NMR Measurements. All measurements were made in $CDCl_3$ on a JEOL FX-90Q spectrometer for ^{15}N (at 9.04 MHz) at natural abundance and a Varian XL-300 spectrometer with a 5-mm broadband probe for enriched samples. Operation frequencies for ^{13}C and ^{15}N on the Varian XL-300 were 75.429 and 30.406 MHz, respectively. The ^{13}C NMR spectra were based on Me_4Si as the internal standard; the ^{15}N spectra were referenced externally to CH_3NO_2, where δ CH_3NO_2 = 380.2 with liquid NH_3 as zero. All ^{15}N measurements were run using full proton decoupling. Samples were enriched to contain about 23% ^{15}N.

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Synthesis of δ-Lactones via Radical C-C Bond Formation Using Chiral Radical Precursors

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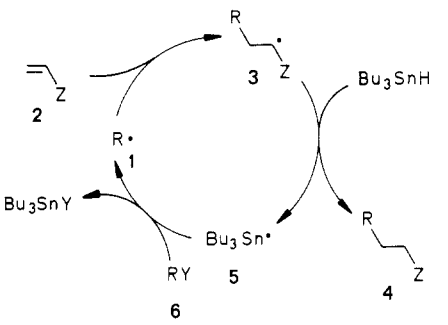
Carbon–carbon bond formation reactions employing addition of radical **1** to alkenes **2** have been successfully applied in organic synthesis.[1] Alkylmercury hydrides and tri-*n*-butyltin hydride act as efficient traps which convert adduct radicals **3** to products **4** before polymerization can occur (Scheme I).[2] In the case of the tin method, radicals **5** propagate the chain by reaction with suitable educts **6** to form radicals **1**. Halides, xanthanes, selenides, and tertiary nitro compounds can be used as radical precursors **6**.[2]

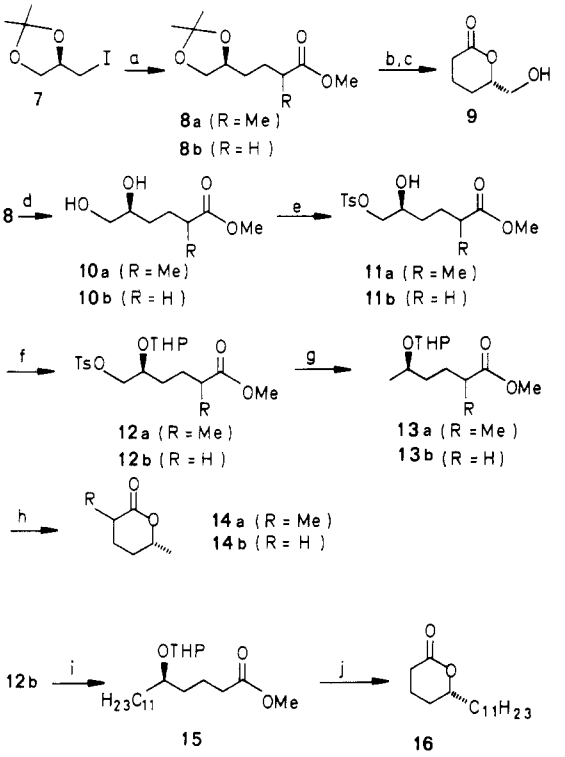
Since these radical reactions are very fast and occur under mild conditions, molecules containing sensitive chiral centers can be used. Therefore, we have applied this method to the synthesis of chiral δ-lactones starting from the readily available chiral precursors **7** and **17**. The δ-lactonic structure is found in several pheromones and could be a useful intermediate in the synthesis of other natural products.[3]

The synthesis that we have developed involves the generation of radicals with the radical center α to a chiral carbon atom and addition of these radicals to electron-poor alkenes. The radicals were generated from the chiral iodide **7**,[4] which was synthesized from (*R*)-(+)-2,3-*O*-isopropylideneglyceraldehyde.[5] The resulting adducts **8a** and **8b** were, after a series of transformations, converted to the lactonic pheromones of the carpenter bee **14a**[6] (cis and trans mixture) and the oriental hornet **16** (Scheme II).[7] Direct conversion of alcohol **9** to **14b** and **16** was not successful because of difficulties encountered in separating the product lactones from the reaction mixtures. However, **9** could be a useful "chiral building block" for other syntheses.

Scheme I



Scheme II[a]



[a] (a) $H_2C{=}CRCO_2Me$, Bu_3SnCl, $NaBH_4$, *hν*, EtOH, 20 °C, 45% (R = Me), 58% (R = H); (b) KOH, EtOH; (c) proton-exchange resin, MeCN, 25 °C, 67%; (d) TsOH, MeOH, 25 °C, 89% (R = Me), 81% (R = H); (e) TsCl, pyridine, 0 °C, 18 h, 70% (R = Me), 73% (R = H); (f) TsOH, DHP, CH_2Cl_2, 25 °C, 1 h, 93% (R = Me), 95% (R = H); (g) NaI, Bu_3SnH, AIBN, glyme, reflux, 3 h, 82% (R = Me), 78% (R = H); (h) proton-exchange resin, CH_3CN, 25 °C, 83% (R = Me), 94% (R = H); (i) $(C_{10}H_{21})_2CuLi$, ether, −30 °C, 4 h, 65%; (j) proton-exchange resin, CH_3CN, 25 °C, 88%.

In a similar scheme, L-(+)-2-(benzyloxy)propanol[8] was converted to the chiral iodide **17**,[9] which reacted in C–C bond formation reactions to give adducts **18**, **20a**, and **20b** (Scheme III). The yield of **20b** was unexpectedly lower than that for **20a** because of the formation of a new unidentified side product. Adducts **20a** and **20b** were deprotected and converted to lactones **21a** and **21b**.

The enantiometric purity of **14b** and **21b** was estimated to be in excess of 95% by using the chiral shift reagent

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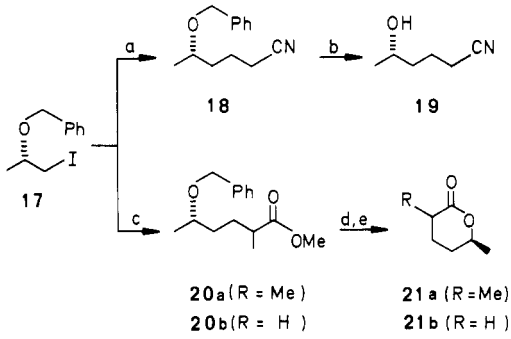
Scheme III[a]



[a] (a) H_2C=CHCN, Bu_3SnCl, $NaBH_4$, $h\nu$, EtOH, 20 °C, 51%; (b) H_2, 10% Pd/C, EtOH, 25 °C, 93%; (c) H_2C=$CRCO_2Me$, Bu_3SnCl, $NaBH_4$, $h\nu$, EtOH, 20 °C, 35% (R = Me), 30% (R = H); (d) H_2, 10% Pd/C, EtOH, (e) proton-exchange resin, CH_3CN, 25 °C, 58% (R = Me), 83% (R = H).

method of Jacovac and Jones.[10] NMR analysis of **14a** and **21a** showed that the cis/trans ratio for both compounds was about 1:1; therefore, the hydrogen abstraction from tributyltin hydride by the adduct radicals showed no selectivity.

Experimental Section

Proton nuclear magnetic resonance spectra were recorded on a Varian EM 360 A (60-Hz) or a Bruker WM 300 (300-Hz) spectrometer. Chemical shifts are expressed as parts per million (ppm) downfield from internal tetramethylsilane (Me_4Si); coupling patterns are designated s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). IR spectra were obtained as neat liquid films or as Nujol mulls between sodium chloride plates on a Perkin-Elmer 297 spectrometer. Intensities are reported as s (strong), m (medium), w (weak), and br (broad). Optical rotations were measured on a Perkin-Elmer 141 polarimeter equipped with sodium and mercury light sources in a 1-dm constant-temperature cell; reported temperatures are uncorrected. Melting points were observed on an electrothermal melting point apparatus and are uncorrected. Mass spectra were obtained from a Varian MAT 311-A spectrometer combined with an ET-FT source.

Methyl (*S*)-5,6-(Isopropylidenedioxy)-2(*R*,*S*)-methylhexanoate (8a). In a typical procedure, a solution of 3.0 g (12.4 mmol) of iodide 7,[4] 12.4 g (124 mmol) of methyl methacrylate, and 700 mg (18.5 mmol) of $NaBH_4$ in 130 mL of dry EtOH was irradiated (Pyrex reaction vessel) with a medium-pressure Hg lamp at 20 °C, and 800 mg (2.5 mmol) of Bu_3SnCl in 6 mL of dry EtOH was added over 15 min. After 45 min of irradiation, the mixture was treated with a KF solution (3.0 g of KF in 1.5 mL of H_2O) for 4 h at 25 °C. After the mixture was filtered through magnesium sulfate and dried over $MgSO_4$, the solvent was removed in vacuo. Chromatographic separation of the residue (20% EtOAc/hexane, silica) gave 1.2 g (45%) of methyl-5,6-(isopropylidenedioxy)-2(*R*,*S*)-methylhexanoate: IR (neat) 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.20 (d, J = 7.0 Hz, 3 H), 1.40 (d, J = 3.0 Hz, 6 H), 1.5–1.8 (m, 4 H), 2.2–2.7 (m, 1 H), 3.3–3.6 (m, 1 H), 3.7 (s, 3 H), 3.8–4.2 (m, 2 H). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.11; H, 9.26. Found: C, 60.93; H, 9.25.

Methyl (*S*)-5,6-(Isopropylidenedioxy)hexanoate (8b). With the same procedure as for adduct **8a**, 3.0 g (12.4 mmol) of iodide **7** reacted with 10.6 g (124 mmol) of methyl acrylate to give 1.45 g (58%) of methyl (*S*)-(+)-5,6-(isopropylidenedioxy)hexanoate: IR (neat) 1737 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.38 (d, J = 3.0 Hz, 6 H), 1.5–1.8 (m, 4 H), 2.2–2.5 (m, 2 H), 3.3–3.8 (m, 1 H), 3.70 (s, 3 H), 3.9–4.3 (m, 2 H); $[\alpha]^{20}_D$ 6.7° (*c* 5.0, EtOH).

Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.41; H, 8.91. Found: C, 59.10; H, 8.93.

5(*S*)-(Hydroxymethyl)-δ-valerolactone (9). A solution of 1.8 g (8.91 mmol) of ester **8b** and 750 mg (13.4 mmol) of KOH in 5 mL of 95% EtOH was stirred for 3 h at 25 °C, acidified to a pH 3 with 2 N HCl, and extracted 3× with 80 mL of CH_2Cl_2. The combined extracts were dried over $MgSO_4$, and the solvent was removed in vacuo. The resulting crude product was stirred with 250 mg of H^+ ion-exchange resin in 140 mL of CH_3CN for 4.5 h. The solvent was removed in vacuo, and the remaining residue was chromatographed (100% CH_3CN, silica) to give 780 mg (67%) of **9**: IR (neat) 1725 (s), 3400 (br) cm^{-1}; NMR ($CDCl_3$) δ 1.7–2.3 (m, 4 H), 2.4–2.8 (m, 2 H), 3.2–3.7 (br s, 1 H), 3.7 (d, J = 6.0 Hz, 2 H), 4.2–4.7 (m, 1 H); $[\alpha]^{20}_D$ +28.2° (*c* 5.3, EtOH).

Anal. Calcd for $C_6H_{10}O_3$: C, 55.38; H, 7.69. Found: C, 55.04; H, 7.74.

Methyl (*S*)-5,6-Dihydroxy-2(*R*,*S*)-methylhexanoate (10a). A solution of 1.5 g (6.9 mmol) of **8a** and 50 mg (0.3 mmol) of TsOH in 35 mL of MeOH was stirred for 3 h at 25 °C. The solvent was removed in vacuo, and the remaining oil was diluted with 35 mL of MeOH. After 15 min, the mixture was neutralized with Et_3N. After removal of the solvent, the remaining oil was chromatographed (EtOAc, silica) to give 1.1 g (89%) of methyl (*S*)-5,6-dihydroxy-2(*R*,*S*)-methylhexanoate: IR (neat) 3400 (br), 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.17 (d, J = 7.0 Hz, 6 H), 1.4–1.8 (m, 4 H), 2.2–2.8 (m, 1 H), 3.0–3.4 (m, 3 H), 3.4–3.8 (m, 2 H), 3.70 (s, 3 H).

Anal. Calcd for $C_8H_{16}O_4$: C, 54.55; H, 9.09. Found: C, 54.38; H, 8.93.

Methyl (*S*)-5,6-Dihydroxyhexanoate (10b). With the same procedure as for **10a**, 2.2 g (10.9 mmol) of ester **8b** reacted to give 1.42 g (80.5%) of methyl (*S*)-5,6-dihydroxyhexanoate: IR (neat) 3400 (br), 1740 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.0 (m, 4 H), 2.2–2.6 (m, 2 H), 3.4–3.8 (br s, 2 H), 3.6–3.9 (br s, 3 H), 3.68 (s, 3 H); $[\alpha]^{20}_D$ −26.7° (*c* 4.8, EtOH).

Anal. Calcd for $C_7H_{14}O_4$: C, 51.85; H, 8.64. Found: C, 51.49; H, 8.79.

Methyl 5(*S*)-Hydroxy-2(*R*,*S*)-methyl-6-[(tolylsulfonyl)oxy]hexanoate (11a). To a solution of 870 mg (4.9 mmol) of diol **10a** in 12 mL of pyridine at 0 °C was added 1.13 g (5.9 mmol) of TsCl over 30 min. The mixture was placed in the refrigerator overnight, poured into 100 g of ice–water, and extracted three times with 50 mL of CH_2Cl_2. The combined extracts were dried over $MgSO_4$, and the solvent was removed in vacuo. The pyridine was azeotropically distilled with benzene in vacuo, and the resulting oil was chromatographed (1:1 EtOAc/hexane, silica) to give 1.15 g (70%) of **11a**: IR (neat) 3520 (br), 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.18 (d, J = 7.0 Hz, 3 H), 1.4–1.7 (m, 4 H), 2.50 (s, 3 H), 2.2–2.6 (m, 1 H), 3.7 (s, 3 H), 3.5–4.1 (m, 4 H), 7.2–7.9 (m, 4 H).

Anal. Calcd for $C_{15}H_{22}SO_6$: C, 54.55; H, 9.09. Found: C, 54.38; H, 8.93.

Methyl 5(*S*)-Hydroxy-6-[(tolylsulfonyl)oxy]hexanoate (11b). With the same procedure as for **11a**, 1.1 g (6.8 mmol) of diol **10b** reacted to give 1.6 g (73%) of **11b**: IR (neat) 3520 (br), 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.2–1.9 (m, 4 H), 2.2–2.5 (m, 2 H), 2.48 (s, 3 H), 2.6–2.8 (br s, 1 H), 3.6–4.1 (m, 1 H), 3.68 (s, 3 H), 3.8–4.2 (m, 2 H), 7.2–7.9 (m, 4 H); $[\alpha]^{20}_D$ −4.9° (*c* 4.7, EtOH).

Anal. Calcd for $C_{14}H_{20}SO_6$: C, 52.83; H, 6.29. Found: C, 52.70; H, 6.12.

Methyl 2(*R*,*S*)-Methyl-5(*S*)-(tetrahydropyranyloxy)-6-[(tolylsulfonyl)oxy]hexanoate (12a). A solution of 800 mg (2.4 mmol) of tosylate **11a**, 1.02 g (12.1 mmol) of 3,4-dihydro-2*H*-pyran, and a few milligrams of TsOH in 16 mL of CH_2Cl_2 was stirred for 1 h at 25 °C, diluted with 100 mL of ether, and washed with dilute aqueous $NaHCO_3$. After drying over $MgSO_4$, the solvent was removed in vacuo and the remaining oil chromatographed (1:3 EtOAc/hexane, silica) to give 940 mg (93%) of **12a**: IR (neat) 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.17 (d, J = 7.0 Hz, 3 H), 1.0–2.0 (m, 10 H), 2.1–2.6 (m, 1 H), 2.45 (s, 3 H), 3.2–4.3 (m, 5 H), 3.71 (s, 3 H), 4.4–4.7 (m, 1 H), 7.2–7.9 (m, 4 H).

Anal. Calcd for $C_{20}H_{30}SO_7$: C, 57.97; H, 7.25. Found: C, 58.20; H, 7.15.

Methyl 5(*S*)-(Tetrahydropyranyloxy)-6-[(tolylsulfonyl)oxy]hexanoate (12b). With the same procedure as for **12a**, 750 mg (2.4 mmol) of tosylate **11b** reacted to give 900 mg (95%) of **12b**: IR (neat) 1738 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.2–1.9 (m, 10 H), 2.2–2.5 (m, 2 H), 2.48 (s, 3 H), 3.2–4.3 (m, 5 H), 3.68 (s, 3 H), 4.5–4.8 (m, 1 H), 7.2–7.9 (m, 4 H); $[\alpha]^{20}_D$ −8.7° (*c* 4.7, EtOH).

Anal. Calcd for $C_{19}H_{28}SO_7$: C, 57.00; H, 7.00. Found: C, 56.96; H, 6.96.

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Methyl 2(*R*,*S*)-Methyl-5(*R*)-(tetrahydropyranyloxy)-hexanoate (13a). To a refluxing mixture of 434 mg (1.05 mmol) of tosylate **12a**, 276 mg (1.84 mmol) of NaI, and a catalytic amount of azoisobutyronitrile in 8 mL of dry glyme was added dropwise 0.32 mL of Bu_3SnH (1.19 mmol). After 1.5 h, an additional 0.32 mL of Bu_3SnH was added. The solution was refluxed for another 1.5 h, and 2 mL of a saturated KF solution was added. After the mixture was stirred overnight at 25 °C and the solvent was removed in vacuo, the remaining oil was taken up in 100 mL of ether and dried over $MgSO_4$ and the ether removed. The oil was chromatographed (4:1 EtOAc/hexane, silica) to give 210 mg (82%) of **13a**: IR (neat) 1740 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.0–1.3 (m, 6 H), 1.3–1.9 (m, 10 H), 2.1–2.6 (m, 1 H), 3.2–4.1 (m, 3 H), 3.70 (s, 3 H), 4.4–4.7 (m, 1 H).

Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.93; H, 9.84. Found: C, 63.64; H, 9.89.

Methyl 5(*R*)-(Tetrahydropyranyloxy)hexanoate (13b). With the same procedure as for **13a**, 650 mg (1.62 mmol) of tosylate **12b** reacted to give 293 mg (78%) of methyl 5(*R*)-(tetrahydropyranyloxy)hexanoate: IR (neat) 1740 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.15 (t, J = 6.0 Hz, 3 H), 1.35–2.0 (m, 10 H), 2.2–2.6 (m, 2 H), 3.2–4.2 (m, 3 H), 3.68 (s, 3 H), 4.5–4.8 (m, 1 H), $[\alpha]^{20}_D$ −13.8° (*c* 5.4, EtOH).

Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.61; H, 9.56. Found: C, 63.10; H, 9.75.

2(*R*,*S*),5(*R*)-Dimethyl-δ-valerolactone (14a). A solution of 481 mg (1.96 mmol) of **13a**, a catalytic amount of H^+ ion-exchange resin (Amberlyst 15), and a few 4-Å molecular sieves in 20 mL of dry CH_3CN was stirred for 4 h at 25 °C. The reaction mixture was filtered, and the solvent was removed in vacuo. The remaining residue was taken up in ether and dried over $MgSO_4$. The solvent was removed in vacuo, and the remaining oil was chromatographed (50% EtOAc/hexane, silica) to give 210 mg (83%) of a 1:1 mixture of 2(*R*),5(*S*)- and 2(*S*),5(*R*)-dimethyl-δ-valerolactone: mp 53 °C; IR (Nujol) 1743 (s); NMR ($CDCl_3$) δ 1.24 (d, J = 7.1 Hz, 1.5 H), 1.32 (d, J = 7.1 Hz, 1.5 H), 1.36 (d, J = 6.2 Hz, 1.5 H), 1.38 (d, J = 6.2 Hz, 1.5 H), 1.4–1.7 (m, 2 H), 1.8–2.2 (m, 2 H), 2.35–2.70 (m, 1 H), 4.35–4.40 (m, 1 H).

Anal. Calcd for $C_7H_{12}O_2$: 128.0834. Found: 128.0837.

5(*R*)-Methyl-δ-valerolactone (14b). With the same procedure as for **14a**, 402 mg (1.74 mmol) of ester **13b** reacted to give 186 mg (94%) of 5(*R*)-methyl-δ-valerolactone: IR (neat) 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.38 (d, J = 6.5 Hz, 3 H), 1.4–1.6 (m, 1 H), 1.8–2.0 (m, 3 H), 2.3–2.6 (m, 2 H), 4.4–4.6 (m, 1 H); $[\alpha]^{20}_D$ +33.1° (*c* 3.0, MeOH) [lit.[6b] $[\alpha]^{20}_D$ +37.2° (*c* 1.8, EtOH].

Anal. Calcd for $C_6H_{10}O_2$: 114.0678. Found: 114.06848.

Methyl 5(*R*)-(Tetrahydropyranyloxy)hexadecanoate (15). Decyllithium was prepared by using the procedure of H. Gilman.[11] To a suspension of 712 mg (3.74 mmol) of purified CuI[12] in 40 mL of dry ether at −20 °C under dry N_2 was added 8.15 mL of 0.92 M $C_{10}H_{21}Li$ (ether solution) over 30 min. The mixture was stirred for an additional 30 min until it turned a pale, clear brown color. It was cooled to −30 °C, and 500 mg (1.25 mmol) of tosylate **12b** in 5 mL of dry ether was slowly added over 45 min. The mixture was stirred for 4 h at −30 °C and quenched with 5 mL of saturated NH_4Cl solution. After dilution with 100 mL of ether, it was washed three times with a saturated NaCl solution and dried over $MgSO_4$. The solvent was removed in vacuo, and the remaining oil was twice chromatographed (20% EtOAc/hexane, silica) to give 300 mg (65%) methyl 5(*R*)-(tetrahydropyranyloxy)hexadecanoate: IR (neat) 1745 (s) cm^{-1}; NMR ($CDCl_3$) δ 0.8–1.0 (m, 3 H), 1.1–1.5 (m, 20 H), 1.4–1.8 (m, 10 H), 2.1–2.5 (m, 2 H), 3.4–3.9 (m, 3 H), 3.65 (s, 3 H), 4.5–4.8 (m, 1 H); $[\alpha]^{20}_D$ −0.43° (*c* 5.3, EtOH).

Anal. Calcd for $C_{17}H_{33}O_4$ ($[M - 101]^+$): 269.2472. Found: 269.2482.

5(*R*)-Undecanyl-δ-valerolactone (16). With the same procedure as for **14a**, 200 mg (0.54 mmol) of ester **15** reacted to give 120 mg (88%) of **16**: mp 37 °C; IR (Nujol) 1745 (s) cm^{-1}; NMR ($CDCl_3$) δ 0.8–0.9 (m, 3 H), 1.30 (s, 20 H), 1.4–2.0 (m, 4 H), 2.3–2.7 (m, 2 H), 4.2–4.3 (m, 1 H); $[\alpha]^{20}_D$ +38.2 (0.74, THF) [lit.[7a] $[\alpha]^{23}_D$ +40.8° (0.76, THF)].

Anal. Calcd for $C_{16}H_{30}O_2$: 254.2240. Found: 254.2250.

Methyl 5(*S*)-(Benzyloxy)-2(*R*,*S*)-methylhexanoate (20a). With the same procedure as for **8a**, 2 g (7.2 mmol) of iodide **17** reacted with 7.2 g (72 mmol) of methyl methacrylate to give 630 mg (35%) of **20a**: IR (neat) 1740 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.10 (d, J = 6.0 Hz, 3 H), 1.18 (d, J = 6.0 Hz, 3 H), 1.4–1.9 (m, 4 H), 2.1–2.6 (m, 1 H), 3.1–3.8 (m, 1 H), 3.7 (s, 3 H), 4.5 (d, J = 2.0 Hz, 2 H), 7.4 (s, 5 H).

Anal. Calcd for $C_{15}H_{22}O_3$: C, 72.00; H, 8.80. Found: C, 71.67; H, 8.95.

Methyl 5(*S*)-(Benzyloxy)hexanoate (20b). With the same procedure as for educt **8a**, 2 g (7.2 mmol) of iodide **17** reacted with 6.2 g (72 mmol) of methyl acrylate to give 520 mg (30%) of **20b**: IR (neat) 1740 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.18 (d, J = 6.0 Hz, 3 H), 1.4–2.0 (m, 4 H), 2.1–2.4 (m, 2 H), 3.68 (s, 3 H), 3.2–3.8 (m, 1 H), 4.50 (d, J = 2.0 Hz, 2 H), 7.3 (s, 5 H); $[\alpha]^{20}$ +25.0° (*c* 4.9, EtOH).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.19; H, 8.47. Found: C, 70.89; H, 8.62.

2(*R*,*S*),5(*S*)-Dimethyl-δ-valerolactone (21a). A solution of 480 mg (1.92 mmol) of ester **20a** and 50 mg of 10% Pd/C in 10 mL of dry EtOH was hydrogenated (1 atm) for 2 h. The Pd/C was filtered off, and the solvent was removed in vacuo. The remaining residue was chromatographed (50% EtOAc/hexane, silica) to give 303 mg of a mixture of methyl and ethyl esters. A solution of 204 mg of this ester mixture, a catalytic amount of H^+ ion-exchange resin, and a few 4-Å molecular sieves in 10 mL of dry CH_3CN was stirred for 3 h at 25 °C. The reaction mixture was filtered, and the solvent was removed in vacuo. The remaining residue was taken up in 150 mL of ether and dried over $MgSO_4$. The solvent was removed in vacuo, and the remaining oil was chromatographed (50% EtOAc/hexane, silica) to give 142 mg (58%) of a 1:1 mixture of 2(*R*),5(*S*)- and 2(*S*),5(*S*)-dimethyl-δ-valerolactone: mp 55 °C; IR (neat) 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.24 (d, J = 7.1 Hz, 1.5 H), 1.32 (d, J = 7.1 Hz, 1.5 H), 1.36 (d, J = 6.2 Hz, 1.5 H), 1.38 (d, J = 6.2 Hz, 1.5 H), 1.4–1.7 (m, 2 H), 1.8–2.2 (m, 2 H), 2.3–2.7 (m, 1 H), 4.3–4.5 (m, 1 H).

Anal. Calcd for $C_8H_{12}O_2$: 128.0834. Found: 128.0836.

5(*S*)-Methyl-δ-valerolactone (21b). With the same procedure as for lactone **21a**, 600 mg (2.54 mmol) of **20b** reacted to give 380 mg of a mixture of methyl and ethyl esters. Lactonization of 367 mg of this mixture gave 241 mg (94%) of 5(*S*)-methyl-δ-valerolactone: IR (neat) 1735 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.38 (d, J = 6.5 Hz, 3 H), 1.4–1.6 (m, 1 H), 1.8–2.0 (m, 3 H), 2.3–2.6 (m, 2 H), 4.4–4.6 (m, 1 H); $[\alpha]^{20}_D$ −33.5° (*c* 3.3 MeOH) [lit.[6b] $[\alpha]^{21.5}_D$ 34.3° (*c* 2.08, EtOH)].

4(*S*)-(Benzyloxy)-1-cyanopentane (18). With the same procedure as for **8a**, 3.3 g (12.0 mmol) of iodide **17**, reacted with 6.3 g (120 mmol) of acrylonitrile to give 2.5 g (51%) of **18**: IR (neat) 2220 (m) cm^{-1}; NMR ($CDCl_3$) δ (d, J = 6.0 Hz, 3 H), 1.5–2.0 (m, 4 H), 2.1–2.4 (m, 2 H), 3.3–3.8 (m, 1 H), 4.2–4.7 (m, 2 H), 7.35 (s, 5 H); $[\alpha]^{20}_D$ +38.1° (*c* 5.1, EtOH).

Anal. Calcd for $C_{13}H_{17}NO$: 203.1305. Found: 203.1317.

1-Cyano-4(*S*)-hydroxypentane (19). A solution of 2.3 g (11.3 mmol) of **18** and 150 mg of 10% Pd/C in 60 mL of dry EtOH was hydrogenated (1 atm) overnight; the Pd/C was filtered off, and the solvent was removed in vacuo. The residue was taken up in ether and dried over $MgSO_4$. The ether was removed in vacuo, and the remaining oil was chromatographed (EtOAc, silica) to give 1.19 g (93%) of **19**: IR (neat) 3440 (br), 2250 (m) cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, J = 6.0 Hz, 3 H), 1.4–1.9 (m, 4 H), 2.2–2.5 (m, 2 H), 2.6–3.0 (br s, 1 H), 3.5–4.0 (m, 1 H); $[\alpha]^{20}_D$ +22.8° (*c* 5.3, EtOH) [lit.[6a] $[\alpha]^{22.4}_D$ +13.7° (*c* 4.3, EtOH)].

Anal. Calcd for C_5H_8NO ($[M - 15]^+$): 98.0603. Found: 98.0609.

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Registry No. **7**, 23735-39-9; **8a** (isomer 1), 103367-29-9; **8a** (isomer 2), 103367-43-7; **8b**, 103367-30-2; **9**, 89408-86-6; **10a** (isomer 1), 103367-31-3; **10a** (isomer 2), 103367-44-8; **10b**, 103367-32-4;

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11a (isomer 1), 103367-33-5; **11a** (isomer 2), 103367-45-9; **11b**, 103367-34-6; **12a** (isomer 1), 103367-35-7; **12a** (isomer 2), 103421-23-4; **12b**, 103367-36-8; **13a** (isomer 1), 103367-37-9; **13a** (isomer 2), 103421-24-5; **13b**, 103367-38-0; **14a** (isomer 1), 65451-95-8; **14a** (isomer 2), 65451-94-7; **14b**, 43112-32-9; **15**, 103367-39-1; **16**, 59812-96-3; **17**, 33106-37-5; **18**, 103367-42-6; **19**, 65451-90-3; **20a** (isomer 1), 103367-40-4; **20a** (isomer 2), 103367-46-0; **20b**, 103367-41-5; **21a** (isomer 1), 65451-93-6; **21a** (isomer 2), 65451-92-5; **21b**, 16320-13-1; $H_2C{=}C(CH_3)CO_2CH_3$, 80-62-6; $H_2C{=}CHCO_2CH_3$, 96-33-3; $H_3C(CH_2)_9Li$, 4416-59-5.

High Pressure [4 + 2] Cycloaddition Reactions of 3,4-Dimethoxyfuran with Dichloromaleic Anhydride and with Cyclopropane Derivatives

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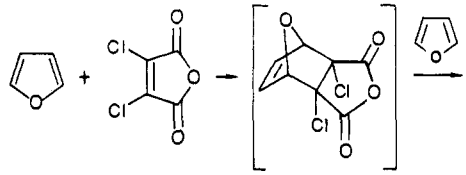
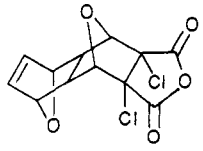
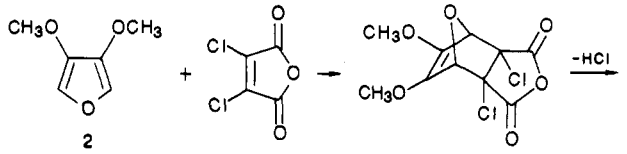
The failure of the [4 + 2] cycloaddition of dimethylmaleic anhydride with furan was a result of both electronic and steric hindrance of the methyl group. Another reason for the failure of the cycloaddition was due to the poor Diels–Alder rectivity of furan.[1]

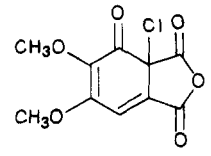
Recently the more reactive diene isobenzofuran was found to react quantitatively with dimethylmaleic anhydride (**1**) in reluxing xylene to give the cycloaddition product, benzocantharidine.[2] Another reactive furan, 3,4-dimethoxyfuran (**2**), undergoes cycloaddition with **1** under high pressure (22 kbar) at room temperature. The reaction, however, did not proceed at lower pressure, e.g., 10 kbar.[3] We have also demonstrated that when the methyl groups of **1** were replaced by chlorines, it reacted with furan under 5 kbar of pressure to yield a cycloadduct.[4] This result showed that the electron-withdrawing chlorine groups increased its dienophilicity, and the application of high pressure overcomes the steric hindrance. The reaction first yields the 1:1 cycloadduct, which is still reactive as a dienophile, and adds a second molecule of furan giving the 1:2 addition product. Thus, we expect that a reactive diene (**2**) and dichloromaleic anhydride (**3**) may react under more moderate conditions to yield a stable 1:1 cycloaddition product. When **2** and **3** were refluxed in toluene,



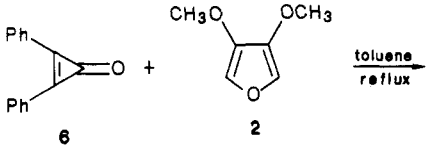


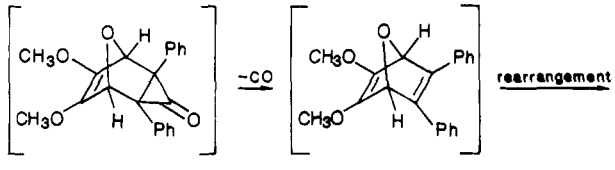
a polymerization was initiated with the elimination of hydrogen chloride and a black solid was produced. The cycloaddition reaction of **2** and **3** in THF solution was found to proceed under 10 kbar at room temperature. (The reaction failed at lower pressure, 5–6 kbar.) The product **5** was isolated in 67% yield after chromatographic purification. The compound **5** probably arose via 1:1 addition (**4**) followed by dehydrochlorination and rearrangement.

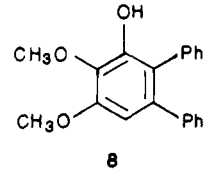




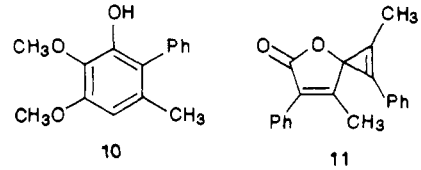
The reaction of furan with diphenylcyclopropenone (**6**) has been reported to be unsuccessful, yielding only the dimer of **6**.[5] We have found that the cycloaddition reaction does not occur even under high pressure (~10 kbar). The more reactive furan **2**, however, underwent the cycloaddition with **6** on refluxing in toluene to give 2,3-dimethoxy-5,6-diphenylphenol (**8**) in 24% yield. The compound **8** may be obtained via the decarbonylation and rearrangement of the initially formed adduct (**7**).







Similarly, methylphenylcyclopropenone (**9**) reacts with **2** in refluxing toluene producing 2,3-dimethoxy-5-methyl-6-phenylphenol (**10**) in 9% yield along with the dimer (**11**)[6] of **9**.



The yields of these phenols **8** and **10** were greatly improved when the reactions were performed at high pressure, 8–10 kbar. The yields were increased to 51% and

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