Experimental Section

The materials required for this work are obtained from the respective companies as follows: diethyl oxalate and diethyl glutarate, Aldrich; glutamate dehydrogenase and other biochemicals, Sigma. Instruments required are the Beckman DU-6 UV–vis spectrophotometer for enzyme assays where NADH consumption is monitored at 340 nm. An EM-390 (90 MHz) instrument was used for ^{1}H NMR analysis.

Enzyme Assays. The method used herein is a modification of the procedures described previously.[3] Determination of the Michaelis–Menten constants is done as follows. Starting with stock solutions of 10 mM NADH, 100 mM 2-ketoadipate, and triethanol amine buffer (pH 7.8, 50 mM) containing ADP (1 mM), ammonium acetate (125 mM), and GluDH (type III dissolved in water, 400 U/mL) cuvette solutions with final volume of 1 mL are made. Thus, to a 1-mL buffer solution was added 25 μL of NADH, 10 μL of enzyme, and various amount of substrate (10 to 50 μL). The change of absorbance at 340 nm (ϵ at 340 nm for NADH = 6.22 mM^{-1} cm^{-1}) was then recorded and used for calculation of velocities. Double reciprocal plots of velocity vs. substrate concentrations gave K_m(2-ketoadipate) = 5.3 mM and V_{max} = 3 U/mg, where 1 U is defined as 1 μmol of product formed per min.

Preparation of 2-Ketoadipate. The method used here is a modified procedure of that used in the preparation of 2-oxoglutarate.[11] To 32 mL of diethyl glutarate in 400 mL of anhydrous ether and 15 mL of ethanol is added 12.25 g of sodium ethoxide. The mixture was refluxed for 60 min to allow for dissolution of sodium ethoxide followed by rapid addition of diethyl oxalate (23.6 mL) while vigorously stirring the solution. The reaction is allowed to proceed for 3.5 h and then the mixture concentrated to an oil. The oil is taken up in 275 mL of 3.5 N HCl and the solution quickly extracted with ether until the aqueous layer is almost colorless (4 × 25 mL). The ether is dried over anhydrous Na_2SO_4, then concentrated under vacuum. The resulting oil is taken up in 135 mL of concentrated HCl and the mixture kept at room temperature for 18 h. The solution is evaporated to dryness. The solid is dissolved in acetone and decolorized with activated carbon. The acetone is evaporated and the solid dissolved in water and adjusted to pH 4 with NaOH solution. Precipitation is brought about by addition of 2-propanol until precipitation is no longer observed. The mixture is then stored for 1 h at 0–4 °C, the precipitate is filtered off, and further precipitation brought about with more 2-propanol. This step is repeated until precipitate is no longer observed (usually 4–5 volumes of 2-proponal are required). The brown product can be recrystallized by repeating the above procedure. The 2-ketoadipate monosodium salt obtained after recrystallization is slightly tan and has the same ^{1}H NMR shifts as a standard sample from Sigma. Yield, 85–90%; mp 175–180 °C dec; ^{1}H NMR (D_2O) δ 2.48 (t, 2 H, C_3-H), 2.45 (t, 2 H, C_5-H), 1.87 (m, 2 H, C_4H).

Preparation of L-α-Aminoadipate and (+)-(1*R*,6*S*)-*cis*-8-Oxabicyclononan-7-one. The procedure is similar to that described previously.[3] To a 900-mL solution containing 2-ketoadipate monosodium salt (50 mmol) and *cis*-1,2-bis(hydroxymethyl)cyclohexane (50 mmol) is added concentrated NH_4OH until pH 8.1 is reached. The enzymes GluDH (400 U) and HLADH (70 U) and the cofactor NAD (1 mmol) are added. Hexane (1 L) is carefully added to the solution without disturbing the water layer. Two days later 40 U GluDH, 100 U of HLADH, and 25 mmol of 2-ketoadipate monosodium salt (in 100 mL of water with pH adjusted to 8.1 with NH_4OH) are added. Two days later, the reactions are complete according enzymatic assays. The residual activities of HLADH and GluDH are about 47% and 60%, respectively, of their original activities. The two layers are separated and the aqueous layer is acidified to pH 4 and stored in refrigerator overnight to give the precipitated L-α-aminoadipic acid in 60–70% yield. The aqueous solution recovered after filtration is then concentrated to 500 mL and stored at 0 °C for 5 h allowing for further crystallization, and approximately 15% more of theoretical yield is obtained (overall yield = 84%): mp 205–206 °C (same as lit.[8,12] mp 205–210 °C); ^{1}H NMR (D_2O) δ 3.8 (t, 1 H, H-2), 2.48 (t, 2 H, H-5), 1.83 (m, 4 H, H-3,4), (D_2O, NaOD) δ 3.2 (t, 1 H, H-2), 2.19 (t, 2 H, H-3), 1.55 (m, 4 H, H-3,4); $[\alpha]^{23}_D$ +24° (*c* 5, 5 N HCl), $[\alpha]^{23}_D$ +12° (*c* 5, 0.5 N NaOH) [lit.[8] +24 (*c* 5, 5 N HCl)]. After filtration of the α-aminoadipic acid, the solution is extracted with ether (4 × 55 mL). The ether solution is dried over $MgSO_4$ and added to the reaction hexane layer which has been previously dried. The collected organic layers are concentrated in vacuo. The oil is further purified by distillation, bp 80 °C (0.9 mmHg); $[\alpha]^{23}_D$ +48.8 (*c* 0.5, $CHCl_3$) (100% ee) [lit.[13] $[\alpha]^{25}_D$ +48.8 (*c* 0.5, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 0.8–2.8 (m, 10 H), 3.8–4.4 (m, 2 H), same as literature values.[13] Yield, 79%.

Acknowledgment. Support of this work by the National Science Foundation (CHE 8318217) and the Robert A. Welch Foundation (A-1004) is gratefully acknowledged.

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(11) Friedman, L.; Kosower, E. *Organic Syntheses*, Wiley: New York, 1955; Collect. Vol. 3, p 510.
(12) Waalkes, T. P.; Fones, W. S.; White, J. *J. Am. Chem. Soc.* **1950**, *72*, 5760.
(13) Jakovac, I. J.; Goodbrand, H. B.; Lok, K. P.; Jones, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 4659.

Communications

A Novel Synthesis of β-Trichlorostannyl Ketones from Siloxycyclopropanes and Their Facile Dehydrostannation Affording 2-Methylene Ketones

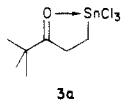
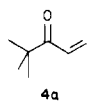
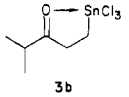
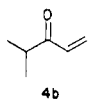
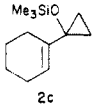
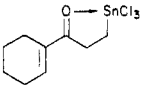
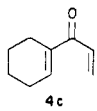
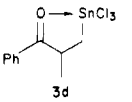
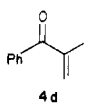
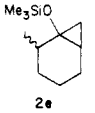
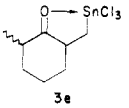
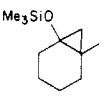
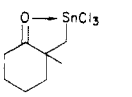
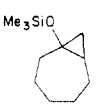
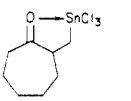
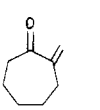
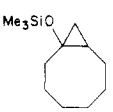
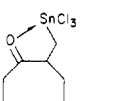
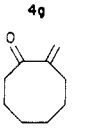
Summary: Site-selective ring cleavage of siloxycyclopropanes **2** with stannic chloride ($SnCl_4$) leads to good yields of β-trichlorostannyl ketones **3**. Subsequent treatment of **3** with dimethyl sulfoxide (Me_2SO) in chloroform at 60 °C results in the facile dehydrostannation to give good yields of 2-methylene ketones **4**.

Sir: Although α-metallo ketones or metal enolates have found widespread use in organic synthesis, the use of β-metallo ketones **1** in synthesis is only just being realized.[1] One of the main reasons for this lies in their limited accessibility, and, in this context, we have been interested in the electrophilic ring opening of siloxycyclopropanes **2** with metal ions as a route to **1**.[2-4] We report here a synthesis and a highly efficient dehydrostannation reaction

(1) For a review, see: Ryu, I.; Sonoda, N. *J. Synth. Org. Chem. Jpn.* **1985**, *43*, 112; *Chem. Abstr.* **1985**, *102*, 166796p.
(2) Ryu, I.; Matumoto, K.; Ando, M.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1980**, *21*, 4283.
(3) Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 7192.
(4) Ryu, I.; Ogawa, A.; Sonoda, N. *Nippon Kagaku Kaishi*, **1985**, 442; *Chem. Abstr.* **1985**, *103*, 214888q.

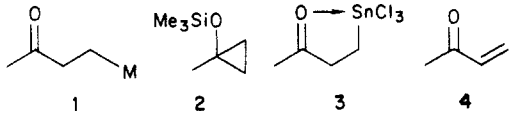
0022-3263/86/1951-2389$01.50/0

Table I. Synthesis of β-Stannyl Ketones 3 and Their Conversion to 2-Methylene Ketones 4

entry	substrate[a] 2	β-Sn ketone 3	yield[b,c] (%)	mp (°C) IR ($\nu_{C=O}$, cm^{-1})	temp, time (°C, h)	enone 4	yield (%)
1	 2a	 3a	(96)	178–179 1632	60, 5	 4a	*d*
2	 2b	 3b	(96)	82–83 1640	60, 5	 4b	*d*
3	 2c	 3c	(80)	182–183 1585	60, 5	 4c	*d*
4	 2d	 3d	(70)	151–152 *e*	60, 2	 4d	*d* (70)[f]
5	 2e	 3e	(83)[g]	136–137.5 1645	60, 2	 4e	*d*
6	 2f	 3f	(66)	148–151 1640	60, 24	NR	
7	 2g		(83)	130–134 1630	60, 3	 4g	(80)[f] 98[h]
8	 2h	 3h	(84)	154.5–156 1625	60, 3	 4h	(70)[f]

[a] Prepared by the cyclopropanation of enol silyl ethers with zinc carbenoids: Ryu, I.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1977**, 4611; **1978**, 856. [b] Carried out on a 5-mmol scale as described in the text. Isolated yields of purified (recrystallization) products are given. [c] All products exhibited the satisfactory spectral and analytical data, consistent with assigned structures. [d] Carried out using NMR tube (Me_2SO or Me_2SO-d_6, 10 equiv, in $CDCl_3$, 60 °C). Quantitative conversion of **3** to **4** was checked by ^1H NMR. [e] Three strong peaks near 1600 cm^{-1} (1618, 1595, 1575 cm^{-1}). [f] Carried out on a 1-mmol scale as described in the text. Isolated yield. [g] Obtained as a mixture of two diastereoisomers (two doublets of methyl protons at 1.19 (d, J = 6 Hz) and 1.32 (d, J = 8 Hz) ppm with nearly equal intensity by ^1H NMR. During recrystallization from $CHCl_3$, isomerization to one diastereoisomer (1.19 ppm) took place. [h] GLC yield.

of β-trichlorostannyl ketones **3** leading to 2-methylene ketones **4**.[5]



1 2 3 4

The present route to **3**, which consists of the electrophilic ring opening of **2** by $SnCl_4$, involves mild reaction conditions and a simple procedure as well as high product selectivity. A typical procedure is exemplified by the synthesis of 5-(trichlorostannyl)-2,2-dimethylpentan-3-one (**3a**). 1-*tert*-Butyl-1-siloxycyclopropane **2a** (5 mmol) was added to a solution of $SnCl_4$ (5 mmol) in CH_2Cl_2 (10 mL) at 15 °C and the solution was stirred for 0.5 h. The solvent and produced Me_3SiCl were evaporated to give a colorless solid, which was essentially pure β-stannyl ketone **3a** (yield, 96%; mp 178–179 °C, recrystallized from $CHCl_3$). The results of β-trichlorostannyl ketone synthesis are listed in Table I. The reaction of 2-methyl-substituted siloxycyclopropane **2d** with $SnCl_4$ gave **3d**, which resulted from site-selective ring cleavage at the methylene carbon.[6] This site selectivity was also observed in the case of bicyclic siloxycyclopropanes **2e–h**, where **3e–h** were obtained in good yields.[7]

The resulting β-stannyl ketones **3** are thermally stable. However, interestingly, facile dehydrostannation of these β-trichlorostannyl ketones **3** leading to 2-methylene ketones **4** took place upon treatment with dimethyl sulfoxide (Me_2SO). For example, when **3g** (1 mmol) was treated with Me_2SO (0.2 mL, 2.8 mmol)/$CHCl_3$ (2 mL) at 60 °C,[8] a colorless precipitate of the hydrostannane complex appeared gradually in the bottom of reaction flask and,

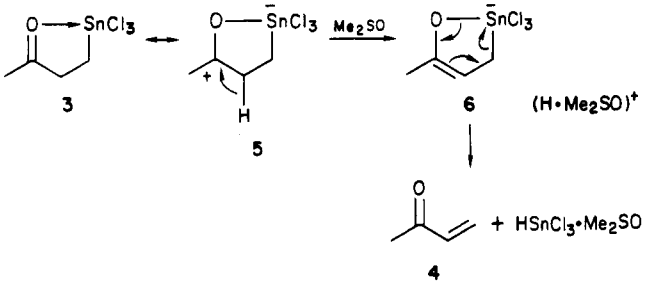
(5) Preparation of β-metallo esters including β-stannyl ester based on a similar siloxycyclopropane approach has been reported, see: Nakamura, E.; Shimada, J.-i.; Kuwajima, I. *Organometallics* **1985**, *4*, 641.

(6) ^1H NMR ($CDCl_3$, 100 MHz) δ 1.25 (d, J = 7 Hz, 3 H), 1.95 (dd, J = 1.5, 12 Hz, 1 H), 2.17 (dd, J = 7, 12 Hz, 1 H), 4.31 (dq, J = 7, 1.5 Hz, 1 H), 7.4–8.3 (m, 5 H). Anal. Calcd for $C_{10}H_{11}OCl_3Sn$: C, 32.26; H, 2.98. Found: C, 32.53; H, 3.13.

(7) The observed site selectivity appears to be a common phenomena in the siloxycyclopropane cleavages mediated by electrophiles. For a review, see: Murai, S.; Ryu, I.; Sonoda, N. *J. Organomet. Chem.* **1983**, *250*, 121. Cf. Rubottom, G. M.; Beedle, E. C.; Kim, C. W. *J. Am. Chem. Soc.* **1985**, *107*, 4230.

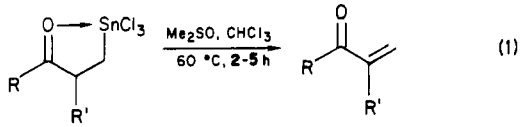
(8) As a general procedure, the use of more than 3 equiv of Me_2SO to β-stannyl ketones may be recommended. With the smaller equiv of Me_2SO, the dehydrostannation proceeded quite slowly; for example, conversion of **3d** to **4d** with 1.6 equiv of Me_2SO required 20 h at 60 °C.

Scheme I



3 5 6 4

concomitantly, 2-methylene ketone **4g** was formed (monitored by ^{1}H NMR). After 4 h, dehydrostannation was complete, and the precipitate was filtered off. Aqueous workup of the filtrate (pentane/aqueous NH_4Cl) followed by evaporation of the solvents and bulb-to-bulb distillation afforded 2-methylenecycloheptanone (**4g**) in 80% yield. Similarly, essentially quantitative conversion of **3** to **4** (eq 1) was observed in the reaction of **3** with Me_2SO-d_6/$CDCl_3$

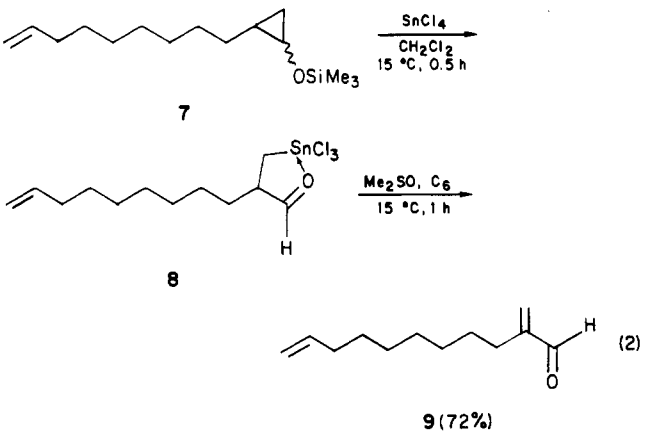


(1)

3 4

at 60 °C (by ^{1}H NMR) except for **3f** which did not bear hydrogen β to the stannyl group.[9] The results are shown in Table I. The dehydrostannation of **3d,e,g,h** proceeded with shorter reaction time than **3a–c**. It seems that for dehydrostannation to occur, the intramolecular coordination of the carbonyl oxygen to the Sn atom (as indicated by IR) may play a key role. In fact, dehydrostannation did not take place with simple *n*-$BuSnCl_3$ even under more forcing conditions (60 °C, 1 day). One plausible explanation for the present reaction is shown in Scheme I. The initial role of Me_2SO may be the one as a base toward β-hydrogen[10] which may be sufficiently acidic due to the inductive effect of the adjacent carbonyl coordinated to the Sn. Thus, the deprotonation from **5** and subsequent destannylation via **6** would occur to lead to **4** and $HSnCl_3(Me_2SO)_n$ complex.[11,12]

Interestingly, the reaction of siloxycyclopropane **7** with $SnCl_4$ in CH_2Cl_2 proceeded similarly and afforded β-trichlorostannyl aldehyde **8** (semisolid, $\nu_{C=O}$ 1680 cm^{-1}). The resulting crude **8** (4 mmol) was treated with Me_2SO (1 mL) in hexane (5 mL)[13] at 15 °C for 1 h, followed by separation of a white precipitate and aqueous treatment (Et_2O/aqueous NH_4Cl). After removal of the solvents, the residue was chromatographed on silica gel to give a 72% yield of 2-methylene-10-undecenal (**9**) (eq 2).



7 8

(2)

9 (72%)

Further synthetic application of β-stannyl ketones and aldehydes is now in progress.

Acknowledgment. We thank Shin-Etsu Chem. Ind. Co. Ltd. for a gift of trimethylchlorosilane.

Registry No. **2a**, 38858-75-2; **2b**, 101653-02-5; **2c**, 54781-38-3; **2d**, 56011-29-1; **2e**, 50338-51-7; **2f**, 50338-50-6; **2g**, 50338-48-2; **2h**, 50338-49-3; **3a** (coordinate), 101653-11-6; **3a** (stannane), 101653-04-7; **3b** (coordinate), 101653-12-7; **3b** (stannane), 101653-05-8; **3c** (coordinate), 101653-13-8; **3c** (stannane), 101653-06-9; **3d** (coordinate), 101653-14-9; **3d** (stannane), 101653-07-0; **3e** (coordinate), 101653-15-0; **3e** (stannane), 101653-08-1; **3f** (coordinate), 101653-16-1; **3f** (stannane), 101653-09-2; **3g** (coordinate), 101653-17-2; **3g** (stannane), 101653-10-5; **3h**, 101653-18-3; **3h** (stannane), 101670-94-4; **4a**, 2177-30-2; **4b**, 1606-47-9; **4c**, 62672-77-9; **4d**, 769-60-8; **4e**, 42858-50-4; **4g**, 3045-99-6; **4h**, 3045-71-4; **7**, 101653-03-6; **8**, 101653-19-4; **9**, 22414-69-3; $SnCl_4$, 7646-78-8.

(9) As the preparative method of β-stannyl ketones **3**, hydrostannation of α,β-unsaturated ketones with $HSnCl_3$ (in situ generated under acidic conditions: HCl and $SnCl_2$) has been known. The observed dehydrostannation promoted by Me_2SO formally corresponds to its reverse reaction. See: Hutton, R. E.; Burley, J. W.; Oakes, B. *J. Organomet. Chem.* **1978**, *156*, 369.

(10) The use of some amines such as pyridine, instead of Me_2SO, was also effective. DMF and methylformamide also promoted the dehydrostannation to some extent. For examples of Me_2SO promoted 1,2-elimination, see, pp 328–329 in a review: Martin, D.; Weise, A.; Niclas, H. J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 318.

(11) Colorless crystals were obtained (mp >300 °C). The IR spectra (KBr) of this compound showed strong absorption at 900 cm^{-1}, which should be ascribed to the coordinated $\nu_{S=O}$. The spectra was identical with that of the Me_2SO complex separately prepared according to the reaction of Me_2SO with in situ generated $HSnCl_3$[9] (by treating $SnCl_2 \cdot 2H_2O$ with Me_3SiCl in ether). The number of coordinated Me_2SO molecules is not clear at the present time (1 and/or 2). Cf. Wayland, B. B.; Schramm, R. F. *J. Chem. Soc., Chem. Commun.* **1968**, 1465. Nametkin, N. S.; Kuz'min, O. V.; Korelov, V. K.; Kobrakov, K. I.; Patrikeev, A. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1978**, 676; *Chem. Abstr.* **1978**, *89*, 42292q.

(12) We have also shown previously that bicyclic siloxycyclopropanes **2** can be converted to the corresponding 2-methylenecycloalkanones **4** based on a β-metallo ketone approach involving the ring cleavage reaction of **2** with $Hg(OAc)_2/PdCl_2$[2] or CuF_2.[4] As referred to in our previous reports, these methods were often bothered by the contamination of side products (endocyclic alkenones or coupling dimers, respectively).

(13) The use of hexane instead of $CHCl_3$ was advantageous for the formation of an easily separable hydrostannane precipitate.

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New C4-Chiral 1,3-Thiazolidine-2-thiones: Excellent Chiral Auxiliaries for Highly Diastereocontrolled Aldol-Type Reactions of Acetic Acid and α,β-Unsaturated Aldehydes

Summary: Diastereocontrolled aldol-type reactions between tin(II) enolates of 3-acetyl-4(*S*)-ETT (**6a**) and 3-acetyl-4(*S*)-IPTT (**6b**) and α,β-unsaturated aldehydes **7a–c** were successfully carried out to give, with high diastereoselectivity, compounds **9a–e** (major products) and **10a–e** (minor products). The reaction conditions were also investigated in detail.

Sir: A chiral synthon, α-nonsubstituted-β-hydroxy-γ,δ-unsaturated carbonyl system (**1**) would be remarkably useful for construction of synthons **2–5** (eq 1). Chiral synthons **1–5** have often appeared in the complicated

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