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Organotin Triflate as Practical Catalyst for Michael Addition of Enol Silyl Ethers

Tsuneo Sato, Yoshiyuki Wakahara, Junzo Otera,* and Hitosi Nozaki

Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700, Japan

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Abstract: Dibutyltin bis(triflate) is a mild Lewis acid which catalyzes clean Michael addition of enol silyl ethers. The new catalyst allows to employ various labile acceptors such as methyl vinyl ketone and 2-cyclopentenone which do not undergo smooth reaction with conventional Lewis acids. A variety of enol silyl ethers are also employable and thus 2-(trimethylsiloxy)propene, the simplest one in this class of compounds, can be used. The adducts of enol silyl ethers of cycloalkanones with vinyl ketones are readily cyclized to give the desired annulated enones free from isomers. Consequently, a practical version of the Robinson annulation has been realized.

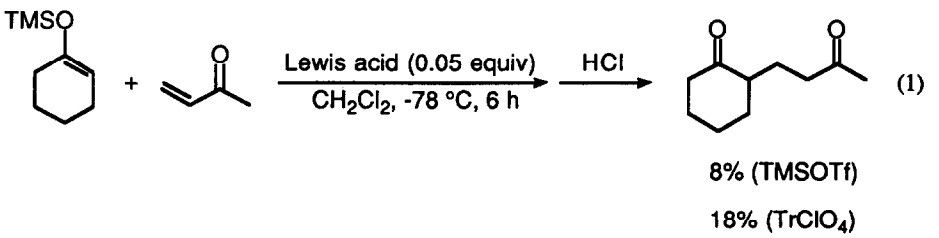
Introduction

The Lewis acid-promoted Michael addition of enol silyl ethers to α-enones originally devised by Mukaiyama et al. plays an important role in modern synthetic organic chemistry.[1] The Mukaiyama modification is of great significance in that it has enabled the Michael reaction to proceed under acidic conditions, otherwise the reaction had to be conducted under basic conditions.[2] As a result of this alteration, we are now able to deal with base-sensitive substrates. However, this advantage is naturally counterbalanced by the drawback that restricts to use acid-sensitive substrates. Despite a number of efforts devoted to overcome this disadvantage, particularly focusing on development of milder Lewis acids, there still remain considerable limitations.[3,4] For instance, methyl vinyl ketone, the simplest α-enone, cannot be employed due to its high tendency to polymerize under acidic conditions. Mukaiyama et al.[1], and Huffman et al.[5] later, reported successful results with methyl vinyl ketone acetal but the unproteced one was not their choice except for the reaction with 2-dimethyl-1-(trimethylsiloxy)propene.[5] Another precedent which met with exceptional but limited success is the reaction with 1-[1-(trimethylsiloxy)vinyl]cyclohexene as a silyl enolate component reported by Uda et al.[6] They screened Lewis acids and obtained the best result with Et_2AlCl (3 equiv, 56% yield). 2-Cycloalkenones are also difficult to work as Michael acceptors. For example, 2-cyclopentenone is highly acid-labile and therefore Michael addition of ketone enolates has not been reported though there appeared the reaction of more nucleophilic ketene silyl acetals with the aid of fluoride ion or by thermal treatment in a polar solvent.[7] A restriction exists also with respect to the enol silyl ether component in the conventional methods. For example, the silyl enolate of acetone which may serve as an acetonylating reagent is highly hydrolyzable and an only successful usage of this reagent has been reported with a $TiCl_4$-$Ti(OPr^i)_4$ promotor.[1]

We previously disclosed organotin triflates to be mild Lewis acids effective for thiostannane-mediated 1,3-dithiane synthesis[8] and aldol-type reaction of enol silyl ethers.[9] In these reactions, delicate reactivity differences between aldehyde and ketones or between their acetals could be discriminated in an unprecedented manner. The present study stemmed from the expectation that such unique mildness of organotin triflates should give a clue to solve the problems encountered in the Michael-type reaction. Indeed we have discovered that $Bu_2Sn(OTf)_2$ (**1**) smoothly catalyzes reaction of a variety of hitherto unemployable acceptors and donors.[10]

Results and Discussion

Methyl Vinyl Ketone Acceptor. Treatment of 1-(trimethylsiloxy)cyclohexene (**2a**) (1 equiv) with methyl vinyl ketone (1.3 equiv) in the presence of **1** (0.05 equiv) furnishes the desired Michael adduct **3a** in 70% yield (Table 1). The reaction is clean and no polymerization of the vinyl ketone is detected. This is the first example of coupling between cyclohexanone and unmasked methyl vinyl ketone (vide infra). The reaction of the corresponding cyclopentanone enolate (**2f**) also proceeds smoothly but in somewhat lower yield. Reasonable yields of the adducts are obtained with substituted cyclohexanone derivatives. Of synthetic importance is the perfect regioselectivities with methylcyclohexanones **2c** and **2d** because the reaction under basic or acidic conditions results in preferential incorporation of an enolate moiety at the more hindered carbon. An acyclic enol silyl ether **2g** and a ketene silyl acetal **2h** are employable as well. The speciality of **1** as a Lewis acid promotor is highlighted by comparison with the other promotors which are believed to be relatively mild. As shown in eq. 1, trimethylsilyl triflate (TMSOTf) and trityl perchlorate ($TrClO_4$), under analogous conditions, furnishes only 8% and 18% yields, respectively.



It is to be noted that the clean reaction takes place as well with α-enones other than methyl vinyl ketones (eqs. 2 and 3).

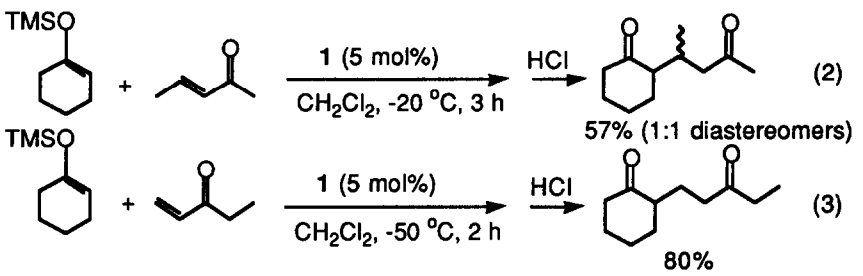
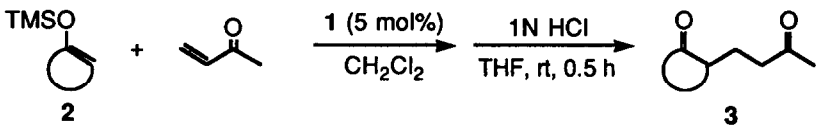
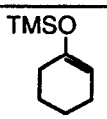
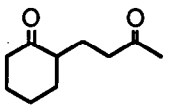
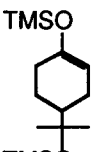
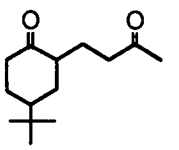
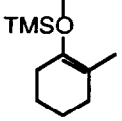
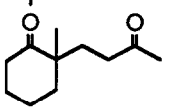
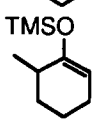
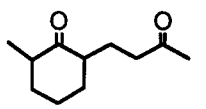
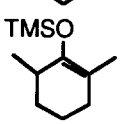
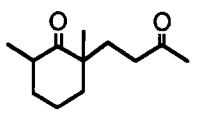
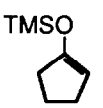
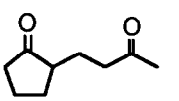
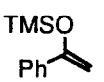
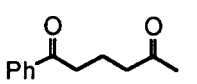
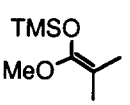
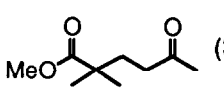


Table 1. Michael Addition of Sily Enol Ethers to Methyl Vinyl Ketone.



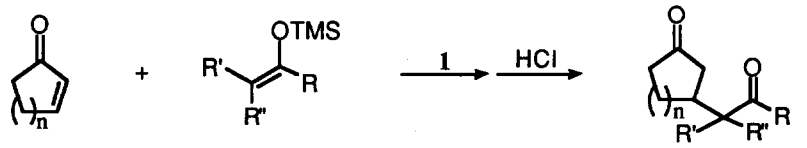
2 3

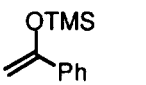
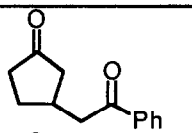
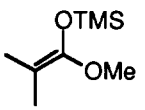
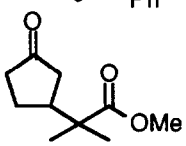
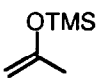
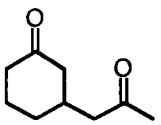
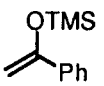
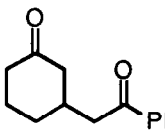
entry	2	conditions	3	yield,%
1	 (2a)	-78 °C, 5 h	 (3a)	70
2	 (2b)	-78 °C, 10 h	 (3b)	76[a]
3	 (2c)	-78 °C, 3 h	 (3c)	64
4	 (2d)	-50 °C, 6 h	 (3d)	77[b]
5	 (2e)	-50 °C, 3 h	 (3e)	61[c]
6	 (2f)	-78 °C, 5 h	 (3f)	61
7	 (2g)	-78 °C, 2 h	 (3g)	98
8	 (2h)	-78 °C, 4 h	 (3h)	71

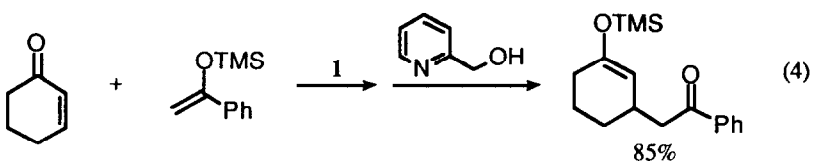
[a] *cis-trans* Mixture (63:37). [b] *cis-trans* Mixture (16:84).
[c] Mixture (78:22). Stereochemistry has not been assigned.

2-Cycloalkenone Acceptors. 2-Cyclopentenone (**4**) undergoes the 1,4-addition with **2g** to give the adducts in 70% yield (Table 2). A smooth reaction occurs with ketene silyl acetal **2h**, too. Furthermore, 2-cyclohexenone (**5**) works as an acceptor. Note that the enol silyl ether of acetone (**2i**) provides a good yield of the Michael product. The reaction with 2-cycloakenones proceeds smoothly in toluene as well as CH_2Cl_2 in the presence of 5 mol% of **1**. However, increase of the catalyst concentration to 10 mol% accelerates the reaction rate efficiently. When the reaction is quenched with 2-(hydroxymethyl)pyridine[4b,d] in place of aqueous HCl, a silyl enol ether is accesible (eq. 4). It follows that the catalysis is driven by transmetallation of a stannyl enolate intermediate by TMSOTf which has been generated in situ . Since we have already proved that TMSOTf is not effective for this sort of reaction, **1** no doubt plays a crucial role for promoting the reaction.

Table 2. Michael Addition of 2-Cyclopentenone and -hexenone.



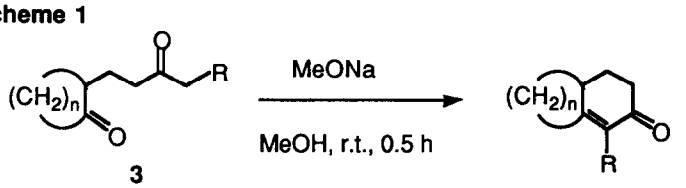
enone	enol silyl ether		product	yield,%
4 (n = 1)		(**2g**)		70
		(**2h**)		75
5 (n = 2)		(**2i**)		78
		(**2g**)		92



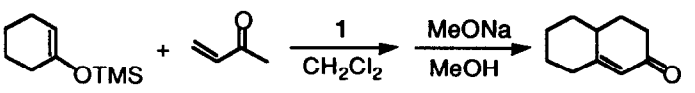
Robinson Annulation. The Robinson annulation is a classical but still widely used methodology for synthesis of polycyclic compounds.[11] Unfortunately, however, the original procedure consisting of Michael addition of enolates to α,β-unsaturated systems suffers from some restrictions.[12] Under highly basic conditions, some of the acceptors readily polymerize and intermediary enolates frequently undergo intramolecular proton transfer resulting in dialkylation. For example, methyl vinyl ketone, the most commonly demanded acceptor, is susceptible to these side reactions. In fact, the coupling of cyclohexanone with methyl vinyl ketone has seldom been realized although this is the simplest donor-acceptor combination. Several improvements have appeared. Marshall et al. isolated ketols which were then dehydrated to the final products.[13] This procedure afforded the ketol from 2-methylcyclohexanone and methyl vinyl ketone in 52% yield, but resulted in only a 17% yield for the cyclohexanone-methyl vinyl ketone reaction. Heathcock et al. utilized acidic conditions (H_2SO_4) to obtain the methylcyclohexanone-methyl vinyl ketone adduct in 55% yield, but did not refer to the cyclohexanone-methyl vinyl ketone combination.[14] Modification of acceptors has been performed with Mannich bases,[15] β-haloketones,[16] β-alkoxyketones,[17] and a methyl vinyl ketone-iron complex[18] which work to some extent. The successful cyclohexanone-methyl vinyl ketone coupling to give pure $\Delta^{1,9}$-octalone-2 was achieved only by employing α-silylated methyl vinyl ketone.[19,20] Stork et al. also devised the enamine method.[21] Despite considerable success, this method encounters double bond migration of the cyclohexanone-methyl vinyl ketone adduct.

With an efficient tool for coupling these two components in hand, we have turned our attention to cyclize the Michael adduct. Treatment of **3** with sodium methoxide in MeOH at room temperature furnishes the desired annulation products in excellent yields (Scheme 1).[22]

Scheme 1



Of more synthetic significance is a one-pot synthesis of $\Delta^{1,9}$-octalone-2 directly from the enol silyl ether of cyclohexanone and methyl vinyl ketone (eq. 5). A mixture of these two reactants in a 1.3:1 molar ratio[23] was stirred in dichloromethane containing 0.05 equiv of **1** at -78 °C. After 5 h, MeONa in methanol was added to this solution, and then, the mixture was stirred at room temperature for 3 h. Usual workup provided the octalone in 89 % yield based on methyl vinyl ketone. The product is entirely free from isomers which are frequently encountered in the conventional methods.[21]



(5)

In conclusion, organotin triflate is acidic enough to trigger the Michael addition but moderate enough that polymerization of α-enones and double alkylation are completely suppressed. Consequently, the serious side reactions which otherwise are liable to occur are retarded in the present case.

Experimental

NMR spectra were recorded on JEOL JNM-FX 100 and GSX-400 spectrometers. Mass spectra were obtained with a JEOL JMS-DX 303-HF mass spectrometer using electron impact ionization. IR spectra were measured with a Hitachi 260-10 infrared spectrometer. GLC analysis was performed on a Shimadzu GC-14A capillary gas chromatograph with Shimadzu CBP-10 (0.25 x 25000 mm). High performance liquid chromatography (HPLC) was performed on a Shimadzu LC-8A with Develosil Si 30 (30 μm, 50 x 3000 mm). Column chromatography was performed on Kieselgel 60 (70-230 mesh) (E. Merck). TLC was carried out on Merck Kieselgel 60 F_{254}. All solvents were purified by standard methods before use. Ethyl vinyl ketone, 2-cyclopentenone, 2-cyclohexenone, sodium methoxide, and TMSOTf were purchased from Aldrich. 2-(Trimethylsiloxy)propene (**2i**) was obtained from Shin-etsu Silicon Chemicals and other reagents were from Wako Chemicals and Tokyo Kasei Kogyo. These commercially available reagents were used without purification. The following compounds were prepared according to the methods described in literatures: **2a**,[24] **2b**,[24] **2d**,[24] **2e**,[24] **2f**,[24] **2g**,[24] **2c**,[25] **2h**,[26] 2-(3-oxopentyl)cyclohexanone,[21] 2-(3-oxobutyl)cyclopentanone,[19] 2-(3-oxobutyl)cyclohexanone,[19] 2-methyl-2-(3-oxobutyl)cyclohexanone,[19] 2,6-dimethyl-2-(3-oxobutyl)cyclohexanone,[19] $\Delta^{1,9}$-octalone-2,[21] $\Delta^{9,10}$-octalone-2[21] [IR (CCl_4) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.62 (m, 4H), 1.89 (m, 2H), 1.97 (m, 2H), 2.35 (m, 2H), 2.48 (t-like, J = 6.60 Hz, 2H), 2.73 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.0, 22.5, 29.3, 29.4, 30.3, 38.5, 44.0, 125.4, 128.2, 210.2], 1-methyl-$\Delta^{1,9}$-octalone-2,[21] 5,6,7,8-tetrahydroindanone-5,[21] $TrClO_4$,[27] 6-methyl-2-(3-oxobutyl)cyclohexanone,[28] 1-phenyl-1,5-hexanedione,[1a,b] 3-[1-(methoxycarbonyl)-1-methylethyl]cyclopentanone,[7c] 3-(2-oxo-2-phenylethyl)-cyclohexanone,[1a,b,4a] and **1**.[29]

Reaction of 1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone in the presence of 1. A mixture of 1-(trimethylsiloxy)cyclohexene (170 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 5 h. The reaction mixture was combined with aqueous $NaHCO_3$ and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and evaporated. The resulting oil was treated with 1N HCl (1 ml)-THF (3 ml) at room temperature for 0.5 h, and quenched with aqueous $NaHCO_3$. Extraction with ethyl acetate, drying the organic layer (Na_2SO_4), and evaporation left an oil. Column chromatography (93:7 hexane-ethyl acetate) of this oil afforded 2-(3-oxobutyl)cyclohexanone (**3a**) (117 mg, 70%) having the identical spectral data with those of the authentic sample separately prepared by the literature method;[19] IR (CCl_4) 1713 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35-1.55 (m, 2H), 1.60-1.75 (m, 2H), 1.80-2.10 (m, 4H), 2.12 (s, 3H), 2.25-2.60 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.4, 24.7, 27.8, 29.5, 34.1, 41.0, 41.8, 49.4, 208.5, 212.6; MS (*m/z*) 168 (M^+); HRMS calcd for $C_{10}H_{16}O_2$ (M^+) 168.1150, found 168.1129.

Reaction of 1-(trimethylsiloxy)cyclopentene with methyl vinyl ketone. A mixture of 1-(trimethylsiloxy)cyclopentene (156 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 5 h. Usual workup gave 2-(3-oxobutyl)cyclopentanone (**3f**) (94 mg, 61%): IR (CCl_4) 1738, 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45-1.70 (m, 2H), 1.72-1.85 (m, 2H), 1.90-2.35 (m, 5H), 2.15 (s, 3H), 2.50-2.65 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.2, 23.2, 29.3, 29.4, 37.6, 40.7, 47.4, 207.9, 220.2; MS (*m/z*) 154 (M^+); HRMS calcd for $C_9H_{14}O_2$ (M^+) 154.0994, found 154.0988. These spectral data were superimposable on those of the authentic sample prepared by the method of literature[19].

Reaction of 4-*tert*-butyl-1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone. A mixture of 4-*tert*-butyl-1-(trimethylsiloxy)cyclohexene (226 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 10 h. Workup and column chromatography (95:5 hexane-ethyl acetate) provided 4-*tert*-butyl-2-(3-oxobutyl)cyclohexanone (**3b**) (170 mg, 76%, *cis*:*trans* = 63:37). The *cis*/*trans* ratio was determined by GLC. Pure *cis*- and *trans*-isomers were obtained by HPLC. *cis*-4-*tert*-Butyl-2-(3-oxobutyl)cyclohexanone: IR (CCl_4) 1717 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (s, 9H), 1.35-1.65 (m, 4H), 1.91 (m, 1H), 2.05-2.15 (m, 2H), 2.13 (s, 3H), 2.25-2.50 (m, 4H), 2.60 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 23.8, 27.6, 28.8, 29.8, 32.4, 35.5, 41.3, 41.7, 47.0, 48.7, 209.0, 213.2; MS (*m/z*) 224 (M^+); HRMS calcd for $C_{14}H_{24}O_2$ (M^+) 224.1776, found 224.1752. *trans*-4-*tert*-Butyl-2-(3-oxobutyl)cyclohexanone: IR (CCl_4) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 9H), 1.4-2.1 (m, 7H), 2.13 (s, 3H), 2.2-2.5 (m, 5H); ^{13}C NMR ($CDCl_3$) δ

25.4, 26.7, 27.4, 30.1, 32.2, 32.3, 38.4, 41.2, 41.3, 48.5, 208.1, 215.5; MS (*m/z*) 224 (M^+); HRMS calcd for $C_{14}H_{24}O_2$ (M^+) 224.1776, found 224.1745.

Reaction of 2-methyl-1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone. A mixture of 2-methyl-1-(trimethylsiloxy)cyclohexene (184 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 3 h. Usual workup gave 2-methyl-2-(3-oxobutyl)-cyclohexanone (**3c**) (116 mg, 64%) having the identical spectral data with those of the authentic sample separately prepared by the literature method:[19] IR (CCl_4) 1720, 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (s, 3H), 1.5-2.1 (m, 8H), 2.13 (s, 3H), 2.2-2.5 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 20.8, 22.5, 27.3, 29.8, 30.9, 38.2, 38.6 39.4, 47.6, 208.2, 215.4; MS (*m/z*) 182 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found 182.1311.

Reaction of 6-methyl-1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone. A mixture of 6-methyl-1-(trimethylsiloxy)cyclohexene (184 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -50 °C for 6 h. Usual workup afforded 2-methyl-6-(3-oxobutyl)-cyclohexanone (**3d**) (140 mg, 77%, *cis/trans* = 16:84) having the identical spectral data with those of the authentic sample separately prepared by the literature method.[28] The *cis/trans* ratio was determined by GLC. Pure *cis*- and *trans* isomers were obtained by HPLC. *cis*-6-Methyl-2-(3-oxobutyl)cyclohexanone: IR (CCl_4) 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, J = 6.23 Hz, 3H), 1.25-1.55 (m, 3H), 1.70-2.00 (m, 3H), 2.10 (m, 2H), 2.12 (s, 3H), 2.25-2.50 (m, 3H), 2.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.3, 23.5, 25.4, 29.7, 35.4, 37.3, 41.3, 45.6, 49.7, 208.9, 213.9: MS (*m/z*) 182 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found 182.1306. *trans*-6-Methyl-2-(3-oxobutyl)cyclohexanone: IR (CCl_4) 1720, 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (d, J = 6.96 Hz, 3H), 1.45-2.10 (m, 8H), 2.12 (s, 3H), 2.30-2.50 (m, 3H), 2.58 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 15.5, 20.5, 24.8, 30.0, 33.0, 35.1, 41.3, 42.7, 48.2, 208.3, 216.4; MS (*m/z*) 182 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found 182.1283.

Reaction of 2,6-dimethyl-1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone. A mixture of 2,6-dimethyl-1-(trimethylsiloxy)cyclohexene (198 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -50 °C for 3 h. Usual workup provided 2,6-dimethyl-2-(3-oxobutyl)cyclohexanone (**3e**) (120 mg, 61%, 78:12 mixture by GLC): IR (CCl_4) 1716, 1703 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3H x 78/100), 0.98 (d, J = 6.23 Hz, 3H), 1.18 (s, 3H x 22/100), 1.25-1.40 (m, 1H), 1.50-1.75 (m, 3H), 1.83-2.15 (m, 4H), 2.12 (s, 3H x 78/100), 2.15 (s, 3H x 22/100), 2.22 (m. 1H), 2.38-2.70 (m, 2H); ^{13}C NMR ($CDCl_3$) δ (major isomer) 14.6, 20.7, 22.0, 29.7, 30.6, 36.3, 37.8, 40.7, 41.0, 47.6, 207.7, 216.4, (minor isomer) 14.6, 20.9, 23.0, 29.5, 31.9, 38.7, 38.9, 40.7, 47.2, 208.9, 216.3; MS (*m/z*) 196 (M^+); HRMS calcd for $C_{12}H_{20}O_2$ (M^+) 196.1463, found 196.1434. These compounds showed the spectral data identical with that of the authentic sample.[19]

Reaction of 1-phenyl-1-(trimethylsiloxy)ethene with methyl vinyl ketone. A mixture of 1-phenyl-1-(trimethylsiloxy)ethene (192 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and CH_2Cl_2 (5 ml) was stirred at -78°C for 2 h. Acidic workup and column chromatography (95:5 hexane-ethyl acetate) gave 1-phenyl-1,5-hexanedione (**3g**) (186 mg, 98%) having the identical spectral data with those of the authentic sample:[1a,b] ^1H NMR ($CDCl_3$) δ 2.04 (m, 2H), 2.14 (s, 3H), 2.57 (t, J = 6.83 Hz, 2H), 3.01 (t, J = 7.08 Hz, 2H), 7.2-8.1 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 18.2, 29.7, 37.3, 42.5, 127.9, 128.4, 132.9, 136.8, 199.4, 208.0; MS (*m/z*) 190 (M^+); HRMS calcd for $C_{12}H_{14}O_2$ (M^+) 190.0994, found 190.0987.

Reaction of 1-methoxy-2-methyl-1-(trimethylsiloxy)propene with methyl vinyl ketone. A mixture of 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (174 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 4 h. Usual workup afforded methyl 2,2-dimethyl-5-oxohexanoate (**3h**) (123mg, 71%): IR (neat) 1726 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (s, 6H), 1.79 (t, J = 8.54 Hz, 2H), 2.13 (s, 3H), 2.40 (t, J = 8.54 Hz, 2H), 3.66 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 24.9, 29.6, 33.8, 39.2, 41.3, 51.4, 177.4, 207.6; MS (*m/z*) 172 (M^+): HRMS calcd for $C_9H_{16}O_3$ (M^+) 172.1099, found 172.1084.

Reaction of 1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone in the presence of TMSOTf. A mixture of 1-(trimethylsiloxy)cyclohexene (170 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), TMSOTf (12 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 C for 6 h. Usual workup afforded an oil. GLC analysis of this oil revealed the formation of **3a** in 8% yield.

Reaction of 1-(trimethylsiloxy)cyclohexene with methyl vinyl ketone in the presence of $TrClO_4$. A mixture of 1-(trimethylsiloxy)cyclohexene (170 mg, 1 mmol), methyl vinyl ketone (91 mg, 1.3 mmol), $TrClO_4$ (17 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 °C for 6 h. Workup and subsequent GLC analysis showed **3a** to be formed in 18% yield.

Reaction of 1-(trimethylsiloxy)cyclohexene with (*E*)-3-penten-2-one. A mixture of 1-(trimethylsiloxy)cyclohexene (170 mg, 1 mmol), (*E*)-3-penten-2-one (109 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -20 °C for 3 h. Usual workup afforded 2-(1-methyl-3-oxobutyl)-cyclohexanone (103 mg, 57%, 1:1 mixture): IR (CCl_4) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, J = 6.96 Hz, 3H x 1/2), 0.93 (d, J = 6.60 Hz, 3H x 1/2), 1.45-1.75 (m, 3H), 1.85-2.08 (m, 4H), 2.13 (s, 3H x 1/2), 2.15 (s, 3H x 1/2), 2.20-2.60 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.9 and 17.3, 24.5 and 24.8, 27.5 and 27.7, 27.7 and 28.1, 29.3 and 29.5, 30.1, 42.2 and 42.3, 47.7 and 48.7, 54.7 and 54.9, 208.5 and 208.8, 212.4 and 212.7; MS (*m/z*) 182 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found 182.1292.

Reaction of 1-(trimethylsiloxy)cyclohexene with ethyl vinyl ketone. A mixture of 1-(trimethylsiloxy)cyclohexene (170 mg, 1 mmol), ethyl vinyl ketone (109 mg, 1.3 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (5 ml) was stirred at -50 °C for 2 h. Workup gave 2-(3-oxopentyl)cyclohexanone (145 mg, 80%): IR (CCl_4) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (t, J = 7.33 Hz, 3H), 1.35-1.78 (m, 4H), 1.80-2.15 (m, 4H), 2.20-2.60 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 7.1, 23.1, 24.3, 27.4, 33.6, 34.9, 39.1, 41.3, 49.1, 210.1, 211.6; MS (*m/z*) 182 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ (M^+) 182.1307, found 182.1303. The product was identical in all respects with an authentic sample.[21]

Reaction of 2-cyclopentenone with 1-phenyl-1-(trimethylsiloxy)ethene (2g). A mixture of 2-cyclopentenone (82 mg, 1 mmol), 1-phenyl-1-(trimethylsiloxy)ethene (250 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and toluene (5 ml) was stirred at -78 °C for 2 h and 0°C for 5 h. Acidic workup and column chromatography (80:20 hexane-ethyl acetate) provided 3-(2-oxo-2-phenylethyl)cyclopentanone (141 mg, 70%): IR (neat) 1738, 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-3.2 (m, 9H), 7.2-8.2 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 29.2, 32.5, 38.1, 43.7, 44.6, 127.7, 128.4, 132.9, 136.6, 198.2, 218.1; MS (*m/z*) 202 (M^+); HRMS calcd for $C_{13}H_{14}O_2$ (M^+) 202.0994, found 202.1012.

Reaction of 2-cyclopentenone with 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (2h). A mixture of 2-cyclopentenone (82 mg, 1 mmol), 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (226 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and toluene (5 ml) was stirred at -78 °C for 5 h. Usual workup afforded 3-[(1-(methoxycarbonyl)-1-methylethyl)]cyclopentanone (138 mg, 75%) identical in all respects with the authentic sample:[7c] ^1H NMR ($CDCl_3$) δ 1.20 (s, 6H), 1.4-2.7 (m, 7H), 3.68 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 22.4, 24.1, 38.5, 40.1, 43.6, 44.8, 51.4, 176.7, 217.3; MS (*m/z*) 184 (M^+); HRMS calcd for $C_{10}H_{16}O_3$ (M^+) 184.1099, found 184.1100.

Reaction of 2-cyclohexenone with 2-(trimethylsiloxy)propene (2i). A mixture of 2-cyclohexenone (96 mg, 1 mmol), 2-(trimethylsiloxy)propene (169 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and CH_2Cl_2 (5 ml) was stirred at -50 °C for 2 h. Acidic workup and column chromatography (90:10 hexane-ethyl acetate) afforded 3-(2-oxopropyl)cyclohexanone (121 mg, 78%): IR (neat) 1705, 1718 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-2.5 (m, 11H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 24.7, 30.3, 30.7, 34.1, 41.0, 47.3, 49.5, 206.8, 210.5; MS (*m/z*) 154 (M^+); HRMS calcd for $C_9H_{14}O_2$ (M^+) 154.0994, found 154.0999.

Reaction of 2-cyclohexenone with 1-phenyl-1-(trimethylsiloxy)ethene (2g). 1N HCl treatment. A mixture of 2-cyclohexenone (96 mg, 1 mmol), 1-phenyl-1-(trimethylsiloxy)ethene (250 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and toluene (5 ml) was stirred at -78 to -10 °C for 3 h. The reaction mixture was combined with aqueous $NaHCO_3$ and extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and evaporated to give an oil. This oil was treated with 1N HCl (1 ml) and THF (3 ml) at room temperature for 0.5 h. Aqueous $NaHCO_3$ was added to this solution, and the mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and evaporated. The residue was subjected to column chromatography (80:20 hexane-ethyl acetate) to give 3-(2-oxo-2-phenylethyl)cyclohexanone (199 mg, 92%) identical in all respects with the authentic sample:[1a, b, 4a] IR (neat) 1710, 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-3.1 (m, 11H), 7.2-8.1 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.6, 30.8, 34.6, 40.9, 44.3, 47.4, 127.6, 128.3, 132.8, 136.7, 198.0, 210.0; MS (*m/z*) 216 (M^+); HRMS calcd for $C_{14}H_{16}O_2$ (M^+) 216.1150, found 216.1151.

2-(Hydroxymethyl)pyridine treatment.[4b,d] A mixture of 2-cyclohexenone (96 mg, 1 mmol), 1-phenyl-1-(trimethylsiloxy)ethene (250 mg, 1.3 mmol), **1** (53 mg, 0.1 mmol), and CH_2Cl_2 (5 ml) was stirred at -78 to -10 °C for 3 h. To this mixture 2-(hydroxymethyl)pyridine (33 mg, 0.3 mmol) and pyridine (0.1 ml) were added. The resulting mixture was diluted with hexane (70 ml) and washed with aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and evaporated. The residual oil was chromatographed on silica gel (pretreated with NH_3) afforded 3-(2-oxo-2-phenylethyl)-1-(trimethylsiloxy)cyclohexene (245 mg, 85%): ^1H NMR ($CDCl_3$) δ 0.25 (s, 9H), 1.2-2.2 (m, 7H), 2.99 (br s, 2H), 4.92 (br s, 1H), 7.2-8.2 (m, 5H); ^{13}C NMR ($CDCl_3$) δ, 0.17, 21.1, 28.6, 29.7, 31.0, 45.3, 107.9, 127.8, 128.2, 132.5, 137.2, 151.0, 199.2.

Cyclization of 2-(3-oxobutyl)cyclopentanone. A mixture of 2-(3-oxobutyl)cyclopentanone (64 mg, 0.41 mmol), $NaOCH_3$ (33 mg, 0.61 mmol), and CH_3OH (2.6 ml) was stirred at room temperature for 0.5 h. The mixture was combined with aqueous NH_4Cl and extracted with ethyl acetate. Evaporation and column chromatography (80:20 hexane-ethyl acetate) provided 5,6,7,8-tetrahydroindanone-5 (55 mg, 98%): IR (CCl_4) 1680, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-2.8 (m, 11H), 5.90 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.9, 28.3, 30.8, 31.8, 36.4, 42.1, 121.1, 174.4, 198.2; MS (*m/z*) 136 (M^+); HRMS calcd for $C_9H_{12}O$ (M^+) 136.0880, found 136.0840. The product was identical in all respects with the authentic sample.[21]

Cyclization of 2-(3-oxobutyl)cyclohexanone. A mixture of 2-(3-oxobutyl)cyclohexanone (168 mg, 1 mmol), $NaOCH_3$ (81 mg, 1.5 mmol), and CH_3OH (5 ml) was stirred at room temperature for 0.5 h. Workup afforded $\Delta^{1,9}$-octalone-2 (134 mg, 89%). Contamination by $\Delta^{9,10}$-octalone-2 was checked on the basis of GLC and ^{13}C NMR analysis: IR (CCl_4) 1677, 1623 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1-2.5 (m, 13H), 5.81 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 25.2, 26.6, 28.9, 34.1, 35.3, 36.2, 37.6, 123.9, 167.2, 199.8; MS (*m/z*) 150 (M^+); HRMS calcd for $C_{10}H_{14}O$ (M^+) 150.1045, found 150.1024. These spectral data were superimposable on those of the authentic sample.[21]

Cyclization of 2-(3-oxopentyl)cyclohexanone. A mixture of 2-(3-oxopentyl)cyclohexanone (182 mg, 1 mmol), $NaOCH_3$ (81 mg, 1.5 mmol), and CH_3OH (5 ml) was stirred at room temperature for 0.5 h. Workup provided 1-methyl-$\Delta^{1,9}$-octalone-2 (149 mg, 91%) having the identical spectral data with those of the authentic sample:[21] IR (CCl_4) 1670, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2-2.9 (m, 13H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 10.6, 25.5, 26.7, 28.8, 31.3, 34.8, 36.3, 38.8, 128.5, 159.9, 199.7; MS (*m/z*) 164 (M^+); HRMS calcd for $C_{11}H_{16}O$ (M^+) 164.1201, found 164.1206.

One-pot synthesis of $\Delta^{1,9}$-octalone-2 from 1-(trimethylsiloxy)cyclohexene and methyl vinyl ketone. A mixture of 1-(trimethylsiloxy)cyclohexene (221 mg, 1.3 mmol), methyl vinyl ketone (70 mg, 1 mmol), **1** (27 mg, 0.05 mmol), and CH_2Cl_2 (3 ml) was stirred at -78°C for 5 h. To this mixture were added $NaOCH_3$ (81 mg, 1.5 mmol) and CH_3OH (2 ml). The resulting solution was further stirred at room temperature for 3 h, and quenched with aqueous NH_4Cl. Extraction with ethyl acetate, drying the organic layer (Na_2SO_4), and evaporation left an oil. Column chromatography (80:20 hexane-ethyl acetate) of this oil gave $\Delta^{1,9}$-octalone-2 (133 mg, 89% yield based on methyl vinyl ketone).

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