a dry septum. After three cycles of evacuation and flushing with nitrogen, the sulfonamide was dissolved in dry dichloromethane (3 mL), boron tribromide solution in dichloromethane (0.5 M solution, 0.50 mL) was added, and the reaction mixture was stirred at room temperature for 24 h to form bromoborane **1**. Solvent was evaporated completely at 25 mmHg through calcium chloride and sodium hydroxide traps, and dry dichloromethane (3 mL) was added and evaporated in vacuo. After admission of nitrogen, toluene (4 mL) was added and the flask was warmed with a heat gun to dissolve **1**. After cooling to −78 °C (dry ice–acetone), cinnamyl phenylacetate (29.7 mL, 0.9 equiv) was added, the bath was removed to dissolve the solidified ester, and the mixture was recooled to −78 °C. Triethylamine (18.6 μL, 1.0 equiv) was added slowly at −78 °C. The reaction mixture was stirred at −78 °C for 24 h and stored at +4 °C for 2 days. The reaction mixture was quenched with aqueous acid (pH ca. 1) and stirred for 30 min. The organic layer was washed with water and extracted with dilute sodium hydroxide solution. Evaporation of the organic layer and silica gel chromatography furnished >85% recovery of the starting bis-sulfonamide. The aqueous layer was washed with ether, acidified with 10% hydrochloric acid, and extracted with ether. The organic layer was dried and evaporated to produce pure (2*S*,3*R*)-diphenyl-4-pentenoic acid (29.6 mg, 99%). This acid was transformed into the corresponding methyl ester with diazomethane.

R_f: 0.54 (hexane:ethyl acetate = 5:1). $[\alpha]_D$: +119.9° (*c* 1.46, $CHCl_3$). Mp: 127–128 °C. GC (DB1-30W capillary column from J & W Scientific, 25 m): 24.81 min at 140 °C. HPLC (Du Pont Zorbax silica gel): 8.62 min (hexane:ethyl acetate = 100:1, 2mL/min). IR (neat): 1736, 1266, 1180, 734 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.34 (s, 3 H), 3.92 (d, J = 11.6 Hz, 1 H), 4.00 (m, 1 H), 4.68 (d, J = 17 Hz, 1 H), 4.79 (d, J = 10 Hz, 1 H), 5.67 (m, 1 H), 7.20–7.40 (m, 10 H). FABMS: *m/e* 267 ($M + H^+$).[8]

Supplementary Material Available: Physical data on Claisen rearrangement products and experimental procedures for correlation of absolute configuration (22 pages). Ordering information is given on any current masthead page.

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Importance of Lewis Acid Mediated Electron Transfer in Mukaiyama–Michael Reaction of Ketene Silyl Acetals

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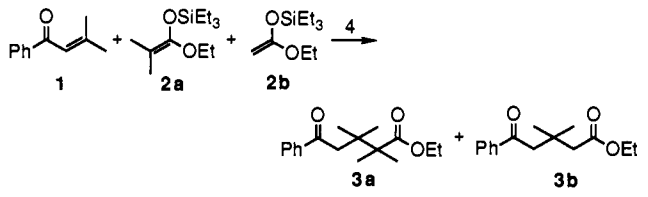
Ketene silyl acetals have received increasing attention in organic synthesis.[1] The Mukaiyama–Michael reaction of these compounds, in particular, offers a convenient route for 1,5-keto esters.[2] The importance of Lewis acids in promotion of this reaction has led one quite naturally to postulate initial nucleophilic attack of the ketene silyl acetal (or its transmetalation species) toward electrophiles. We disclose herein that this postulate is not always the case. Initial electron transfer plays a key role on some occasions, thus allowing smooth connection of contiguous quaternary carbon centers which would otherwise be difficult to achieve.[2,3]

Scheme I[a]



promotor 4	yield,% 3a	3b	3a/3b
4a (0.05 equiv)	85	0	100:0
4b (0.10 equiv)	95	0	100:0
4c (0.10 equiv)	93	0	100:0
4d (1.0 equiv)	98	2.4	97:3

[a] Reaction conditions: α-enone:ketene acetal:ketene acetal = 1:1:1, CH_2Cl_2, −78 °C, 4 h.

In the context of synthetic applications of organotin triflates as functional Lewis acids,[4] we conducted the crossover reaction of an equimolar mixture of ketene silyl acetal **2b** and its β,β-disubstituted derivative **2a** with a hindered α-enone **1** in the presence of a catalytic amount of $Bu_2Sn(OTf)_2$ (**4a**) (Scheme I). More sterically demanding **2a** reacted exclusively to give the adduct **3a** bearing contiguous quaternary carbon centers. The preference holds with other promotors, $SnCl_4$ (**4b**), Et_3SiClO_4 (**4c**),[5] and $TiCl_4$ (**4d**).[6]

These results cannot be interpreted in terms of the nucleophilic attack of ketene silyl acetals which should favor the coupling between less hindered carbons. In fact, RajanBabu revealed that the relevant thermal reaction in highly polar solvents which proceeds through nucleophilic attack of an ester enolate ion toward an α-enone exhibited a quite different tendency: crossover reaction of β,β-disubstituted and β-monosubstituted ketene silyl acetals with 2-cyclopentenone gave rise to the adducts derived from the respective ketene silyl acetals in a nearly equal ratio.[7] Since the preferred connection of more hindered carbons is characteristic of radical coupling,[3o] a plausible explanation is put forth by assuming an initial electron transfer. Scheme II representatively

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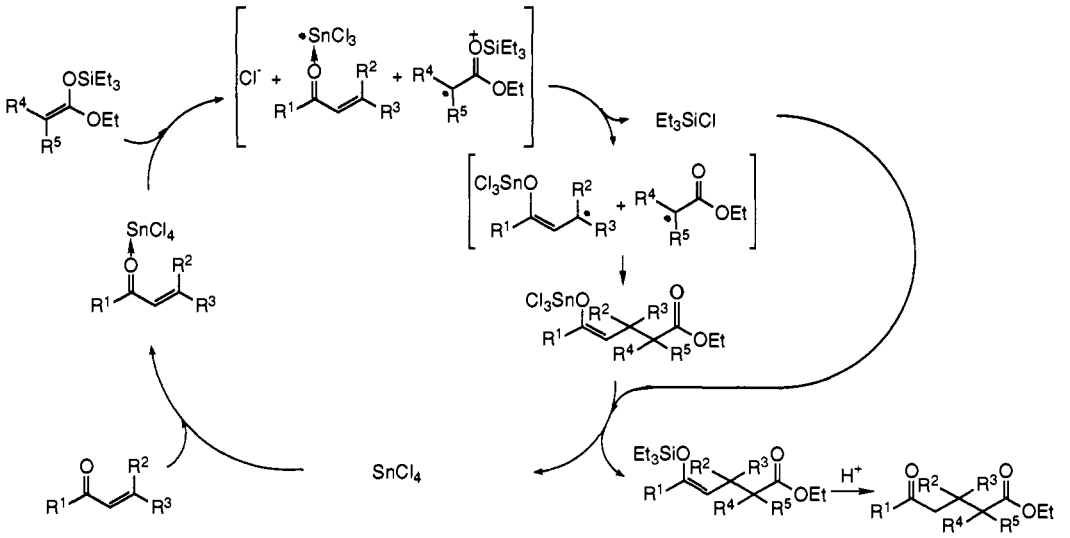
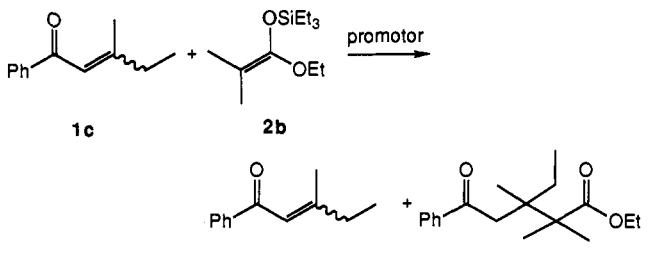
Scheme II



Scheme III



1c *E:Z*	promotor	conversion,%	1c-recovered *E:Z*
99:1	4a	44	90:10
	4b	74	92:8
1:99	4a	49	22:78
	4b	61	22:78

illustrates pathways for the $SnCl_4$-promoted reaction. A ketene silyl acetal is oxidized to a silyloxonium radical[8] while $SnCl_4$ coordinated by the α-enone is reduced to an $SnCl_4$ anion radical, which then undergoes spontaneous fragmentation to $^{\bullet}SnCl_3$ and Cl^-. The $^{\bullet}SnCl_3$ radical adds to α-enone to give a stannyl enol radical, which subsequently couples with the α-ethoxy carbonyl radical. The reaction with other promotors may proceed in a like manner.[9] The stannyl enolate thus formed is replaced by Et_3SiCl so that the catalytic cycle could be completed.[10] In this process, the close contact between sterically demanding reaction sites at an early stage is of no virtual importance.

Examination of the α-enone stereochemistry is consistent with involvement of the radicaloid species (Scheme III). When (*E*)- and (*Z*)-**5** were exposed to Lewis acids under conditions analogous to those employed for the Michael reaction, no isomerization was seen. Then, stereochemically pure **5** was treated with **2a**, and the reactions were quenched at low conversions. HPLC analyses of recovered **5** indicated that the *E*–*Z* isomerization had indeed occurred, consistent with the enol radical intermediacy.[11]

The unexpectedly facile one-electron oxidation of ketene silyl acetals was confirmed by photoinduced electron-transfer reactions to the singlet excited states of electron acceptors ($[Ru(bpy)_3]^{2+}$, pyrene, naphthalene, and 9,10-dicyanoanthrathene).[12] The strong electron-donating character is further demonstrated by the fact that **2a** can transfer an electron thermally to a mild one-electron oxidant, $Fe(C_5H_5)_2^+$ (k_{et} = 6.7 M^{-1} s^{-1} in CH_3CN at 298 K). On the basis of these observations, the one-electron oxidation potentials ($E°_{ox}$) and $\Delta G^{\ddagger}_0$ are obtained[13] as $E°_{ox}$ = 0.89 ± 0.05 and 1.29 ± 0.05 V (vs SCE), and $\Delta G^{\ddagger}_0$ = 5.3 ± 0.5 and 4.6 ± 0.5 kcal mol^{-1} for **2a** and **2b**, respectively.

Meanwhile, Lewis acids which are usually employed in the Mukaiyama reaction were not regarded as strong one-electron oxidants.[14] Yet ferrocene ($Fe(C_5H_5)_2$), a mild one-electron reductant, has proved to be readily oxidized by $SnCl_4$, Ph_3SiClO_4, and Et_3SiClO_4 to yield ferrocenium ion in CH_2Cl_2 at 298 K (k_{et} = 0.72, 0.21, and 1.0 × 10^{-2} M^{-1} s^{-1}, respectively). For the methyl-substituted ferrocenes, $Fe(MeC_5H_4)_2$ and $Fe(Me_5C_5)_2$, the rate constants with Et_3SiClO_4 (0.22 × 10^3 and 6.8 × 10^3 M^{-1} s^{-1}, respectively) increase with a decrease in the $E°_{ox}$ values of the ferrocenes.[15] To the best of our knowledge, this is the first example that reveals the tendency of the conventional Lewis acids to undergo facile one-electron reduction.

Since the hindered ketene silyl acetals can transfer an electron to $Fe(C_5H_5)_2^+$ efficiently and $Fe(C_5H_5)_2$ does so to the Lewis acids, the electron transfer from the hindered ketene silyl acetal to the Lewis acid is energetically allowed to occur. It should be noted that the enone **1** has no ability to oxidize the ferrocene derivatives.[16] In the presence of the Lewis acids, however, the one-electron oxidation of $Fe(C_5H_5)_2$ does occur,[17] a result consistent with the proposal that electron transfer occurs initially from a ketene silyl

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(16) The cyclic voltammogram of this compound indicated that the reduction in CH_2Cl_2 occurred at largely negative electrode potential, *E* (vs SCE) < −1.7 V.

(17) The rate constants of electron transfer from $Fe(C_5H_5)_2$ to the Lewis acids were somewhat diminished by the presence of **1** (for example, 1.6 × 10^{-3} M^{-1} s^{-1} in CH_2Cl_2 at 298 K with $SnCl_4$), suggestive of weak interactions between **1** and $SnCl_4$. Nevertheless, the cathodic peak potentials observed in the cyclic voltammograms of the **1**–Et_3SiClO_4 system in CH_2Cl_2 at 298 K exhibited no appreciable changes as compared with those of the superposition of each component at various sweep rates (20–500 mV s^{-1}), indicating that the susceptibility to the one-electron reduction of both components had not been altered significantly upon mixing.

acetal to a Lewis acid rather than to an α-enone. These results hence provide a rationale for the above mechanism on the basis of energetics.

In summary, the mechanism of the Mukaiyama reaction has never been examined from the standpoint of electron transfer. We conclude here that the Lewis acid mediated electron transfer from hindered ketene silyl acetals to α-enones plays an essential role in connecting quaternary carbon centers. The conclusion sheds light on a novel facet of the ketene silyl acetal chemistry, and consequently relevant reactions should be reexamined along this line, particularly in terms of stereochemistry.[18]

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectral data of **3a–c** and **7a,b**, results of the crossover reaction employing other ketene silyl acetals and an α-enone, and a figure exhibiting relations of the log k_{et} values with $E°_{red}$ or $E°_{ox}$ (3 pages). Ordering information is given on any current masthead page.

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Variable-Temperature Magnetic Circular Dichroism Spectroscopy as a Probe of the Electronic and Magnetic Properties of Nickel in Jack Bean Urease

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Urease catalyzes the hydrolysis of urea to yield ammonia and carbamate, which spontaneously hydrolyzes to form carbonic acid and a second molecule of ammonia.[1] The best characterized example is jack bean urease, which is a hexamer of identical 90 770-Da subunits,[2] each containing one catalytic site and two Ni(II) ions, which are required for activity.[3] Although information concerning the Ni(II) active site is now beginning to emerge, its structure and electronic properties are still poorly characterized. Weak absorption bands superimposed on the scattering background of the globular protein have been assigned to the spin-allowed d–d transitions of octahedral Ni(II),[4] and studies using X-ray absorption spectroscopy (XAS) are consistent with pseudooctahedral coordination by O or N donor atoms.[5]

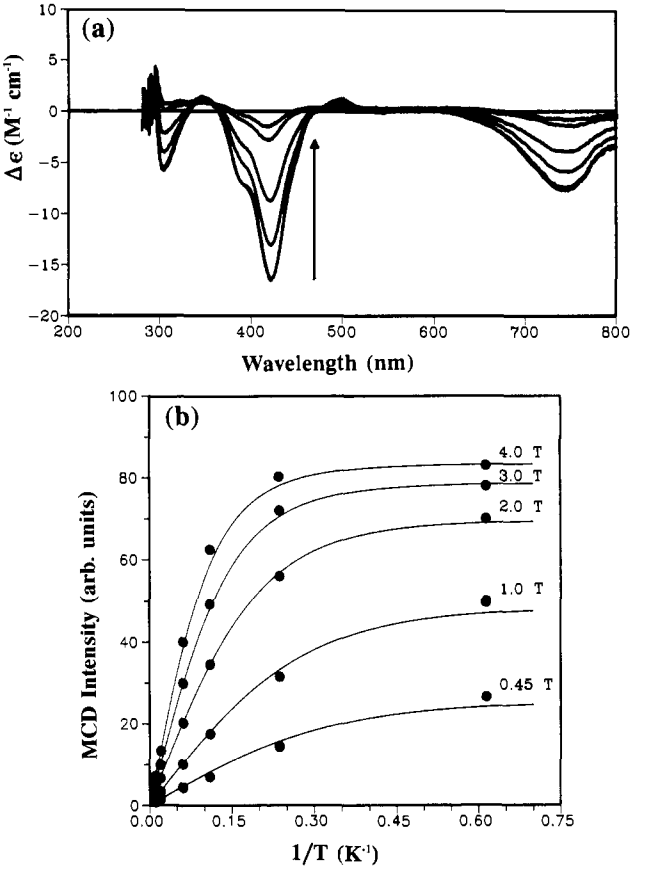

Figure 1. Variable-temperature MCD spectra of native jack bean urease. The urease sample, in 20 mM phosphate buffer containing 65% (v/v) glycerol, pH 6.6, was 2.8 mM in Ni. (a) MCD spectra with a magnetic field of 4.5 T at 1.63, 4.22, 9.1, 16, 49, and 91 K. The arrow indicates the direction of change in the MCD intensity with increasing temperature. (The spectra at 1.63 and 4.22 K are almost superimposed.) (b) Temperature dependence of the MCD intensity at 420 nm at 4.0, 3.0, 2.0, 1.0, and 0.45 T. Solid lines are the best fit to eq 6 of ref 14, with $g_\perp = 7.3$ and $\delta = 4.1$ cm^{-1}.

Evidence for a binuclear Ni(II) active site has come from magnetic susceptibility studies of jack bean urease which indicate that ~80% of the Ni(II) is in an antiferromagnetically exchange coupled binuclear active site ($J = -6.3$ cm^{-1}, using an isotropic exchange Hamiltonian $H = -2J\mathbf{S}_1\cdot\mathbf{S}_2$) with the remaining ~20% as magnetically isolated high spin ($S = 1$) Ni(II).[6] On binding of the competitive inhibitor 2-mercaptoethanol (2-ME, $K_i = 0.72 \pm 0.26$ mM at 25 °C[3b]) to the jack bean enzyme, a large decrease in paramagnetism is observed, and this has been ascribed to the formation of a strongly antiferromagnetically coupled binuclear Ni(II) center.[6] In contrast, subsequent magnetic susceptibility studies of native *Klebsiella aerogenes* urease were interpreted in terms of a mixture of low-spin ($S = 0$) and high-spin ($S = 1$) Ni(II) without invoking an exchange-coupled binuclear center.[7]

Here we report the results of variable-temperature MCD studies[8] of native and 2-ME-inhibited jack bean urease. The enzyme samples used in this work were prepared as previously reported,[6] contained 65% (v/v) glycerol, exhibited specific activities >75% of the maximum reported[9] (~2700 IU/mg), and contained

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