Aldol Reaction of Aluminium Enolate Resulting from 1,4-Addition of R_2AlX to α,β-Unsaturated Carbonyl Compound. A 1-Acylethenyl Anion Equivalent[1)]

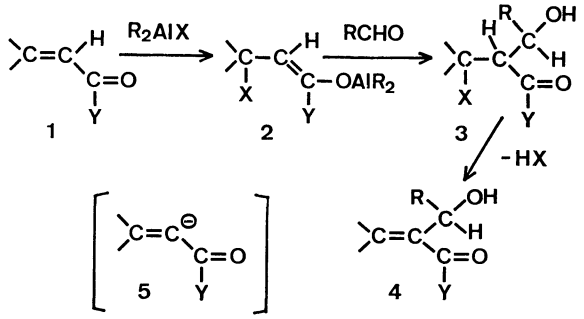
Akira Itoh, Shuji Ozawa, Koichiro Oshima,* and Hitosi Nozaki

Department of Industrial Chemistry, Faculty of Engineering, Kyoto Univesity, Yoshida, Sakyo-ku, Kyoto 606

(Received July 16, 1980)

Organoaluminium reagents R_2AlX (X=SPh, SeMe) easily add to α,β-unsaturated carbonyl compounds in 1,4-fashion. The resulting aluminium enolates react with aldehydes to give aldol adducts in fair to good yields. Formal elimination of HX from the adducts provides α-substituted α,β-unsaturated carbonyl compounds. The overall transformation is an addition of aldehydes to 1-acylethenyl anion equivalent. Diethylaluminium iodide also is found to be an efficient reagent for the same type transformation.

The aldol condensation is one of the most versatile synthetic methods in organic chemistry. Recently, organoaluminium enolates as produced *via* several routes have been utilized as a vast potential agent of the reaction.[2-5)] Conjugate addition of organoaluminium reagents R_2AlX to α,β-unsaturated carbonyl compounds provides another route to aluminium enolates (Scheme 1).[6)] The aldol reaction with an aldehyde component followed by elimination of HX gives α-substituted α,β-unsaturated carbonyl compound **4**. The overall transformation therefore provides an α-carbanion equivalent of the substrate **5** adding to the aldehyde component to form **4**. The sequence gives a solution to the recurring synthetic problem to introduce α-substituent directly to α,β-unsaturated carbonyl compounds.[7)]



Scheme 1.

Among many candidates for R_2AlX, dimethylaluminium benzenethiolate[8)] (reagent A) and dimethylaluminium methaneselenolate[9)] (reagent B) have been found to be effective (Table 1). Dimethylaluminium benzenethiolate was prepared from trimethylaluminium and thiophenol in dichloromethane and dimethylaluminium methaneselenolate from trimethylaluminium and selenium metal in toluene. These reagents were used directly without isolation. In an attempt to find the suitable solvent for the aldol reaction, the reaction between 2-cyclohexenone and acetaldehyde mediated by Me_2AlSPh was examined in various solvents (solvent, isolated yield of **3**): hexane, 42%; CH_2Cl_2, 43%; toluene, 45%; tetrahydrofuran (THF), 94%. After completion of 1,4-addition of R_2AlX (X=SPh, SeMe) to α,β-unsaturated carbonyl compounds, the reaction mixture was diluted with THF which was found to be the best solvent.

Unfortunately dimethylaluminium benzenethiolate was not effective in the reaction of α,β-unsaturated esters because of sluggishly proceeding 1,4-addition, where a quantity of the corresponding thiocarboxylic *S*-ester was formed[11)] The use of a new ate complex $Me_3Al^-SPhLi^+$ (reagent C) has been found to be much more advantageous possibly due to the increased reactivity of thiolate ion itself as well as of the resulting enolate anion corresponding to **2**.

Erythro and threo ratios of the aldol product **3** have been examined. The aldol product 2-(1-hydroxyethyl)-3-phenylthiocyclohexanone was desulfurized with Raney Ni in ethanol. Analysis of the NMR spectra[12)] revealed that the product was a 1:1 mixture of erythro and threo isomers. Similarly, the aldol products between acetaldehyde and methyl vinyl ketone (run 7) or ethyl acrylate (run 11) were found to be 1:1 and 1:2 mixture of isomers by NMR analysis.[13)]

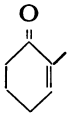
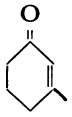
Spontaneous elimination of phenylthio group in the reaction mixture was observed in run 6. More easily the conversion of **3** to **4** was achieved by the oxidation (sodium periodate for SPh and hydrogen peroxide for SeMe), which facilitates successive elimination[14)] as given in Table 1. Moreover, the overall transformation could be performed in one pot, for instance, the addition of copper(II) chloride and sodium acetate directly to the product in the run 1 without workup afforded the desired compound **4** in 52% yield.

Diethylaluminium iodide[15)] was found to be more effective for the same type transformation. Addition of diethylaluminium iodide to a mixture of aldehyde and α,β-unsaturated ketone in dichloromethane gave α-substituted α,β-unsaturated ketone **4** directly. The whole sequence involving conjugate addition of the iodide, aldol condensation of the resulting aluminium enolate, and elimination of HI element proceeded in one pot. The results are summarized in Table 2.

Tetrahydrofuran was not a suitable solvent for the reaction of Et_2AlI because of the ring cleavage producing 4-iodo-1-butanol. Reaction between ethyl acrylate and acetaldehyde gave the adduct **3** (X=I). Elimination of HI did not proceed spontaneously in this case and treatment with 1,8-diazabicyclo[5.4.0]-undec-5-ene was necessary in order to obtain the product **4**.

Although aldehydes successfully trapped the aluminium enolates in high yields, ketones and other electrophiles such as allyl bromide, acetyl chloride, 2-phenyl-1,3-dioxolane, and cyclohexene oxide failed to react.

Table 1. Reaction between α,β-unsaturated carbonyl compounds and aldehydes by means of Me_2AlSPh or $Me_2AlSeMe$

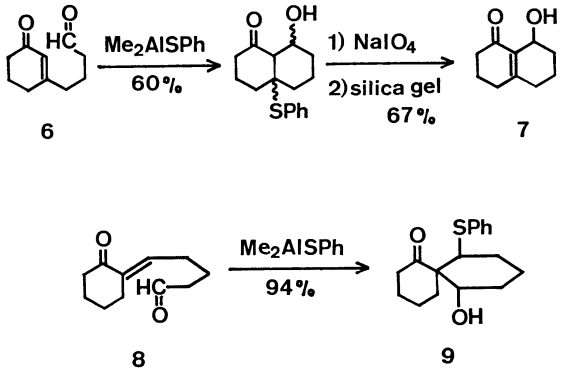
Run	α,β-Unsaturated carbonyl compound	Reagent[a]	Aldehyde RCHO	3 Yield %	4 Yield %[b]
1	2-Cyclohexenone	A	$CH_3(CH_2)_7CHO$	90	71
2	2-Cyclohexenone	A	CH_3CHO	94	92
3	2-Cyclohexenone	B	CH_3CHO	77	77
4	2-Cyclohexenone	A	methacrolein	97	84
5		A	CH_3CHO	75	—
6		A	CH_3CHO	—	50[c]
7	CH_2=CHCOCH$_3$	A	CH_3CHO	60	57
8	CH_2=CHCOCH$_3$	B	CH_3CHO	55	50
9	2-Cyclopentenone	A	HCHO	56	80[d]
10	2-Cyclopentenone	A	$CH_3(CH_2)_7CHO$	76	60
11	CH_2=CHCOOC$_2$H$_5$	C	CH_3CHO	73	87
12		C	PhCHO	77	74

a) A: Me_2AlSPh, B: $Me_2AlSeMe$, C: $Me_3Al^-SPhLi^+$. b) Yields were based on **3**. c) Phenylthio group has been spontaneously eliminated in this case. d) See Ref. 10.

Table 2. Reaction between α,β-unsaturated carbonyl compounds and aldehydes by means of Et_2AlI

Run	α,β-Uusaturated carbonyl compound	Aldehyde RCHO	4 Yield/%
1	2-Cyclohexenone	CH_3CHO	81
2	2-Cyclohexenone	$CH_3(CH_2)_7CHO$	88
3	CH_2=CHCOCH$_3$	CH_3CHO	61
4	CH_2=CHCOOC$_2$H$_5$	CH_3CHO	62[a]

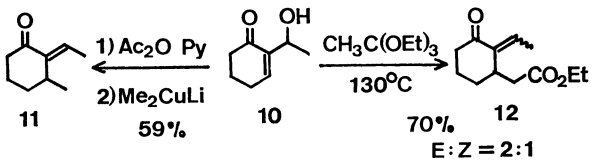
a) Further treatment with DBU was necessary. See experimental part.



Scheme 2.

Treatment of the α,β-unsaturated carbonyl compounds **6**[16] or **8** with dimethylaluminium benzenethiolate provided an efficient method for the cyclization affording **7** or **9**.

Finally, further synthetic applications of the adduct **10** have been examined (Scheme 3). Treatment of the acetate of **10** with lithium dimethylcuprate(I)[17] afforded **11** in 59% yield. No regio- and stereoisomers were detected. Orthoester Claisen rearrangement[18] of **10** gave a stereoisomeric mixture of **12** in 70% yield. These transformations enable us to introduce a variety of groups on α and β positions of α,β-unsaturated carbonyl compounds.



Scheme 3.

Experimental

The infrared spectra were determined on a Shimadzu IR-27-G spectrometer; the mass spectra on a Hitachi RMU-6L machine; the GLPC analyses on a Yanagimoto GCG-550F; and the NMR spectra on a JEOL C-60H or Varian EM-390H spectrometer. The chemical shifts are given in δ in ppm with TMS as the internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. The microanalyses were carried out by the staffs at the Elemental Analyses Center of Kyoto University. All experiments were carried out under an atmosphere of dry argon. Tetrahydrofuran was dried by distillation from sodium-benzophenone. Thin layer or thick layer plates were made of E. Merck PF-254, and preparative columns silica gel E. Merck Art. 7734.

2-(1-Hydroxynonyl)-2-cyclohexenone. A solution of thiophenol (0.26 g, 2.4 mmol) in dichloromethane (2.0 ml) was added to a solution of trimethylaluminium in hexane (1.0 M, 2.4 ml, 2.4 mmol) at 0 °C and the mixture was stirred for 20 min. A solution of 2-cyclohexenone (0.19 g,

2.0 mmol) in dichloromethane (2.0 ml) was added at −78 °C and, after 15 min, the resulting white suspension was diluted with THF (10 ml) to give a colorless solution. After additional 5 min, a solution of nonanal (0.34 g, 2.4 mmol) in THF (2.0 ml) was added and stirring was continued for 20 min at −78 °C. The reaction mixture was poured into ice-water and the organic phase was washed with 1 M HCl twice. The aqueous phase was extracted twice with ethyl acetate and the combined organic layers were washed with brine, dried, and freed of the solvent. Purification by column chromatography on silica gel (hexane:ether=2:1) gave 2-(1-hydroxynonyl)-3-(phenylthio)cyclohexanone (0.64 g, 90% yield): IR (neat) 3450, 1700 cm^{-1}; NMR (CCl_4) δ 0.88 (t, J=4.5 Hz, 3H), 1.20—2.40 (m, 22H), 3.46 (m, 1H), 4.00 (m, 1H), 7.20—7.48 (m, 5H); MS *m/e* (%) 238 (2), 220 (7), 206 (24), 140 (13), 135 (16), 125 (100), 110 (98).

The sulfide (0.28 g, 0.72 mmol) was dissolved in 50% aqueous methanol (5.0 ml) and treated with sodium periodate (0.23 g, 1.1 mmol) at 25 °C for 3 d. After purification by column chromatography on silica gel, the obtained sulfoxide was dissolved in toluene (3.0 ml) and heated at reflux for 30 min to give the title compound (0.12 g, 71% yield based on the hydroxy sulfide): bp 185 °C (bath temp, 2 Torr, 1 Torr=133.322 Pa); IR (neat) 3445, 1665, 1653 cm^{-1}; NMR (CCl_4) δ 0.87 (t, J=4.8 Hz, 3H), 1.28 (m, 14H), 1.82—2.07 (m, 2H), 2.24—2.44 (m, 5H), 4.15 (m, 1H), 6.74 (t, J=3.9 Hz, 1H); MS *m/e* (%) 238 (M^+, 3), 221 (3), 220 (11), 141 (13), 136 (18), 126 (100). Microanalysis was performed after trimethylsilylation of the hydroxyl group.[19] Found: C, 69.56; H, 11.01%. Calcd for $C_{18}H_{34}O_2Si$: C, 69.62; H, 11.04%.

2-(1-Hydroxyethyl)-2-cyclohexenone ***10***. Bp 130 °C (bath temp, 2 Torr); IR (neat) 3440, 1665, 1655 cm^{-1}; NMR (CCl_4) δ 1.23 (d, J=6.5 Hz, 3H), 1.96 (m, 2H), 2.36 (m, 4H), 2.69 (bs, 1H), 4.42 (qd, J=6.5 and 1.2 Hz, 1H), 6.80 (td, J=4.1 and 1.2 Hz, 1H); MS *m/e* (%) 141 (9), 140 (M^+, 38), 139 (9), 125 (100), 97 (54). Found: C, 62.07; H, 9.40%. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49%.[19]

Joining Reaction of 2-Cyclohexenone and Acetaldehyde Mediated by $Me_2AlSeMe$. A mixture of selenium (0.23 g, 2.9 mg-atom), trimethylaluminium (1.0 M hexane solution, 3.0 ml, 3.0 mmol), and toluene (3.0 ml) was refluxed for 2.5 h.[9] The resulting homogeneous solution was diluted with THF (10 ml) and treated with 2-cyclohexenone (0.11 g, 1.1 mmol) at −78 °C. After 70 min, acetaldehyde (0.1 ml, 1.8 mmol) was added and the mixture was stirred for 30 min at −78 °C and for 5 min at 0 °C. Purification by preparative TLC (hexane:ether=1:2) afforded 2-(1-hydroxyethyl)-3-(methylseleno)cyclohexanone (0.20 g, 0.85 mmol) in 77% yield. The selenide (0.20 g, 0.85 mmol) was dissolved in a mixture of dichloromethane (10 ml) and pyridine (0.35 ml, 4.3 mmol) and treated with 30% H_2O_2 (0.55 g, 4.8 mmol) at 25 °C for 30 min to give **10** (91 mg, 77% yield).

2-(1-Hydroxy-2-methyl-2-propenyl)-2-cyclohexenone. IR (neat) 3430, 1664, 1655, 893 cm^{-1}; NMR (CCl_4) δ 1.65 (s, 3H), 2.01 (m, 2H), 2.38 (m, 4H), 2.85 (bs, 1H), 4.75 (s, 1H), 4.82 (s, 1H), 4.95 (s, 1H), 6.78 (t, J=4.2 Hz, 1H); MS *m/e* (%) 166 (M^+, 47), 165 (18), 151 (27), 149 (12), 148 (16), 147 (20), 137 (100); bp 95 °C (bath temp, 2 Torr).[20] Found: C, 65.21; H, 9.08%. Calcd for $C_{13}H_{22}O_2Si$: C, 65.50; H, 9.30%.[19]

2-(1-Hydroxyethyl)-2-methyl-3-(phenylthio)cyclohexanone. IR (neat) 3460, 1703 cm^{-1}; NMR (CCl_4) δ 1.16 (s, 3H), 1.35 (d, J=6.3 Hz, 3H), 1.63—2.55 (m, 7H), 3.66—4.29 (m, 2H), 7.13—7.50 (m, 5H); MS *m/e* (%) 220 (5), 154 (1), 139 (1), 111 (15), 110 (100), 109 (19), 82 (56); bp 140 °C (bath temp, 2 Torr).[20] Found: C, 64.16; H, 8.44%. Calcd for $C_{18}H_{28}O_2SSi$: C, 64.23; H, 8.39%.[19]

2-(1-Hydroxyethyl)-3-methyl-2-cyclohexenone. IR (neat) 3470, 1643, 1625 cm^{-1}; NMR (CCl_4) δ 1.26 (d, J=6.3 Hz, 3H), 1.95 (s, 3H), 1.75—2.05 (m, 2H), 2.25—2.50 (m, 4H), 4.27 (bs, 1H), 4.52 (q, J=6.3 Hz, 1H); MS *m/e* (%) 154 (M^+, 7), 140 (12), 139 (100), 136 (13), 121 (11), 111 (15); bp 94 °C (bath temp, 2 Torr).[20] Found: C, 63.20; H, 9.91%. Calcd for $C_{12}H_{22}O_2Si$: C, 63.66; H, 9.79%.[19]

4-Hydroxy-3-methylene-2-pentanone. IR (neat) 3415, 1665, 1635, 1088 cm^{-1}; NMR (CCl_4) δ 1.23 (d, J=6.6 Hz, 3H), 2.30 (s, 3H), 2.65 (bs, 1H), 4.53 (q, J=6.6 Hz, 1H), 5.98 (s, 2H); MS *m/e* (%) 114 (M^+, 1), 113 (1), 100 (7), 99 (100), 81 (12), 71 (16); bp 45 °C (bath temp, 2 Torr).[20] Found: C, 57.78; H, 9.67%. Calcd for $C_9H_{18}O_2Si$: C, 58.02; H, 9.74%.[19]

2-Hydroxymethyl-2-cyclopontenone. NMR and IR spectra and mp agreed with published data.[7b]

2-(1-Hydroxynonyl)-2-cyclopentenone. IR (neat) 3432, 1686, 1631 cm^{-1}; NMR (CCl_4) δ 0.86 (t, J=5.4 Hz, 3H), 1.29 (m, 14H), 2.33 (m, 2H), 2.56 (m, 2H), 2.87 (bs, 1H), 4.26 (bt, J=5.1 Hz, 1H), 7.32 (bs, 1H); MS *m/e* (%) 224 (M^+, 0.3), 207 (2), 206 (9), 149 (3), 145 (3), 135 (5), 111 (100); bp 124 °C (bath temp, 2 Torr).[20] Found: C, 68.84; H, 10.84%. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88%.[19]

Ethyl 3-Hydroxy-2-methylenebutyrate. A solution of trimethylaluminium in hexane (1.0 M, 1.2 ml, 1.2 mmol) was added to a solution of lithium benzenethiolate (1.2 mmol, prepared *in situ* from thiophenol and butyllithium at 0 °C) in THF (5.0 ml) at 0 °C. After 1 h, the mixture was cooled to −78 °C and treated with a solution of ethyl acrylate (0.11 g, 1.1 mmol) in THF (1.0 ml) and kept there for 15 min. Acetaldehyde (0.1 ml, 1.8 mmol) was added and the mixture was stirred for 10 min at −78 °C and for 5 min at 0 °C. The crude product was submitted to preparative TLC (hexane:ether=1:1) to afford ethyl 3-hydroxy-2-(phenylthiomethyl)butyrate (0.21 g, 0.81 mmol) in 73% yield. Following the previously described procedure, this hydroxy ester (0.15 g, 0.6 mmol) was subsequently transformed to the title compound (75 mg, 87% yield): IR (neat) 3440, 1713, 1630 cm^{-1}; NMR (CCl_4) δ 1.29 (d, J=6.4 Hz, 3H), 1.32 (t, J=7.2 Hz, 3H), 2.90 (bs, 1H), 4.17 (q, J=7.2 Hz, 2H), 4.50 (q, J=6.4 Hz, 1H), 5.76 (s, 1H), 6.10 (s, 1H); MS *m/e* (%) 129 (51), 101 (75), 99 (44), 98 (34), 97 (21), 83 (100), 73 (37); bp 54 °C (bath temp, 2 Torr).[20] Found: C, 55.61; H, 9.57%. Calcd for $C_{10}H_{20}O_3Si$: C, 55.52; H, 9.32%.[19]

2-(1-Hydroxybenzyl)-2-buten-4-olide. NMR, IR, and mass spectra were found to be in accord with published data.[6]

Desulfurization of 2-(1-Hydroxyethyl)-3-(penylthio)cyclohexanone with Raney Ni. Stirring the hydroxy sulfide (0.11 g) in ethanol (3.0 ml) with Raney Ni W-2 (0.3 g) under hydrogen atmosphere at 25 °C for 14 h followed by preparative TLC isolation (benzene:ethyl acetate=3:1, two developments) gave 2-(1-hydroxyethyl)cyclohexanone (31 mg) in 51% yield. The NMR spectrum (CCl_4) indicated this being a 1:1 mixture of erythro and threo isomers by exhibiting a pair of multiplets at δ 3.82 and 4.13 in a 1:1 ratio as well as a pair of doublets of equal intensities at δ 1.07 (J=6.6 Hz) and 1.09 (J=6.6 Hz).[12]

One Pot Synthesis of ***10***. After successive treatment of 2-cyclohexenone (92 mg, 1.0 mmol) with Me_2AlSPh (1.2 mmol) and acetaldehyde (0.1 ml, 1.8 mmol) in hexane (3.0 ml) and THF (7.0 ml), the reaction mixture was allowed to react with copper(II) chloride (0.68 g, 5.1 mmol) and sodium acetate (0.44 g, 5.3 mmol). The mixture was re-

fluxed for 2 h, poured into water, and filtered through a pad of Celite 545. The organic phase was washed with brine, dried, and freed of the solvent. The residue was submitted to preparative TLC (hexane:ethyl acetate=1:1, two developments) to give **10** (70 mg, 0.50 mmol) in 52% yield.

Joining Reaction of 2-Cyclohexenone and Acetaldehyde Mediated by Et_2AlI. A solution of diethylaluminium iodide in toluene (1.15 M, 1.6 ml, 1.8 mmol) was added to a solution of 2-cyclohexenone (0.12 g, 1.2 mmol) and acetaldehyde (0.10 ml, 1.8 mmol) in dichloromethane (7.0 ml) at 0 °C. After stirring for 20 min at 0 °C, the mixture was diluted with ether and washed with 1 M HCl and brine. Purification by column chromatography on silica gel (hexane:ethyl acetate=3:1) afforded **10** (0.14 g) in 81% yield.

Joining Reaction of Ethyl Acrylate and Acetaldehyde by Means of Et_2AlI. Similar treatment of a solution of ethyl acrylate (0.15 g, 1.5 mmol) and acetaldehyde (0.13 ml, 2.3 mmol) in dichloromethane (7.0 ml) followed by silica gel column chromatography gave ethyl 3-hydroxy-2-(iodomethyl)butyrate (0.44 g, 72% yield): IR (neat) 3470, 1730 cm^{-1}; NMR (CCl_4) δ 1.05 (d, J=6.0 Hz, 3H), 1.33 (t, J=6.9 Hz, 3H), 2.17 (bs, 1H), 2.66 (m, 1H), 3.36 (d, J=6.6 Hz, 2H), 3.90 (m, 1H), 4.18 (q, J=6.9 Hz, 2H); MS *m/e* (%) 272 (M^+, 3), 227 (5), 145 (6), 101 (100), 73 (70), 55 (80). The iodide (0.44 g, 1.1 mmol) was dissolved in benzene (15 ml) and treated with 1,8-diazabicyclo[5.4.0]-5-undecene (0.66 g, 4.3 mmol) at 25 °C for 1 h to give ethyl 3-hydroxy-2-methylenebutyrate (0.12 g, 0.93 mmol) in 86% yield.

10-Hydroxybicyclo[4.4.0]dec-1(6)-en-2-one **7**. A solution of **6**[16] (0.17 g, 1.0 mmol) in THF (2.0 ml) was added to a solution of Me_2AlSPh (3.0 mmol) in hexane (3.0 ml) and THF (9.0 ml) at 0 °C over a period of 40 min. After stirring for additional 20 min, the mixture was poured into ice–water and extracted with ethyl acetate. The cyclized product (0.17 g, 60% yield) was treated with sodium periodate (0.20 g) in 50% aqueous methanol (6.0 ml) at 25 °C for 1 h. The crude sulfoxide was dissolved in ethyl acetate (6.0 ml) and stirred at 25 °C for 9 h in the presence of silica gel (Merck, PF-254, 1.0 g). The reaction mixture was filtered and the filtrate was concentrated. Purification by preparative TLC (ethyl acetate) gave the title compound **7** (67 mg, 40% yield based on the keto aldehyde **6**): IR (neat) 3480, 1655, 1630 cm^{-1}; NMR (CCl_4) δ 1.60—2.40 (m, 11H), 2.99 (m, 2H), 4.42 (bs, 1H); MS *m/e* (%) 166 (M^+, 32), 148 (6), 138 (41), 123 (14), 120 (15), 110 (100). Found: *m/e* 166.0980. Calcd for $C_{10}H_{14}O_2$: M, 166.0992.

5-(2-Oxocyclohexylidene)pentanal **8**. Following the Corey's procedure,[21] 2-[1-hydroxy-5-(2-tetrahydropyranyloxy)pentyl]cyclohexanone was obtained in 54% yield based on cyclohexanone dimethyldrazone. This hydroxy ketone (5.8 g, 20 mmol) was mesylated at 0 °C and the crude mesylate was treated with sodium methoxide (28% solution in methanol, 42 mmol) in methanol at −78 °C. After 12 min at 0 °C, the mixture was diluted with brine and extracted with ethyl acetate. The product was purified by column chromatography on silica gel to give 2-[5-(2-tetrahydropyranyloxy)pentylidene]cyclohexanone (3.7 g) in 68% yield. The tetrahydropyranyl group was removed by treatment with pyridinium *p*-toluenesulfonate (1.5 g) in methanol (45 ml) at 25 °C for 4 h and the product was oxidized with $CrO_3 \cdot 2py$ in dichloromethane to give the title compound **8** in 34% yield: IR (neat) 1724, 1685, 1616 cm^{-1}; NMR (CCl_4) δ 1.59—2.49 (m, 14H), 6.39 (m, 1H), 9.70 (t, J=1.5 Hz, 1H); MS *m/e* (%) 180 (M^+, 21), 162 (13), 152 (12), 124 (70), 93 (63), 81 (54), 79 (63), 67 (100). Found: *m/e* 180.1162. Calcd for $C_{11}H_{16}O_2$: M, 180.1151.

Cyclization of **8** *by Means of Me_2AlSPh.* The keto aldehyde **8** (94 mg, 0.5 mmol) was treated with Me_2AlSPh (1.5 mmol) as described above to afford **9** (0.14 g, 94% yield): bp 152 °C (bath temp, 3 Torr); IR (neat) 3440, 1702 cm^{-1}; NMR (CCl_4) δ 1.47—2.09 (m, 12H), 2.28—2.47 (m, 2H), 2.93 (bs, 1H), 3.81 (m, 2H), 7.13—7.48 (m, 5H); MS *m/e* (%) 180 (14), 162 (8), 137 (17), 135 (14), 124 (32), 110 (100). Found: *m/e* 290.1329. Calcd for $C_{17}H_{22}O_2S$: M, 290.1339.

(E)-2-Ethylidene-3-methylcyclohexanone **11**: A solution of the acetate of the keto alcohol **10** (0.13 g, 0.7 mmol) in ether (1.0 ml) was added to a solution of lithium dimethylcuparte (0.9 mmol) in ether (3.0 ml) at −23 °C. After 17 min at −23 °C and 5 min at 0 °C, saturated NH_4Cl solution was added and the mixture was filtered. The filtrate was washed with water and brine, dried, and freed of the solvent. Purification by column chromatography on silica gel afforded **11** (57 mg) in 59% yield. The absence of *Z*-isomer was confirmed by the examination of its NMR spectrum.[22]

Ethyl (2-Ethylidene-3-oxocyclohexyl)acetate **12**: A mixture of **10** (0.13 g, 0.9 mmol) triethyl orthoacetate (1.7 ml, 9.2 mmol), and propionic acid (catalytic amount) was heated at 130 °C for 20 min. The mixture was diluted with ethyl acetate and washed with saturated aqueous solution of sodium hydrogencarbonate. The aqueous phase was extracted with ethyl acetate and the combined organic layer was washed with brine, dried, and freed of the solvent. The crude product was submitted to preparative TLC (hexane:ether=1:1, two developments) to give the title compound **12** (*E*-isomer, 89 mg; *Z*-isomer, 45 mg) in 70% yield. The stereochemical assignment was based on the examination of the NMR spectrum.[23]

E-Isomer: Bp 105 °C (bath temp, 0.5 Torr); IR (neat) 1740, 1695, 1620 cm^{-1}; NMR (CCl_4) δ 1.26 (t, J=7.0 Hz, 3H), 1.79 (d, J=7.5 Hz, 3H), 1.70—1.90 (m, 4H), 2.28 (m, 4H), 3.43 (m, 1H), 4.06 (q, J=7.0 Hz, 2H), 6.45 (qd, J=7.5 and 1.2 Hz, 1H); MS *m/e* (%) 211 (5), 210 (M^+, 10), 165 (17), 153 (11), 123 (100), 122 (79), 95 (56). Found: C, 68.50; H, 8.69%. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%.

Z-Isomer: IR (neat) 1740, 1695, 1635 cm^{-1}; NMR (CCl_4) δ 1.24 (t, J=7.0 Hz, 3H), 1.80 (d, J=7.5 Hz, 3H), 1.70—1.94 (m, 4H), 2.30 (m, 4H), 2.69 (m, 1H), 4.05 (q, J=7.0 Hz, 2H), 5.65 (qd, J=7.5 and 1.4 Hz, 1H); MS *m/e* (%) 211 (3), 210 (M^+, 8), 165 (16), 153 (11), 123 (100), 122 (77), 95 (55). Found: C, 68.49; H, 8.68%. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%.

The authors wish to thank the Ministry of Education, Science and Culture, Japan, for the Grant-in-Aid (403022).

References

1) Preliminary account of this work has appeared: A. Itoh, S. Ozawa, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, **21**, 361 (1980).

2) E. A. Jeffery, A. Meisters, and T. Mole, *J. Organomet. Chem.*, **74**, 373 (1974).

3) J. Tsuji, T. Yamada, M. Kaito, and T. Mandai, *Tetrahedron Lett.*, **1979**, 2257.

4) K. Maruoka, S. Hashimoto, Y. Kitagawa, H. Yamamoto, and H. Nozaki, *J. Am. Chem. Soc.*, **99**, 7705 (1977).

5) H. Nozaki, K. Oshima, K. Takai, and S. Ozawa, *Chem. Lett.*, **1979**, 379.

6) a) T. Mukaiyama, K. Inomata, and M. Muraki,

J. Am. Chem. Soc., **95**, 967 (1973); b) T. Shono, Y. Matsumura, S. Kashimura, and K. Hatanaka, *ibid.*, **101**, 4752 (1979); c) M. Watanabe, K. Shirai, and T. Kumamoto, *Bull. Chem. Soc. Jpn.*, **52**, 3318 (1979).

7) a) D. J. Ager and I. Fleming, *J. Chem. Soc., Chem. Commun.*, **1978**, 177; b) S. J. Branca and A. B. Smith, III, *J. Am. Chem. Soc.*, **100**, 7767 (1978); c) M. A. Guaciaro, P. M. Wovkulich, and A. B. Smith, III, *Tetrahedron Lett.*, **1978**, 4661.

8) N. Davidson and H. C. Brown, *J. Am. Chem. Soc.*, **64**, 316 (1942).

9) A. P. Kozikowski and A. Ames, *J. Org. Chem.*, **43**, 2735 (1978).

10) This product is a key compound for the synthesis of cyclopentenoid antibiotics (see Ref. 7b). The research described here was started to exploit an another versatile route to this compound.

11) T. Cohen and R. E. Gapinsky, *Tetrahedron Lett.*, **1978**, 4319.

12) J-E Dubois and M. Dubois, *Bull. Soc. Chim. Fr.*, **1969**, 3126.

13) D. A. Evans, E. Vogel, and J. V. Nelson, *J. Am. Chem. Soc.*, **101**, 6120 (1979).

14) a) P. A. Grieco and M. Miyashita, *J. Org. Chem.*, **40**, 1181 (1975); b) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975).

15) Diethylaluminum iodide was purchased from Aldrich Chemical Co.; E. C. Ashby and S. A. Noding, *J. Org. Chem.*, **44**, 4792 (1979).

16) F. Naef, R. Decorzant, and W. Thommen, *Helv. Chim. Acta*, **58**, 1808 (1975).

17) R. J. Anderson, C. A. Henrick, and J. B. Siddall, *J. Am. Chem. Soc.*, **92**, 735 (1970).

18) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T-t. Li, D. J. Faulkner, and M. R. Petersen, *J. Am. Chem. Soc.*, **92**, 741 (1970).

19) All the hydroxy compounds in Table 1 were transformed to trimethylsilyl ethers in order to obtain analytical samples.

20) Boiling point of the trimethylsilyl ether was recorded.

21) E. J. Corey and D. Enders, *Chem. Ber.*, **111**, 1337, 1362 (1978).

22) M. Bortoluss, R. Bloch, and J. M. Conia, *Bull. Soc. Chim. Fr.*, **1975**, 2722.

23) R. M. Silverstein, C. G. Bassler, and T. C. Morrill, "Spectrometric Identification of Organic Compounds," 3rd ed, John Wiley and Sons, New York, N. Y. (1974), pp. 168—169.