integration ratio of the two former peaks (CH_3SiF:CH_3SiCl) was 1.6:1.

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Synthesis of Hydroxy Lactones by Bis(tributyltin) Oxide Promoted Ring Expansion of Halo Lactones

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Halo lactones are easily prepared by cyclofunctionalization of unsaturated carboxylic acids on treatment with halogen under basic conditions.[1] This halolactonization had proven useful in organic synthesis because of advantages in operational convenience and high stereoselectivity. We have reported the synthesis of heterocyclic compounds by the cleavage of halo lactones with organotin alkoxide.[2] Organotin alkoxides cleave β-lactone rings easily to provide tin alkoxides, and tin has a great affinity toward halogens.[3-5]

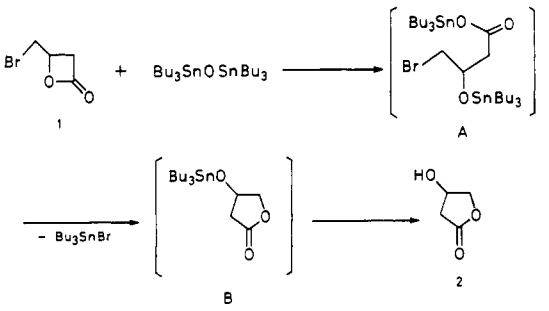
On the basis of these features, we have found a novel synthetic method for ring expansion of halo lactones with bis(tributyltin) oxide [$(Bu_3Sn)_2O$].

The reaction of $(Bu_3Sn)_2O$ with β-lactone **1** at 80 °C for 5 h gave β-hydroxy-γ-butyrolactone[6] (**2**) in 80% yield. As shown in Scheme I, the reaction course may be explained as follows. First, the β-lactone is cleaved to afford the intermediate A. Subsequently, the stannyl carboxylate moiety of A attacks the terminal organic bromide[7] to produce B, which on work up with MeOH gives the product **2**.

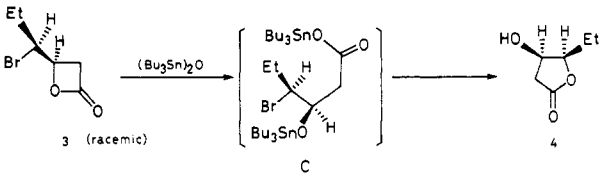
When the β-lactone bearing a secondary alkyl bromide **3** is used, the stannyl carboxylate moiety of C attacks at the back side of the terminal secondary alkyl bromide in a S_N2 process to give the stereoisomerically pure product, 3,4-*cis*-substituted lactone **4** in 77% yield (Scheme II). The lactone **3** was prepared from the stereospecific bromolactonization of *trans*-hexenoic acid.[1g]

We examined the use of α,β-*trans*-substituted β-lactones, **5-7**, as substrates. These compounds were prepared from the stereoselective bromolactonization of α-substituted

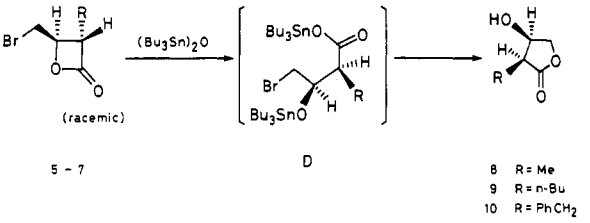
Scheme I



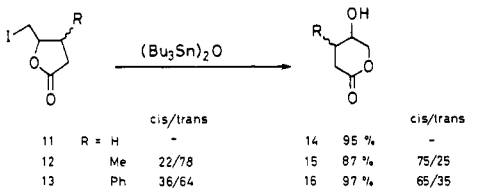
Scheme II



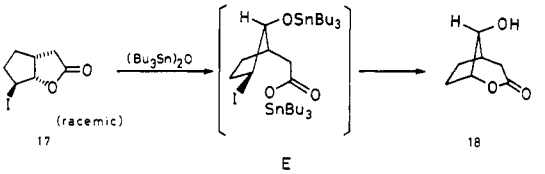
Scheme III



Scheme IV



Scheme V



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β,γ-unsaturated carboxylic acids.[1h] The reactions were performed at 100 °C for 5 h. As shown in Scheme III, the ring cleavage by $(Bu_3Sn)_2O$ and the subsequent cyclization of D provides α-*cis*-substituted β-hydroxy-γ-lactones **8**, **9**, and **10** in 99%, 99%, and 90% yields, respectively.

The α-cis isomers prepared here are noteworthy, because previous reports of α-alkyl β-hydroxy lactones show only the trans isomers to be prepared by direct α-alkylation of β-hydroxy-γ-butyrolactones.[6b,8]

As shown in Scheme IV, the ring expansions of γ-lactones **11**–**13** also proceeds in good yields, although more severe conditions are required (100 °C, 5 h). Thus the γ-hydroxy-δ-valerolactones **14**, **15**, and **16** were obtained in 95, 87, and 97% yields, respectively.

When bicyclic substrate **17** was used, the transformation also proceeded cleanly, affording **18** in 70% yield (Scheme V).

In summary, $(Bu_3Sn)_2O$-promoted ring expansion reaction of halo lactones provides various hydroxy lactones in good yields.

Experimental Section

Melting points were taken on a Yanaco melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra (tetramethylsilane as an internal standard) were recorded on a Hitachi R-90H (90 MHz) or a JEOL JNM-GSX-400 (400 MHz) spectrometer. Infrared spectra were recorded with a Hitachi 260-30 instrument. Mass spectra were obtained with a JEOL JMS-DS303 spectrometer. Analytical GLC was performed on a Shimadzu GC-3B with TCD using 2 m × 3 mm glass column packed with Silicone OV-17 on Uniport HP (5%, 60–80 mesh) or a Shimadzu GC-14A with FID using 25 m × 0.3 mm capillary column packed with CBP-10. Column chromatography was performed on silica gel (Wakogel C-200 or C-300).

Bis(tributyltin) oxide [$(Bu_3Sn)_2O$], a commercial product, was used (Sankyo Yuki Gosei Co.). Halo lactones **1**, **3**, **11**, **12**, **13**, and **17** were prepared by the standard procedure.[1] α-Alkyl-γ-bromo β-lactones, **5**, **6**, and **7**, were synthesized by our method.[1h]

β-Hydroxy-γ-butyrolactone (2). General Procedure. $(Bu_3Sn)_2O$ (1.79 g, 3 mmol) was added to **1** (0.50 g, 3 mmol) under nitrogen atmosphere. This mixture was stirred at 80 °C for 2 h to give the intermediate A. The mixture was quenched by MeOH and chromatographed on silica gel. Compound **2** was obtained as a colorless oil, which was purified by Kugelrohr at 80 °C (10^{-2} mmHg) [lit.[6a] bp 103–105 °C (0.4 mmHg)]; IR (neat) 3300, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80 (br, 1 H, OH), 2.40–2.75 (m, 2 H, $COCH_2$), 4.20–4.80 (m, 3 H, OCH_2 and C*H*OH); MS *m*/*z* 103 (M^+).

β-Hydroxy-γ-ethyl-γ-butyrolactone (4): colorless oil, purified by Kugelrohr at 100 °C (10^{-2} mmHg); IR (neat) 3300, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (t, 3 H, *J* = 7.6 Hz, CH_3), 1.70–1.95 (m, 2 H, CH_2Me), 2.58 (dd, 1 H, *J* = <1 and 17.8 Hz, one of C=OCH_2), 2.65 (br, 1 H, OH), 2.77 (dd, 1 H, *J* = 5.4 and 17.8 Hz, one of C=OCH_2), 4.31 (m, 1 H, C*H*OH), 4.49 (m, 1 H, OCHEt): ^{13}C NMR ($CDCl_3$) δ 9.8, 21.5, 39.5, 68.7, 86.3, 175.8; MS *m*/*z* 131 (M^+). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.36; H, 7.57.

α-Methyl-β-hydroxy-γ-butyrolactone (8): colorless oil, purified by Kugelrohr at 100 °C (10^{-2} mmHg); IR (neat) 3250, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (d, 3 H, *J* = 7.3 Hz, CH_3), 1.97 (br, 1 H, OH), 2.65 (qd, 1 H, *J* = 7.3 and 5.4 Hz, C=OCH), 4.29 (dd, 1 H, *J* = 1.0 and 10.3 Hz, one of OCH_2), 4.32 (dd, 1 H, *J* = 3.4 and 10.3 Hz, one of OCH_2), 4.54 (m, 1 H, C*H*OH): ^{13}C NMR ($CDCl_3$) δ 7.7, 40.0, 69.5, 74.5, 179.6; MS *m*/*z* 116 (M^+). Anal. Calcd for $C_5H_8O_3$: C, 51.72; H, 6.94. Found: C, 51.61; H, 7.07.

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α-*n*-Butyl-β-hydroxy-γ-butyrolactone (9): colorless oil, purified by Kugelrohr at 100 °C (10^{-2} mmHg); IR (neat) 3300, 1760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–1.90 (m, 9 H, Bu), 2.30 (br, 1 H, OH), 2.46 (td, 1 H, *J* = 5.1 and 10.3 Hz, C=OCH), 4.25–4.35 (m, 2 H, one of OCH_2 and C*H*OH), 4.55–4.65 (dd, 1 H, *J* = 4.4 and 2.2 Hz, one of OCH_2); ^{13}C NMR ($CDCl_3$) δ 13.6, 22.3, 22.8, 29.4, 45.2, 68.5, 74.5, 178.5; MS *m*/*z* 158 (M^+). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.91. Found: C, 60.58; H, 8.66.

α-Benzyl-β-hydroxy-γ-butyrolactone (10): mp 84–85 °C; IR (KBr) 3200, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (s, 1 H, OH), 2.80–2.90 (m, 1 H, C=OCHBn), 3.00 (dd, 1 H, *J* = 11.5 and 14.3 Hz, one of CH_2Ph), 3.20 (dd, 1 H, *J* = 3.9 and 14.3 Hz, one of CH_2Ph), 4.25–4.32 (m, 2 H, OCH_2), 4.38–4.43 (m, 1 H, C*H*OH), 7.20–7.40 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 29.50, 47.55, 68.77, 74.62, 126.70, 128.65, 128.80, 138.99, 177.25; MS *m*/*z* 192 (M^+). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.65; H, 6.24.

γ-Hydroxy-δ-valerolactone (14): $(Bu_3Sn)_2O$ (1.79 g, 3 mmol) was added to **1** (0.50 g, 3 mmol) under nitrogen atmosphere. This mixture was stirred at 100 °C for 5 h. The mixture was quenched by MeOH and chromatographed on silica gel. Compound **14** was obtained as a colorless oil, which was purified by Kugelrohr at 80 °C (10^{-2} mmHg): IR (neat) 3300, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10–2.30 (m, 2 H, CH_2), 2.45 (s, 1 H, OH), 2.50–2.70 (m, 2 H, C=OCH_2), 3.64 (dd, 1 H, *J* = 4.5 and 12.4 Hz, one of OCH_2), 3.91 (dd, 1 H, *J* = 3.2 and 12.4 Hz, one of OCH_2), 4.50–4.80 (m, 1 H, C*H*OH); MS *m*/*z* 116 (M^+).

***cis*- and *trans*-β-methyl-γ-hydroxy-δ-valerolactone (15)**: colorless oil which was purified by Kugelrohr at 80 °C (10^{-2} mmHg); IR (neat) 3200, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) (cis isomer) δ 1.18 (d, 3 H, *J* = 6.8 Hz, CH_3), 2.23 (dd, 1 H, *J* = 9.0 and 17.3 Hz, one of C=OCH_2) 2.32 (s, 1 H, OH), 2.50–2.60 (m, 1 H, CHMe), 2.76 (dd, 1 H, *J* = 9.8 and 17.3 Hz, one of C=OCH_2), 3.80–3.95 (m, 2 H, OCH_2), 4.12–4.18 (m, 1 H, C*H*OH); (trans isomer) δ 1.15 (d, 3 H, *J* = 6.8 Hz, CH_3), 2.32 (s, 1 H, OH), 2.37 (dd, 1 H, *J* = 8.0 and 17.3 Hz, one of C=OCH_2), 2.63 (dd, 1 H, *J* = 8.5 and 17.3 Hz, one of C=OCH_2), 2.72–2.78 (m, 1 H, CHMe), 3.65–3.72 (m, 2 H, OCH_2), 4.50–4.55 (m, 1 H, C*H*OH); ^{13}C NMR ($CDCl_3$) (cis isomer) δ 18.1, 31.4, 37.3, 62.6, 87.9, 177.6; (trans isomer) δ 14.0, 32.3, 37.1, 61.7, 83.6, 178.1; MS *m*/*z* 130 (M^+). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.63; H, 7.74.

***cis*- and *trans*-β-phenyl-γ-hydroxy-δ-valerolactone (16)**: mp 107 °C; IR (KBr) 3350, 1770 cm^{-1}; ^1H NMR ($CDCl_3$) (cis isomer) δ 2.65 (br, 1 H, OH), 2.79 (dd, 1 H, *J* = 9.8 and 17.6 Hz, one of C=OCH_2), 3.04 (dd, 1 H, *J* = 8.8 and 17.6 Hz, one of C=OCH_2), 3.65–3.75 (m, 2 H, CHPh and one of OCH_2), 3.95 (dd, 1 H, *J* = 2.4 and 12.8 Hz, one of OCH_2), 4.50–4.58 (m, 1 H, C*H*OH), 7.20–7.40 (m, 5 H, Ph); (trans isomer) δ 2.65 (br, 1 H, OH), 2.88 (dd, 1 H, *J* = 8.8 and 17.6 Hz, one of C=OCH_2), 3.04 (dd, 1 H, *J* = 8.8 and 17.6 Hz, one of C=OCH_2), 3.35–3.45 (m, 1 H, PhCH), 3.52 (dd, 1 H, *J* = 3.4 and 12.7 Hz, one of OCH_2), 3.85–3.95 (m, 1 H, one of OCH_2), 4.75–4.85 (m, 1 H, C*H*OH), 7.20–7.40 (m, 5 H, Ph); ^{13}C ($CDCl_3$) (cis isomer) δ 37.2, 42.0, 61.9, 87.0, 127.1, 127.6, 129.1, 139.1, 175.9; (trans isomer) δ 34.6, 43.5, 62.0, 83.4, 127.1, 127.6, 129.1, 139.1, 175.9; MS *m*/*z* 192 (M^+). Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.51; H, 6.13.

2-Oxa-8-hydroxybicyclo[3.2.1]octan-3-one (18): colorless oil, purified by Kugelrohr at 120 °C (10^{-2} mmHg); IR (neat) 3350, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.58–1.78 (m, 2 H, CH_2), 1.99–1.82 (m, 2 H, CH_2), 2.17 (s, 1 H, OH), 2.29–2.37 (m, 1 H, CH), 2.80–2.95 (m, 2 H, C=OCH_2) 4.13–4.17 (m, 1 H, C*H*OH), 4.78–4.81 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$) δ 29.6, 31.1, 35.3, 37.0, 74.1, 166.2, 178.1; MS *m*/*z* 142 (M^+). Anal. Calcd for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.03; H, 7.23.

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