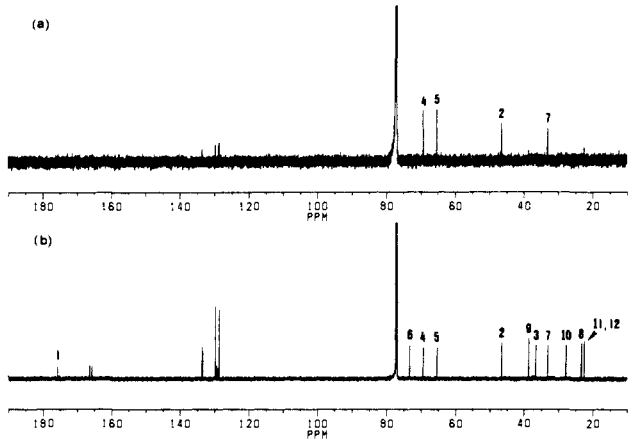

Figure 1. ^{13}C NMR spectra of **1a**: (a) derived from [1,3-^{13}C]glycerol (0.062 mg in 0.6 mL of $CDCl_3$, 18211 transients) and (b) natural abundance (3.0 mg in $CDCl_3$, 1515 transients).

(100 mg) was added to the culture twice at 24 and 48 h since the addition of it increased the yield of **1**. After a total of 96 h of incubation, the broth (10 × 100 mL) was treated with charcoal and SEP-PAK C_{18} cartridge to obtain the crude **1**. Benzoylation of crude **1** and further purification by HPLC gave 1 mg of **1a**.

Next, instead of sodium acetate, a mixture of sodium acetate (50 mg) and sodium [1-^{13}C]acetate (99 atom % ^{13}C, 50 mg) was administered to the culture (15 × 100 mL broth), and workup yielded 1.87 mg of **1a**. The 150.9-MHz ^{13}C NMR spectrum[10] of this sample showed enrichment at C-1 (6.6%) and C-6 (5.8%). Sodium [2-^{13}C]acetate (99 atom % ^{13}C, 50 mg) was fed next (15 × 100 mL broth), and the ^{13}C NMR spectrum of the obtained **1a** (1.88 mg) revealed enrichment at C-2 (10.7%) and C-7 (9.3%). In the next experiment, sodium [1-^{13}C]isovalerate[11] (2.5 mg) was fed (5 × 100 mL broths) eight times, so as to avoid the growth inhibition by too much addition of it at one time. The ^{13}C NMR spectrum of the obtained **1a** (0.33 mg) showed enrichment only at C-8 (7.3%), revealing that isovaleric acid was incorporated into the five carbons of **1** from C-8 to C-12.

Labeled glycerol was fed in a medium without glycerol in spite of a drastic decrease in the yield to avoid the high dilution of labeled glycerol. [1,3-^{13}C]Glycerol[12] (50 mg) was administered to the culture (5 × 100 mL broth) twice at 24 and 48 h, and 0.062 mg of **1a** was obtained. The ^{13}C NMR spectrum of **1a** (Figure 1) clearly showed enrichment at C-4 (6.2%) and C-5 (6.1%) and also C-2 (4.5%) and C-7 (3.7%) due to offshoot [2-^{13}C]acetate. Unfortunately, an expected two-bond coupling between C-4 and C-5 could not be observed under the measurement condition[10] because of its small value.[13] But its CI-MS spectrum revealed that non-, mono-, and di-^{13}C-labeled molecular species were present in it with the ratio of their relative abundances of 100:8.5:6.1.[14] Since the majority of dilabeled molecules must be the molecule labeled at C-4 and -5, and the mol % of a dilabeled one (5.3%) calibrated from the ratio was approximately consistent with the incorporation % estimated by NMR of C-4 (4.5%)[15] or C-5 (4.4%),[15] it was concluded that C-4 and C-5 resulted from an intact glycerol molecule.

(10) Spectra were taken on a Brucker AM 600 spectrometer with power gated broad band proton decoupling (sweep width = 38 462 Hz, 128 K data points, pulse width = 43°, acquisition time = 1.704 s). Each signal was unambiguously assigned by DEPT, COSY, and C-H COSY experiments.

(11) [1-^{13}C]Isovaleric acid was synthesized from $K^{13}CN$ (99 atom % ^{13}C) and isobutyl bromide.

(12) [1,3-^{13}C]Glycerol (77 atom % ^{13}C at C-1, 99 atom % ^{13}C at C-3) was synthesized from $K^{13}CN$ and sodium [1-^{13}C]acetate (99.4 atom % ^{13}C) as described in the following: Chen, T. S. S.; Chang, C.; Floss, H. G. *J. Am. Chem. Soc.* **1981**, *103*, 4565-4568.

(13) Marshall, J. L. In *Methods in Stereochemical Analysis*; Marchand, A. P., Ed.; Verlag Chemie International: FL, 1983; Vol. 2, pp 193-195.

(14) Caprioli, R. M. *Biochemical Applications of Mass Spectrometry*; Wiley: New York, 1972; pp 735-776.

(15) These values were deduced from the enrichment % of peaks and the contamination % of [1-^{13}C]glycerol.

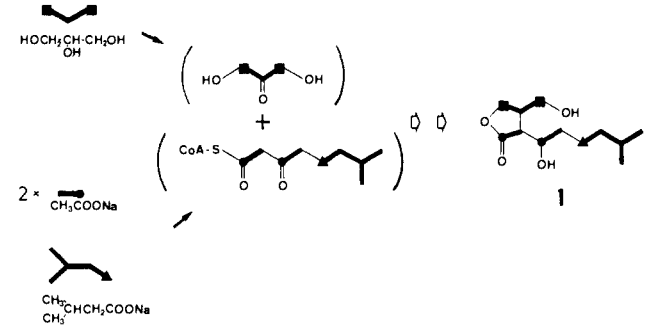

Figure 2. Biosynthetic origin of **1**.

The origin of the skeleton of **1** is summarized in Figure 2, and we believe that these subunits except for isovaleric acid moiety are common in all signal molecules of 2-(1′-hydroxyalkyl)-3-(hydroxymethyl)butanolides produced by *Streptomyces*. A probable route for its formation is a reductive coupling between the β-ketoacid started from isovaleryl-CoA and the C_3 unit from glycerol, such as dihydroxyacetone or its derivatives (Figure 2). Work to prove this hypothesis is now in progress.

Acknowledgment. This work is supported in part by a Grant-in-Aid for scientific research (No. 1760093) from the Ministry of Education.

Registry No. **1**, 109215-47-6; $HOCH_2CH(OH)CH_2OH$, 56-81-5; acetic acid, 64-19-7; isovaleric acid, 503-74-2.

A Water-Stable Manganese(V)-Oxo Complex: Definitive Assignment of a $\nu_{Mn^V=O}$ Infrared Vibration

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Although there are over 120 000 entries in the *Chemical Abstracts Formula Index* for manganese, fewer than ten unique fully characterized species of manganese(V), -(VI), and -(VII) are stable under normal conditions.[2,3] The preponderance of lower oxidation state compounds is typical of the middle and later transition metals, yet the rareness of higher oxidation state complexes does not imply lack of importance. These compounds provide the major source of prima facie metallooxidants,[3] and in manganese chemistry, permanganate is a classic example. Manganese(V)-oxo complexes are the subject of considerable current interest as reactive intermediates in oxidation reactions with porphyrin[4a-c] and salen[4d] systems, and manganese-oxo complexes of a number of lower oxidation states have a probable role in the oxygen-evolving complex in photosynthesis.[5] Man-

(1) (a) Dreyfus Teacher-Scholar, 1986-1990; Alfred P. Sloan Research Fellow, 1986-1989. (b) California Institute of Technology; current address, Department of Chemistry, Carnegie Mellon University.

(2) (a) Nugent, W. A.; Mayer, J. M. *Metal-Ligand Multiple Bonds*; Wiley-Interscience: New York, 1988. (b) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley: New York, 1988.

(3) Collins, T. J.; Gordon-Wylie, S. W. *J. Am. Chem. Soc.* **1989**, *111*, 4511-4513.

(4) For a set of references on this rapidly developing area, see: (a) Groves, J. T.; Stern, M. K. *J. Am. Chem. Soc.* **1988**, *110*, 8628-8638. Also see: (b) Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. *J. Chem. Soc., Chem. Commun.* **1989**, 779-780. (c) Holm, R. H. *Chem. Rev.* **1987**, *87*, 1401-1449. (d) Srinivasan, K.; Michaud, P.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 2309-2320.

(5) (a) Amesz, J. *Biochim. Biophys. Acta* **1983**, *726*, 1-12. (b) Babcock, G. T. In *New Comprehensive Biochemistry—Photosynthesis*; Amesz, J., Ed.; Elsevier: Amsterdam, 1988. (c) Pecoraro, V. L. *Photochem. Photobiol.* **1988**, *48*, 249-264.

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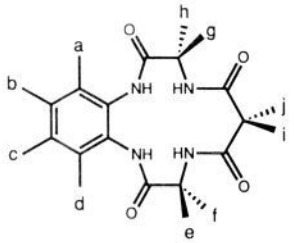

Figure 1. Macrocyclic tetraamide ligands $H_4[L]$ showing modifiable positions. For $H_4[\mathbf{1}]$, a = d = H, b = c = Cl, e = f = g = h = CH_3, i = j = CH_2CH_3.

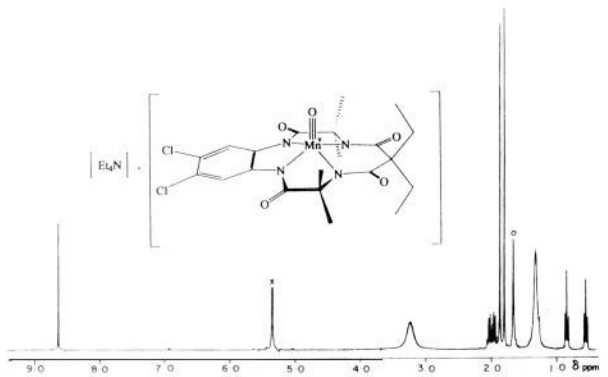

Figure 2. ^1H NMR (300 MHz, CD_2Cl_2) spectrum of $[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$ [δ ppm: 8.59, s, 2 H (aromatic); 3.23, br, 8 H ($[CH_3CH_2)_4N]^+$); 2.02, q, 2 H (CH_3CH_2); 1.94, q, 2 H (CH_3CH_2); 1.86, s, 6 H ($C(CH_3)CH_3$); 1.80, s, 6 H ($C(CH_3)(CH_3)$); 1.35, br, 12 H ($[(CH_3CH_2)_4N]^+$); 0.86, t, 3 H (CH_3CH_2); 0.56, t, 3 H (CH_3CH_2) (x = $CHDCl_2$ signals, used as reference; o = H_2O)].

ganese is also present in the active sites of several enzymes that catalyze redox reactions of oxygen species: manganese superoxide dismutase[6] and azide-insensitive catalase.[7] The scarcity of highly oxidized middle- and later-transition-metal complexes challenges chemists to develop ligand complements compatible with oxidizing metal centers.

Recently we reported the synthesis of the first stable manganese(V)–monooxo species[3] supported by an acyclic polyanionic chelating ligand.[8] Unfortunately, this compound is not stable in water, and a major goal has been to develop systems compatible with aqueous environments. Here we describe a manganese(V)–monooxo complex of a new macrocyclic tetraamide, $[Mn(O)(\eta^4\text{-}\mathbf{1})]^-$, which is water-stable. The oxo ligand exchanges in ^{18}O-labeled water, permitting the first assignment of a $\nu_{Mn=O}$ infrared vibration.

$[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$ was prepared as follows: $H_4[\mathbf{1}]$ (58 mg, 0.12 mmol, Figure 1) was dissolved in dry, deoxygenated THF, and a stoichiometric amount of lithium bis(trimethylsilyl)amide (1.0 M solution in THF) was added at 20 °C under N_2 and stirred (5 min). A 25% excess of anhydrous $MnCl_2$ was added, and the mixture was stirred (2 h), to yield a yellowish-white suspension, presumably a manganese(II) complex. A 5-fold excess of *tert*-butyl hydroperoxide (3.0 M solution in 2,2,4-trimethylpentane) was added, and the mixture was stirred overnight, to yield a dark greenish-brown solution. The solvents were removed under vacuum, and the solid residue was washed with CH_2Cl_2, extracted with CH_3CN, and passed through a diatomaceous earth pad, to give $Li[Mn(O)(\eta^4\text{-}\mathbf{1})]$ (yield approximately 75%). A stoichiometric amount of $[Et_4N]Cl$ was added to a CH_3CN solution of the complex, and the CH_3CN was then removed in vacuo. The residue was extracted with CH_2Cl_2, to yield a solution of $[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$, which gave green X-ray quality crystals from CH_2Cl_2/C_6H_6. The ^1H NMR spectrum in CD_2Cl_2 (Figure 2) shows that $[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$ is diamagnetic and possesses the C_s symmetry expected for a low-spin d^2 square-pyramidal complex with a triply bonded axial oxo ligand. An oxygen-18-substituted species was produced by dissolving $Li[Mn(O)(\eta^4\text{-}\mathbf{1})]$ (10 mg) in $H_2{}^{18}O$ (1 mL), stirring for 48 h under N_2, removing the excess water in vacuo, and then crystallizing as the $[Et_4N]^+$ salt as described above. The pertinent IR data for the $\nu_{Mn=O}$ bands are as follows: ^{16}O-labeled, 979 cm^{-1}; ^{18}O-labeled, 942 cm^{-1}. The vibrational properties of high-spin d^3 $Mn^{IV}{=}O$ units in porphyrin complexes were recently determined by IR and resonance Raman spectroscopy.[9] For the five-coordinate species in that study, $\nu_{Mn=O}$ occurs at the notably low frequency of 754 cm^{-1}.

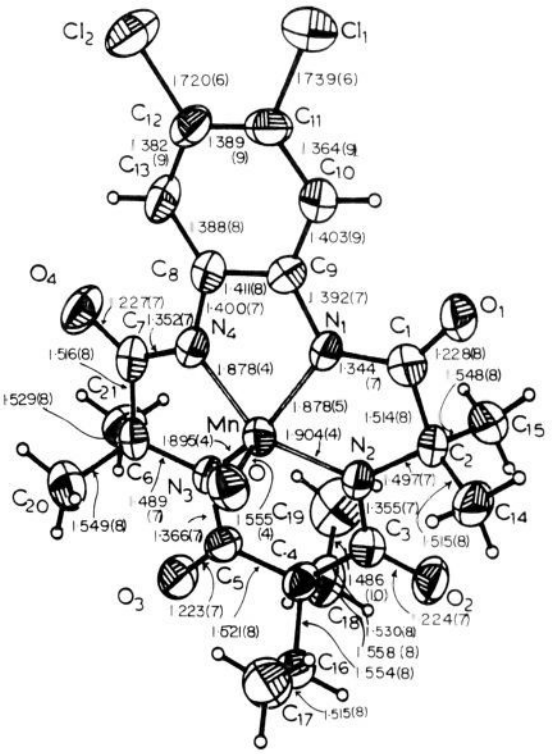

Figure 3. Molecular structure of $[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$; ORTEP drawing with all nonhydrogen atoms drawn to encompass 50% of electron density.

The results of the structural study for $[Et_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$ are shown in Figure 3.[10] The Mn≡O distance of 1.555 (4) Å is similar to the distance in our previously reported complex (1.548 (4) Å).[3] The four nitrogens lie nearly in a plane (largest deviation 0.026 Å), and the manganese atom sits 0.60 Å above the mean plane, virtually equidistant from all four nitrogens (1.878 (5) Å from both aromatic amide nitrogens and 1.904 (4) and 1.895 (4) Å from the aliphatic amide nitrogens). The bond distances in the benzene ring are consistent with an aromatic unit, and the bond distances from the ring to the amide nitrogen atoms are consistent with a single bond between the two sp^2 atoms.

(6) Ludwig, M.; Pattridge, K. A.; Stallings, W. C. *Manganese in Metabolism and Enzyme Function*; Academic Press: New York, 1986; Chapter 21, p 405.

(7) Beyer, W., Jr.; Frodovich, I. *Manganese in Metabolism and Enzyme Function*; Academic Press: New York, 1986; Chapter 12, p 193.

(8) (a) Anson, F. C.; Christie, J. A.; Collins, T. J.; Coots, R. J.; Furutani, T. T.; Gipson, S. L.; Keech, J. T.; Krafft, T. E.; Santarsiero, B. D.; Spies, G. H. *J. Am. Chem. Soc.* **1984**, *106*, 4460–4472. (b) Anson, F. C.; Collins, T. J.; Richmond, T. G.; Santarsiero, B. D.; Toth, J. E.; Treco, B. G. R. T. *J. Am. Chem. Soc.* **1987**, *109*, 2974–2979.

(9) Czernuszewicz, R. S.; Su, Y. O.; Stern, M. K.; Macor, K. A.; Kim, D.; Groves, J. T.; Spiro, T. G. *J. Am. Chem. Soc.* **1988**, *110*, 4158–4165.

(10) Crystal data: The structure was solved by Crystalytics Company. Single crystals of $[(C_2H_5)_4N][Mn(O)(\eta^4\text{-}\mathbf{1})]$ at 20 ± 1 °C are monoclinic, space group $P2_1/c\text{-}C_{2h}^5$ (No. 14) with a = 9.853 (2) Å, b = 14.890 (3) Å, c = 22.432 (5) Å, β = 95.43 (1)°, V = 3276 (1) Å^3, and Z = 4 (d_{calcd} = 1.356 g cm^{-3}; μ_a(CuK$\bar{\alpha}$) = 5.2 mm^{-1}). A total of 4505 independent absorption-corrected reflections having 2θ(CuK$\bar{\alpha}$) < 115.0° were collected using θ–2θ scans and Ni-filtered Cu K$\bar{\alpha}$ radiation. The structural parameters have been refined to a convergence of R_1 (unweighted, based on F) = 0.046 for 2447 independent reflections having $2\theta_{CuK\bar{\alpha}}$ < 115.0° and $I > 3\sigma(I)$. Figure 2 does not show the disorder in the Mn–O unit (92% "above" the plane and 8% "below" the plane).

The macrocyclic tetraamido-*N* ligand class used here is unique. In spite of the voluminous literature of macrocyclic polyamines and Schiff bases, only one example, prior to our work, of a complex of a macrocyclic tetraamido-*N* ligand (a cyclic tetrapeptide) has been reported (as part of a classic study of copper(III) chemistry by Margerum et al.[11,12]). That copper(III) complex proved susceptible to degradation via chemistry involving hydrogen substituents β to the amido-*N* donor.[11b] The ligand class shown in Figure 1 possesses no β-hydrogens and can be systematically varied at the "a" through "j" positions. We are currently studying the reactions and physical properties of these unprecedented oxo complexes and the broader chemistry of a family of complexes of the tetraamide ligands.

Acknowledgment. We gratefully acknowledge the National Science Foundation (Grant No. CHE-8714720) for support. E.S.U. thanks Sonny Lee for useful discussions and the NSF for a Predoctoral Fellowship (1984-1987).

Supplementary Material Available: A listing of atomic coordinates, anisotropic thermal parameters for non-hydrogen atoms, bond lengths involving non-hydrogen atoms, bond angles involving non-hydrogen atoms, and complete details of the analysis of $[Et_4N][Mn(O)(\eta^4\text{-}1)]$ (29 pages); a listing of structure factor amplitudes for $[Et_4N][Mn(O)(\eta^4\text{-}1)]$ (12 pages). Ordering information is given on any current masthead page.

(11) (a) Margerum, D. W.; Rybka, J. S. *Inorg. Chem.* **1980**, *19*, 2784-2790. (b) Rybka, J. S.; Margerum, D. W. *Inorg. Chem.* **1981**, *20*, 1453-1458.

(12) For a summary of work performed with macrocyclic ligands containing one, two, or three amides, see: Kimura, E. *J. Coord. Chem.* **1986**, *15*, 1-28.

Organotin Triflate Promoted Carbonyl Activation. Does Acetalization Deactivate or Activate Carbonyl Groups?

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Addition of nucleophiles to carbonyl groups constitutes one of the most fundamental reactions in organic synthesis. Mukaiyama found acetals to serve as carbonyl equivalents in the Lewis acid promoted reaction with enol silyl ethers.[1] In this respect, acetalization works not to protect (or deactivate) but to activate carbonyls. It would be of great synthetic value if we could control at will reactivities of carbonyls through acetalization. As an example along this line, Noyori et al. reported that trimethylsilyl triflate (TMSOTf) was milder than the usual Lewis acids to preferentially promote the reaction of acetals with enol silyl ethers in competing reactions with a carbonyl compound.[2] Reetz,[3] and Yamamoto[4] later, disclosed that an aldehyde underwent selective protection through titanium or aluminum amide mediated aminoacetalization, leaving a coexisting ketone intact, and subsequently the ketone was alkylated. Luche also utilized the same concept for the selective $NaBH_4$ reduction of ketones in the presence of an aldehyde which was preferentially deactivated as a hydrated form with the aid of $CeCl_3$.[5] Now we have found that dibutyltin bis(triflate) (**1**) catalyzes the reaction with a variety of silyl nucleophiles in a quite unusual manner leading to synthetically promising differentiation of carbonyl groups. Namely, in contrast to smooth reaction with aldehydes, no reaction takes place with ketones. However, through acetalization, ketones are activated and are capable of undergoing addition of silyl nucleophiles while aldehydes are deactivated, giving rise to inert acetals. This finding has allowed ketones to react in preference to an aldehyde in a one-pot manner.

Scheme I

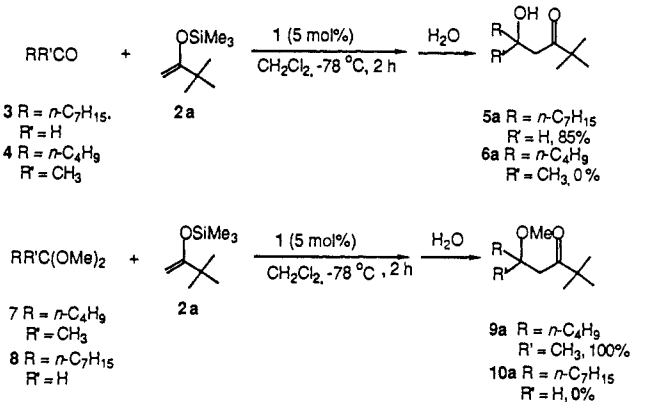
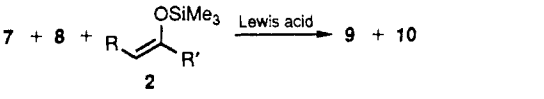


Table I. Crossover Aldol Reaction between Acetals of Ketone and Aldehyde[a]



2			yield,[b] %		
R	R'	Lewis acid[c]	9	10	9:10
H	C_6H_5	**1** (0.05)	78	1	99:1
CH_3	C_2H_5	**1** (0.05)	80	1	99:1
H	t-C_4H_9	**1** (0.05)	80	0	100:0
		$TiCl_4$ (1.0)	28	8	78:22
		$SnCl_4$ (1.0)	72	28	72:28
		$AlCl_3$ (1.0)	30	21	58:42
		TMSOTf (0.1)	50	9	85:15
		$TrClO_4$ (0.1)	49	6	89:11
		$SnCl_2$ (0.1)-TMSCl (0.2)	37	13	74:26
		CF_3SO_3H (0.1)	81	19	81:19

[a] Reaction conditions: **7**:**8**:**2** = 1:1:1, dichloromethane, -78 °C, 2 h. [b] Determined on the basis of GLC analysis. [c] The amount employed is given in parentheses.

Exposure of octanal (**3**) to the enol silyl ether **2a** in the presence of **1**[6,7] at -78 °C afforded the aldol product **5a** in 80% yield after column chromatographic isolation while no reaction occurred with 2-hexanone (**4**) (Scheme I),[8] in accord with the known relative reactivities of aldehydes and ketones. Note, however, that TMSOTf failed to activate either type of carbonyl under similar conditions.[2] In this sense, **1** is more active than the silicon analogue.

Next, acetals were subjected to the same reaction (Scheme I). The ketone acetal **7** reacted smoothly while the aldehyde acetal **8** reacted quite sluggishly. Other enol ethers gave similar results (Table I). Of more importance is the fact that no such distinct discrimination was observed with other Lewis acids such as $TiCl_4$,[9] $SnCl_4$, $AlCl_3$, TMSOTf,[10] trityl perchlorate ($TrClO_4$),[11]

(1) Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043.

(2) Murata, S.; Suzuki, M.; Noyori, R. *Tetrahedron* **1988**, *44*, 4259.

(3) Reetz, M. T.; Wenderoth, B.; Peter, R. *J. Chem. Soc., Chem. Commun.* **1983**, 406. Reetz, M. T.; Wenderoth, B. *Tetrahedron Lett.* **1982**, *23*, 5259. Okazoe, T.; Hibino, J.; Takai, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5581.

(4) Maruoka, K.; Araki, Y.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 3101.

(5) Luche, J.-L.; Gemal, A. L. *J. Am. Chem. Soc.* **1979**, *101*, 5848.

(6) $Bu_2Sn(OTf)_2$ was prepared easily from Bu_2SnCl_2 and AgOTf: Schmeisser, M.; Sartori, P.; Lippsmeier, B. *Chem. Ber.* **1970**, *103*, 868.

(7) For precedent application of **1** to selective reactions, see: Sato, T.; Yoshida, E.; Kobayashi, T.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1988**, *29*, 3971.

(8) All the products in this study were confirmed by comparison with authentic specimens.

(9) Mukaiyama, T.; Murakami, M. *Chem. Lett.* **1974**, 15. Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1976**, 769. Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941.

(10) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1979**, *101*, 2738. Noyori, R.; Murata, S.; Suzuki, M. *Tetrahedron* **1981**, *37*, 3899.

0002-7863/90/1512-901$02.50/0