Journal of Organometallic Chemistry, 321 (1987) 307–316
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

MICHAEL-TYPE ADDITION OF *O*-ETHYL-*C*,*O*-BIS(TRIMETHYLSILYL)KETENE ACETAL AND ITS APPLICATION TO THE SYNTHESIS OF α-YLIDENE-δ-LACTONES

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(Received August 25th, 1986)

Summary

O-Ethyl-*C*,*O*-bis(trimethylsilyl)ketene acetal behaves as an active C_2 chain-lenghtening unit when treated with α,β-unsaturated ketones yielding δ-keto-α-trimethylsilylesters with the aid of titanium tetrachloride. The products readily form α-ylidene-δ-lactone derivatives after selective reduction of the ketone carbonyl and subsequent Peterson type olefination.

Introduction

Bis(trimethylsilyl)ketene acetal (**1**) is a good C_2 chain-lengthening unit, which behaves as a nucleophilic equivalent to the methyl acetate anion with the aid of titanium tetrachloride ($TiCl_4$). The reaction of **1a** with aldehydes leads to stereoselective formation of ($2R^*$, $3S^*$)-aldol type products **2** or (*Z*)-α,β-unsaturated esters (**3**) depending on reaction temperature [1]. The trimethylsilyl group retained in **2** plays an important role in controlling the stereochemistry of **3**. On the other hand **1a** reacts with conjugated cycloalkenones to give Michael-type products **4** selectively, which are exploited in the synthesis of methyl jasmonate [2]. It is imperative that a trimethylsilyl group is located on the anionic carbon for the Peterson type of chain-lengthening [3–7], therefore, the structure of **4** is expedient for the selective chain-lengthening at the less acidic site (see Scheme 1).

Interest in the α-methylene-δ-lactones has been aroused in relation to the total synthesis of vernolepin [8–11]. This prompted us to apply the Michael-type products (**4**) to the general synthesis of α-ylidene-δ-lactones (**9**). Here we report on the Michael-type addition of *O*-ethyl-*C*,*O*-bis(trimethylsilyl)ketene acetal **1b** to α,β-unsaturated ketones and the subsequent transformation of **7** into α-ylidene-δ-lactones, **9** and **10**.

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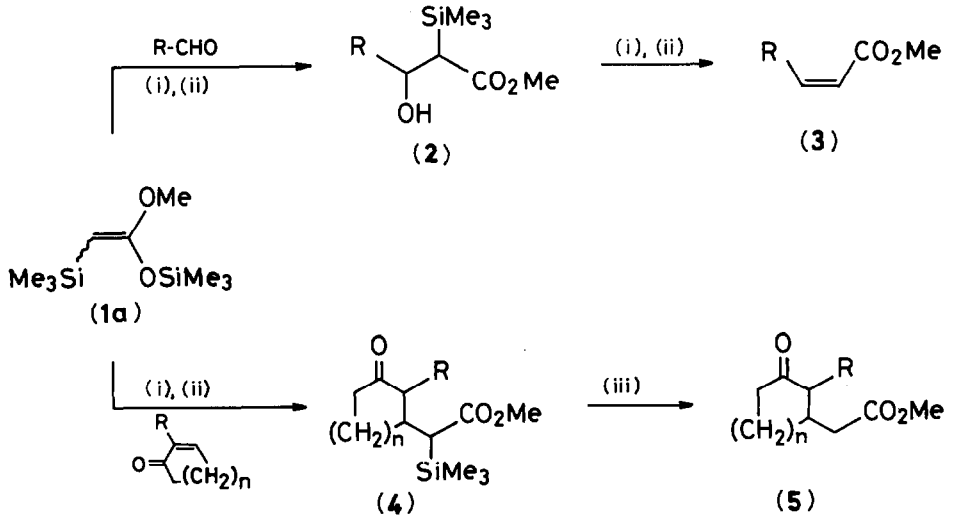


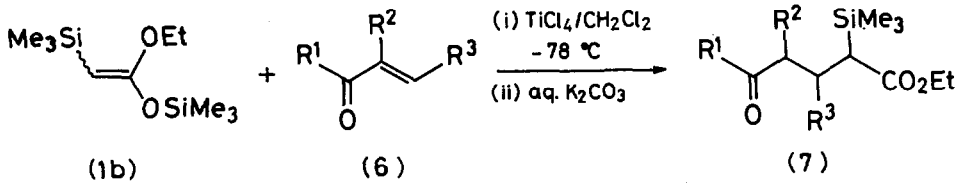
SCHEME 1. (i) $TiCl_4/CH_2Cl_2$, −78°C. (ii) aq. K_2CO_3. (iii) KF/aq. MeOH, room temperature.

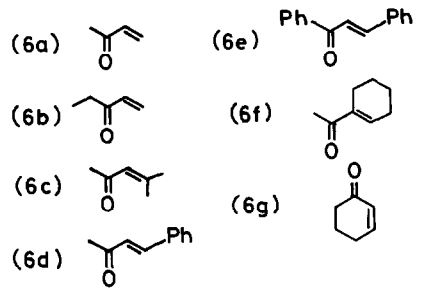
Resolution and discussion

Michael-type addition of ***1b*** *to α,β-unsaturated ketones*

In spite of the presence of the bulky trimethylsilyl group, ketene acetal **1b** readily reacts with α,β-unsaturated ketones (**6**) to give δ-keto-α-trimethylsilylesters (**7**) in good yields, with the aid of an equimolar amount of $TiCl_4$ at −78°C. A mixed ligand titanium compound derived from $TiCl_4$ and half a mole of $Ti(O^iPr)_4$ gave higher yields of **7** in the case of the susceptible α,β-enones **6a**, **6b**, and **6g** [12]. The disproportionation between $TiCl_4$ and $Ti(O^iPr)_4$ would lower the Lewis acidity of titanium reagent and prevent unwanted consumption of α,β-enones. A similar improvement of yield was also observed by simultaneous addition of **1b** and **6** to a cooled dichloromethane solution of $TiCl_4$. The competitive formation of the aldol product **2** was confined to 2% for all types of α,β-enones **6**, although the aldol product **2** (R; PhCH=CH–) was selectively isolated in the case of cinnamaldehyde under the similar conditions. The structure of **7** was determined from its IR and ^1H NMR spectra and elemental analysis. The trimethylsilyl group is unambiguously present on the α-carbon of ester group. Although the following two procedures, Michael-type addition of *O*-methyl-*O*-(t-butyldimethylsilyl)ketene acetal [13,14] and ethyl trimethylsilylacetate [15] to α,β-enone and C-diphenylmethylsilylation of ester [6] have been published, the selective synthesis of **7** cannot be attained by the two-step method. Thus, the present bimolecular coupling to give **7** which, from a synthetic point of view, offers an efficient entry for the selective activation of the less acidic α-proton in the δ-keto ester.

In contrast to the successful regiocontrol, diastereomeric control does not favor construction of **7d–7g**. However, **7d** and **7e** have a pair of diastereomers which can be separated by column chromatography. The ratio (45/55) of each pair of the diastereomers is estimated by comparison of the well separated trimethylsilyl group in the ^1H NMR spectra with **7d** and **7e**. Since the trimethylsilyl group is removed in





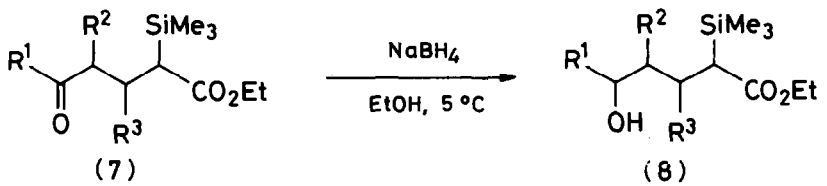
the olefination stage, ester **7** was used for the following reduction, without precise diastereomer assignment at that time.

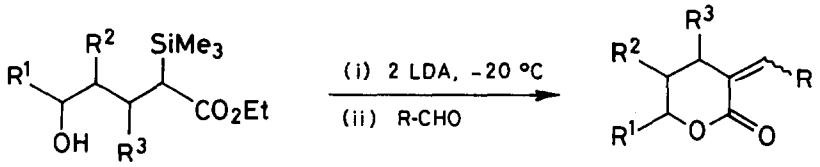
Reduction of 7 with $NaBH_4$

Selective reduction of the ketone carbonyl group in **7** was achieved in good yield by the reaction of $NaBH_4$ in ethanol at 5°C. The trimethylsilyl group of **7**, which was relatively susceptible under basic conditions, remained intact during the reduction within 1 h. In contrast to the chemoselectivity, the diastereoselectivity was not observed in the reduction with $NaBH_4$. For example, the isolated isomer, **7e**-I, gave a mixture of two diastereomers, **8e**-I and **8e**-II, in an almost equal ratio, which was estimated by comparison of the trimethylsilyl groups in the ^1H NMR spectrum (δ 0.00 and 0.15). Analogously **7e**-II gave another pair of diastereo mixtures, **8e**-III and **8e**-IV (δ −0.33 and −0.23).

Synthesis of α-ylidene-δ-lactones 9 and 10 from 8

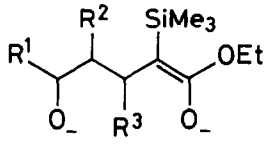
The transformation of δ-hydroxy esters **8** into α-benzylidene-δ-lactones **9** was successfully achieved by way of the following procedure. The addition of **8** to a 1,3-dimethoxyethane (DME) solution of two equivalents of lithium diisopropyl-





(8)

(9) R = Ph
(10) R = H



(11)

amide (LDA) gave dianion **11**. An excess of benzaldehyde was then added to the resultant solution at −78°C. The usual work-up of the mixture, stirring for 2 h at the same temperature and refluxing for 1 h, gave desired δ-lactones **9** in relatively good yields. Although stereochemistry of the olefin part was not controlled during this transformation as in other Peterson-type olefinations [3–5], stereocontrolled formation of ester enolate anion [17,18] or titanium mediated olefin formation of silylketene acetal [1,19] would attain the stereodefined synthesis of **9**. It should be noted that the transformation from **8** to **9** is applicable to formaldehyde in the one-pot reaction. In fact, bubbling of an excess of formaldehyde gas into a tetrahydrofuran (THF) solution of **11** also gave α-methylene-δ-lactone **10** without problems. This is in contrast to another study in which it was found that α-silyl-γ-lactone anion did not give the expected product with formaldehyde [20].

Thus, the present route is a facile synthesis method requiring three readily available components, **1b**, α,β-unsaturated ketone, and aldehyde.

Experimental

All reactions were carried out under argon. The IR spectra in carbon tetrachloride were recorded on a JASCO IR-403G. A JEOL C-60HL instrument was used to record the ^{1}H NMR spectra in carbon tetrachloride with tetramethylsilane as internal standard. Bath temperatures of the bulb-to-bulb distillation apparatus were taken as the boiling points except for **1b**.

Preparation of O-ethyl-C,O-bis(trimethylsilyl)ketene acetal (1b)

To a THF solution (205 ml) of lithium diisopropylamide, generated from butyllithium (0.271 mol) and diisopropylamine (28.1 g, 0.278 mol), was added ethyl trimethylsilylacetate (30.3 g, 0.189 mol) at −78°C and stirred for 3 h (at −78°C). The reaction mixture was quenched with an excess of chlorotrimethylsilane (34.4 g, 0.32 mol) at the same temperature. The mixture was stirred for a further 1.5 h at

room temperature and concentrated under reduced pressure. Distillation of the residual liquid yielded 37.1 g (85%) of **1b** as a colorless liquid: B.p.: 55–60°C/0.3 Torr. Anal. Found: C, 51.39; H, 10.53. $C_{10}H_{24}O_2Si_2$ calc: C, 51.67; H, 10.41%. IR: 1609 (C=C) cm^{-1}, 1252, 1245(SiC_3)cm^{-1}. ^1H NMR: major isomer δ 0.00 ($SiCH_3$, 9H, s), 0.27 ($SiCH_3$, 9H, s), 1.21 (CH_2CH_3, 3H, t, *J* 6.9 Hz), 2.94 (C=C*H*, 1H, s), and 3.80 (CH_2CH_3, 2H, q, *J* 6.9 Hz) ppm; minor isomer δ 0.00 ($SiCH_3$, 9H, s), 0.19 ($SiCH_3$, 9H, s), 1.28 (CH_2CH_3, 3H, t, *J* 6.9 Hz), 2.81 (C=C*H*, 1H, s), and 3.73 (CH_2CH_3, 2H, q, *J* 6.9 Hz) ppm.

Synthesis of δ-keto-α-trimethylsilylesters (7)

Ethyl 5-oxo-2-trimethylsilylhexanoate (7a). To a solution of $TiCl_4$ (1.02 g, 5.38 mmol) and $Ti(O^iPr)_4$ (0.29 g, 1.54 mmol) in dichloromethane (18 ml) dropwise was added a solution of 3-buten-2-one (**6a**) (0.267 g, 3.81 mmol) and **1b** (1.120 g, 4.82 mmol) in dichloromethane (3 ml) at −78°C. The color of the mixture immediately changed to red brown. After stirring for 3 h at −78°C, the reaction mixture was quenched with aqueous K_2CO_3 solution at the same temperature. The organic portion was decanted and diethyl ether (50 ml) was poured into the residue. The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 30 ml). The organic part was washed with brine (2 × 30 ml) and dried over anhydrous $MgSO_4$. The solvent was evaporated off under reduced pressure and the residual oil was purified by column chromatography, eluting with a mixed solvent (hexane/benzene/ethyl acetate = 48/18/1) gave **7a** (0.567 g, 51%) as a colorless liquid: B.p.: 88°C/0.2 Torr. Anal. Found: C, 57.08; H, 9.69. $C_{11}H_{22}O_3Si$ calc: C, 57.35; H, 9.63%. IR: 1715 (C=O), 1248 (SiC_3) cm^{-1}. ^1H NMR: δ 0.08 ($SiCH_3$, 9H, s), 1.22 (CH_2CH_3, 3H, t, *J* 7.1 Hz), 1.6–1.9 (CH_2 and C*H*, 3H, m), 2.02 (CH_3, 3H, s), 2.2–2.5 (CH_2C=O, 2H, m), and 4.00 (CH_2CH_3, 2H, q, *J* 7.1 Hz) ppm.

Ethyl 5-oxo-2-trimethylsilylheptanoate (7b). Treatment, similar to above, of 1-penten-3-one (**6b**) (1.528 g, 18.17 mmol), **1b** (4.688 g, 20.17 mmol), and $TiCl_4$ (3.784g, 19.94 mmol) in CH_2Cl_2 (100 ml) gave **7b** (3.286 g, 74%) as a colorless liquid: B.p.: 83°C/0.1 Torr. Anal. Found: C, 58.72; H, 9.99. $C_{12}H_{24}O_3Si$ calc: C, 58.97; H, 9.90%. IR: 1715 (C=O), 1249 (SiC_3) cm^{-1}. ^1H NMR: δ 0.08 ($SiCH_3$, 9H, s), 1.12 (CH_3, 3H, t, *J* 6.8 Hz), 1.34 (CH_3, 3H, t, *J* 6.8 Hz), 1.7–1.9 (CH_2 and C*H*, 3H, m), 2.1–2.5 (CH_2 × 2, 4H, m), and 4.16 (CH_2, 2H, q, *J* 6.8 Hz) ppm.

Ethyl 3,3-dimethyl-5-oxo-2-trimethylsilylhexanoate (7c). Treatment, similar to above, of 4-methyl-3-penten-2-one (**6c**) (2.077 g, 21.16 mmol), **1b** (5.519 g, 23.74 mmol), and $TiCl_4$ (5.16 g, 27.2 mmol) in CH_2Cl_2 (12 ml) gave **7c** (4.539 g, 83%) as a colorless liquid: B.p.: 85°C/0.1 Torr. Anal. Found: C, 60.32; H, 10.14. $C_{13}H_{26}O_3Si$ calc: C, 60.42; H, 10.14%. IR: 1720 (C=O, sh.), 1713 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ 0.13 ($SiCH_3$, 9H, s), 1.15 (CH_3 × 2, 6H, s), 1.23 (CH_3, t, *J* 7.2 Hz), 2.02 (CH_3, 3H, s), 2.32 (CH_2, 2H, s), 2.62 (C*H*, 1H, s), and 4.02 (CH_2, 2H, q, *J* 7.2 Hz) ppm.

Ethyl 5-oxo-3-phenyl-2-trimethylsilylhexanoate (7d). Treatment, similar to above, of 4-phenyl-3-buten-2-one (**6d**) (1.789 g, 12.24 mmol), **1b** (3.649 g, 15.69 mmol) and $TiCl_4$ (2.58 g, 13.60 mmol) in CH_2Cl_2 gave **7d** (3.676 g, 98%) as a colorless oil: B.p.: 135°C/0.2 Torr. Anal. Found: C, 66.43; H, 8.37. $C_{17}H_{26}O_3Si$ calc: C, 66.62; H, 8.55%. IR: 1715 (C=O), 1247 (SiC_3) cm^{-1}. ^1H NMR: Isomer I, δ 0.12 ($SiCH_3$, 9H, s), 0.91 (CH_3, 3H, t, *J* 7.4 Hz), 1.74 (CH_3, 3H, s), 2.37 (C*H*, 1H, d, *J* 11.0 Hz), 2.61 (CH_2, 2H, *J* 7.5 Hz), 3.46 (C*H*, 1H, d.t., *J* 7.5 and 11.0 Hz), 3.72 (CH_2, 2H, q, *J*

7.4 Hz), 7.09 (Ph, 5H, broad, s) ppm. Isomer II, δ −0.23 ($SiCH_3$, 9H, s), 1.24 (CH_3, 3H, t, J 6.9 Hz), 1.80 (CH_3, 3H, s), 2.26 (CH, 1H, d, J 1.2 Hz), 2.7–3.0 (CH_2, 2H, m), 3.5–3.9 (CH, 1H, m), 4.02 (CH_2, 2H, q, J 6.9 Hz), 7.12 (Ph, 5H, broad s) ppm.

Ethyl 5-oxo-3,5-diphenyl-1-trimethylsilylpentanoate (7e). Treatment, similar to above, of 1,3-diphenyl-2-propen-1-one (**6e**) (4.357 g, 20.92 mmol), **1b** (5.217 g, 22.44 mmol) and $TiCl_4$ in CH_2Cl_2 (55 ml) gave **7e** (7.324 g, 95%) as colorless needles. Anal. Found: C, 71.74; H, 7.74. $C_{22}H_{28}O_3Si$ calc: C, 71.70; H, 7.66%.

Isomer I, M.p.: 89.5–91.5°C. IR (KBr disk): 1709 (C=O), 1686 (C=O), 1261 (SiC_3) cm^{-1}. ^1H NMR: δ 0.12 ($SiCH_3$, 9H, s), 0.93 (CH_3, 3H, t, J 7.1 Hz), 2.57 (CH, 1H, d, J 9.9 Hz), 3.23 (CH_2, 2H, d, J 6.9 Hz), 3.8–4.1 (CH, 1H, m), 3.80 (CH_2, 2H, q, J 7.1 Hz), 7.0–7.8 (Ph × 2, 10H, m) ppm.

Isomer II, M.p.: 36.0–48.0°C. IR (KBr disk): 1712 (C=O), 1689 (C=O), 1252 (SiC_3) cm^{-1}. ^1H NMR: δ −0.21 ($SiCH_3$, 9H, s), 1.27 (CH_3, 3H, t, J 7.1 Hz), 2.43 (CH, 1H, d, J 10.8 Hz), 3.22 (CH_2, 2H, d, J 7.7 Hz), 3.1–4.0 (CH, 1H, m), 4.12 (CH_2, 2H, q, J 7.1 Hz), 7.1–7.9 (Ph × 2, 10H, m) ppm.

1-Acetyl-2-[(ethoxycarbonyl)(trimethylsilyl)methyl]cyclohexane (7f). Treatment, similar to above, of 1-acetylcyclohexene (**6f**) (2.010 g, 16.18 mmol), **1b** (4.181 g, 17.99 mmol), and $TiCl_4$ (3.78 g, 19.9 mmol) in CH_2Cl_2 (80 ml) gave **7f** (3.933 g, 85%) as a colorless oil: B.p.: 118–122°C/0.2 Torr. Anal. Found: C, 63.41; H, 10.20. $C_{15}H_{28}O_3Si$ calc: C, 63.33; H, 9.92%. IR: 1712 (C=O), 1249 (SiC_3). ^1H NMR: δ 0.07, 0.11 ($SiCH_3$, 9H, each s), 1.25 (CH_3, 3H, t, J 7.0 Hz), 1.2–2.0 (cyclohexyl, 9H, m), 2.01, 2.06 (CH_3, 3H, each s), 2.0–2.3 (CH, 1H, m), 2.7–3.0 (CH, 1H, m), 4.03 (CH_2, 2H, q, J 7.0 Hz) ppm.

3-[2-(Ethoxycarbonyl)(trimethylsilyl)methyl]cyclohexanone (7g). Treatment, similar to above, of 2-cyclohexenone (**6g**) (1.758g, 18.57 mmol), **1b** (4.729 g, 20.34 mmol), and $TiCl_4$ (3.96 g, 20.86 mmol) gave **7g** (4.095 g, 86%) as a colorless oil: B.p.: 120°C/0.1 Torr. Anal. Found: C, 61.01; H, 9.53. $C_{13}H_{24}O_3Si$ calc: C, 60.89; H, 9.43%. IR: 1715 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ 0.10 ($SiCH_3$, 9H, s), 1.25 (CH_3, 3H, t, J 7.1 Hz), 1.5–2.4 (cyclohexyl and CH, 10H, m), 4.05 (CH_2, 2H, q, J 6.7 Hz) ppm.

Synthesis of δ-hydroxy-α-trimethylsilylcarboxylic esters (8)

Ethyl 5-hydroxy-2-trimethylsilylhexanoate (8a). To a solution of **7a** (0.750 g, 3.25 mmol) in ethanol (15 ml), was added $NaBH_4$ (0.148 g, 3.92 mmol) in small portions at 0°C. After all the $NaBH_4$ had been added, the mixture was stirred for 25 min at 5°C and quenched with 1 M aqueous HCl (10 ml) and stripped of ethanol under reduced pressure. The residual aqueous layer was extracted with ethyl acetate (4 × 20 ml). These extracts were collected, washed with brine (2 × 20 ml), and dried over anhydrous $MgSO_4$. After the solvent had been evaporated off, the residual oil was purified by silica gel column chromatography, eluting with a mixed solvent (hexane/benzene/ethyl acetate = 3/3/1) gave **8a** (0.754 g, 98%) as a colorless oil: B.p.: 90°C/0.2 Torr. Anal. Found: C, 56.59; H, 10.50. $C_{11}H_{24}O_3Si$ calc: C, 56.85; H, 10.41%. IR: 1716 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ 0.07 ($SiCH_3$, 9H, s), 1.12 (CH_3, 3H, d, J 6.0 Hz), 1.25 (CH_3, 3H, t, J 7.4 Hz), 1.3–1.9 (CH_2 × 2, CH × 2, 6H, m), 2.80 (OH, 1H, broad s), 4.09 (CH_2, 2H, q, J 7.4 Hz) ppm.

Ethyl 5-hydroxy-2-trimethylsilylheptanoate (8b). When **7b** (1.571 g, 5.53 mmol) and $NaBH_4$ (0.29 g, 7.69 mmol) were treated in a manner similar to that for **8a**, in ethanol (20 ml), **8b** (1.267 g, 93%) was obtained as a colorless oil: B.p.: 120°C/0.2

Torr. Anal. Found: C, 58.36; H, 10.66. $C_{12}H_{26}O_3Si$ calc: C, 58.49; H, 10.64%. IR: 1714 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ 0.06 ($SiCH_3$, 9H, s), 0.91 (CH_3, 3H, t, 6.3 Hz), 1.24 (CH_3, 3H, t, *J* 7.2 Hz), 1.3–2.1 ($CH_2 \times 3$, CH, 7H, m), 2.49 (OH, 1H, broad s), 3.2–3.6 (CH, 1H, m), 4.08 (CH_2, 2H, q, *J* 7.2 Hz) ppm.

*Ethyl 5-hydroxy-3,3-dimethyl-2-trimethylsilylhexanoate (**8c**).* When **7c** (5.441 g, 21.05 mmol) and $NaBH_4$ (0.844 g, 22.30 mmol) were treated in a manner similar to that for **8a** in ethanol (40 ml), **8c** (4.169 g, 76%) was obtained as a colorless oil. B.p.: 85°C/0.1 Torr. Anal. Found: C, 59.84; H, 11.10. $C_{13}H_{28}O_3Si$ calc: C, 59.95; H, 11.01%. IR: 1714 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ 0.12 ($SiCH_3$, 9H, s), 1.12 ($CH_3 \times 2$, 6H, s), 1.14 (CH_3, 3H, d, *J* 5.2 Hz), 1.18 (CH_3, 3H, t, *J* 7.1 Hz), 1.3–1.7 (CH_2, 2H, m), 1.8–2.1 (OH, 1H, broad peak), 2.20, 2.23 (CH, 1H, s), 3.7–3.9 (CH, 1H, m), 4.04, 4.07 (CH_2, 2H, q, *J* 7.1 Hz) ppm.

*Ethyl 5-hydroxy-2-trimethylsilyl-3-phenylhexanoate (**8d**).* When **7d** (6.12 g, 20.00 mmol) and $NaBH_4$ (0.730 g, 19.31 mmol) were treated in a manner similar to that for **8a** in ethanol (50 ml), **8d** (5.804 g, 94%) was obtained as a colorless oil. Anal. Found: C, 66.25; H, 9.15. $C_{17}H_{28}O_3Si$ calc: C, 66.19; H, 9.15%. IR: 1721 (C=O), 1249 (SiC_3) cm^{-1}. ^1H NMR: δ −0.29, −0.27, 0.16 ($SiCH_3$, 9H, each s), 0.87, 1.22, 1.28 (CH_2CH_3, 3H, each t, *J* 7.4 Hz), 1.04, 1.08 ($CHCH_3$, 3H, each d, *J* 5.3 Hz), 1.5–2.5 (CH_2, SiCH, PhCH, OH, 5H, m), 2.7–3.5 (OCH, 1H, m), 3.68, 4.03, 4.09 (CH_2, each q, *J* 7.4 Hz), 7.0–7.4 (Ph, 5H, m) ppm.

*Ethyl 5-hydroxy-2-trimethylsilyl-3,5-diphenylpentanoate (**8e**).* When **7e** (9.082 g, 24.64 mmol) and $NaBH_4$ (0.945 g, 24.98 mmol) were treated in a similar manner to that for **8a**, in ethanol (90 ml), **8e** (8.035 g, 88%) was obtained as a colorless oil. Anal. Found: C, 71.33; H, 8.17. $C_{22}H_{30}O_3Si$ calc: C, 71.31; H, 8.16%. IR: 1717 (C=O), 1251 (SiC_3) cm^{-1}. ^1H NMR: Isomer I, δ −0.33 ($SiCH_3$, 9H, s), 1.22 (CH_3, 3H, t, *J* 7.2 Hz), 1.9–2.1 (CH_2, 2H, m), 2.23 (CHSi, 1H, d, *J* 10.9 Hz), 2.5–3.0 (CHPh, OH, 2H, m), 3.8–4.2 (CHO, 1H, m), 4.00 (CH_2, 2H, q, *J* 7.1 Hz), and 6.8–7.2 (Ph × 2, 10H, m). Isomer II, δ −0.23 ($SiCH_3$, 9H, s), 1.21 (CH_3, 3H, t, *J* 7.4 Hz), 1.6–2.8 (CH_2, CH × 2, OH, 5H, m), 3.2–3.6 (CH, 1H, m), 3.96 (CH_2, 2H, q, *J* 7.4 Hz), 6.8–7.2 (Ph × 2, 10H, m). Isomer III, δ 0.00 ($SiCH_3$, 9H, s), 0.83 (CH_3, 3H, t, *J* 7.4 Hz), 1.9–2.8 (CH_2, CH × 2, OH, 5H, m), 3.62 (CH_2, 2H, q, *J* 7.4 Hz), 4.09 (O–CH, 1H, t, *J* 7.4 Hz), and 6.9–7.3 (Ph × 2, 10H, m). Isomer IV, δ 0.15 ($SiCH_3$, 9H, s), 0.86 (CH_3, 3H, t, *J* 7.5 Hz), 1.6–2.8 (CH_2, CH × 2, OH, 5H, m), 3.66 (CH_2, 2H, q, *J* 7.5 Hz), 4.07 (OCH, 1H, t, *J* 6.9 Hz), and 7.0–7.4 (Ph × 2, 10H, m) ppm.

*2-(1′-Hydroxyethyl)-1-[(ethoxycarbonyl)(trimethylsilyl)methyl]cyclohexane (**8f**).* When **7f** (1.57 g, 5.53 mmol) and $NaBH_4$ (0.29 g, 7.69 mmol) were treated in a manner similar to that for **8a**, in ethanol (20 ml), **8f** (1.347 g, 85%) was obtained as a colorless oil: B.p.: 120°C/0.2 Torr. Anal. Found: C, 62.59; H, 10.80. $C_{15}H_{30}O_3Si$ calc: C, 62.89; H, 10.55%. IR: 1713 (C=O), 1693 (C=O), 1250 (SiC_3) cm^{-1}. ^1H NMR: δ −0.03, 0.03 ($SiCH_3$, 9H, each s), 0.98, 1.10 ($OCHCH_3$, 3H, each d, *J* 6.2 Hz), 1.16, 1.19 (CH_2CH_3, each t, *J* 7.4 Hz), 1.2–2.2 (cyclohexyl, 10H, m), 2.43 (OH, 1H, broad s), 2.6–2.8 (SiCH, 1H, m), 2.9–3.2 (O–CH, 1H, m), 3.96, 4.02 (CH_2CH_3, 2H, each q, *J* 7.4 Hz) ppm.

*3-[(Ethoxycarbonyl)(trimethylsilyl)methyl]cyclohexane-1-ol (**8g**).* When **7g** (4.693 g, 18.30 mmol) and $NaBH_4$ (0.732 g, 19.35 mmol) were treated in a manner similar to that for **8a**, in ethanol (50 ml), **8g** (3.641 g, 77%) was obtained as a colorless oil: B.p.: 120°C/0.15 Torr. Anal. Found: C, 60.49; H, 10.01. $C_{13}H_{26}O_3Si$ calc: C,

60.42; H, 10.14%. IR: 1720 (C=O), 1251 (SiC_3) cm^{-1}. ^1H NMR: δ 0.08 ($SiCH_3$, 9H, s), 1.25 (CH_2CH_3, 3H, t, J 7.5 Hz), 0.7–2.0 (cyclohexyl, 9H, m), 2.8–3.0 (SiC*H*, O*H*, 2H, m), 3.2–3.6 (OC*H*, 1H, m), 4.07 (CH_2CH_3, 2H, q, J 7.5 Hz) ppm.

Synthesis of α-benzylidene-δ-valerolactone (9)

2-Benzylidene-5-hexanolide (9a). A solution of **8a** (0.266 g, 1.13 mmol) in DME (3 ml) was added dropwise at −78°C to LDA (2.8 mmol) in DME (20 ml), prepared from diisopropylamine (0.399 g, 3.94 mmol) and butyllithium (2.8 mmol), and stirred for 2 h at −20°C. A solution of benzaldehyde (0.257, 2.42 mmol) in DME (3 ml) was then added to the above reaction mixture at −78°C. The color of the mixture immediately changed to yellow. After all the benzaldehyde had been added the mixture was stirred for 2 h at −78°C, for a further 13 h at room temperature, and then for 1 h while heating under reflux. The resulting solution was quenched with 1 *M* aqueous HCl (30 ml), the phases were separated, and the water layer was extracted with ethyl acetate (4 × 20 ml). The organic layer and the extracts were collected, washed with brine (2 × 30 ml), and dried over anhydrous $MgSO_4$. After the solvent had been evaporated off under reduced pressure, the residual oil was purified by silica gel column chromatography eluting with a mixture of hexane/benzene/ethyl acetate (23/23/4), and recrystallizing from a mixed solvent of benzene and hexane gave **9a** (0.150 g, 66%) as colorless needles: M.p.: 65.5–66.0°C. Anal. Found: C, 76.90; H, 6.95. $C_{13}H_{14}O_2$ calc: C, 77.20; H, 6.98%. IR: 1720 (C=O), 1617 (C=C) cm^{-1}. ^1H NMR: δ 1.33 (CH_3, 3H, d, J 6.3 Hz), 1.6–2.8 (CH_2 × 2, 4H, m), 4.1–4.6 (OC*H*, 1H, m), 6.56 (*Z*), 7.62 (*E*) Ph(*H*)C=C ~ , 1H, each t, J 1.9 Hz), 7.0–7.4 (Ph, 5H, m) ppm.

2-Benzylidene-5-heptanolide (9b). When **8b** (0.171 g, 0.69 mmol) and benzaldehyde (0.135 g, 1.27 mmol) were treated in a manner similar to that for **9a**, the pale yellow oil, **9b** (0.133 g, 89%), was obtained. Anal. Found: C, 77.79; H, 7.49. $C_{14}H_{16}O_2$ calc: C, 77.75; H, 7.46%. B.p.: 125°C/0.1 Torr. IR: 1722 (C=O), 1620 (C=C) cm^{-1}. ^1H NMR: δ 1.01 (CH_2CH_3, t, J 7.0 Hz), 1.4–2.9 (CH_2 × 3, 6H, m), 3.8–4.3 (OC*H*, 1H, m), 6.53 (*Z*), 7.60 (*E*) Ph(*H*)C=C ~ 1H, each t, J 1.8 Hz), 7.0–7.4 (Ph, 5H, m).

2-Benzylidene-3,3-dimethyl-5-hexanoate (9c). When **8c** (0.447 g, 1.72 mmol) and benzaldehyde (0.364 g, 3.43 mmol) were treated in a manner similar to that for **9a**, a yellow oil **9c** (0.226 g, 57%), was obtained. B.p. 98°C/0.2 Torr. Anal. Found: C, 78.53; H, 8.04. $C_{15}H_{18}O_2$ calc: C, 78.23; H, 7.88%. IR: 1713 (C=O), 1624 (C=C) cm^{-1}. ^1H NMR: δ 1.24 (CH_3, 3H, s), 1.32 (CH_3, 3H, s), 1.33 (CH_3, 3H, d, J 6.2 Hz), 1.6–1.8 (CH_2, 2H, m), 4.1–4.6 (OC*H*, 1H, m), 6.64 (*Z*), 7.89 (*E*) Ph(*H*)C=C ~ 1H, each s), 7.1–7.4 (Ph, 5H, m) ppm.

2-Benzylidene-3-phenyl-5-hexanolide (9d). When **8d** (0.136 g, 0.44 mmol) and benzaldehyde (0.169 g, 1.59 mmol) were treated in a manner similar to that for **9a**, colorless needles, **9d** (0.092 g, 75%), were obtained. B.p 185°C/0.2 Torr. M.p.: 80.5–83.5°C. Anal. Found: C, 81.97; H, 6.57. $C_{19}H_{18}O_2$ calc: C, 81.99; H, 6.52%. IR: 1715 (C=O), 1619 (C=C) cm^{-1}. ^1H NMR: δ 1.27 (CH_3, 3H, t, J 6.0 Hz), 1.9–2.2 (CH_2, 2H, m), 4.0–4.4 (PhC*H*, OC*H*, 2H, m), 7.0–7.5 (Ph × 2, 10H, m), 8.04 Ph(*H*)C=C ~ 1H, s) ppm.

2-Benzylidene-3,5-diphenyl-5-pentanolide (9e). When **8e** (0.185 g, 0.50 mmol) and benzaldehyde (0.089 g, 0.84 mmol) were treated in a manner similar to that for **9a**, a yellow oil, **9e** (0.129 g, 76%) was obtained. B.p. 180°C/0.1 Torr. Anal. Found: C,

84.44; H, 5.98. $C_{24}H_{20}O_2$ calc: C, 84.68,; H, 5.92%. IR: 1719 (C=O), 1619 (C=C) cm^{-1}. ^1H NMR: δ 2.1–2.4 (CH_2, 2H, m), 4.40 (PhC*H*, 1H, t, *J* 3.2 Hz), 5.09 (Ph(O)C*H*, 1H, t, *J* 7.5 Hz), 7.1–7.4 (Ph × 3, 15H, m), 8.08 Ph(*H*)C=C ~ 1H, s) ppm.

*5-Benzylidene-2-methyl-3-oxabicyclo[4.4.0]decan-4-one (**9f**).* When **8f** (0.222g, 0.78 mmol) and benzaldehyde (0.234 g, 2.21 mmol) were treated in a manner similar to that for **9a**, a pale yellow oil, **9f** (0.125 g, 63%), was obtained. B.p.: 120°C/2.0 Torr. Anal. Found: C, 79.80; H, 7.88. $C_{17}H_{20}O_2$ calc: C, 79.65; H, 7.86%. IR: 1723 (C=O), 1616 (C=C) cm^{-1}. ^1H NMR: δ 1.32, 1.36 (CH_3, 3H, each d, *J* 6.7 Hz), 0.9–2.2 (CH_2 × 4, C*H*, 9H, m), 2.5–3.0 (C*H*, 1H, m), 4.0–4.5 (OC*H*, 1H, m), 6.6–6.8 (*Z*), 7.55–7.7 (*E*) Ph(*H*)C=C ~ 1H, each m), 7.1–7.5 (Ph, 5H, m) ppm.

*4-Benzylidene-2-oxabicyclo[3.3.1]nonan-3-one (**9g**).* When **8g** (0.234 g, 1.80 mmol) and benzaldehyde (0.191 g, 1.80 mmol) were treated in a manner similar to that for **9a**, a yellow oil, **9g** (0.092 g, 45%), was obtained. B.p.: 110°C/0.3 Torr. Anal. Found: C, 78.69; H, 7.24. $C_{15}H_{16}O_2$ calc: C, 78.92; H, 7.06%. IR: 1716 (C=O), 1621 (C=C) cm^{-1}. ^1H NMR: δ 0.9–2.6 (CH_2 × 4, 8H, m), 3.14–3.42 (C*H*, 1H, broad peak), 4.5–4.7 (OC*H*, 1H, broad peak), 7.30 (Ph, 5H, broad s), 7.78 Ph(*H*)C=C ~ 1H, s) ppm.

*Synthesis of α-methylene-δ-valeroactone (**10**)*

*2-Methylene-5-heptanolide (**10b**).* A THF (15 ml) solution of **8a** (0.445 g, 1.80 mmol) was added, dropwise at −78°C to LDA (4.1 mmol) in THF (35 ml). After stirring for 2 h at −20°C, the reaction mixture was cooled to −78°C, and formaldehyde gas (prepared by cracking of 10–20 mmol of dry paraformaldehyde) was bubbled through it with a vigorous nitrogen stream. Then the reaction mixture was stirred for 2 h at −20°C, for a further 10 h at room temperature, and for 1 h at while heating under reflux. The resulting solution was quenched with 1 *M* aqueous HCl (40 ml). The phases were separated and the water layer was extracted with ethyl acetate (4 × 30 ml). The organic layer and the extracts were collected, washed with brine (2 × 30 ml), and dried over anhydrous $MgSO_4$. After the solvent had been evaporated off under reduced pressure, the residual oil was purified by silica gel column chromatography eluting with a mixture hexane/benzene/ethyl acetate (10/10/1) gave **10b** (0.113 g, 45%) as a colorless oil: B.p.: 98°C/0.21 Torr. Anal. Found: C, 68.71; H, 8.78. $C_8H_{12}O_2$ calc: C, 68.54; H, 8.63%. IR: 1731 (C=O), 1629 (C=C) cm^{-1}. ^1H NMR: δ 1.03 (CH_3, t, *J* 7.0 Hz), 1.3–2.3 (CH_2 × 2, 4H, m), 2.4–2.8 (CH_2, 2H, m), 3.9–4.4 (OC*H*, 1H, m) 5.44 ($HC{=}CC(=O)_{trans}$, 1H, d. t, *J* 2.4 and 3.8 Hz), 6.24, ($HC{=}CC(=O)_{cis}$, 1H, d. t, *J* = 2.7 and 3.8 Hz) ppm.

*2-Methylene-3,3-dimethyl-5-hexanolide (**10c**).* When **8c** (0.425 g, g, 1.63 mmol) and formaldehyde gas were treated in a manner similar to that for **10b**, a colorless oil, **10c** (0.100 g, 40%), was obtained: B.p.: 91°C/0.2 Torr. Anal. Found: C, 69.89; H, 9.44. $C_9H_{14}O_2$ calc: C, 70.10; H, 9.15%. IR: 1729 (C=O), 1622 (C=C) cm^{-1}. ^1H NMR: δ 1.25 (CH_3 × 2, 6H, s), 1.35 (CH_3, 3H, d *J* 6.2 Hz), 1.5–1.8 (CH_2, 2H, m), 4.2–4.7 (OC*H*, 1H, m), 5.56 ($HC{=}CC(=O)_{trans}$, 1H, d, *J* 1.9 Hz), 6.24 ($HC{=}CC(=O)_{cis}$, 1H, d, *J* 1.9 Hz).

*2-Methylene-3-phenyl-5-hexanolide (**10d**).* When **8d** (0.314 g, 1.02 mmol) and formaldehyde gas were treated in a manner similar to that for **10b**, a colorless oil, **10d** (0.110 g, 54%), was obtained. B.p.: 93°C/1.9 Torr. Anal. Found: C, 77.07; H, 6.87. $C_{13}H_{14}O_2$ calc: C, 77.20; H, 6.98%. IR: 1730 (C=O), 1625 (C=C) cm^{-1}. ^1H

NMR: Isomer I; δ 1.34 (CH_3, 3H, d, J 6.5 Hz), 1.9–2.1 (CH_2, 2H, m), 3.5–4.8 (PhC*H*, OC*H*, 2H, m), 5.44 ($HC{=}CC(=O)_{trans}$, 1H, dd., J 1.5 and 1.5 Hz), 6.54 ($HC{=}CC(=O)_{cis}$, 1H, d.d., J 1.5 and 2.1 Hz), 7.0–7.5 (Ph, 5H, m) ppm. Isomer II; δ 1.41 (CH_3, 3H, d, J 6.5 Hz), 2.0–2.2 (CH_2, 2H, m), 3.5–4.8 (PhC*H*, OC*H*, 2H, m), 5.14 ($HC{=}CC(=O)_{trans}$, 1H, d.d., J 2.3 and 3.0 Hz), 6.44 ($HC{=}CC(=O)_{cis}$, 1H, dd., J 2.6 and 3.0 Hz), 7.0–7.5 (Ph, 5H, m) ppm.

*2-Methylene-3,5-diphenyl-5-pentanolide (**10e**).* When **8e** (0.389 g, 1.05 mmol) and formaldehyde gas were treated in a manner similar to that for **10b**, a colorless oil, **10e** (0.131 g, 47%), was obtained. B.p.: 105°C/0.22 Torr. Anal. Found: C, 81.81; H, 6.12. $C_{18}H_{16}O_2$ calc: C, 81.79; H, 6.10%. IR: 1732 (C=O), 1625 (C=C) cm^{-1}. ^1H NMR: δ 2.35 (CH_2, 2H, t, J 5.8 Hz), 3.93 (PhC*H*, 1H, broad t, J 6.0 Hz), 5.1–5.3 (OC*H*, 1H, m), 5.38 ($HC{=}CC(=O)_{trans}$, 1H, d.d., J 1.6 and 1.9 Hz), 6.57 ($HC{=}CC(=O)_{cis}$, 1H, d.d., J 1.7 and 2.0 Hz), 7.0–7.3 (Ph × 2, 10H, m).

*5-Methylene-2-methyl-3-oxabicyclo[4.4.0]decan-4-one (**10f**).* When **8f** (0.419 g, 1.46 mmol) and formaldehyde gas were treated in a manner similar to that for **10b**, a colorless oil, **10f** (0.140 g, 53 5), was obtained. B.p.: 105°C/0.25 Torr. Anal. Found: C, 73.52; H, 9.09. $C_{11}H_{16}O_2$ calc: C, 73.30; H, 8.95%. IR: 1728 (C=O), 1623 (C=C) cm^{-1}. ^1H NMR: δ 1.29 (CH_3, 3H, d, J 6.8 Hz), 0.7–2.6 ($CH_2 \times 4$, $CH \times 2$, 10H, m), 3.9–4.8 (OC*H*, 1H, m), 5.4–5.6 ($HC{=}CC(=O)_{trans}$, 1H, m), 6.2–6.4 ($HC{=}CC(=O)_{cis}$, 1H, m).

Acknowledgement

The author thanks The Kurata Foundation for the Kurata Reserach Grant and Shin-Etsu Chemical Co. Ltd. for a gift of chlorotrimethylsilane.

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