) and trituration with a small amount of hexane. On the other hand, ethyl mesityl ketone (**3,** 92% (*E*)-enolate, 8% (*Z*)-enolate) reacts with benzaldehyde to afford 92% of *threo* aldol **4** and 8% of *erythro* aldol **5.** Pure **4** (mp 97–99 °C) is obtained in 52% yield after two recrystallizations from hexane. To gain further support for the supposition that (*Z*)-enolates give *erythro* aldols and (*E*)-enolates give *threo* aldols, we have prepared mixtures of (*E*)- and (*Z*)-enolates of varying composition from ketone **3**[5] and allowed these mixtures to react with benzaldehyde. In each case, the *erythro*/*threo* ratio is identical within experimental error to the (*Z*)/(*E*) ratio.



1, R = *tert*-butyl **2,** R = *tert*-butyl
3, R = mesityl **5,** R = mesityl
4

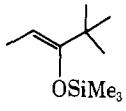
Our results are explicable in terms of a six-center transition state, depicted in structure I for a (*Z*)-enolate, in which the

metal cation is chelated by the two oxygens of the reacting array. Kinetic stereoselectivity is maintained even when the condensation is carried out in the presence of large amounts of the highly ionizing solvent HMPT.[7]

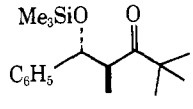


I

The tetraalkylammonium enolate[8] derived from ketone **1** gives equally high but *opposite* kinetic stereoselectivity in its reaction with benzaldehyde. Thus, when an equimolar mixture of enol ether **6** and benzaldehyde is treated with a catalytic quantity (3–6 mol %) of benzyltrimethylammonium fluoride in THF at 25 °C for 2 h, the sole reaction product (52% isolated yield) is the silylated aldol **7**.[9]

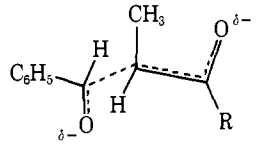


6



7

In the case of the tetraalkylammonium enolate, in which the cation cannot accept the two partially negative oxygens as ligands, we believe that a transition state such as that depicted in structure II is involved. In this case, to minimize electrostatic repulsion, the oxygens must be directed in generally opposite directions. Consequently, the enolate now attacks the other face of the carbonyl group.



II

Thus, by using a diastereomerically pure lithium enolate derived from a ketone in which one alkyl group is sterically demanding, one may achieve total diastereoselection in the aldol condensation. From a practical standpoint, *erythro* stereoselection is easily achieved with ketones in which one alkyl group is tertiary, such as ethyl *tert*-butyl ketone (**1**) or ethyl 1-adamantyl ketone, since these ketones yield only the (*Z*)-enolate on deprotonation with LDA at −72 °C. In some cases, *threo* stereoselection may be achieved by using tetraalkylammonium enolates derived from these same ketones.[9] *Threo* stereoselection may also be realized by using the lithium (*E*)-enolate. The only acyclic ketone we have studied which meets the two criteria of having a sterically demanding group bound to the carbonyl *and* an easily accessible (*E*)-enolate is ethyl mesityl ketone, which gives a kinetic enolate mixture containing 92% (*E*)-enolate.[10] We are currently exploring ways to extend this discovery to an equivalent of the Reformatsky reaction by creating a ketone such as **1** or **3** in which R is easily convertible to OH.[11]

Acknowledgments. Support for this work was provided by the National Science Foundation (Grant No. GP-31321X), and the United States Public Health Service (Grant No. AI-11607).

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(3) Enolate composition is determined in an independent experiment by silylation with trimethylsilyl chloride.[4]
(4) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).
(5) Enolate diastereomer composition was varied by deprotonating with LDA in the presence of varying amounts of HMPT.[6]
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(7) The similarity of the hypothetical transition state depicted in structure I to that believed to intervene in pericyclic reactions such as the Diels–Alder reaction, ene reaction, and Cope rearrangement is striking. In fact, it is tempting to attribute the remarkable facility of the lithium enolate reaction to the stability of such an "aromatic" transition state.
(8) I. Kuwajima and E. Nakamura, *J. Am. Chem. Soc.*, **97**, 3257 (1975).
(9) Compound **7** is a true kinetic product. If the reaction is allowed to proceed for 15 *h*, the product isolated is a 2:3 mixture of **7** and its *erythro* counterpart. Unfortunately, this reaction appears to be of limited generality. In several systems we have examined, the product β-trimethylsilyloxy ketone appears to undergo elimination at a rate comparable to its rate of formation, resulting in the formation of the α,β-unsaturated ketone.
(10) Reaction of this enolate mixture with trimethylsilyl chloride affords a silyl enol ether mixture which may be fractionated through a spinning-band column to yield >98% pure (*E*)-silyl enol ether. Although we have not yet done the experiment, in principle this ether can be converted back to an enolate mixture of comparable purity.
(11) Attempts to perform Baeyer–Villiger oxidations and Beckmann rearrangements on aldols such as **2** and **4** have been unsuccessful.

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β-Lactam Antibiotics. Novel Synthetic Routes to Cephem-Ring System from β-Lactam Thiazolines via Hydrazinothioazetidinones

Sir:

Acid-catalyzed oxidative ring opening of **1c**[1-3] (X = H) with dimethyl azodicarboxylate (2–3 mol excess) and toluene-*p*-sulfonic acid (1 equiv) in 2% aqueous acetone (20 °C, 4–6 h) afforded **2c** (X = H), 80%: mp 133–135 °C.[4,5] Similarly hydrazinothioazetidinones, **2a, b, d** (X = H), were obtained from **1a, b, d** (X = H).[6] We suggest that this transformation proceeds through a transition state **4**, which undergoes hydrolytic cleavage to **2a–d.** An outstanding property of compounds **2a–d** (X = H)[7] is their tendency to be cleanly converted to deacetoxycephalosporins **3a–d** (80–85% yield) (X = H) by stirring the benzene solution with 30% aqueous KOH or with aluminum oxide at room temperature. This cyclization can be explained by an initial abstraction of the α proton and concomitant attack of the activated double bond on the sulfur atom, resulting in the formation of the C–S bond and of the six-membered ring system, as outlined in **2.** Alternatively, **2a–d** (X = H) were cyclized by treatment with *tert*-butyl hypochlorite (THF, −78 °C) to the corresponding 3-chlorocepham[8] (presumably via an intermediate sulfenyl chloride) which gave, by further dehydrohalogenation, the 3-cephem derivatives **3a–d** (X = H).

Compounds of formula **2a, b** (X = OAc) were obtained with a five-step procedure starting from thiazolines **1a, b** (X = H). Treatment of **1a–d** (X = H) with NBS and aluminum oxide (benzene, 20 °C, 20 h) yielded, almost quantitatively, the monobromides **5** and **6** in 70:30 ratio.[9] Alternatively bromine was quantitatively added to the isopropenyl double bond of **1c** (CH_2Cl_2, 30 min, 20 °C), in the presence of CaO, to give dibromide **28** (as a 1:1 mixture of two diastereoisomers) which was transformed into monobromides **5** and **6** by treatment with triethylamine or simply by passing through a silica gel bed. Monobromides **5** and **6** and dibromide **28** were quantitatively converted to monoacetates **7** and **8** by nucleophilic displacement with potassium acetate (acetone, 40 °C), the resulting mixture of *E*–*Z* isomers being separated either by column