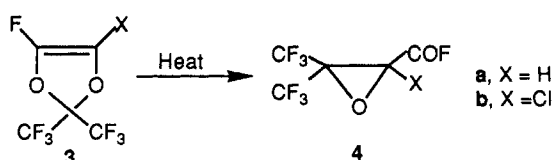


Table I. Yield and ^{19}F Nuclear Magnetic Resonance Data of Epoxy Acid Fluorides^a

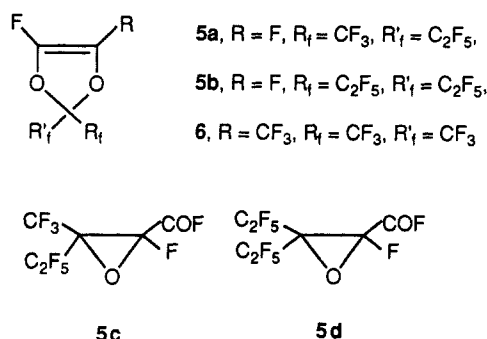
compd	yield, ^b %	bp, °C	^{19}F NMR ^c
2	86	35	-68.9 (3 F), -71.1 (3 F), -148.6 (1 F), +28.7 (1 F)
2a	72	91	-68.6 (3 F), -71.3 (3 F), -145.8 (1 F); 3.80 ^d
4a	72	73	-69.8 (3 F), -74.5 (3 F), +37.8 (1 F); 4.18 ^d
4b	88	63	-67.6 (3 F), -71.2 (3 F), +25.0 (1 F)
5c	90	45	-68.0 (3 F), -83.8 (3 F), -118.9 (2 F), -149.7 (1 F), +27.2 (1 F) (major isomer); -70.3 (3 F), -84.0 (3 F), -117.0 (2 F), 147.5 (1 F), +27.8 (1 F) (minor isomer)
5d	90	55	-114.0 (4 F), -82.0 (6 F), -145.7 (1 F), +25.8 (1 F)
12	100	45	-66.7 (3 F), -68.0 (3 F), -71.3 (3 F), +37.7 (1 F)

^a All new compounds have been fully characterized by spectral means and elemental compositions determined by combustion analysis or high-resolution mass spectrometry. ^b Isolated yields. ^c Neat, CFCl_3 as reference. ^d ^1H NMR, tetramethylsilane as reference.

Thermal rearrangement of dioxoles **3a** and **3b**⁵ resulted in the formation of acyl fluorides **4a** and **4b**, respectively, as the sole products. No aldehyde or acid chloride was detected.

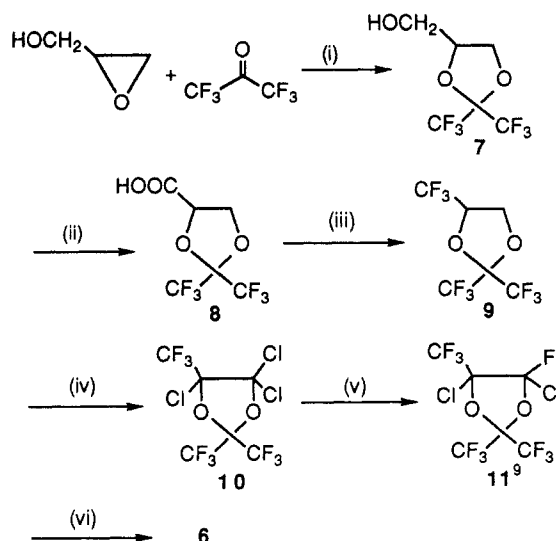


The rate of rearrangement increased as the size of the substituents at the 2-position of the 1,3-dioxole ring increased. Rearrangement of **1**, **5a**, and **5b**⁶ at 100 °C were followed chromatographically.⁷ After 0.5 h, dioxole **1** was unchanged, while 11–12 mol % of **5a** and 28–29 mol % of **5b** had rearranged to the corresponding epoxides, **5c**, two isomers in a ratio of 3.2:1.0, and **5d**, respectively. The difference in rate may be due to increased steric congestion in the series of **1**, **5a**, and **5b** as the electronic effects of trifluoromethyl and pentafluoroethyl groups are quite similar.⁸



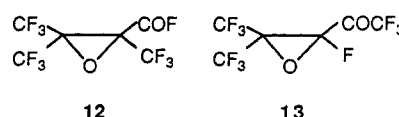
Dioxole **6** was synthesized in six steps from hexafluoroacetone as shown in Scheme I. Heating **6** at 200 °C for 15 min followed by heating at 240 °C for 30 min resulted in almost quantitative conversion to the acid fluoride **12**, characterized by its ^{19}F NMR spectrum, (Table I). None of the isomeric ketone, **13**, was observed.

One plausible mechanism for this rearrangement involves the formation of a biradical intermediate followed by ring closure to

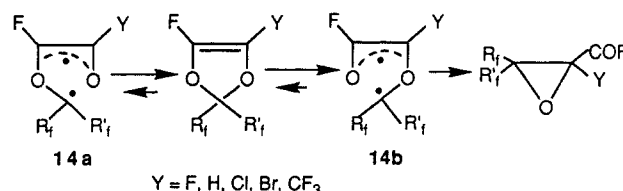
Scheme I^a

^a Reagents and conditions: (i) $n\text{-Bu}_4\text{NBr}$, 0.15%, H_2O , 0.15%, 125 °C, 5 h, 93%; (ii) $\text{KMnO}_4/\text{Na}_2\text{CO}_3/\text{water}$, 25 °C, 16 h, 82%; (iii) SF_4/HF , 85 °C, 6 h, 58%; (iv) Cl_2 , neat, 120 °C, 87%; (v) $\text{SbF}_3/\text{SbCl}_3$, neat, 100–110 °C, 8 h, 70%; (vi) $\text{LiAlH}_4/\text{TiCl}_4/\text{THF}$, 25–35 °C, 1–2 h, 88%.

give the epoxide product. The increased stability of **14b** over **14a** is apparently large enough to result in the high regioselective



formation of acyl fluorides. An analogous rearrangement of 2,2-bis(trifluoromethyl)-1,3-dioxole was not observed.



In a typical experiment, a 1-ft glass tube with a 1-in. diameter was filled with glass beads and heated to 280 °C, and dioxole **1** (17.4 g, 71 mmol) was added at a rate of 0.48 mL/min. The effluent was trapped at -78 °C and distilled to give epoxide **2** (15.0 g, 86% yield) as a clear, colorless liquid, boiling at 35 °C.

In conclusion, we have discovered an unusual thermal rearrangement reaction that involves the conversion of a fluorinated dioxole to an epoxy acid fluoride. These epoxy-containing acyl compounds are highly useful in further synthetic applications.

A Silicon-Directed Aldol Condensation. Synthesis of Enantiomerically Pure Anti Aldols

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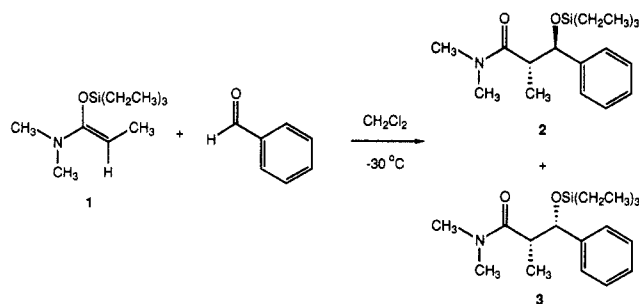
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A new type of aldol addition reaction involving the direct condensation of *O*-silyl ketene *N,O*-acetals with aldehydes is re-

(5) Squire, E. N. U.S. Pat. 4,431,786, 1984.
(6) Hung, M.-H. U.S. Pat. 4,908,461, 1990.
(7) Six feet $\times$ 1/4 in. 20% OV-210 on Chromosorb P (AW-DMCS) at 100 °C.
(8) Smart, B. E. *The Chemistry of Functional Groups, Supplement D*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: New York, 1983; Chapter 14.
(9) Compound **11** was obtained as an isomeric mixture with the mole ratio *Z/E* = 7:1. This isomeric mixture was used directly for next step synthesis. For compound (*Z*)-**11**: ^{19}F NMR (neat, CFCl_3) -54.3 (m, 1 F). For (*E*)-**11**: -40.7 (m, 1 F).

ported.¹ The reaction proceeds without apparent catalysis and is believed to occur through a pericyclic transition state containing hypervalent silicon. This silicon-directed aldol condensation is exploited in a highly stereoselective synthesis of enantiomerically pure anti aldols.²

O-Silyl enol derivatives of aldehydes, ketones, and esters (*O*-silyl ketene acetals) form aldol addition products with aldehydes in the presence of a coreactant such as fluoride ion³ or a Lewis acid.^{4,5} Open or extended transition states are frequently invoked in mechanistic proposals for these reactions.^{3a,c,4d} We have discovered that *O*-silyl enol derivatives of amides (*O*-silyl ketene *N,O*-acetals)⁶ undergo facile noncatalyzed aldol addition with aldehydes at or below ambient temperature. For example, equimolar quantities of benzaldehyde and (*Z*)-*N,N*-dimethylpropionamide *O*-triethylsilyl ketene *N,O*-acetal (**1**; 1.1 M)⁷ react smoothly in di-



chloromethane at $-30\text{ }^{\circ}\text{C}$ within 4 h to form a 1.8:1 mixture of anti and syn aldol products **2** and **3**, respectively, in 80% combined yield. This transformation is likely mechanistically distinct from known aldol processes; a reasonable proposal involves a pericyclic transition state with transfer of silicon from enol to aldehyde oxygens and concerted or near-concerted carbon-carbon bond formation. This mechanism implies that the reaction is directed by silicon, presenting new possibilities for stereocontrol in the aldol addition reaction, as illustrated below.

(1) Aldol condensation, general references: (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top Stereochem.* **1982**, *13*, 1. (b) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, Chapter 2.

(2) Other anti-selective aldol condensations forming optically active products: (a) Meyers, A. I.; Yamamoto, Y. *Tetrahedron* **1984**, *40*, 2309. (b) Helmchen, G.; Leikauf, U.; Tauber-Knöpfer, I. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 874. (c) Gennari, C.; Bernardi, A.; Colombo, L.; Scolastico, C. *J. Am. Chem. Soc.* **1985**, *107*, 5812. (d) Palazzi, C.; Colombo, L.; Gennari, C. *Tetrahedron Lett.* **1986**, *27*, 1735. (e) Oppolzer, W.; Marco-Contelles, J. *Helv. Chim. Acta* **1986**, *69*, 1699. (f) Masamune, S.; Sato, T.; Kim, B. M.; Wollman, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 8279. (g) Danda, H.; Hansen, M. M.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 173. (h) Corey, E. J.; Kim, S. S. *Tetrahedron Lett.* **1990**, *31*, 3715. (i) Corey, E. J.; Kim, S. S. *J. Am. Chem. Soc.* **1990**, *112*, 4976.

(3) (a) Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247. (b) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1977**, *99*, 1265. (c) Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 932. (d) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181.

(4) (a) Mukaiyama, T.; Banno, K.; Narasaka, K. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (b) Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1975**, 989. (c) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029. (d) Heathcock, C. H.; Davidsen, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027. (e) Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1986**, *27*, 5517. (f) Reetz, M. T.; Vougioukas, A. E. *Tetrahedron Lett.* **1987**, *28*, 793.

(5) The direct condensation of aromatic aldehydes and *O*-silyl ketene acetals at $150\text{ }^{\circ}\text{C}$ has been reported: (a) Creger, P. L. *Tetrahedron Lett.* **1972**, 79. *O*-Silyl ketene acetals also undergo Michael addition with enones in acetonitrile: (b) Kita, Y.; Segawa, J.; Haruta, J.; Fujii, T.; Tamura, Y. *Tetrahedron Lett.* **1980**, *21*, 3779.

(6) (a) Hudrlik, P. F.; Peterson, D.; Chou, D. *Synth. Commun.* **1975**, *5*, 359. (b) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 881, and references therein.

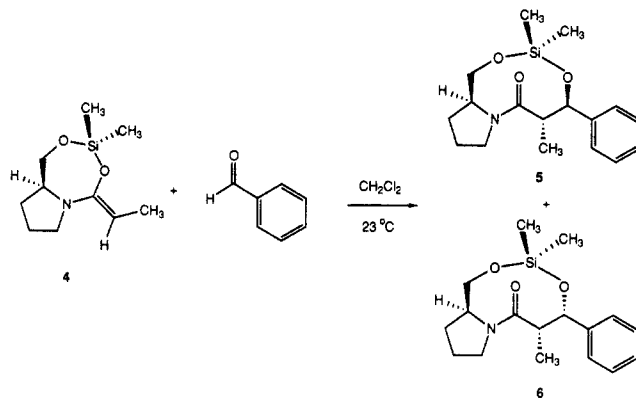
(7) Hydrosilylation is found to be a convenient method for large-scale preparation of these derivatives. Reaction of equimolar quantities of *N,N*-dimethylacrylamide and triethylsilane, neat, at $50\text{ }^{\circ}\text{C}$ for 8 h using Wilkinson's catalyst (0.1 mol %) affords **1** as a single stereoisomer (bp $70\text{--}77\text{ }^{\circ}\text{C}$ (12 mmHg), 60% yield, 8-g scale). Hydrosilylation of α,β -unsaturated ketones and aldehydes: Ojima, I.; Kogure, T. *Organometallics* **1982**, *1*, 1390.

Table I. Diastereoselective Addition Reactions of **4** with Aldehydes

RCHO	diastereoselectivity, ^a %			(2- <i>S</i>)- <i>anti</i>	
	(2- <i>S</i>)- <i>anti</i>	(2- <i>S</i>)- <i>syn</i>	(2- <i>R</i>)- <i>anti</i> , ^b <i>syn</i> ^b	yield, ^c %	mp, $^{\circ}\text{C}$
C_6H_5	97.2	2.5	0.3	77	139–142
<i>i</i> -Pr ^d	99.6	0.2	0.2	72	99–100
Et ^e	97.4	1.3	1.3	58	46–47

^a Based on capillary GC and high-field NMR analysis of crude reaction mixtures. Numbers for (2-*S*)-*anti* diastereomers are minimum values. ^b Maximum combined yield of 2-*R* diastereomers as estimated by capillary GC. ^c Isolated yield of pure (2-*S*)-*anti* diastereomer. ^d Reaction conducted in CH_2Cl_2 at $23\text{ }^{\circ}\text{C}$ for 26 h. ^e Reaction conducted in CH_2Cl_2 at $0\text{ }^{\circ}\text{C}$ for 16 h.

Metallation of (*S*)-prolinol propionamide (9.21 g, 58.6 mmol)^{8,9} with lithium diisopropylamide (2.30 equiv) in tetrahydrofuran (250 mL) at $-78\text{ }^{\circ}\text{C}$ for 1 h, sequential addition of tetrahydrofuran (500 mL, at $0\text{ }^{\circ}\text{C}$) and dichlorodimethylsilane (9.00 mL, 74.2 mmol, 1.27 equiv, added at $23\text{ }^{\circ}\text{C}$ over 10 min, distilled from magnesium), removal of volatiles in vacuo, and distillation of the residue affords the bicyclic dimethylsiloxane **4** as a colorless, nonviscous liquid (bp $72\text{--}83\text{ }^{\circ}\text{C}$ (0.2 mmHg), 9.70 g, 78%). Siloxane **4** is moisture-sensitive but can be stored for extended periods under an inert atmosphere without decomposition and is shown to be a single stereoisomer by ^1H and ^{13}C NMR spectroscopy. The olefin geometry is assigned as *Z* based on literature precedent⁸ and the observation of nuclear Overhauser enhancement of the vinyl proton upon irradiation at an NCH_2 resonance frequency. Siloxane **4** undergoes efficient and highly diastereoselective condensation with aldehydes at ambient temperature to form silicon-bridged nine-membered ring anti aldol products (Table I).¹⁰ Its reaction with benzaldehyde is illustrative: siloxane **4** (0.503 g, 2.36 mmol) and benzaldehyde (0.247 mL, 2.43 mmol,



1.03 equiv) are combined at $23\text{ }^{\circ}\text{C}$, using hexanes for quantitative material transfer (0.1 mL). After stirring for 10 h at $23\text{ }^{\circ}\text{C}$, the crystalline product is suspended in fresh hexanes (2 mL) and the mixture is cooled to $-20\text{ }^{\circ}\text{C}$ to complete precipitation of the product. The colorless crystals are collected by filtration and washed with two 1-mL portions of cold hexanes ($-20\text{ }^{\circ}\text{C}$) to afford pure anti aldol **5** (mp $139\text{--}142\text{ }^{\circ}\text{C}$, 0.752 g, 77%). The diastereomeric purity of **5** is ascertained by ^1H NMR and ^{13}C NMR spectroscopy and capillary GC analysis.¹¹ The anti stereochemical assignment is suggested by the observation of a 9.7-Hz coupling between protons on the adjacent stereogenic centers and is con-

(8) Synthesis, metallation, and alkylation of (*S*)-prolinol propionamide: Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233. See also ref 9.

(9) Alkylations of bicyclic boron enolates derived from (*S*)-prolinol propionamide dianion have been studied: Takacs, J. M. Ph.D. Thesis, California Institute of Technology, 1981.

(10) Conditions for the hydrolysis of prolinol amide derived aldol products have been developed: Evans, D. A.; McGee, L. R. *J. Am. Chem. Soc.* **1981**, *103*, 2876. The silicon-bridged products described herein may provide new opportunities for elaboration of prolinol amide derived aldol products.

(11) Since the (*S*)-prolinol employed in this study is enantiomerically pure, **5** can be confidently assumed to be enantiomerically pure as well.

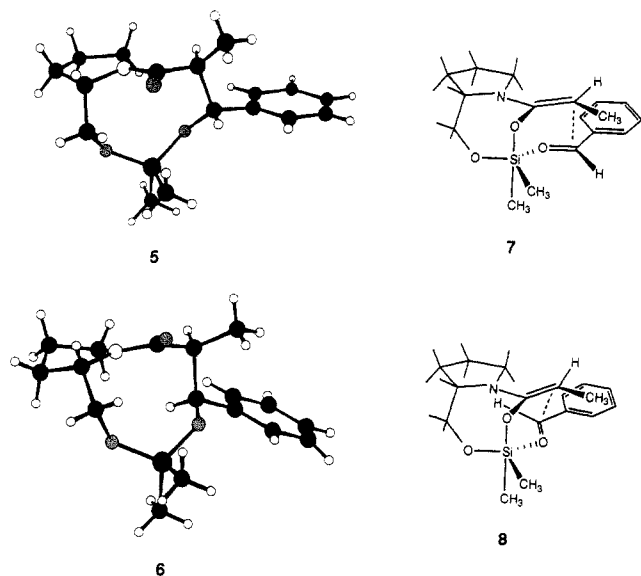


Figure 1.

firmed by single-crystal X-ray analysis.¹² The latter also establishes the product to be the (2-*S*,3-*R*)-*anti* stereoisomer. This requires that aldehyde attack occur on the more hindered, concave surface of the enol, supporting the notion that the aldehyde is directed to that face by coordination to the silicon atom. Careful analysis of the crude reaction mixture shows that a small amount of the (2-*S*,3-*S*)-*syn* diastereomer **6** is also produced ($[5]:[6] = 39:1$). This minor contaminant is easily removed upon purification by crystallization (as described) or flash chromatography (eluent, 30% ethyl acetate–hexanes). The *syn* stereochemistry of **6** is suggested by the smaller coupling between protons on the adjacent stereocenters (3.9 Hz) and is confirmed by single-crystal X-ray analysis.¹² We have found no evidence of the aldol diastereomers resulting from attack on the convex enol π face in high-field NMR spectra of the crude reaction mixture and estimate an upper limit for their formation to be 0.25% by capillary GC analysis. The corresponding aldol addition reactions of **4** with isobutyraldehyde

and propionaldehyde proceed with even greater stereoselectivity (Table I). The stereochemistry of these products is assigned in analogy to the benzaldehyde addition products and is supported by proton–proton coupling constants between the newly formed stereogenic centers.

In addition to establishing stereochemical assignments, X-ray crystal structures of **5** and **6** (Figure 1) provide insights into the mechanism of the aldol reaction and the origin of *anti* selectivity. In each structure, the amide carbonyl group lies over one face of the silicon-centered tetrahedron, in van der Waals contact with the silicon atom. The reasonable transition-state structure **7** (Figure 1) can be derived from **5** by reversing the proposed pericyclic aldol process. Salient features of this hypothetical transition structure are the following: (1) silicon is trigonal bipyramidal with methyl and enol oxygen substituents in the apical positions; (2) the aldehyde is equatorially oriented, coordinated through the lone pair trans to the phenyl group; (3) silicon is bound to the enol through an oxygen p-type orbital; (4) overlap between the bonding carbons is greater in the boatlike transition state **7** than the chairlike transition state **8**, providing a rationale for the observed *anti* selectivity. Modeling studies suggest that proper overlap for *syn* bond formation can best be achieved by a conformational change in the bicyclic system, leading to a higher energy transition-state structure.

In summary, *O*-silyl ketene *N,O*-acetals have been shown to undergo a facile and highly diastereoselective carbon–carbon bond-forming reaction with aldehydes. Preliminary experiments show that Michael additions with these substrates proceed with even greater facility. It is anticipated that these observations will prove of value in extension of these results and in the development of related condensation reactions employing this reactive functional group.

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Supplementary Material Available: Complete spectral and analytical data for **4–6** and *anti* aldol products from propionaldehyde and isobutyraldehyde (30 pages). Ordering information is given on any current masthead page.

(12) Schaefer, W. P.; Widdowson, K. L.; Myers, A. G., submitted for publication in *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*