was ineffective for this purpose (run 4), and about 60% of the starting diol 1 was recovered.

In conclusion, we have found the first practical transformation of *vic*-diols into α-ketols using hydrogen peroxide. This method possesses several advantages: (1) the reaction is carried out catalytically using a cheap and clean oxidant (35% H_2O_2), and the isolation of α-ketols is accomplished easily since the reaction is carried out in a biphasic system; (2) the reaction is particularly useful for oxidation of terminal diols to afford acyloins which are difficult to prepare by conventional methods; and (3) the preparation of α-ketols from *vic*-diols offers a wider range of substrate opportunities.

Experimental Section

GLC analyses were performed employing a thermal conductivity detector using a 2.6 mm × 5.4 m column (5% silicon OV-7 on Chromosorb W). Infrared spectra were measured as KBr pellets (4-cm^{-1} resolution). ^1H and ^{13}C NMR were measured at 400 MHz in $CDCl_3$ using $MeSi_4$ as the internal standard. The yield of products was estimated from peak areas based on an internal standard.

Preparation of Peroxotungsten Complex (PCWP). PCWP was prepared by the method reported previously.[19] The active oxygen content of PCWP was estimated to 3.7–3.9 mmol/g (theoretical 3.8 mmol/g) from iodometry improved by Venturello.[16] PCWP: IR (KBr/Nujol) 2900, 2850, 1633, 1486, 1466, 1090, 1055, 957, 842, 774, 722, 684, 648, 625, 571, 552, 524 cm^{-1}. Anal. Calcd for $C_{63}H_{114}N_3O_{24}PW_4$ (PCWP): C, 36.66; H, 5.57; N, 2.04. Found: C, 36.41; H, 5.47; N, 2.01.

General Procedure for Oxidation of *vic*-Diols. To a stirred solution of PCWP (0.1 g, 0.048 mmol) and 35% H_2O_2 (18 mmol) in chloroform (15 mL) was added the *vic*-diol (3 mmol), and the mixture was refluxed for 16 h. The reactant was treated with a solution of 10% $NaHSO_3$ (20 mL) to decompose unreacted H_2O_2 and extracted with $CHCl_3$. The products were purified by silica gel column chromatography (hexane/ethyl acetate (10–20/1)). Spectral data of the products were identical with those reported.[1b,5,6,9,10]

Registry No. 1, 6920-22-5; 2, 73397-68-9; 3, 109-52-4; 4, 1117-86-8; 5, 7019-19-4; 6, 584-03-2; 7, 5077-67-8; 8, 93-56-1; 9, 582-24-1; 10, 56255-50-6; 11, 20653-90-1; 12a, 52279-26-2; 12b, 52279-26-2; 13, 1460-57-7; 14, 124-04-9; 15, 4277-32-1; 16, 496-82-2; H_2O_2, 7722-84-1.

Supplementary Material Available: Spectral data for acyloins in Table I (2 pages). Ordering information is given on any current masthead page.

Synthesis of Functionalized Endocyclic α,β-Unsaturated and α-Methylene Eudesmanolides[1]

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Although a number of sesquiterpenes possessing C_{12}-functionalized endocyclic α,β-unsaturated γ-lactones such as A (X = CH_3, CH_2OH, CH_2OAc, CHO)[3] and 7-hydroxy-α-methylene γ-lactones[4] such as B (Figure 1) have been reported, efficient methodology for synthesis of these functional groups has not yet been reported.[5] In the course of our studies of sesquiterpene lactones, we were interested in the syntheses of compounds possessing these functional groups because of literature reports concerning their biological activities.[6] In this paper we report the

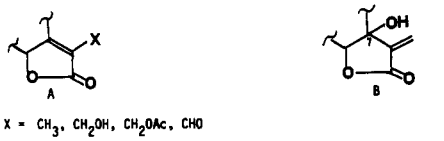
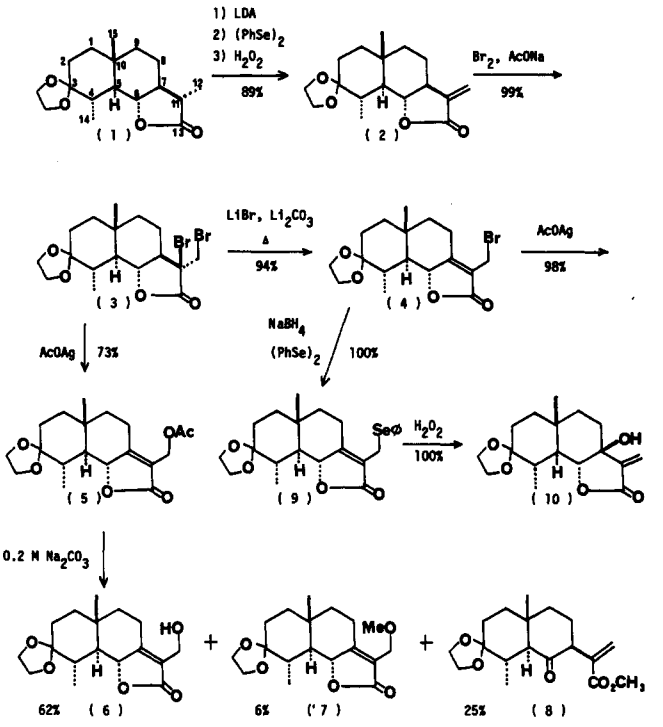
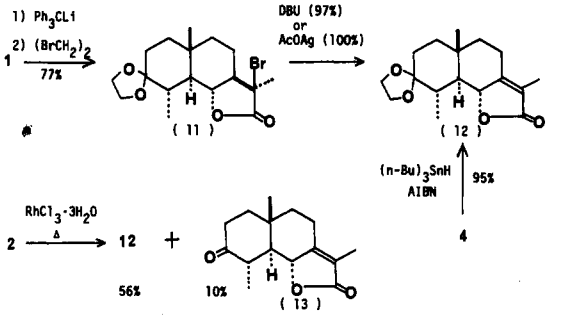


Figure 1.

Scheme I



Scheme II



(1) Studies on the Syntheses of Sesquiterpene Lactones. 13. Preliminary reports of this work were presented at the 26th and 31th Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics, Yamagata, Oct 1982; Abstract pp 224–227 and Kyoto, Sept 1987, pp 137–139.

(2) (a) Department of Applied Chemistry, Faculty of Engineering, Niigata University. (b) Department of Chemistry, Faculty of Science, Tohoku University.

(3) Fisher, N. H.; Olivier, E. J.; Fisher, H. D. *Prog. Chem. Org. Nat. Prod.* **1979**, *38*, 47 and references cited therein.

(4) (a) Bohlmann, F.; Le Van, N. *Phytochemistry* **1978**, *17*, 1957. (b) Herz, W.; Govindan, S. V.; Blount, J. F. *J. Org. Chem.* **1980**, *45*, 1113. (c) Bohlmann, F.; Castro, V.; Jakupovic, J. *Phytochemistry* **1983**, *22*, 1223. (d) Christensen, S. B.; Norup, E.; Rasmussen, U.; Madsen, J. Ø. *Ibid.* **1984**, *23*, 1659. (e) Seaman, F. C.; Malcolm, A. J.; Fisher, N. H. *Ibid.* **1985**, *24*, 2003. (f) de Luengo, D. H.; Miski, M.; Gage, D. A.; Mabry, T. J. *Ibid*, **1986**, *25*, 1917. (g) Gogte, M. G.; Ananthasubramanian, L.; Nargud, K. S.; Bhattacharyya, S. C. *Ind. J. Chem.* **1986**, *25*, 223. (h) Jakupovic, J.; Grenz, M.; Bohlmann, F.; Mungai, M. *Phytochemistry* **1990**, *29*, 1213. (i) Fronczeck, F. R.; Vargas, D.; Fisher, N. H.; Hostettmann, K. *J. Nat. Prod.* **1984**, *47*, 1036.

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0022-3263/91/1956-6235$02.50/0

results of our synthetic efforts to elaborate these functional groups from the easily available eudesmanolide derivative (11*S*)-3,3-(ethylenedioxy)eudesmano-13,6α-lactone (**1**)[7] (Scheme I). Although we show only one set of reactions in this paper, the conditions employed here are mild and might be applicable to the syntheses of analogous compounds.

Phenylselenenylation of **1** and successive treatment with 30% hydrogen peroxide in THF in the presence of acetic acid gave α-methylene γ-lactone **2**[7] in 89% yield. Bromination of **2** with bromine in the presence of sodium acetate in dichloromethane gave dibromide **3** in almost quantitative yield. The paramagnetic shift of C_6-H of **3** (0.22) compared with that of **1** indicates the β-orientation of bromine atom at C_{11}. Attempts to effect bromination of **2** with PTAB in THF[8] or bromine in dichloromethane[9] gave several products.

Dehydrobromination of **3** with a mixture of lithium bromide and lithium carbonate in DMF at 70–76 °C gave a C_{12}-brominated endocyclic α,β-unsaturated γ-lactone derivative **4** in 94% yield. Treatment of **4** with silver acetate in DMF at room temperature gave an acetate **5** in 98% yield. Alternatively, treatment of **3** with 3.2 molar equiv of silver acetate at room temperature gave **5** directly, in 73% yield.

Hydrolysis of **5** with a 0.2 M aqueous solution of sodium carbonate in methanol at room temperature gave the corresponding alcohol **6** in 62% yield, accompanied by a methoxy derivative **7** and a methyl ester **8** in 6 and 25% yields, respectively.

Displacement of the C_{12}-bromine atom of **4** with sodium phenyl selenolate, which was formed from diphenyl diselenide and sodium borohydride in ethanol,[10] gave a rather unstable phenyl selenide **9**. Treatment of **9** with 30% hydrogen peroxide in THF in the presence of acetic acid gave a C_7-hydroxy-α-methylene γ-lactone **10** in a quantitative yield. A large paramagnetic shift of C_6-H of **10** (0.53) compared with that of **2** indicates the β-orientation of the newly introduced C_7-hydroxyl group. The formation of **10** is rationalized by a [2,3] sigmatropic rearrangement of the phenyl selenoxide intermediate.[11]

Debromination of **4** by treatment with tri-*n*-butyltin hydride in the presence of AIBN in THF gave an endocyclic α,β-unsaturated γ-lactone **12** in 95% yield (Scheme II). This compound was also prepared by the following alternate two procedures.

Treatment of **1** with (triphenylmethyl)lithium in THF followed by 1,2-dibromoethane[12] gave bromo γ-lactone **11** in 77% yield. The β-orientation of the bromine atom at C_{11} of **11** was deduced by the paramagnetic shift of C_6-H of **11** (0.31) compared with that of **1** in their ^{1}H NMR spectra. Dehydrobromination of **11** with DBU in refluxing benzene gave **12** in 97% yield. Alternatively, treatment of **11** with silver acetate in DMF at room temperature gave **12** in a quantitative yield.

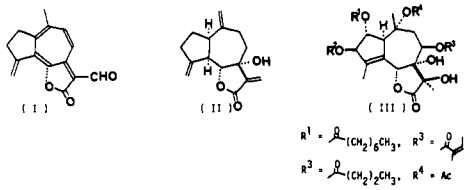
A possible alternative procedure for preparation of **12** is the isomerization of the double bond of the α-methylene γ-lactone. Treatment of **2** with rhodium trichloride hydrate[13] in refluxing ethanol gave **12** in 56% yield, accompanied by the corresponding ketone **13** in 10% yield.

Experimental Section[14]

11β,12-Dibromo-3,3-(ethylenedioxy)eudesmano-13,6α-lactone (3). To a stirred mixture of 3,3-(ethylenedioxy)eudesm-11(12)-eno-13,6α-lactone (**2**)[7] (151.2 mg, 0.517 mmol) and sodium acetate (64.8 mg, 0.79 mmol) in CH_2Cl_2 (6.5 mL) was added a solution of Br_2 (93.0 mg, 0.582 mmol) in CH_2Cl_2 (150 μL) in 15 min. The mixture was stirred for 3 h at 0 °C, poured into a mixture of saturated aqueous NaCl and saturated aqueous $NaHCO_3$, and extracted with $CHCl_3$. The extract was dried (Na_2SO_4) and concentrated to give spectroscopically pure **3** (232 mg, 99%) as a pale yellow oil, which was crystallized from a mixture of ether and hexane at 0 °C to give colorless prisms: mp 132 °C; IR (KBr) 1790 cm^{-1}; ^{1}H NMR δ 1.02 (3 H, s), 1.05 (3 H, d, J = 6.0), 3.78 (1 H, d, J = 10.5), 3.95 (4 H, br s), 4.13 (1 H, d, J = 10.5), 4.13 (1 H, dd, J = 10.5, 9.5); MS m/e (relative intensity) 450 (M^+, 5), 373 (100), 371 (90). Anal. Calcd for $C_{17}H_{24}Br_2O_4$: C, 45.16; H, 5.35. Found: C, 45.56; H, 5.59.

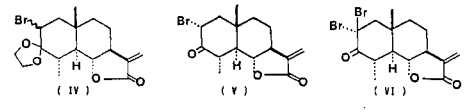
12-Bromo-3,3-(ethylenedioxy)eudesm-7(11)-eno-13,6α-lactone (4). A mixture of **3** (143.9 mg, 0.318 mmol), Li_2CO_3 (59.7 mg, 0.808 mmol), and LiBr (44.9 mg, 0.517 mmol) in DMF (4.5 mL) was stirred at 70–76 °C for 40 min, cooled to rt, poured into water, and extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and concentrated to give a yellow oil, which was purified by TLC (AcOEt–$CHCl_3$ (1:1)) and crystallized from a mixture of benzene, ether, and hexane to give **4** (111.5 mg, 94%) as colorless prisms: mp 185–186 °C; IR (KBr) 1755, 1675

(6) (a) Lettucenin A (I), phytoalexin of lettuce, has been reported as an antifungal compound: Takasugi, M.; Okinaka, S.; Katsui, N.; Masamune, T.; Shirata, A.; Ohuchi, M. *J. Chem. Soc., Chem. Commun.* **1985**, 621. (b) 11,13-Dihydro-7,11-dehydro-13-hydroxy-3-desoxyzaluzanin C (II) has been reported as an molluscidal compound: Fronczeck, F. R.; Vargas, D.; Fisher, N. H. *J. Nat. Prod.* **1984**, *47*, 1036. (c) The dihydroxygenated derivatives of the double bond of endocyclic α,β-unsaturated γ-lactone, such as thapsigargin (III), have been reported as noncytotoxic histamine-releasing compounds: Christensen, S. B.; Norup, E.; Rasmussen, U.; Madsen, J. Ø. *Phytochemistry* **1984**, *23*, 1659 and references cited therein.

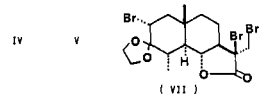


(7) Ando, M.; Wada, T.; Kusaka, H.; Takase, K.; Hirata, N.; Yanagi, Y. *J. Org. Chem.* **1987**, *52*, 4792.

(8) The isolated products were as follows:



(9) The isolated products were as follows:



(10) (a) Sjöberg, B.; Herdevall, S. *Acta Chem. Scan.* **1958**, *12*, 1347. (b) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947. (c) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697. (d) Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *Ibid.* **1973**, *95*, 6137. (e) Scarborough, R. M.; Smith, A. B. *Tetrahedron Lett.* **1977**, 4361. (f) Liotta, D.; Markiewicz, W.; Santiesteban, H. *Ibid.* **1977**, 4365. (g) Liotta, D.; Santiesteban, H. *Tetrahedron Lett.* **1977**, 4369.

(11) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986; pp 143–150 and references cited therein.

(12) Green, A. E.; Muller, J. C.; Ourison, G. *J. Org. Chem.* **1974**, *39*, 186.

(13) Fieser, M.; Fieser, L. F. *Reagents for Organic Synthesis*; John Wiley and Sons: New York, 1972; Vol. 3, p 242.

(14) All melting points are uncorrected. ^{1}H NMR spectra were recorded at 90 MHz in $CDCl_3$. Coupling constants are in hertz (Hz). ^{13}C NMR spectra were recorded at 50.3 or 22.49 MHz in $CDCl_3$. Mass spectra were recorded at 25 eV. Reactions were run under an atmosphere of nitrogen. THF was distilled from sodium benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. DMF was dried by removing by benzene–water azeotropic distillation. Benzene was dried over sodium wire. Absolute ethanol was distilled from magnesium ethoxide. Kiesel gel 60 (Merck 70–200 mesh) was employed for column chromatography, and Kiesel gel 60 GF_{254} (Merck) was used for TLC or preparative TLC (thickness 0.25 mm). HPLC effluent was monitored with a RI detector. To describe HPLC conditions, we designate column, solvent, flow rate (mL/min), and retention time (t_R) in min.

cm^{-1}; ^{1}H NMR δ 1.10 (3 H, d, J = 6.8), 1.11 (3 H, s), 1.43 (1 H, dd, J = 11.0, 11.0), 3.93 (4 H, br s), 4.08 (2 H, s), 4.65 (1 H, d, J = 11.0); ^{13}C NMR δ 12.1 (q), 16.9 (q), 18.6 (t), 23.2 (t), 30.8 (t), 35.2 (s), 37.4 (t), 40.4 (d), 40.5 (t), 53.9 (d), 65.0 (t), 65.2 (t), 82.3 (d), 110.1 (s), 121.5 (s), 167.8 (s), 171.4 (s); HRMS m/e calcd for $C_{17}H_{23}O_4$ (M^+ - Br) 291.15961, found 291.15957. Anal. Calcd for $C_{17}H_{23}BrO_4$: C, 55.00; H, 6.24. Found: C, 54.83; H, 6.29.

12-Acetoxy-3,3-(ethylenedioxy)eudesm-7(11)-eno-13,6α-lactone (5). A mixture of **4** (734 mg, 1.98 mmol) and silver acetate (430 mg, 2.58 mmol) in DMF (30 mL) was stirred at rt for 10 h and filtered. The filtrate was poured into saturated aqueous NaCl and extracted with ethyl acetate. The extract was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give a crude product, which was chromatographed over silica gel (35 g, 70–230 mesh) and eluted with $CHCl_3$ and ethyl acetate. The fraction eluted with ethyl acetate gave spectroscopically pure **5** (679 mg, 98%) as colorless needles, which was recrystallized from a mixture of benzene and hexane to give colorless needles: mp 185–187 °C; IR (KBr) 1755, 1740, 1680 cm^{-1}; ^{1}H NMR δ 1.09 (3 H, d, J = 6.8), 1.10 (3 H, s), 3.91 (4 H, m), 4.68 (1 H, d, J = 11.0), 4.75 (2 H, s). Anal. Calcd for $C_{19}H_{26}O_6$: C, 65.13; H, 7.48. Found: C, 64.86; H. 7.57.

3,3-(Ethylenedioxy)-12-hydroxyeudesm-7(11)-eno-13,6α-lactone (6). A mixture of **5** (251.5 mg, 0.718 mmol) and 0.2 M aqueous Na_2CO_3 (8.5 mL) in MeOH was stirred at rt for 15 min, poured into saturated aqueous NaCl, and extracted with $CHCl_3$. The extract was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give an oily crude product, which was purified by HPLC (30 × 1 cm i.d. glass column packed with 10-μm silica gel (Kyowa gel MIC-SI-10), EtOc–hexane (1:1), 2.5 mL/min).

The first peak (t_R 11.2 min) gave **methyl 3,3-(ethylenedioxy)-6-oxoeudesmane-13-carboxylate (8)** (57.5 mg, 25%) as a colorless oil: IR (neat) 1730, 1720, 1640 cm^{-1}; ^{1}H NMR δ 0.82 (3 H, s), 0.85 (3 H, d, J = 6.0), 2.06 (1 H, dq, J = 11.3, 6.0), 2.62 (1 H, dd, J = 11.3, 1.0), 3.57 (1 H, br t, J = 9.5), 3.69 (3 H, s), 3.93 (4 H, s), 5.50 (1 H, dd, J = 1.0, 1.0), 6.30 (1 H, dd, J = 1.0, 1.0); MS m/e (relative intensity) 322 (M^+, 28), 99 (100).

The second peak (t_R 24.5 min) gave **3,3-(ethylenedioxy)-12-methoxyeudesm-7(11)-eno-13,6α-lactone (7)** (13.8 mg, 6%) as colorless crystals: mp 140–143 °C; IR ($CHCl_3$) 1745, 1680 cm^{-1}; ^{1}H NMR δ 1.09 (3 H, s), 1.09 (3 H, d, J = 6.4), 3.35 (3 H, s), 3.92 (4 H, m), 4.15 (2 H, s), 4.62 (1 H, br d, J = 11.0); MS m/e (relative intensity) 322 (M^+, 4), 99 (100.).

The third peak (t_R 62 min) gave **6** (137.2 mg, 62%) as colorless crystals, which was recrystallized from a mixture of benzene and hexane to give colorless prisms: mp 200–202 °C; IR ($CHCl_3$) 3600, 1740, 1680 cm^{-1}; ^{1}H NMR δ 1.09 (3 H, s), 1.10 (3 H, d, J = 6.5), 3.91 (4 H, m), 4.35 (2 H, s), 4.62 (1 H, d, J = 11.0); MS m/e (relative intensity) 308 (M^+, 33), 167 (32), 99 (100). Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.25; H, 7.85.

3,3-(Ethylenedioxy)-12-(phenylseleno)eudesm-7(11)-eno-13,6α-lactone (9). To a stirred mixture of $NaBH_4$ (5.8 mg, 0.153 mmol) and absolute ethanol (0.5 mL) was added a solution of diphenyl diselenide (22 mg, 0.070 mmol) in absolute ethanol at 0 °C. After the solution was stirred at 0 °C for 25 min, bromide **4** (37.2 mg, 0.10 mmol) in THF (1.5 mL) was added. The mixture was stirred at rt for 3 h and poured into saturated aqueous NaCl and extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give a yellow oil, which was purified by TLC ($CHCl_3$–EtOAc (9:1)).

The first band (R_f 0.87) gave diphenyl diselenide.

The second band (R_f 0.34) gave **9** (45 mg, 100%) as a colorless oil: ^{1}H NMR δ 0.94 (3 H, s), 1.05 (3 H, d, J = 7.0), 3.59 (2 H, s), 3.90 (4 H, br s), 4.45 (1 H, d, J = 10.5), 7.09–7.33 (3 H, m), 7.39–7.59 (2 H, m).

3,3-(Ethylenedioxy)-7β-hydroxyeudesm-11(12)-eno-13,6α-lactone (10). A solution of **9** (44.7 mg, 0.102 mmol) in THF (2.0 mmol) containing acetic acid (15 μL, 0.267 mmol) was treated at 0 °C with 30% H_2O_2 (70 μL, 0.728 mmol) for 2 h. The reaction mixture was poured into cold saturated aqueous $NaHCO_3$ (40 mL) and extracted with $CHCl_3$. The extract was washed with aqueous KI, $Na_2S_2O_3$, and NaCl, successively, dried (Na_2SO_4), and concentrated to give spectroscopically pure **10** (31.5 mg, 100%) as a colorless oil: IR ($CHCl_3$) 3590, 3430, 1760, 980 cm^{-1}; ^{1}H NMR δ 1.00 (3 H, s), 1.01 (3 H, d, J = 6.5), 1.11 (1 H, dd, J = 10.5, 10.5), 1.96 (1 H, dq, J = 10.5, 6.5), 3.90 (4 H, m), 4.31 (1 H, d, J = 10.5), 5.73 (1 H, s), 6.29 (1 H, s); MS m/e (relative intensity) 308 (M^+, 6), 291 (M^+ - OH, 2), 99 (100); HRMS m/e calcd for $C_{17}H_{24}O_5$ 308.16234; found 308.16299.

11β-Bromo-3,3-(ethylenedioxy)eudesmano-13,6α-lactone (11). To a THF solution of (triphenylmethyl)lithium prepared from triphenylmethane (415 mg, 1.70 mmol), 1.6 M butyllithium in hexane (0.64 mL, 1.02 mmol), and THF (2.5 mL) at −75 °C (1.70 mmol) was added dropwise over a period of 10 min 100 mg (0.34 mmol) of **1** in THF (2.0 mL). After the solution was stirred at 0 °C for 2 h, 1,2-dibromoethane (0.74 mL, 8.55 mmol) was added dropwise at 0 °C over a period of 4 min. The reaction mixture was stirred at −78 °C for 1 h, quenched by the addition of saturated aqueous NH_4Cl, and extracted with chloroform. The extract was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give a crude crystalline material, which was purified by TLC ($CHCl_3$–EtOAc (9:1)). The band (R_f 0.40) gave spectroscopically pure **11** (98.2 mg, 77%), which was recrystallized from a mixture of ether and hexane to give colorless crystals: mp 142–143 °C; IR (KBr) 1785 cm^{-1}; ^{1}H NMR δ 1.03 (3 H, s), 1.06 (3 H, d, J = 6.0), 1.69 (1 H, dd, J = 11.3, 10.5), 1.87 (3 H, s), 2.05 (1 H, dq, J = 11.3, 6.0), 4.12 (1 H, dd, J = 10.5, 9.0). Anal. Calcd for $C_{17}H_{25}BrO_4$: C, 54.70; H, 6.75. Found: C, 55.02; H, 6.93.

3,3-(Ethylenedioxy)eudesm-7(11)-eno-13,6α-lactone (12).

A. By Bu_3SnH Reduction of 4. Into a flask containing $NaBH_4$ (183 mg, 4.83 mmol) was added a solution of n-Bu_3SnCl (1.47 mL, 5.32 mmol) in absolute ethanol (6.7 mL) at 0 °C over 15 min. After the mixture was stirred at 0 °C for 15 min, the resulting solution and AIBN (20 mg) were added to a solution of **4** (900 mg, 2.43 mmol) in THF (52 mL). The solution was refluxed for 45 min, cooled, poured into saturated aqueous NaCl, and extracted with ethyl acetate. The extract was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give a crude product, which was crystallized from n-pentane to give **12** (617.8 mg) as colorless prisms. The filtrate was concentrated and chromatographed over silica gel (Merck, 70–230 mesh, 90 g).

The elution with $CHCl_3$ gave n-Bu_3SnCl and n-Bu_3SnBr.

The elution with ethyl acetate gave **12** (55.8 mg).

The combined yield of **12** was 674 mg (95%). The analytical sample was prepared by the recrystallization from a mixture of ether and hexane to give colorless prisms: mp 198 °C; IR (KBr) 1750, 1690 cm^{-1}; ^{1}H NMR δ 1.08 (3 H, s), 1.09 (3 H, d, J = 6.6), 1.80 (3 H, dd, J = 1.5, 1.5), 3.91 (4 H, br s), 4.56 (1 H, br d, J = 11.0); ^{13}C NMR δ 8.3 (q), 12.2 (q), 17.0 (q), 22.7 (t), 31.0 (t), 35.2 (s), 37.8 (t), 40.5 (d), 40.9 (t), 53.7 (d), 65.1 (t), 65.2 (t), 82.2 (d), 110.5 (s), 120.2 (s), 162.3 (s), 174.6 (s); MS m/e (relative intensity) 292 (M^+, 16), 99 (100). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.32; H, 8.67.

B. By Dehydrobromination of 11 with DBU. The mixture of **11** (49.9 mg, 0.134 mmol) and DBU (90 μL, 0.602 mmol) in benzene (1.5 mL) was refluxed for 30 min, cooled, and poured into saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The extract was washed with saturated aqueous NaCl, dried (Na_2SO_4), and concentrated to give a crude product, which was purified by TLC ($CHCl_3$–AcOEt (9:1), R_f 0.87) to give **12** (37.9 mg, 97%).

C. By Dehydrobromination of 11 with AgOAc. The mixture of **11** (36.1 mg, 0.097 mmol) and AgOAc (21.7 mg, 0.13 mmol) in DMF (2.0 mL) was refluxed for 10 h, cooled, diluted with ethyl acetate, and filtered through Celite. The filtrate was poured into saturated aqueous NaCl and extracted with ethyl acetate. The extract was dried (Na_2SO_4) and concentrated to give a crude product, which was purified by TLC to give **12** (28.3 mg, 100%).

D. By Rh(III) Isomerization of 2. The mixture of **2** (43.6 mg, 0.149 mmol) and $RhCl_3 \cdot 3H_2O$ (6.0 mg) in ethanol (3.0 mL) was refluxed for 3.5 h, cooled, diluted with ethyl acetate, and filtered. The filtrate was concentrated and purified by HPLC (30 cm × 1 cm i.d. glass column packed with 10-μm silica gel (Kyowa gel MIC-SI-10), EtOAc–hexane (3:7), 3.0 mL/min).

The first peak (t_R 24 min) gave **12** (24.2 mg, 56%).

The second peak (t_R 54) gave **13** (3.8 mg, 10%) as colorless crystals: mp 124–126 °C; IR ($CHCl_3$) 1750, 1710, 1685 cm^{-1}; ^{1}H NMR δ 1.30 (3 H, s), 1.30 (3 H, d, J = 6.3), 4.67 (1 H, br d, J = 10.5); MS m/e (relative intensity) 248 (M^+, 57). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.45; H, 8.07.

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Methanesulfonate/*p*-Nitrobenzoate and *p*-Toluenesulfonate/*p*-Nitrobenzoate Rate Ratios. Solvolyses of 1-Adamantyl and Benzhydryl Substrates

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Alcohols derivatized as benzoate or sulfonate esters are frequently employed as precursors of carbocationic species generated in solvolytic reactions.[1] Typically, reactivities of a series of compounds having the same leaving group are examined in individual projects. Comparisons of substituent effects on kinetic data for different benzoates OR sulfonates can readily be made,[2] but comparisons of benzoates AND sulfonates (i.e., *p*-nitrobenzoates and tosylates) are difficult because benzoates are about 10^8-fold less reactive than sulfonates.[3]

Improved methods for determining first-order solvolysis rate constants have extended the conveniently accessible range to fast reactions having half-lives of <1 s,[4,5] and sulfonates too unstable to be isolated at room temperature have recently been studied.[6] Also, kinetics of reactions of sparingly soluble substrates can now be examined conveniently by HPLC monitoring of the disappearance of the substrate; as the "infinity" value (equal to zero substrate concentration) can be assumed, this method is well-suited to very slow reactions.[7,8] A combination of these two methods allows reliable, direct measurements of first-order rate constants spanning at least seven orders of magnitude.

We now report rate constants for solvolyses of benzhydryl (1) and 1-adamantyl (2) *p*-nitrobenzoates and methanesulfonates (mesylates) in aqueous ethanol, providing the first reliable measurements of sulfonate/*p*-nitrobenzoate rate ratios. When combined with the known trends in substituent effects[2] and solvent effects (from the Grunwald-Winstein treatment[9]), these new data link an unusually diverse range of published kinetic data.

Table I. Rate Constants (k) for Solvolyses of Benzhydryl Mesylate (1, X = OMs)[a]

solvent	temp, °C	k, s^{-1}	Y_{OMs}[b]
80% EtOH[d]	-17.1	$(1.64 \pm 0.02) \times 10^{-1}$	
	-9.6	$(4.18 \pm 0.05) \times 10^{-1}$	0.0
	0.8	1.31 ± 0.01	
	25.0[c]	14.8	
90% EtOH[d]	-9.2	$(1.34 \pm 0.01) \times 10^{-1}$	-0.82
EtOH	-9.2	$(1.22 \pm 0.05) \times 10^{-2}$	-2.22

[a] Determined conductimetrically at least in duplicate; errors shown are average deviations. [b] Values at 25 °C from ref 9b; an m value of 0.78 ± 0.06 is obtained for solvolyses of 1 at -9 °C. [c] Calculated from rate constants at lower temperatures; $\Delta H^{\ddagger} = 15.5$ kcal mol^{-1}, $\Delta S^{\ddagger} = -0.9$ cal mol^{-1} K^{-1}. [d] % v/v ethanol/water.

Table II. Rate Constants (k) for Solvolyses of Benzhydryl *p*-Nitrobenzoate (1, X = $OCOC_6H_4NO_2$) in 80% Ethanol/Water

temp, °C	k, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal mol^{-1} K^{-1}
100.0[a]	3.48×10^{-5}		
100.3[b]	$(3.34 \pm 0.05) \times 10^{-5}$		
75.2[b]	$(2.70 \pm 0.01) \times 10^{-6}$	25.6	-11.0
59.5[b]	$(4.33 \pm 0.13) \times 10^{-7}$		
25.0[c]	4.5×10^{-9}		

[a] Determined spectrophotometrically from the rate of appearance of acid.[10] [b] Determined in duplicate by HPLC from the rate of disappearance of ester in buffered solution; the rate of appearance of acid gave slightly higher results having greater uncertainty. [c] Calculated from rate constants at higher temperatures.

Table III. Rate Constants (k) for Solvolyses of 1-Adamantyl Esters (2) in 60% v/v Ethanol/Water

leaving group (X)	temp, °C	k, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal mol^{-1} K^{-1}
OMs[a]	25.0	$(5.16 \pm 0.04) \times 10^{-2}$	17.8[b]	-4.7[b]
OMs[a]	35.0	$(1.41 \pm 0.03) \times 10^{-1}$	17.9	-4.4
OMs[a]	50.0	$(5.77 \pm 0.12) \times 10^{-1}$		
OMs[c]	75.0	4.6		
PNB[d]	129.2	$(7.76 \pm 0.2) \times 10^{-6}$		
PNB[d]	101.7	$(5.16 \pm 0.1) \times 10^{-7}$	28.8	-11.0
PNB[c]	75.0	2.5×10^{-8}		

[a] Mesylate (OMs) determined conductimetrically at least in duplicate; errors shown are average deviations. [b] Reference 4c. [c] Calculated from rate constants at other temperatures. [d] *p*-Nitrobenzoate (PNB) determined by HPLC from the rate of disappearance of ester in buffered solution—the rate of appearance of acid gave similar but less precise results; an additional rate constant of $(3.18 \pm 0.03) \times 10^{-6}$ was obtained for 40% ethanol/water at 101.5 °C.

Results

The fast-response conductimetric method[4] was applied to solvolyses of benzhydryl mesylate (1, X = OMs) in pure

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