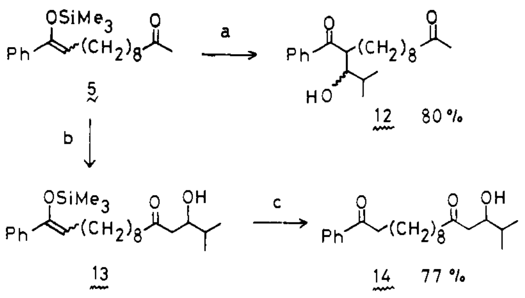
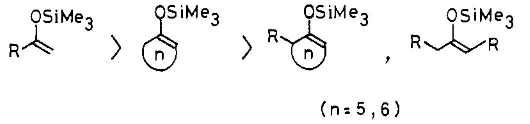
Scheme III



^{a} Isobutyraldehyde (1.1 equiv), $TiCl_4$ (1.1 equiv), CH_2Cl_2, −78 °C. ^{b} LDA (1.1 equiv), THF, −78 °C; isobutyraldehyde (1.2 equiv). ^{c} Aqueous HCl-THF.

of competition reactions using an equimolar mixture of two types of silyl enol ethers have revealed the following guidelines on the selelctivity; (i) an acyclic enol ether except a methyl ketone derivative is not affected by the present method and (ii) an α′- as well as α-substitutent greatly retard the desilylation. Namely, the rate of the reaction drops in the following order.



Such difference of reactivity should account for the selective transformation of cyclic ketones as shown in Scheme II. The desilylation of **7** proceeds cleanly with formation of neither **6** nor **8**. The mono(silyl ethers) of the Wieland–Mischer ketone **6**[2a,7,8] and its hydrogenated ketones **9**[9] and **10**[9] seem to be quite important for terpene and steroid synthesis.

Another synthetic advantage is that this method allows for removal of regioisomeric impurities from thermodynamically favorable silyl enol ethers of methyl ketones. For example, pure 5-methyl-2-(trimethylsiloxy)-2-hexene (**11**) was obtained in 91% yield by treating a mixture of **1** and **11** (14:86) with Bu_3SnF (0.17 equiv) and the Pd catalyst (0.005 equiv) under standard conditions.

A representative procedure for the desilylation is as follows. A mixture of the bis(silyl enol ether) **3** (81 mg, 0.2 mmol), Bu_3SnF (64 mg, 0.205 mmol), and $PdCl_2(P(o\text{-}MeC_6H_4)_3)_2$ (6 mg, 0.006 mmol) in benzene (1 mL) was heated to reflux for 30 min under nitrogen. The reaction mixture was diluted with ether,[10] treated briefly with 1 N NaOH under vigorous stirring, and extracted with ether. Drying and removal of the solvent from the combined extracts followed by silica gel column chromatography[11] afforded the mono(silyl enol ether) **4** (60.2 mg, 91%).

Application of this methodology to further selective transformation has been demonstrated as follows. The reaction of **5** with isobutyraldehyde in the presence of $TiCl_4$ afforded the aldol **12**, whereas treatment of **5** with LDA followed by addition of the same aldehyde gave the isomeric aldol **14** (Scheme III). It is noteworthy that the silyl enol ether is employed for activation of the ketone in the former reaction, while in the latter sequence it acts as a protecting group of the ketone functionality.

Further synthetic application as well as mechanistic studies on the present reaction, especially on the exact role of the palladium catalyst, is now in progress.

Registry No. 1, 73503-97-6; **2**, 86497-50-9; **3**, 86497-36-1; **4**, 86497-37-2; **5**, 86497-38-3; **6**, 20007-72-1; **7**, 86497-39-4; **9**, 4707-05-5; **10**, 4707-04-4; **11**, 86497-40-7; **12**, 86497-41-8; **13**, 86497-42-9; **14**, 86497-43-0; Bu_3SnF, 1983-10-4; $Pd(PPh_3)_4$, 14221-01-3; $PdCl_2(CH_3CN)_2$, 14592-56-4; $PdCl_2(PPh_3)_2$, 13965-03-2; $PdCl_2(P(o\text{-}MeC_6H_4)_3)_2$, 40691-33-6; $TiCl_4$, 7550-45-0; isopentyl methyl ketone, 110-12-3; isobutyraldehyde, 78-84-2; 11-[(bimethylsilyl)oxy]pentadecen-2-one, 86507-85-9; 2,11-pentadecanedione, 86497-44-1; 1-phenyl-1,11-dodecanedione, 15288-89-8; 2,2,16,16-tetramethyl-14-methylene-4-phenyl-3,15-dioxa-2,16-disilaheptadecane, 86497-45-2; 4,4a,7,8-tetrahydro-4a-methyl-5-[(trimethylsilyl)oxy]-2(3*H*)-naphthalenone, 86497-46-3; *cis*-[3,4,4a,5,8,8a(or 3,4,4a,7,8,8a)-hexahydro-8a-methyl-1,6-naphthalenediylbis(oxy)]bis[trimethylsilane], 86497-52-1; *cis*-3,4,4a,7,8,8a-hexahydro-4a-methyl-5-[(trimethylsilyl)oxy]-2(1*H*)-naphthalenone, 86497-47-4; *trans*-[3,4,4a,5,8,8a(or 3,4,4a,7,8,8a)-hexahydro-8a-methyl-1,6-naphthalenediylbis(oxy)]bis[trimethylsilane], 86497-54-3; *trans*-3,4,4a,7,8,8a-hexahydro-4a-methyl-5[(trimethylsilyl)oxy]-2(1*H*)-naphthalenone, 86497-48-5.

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(6) We found that *tert*-butyldimethylsilyl enol ether was not affected even under forcing conditions: cf. the trimethylsilyl enol ether of cyclohexanone suffered desilylation in >85% with 2 equiv of Bu_3SnF and the Pd catalyst for 8 h, while the *tert*-butyldimethylsilyl enol ether was recovered in >85% under the same conditions.

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(10) On using an excess amount of Bu_3SnF (as in Scheme II), the remaining fluoride was readily removed by filtration at this stage.

(11) Flash chromatography (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923) was performed at 4 °C to prevent the possible hydrolysis of silyl enol ethers during the operation.

Reaction-Coordinate Tunneling in Hydride-Transfer Reactions[1]

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Received May 2, 1983

Quantum-mechanical tunneling[3] in the transition state for hydride-transfer reactions, including the action of NAD^+/NADH-dependent dehydrogenases, is shown by model vibrational-analysis calculations[4] to explain observed anomalies in the α-deuterium secondary kinetic isotope effects,[5,6] which exceed the corresponding equilibrium effects in these systems.

α-Deuterium secondary kinetic isotope effects[7-11] lie between unity and the equilibrium isotope effect for reactions in which the proximal atom of the group departing from or arriving at the isotope-bearing center is oxygen or a heavier atom (as in S_N1 reactions[8] and nucleophilic reactions at carbonyl[9-12]). Their magnitudes are taken to reflect progress from reactants toward products at the transition state.[7-12]

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(1) This research was supported by the National Institutes of Health through research grant No. GM-20198 from the National Institute of General Medical Sciences.

(2) Graduate Fellow of the National Science Foundation.

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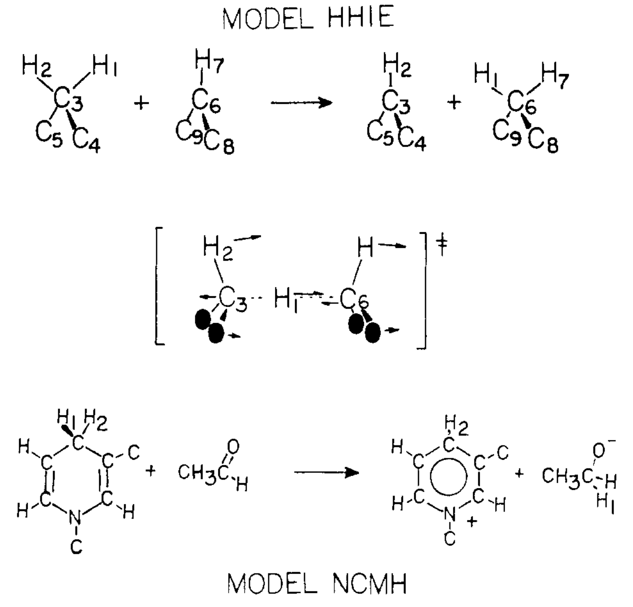

Figure 1. Models used in vibrational-analysis calculations. Model HHIE has only nine atoms and is symmetrical with respect to reactants and products. The computations are inexpensive and fast, and the results are easy to analyze. However, it violates the "cut-off rules" of Wolfsberg and Stern[18,19] and may give inaccurate predictions. Model NCMH has 20 atoms and was used for more accurate simulation of selected cases. Geometrical data were taken from standard studies of molecules related to NAD$^+$, NADH, and other relevant species. Force constants for reactants and products were similarly chosen. For transition states, geometrical and force-field characteristics were estimated by a scheme related to that of Rodgers, Femec, and Schowen,[20] although a more complex method of interpolation was used. The figure in the center of the diagram shows a typical transition-state geometry and reaction-coordinate eigenvector. the $C_3H_1C_6$ angle is taken at 180° in the calculations reported here. Smaller angles lead to smaller $(k_H/k_D)_{pri}$ and very little change in $k_{\alpha H}/k_{\alpha D}$. Even larger tunneling corrections would then be required to match experimental primary isotope effects. The reaction coordinates were generated (caused to have negative eigenvalues) by simultaneous coupling of the C_3–H_1 stretch to the C_6–H_1 stretch and of the inversion coordinates about atoms C_3 and C_6 with the adjacent C–H_1 stretch. The coupling constants for both interactions were varied to obtain different $\nu^‡$ and r_{H2}/r_{H1} values.

In contrast, the following observations of α-deuterium secondary kinetic and equilibrium isotope effects (isotopic labels in NADH) and primary kinetic deuterium isotope effects have been reported for hydride donation from NADH. For nonenzymic reduction of 4-cyano-2,6-dinitrobenzenesulfonate, Kurz and Frieden[5,13] found $k_{\alpha H}/k_{\alpha D} = 1.145 \pm 0.009$, $K_{\alpha H}/K_{\alpha D} = 1.035 \pm 0.009$, and $(k_H/k_D)_{pri} = 5.5$ (from A side of NADH) and 5.3 (from B side). For reduction of acetone catalyzed by yeast alcohol dehydrogenase, Cook, Oppenheimer, Blanchard, and Cleland[6] found $k_{\alpha H}/k_{\alpha D} = 1.38$ (no error limit given), $K_{\alpha H}/K_{\alpha D} = 1.127 \pm 0.006$, and $(k_H/k_D)_{pri} = 4.9$. For reduction of cyclohexanone catalyzed by horse-liver alcohol dehydrogenase, the same authors[6] found $k_{\alpha H}/k_{\alpha D} = 1.50$ (no error limit given), $K_{\alpha H}/K_{\alpha D} = 1.127 \pm 0.006$, and $(k_H/k_D)_{pri} = 5.3$.

To test the hypothesis[5,6] that reaction-coordinate motion of the α-hydrogen is important, we calculated isotope effects for the two models of Figure 1. In Figure 2, the reaction-coordinate frequency $\nu^‡$, which measures curvature at the top of the reaction barrier, is plotted vs. (r_{H2}/r_{H1}), which measures amplitude in the reaction coordinate for the α-hydrogen (H2) relative to the transferring hydrogen (H1), for calculations on both models. The HHIE calculations for a severe cut-off model are included in Figure 2 to show trends and to demonstrate that (for both models) only combinations to the left of the dashed line are permitted (other combinations generate multiple decomposition modes and thus do not model possible transition states). The NCMH results, shown as points A–D, should provide realistic simulations of the actual molecular system to compare with experimental results.

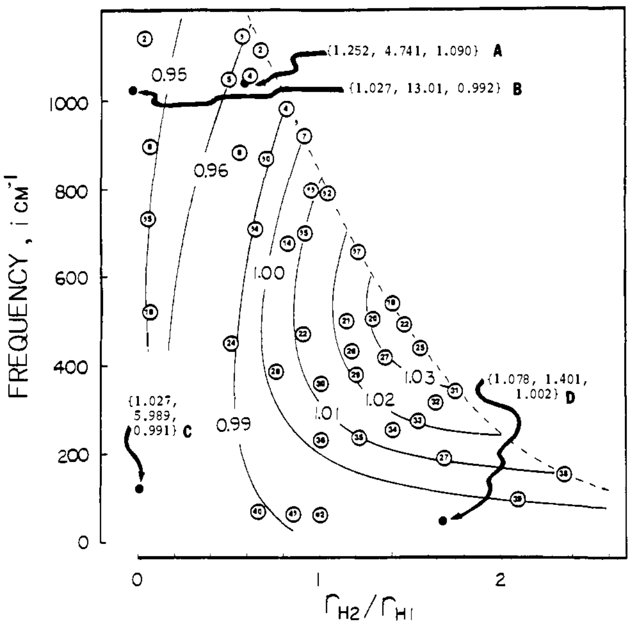

Figure 2. A plot of reaction-coordinate frequencies $\nu^‡$ vs. the relative amplitudes of atoms H_2 and H_1 (r_{H2}/r_{H1}) in the reaction-coordinate motion for 42 model HHIE transition states (numbered points) and four model NCMH transition states (points A, B, C, and D). The contours approximately trace lines of constant zero-point energy contribution to the α-secondary kinetic isotope effect on model HHIE. The numbers in brackets for points A–D are respectively the α-secondary kinetic isotope effect $k_{\alpha H}/k_{\alpha D}$, the primary kinetic isotope effect $(k_H/k_D)_{pri}$, and the ratio of the secondary isotope effect for protium transfer to the same isotope effect for deuterium transfer. Points A, B, C, and D include the truncated Bell[21] tunnel correction to the semiclassical isotope effect. For points A, B, C, and D the respective tunnel corrections for the secondary isotope effects were 1.190, 1.002, 1.000, and 1.000; for the primary isotope effects, the corrections were 1.568, 2.133, 1.006, and 1.000. All calculations were for 25 °C.

Points C and D both have reaction barriers with small $\nu^‡$ and thus little tunneling. Point C has very little motion of the α-hydrogen in the reaction coordinate $(r_{H2}/r_{H1} = 0.06)$. Then $k_{\alpha H}/k_{\alpha D} = 1.027$, well below the calculated $K_{\alpha H}/K_{\alpha D} = 1.069$, thus failing to exhibit the observed anomaly. However, $(k_H/k_D)_{pri} = 5.99$, near the experimental values. When large motion of the α-hydrogen is introduced (point D, $r_{H2}/r_{H1} \sim 1.7$), $k_{\alpha H}/k_{\alpha D} = 1.078$, slightly exceeding $K_{\alpha H}/K_{\alpha D}$, but at the same time $(k_H/k_D)_{pri}$ is sharply reduced to 1.40, far below the experimental values. This is a general result because an increase in α-hydrogen amplitude inevitably "steals" amplitude from the transferring hydrogen and reduces the primary isotope effect. Any amplitude of the α-hydrogen that makes $k_{\alpha H}/k_{\alpha D} > K_{\alpha H}/K_{\alpha D}$ makes $(k_H/k_D)_{pri}$ unacceptably small.

Points A and B have large $\nu^‡$ and thus significant tunneling. Point B has $r_{H2}/r_{H1} = 0.04$ and $(k_{\alpha H}/k_{\alpha D}) = 1.027$, which (as for point C) does not exceed $K_{\alpha H}/K_{\alpha D}$. Extensive tunneling, however, gives $(k_H/k_D)_{pri} = 13$, much above experimental values. Finally, point A, where the features of (a) relatively large α-hydrogen amplitude in the reaction coordinate $(r_{H2}/r_{H1} \sim 0.6)$ *and* (b) tunneling ($\nu^‡ = 1036i$ cm^{-1}) are combined, reproduces the observed phenomena: $k_{\alpha H}/k_{\alpha D} = 1.252 > 1.069$; $(k_H/k_D)_{pri} = 4.7$.

We conclude that the combination of α-hydrogen motion in the reaction coordinate with large curvature along the reaction coordinate and concomitant tunneling provides a simple and realistic explanation of isotope-effect observations on hydride-transfer systems.[14] Two further results of the calculations lend strength

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[13] The isotope effects shown here were calculated from the measurements of ref 5 assuming that a single step determines the rate and that secondary isotope effects for hydride donation from either the A or B sides of NADH are equal.

to this explanation.

First, the calculations reproduce observed changes in the secondary effect when the primary hydrogen is changed from H to D, and vice versa. Experimentally, deuteration at one of the sites *reduces* the isotope effect at the other by factors of 1.03 ± 0.02 (Kurz and Frieden[5,13]) or around 1.14 (cited as ref 11 by Cook, Oppenheimer and Cleland[6]). The calculation for point A predicts a factor of 1.09. Those for points B, C, and D predict respectively 0.99, 0.99, and 1.00.

Second, if the mass of the transferring atom is increased to 16 amu, thus (crudely) simulating solvolysis[8] and acyl-transfer reactions,[9-12] anomalous phenomena disappear. If this mass change but no other alteration is made in the model for point A, $k_{\alpha H}/k_{\alpha D}$ becomes 1.060 and $K_{\alpha H}/K_{\alpha D}$ 1.100. As with deuteration, an increase in reduced mass for the reaction coordinate has greatly reduced the importance of tunneling and the associated anomalies.

The results are consistent with, but do not demand, a ubiquitous importance of tunneling in hydrogen transfer. The similar observations of Saunders and his co-workers[15-17] for proton transfer in elimination reactions add reinforcement to such a suggestion. It is possible that enzymes that catalyze hydrogen transfer have developed part of their catalytic power by not only altering the *height* of the reaction barrier but also its *shape*, thus altering the contribution of tunneling.

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(14) The calculations shown in Figure 2 correspond to a total bond order about H_I of approximately unity, which is usually assumed in hydrogen-transfer reactions (a practice that derives from: Johnston, H. S. "Gas Phase Reaction Rate Theory", Ronald Press: New York, 1966). Any of the models that reproduces approximately the observed secondary and primary isotope effects yet maintains a low imaginary frequency and thus has no tunneling contribution requires extremely low bond orders about the transferring hydrogen. Such models are probably unreasonable for hydrogen-transfer reactions but perhaps not for heavy-atom transfers.

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Group-Transfer Polymerization. 1. A New Concept for Addition Polymerization with Organosilicon Initiators[1]

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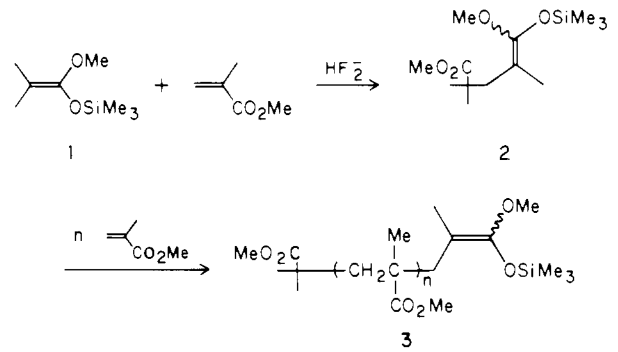
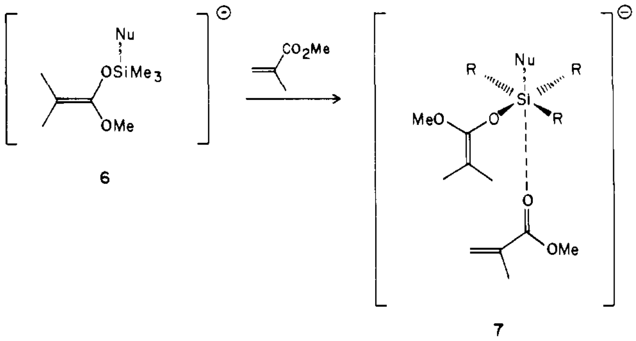
Although the conjugate addition of silyl ketene acetals to α,β-unsaturated carbonyl compounds has been used in organic synthesis,[2] application of this chemistry to polymer formation by sequential additions is unprecedented. This communication describes such a process for the controlled polymerization of α,β-unsaturated esters, ketones, nitriles, and carboxamides. *This new method offers new dimensions in the construction and design of polymer chains from these monomers.*

Scheme I



Scheme II



Scheme I illustrates the polymerization of methyl methacrylate (MMA) with dimethylketene methyl trimethylsilyl acetal[3] (**1**) as initiator. This new method of addition polymerization is termed "group-transfer polymerization" (GTP)[4] since the trimethylsilyl group is transferred from **1** (or **2** or **3**) to the incoming monomer.

A catalyst is required for the polymerization to proceed, and surprisingly, one of the most generally useful catalysts is bifluoride ion. Although fluorides have been widely used for the catalysis of nucleophilic reactions of organosilanes,[2g] this is the first report of the general utility of bifluoride ion in the catalysis of such reactions. Other anions that catalyze GTP are Me_3SiF_2,[5] CN, and N_3.[6,7] Table I summarizes the results.

In general, GTP proceeds rapidly at room temperature and gives living polymer of narrow molecular weight distribution in quantitative yield.[8] The degree of polymerization is controlled by the ratio of monomer to **1**. The living polymers are isolable and characterizable.[9] Hence, further addition of monomer leads to

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[†] Contribution No. 3191.

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(4) This name was suggested by Professor B. M. Trost, University of Wisconsin.

(5) Middleton, W. J. U.S. Patent 3940402, Feb 1976; Middleton, W. J. *Org. Synth.*, in press.

(6) Lewis acids such as zinc halides and alkylaluminum chlorides also catalyze group-transfer polymerization (most likely by activation of the monomer). This work will be published in the near future by O. W. Webster, B. M. Trost, W. R. Hertler, and D. Y. Sogah.

(7) Although tetraalkylammonium bifluorides or even potassium bifluoride can be used, we found tris(dimethylamino)sulfonium bifluoride (TAS HF_2) to give the best overall results. Tris(dimethylamino)sulfonium bifluoride was prepared in quantitative yield by treatment of tris(dimethylamino)sulfonium difluorotrimethylsilicate (27.5 g, 0.10 mol) with water (1.0 mL, 0.055 mol) in acetonitrile (20 mL). Purification was achieved by crystallization from MeCN/THF (1/10, v/v). The product has the expected ^1H and ^{19}F NMR spectral properties, and the elemental analysis was within 0.3% of theory.

(8) In a typical procedure, MMA (360 mmol) is slowly added to a solution of 1-methoxy-1-(trimethylsiloxy)-2-methyl-1-propene (**1**, 8.5 mmol) and tris(dimethylamino)sulfonium bifluoride (0.01 mmol) in tetrahydrofuran (20 mL) at room temperature with exclusion of moisture. When the exothermic reaction is complete, methanol (3 mL) is added, and the solution is evaporated to give a quantitative yield of poly(methyl methacrylate), M_n 4300, M_w 5300 (theory, 4343), dispersity (D) = M_w/M_n = 1.24, as determined by GPC.

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