NH_4Cl/NH_4OH solution (5 mL). The organic layer was separated, washed with brine, and dried (Na_2SO_4). Removal of the solvent and purification by column chromatography on silica gel (eluant: hexane) gave 520 mg of **4** (76% yield): ^1H NMR ($CDCl_3$, 300 Mhz) δ -0.079 (s, 9 H), 0.758 (s, 3 H), 0.823 (s, 3 H), 0.991 (d, 3 H, J = 7 Hz), 1.12 (m, 1 H), 1.34 (m, 1 H), 1.50 (m, 1 H), 1.536 (s, 3 H), 1.94 (m, 2 H), 2.013 (d, 1 H, J = 9 Hz), 4.946 (ddd, 1 H, J_1 = 16 Hz, J_2 = 9 Hz, J_3 = 1 Hz), 5.31 (m, 1 H), 5.356 (ddd, J_1 = 16 Hz, J_2 = 10 Hz, J_3 = 1 Hz); MS m/e (%) 250 (M^+, 5), 73 (100). Anal. Calcd for $C_{16}H_{30}Si$: C, 76.77, H, 12.07. Found: C, 76.07; H, 12.10.

(*E*)-1-(2,6,6-Trimethylcyclohex-1-en-1-yl)-3-(trimethylsilyl)but-1-ene (11). Product **11** was prepared and purified (580 mg, 84% yield) as previously described for **4**: ^1H NMR ($CDCl_3$, 300 MHz) δ -0.050 (s, 9 H), 0.926 (s, 3 H), 0.931 (s, 3 H), 1.044 (d, 1 H, J = 7 Hz), 1.39 (m, 2 H), 1.42 (m, 2 H), 1.53 (m, 3 H), 1.620 (s, 3 H), 1.91 (m, 2 H), 5.326 (dd, 1 H, J_1 = 17 Hz, J_2 = 10 Hz), 5.593 (d, 1 H, J = 17 Hz); MS m/e (%) 250 (M^+), 73 (100). Anal. Calcd for $C_{16}H_{30}Si$: C, 76.77; H, 12.07. Found: C, 76.32; H, 12.11.

1-(2,6,6-Trimethylcyclohex-2-en-1-yl)-3-(trimethylsilyl)-butane-1,2-diol (5). Osmium tetraoxide (2.5 mL of a 2.5 wt % solution in 2-methyl-2-propanol, 0.25 mmol) was added to a solution of trimethylamine *N*-oxide dihydrate (225 mg, 2 mmol in THF/water, 10/1 (2.5 mL)). Allylsilane **4** (500 mg, 2 mmol) dissolved in THF/water 8/1 (1 mL) was added slowly at 0 °C, and the mixture was stirred at room temperature overnight. Methyl sulfide (0.5 mL) was added, the mixture was filtered, and the clear solution was extracted with diethyl ether and washed with a saturated solution of HCl and brine. After drying (Na_2SO_4), the solution was evaporated, and the crude product was purified by column chromatography on silica gel (eluant ethyl acetate), yielding 430 mg (75%); IR (neat) 3450, 2940, 1460, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ -0.020 (s, 9 H), 0.790 (s, 3 H), 0.801 (s, 3 H), 0.830 (d, J = 5 Hz, 3 H), 1.40 (m, 2 H), 1.75 (m, 1 H), 1.556 (s, 3 H), 1.65 (m, 1 H), 1.89 (m, 2 H), 2.10 (m, 2 H, OH), 4.10 (m, 2 H), 5.26 (m, 1 H); MS m/e (%) 266 ($M^+ - H_2O$), 43 (100).

(*E*)-1-(2,6,6-Trimethylcyclohex-2-en-1-yl)but-2-en-1-ol (α-Damascol, 6). Potassium hydride (228 mg of a 35% dispersion in mineral oil, 2 mmol) was washed with pentane under nitrogen atmosphere; THF (5 mL) was added, followed by diol **5** (400 mg, 1.4 mmol). The mixture was stirred at room temperature for 30 min, water was cautiously added, and the product was extracted into ether. The ether was dried over Na_2SO_4 and evaporated in vacuum to give product **6** as an oil. Column chromatography on silica gel (eluant hexane/ethyl acetate 10/1) gave 220 mg, 81% yield: IR (neat) 3450, 2960, 1620, 1450, 980 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), δ 0.968 (s, 3 H), 1.014 (s, 3 H), 1.42 (m, 2 H), 1.506 (s, 3 H), 1.70 (m, 3 H), 1.92 (m, 2 H), 2.10 (d, J = 8 Hz, 1 H), 2.70 (d, 1 H, OH), 4.12 (m, 1 H), 5.36 (m, 1 H), 5.56 (m, 1 H), 5.81 (m, 1 H); MS m/e (%) 194 (M^+, 11), 43 (100). Anal. Calcd for $C_{13}H_{22}O$: C, 80.30; H, 11.41. Found: C, 80.20; H, 11.36.

(*E*)-1-(2,6,6-Trimethylcyclohex-2-en-1-yl)but-2-en-1-one (α-Damascone, 7). To a dispersion of MnO_2 (activated form, purchased from Aldrich) (1 g) in acetone, alcohol **6** (194 mg, 1 mmol) was added, and the mixture was stirred until TLC showed disappearance of the starting material. The liquid was decanted, and the residue was washed several times with Et_2O. The organic layers collected were washed with a saturated solution of NH_4Cl and brine and dried over Na_2SO_4. After evaporation of the solvent, α-damascone (**7**) was purified by PTLC (eluant hexane/ethyl acetate (20/1) to yield 103 mg, 54%: IR (neat) 2980, 1690, 1660, 825 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.835 (s, 3 H), 0.960 (s, 3 H), 1.34 (m, 1 H), 1.40 (m, 1 H), 1.550 (s, 3 H), 1.886 (d, J = 6 Hz, 3 H), 2.796 (s, 1 H), 5.421 (m, 1 H), 6.196 (dq, J_1 = 16 Hz, J_2 = 1 Hz, 1 H), 6.779 (dq, J_1 = 16 Hz, J_2 = 6 Hz, 1 H); $[\alpha]^{20}_D$ = +330° (c = 10, $CHCl_3$) [lit.[7c] $[\alpha]^{20}_D$ = +324° (c = 10, $CHCl_3$)].

(*E*)-1-(2,6,6-Trimethylcyclohex-1-en-1-yl)but-2-en-1-ol (β-Damascol, 12). To a dispersion of MCPBA (431 mg of 80% MCPBA, 2 mmol) in CH_2Cl_2 (5 mL) cooled at -78 °C was added allylsilane **11** (500 mg, 2 mmol) in CH_2Cl_2 (1 mL). The mixture was warmed to room temperature, and then methyl sulfide (1 mL) was added. The mixture was diluted with diethyl ether (20 mL) and washed subsequently with a saturated solution of NH_4Cl and brine. After drying over Na_2SO_4 the solvent was evaporated and the crude product was dissolved in THF (2 mL) and added to a solution of TBAF·$3H_2O$ (540 mg, 2 mmol) in THF (5 mL). The mixture was stirred overnight and then diethyl ether (10 mL) was added; the organic layer was washed with a saturated solution of NH_4Cl and dried over Na_2SO_4. After evaporation of the solvent, **12** was purified by column chromatography on silica gel (eluant hexane/ethyl acetate, 8/1), affording 216 mg, 55%: IR (neat) 3470, 2930, 1655, 1630, 1460, 877 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.968 (s, 3 H), 1.014 (s, 3 H), 1.32 (m, 2 H), 1.406 (s, 3 H), 1.715 (d, J = 5 Hz, 3 H), 1.78 (m, 2 H), 2.783 (br, 1 H, OH), 4.445 (d, J = 7 Hz, 1 H), 5.531 (dq, J_1 = 15 Hz, J_2 = 5 Hz, 1 H), 5.780 (dq, J_1 = 15 Hz, J_2 = 2 Hz, 1 H); MS m/e (%) 194 (M^+, 11), 123 (29), 109 (37), 91 (21), 55 (22), 43 (100). Anal. Calcd for $C_{13}H_{22}O$; C, 80.30; H, 11.41. Found: C, 80.46; H, 11.46.

(*E*)-1-(2,6,6-Trimethylcyclohex-1-en-1-yl)but-2-en-1-one (β-Damascone, 13). Pyridinium dichromate (376 mg, 1 mmol) was dissolved in dry DMF (2 mL), and alcohol **12** (194 mg, 1 mmol) was added. The mixture was stirred at room temperature for 2 h, then Et_2O (10 mL) was added, and the solution was washed with a HCl solution followed by brine. After drying over Na_2SO_4, the solvent was evaporated and **13** was purified by PTLC (eluant hexane/ethyl acetate, 20/1) to give 130 mg, 68% yield: IR (neat) 2940, 1675, 1640, 1615, 970 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), δ 0.986 (s, 3 H), 1.016 (s, 3 H), 1.26 (m, 2 H), 1.41 (m, 2 H), 1.486 (s, 3 H), 1.58 (m, 2 H), 1.906 (dd, J_1 = 6 Hz, J_2 = 1 Hz, 1 H), 6.061 (dq, J_1 = 16 Hz, J_2 = 1 Hz, 1 H), 6.629 (dq, J_1 = 16 Hz, J_2 = 6 Hz, 1 H); MS m/e (%) 192 (M^+, 12), 136 (43), 43 (100). Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.87; H, 10.56.

(*E*)-1-(2,6,6-Trimethylcyclohexa-1,3-dienyl)but-2-en-1-one (β-Damascenone, 14). *N*-Bromosuccinimide (196 mg, 1.1 mmol) was dissolved in dry CH_2Cl_2 (3 mL), ketone **13** (192 mg, 1 mmol) in CCl_4 (3 mL) was added, and the mixture was heated at 50 °C; DABCO (224 mg, 2 mmol) was added, followed by 4-(dimethylamino)pyridine (15 mg). After filtration the solution was poured in a round-bottomed flask, and the solvent was evaporated at a rotavap. The flask was transferred in a Kughelrohr apparatus and heated at 80 °C under vacuum (25 mmHg) for 1 h. The residue was treated with Et_2O (5 mL) and 10% HCl (2 mL). The organic layer was separated, washed with brine, and dried over Na_2SO_4. After evaporation of the solvent product **14** was purified by column chromatography on silica gel (eluant hexane/ethyl acetate, 20/1) to yield 168 mg, 86%: IR (neat) 2940, 1670, 1635, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.005 (s, 3 H), 1.010 (s, 3 H), 1.625 (s, 3 H), 1.930 (dd, J_1 = 7 Hz, J_2 = 1 Hz, 3 H), 2.109 (d, J = 2 Hz, 2 H), 5.79 (m, 2 H), 6.10 (dq, J_1 = 16 Hz, J_2 = 1 Hz, 1 H), 6.750 (dq, J_1 = 1 Hz, J_2 = 7 Hz, 1 H); MS m/e (%) 190 (1), 126 (36), 43 (100). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.46; H, 9.56.

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Registry No. 1, 24190-29-2; **2** (isomer 1), 124152-01-8; **2** (isomer 2), 120523-19-5; **3** (isomer 1), 124152-02-9; **3** (isomer 2), 124152-04-1; **4**, 124099-57-6; **5**, 124099-58-7; **6**, 28102-24-1; **7**, 28102-28-5; **8**, 79-77-6; (±)-**9**, 53078-25-4; (±)-**10**, 124152-03-0; (±)-**11**, 124099-59-8; (±)-**12**, 124099-60-1; **13**, 23726-91-2; **14**, 23726-93-4.

An Efficient Synthesis of α-Silylacetates Having Various Types of Functional Groups in the Molecules

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The synthetic utility of α-silyl esters has been shown in a variety of organic reactions.[1] One of the most practical

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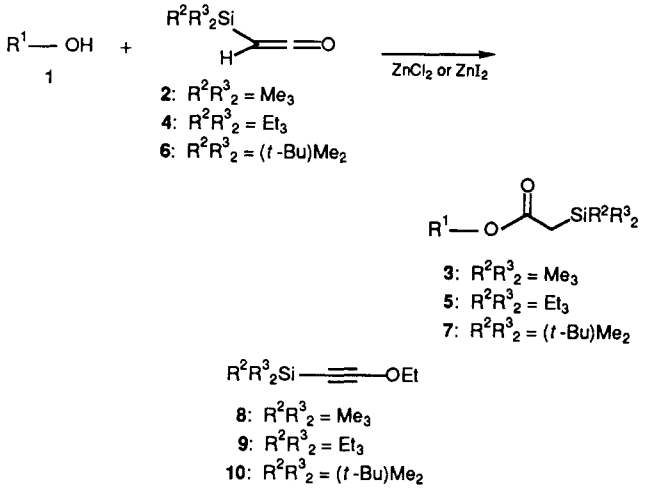
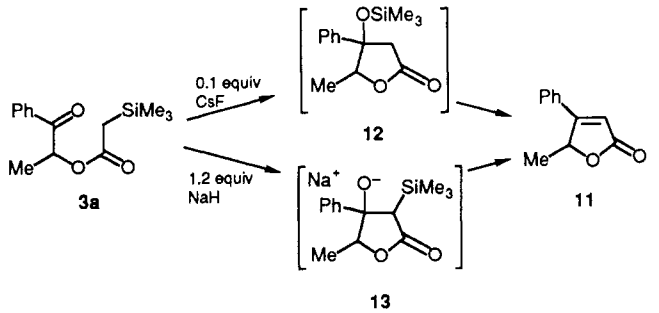
uses of the esters is in carbon–carbon bond-forming reactions such as the Peterson (silyl-Wittig) olefination[2] and a fluoride ion catalyzed aldol type reaction.[3] These reactions have been extensively studied because of their high reactivity and convenience in preparation of the products in high yields. Although it was of obvious interest to see if these reactions could be extended to intramolecular reactions, this aspect has been scarcely explored.[4] One reason for this lack of study may be found in the difficulty of preparation of α-silyl esters having suitable functional groups in the molecules. Generally, α-silyl esters have been prepared by the Reformatsky reaction,[5] C-silylation of esters with trimethylsilyl chloride[6] or methyldiphenylsilyl chloride[7] under basic conditions or by using trimethylsilyl trifluoromethanesulfonate,[8] and silyl migration from acylsilanes.[9] These methods, however, could not be applied to intramolecular reactions owing to incompatibility with other active functional groups and/or the less selective C- vs O-silylation of esters.[10] We now report a convenient synthesis of α-silylacetates (**3**, **5**, and **7**) having various types of functional groups.

Addition of substituted hydroxy compounds (**1**) to silylketenes seems to be a convenient method for the synthesis of α-silyl esters. Previously, Ruden reported two examples of a BF_3·Et_2O-catalyzed addition of bulky alcohols to (trimethylsilyl)ketene (**2**) to give α-(trimethysilyl)acetates (**3**).[11,12] However, addition of phenol (**1d**) having a carbonyl group to **2** by this method resulted in a partial desilylation, and addition of alcohol (**1f**) having an acetal group to **2** resulted in a deacetalization of the product. Employment of a catalytic amount of $SnCl_4$ gave better but still unsatisfactory results. After many unsuccessful trials,[13] it was found that $ZnCl_2$ (for alcohols) and ZnI_2 (for phenols) were efficient catalysts for the synthesis of α-silylacetates (**3**). Thus, **1** and **2** were stirred in the presence of 0.1 equiv of the catalyst in methylene chloride at room temperature for a few hours to give a high yield of **3**. Various α-(trimethylsilyl)acetates (**3a–j**) having carbonyl, acetal, thioacetal, epoxy, and olefinic groups were easily prepared. Formation of acetate (**3g**) from hindered alcohol (**1g**) was also achieved. By this method, other types of α-silylacetates were readily prepared. Thus, (triethylsilyl)ketene (**4**) reacted with hydroxy compounds (**1h** and **1k**) to give α-(triethylsilyl)acetates (**5a** and **5b**) in 84% and 99% yields, respectively. Similarly, (*tert*-butyldimethylsilyl)ketene (**6**) and hydroxy compounds (**1f** and **1k**) gave α-(*tert*-butyldimethylsilyl)acetates (**7a** and **7b**) in 71% and 99% yields, respectively. The structures of all previously unreported products (**3**, **5**, and **7**) were assigned on the basis of their analytical and spectral data. The reaction conditions, yields, and boiling or melting points are summarized in Table I. Since silylketenes (**2**, **4**, and **6**) are readily available by the thermal decomposition of the corresponding silylated ethoxyacetylenes (**8–10**),[11,14] the present method allows general preparation of α-silylacetates having various types of functional groups in the molecules.



A preliminary study on utilization of these α-silylacetates was carried out by cyclization of keto acetate (**3a**). Thus, treatment of **3a** with 0.1 equiv of anhydrous CsF in dry *N*,*N*-dimethylformamide (DMF) at 0 °C gave butenolide (**11**) in 71% yield, via fluoride ion catalyzed aldol type reaction to β-siloxy lactone (**12**),[3] from which silanol eliminated under weak basic conditions. The same product (**11**) was also prepared from **3a** by treatment with 1.2 equiv of NaH under similar conditions in 82% yield via β-silylalkoxide intermediate **13**.

Extended studies on the cycloaddition of other types of α-silylacetates are currently in progress.



Experimental Section

All boiling and melting points are uncorrected. IR absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer with $CHCl_3$ as a solvent. ^1H NMR spectra were measured on

(1) (a) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. (b) Gilday, J. P.; Gallucci, J. C.; Paquette, L. A. *J. Org. Chem.* **1989**, *54*, 1399. (c) Paquette, L. A.; Maynard, G. D.; Ra, C. S.; Hoppe, M. *J. Org. Chem.* **1989**, *54*, 1408.

(2) (a) Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 1620. (b) Hartzell, S. L.; Sullivan, D. F.; Rathke, M. W. *Tetrahedron Lett.* **1974**, 1403. (c) Larson, G. L.; Quiroz, F.; Suarez, J. *Synth. Commun.* **1983**, *13*, 833.

(3) (a) Nakamura, E.; Shimizu, M.; Kuwajima, I. *Tetrahedron Lett.* **1976**, 1699. (b) RajanBabu, T. V. *J. Org. Chem.* **1984**, *49*, 2083.

(4) Only one example has been reported by Taylor: The addition of sodium salts of *o*-acylphenols to (trimethylsilyl)ketene gave the enolate anions of α-silylacetates, which successively added to the carbonyl group in an intramolecular sense to give coumarins: Taylor, R. T.; Cassell, R. A. *Synthesis* **1982**, 672.

(5) Fessenden, R. J.; Fessenden, J. S. *J. Org. Chem.* **1967**, *32*, 3535.

(6) Rathke, M. W.; Sullivan, D. F. *Synth. Commun.* **1973**, *3*, 67.

(7) (a) Larson, G. L.; Fuentes, L. M. *J. Am. Chem. Soc.* **1981**, *103*, 2418. (b) Larson, G. L.; Cruz de Maldonado, V.; Fuentes, L. M.; Torres, L. E. *J. Org. Chem.* **1988**, *53*, 633.

(8) (a) Emde, H.; Simchen, G. *Synthesis* **1977**, 867. (b) *Justus Liebigs Ann. Chem.* **1983**, 816.

(9) Kuwajima, I.; Matsumoto, K.; Inoue, T. *Chem. Lett.* **1979**, 41.

(10) Very recently an effective C-silylation of esters was reported based on metal-catalyzed reaction of α-diazo esters with trialkylsilanes: Bagheri, V.; Doyle, M. P.; Taunton, J.; Claxton, E. E. *J. Org. Chem.* **1988**, *53*, 6158.

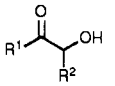
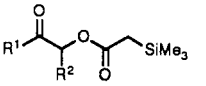
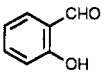
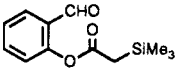
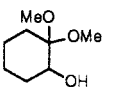
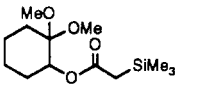
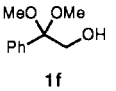
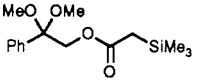
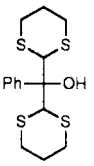
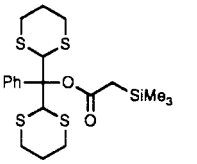
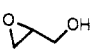
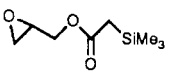
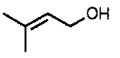
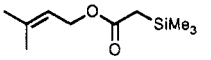
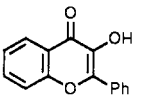
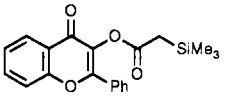
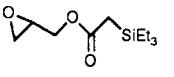
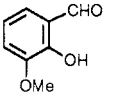
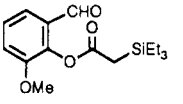
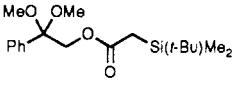
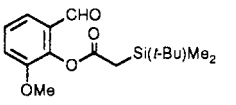
(11) Simple *t*-BuOH and tertiary alcohol having nitro group in the molecule were converted to the corresponding α-silylacetates: Ruden, R. A. *J. Org. Chem.* **1974**, *39*, 3607.

(12) Knaus also reported the derivation of phenolic compounds, cannabinols, to their α-(trimethylsilyl)acetates by using a large excess of **2**: Knaus, E. E.; Coutts, R. T.; Kazakoff, C. W. *J. Chromatogr. Sci.* **1976**, *14*, 525.

(13) Catalytic treatment using other Lewis acids such as $MgBr_2$ or $Ti(O\text{-}i\text{-}Pr)_4$ and also (*N*,*N*-dimethylamino)pyridine gave unsatisfactory results.

(14) These ketenes (**2**, **4**, and **6**) are fairly stable and can be stored in a refrigerator under a nitrogen atmosphere more than half a year.

Table I. Preparation of α-Silylacetates (3, 5, and 7)

silylketene (2, 4, and 6)	hydroxy compound 1	reaction conditions[a]	α-silylacetate (3, 5, and 7)	yield,[b] %	bp,[c] °C/Torr or [mp,[c,d] °C]
					
2	**1a**: R^1 = Ph; R^2 = Me	$ZnCl_2$, 0.75 h	**3a**: R^1 = Ph; R^2 = Me	91	oil
2	**1b**: $R^1 = R^2$ = Ph	$ZnCl_2$, 1 h	**3b**: $R^1 = R^2$ = Ph	93	[40.5–41]
2	**1c**: R^1 = Me; R^2 = H	$ZnCl_2$, 3 h	**3c**: R^1 = Me; R^2 = H	76	85–95/11 (bath temp)
2	 **1d**	ZnI_2, 0.5 h	 **3d**	76	[118.5–120]
2	 **1e**	$ZnCl_2$, 3 h	 **3e**	88	oil
2	 **1f**	$ZnCl_2$, 4 h[e]	 **3f**	78	oil
2	 **1g**	$ZnCl_2$, 5 h	 **3g**	80	gum
2	 **1h**	$ZnCl_2$, 1 h	 **3h**	84	53/0.35
2	 **1i**	$ZnCl_2$, 1 h	 **3i**	86	85–90/10 (bath temp)
2	 **1j**	ZnI_2, 1 h	 **3j**	99	[110–111]
4	**1h**	$ZnCl_2$, 1 h	 **5a**	84	oil
4	 **1k**	ZnI_2, 1.5 h	 **5b**	99	oil
6	**1f**	$ZnCl_2$, 6 h	 **7a**	71	oil
6	**1k**	ZnI_2, 1.5 h	 **7b**	99	[74–75]

[a] Carried out in CH_2Cl_2 at room temperature. [b] Isolated yield of 3, 5, and 7 based on 1. [c] Uncorrected. [d] Recrystallized from ether–*n*-hexane. [e] Carried out at 0 °C.

Hitachi R-22 (90 MHz) and JEOL JNM FX-90Q (90 MHz) spectrometers with $CDCl_3$ as a solvent and with tetramethylsilane as an internal standard. Mass spectra (MS) and high-resolution MS were obtained on ESCO EMD-05A and JEOL JMS-D300 mass spectrometers. E. Merck silica gel 60 (230–400 mesh ASTM) for flash column chromatography and E. Merck precoated TLC plates, silica gel 60 F_{254}, for preparative thin-layer chromatography (prep. TLC) were used. Organic layers were dried with anhydrous $MgSO_4$. Known compounds (**1a**,[15] **1e**,[15] **1f**,[15] **2**,[11] and **8**[16]) were

(15) Moriarty, R. M.; Hou, K.-C. *Tetrahedron Lett.* **1984**, *25*, 691.

prepared by the reported methods. Alcohol **1g**, ketenes **4** and **6**, and acetylenes **9** and **10** were prepared as follows. All other substrates are commercially available.

1,1-Bis(1,3-dithian-2-yl)benzyl alcohol (1g) was prepared by the usual reaction of 2-lithio-1,3-dithiane [prepared from *n*-BuLi (1.5 M in *n*-hexane, 11 mL, 17 mmol) and 1,3-dithiane (1.8 g, 15 mmol) in dry THF (17 mL) at −30 °C for 1.5 h] and benzoyl chloride (2.2 g, 16 mmol) at −78 °C for 0.5 h in 97% yield (2.5 g) as colorless crystals: mp 166–167.5 °C (AcOEt); IR 3510 cm^{-1}; ^1H NMR δ 1.75–2.05 (m, 4 H), 2.7–2.85 (m, 8 H), 4.84 (s, 2 H), 7.25–7.4 (m, 3 H), 7.5–7.65 (m, 2 H); MS *m/e* 344 (M^+). Anal. Calcd for $C_{15}H_{20}OS_4$: C, 52.29; H, 5.85. Found: C, 52.28; H, 5.91.

(Triethylsilyl)ethoxyacetylene (9). Under a nitrogen atmosphere, *n*-BuLi (1.5 M in *n*-hexane, 10.5 mL, 15.8 mmol) was added to a solution of ethoxyacetylene (1.0 g, 14.3 mmol) in dry THF (10 mL) at 0 °C over 10 min. The mixture was stirred for 1.5 h, and hexamethylphosphoric triamide (2.8 mL) was added. After 10 min, triethylsilyl chloride (2.3 g, 15.5 mmol) was added, and the mixture was stirred overnight at room temperature. The reaction mixture was poured to a mixture of ice (10 g) and *n*-pentane (20 mL). The organic layer was separated, and the aqueous layer was extracted with *n*-pentane (20 mL). The combined organic layer was washed with brine (10 mL), dried, and concentrated in vacuo. The crude product was distilled in vacuo (*caution*: bath temperature must be kept below 90 °C to avoid the thermal decomposition of **9**) to give an 86% yield (2.3 g) of pure **9** as a colorless oil: bp 59–63 °C (3 Torr) [lit.[17] bp 73 °C (34 Torr)]; IR 2175 cm^{-1}; ^1H NMR δ 0.4–0.65 (m, 6 H), 0.85–1.05 (m, 9 H), 1.36 (t, 3 H, J = 7 Hz), 4.09 (q, 2 H, J = 7 Hz); MS *m/e* 155 ($M^+ - C_2H_5$).

(*tert*-Butyldimethylsilyl)ethoxyacetylene (10). Similarly as described for **9**, **10** was prepared from ethoxyacetylene (1.0 g, 14.3 mmol) and *tert*-butyldimethylsilyl chloride (2.3 g, 15.5 mmol) in 88% yield (2.3 g) as a colorless oil: bp 66–69 °C (12 Torr); IR 2180 cm^{-1}; ^1H NMR δ 0.07 (s, 6 H), 0.93 (s, 9 H), 1.41 (t, 3 H, J = 7 Hz), 4.13 (q, 2 H, J = 7 Hz). Anal. Calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.94. Found: C, 64.74; H, 10.92.

(Triethylsilyl)ketene (4). Acetylene (**9**, 0.56 g, 3.1 mmol) was slowly distilled to produce **4** at 120–130 °C (at atmospheric pressure during the first 10 min then the pressure was gradually reduced to 120 Torr over 2 h). A second distillation gave pure **4** in 84% yield (0.40 g) as a colorless oil: bp 94–96 °C (73 Torr) [lit.[18] bp 61.5–62.5 °C (20 Torr)]; IR 2110 cm^{-1}; ^1H NMR δ 0.45–0.8 (m, 6 H), 0.9–1.1 (m, 9 H), 1.70 (s, 1 H); MS *m/e* 127 ($M^+ - C_2H_5$).

(*tert*-Butyldimethylsilyl)ketene (6). Similarly as described for **4**, **6** was prepared from **10** (1.5 g, 8.2 mmol) in 86% yield (1.1 g) as a colorless oil: bp 74–76 °C (87 Torr); IR 2130 cm^{-1}; ^1H NMR δ 0.12 (s, 6 H), 0.92 (s, 9 H), 1.74 (s, 1 H); MS *m/e* 99 ($M^+ - C_4H_9$). Anal. Calcd for $C_8H_{16}OSi$: C, 61.50; H, 10.30. Found: C, 61.74; H, 10.56.

General Procedure for the Synthesis of α-Silylacetates (3, 5, and 7). Under a nitrogen atmosphere, a mixture of silylketene (**2**, **4**, and **6**, 1.2 mmol) and anhydrous catalyst ($ZnCl_2$ for alcohols or ZnI_2 for phenols, 0.1 mmol) was stirred in dry CH_2Cl_2 (3 mL) at room temperature for 10 min. To the mixture was added **1** (1.0 mmol), and the whole was stirred at room temperature for the period of time given in Table I. The reaction was quenched with saturated aqueous $NaHCO_3$ (3 mL), and CH_2Cl_2 (20 mL) was added. The organic layer was separated, washed with brine (10 mL), dried, and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel or by prep. TLC on silica gel (1:1–5 ether–*n*-hexane for both methods).

1-Methylphenacyl (trimethylsilyl)acetate (3a): IR 1720 (sh), 1700, 1600 cm^{-1}; ^1H NMR δ 0.16 (s, 9 H), 1.49 (d, 3 H, J = 7 Hz), 1.96 (s, 2 H), 5.96 (q, 1 H, J = 7 Hz), 7.3–7.55 (m, 3 H), 7.93 (dd, 2 H, J = 8, 2 Hz); MS *m/e* 264 (M^+), 249 ($M^+ - CH_3$); high-resolution MS (*m/e*) calcd for $C_{13}H_{17}O_3Si$ ($M^+ - CH_3$) 249.0944, found 249.0934.

1-Phenylphenacyl (trimethylsilyl)acetate (3b): IR 1720, 1700, 1605 cm^{-1}; ^1H NMR δ 0.18 (s, 9 H), 2.01 (s, 2 H), 6.81 (s, 1 H), 7.2–7.45 (m, 8 H), 7.90 (dd, 2 H, J = 8, 3 Hz); MS *m/e* 326 (M^+). Anal. Calcd for $C_{19}H_{22}O_3Si$: C, 69.90; H, 6.79. Found: C, 70.08; H, 6.80.

Acetonyl (trimethylsilyl)acetate (3c): IR 1735, 1720 cm^{-1}; ^1H NMR δ 0.20 (s, 9 H), 2.00 (s, 2 H), 2.16 (s, 3 H), 4.62 (s, 2 H); MS *m/e* 188 (M^+), 173 ($M^+ - CH_3$). Anal. Calcd for $C_8H_{16}O_3Si$: C, 51.03; H, 8.56. Found: C, 51.31; H, 8.80.

***o*-Formylphenyl (trimethylsilyl)acetate (3d)**: IR 1740, 1695, 1605 cm^{-1}; ^1H NMR δ 0.23 (s, 9 H), 2.22 (s, 2 H), 7.13 (dd, 1 H, J = 8, 2 Hz), 7.32 (td, 1 H, J = 8, 2 Hz), 7.62 (td, 1 H, J = 8, 2 Hz), 7.88 (dd, 1 H, J = 8, 2 Hz), 10.32 (s, 1 H); MS *m/e* 236 (M^+), 221 ($M^+ - CH_3$); high-resolution MS (*m/e*) calcd for $C_{11}H_{13}O_3Si$ ($M^+ - CH_3$) 221.0632, found 221.0625.

2,2-Dimethoxycyclohexyl (trimethylsilyl)acetate (3e): IR 1710 cm^{-1}; ^1H NMR δ 0.14 (s, 9 H), 1.35–1.8 (m, 8 H), 1.92 (s, 2 H), 3.12 (s, 3 H), 3.16 (s, 3 H), 5.03 (m, 1 H, $W_{1/2}$ = 6 Hz); MS *m/e* 274 (M^+), 243 ($M^+ - OCH_3$); high-resolution MS (*m/e*) calcd for $C_{13}H_{26}O_4Si$ (M^+) 274.1601, found 274.1607.

2,2-Dimethoxyphenethyl (trimethylsilyl)acetate (3f): IR 1710, 1600 cm^{-1}; ^1H NMR δ 0.20 (s, 9 H), 1.88 (s, 2 H), 3.20 (s, 6 H), 4.30 (s, 2 H), 7.25–7.6 (m, 5 H); MS *m/e* 281 ($M^+ - CH_3$), 265 ($M^+ - OCH_3$); high-resolution MS (*m/e*) calcd for $C_{14}H_{21}O_3Si$ ($M^+ - OCH_3$) 265.1260, found 265.1260.

1,1-Bis(1,3-dithian-2-yl)benzyl (trimethylsilyl)acetate (3g): IR 1720 cm^{-1}; ^1H NMR δ 0.22 (s, 9 H), 1.75–2.05 (m, 4 H), 2.05 (s, 2 H), 2.65–2.9 (m, 8 H), 5.50 (s, 2 H), 7.25–7.4 (m, 3 H), 7.65–7.8 (m, 2 H); MS *m/e* 458 (M^+); high-resolution MS (*m/e*) calcd for $C_{20}H_{30}O_2S_4Si$ (M^+) 458.0897, found 458.0902.

Glycidyl (trimethylsilyl)acetate (3h): IR 1715 cm^{-1}; ^1H NMR δ 0.12 (s, 9 H), 1.95 (s, 2 H), 2.62 (dd, 1 H, J = 5, 3 Hz), 2.81 (t, 1 H, J = 5 Hz), 3.17 (m, 1 H, $W_{1/2}$ = 16 Hz), 3.87 (dd, 1 H, J = 12, 6 Hz), 4.38 (dd, 1 H, J = 12, 3 Hz); MS *m/e* 188 (M^+), 173 ($M^+ - CH_3$). Anal. Calcd for $C_8H_{16}O_3Si$: C, 51.03; H, 8.56. Found: C, 50.86; H, 8.66.

3-Methyl-2-butenyl (trimethylsilyl)acetate (3i): IR 1710 cm^{-1}; ^1H NMR δ 0.11 (s, 9 H), 1.70 (br s, 3 H), 1.74 (br s, 3 H), 1.88 (s, 2 H), 4.50 (br d, 2 H, J = 7 Hz), 5.32 (br t, 1 H, J = 7 Hz); MS *m/e* 200 (M^+); high-resolution MS (*m/e*) calcd for $C_{10}H_{20}O_2Si$ (M^+) 200.1233, found 200.1241.

2-Phenylchromon-3-yl (trimethylsilyl)acetate (3j): IR 1745, 1655 (sh), 1640, 1625 cm^{-1}; ^1H NMR δ 0.23 (s, 9 H), 2.12 (s, 2 H), 7.2–7.8 (m, 8 H), 8.24 (dd, 1 H, J = 8, 2 Hz); MS *m/e* 352 (M^+), 337 ($M^+ - CH_3$). Anal. Calcd for $C_{20}H_{20}O_4Si$: C, 68.15; H, 5.72. Found: C, 68.37; H, 5.73.

Glycidyl (triethylsilyl)acetate (5a): IR 1715 cm^{-1}; ^1H NMR δ 0.65–0.8 (m, 6 H), 0.9–1.1 (m, 9 H), 1.96 (s, 2 H), 2.62 (dd, 1 H, J = 5, 3 Hz), 2.83 (t, 1 H, J = 5 Hz), 3.18 (m, 1 H, $W_{1/2}$ = 16 Hz), 3.86 (dd, 1 H, J = 12, 6 Hz), 4.35 (dd, 1 H, J = 12, 4 Hz); MS *m/e* 201 ($M^+ - C_2H_5$); high-resolution MS (*m/e*) calcd for $C_9H_{17}O_3Si$ ($M^+ - C_2H_5$) 201.0944, found 201.0906.

2-Formyl-6-methoxyphenyl (triethylsilyl)acetate (5b): IR 1740, 1700, 1655, 1585 cm^{-1}; ^1H NMR δ 0.6–1.2 (m, 15 H), 2.24 (s, 2 H), 3.86 (s, 3 H), 7.1–7.5 (m, 3 H), 10.27 (s, 1 H); MS *m/e* 308 (M^+), 279 ($M^+ - C_2H_5$); high-resolution MS (*m/e*) calcd for $C_{16}H_{24}O_4Si$ (M^+) 308.1444, found 308.1447.

2,2-Dimethoxyphenethyl (*tert*-butyldimethylsilyl)acetate (7a): IR 1715 cm^{-1}; ^1H NMR δ 0.13 (s, 3 H), 0.20 (s, 3 H), 0.94 (s, 9 H), 1.90 (s, 2 H), 3.35 (s, 6 H), 4.41 (s, 2 H), 7.35–7.7 (m, 5 H); MS *m/e* 307 ($M^+ - OCH_3$); high-resolution MS (*m/e*) calcd for $C_{17}H_{27}O_3Si$ ($M^+ - OCH_3$) 307.1730, found 307.1741.

2-Formyl-6-methoxyphenyl (*tert*-butyldimethylsilyl)acetate (7b): IR 1745, 1700, 1660, 1590 cm^{-1}; ^1H NMR δ 0.23 (s, 6 H), 0.98 (s, 9 H), 2.22 (s, 2 H), 3.84 (s, 3 H), 7.1–7.5 (m, 3 H), 10.27 (s, 1 H); MS *m/e* 308 (M^+), 251 ($M^+ - C_4H_9$). Anal. Calcd for $C_{16}H_{24}O_4Si$: C, 62.30; H, 7.84. Found: C, 62.57; H, 7.86.

Cyclization of 3a. (a) By Using CsF. Under a nitrogen atmosphere, a suspension of anhydrous CsF (1.7 mg, 0.01 mmol) in dry DMF (1 mL) was vigorously stirred at room temperature for 15 min then cooled to 0 °C. A solution of **3a** (30 mg, 0.11 mmol) in dry DMF (1 mL) was added, and the whole was stirred for 1 h. The mixture was poured into an ice-cold mixture of saturated aqueous NH_4Cl (5 mL) and ether (5 mL). The organic layer was separated, and aqueous layer was extracted with ether (5 mL). The combined organic layer was washed with H_2O (2 × 5 mL), dried, and concentrated in vacuo. The crude product

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(17) Shchukovskaya, L. L.; Pal'chik, R. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1964**, 2228; *Chem. Abstr.* **1965**, *62*, 9167c.
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was purified by prep. TLC on silica gel (1:2 ether–*n*-hexane) to give a 71% yield (14 mg) of pure **11** as colorless crystals: mp 50–53 °C (ether–*n*-hexane) (lit.[19] mp 55–56 °C); IR 1750, 1620 cm^{-1}; ^1H NMR δ 1.55 (d, 3 H, J = 7 Hz), 5.54 (qd, 1 H, J = 7, 1.5 Hz), 6.24 (d, 1 H, J = 1.5 Hz), 7.44 (s, 5 H); MS m/e 174 (M^+).

(b) By Using NaH: Similarly as described in method a, **3a** (50 mg, 0.19 mmol) was treated with NaH (60% oil suspension, 9 mg, 0.23 mmol) in dry DMF (2 mL) at 0 °C for 1 h to give **11** in 82% yield (27 mg), which was identical with **11** prepared by method a.

Acknowledgment. We thank Yasunori Tsuzuki for technical assistance.

Registry No. **1a**, 5650-40-8; **1b**, 119-53-9; **1c**, 116-09-6; **1d**, 90-02-8; **1e**, 63703-34-4; **1f**, 28203-05-6; **1g**, 124513-25-3; **1h**, 556-52-5; **1i**, 556-82-1; **1j**, 577-85-5; **1k**, 148-53-8; **2**, 4071-85-6; **3a**, 124513-11-7; **3b**, 124513-12-8; **3c**, 124513-13-9; **3d**, 124513-14-0; **3e**, 124513-15-1; **3f**, 124513-16-2; **3g**, 124513-17-3; **3h**, 124513-18-4; **3i**, 124513-19-5; **3j**, 124513-20-8; **4**, 19060-98-1; **5a**, 124513-21-9; **5b**, 124513-22-0; **6**, 104992-44-1; **7a**, 124513-23-1; **7b**, 124513-24-2; **9**, 995-00-6; **10**, 124513-26-4; **11**, 74528-46-4; $ZnCl_2$, 7646-85-7; ZnI_2, 10139-47-6; 2-lithio-1,3-dithiane, 36049-90-8; benzoyl chloride, 98-88-4; ethoxyacetylene, 927-80-0; triethylsilyl chloride, 994-30-9; *tert*-butyldimethylsilyl chloride, 18162-48-6.

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Efficient Syntheses for Optically Pure Stereogenically Labile 4-Substituted-2-hydroxytetronic Acids

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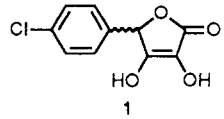
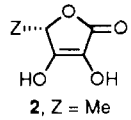
The *aci*-reductone 4-(4-chlorophenyl)-2-hydroxytetronic acid (CHTA, **1**) exhibits antilipidemic and antiaggregatory properties that differ from those of classical phenoxyacetic acids.[1,2] To further explore enzymatic inhibitory mechanisms of action relevant to the treatment and/or prevention of atherosclerosis, we required methods for the synthesis of optically pure 4-alkyl- and 4-aryl-2-hydroxytetronic acids **2** and **3**. The redox functionality present in these species is also found in vitamin C, but outside the scope of vitamin C research this function has received little attention.[3] Although, unsubstituted, 2-alkyl-, and 2-acyltetronic acids are frequently found in nature,[4,5] the 2-hydroxy-substituted redox system, to our knowledge, is only found in vitamin C and the macrolide antibiotic chlorothricin.[6]

Synthesis of 4-monosubstituted-2-hydroxytetronic acids **2** and **3** is complicated by the stereochemical lability of the C-4 stereogenic center. The lability of this center in



1



2, Z = Me
3, Z = Ph

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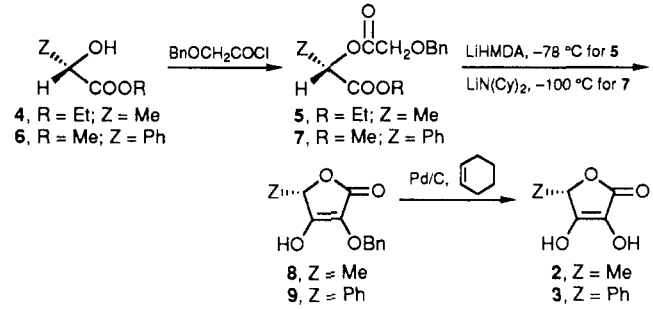
Scheme I



tetronic acid **3** can be compared to the lability of the asymmetric center of mandelic acid[7,8] and phenylglycine.[9,10] Phenylglycine undergoes extensive racemization during peptide synthesis.[9]

Older synthetic methods[11] involving benzoin and intermolecular Claisen condensations employed in the synthesis of L-ascorbic acid would likely produce racemic 4-aryl-2-hydroxytetronic acids. Elegant syntheses published for the naturally occuring chiral tetronic acids such as (−)-vertinolide,[12] (*S*)-carlosic acid,[13] chlorothricin,[14] related 2-acylated[15] or 2-unsubstituted[16] tetronic acids, and chiral tetronic acid intermediates useful for the synthesis of the seco acid of erythronolide B[17] were not applicable for the synthesis of optically pure enantiomers of 4-aryl-2-hydroxytetronic acids. Some targets contain quaternary chiral centers not expected to undergo racemization during their preparation.[12,14] Other syntheses are dependent upon intramolecular Claisen condensations facilitated by a second carbonyl function, thereby affording 2-acyltetronic acids.[13,15] In some cases the 4-substituent at the chiral center is alkyl[16,17] and, therefore, racemization under reaction conditions employed is more easily prevented.

Results and Discussion

The intramolecular Claisen condensation involving use of a nonnucleophilic sterically hindered base was anticipated to be a useful approach for the synthesis of optically pure 4-alkyl- and 4-aryl-2-hydroxytetronic acids of known absolute configuration [(*S*)-**2** and (*S*)-**3**] from accessible asymmetric α-hydroxy esters **4** and **6**, respectively (Scheme I). Such a Claisen condensation is a particularly facile intramolecular process suitable for the construction of tetronic acids via C2–C3 bond connection. Thus (phenylmethoxy)acetyl derivative **5**, prepared from ester **4** and (phenylmethoxy)acetyl chloride in 86% yield, underwent intramolecular Claisen condensation with lithium hexamethyldisilazide (LiHMDA) (−78 °C) to afford 2-(phenylmethoxy)tetronic acid (**8**) in 82% yield without detectable epimerization. The enantiomeric purity of the protected tetronic acid (*S*)-(+)-**8** (>98% ee) was determined by using high resolution NMR (500 MHz) analysis

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