A Simple Synthesis of α-Ylidene γ-Lactones from γ-Trimethylsiloxy Nitriles

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(Received January 5, 1979)

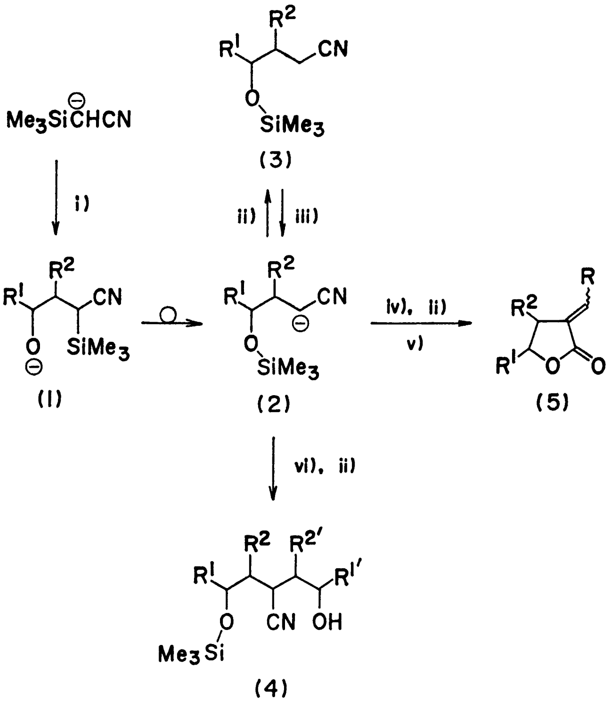
α-Cyano carbanions which are generated from γ-trimethylsiloxy nitriles have been found to react with aldehydes to give α-(1-hydroxyalkyl)-γ-trimethylsiloxy nitriles (**6**). α-Ylidene γ-lactones (**5**) are derived from **6** in two steps; hydrolytic lactonization to α-(1-hydroxyalkyl) γ-lactones and dehydration. The stereochemistry of the lactones **5** with one exception have been found to be of the *E* form on the basis of the NMR spectra.

α-Methylene-γ-butyrolactones have recently been the subject of extensive research since several sesquiterpenes possess cytotoxic and/or antitumor properties, largely attributed to this system.[1,2] A variety of methods have been developed for the synthesis of this moiety,[3,4] most of the procedures involving the introduction of the α-methylene group into a preformed lactone *via* the enolate anion.[5,6]

In a previous paper,[7] it was shown that the trimethylsilylacetonitrile (TMSAN) anion reacts readily and selectively with epoxides to produce γ-trimethylsiloxy nitriles **3** which are a possible synthetic equivalent of γ-lactones. This paper will report a method for the facile introduction of the α-methylene or alkylidene equivalent group into γ-lactones by the reaction of α-cyano carbanions **2** with aldehydes as a demonstration of the synthetic versatility of γ-trimethylsiloxy nitriles **3**.

Results and Discussion

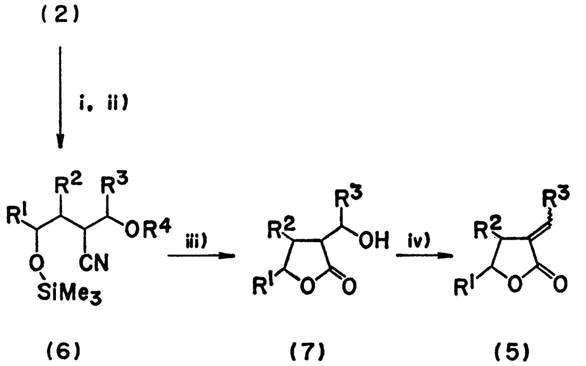
The dianion character of TMSAN has been suggested in the stepwise ring opening of two equivalents of epoxide.[7] This unusual character is brought about by the intermediate **2** which is generated as a result of the migration of the trimethylsilyl group from the carbon atom to the oxy anion in **1** as shown in Scheme 1. The intermediate **2** has been confirmed by the stepwise addition of different types of epoxide. Substitution of aldehydes in place of epoxides in the reaction of the anion **2** would be expected to give the α-(1-hydroxyalkyl)-γ-trimethylsiloxy nitriles as products which lead to α-alkylidene γ-lactones by additional two steps.



Scheme 1. i) $R^1CH\underset{O}{—}CHR^2$, ii) aq NH_4Cl, iii) LDA, iv) RCHO, v) Silica gel, vi) $R^1CH\underset{O}{—}CHR^2$.

An equivalent of benzaldehyde was added to a solution of **2b** (R^1=Me, R^2=H) formed from the TMSAN anion and propylene oxide in 1,2-dimethoxyethane (DME) and quenched with water, which produced an unexpected product, α-benzylidene γ-lactone **5b** (7%) in addition to other products. Lactone **5c** (6%) was obtained by a similar reaction of benzaldehyde with **2c** [R^1, R^2=$-(CH_2)_4-$]. Lactones **5b** and **5c** were given after purification of the reaction mixture by column chromatography on silica gel. Despite the low yield of **5** under optimum conditions, the result is noteworthy since this one pot reaction provides a general synthetic method for **5**. The reactivity of the anion **2** to aldehydes may decrease since it takes several hours to complete the formation of **2**. Therefore, alternative anions **2** from γ-trimethylsiloxy nitriles **3** have been used in order to enhance the selectivity of nucleophilic attack on the aldehydes. An efficient preparative method for γ-trimethylsiloxy nitriles **3** has been exploited on a large scale.[8] The outline of the procedure is summarized in Scheme 2.

α-Cyano carbanions **2** are generated smoothly by the interaction of nitriles **3** with an equivalent of butyl-



Scheme 2. i) R^3CHO, ii) aq NH_4Cl or Me_3SiCl, iii) 1.5 M. HCl, iv) $MeSO_2Cl$/pyridine, reflux.

TABLE 1. YIELDS OF PRODUCTS AND STEREOISOMERS OF 5

	R^1	R^2	R^3	R^4	6	7	5	
					Yield/%	Yield/%	Yield/%	Stereoisomers
a	H	H	Ph	H	63	77	87	*E*
b	Me	H	Ph	H	82	73	63	*E*
c	$-(CH_2)_4-$		Ph	H	84	48	45	*Z*
d	H	H	Me	Me_3Si	65	63	66	*E*
e	Me	H	Me	Me_3Si	69	70	82	*E*
f	$-(CH_2)_4-$		Me	H	64	69	39	*E*
g	Me	H	H	H	59	63	21	—
h	$-(CH_2)_4-$		H	H	77	85	47	—

lithium or lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C and react with aldehydes at ambient temperature. After quenching the reaction mixture with either aqueous ammonium chloride (a, b, c, f, g, and h) or chlorotrimethylsilane (d and e), α-(1-hydroxyalkyl)- or (1-trimethylsiloxyalkyl)-γ-trimethylsiloxy nitriles **6** are given. Compounds **6** hydrolyzed with 1.3 M hydrochloric acid in aqueous methanol spontaneously give α-(1-hydroxyalkyl)-γ-lactones **7**. The elimination of water from **7** is achieved by the use of methanesulfonyl chloride in pyridine giving α-alkylidene γ-lactones **5**, the results of which are summarized in the Table.

The structure of **5**, **6**, and **7** have been elucidated on the basis of IR, NMR, and elemental analyses. The IR spectra of **6** is analogous to **4**. The splitting of the trimethylsilyl group in the NMR spectra of **6** reflects the discrimination of diastereomers caused by asymmetric carbon atoms.[7] For example, two separate signals of the trimethylsilyl group at 0.16 and 0.20 ppm are observed and the terminal methyl group is clearly distinguished at 1.28 and 1.40 ppm in the case of **6f**.

The NMR spectra of **7** are more complicated due to the increase in rigidity of the conformations with the formation of lactone rings. The ring methyl group of **7e** appears as a double doublet (J=6.45 and 2.1 Hz) including long range coupling at 1.18 ppm while a pair of doublet at 1.37 and 1.43 ppm (J=6.3 Hz) has been assigned to the terminal methyl of the 1-hydroxyethyl group.

From the NMR spectra and an inspection of the CPK models it was possible to establish the stereochemistry around the olefinic part of the obtained α-alkylidene γ-lactones **5**. The chemical shift of the olefinic proton (6.81 and 6.36 ppm for *E* and *Z* isomers, respectively) is the most remarkable diagnostic point to discriminate between the geometrical isomers of α-ethylidene-γ-butyrolactone **5d**.[9] The observed values of the olefinic proton, 6.77, 6.64, and 6.51 ppm in a series of α-ethylidene γ-lactones (**5d**, **5e**, and **5f**) enabled the *E* isomers to be differentiated. This was coupled with the knowledge that the vinyl proton located in the cis position to the carbonyl group shows significant down field shift (0.6—0.9 ppm) compared with the trans proton in the cases of α-methylene cycloalkanones[10] and α-methylene γ-lactones **5g** and **5h**.

With respect to the α-benzylidene γ-lactones **5a**, **5b**, and **5c**, the olefinic protons show peaks at 7.54, 7.3, and 6.53 ppm, respectively. Relatively sharp peaks at 7.45 and 7.30 ppm have been observed for the phenyl protons of **5a** and **5b**. The multiplet pattern of the phenyl protons divided in two groups with a 3:2 intensity ratio at 7.3 and 7.7 ppm for **5c**, reflecting the different susceptibility among the phenyl protons towards the magnetic anisotropy effect by the carbonyl group. Therefore, it has been concluded that lactones **5a**[11] and **5b** are the *E* isomers whereas **5c** is the *Z* isomer based on the above data. The other isomer is not detectable from the NMR spectra. The selective formation of the isomer **5a**—**5f** shows that the elimination step (**7** to **5**) is a thermodynamically controlled reaction *via* a carbocation intermediate under the above conditions. The formation of the *Z* isomer in **5c** is consistent according to a comparison of both isomers by the CPK models. The *Z* isomer of **5c** is sterically less hindered than the *E* isomer.

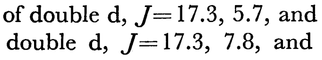
The ring juncture in the bicyclo system **5c**, **5f**, and **5g** has been designated trans based on the following. The starting material **3c** has been prepared by the ring opening of cyclohexene oxide with the acetonitrile anion, which arranges the trans relationship between the two substituents.[12] The coupling pattern of the junctional proton in close proximity to the oxygen atom in **5c**, **5f**, and **5g** shows a typical doublet of triplet composed of six peaks (see Experimental). The coupling constants of this pattern reflect the presence of two axial and an equatorial vicinal protons, which suggests a trans juncture in **5**.

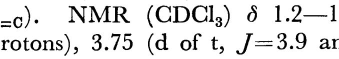
The synthesis is attractive as one of the preparative methods of versatile α-ylidene γ-lactones since the preparation involves no specific reagent.

Experimental

The IR spectra were recorded on JASCO IR-403G and IR-S instruments. A JEOL C-60 HL instrument was used to record the ^1H NMR spectra using tetramethylsilane as the internal standard. Trimethylsilylacetonitrile[7] and γ-trimethylsiloxy nitriles[8] were prepared according to the literature. Formaldehyde was generated by the cracking of dried paraformaldehyde. Acetaldehyde was distilled prior to use. Purification of the products was conducted by column chromatography on silica gel using a mixed solvent as eluent (benzene: hexane: ethanol=1: 1: 1/20—1/40).

Synthesis of 5. *α-Benzylidene-γ-valerolactone (5b)*: To a DME (25 ml) solution of the TMSAN anion prepared from TMSAN (1.70 g, 15.0 mmol) and an equivalent of LDA was added a DME (3 ml) solution of propylene oxide (0.87 g, 14.9 mmol) at −78 °C. After stirring for 5 h at −30 °C—

−20 °C, the reaction mixture was cooled to −78 °C and a DME (5 ml) solution of benzaldehyde (1.59 g, 15.0 mmol) added at the same temperature. After the addition, the mixture was stirred for 1 h at −30 °C and for 14 h at ambient temperature and quenched with saturated aqueous NH_4Cl (25 ml). The organic layer was extracted with dichloromethane (20 ml × 5). The combined extracts were washed with saturated brine and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure. Column chromatography of the residue gave 1.20 g (47%) of **3b** and 0.614 g of a yellow oily product ($\nu_{C=O}$ 1750 cm^{-1}). The oily product gave the pure lactone **5b** (0.196 g, 7%) as a yellow oil after purification, which crystallized on standing, mp 54—54.5 °C. Found: C, 76.65; H, 6.73%. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43%. IR (KBr disk) 1741 ($\nu_{C=O}$) and 1652 cm^{-1} ($\nu_{C=C}$). ^{1}H NMR (CCl_4) δ 1.42 (d, J=6.3 Hz, 3H, $\mathrm{C\underline{H}_3}$), 2.63 (d of double d, J=17.3, 5.7, and 3.3 Hz, 1H, $\mathrm{C\underline{H}_2}$), 3.28 (d of double d, J=17.3, 7.8, and 3.1 Hz, 1H, $\mathrm{C\underline{H}_2}$), 4.59 (dd of quartet, J=7.8, 5.7, and 6.3 Hz, 1H, $\mathrm{C\underline{H}{-}O}$), and 7.30 ppm  $\left(\text{m, 6H, Ph and } \mathrm{C{=}C}\genfrac{}{}{0pt}{}{\diagup\underline{\mathrm{H}}}{\diagdown\mathrm{Ph}}\right)$.

trans-9-Benzylidene-7-oxabicyclo[4.3.0]nonan-8-one **(5c)**: Similarly, from a DME (25 ml) solution of the TMSAN anion (8.05 mmol), cyclohexene oxide (0.793 g, 8.08 mmol), and benzaldehyde (1.02 g, 9.59 mmol), pure **5c** (0.11 g, 6%) was obtained as colorless needles in addition to **3c** (0.989 g, 58%), mp 146—147.5 °C. Found: C, 78.93; H, 7.37%. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.07%. IR (KBr disk) 1740 ($\nu_{C=O}$) and 1652 cm^{-1} ($\nu_{C=C}$). NMR ($CDCl_3$) δ 1.2—1.7 (m, 9H, cyclohexyl ring protons), 3.75 (d of t, J=3.9 and 10.7 Hz, 1H, $\mathrm{C\underline{H}{-}O}$), 6.35  $\left(\text{d, } J\text{=3.0 Hz, 1H, } \mathrm{C{=}C}\genfrac{}{}{0pt}{}{\diagup\underline{\mathrm{H}}}{\diagdown}\right)$, 7.3 (m, 3H, Ph), and 7.7 ppm (m, 2H, Ph).

Synthesis of α-(1-Hydroxyalkyl)-γ-trimethylsiloxy Nitriles **(6)**. *2-Cyano-1-phenyl-4-trimethylsiloxy-1-butanol* **(6a)**: To a THF solution of LDA (10.5 mmol) was added a THF (5 ml) solution of **3a** (1.57 g, 9.99 mmol) at −78 °C. The mixture was stirred for 1 h at the same temperature to complete the formation of the anion **2a**. A THF (5 ml) solution of benzaldehyde (0.536 g, 5.05 mmol) was added to the anion solution at −78 °C. The mixture was stirred for 30 min at −78 °C and for 15 h at ambient temperature and the reaction mixture quenched with saturated aq NH_4Cl (30 ml). The organic layer was decanted and the water layer extracted with dichloromethane (20 ml × 5). The organic layer and the extracts were collected, washed with saturated brine, and dried over $MgSO_4$. The residue obtained after evaporation of the solvent under reduced pressure was chromatographed to give 1.65 g (63%) of a pale yellow oil, **6a**. Found: C, 63.72; H, 8.13; N, 5.41%. Calcd for $C_{14}H_{21}NO_2Si$: C, 63.84; H, 8.04; N, 5.32%. IR (CCl_4) 3620, 3440, (ν_{O-H}), 2270 ($\nu_{C\equiv N}$), and 1250 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.12 (s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.6—2.0 (broad m, 2H, $\mathrm{C\underline{H}_2CCN}$), 3.12 (q, J=6.0 Hz, 1H, $\mathrm{C\underline{H}{-}CN}$), 3.80 (t, J=6.0 Hz, 2H, $\mathrm{C\underline{H}_2{-}O{-}Si}$), 4.2 (broad, 1H, $\mathrm{O\underline{H}}$), 4.9 (broad, 1H, $\mathrm{C\underline{H}{-}Ph}$), and 7.50 ppm (s, 5H, Ph).

2-Cyano-1-phenyl-4-trimethylsiloxy-1-pentanol **(6b)**: The analogous treatment of **3b** (0.957 g, 5.59 mmol) with butyllithium (5.1 mmol) and benzaldehyde (0.536 g, 5.05 mmol) in THF (25 ml) gave pure **6b** as a yellow oil (1.14 g, 82%). Found: C, 64.71; H, 8.57; N, 5.13%. Calcd for $C_{15}H_{23}NO_2Si$: C, 64.94; H, 8.34; N, 5.05%. IR (CCl_4) 3620, 3430 (ν_{O-H}), 2260 ($\nu_{C\equiv N}$), and 1249 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.10 (s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.12 (d, J=6.0 Hz, 3H, $\mathrm{C\underline{H}_3}$), 1.55 (m, 2H, $\mathrm{C\underline{H}_2}$), 2.78 (m, 1H, $\mathrm{C\underline{H}{-}CN}$), 3.9 (broad m, 2H, $\mathrm{O{-}\underline{H}}$ and $\mathrm{SiO{-}C\underline{H}}$), 4.57 (broad, 1H, $\mathrm{Ph{-}C\underline{H}{-}O}$), and 7.23 ppm (s, 5H, Ph).

3-Hydroxy-3-phenyl-2-(trans-2-trimethylsiloxycyclohexyl)propionitrile **(6c)**: The analogous treatment of **3c** (1.50 g, 7.09 mmol) with LDA (7.40 mmol) and benzaldehyde (0.781 g, 7.40 mmol) in THF (25 ml) gave **6c** as a yellow oil (1.88 g, 84%). Found: C, 68.13; H, 8.62; N, 4.48%. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57; N, 4.41%. IR (CCl_4) 3640, 3430 (ν_{O-H}), 2265 ($\nu_{C\equiv N}$), and 1249 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.10 (s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.0—2.1 (broad m, 9H), 2.96 (broad s, 1H, $\mathrm{O\underline{H}}$), 3.26 (double d, J=9.2 and 2.9 Hz, 1H, $\mathrm{C\underline{H}{-}CN}$), 3.4 (broad m, 1H, $\mathrm{C\underline{H}{-}OSi}$), 4.68 (d, J=9.2 Hz, 1H, $\mathrm{Ph{-}C\underline{H}{-}O}$), and 7.34 ppm (m, 5H, Ph).

3-Cyano-1,4-bis(trimethylsiloxy)pentane **(6d)**: LDA (10.4 mmol), **3a** (1.55 g, 10.1 mmol), and acetaldehyde (0.6 ml, 10.7 mmol) were mixed in a similar manner in THF (30 ml) and quenched with Me_3SiCl (1.56 g, 14.4 mmol). After evaporation of the solvent, the residue was diluted with Et_2O (30 ml) and the solution filtered. Pure **6d** (1.77 g, 65%) was obtained as a yellow liquid. Found: C, 52.43; H, 9.75; N, 5.40%. Calcd for $C_{12}H_{27}NO_2Si_2$: C, 52.69; H, 9.95; N, 5.12%. IR (CCl_4) 2280 ($\nu_{C\equiv N}$) and 1248 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.14, 0.16 (each s, 18H, $\mathrm{Si{-}C\underline{H}_3}$), 1.29 (d, J=6.3 Hz, 3H, $\mathrm{C\underline{H}_3}$), 1.74 (q, J=6.3 Hz, 2H, $\mathrm{C\underline{H}_2CCN}$), 2.2—2.9 (m, 1H, $\mathrm{C\underline{H}{-}CN}$), 3.74 (t, J=6.3 Hz, 2H, $\mathrm{C\underline{H}_2{-}O}$), and 3.93 ppm (q, J=6.3 Hz, 1H, $\mathrm{C\underline{H}{-}O}$).

3-Cyano-2,5-bis(trimethylsiloxy)hexane **(6e)**: The analogous treatment of **3b** (1.38 g, 8.03 mmol) with acetaldehyde (0.5 ml, 8.9 mmol) and Me_3SiCl (1.31 g, 12.1 mmol) gave pure **6e** (1.59 g, 69%) as a pale yellow liquid. Found: C, 54.54; H, 10.02; N, 4.91%. Calcd for $C_{13}H_{29}NO_2Si_2$: C, 54.30; H, 10.17; N, 4.87%. IR (CCl_4) 2265 ($\nu_{C\equiv N}$) and 1249 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.12, 0.14 (each s, 18H, $\mathrm{Si{-}C\underline{H}_3}$), 1.18 (d, J=6.9 Hz, 3H, $\mathrm{O{-}C{-}C\underline{H}_3}$), 1.25 (d, J=7.2 Hz, 3H, $\mathrm{O{-}C{-}C\underline{H}_3}$), 1.65 (t, J=6.9 Hz, 2H, $\mathrm{C\underline{H}_2}$), 2.43 (m, 1H, $\mathrm{C\underline{H}{-}CN}$), and 3.89 ppm (m, 2H, 2 × $\mathrm{C\underline{H}{-}O}$).

3-Hydroxy-2-(trans-2-trimethylsiloxycyclohexyl)butyronitrile **(6f)**: The analogous treatment of **3c** (3.85 g, 18.2 mmol) with LDA (18.7 mmol) and acetaldehyde (1.1 ml, 19 mmol) in THF (60 ml) gave a colorless oil of pure **6f** (2.96 g, 64%). Found: C, 61.10; H, 9.80; N, 5.44%. Calcd for $C_{13}H_{25}NO_2Si$: C, 61.13; H, 9.87; N, 5.48%. IR (CCl_4) 3660, 3390 (ν_{O-H}), 2275 ($\nu_{C\equiv N}$), and 1250 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.16, 0.20 (each s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.28, 1.40 (each d, J=6.0 Hz, 3H, $\mathrm{C\underline{H}_3}$), 1.1—2.1 (m, 9H, ring protons), 2.4—2.9 (m, 1H, $\mathrm{C\underline{H}{-}CN}$), and 3.2—4.1 ppm (m, 3H, O–H and 2 × $\mathrm{C\underline{H}{-}O}$).

2-Hydroxymethyl-4-(trimethylsiloxy)pentanenitrile **(6g)**: Into a solution of **2b** formed from LDA (10.5 mmol) and **3b** (1.71 g, 9.99 mmol) was bubbled gaseous formaldehyde (0.61 g, 20.4 mmol) in a stream of nitrogen at −78 °C in THF (40 ml). After a work up of the mixture similar to that described above, pure **6g** (1.18 g, 59%) was obtained as a colorless oil. Found: C, 53.45; H, 9.74; N, 7.05%. Calcd for $C_9H_{19}NO_2Si$: C, 53.69; H, 9.51; N, 6.96%. IR (CCl_4) 3650, 3460 (ν_{O-H}), 2270 ($\nu_{C\equiv N}$), and 1246 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.13, 0.15 (each s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.20 (d, J=6.0 Hz, $\mathrm{C\underline{H}_3}$), 1.45—1.93 (m, 2H, $\mathrm{C\underline{H}_2{-}C{-}O}$), 2.7 (m, 1H, $\mathrm{C\underline{H}{-}CN}$), 3.72 (d, J=6.0 Hz, 2H, $\mathrm{C\underline{H}_2{-}O}$), 3.7 (broad, 1H, $\mathrm{O{-}\underline{H}}$), and 3.93 ppm (quint, J=6.0 Hz, $\mathrm{C\underline{H}{-}O}$).

3-Hydroxy-2-(trans-2-trimethylsiloxycyclohexyl)propionitrile **(6h)**: The analogous treatment of **3c** (2.55 g, 12.0 mmol) with LDA (12.5 mmol) and formaldehyde (30 mmol) gave pure **6h** as a colorless oil (2.22 g, 77%). Found: C, 59.93; H, 9.88; N, 6.16%. Calcd for $C_{12}H_{23}NO_2Si$: C, 59.71; H, 9.60; N, 5.80%. IR (CCl_4) 3660, 3440 (ν_{O-H}), 2270 ($\nu_{C\equiv N}$), and 1249 cm^{-1} ($\delta_{s,Si-C_s}$). NMR (CCl_4) δ 0.15 (s, 9H, $\mathrm{Si{-}C\underline{H}_3}$), 1.1—2.0 (broad, 9H, ring protons), 2.93 (broad s, 1H, $\mathrm{O{-}\underline{H}}$), 3.0—3.6

(m, 2H, C$\underline{\mathrm{H}}$-CN and C$\underline{\mathrm{H}}$-O), and 3.6—3.85 ppm (m, 2H, C$\underline{\mathrm{H}}_2$-O).

Synthesis of α-(1-Hydroxyalkyl) γ-Lactones (7). *α-(α-Hydroxybenzyl)-γ-butyrolactone (7a)*: A solution of **6a** (1.27 g, 4.71 mmol) in concd HCl (3 ml) and MeOH (22 ml) was refluxed for 4 h. The mixture was poured into H_2O (100 ml), neutralized with aq $NaHCO_3$, and extracted with dichloromethane (20 ml×5). The extracts were combined, washed with water, and dried over $MgSO_4$. The crude product obtained after evaporation of the solvent was purified by chromatography to give pure **7a** (0.697 g, 77%) as colorless needles, mp 107—109 °C. Found: C, 68.81; H, 6.29%. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29%. IR (KBr disk) 3420 ($\nu_{\mathrm{O-H}}$) and 1744 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR ($CDCl_3$) δ 1.75—2.7 (m, 2H, CH-C$\underline{\mathrm{H}}_2$), 2.75—3.1 (m, 2H, C$\underline{\mathrm{H}}$-C=O and O-$\underline{\mathrm{H}}$), 3.9—4.4 (m, 2H, C$\underline{\mathrm{H}}_2$-O), 4.81, 4.84 (each d, J=8.7 Hz), 5.38, 5.39 (each d, J=5.0 Hz, 1H for 4 peaks, C$\underline{\mathrm{H}}$-O), and 7.30 ppm (s, 5H, Ph).

α-(α-Hydroxybenzyl)-γ-valerolactone (7b): The treatment of **6b** (2.06 g, 7.43 mmol) with concd HCl (4 ml) in MeOH (25 ml) gave pure **7b** (1.17 g, 73%) as a yellow oil. Found: C, 69.80; H, 7.14%. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84%. IR (CCl_4) 3630, 3460 ($\nu_{\mathrm{O-H}}$), and 1765 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR (CCl_4) δ 1.22 (d, J=6.4 Hz), 1.32 (d, J=5.5 Hz, 3H for two signals, C$\underline{\mathrm{H}}_3$), 1.5—2.5 (m, 2H, C$\underline{\mathrm{H}}_2$), 2.6—3.0 (m, 1H, C$\underline{\mathrm{H}}$-C=O), 4.0 (broad, 1H, O-$\underline{\mathrm{H}}$), 4.1—5.2 (m, 2H, 2×C$\underline{\mathrm{H}}$-O), and 7.20 ppm (m, 5H, Ph).

trans-*9-(α-Hydroxybenzyl)-7-oxabicyclo[4.3.0]nonan-8-one (7c)*: **6c** was treated (1.53 g, 4.83 mmol) with concd HCl (3 ml) in DME (30 ml) and pure **7c** (0.571 g, 48%) was obtained as pale yellow needles, mp 180—183 °C. Found: C, 73.42; H, 7.67%. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37%. IR (KBr disk) 3450 ($\nu_{\mathrm{O-H}}$) and 1755 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR ($CDCl_3$) δ 1.0—2.3 (m, 9H, ring protons), 2.73 (double d, J=12.0 and 3.0 Hz, 1H, C$\underline{\mathrm{H}}$-C=O), 2.93 (broad, 1H, O-$\underline{\mathrm{H}}$), 3.64 (m, 1H, C$\underline{\mathrm{H}}$-O), 5.38 (broad d, J=3 Hz, 1H, Ph-C$\underline{\mathrm{H}}$-O), and 7.32 ppm (m, 5H, Ph).

α-(1-Hydroxyethyl)-γ-butyrolactone (7d): Treatment of **6d** (1.33 g, 4.87 mmol) with concd HCl (4 ml) in MeOH (30 ml) gave **7d** (0.397 g, 63%) as a pale yellow liquid. Found: C, 55.18; H, 7.96%. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.75%. IR ($CHCl_3$) 3620, 3480 ($\nu_{\mathrm{O-H}}$), and 1764 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR (CCl_4) δ 1.30 (d, J=6.2 Hz, 3H, C$\underline{\mathrm{H}}_3$), 1.8—2.6 (m, 3H, C$\underline{\mathrm{H}}$-C=O and C$\underline{\mathrm{H}}_2$-CH), and 3.3—4.5 ppm (m, 4H, O-$\underline{\mathrm{H}}$, C$\underline{\mathrm{H}}$-OH, and C$\underline{\mathrm{H}}_2$-O).

α-(1-Hydroxyethyl)-γ-valerolactone (7e): Treatment of **6e** 0.68 g, 2.36 mmol) with concd HCl (2 ml) in MeOH (15 ml) gave **7e** (0.237 g, 70%) as a yellow liquid. Found: C, 58.05; H, 8.55%. Calcd for $C_7H_{17}O_3$: C, 58.31; H, 8.39%. IR ($CHCl_3$) 3480 ($\nu_{\mathrm{O-H}}$) and 1755 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR (CCl_4) δ 1.18 (double d, J=6.45 and 2.1 Hz, 3H, C$\underline{\mathrm{H}}_3$-CH), 1.37 (d, J=6.3 Hz), 1.43 (d, J=6.3 Hz, 3H for two signals, C$\underline{\mathrm{H}}_3$-C-O), 1.9—2.7 (m, 3H, C$\underline{\mathrm{H}}_2$ and C$\underline{\mathrm{H}}$-C=O), 3.7—4.0 (m, 2H, O-$\underline{\mathrm{H}}$ and C$\underline{\mathrm{H}}$-O-C=O), and 4.3—4.8 ppm (m, 1H, C$\underline{\mathrm{H}}$-O).

trans-*9-(1-Hydroxyethyl)-7-oxabicyclo[4.3.0]nonan-8-one (7f)*: Treatment of **6f** (1.75 g, 6.84 mmol) with concd HCl (4 ml) in DME (25 ml) gave pure **7f** (0.865 g, 69%) as colorless needles, mp 99—105 °C. Found: C, 65.10; H, 8.98%. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75%. IR (KBr disk) 3430 ($\nu_{\mathrm{O-H}}$), 1764 and 1749 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR ($CDCl_3$) δ 1.42 (d, J=6.2 Hz, 3H, C$\underline{\mathrm{H}}_3$), 1.2—2.5 (m, 10H), and 4.2 ppm (broad, 3H, O-$\underline{\mathrm{H}}$ and 2×C$\underline{\mathrm{H}}$-O).

α-Hydroxymethyl-γ-valerolactone (7g): Treatment of **6g** (1.08 g, 15.36 mmol) with concd HCl (3 ml) in MeOH (25 ml) gave pure **7g** (0.445 g, 63%) as a colorless liquid. Found: C, 55.55; H, 7.99%. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.75%. IR ($CHCl_3$) 3400 ($\nu_{\mathrm{O-H}}$) and 1759 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR (CCl_4) δ 1.25—1.50 (m, 3H, C$\underline{\mathrm{H}}_3$), 1.9—2.9 (m, 2H, C$\underline{\mathrm{H}}_2$), and 3.5—4.9 ppm (m, 4H, O-$\underline{\mathrm{H}}$, C$\underline{\mathrm{H}}$-O, and C$\underline{\mathrm{H}}_2$-O).

trans-*9-Hydroxymethyl-7-oxabicyclo[4.3.0]nonan-8-one (7h)*: Treatment of **6h** (0.490 g, 2.03 mmol) with concd HCl (2 ml) in DME (15 ml) gave pure **7h** (0.293 g, 85%) as a colorless solid, mp 55—56 °C. Found: C, 63.54; H, 8.43%. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29%. IR (KBr disk) 3415 ($\nu_{\mathrm{O-H}}$) and 1756 cm^{-1} ($\nu_{\mathrm{C=O}}$). NMR ($CDCl_3$) δ 1.2—2.8 (m, 11H, ring protons, C$\underline{\mathrm{H}}$-C=O, and O-$\underline{\mathrm{H}}$), and 3.7—4.3 ppm (m, 3H, C$\underline{\mathrm{H}}_2$-O and C$\underline{\mathrm{H}}$-O).

Synthesis of α-Alkylidene γ-Lactones (5). *α-Benzylidene-γ-butyrolactone (5a)*: A mixture of **7a** (0.305 g, 1.48 mmol) and methanesulfonyl chloride (0.14 ml) in pyridine (5 ml) was refluxed for 3 h. The reaction mixture was poured into ice (50 g) and concd HCl (15 ml) and the organic materials extracted with dichloromethane (20 ml×5). The extracts were combined and washed with 1 M HCl, water, and 5% aq $NaHCO_3$. After drying over $MgSO_4$, the solvent was evaporated under reduced pressure. The residue was chromatographed to give **5a** (0.153 g, 87%) as colorless needles, mp 115—115.5 °C. Found: C, 75.75; H, 5.75%. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79%. IR (KBr disk) 1739 ($\nu_{\mathrm{C=O}}$) and 1650 cm^{-1} ($\nu_{\mathrm{C=C}}$). NMR ($CDCl_3$) δ 3.20 (doublet of t, J=2.7 and 7.1 Hz, 2H, C$\underline{\mathrm{H}}_2$-C-C=O), 4.45 (t, J=7.1 Hz, 2H, C$\underline{\mathrm{H}}_2$-O), 7.45 (s, 5H, Ph), and 7.54 ppm $\left(\text{t, } J\text{=2.7 Hz, 1H, C=C}\begin{smallmatrix}\diagup\underline{\mathrm{H}}\\ \diagdown\end{smallmatrix}\right)$.

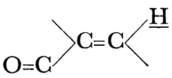
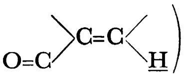
α-Benzylidene-γ-valerolactone (5b): Similarly, from **7b** (0.305 g, 1.48 mmol), pure **5b** (0.174 g, 63%) was obtained as a yellow oil which solidified in storage.

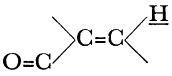
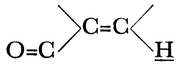
trans-*9-Benzylidene-7-oxabicyclo[4.3.0]nonan-8-one (5c)*: Similarly, from **7c** (0.607 g, 2.46 mmol), pure **5c** (0.253 g, 45%) was obtained as colorless needles.

α-Ethylidene-γ-butyrolactone (5d): **7d** (0.397 g, 3.07 mmol) gave **5d** (0.228 g, 66%) as a pale yellow liquid by a similar treatment to that described above. Found: C, 64.01; H, 7.45%. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19%. IR (CCl_4) 1768 ($\nu_{\mathrm{C=O}}$) and 1685 cm^{-1} ($\nu_{\mathrm{C=C}}$). NMR (CCl_4) δ 1.91 (t of doublet, J=2.0 and 7.4 Hz, 3H, C$\underline{\mathrm{H}}_3$), 2.88 (m, 2H, C$\underline{\mathrm{H}}_2$-C=C), 4.41 (t, J=7.2 Hz, 2H, C$\underline{\mathrm{H}}_2$-O), and 6.77 ppm (t of quartet, J=3.0 and 7.4 Hz, 1H, vinyl proton).

α-Ethylidene-γ-valerolactone (5e): **7e** (0.237 g, 1.64 mmol) gave **5e** (0.170 g, 82%) as a yellow liquid by a similar treatment. Found: C, 66.35; H, 8.29%. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99%. IR (CCl_4) 1767 ($\nu_{\mathrm{C=O}}$) and 1683 cm^{-1} ($\nu_{\mathrm{C=C}}$). NMR (CCl_4) δ 1.41 (d, J=6.5 Hz, 3H, C$\underline{\mathrm{H}}_3$-CH), 1.83 (t of d, J=2.2 and 7.4 Hz, 3H, C$\underline{\mathrm{H}}_3$-C=C), 2.35 (t of double d, J=3.4, 6.1, and 17.0 Hz, 1H, C$\underline{\mathrm{H}}_2$-C=C), 3.03 (t of double d, J=3.4, 7.7, and 17.0 Hz, 1H, C$\underline{\mathrm{H}}_2$-C=C), 4.60 (double d of quartet, J=7.7, 6.1, and 6.5 Hz, 1H, C$\underline{\mathrm{H}}$-O), and 6.64 ppm (t of quart, J=3.4 and 7.4 Hz, 1H, vinyl proton).

trans-*9-Ethylidene-7-oxabicyclo[4.3.0]nonan-8-one (5f)*: **7f** (0.917 g, 4.96 mmol) gave **5f** (0.318 g, 39%) as a yellow oil by a similar treatment. Found: C, 72.21; H, 8.72%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%. IR (CCl_4) 1778 ($\nu_{\mathrm{C=O}}$) and 1689 cm^{-1} ($\nu_{\mathrm{C=C}}$). NMR (CCl_4) δ 1.3—2.6 (m, 9H, ring protons), 1.86 (double d, J=7.2 and 1.7 Hz, 3H, CH_3), 3.56 (doublet of t, J=3.7 Hz and 9.0 Hz, 1H, C$\underline{\mathrm{H}}$-O), and 6.51 ppm (d of quart, J=3.0 and 7.5 Hz, 1H, vinyl proton).

α-Methylene-γ-butyrolactone (5g): A benzene solution of **7g** (0.445 g, 3.42 mmol), methanesulfonyl chloride (0.35 ml), and 1,5-diazabicyclo[5.4.0]undec-5-ene (1 ml) was stirred for 1 h at ambient temperature. The mixture was poured into water (20 ml) and extracted with dichloromethane (10 ml × 7). The extracts were combined, washed with 1 M HCl (20 ml) and water (20 ml), and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, the residue was chromatographed to give a pale yellow liquid **5g** (0.081 g, 21%). Found: C, 64.05; H, 7.44%. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19%. IR (CCl_4)$^{13)}$ 1772 ($\nu_{C=O}$) and 1671 cm^{-1} ($\nu_{C=C}$). NMR (CCl_4)$^{13)}$ δ 1.39 (d, J=6.1 Hz, 3H, C$\underline{H}_3$), 2.42 (t of double d, J=3.3, 6.6, and 16.7 Hz, 1H, C$\underline{H}_2$), 3.06 (t of double d, J=2.4, 7.2, and 16.7 Hz, 1H, C$\underline{H}_2$), 4.55 (quart of double d, J=6.1, 6.6, and 7.2 Hz, 1H, C$\underline{H}$–O), 5.50 (double d, J=6.6 and 7.2 Hz, 1H, ), and 6.06 ppm (double d, J=6.6 and 7.2 Hz, 1H, ).

trans-*9-Methylene-7-oxabicyclo*[*4.3.0*]*nonan-8-one* (**5h**): In a similar manner, **7h** (0.745 g, 4.38 mmol) gave colorless needles of **5h** (0.315 g, 47%), mp 39—41 °C. (lit,$^{14)}$ 39—41 °C). Found: C, 71.09; H, 8.03%. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95%. IR (KBr disk)$^{5)}$ 1758 ($\nu_{C=O}$) and 1673 cm^{-1} ($\nu_{C=C}$). NMR (CCl_4)$^{6)}$ δ 1.1—2.6 (m, 9H, ring protons), 3.63 (double t, J=3.8 and 10.5 Hz, 1H, C$\underline{H}$–O), 5.32 (d, J=3.0 Hz, 1H, ), and 5.96 ppm (d, J=3.0 Hz, 1H, ).

The authors would like to thank the Ministry of Education, Japan, for a Grant-in-Aid 375469 and Shinetsu Chemical Company for the supply of chlorotrimethylsilane.

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