a 20% sodium hydroxide solution, stirred for 4 hr at room temperature, filtered, and added to 500 ml of 0.5 *N* sodium hydroxide in tetrahydrofuran. After stirring for an additional 4 hr, the resin was filtered, washed with tetrahydrofuran, and dried under vacuum (6 hr, 100°, 0.1 mm). Reaction of regenerated **1** with 1-undecanol using the small-scale procedure produced a 76% yield of 1-chloroundecane.

Acknowledgment. We are grateful to Professor Heitz for communicating valuable experimental procedures to us prior to publication.

Registry No.—Polystyrene, 9003-53-6; chlorodiphenylphosphine, 1079-66-9.

References and Notes

(1) Supported by the Research Corporation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Marquette University Committee on Research.
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(6) All ^{1}H NMR spectra were recorded using a Varian A-60 spectrometer. Product mixtures were analyzed by GLC on a Hewlett-Packard Model 5711A flame ionization instrument.
(7) Phosphorus analyses for such samples were usually high and were not lowered by extensive washing.
(8) In order to determine the number of reactive phosphine sites along the polymer backbone, we treated **1** with 2 equiv of benzyl alcohol (based upon phosphorus content) using the procedure described for the small-scale reactions. Analysis of the benzyl chloride produced indicated that 100% of the phosphorus present was active in the halogenation reaction.

Oxygenated α-Methylene-γ-butyrolactones[1]

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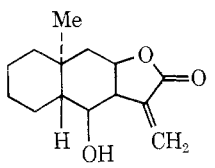
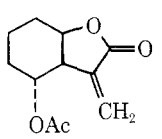
Synthetic efforts to date[3] have concentrated on the construction of α-methylene-γ-butyrolactones with almost no attention being devoted to the homoallylic oxygenated α-methylene-γ-butyrolactones. Two recent publications have reported syntheses of the oxygenated α-methylene lactones I[4] and II.[5] Interest in such oxygenated α-methylene lactones stems from recent studies[6] which have demonstrated that the presence of a lipophilic, conjugated ester or halo ester situated homoallylic to the exocyclic double bond of many naturally occurring α-methylene-γ-butyrolactones contributes to the enhancement of cytotoxic activity. Such oxygenated α-methylene lactone structural types are commonly found fused to six-, seven-, and ten-membered rings.[3]



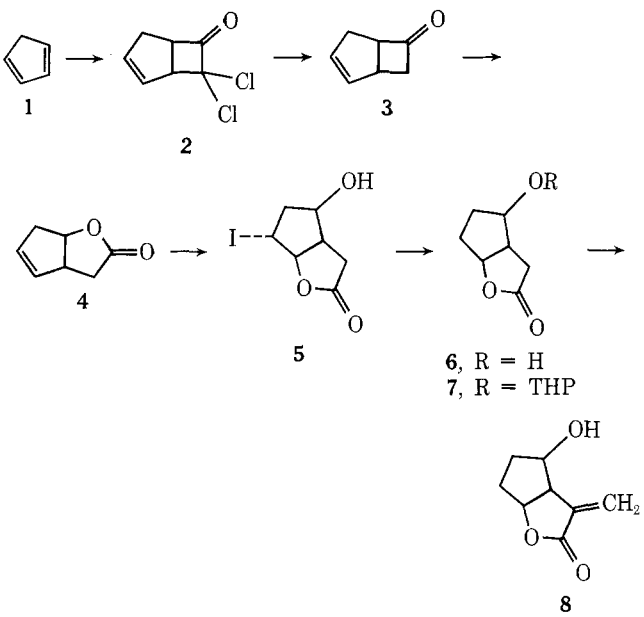
I



II

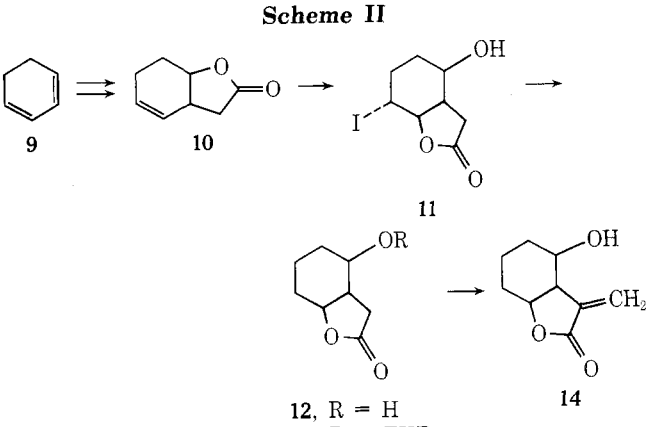
We wish to detail here a method for the construction of oxygenated α-methylene-γ-butyrolactones fused to five- and six-membered rings of type I. The method is applicable to other ring systems as well.[7] As illustrated in Scheme I, the approach involves the position-specific addition of dichloroketene[8] to an appropriate diene followed by dechlorination. Baeyer–Villiger oxidation results in formation of an olefinic γ-butyrolactone, which when subjected to the conditions of saponification and subsequent iodolactonization results in formation of the oxygenated γ-butyrolactone structural unit. Deiodination is cleanly carried out on the free hydroxy lactone followed by methylenation of the γ-lactone ring.

Scheme I



Addition of dichloroketene to cyclopentadiene followed by dechlorination and Baeyer–Villiger oxidation as previously described[9] results in the formation of the bicyclic lactone **4**. Saponification of **4** in water followed by neutralization with carbon dioxide and treatment with potassium triiodide at 5° causes iodolactonization with formation of **5** (95%). Deiodination of **5** using tributyltin hydride (initiation with azobisisobutyronitrile) in benzene at an elevated temperature affords hydroxy lactone **6** (91%). Protection of the free hydroxyl of **6** as its tetrahydropyranyl ether **7** followed by methylenation employing the α-hydroxymethylation procedure for lactone enolates[10] produces the oxygenated α-methylene-γ-butyrolactone **8**. During the elimination (anhydrous pyridine, ca. 130°) of the mesylate derived from the hydroxymethylated derivative of lactone **7**, simultaneous formation of the α-methylene unit and cleavage of the tetrahydropyranyl ether occur.[11]

Scheme II



The application of this sequence of reactions to the synthesis of **14** was also realized (Scheme II). Transformation of cyclohexadiene (**9**) to the bicyclic lactone **10** was carried out in ca. 70% overall yield by addition of dichloroketene followed by dechlorination and Baeyer–Villiger oxidation.[12] Conversion of **10** to the iodolactone **11** via the iodolactonization reaction (95%) and subsequent deiodination (99%) affords the oxygenated γ-butyrolactone **12.** Tetrahydropyranylation of **12** (98%) followed by α-hydroxymethylation (74%), mesylation (99%), and elimination (83%) affords directly the oxygenated α-methylene-γ-butrolactone **14.**

Experimental Section

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting and boiling points are uncorrected. The following spectrometers were used: nuclear magnetic resonance (NMR), Varian T-60 and A-60D (in δ units, with Me_4Si as internal reference in CCl_4 unless stated otherwise); infrared (ir), Perkin-Elmer Model 247 and Beckman IR-8; mass spectrometer (MS), LKB-9000.

***cis,cis*-2,5-Dihydroxy-*trans*-3-iodocyclopentylacetic Acid Lactone (5).** Lactone **4** (1.00 g, 8.08 mmol) was dissolved in an aqueous solution of sodium hydroxide (880 mg in 40 ml of water). After ca. 20 min the resulting homogeneous solution was cooled to 0° and carbon dioxide was introduced for ca. 15 min until pH 7 was reached. A solution of potassium iodide (12.0 g, 72 mmol) and iodine (6.10 g, 24 mmol) in water (20 ml) was added all at once to the neutralized solution cooled to 0°. The reaction was allowed to stir for 24 hr at 0–5°. The reaction was quenched by the addition of methylene chloride and solid sodium sulfite. The resulting decolorized solution was saturated with potassium sodium tartrate and extracted exhaustively with methylene chloride. The combined organic layers were washed with saturated brine, dried over anhydrous magnesium sulfate, and concentrated in vacuo. Passage of the crude iodolactone through a short column of silica gel (benzene) afforded 2.00 g (95%) of **5** which was homogeneous by TLC [benzene–ethyl acetate (1:1)]: ir ($CHCl_3$) 3425, 1755 cm^{-1}; NMR ($CDCl_3$) 5.02 (m, 1 H), 4.38 ppm (m, 2 H).

***cis,cis*-2,5-Dihydroxycyclopentylacetic Acid Lactone (6).** To a solution of iodolactone **5** (1.42 g, 5.32 mmol) in 60 ml of dry benzene heated to 50° was added 2.56 g (8.78 mmol) of freshly prepared tri-*n*-butyltin hydride[13] and 65 mg of azobisisobutyronitrile. The mixture was stirred at 50° for 1 hr. Removal of the benzene on a rotary evaporator afforded the crude hydroxylactone **6,** which was purified by passage through a column of silica gel (40 g). Elution with benzene–ethyl acetate gave 688 mg (91%) of pure **6:** ir (film) 3450, 1755 cm^{-1}; NMR ($CDCl_3$) 4.90 (m, 1 H, CHOCO–), 4.25 ppm (m, 1 H, CHOH); MS *m/e* 142.

Anal. Calcd for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.17; H, 7.16.

***cis*-2-Hydroxy-*cis*-5-tetrahydropyranyloxycyclopentylacetic Acid Lactone (7).** A solution of hydroxylactone **6** (500 mg, 3.52 mmol) and dihydropyran (443 mg, 5.28 mmol) in dry methylene chloride (8.0 ml) containing *p*-toluenesulfonic acid (2.5 mg) was stirred at 0° for 25 min. The reaction was quenched by the addition of six drops of pyridine. The mixture was diluted with methylene chloride and washed with brine and the resulting organic phase was dried over anhydrous magnesium sulfate. Concentration of the organic layer in vacuo afforded the crude product (**7**), which was passed through a short column of silica gel, affording 790 mg (99%) of pure **7** as a colorless oil. An analytical sample was prepared by distillation [114° (0.14 mmHg)].

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.83; H, 7.82.

2-(*cis,cis*-2,5-Dihydroxycyclopentyl)propenoic Acid Lactone (8). A solution of lactone **7** (468 mg, 2.07 mmol) in 3.0 ml of anhydrous THF (freshly distilled from lithium aluminum hydride) was added dropwise via a mechanically driven syringe over a period of 40 min to a cooled (−78°) solution of lithium diisopropylamide (LDA) in anhydrous THF [prepared from diisopropylamine (333 mg, 3.3 mmol) and 2.0 ml of 1.51 *M* *n*-butyllithium in 8.0 ml of THF]. After enolate formation was complete, the reaction mixture was warmed to −23° and the lactone enolate was trapped with formaldehyde. Paraformaldehyde (700 mg, dried over P_2O_5 under vacuum) was depolymerized at 150–160° and the monomeric formaldehyde was carried by a stream of nitrogen (flow rate 200 ml/min) into the reaction vessel. The reaction was terminated 40 min after complete depolymerization by addition of a saturated solution of ammonium chloride. The product was extracted with ethyl acetate. The combined organic extracts were washed with water, saturated sodium bicarbonate, and saturated brine. Drying over anhydrous magnesium sulfate followed by removal of the solvent on a rotary evaporator afforded 526 mg (99%) of crude hydroxymethyl lactone. After purification by column chromatography on silica gel (32 g) using ethyl acetate–benzene there was obtained 414 mg (78%) of pure α-hydroxymethyl lactone [ir (film) 3430, 1760 cm^{-1}].

To a solution of the above α-hydroxymethyl lactone (280 mg, 1.09 mmol) in 5.0 ml of dry pyridine cooled to 0° was added methanesulfonyl chloride (229 mg, 2.0 mmol). After 15 hr at 5°, the reaction mixture was warmed to room temperature and the solvent was removed in vacuo (high vacuum pump). The product was dissolved in ethyl acetate and was washed with brine (saturated). Concentration of the dried (magnesium sulfate) organic phase yielded 331 mg (90%) of crude mesylate (homogeneous on TLC analysis) which was immediately used in the next reaction.

A solution of crude mesylate (320 mg, 0.96 mmol) in 5.0 ml of dry pyridine was refluxed for 6 hr (bath temperature 130°). After removal of pyridine in vacuo (high vacuum pump), the resulting residue was taken up in ethyl acetate and washed with saturated brine. Concentration of the dried (magnesium sulfate) organic layer followed by removal of solvent on a rotary evaporator afforded 145 mg (99%) of crude **8.** Purification by column chromatography on silica gel yielded 103 mg (70%) of pure crystalline hydroxy-α-methylene lactone **8:** mp 79.5° (benzene–ethyl acetate); ir (KBr) 3344, 3003, 1740, 1661 cm^{-1}; NMR ($CDCl_3$) 6.38 (d, J = 2.5 Hz, 1 H), 5.78; (d, J = 2.5 Hz, 1 H), 4.94 (m, 1 H, –CHOCO), 4.25 (m, 1 H, –CHOH), 3.42 (m, 1 H, –CHC=), 2.58 ppm (s, 1 H, OH); MS *m/e* 152.

Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.10; H, 6.42.

In addition, chromatography yielded 9 mg (6%) of the THP ether of **8.**

***cis,cis*-2,6-Dihydroxy-*trans*-3-iodocyclohexylacetic Acid Lactone (11).** Lactone **10** (544 mg, 4.0 mmol) was dissolved in 15.0 ml of water containing 432 mg (10.8 mmol) of sodium hydroxide. After stirring at room temperature for 15 min, the homogeneous solution was cooled to 0° and the excess base was neutralized with carbon dioxide until pH 7 was reached (approximately 10 min). To the cooled, neutralized solution was added a solution of potassium iodide (5.98 g, 36 mmol) and iodine (3.05 g, 12.0 mmol) in 7.5 ml of water. After stirring at 0–5° for 23 hr, methylene chloride was added to the reaction mixture followed by solid sodium sulfite to decolorize the solution. The aqueous layer was saturated with potassium sodium tartrate and then extracted four times with methylene chloride. The combined organic layers were washed with aqueous sodium thiosulfate solution, water, and saturated brine. Removal of the solvent in vacuo gave 1.17 g of a colorless oil which crystallized on standing. Recrystallization from benzene–ethyl acetate gave 1.07 g (95.5%) of hydroxy iodolactone **11:** mp 95–97° dec; NMR ($CDCl_3$) 4.61 (m, 1 H), 4.38 (m, 1 H), 4.10 ppm (m, 1 H).

Anal. Calcd for $C_8H_{11}IO_3$: C, 34.06; H, 3.93. Found: C, 34.18; H, 4.03.

***cis,cis*-2,6-Dihydroxycyclohexylacetic Acid Lactone (12).** To a solution of iodolactone **11** (392 mg, 1.40 mmol) in 6.0 ml of dry benzene warmed to 50° was added tri-*n*-butyltin hydride[13] (610 mg, 2.10 mmol) and azobisisobutyronitrile (3.0 mg). The mixture was stirred at 50° for 40 min. Removal of the solvent in vacuo gave an oil which was chromatographed on silica gel (14.0 g). Benzene–ether (3:1) eluted the hydroxylactone **12** (219 mg, 99%) as a colorless oil: ir ($CHCl_3$) 3610, 3450, 1762 cm^{-1}; NMR ($CDCl_3$) 4.58 (m, 1 H, –CHOCO), 3.98 ppm (m, 1 H, CHOH). An analytical sample was prepared by distillation [115° (bath temperature) (0.35 mmHg].

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.31; H, 7.60.

***cis*-2-Hydroxy-*cis*-6-tetrahydropyranyloxycyclohexylacetic Acid Lactone (13).** A solution of hydroxylactone **12** (234 mg, 1.5 mmol), *p*-toluenesulfonic acid (5 mg), and dihydropyran (189 mg, 2.25 mmol) in 7.0 ml of dry methylene chloride was stirred for 40 min at 0°. The reaction was quenched by the addition of 5 drops of pyridine and then washed with saturated brine. Removal of the solvent in vacuo gave 414 mg of crude THP ether which was chromatographed on silica gel (25 g). Elution with benzene–ether (8:1) afforded the THP ether **13** (355 mg, 99%) as a colorless oil. An analytical sample was prepared by distillation [125–130° (bath temperature) (0.4 mmHg)].

Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 65.12; H, 8.56.

2-(*cis,cis*-2,6-Dihydroxycyclohexyl)propenoic Acid Lactone (14). A solution of lactone **13** (240 mg, 1.0 mmol) in 4.0 ml of dry THF was added slowly over a period of 1 hr to a cooled (−78°) solution of LDA under nitrogen. LDA was prepared from diisopropylamine (131 mg, 1.30 mmol) and *n*-butyllithium (0.81 ml of 1.6 *M* solution in hexane) in THF (3.5 ml) cooled to −78°. After enolate formation was complete, the reaction mixture was warmed to −30° and formaldehyde was passed into the reaction vessel via a stream of nitrogen (flow rate 200 ml/min) by heating paraformaldehyde (450 mg, 15.0 mmol) at 155° until depolymerization was complete. Stirring was continued for an additional 1.5 hr. The reaction was quenched by the addition of saturated aqueous ammonium chloride. The solvent was removed under reduced pressure on a rotary evaporator and the remaining residue was dissolved in methylene chloride (40 ml). The organic solution was washed with water and saturated brine. Evaporation of the solvent in vacuo gave an oil (381 mg) which was chromatographed on silica gel (13 g). Benzene–ether (15:1) eluted pure hydroxymethylated lactone (200 mg, 74%). In addition 30 mg of starting lactone was recovered.

A solution of the above pure hydroxymethylated lactones (189 mg, 0.7 mmol) and methanesulfonyl chloride (96.6 mg, 0.84 mmol) in dry pyridine (3.0 ml) was stirred at 3° for 16 hr. The solvent was evaporated in vacuo and the residue was dissolved in ethyl acetate. The organic solution was washed with brine and dried (magnesium sulfate). Removal of the solvent afforded 250 mg (100%) of mesylate which was homogeneous by TLC analysis.

A solution of the crude mesylate (244 mg, 0.7 mmol) in 4.0 ml of dry pyridine was heated at 135° (bath temperature) under nitrogen. After 6 hr, the solvent was evaporated in vacuo (high vacuum pump). The residue was dissolved in methylene chloride and was washed with saturated brine. After drying and removal of the solvent, there was obtained 126 mg of an oil which was chromatographed on silica gel (6 g). Benzene–ether (20:1) eluted the THP ether of lactone **14** (40 mg, 23%). Benzene–ether (15:1) eluted the oxygenated α-methylene lactone **14** (71 mg, 60%): ir (film) 3450, 1760, 1668 cm^{-1}; NMR ($CDCl_3$) 6.24 (d, J = 2 Hz, 1 H, $=CH_2$), 5.92 (d, J = 2 Hz, 1 H, $=CH_2$), 4.62 (m, 1 H, CHOCO–), 4.08 (m, 1 H, –CHOH), 3.22 (m, 1 H, –CHC=)]. An analytical sample was prepared by distillation [115° (bath temperature) (0.35 mmHg)].

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.19; H, 7.26.

A solution of the THP ether of lactone **14** (40 mg, 0.16 mmol) in 2.0 ml of methanol containing *p*-toluenesulfonic acid (1.0 mg) was stirred at room temperature for 6 hr. The reaction was quenched with pyridine (2 drops). The solvent was evaporated in vacuo, affording 29 mg of an oil which was through a short column of silica gel. Elution with benzene–ether (1:1) yielded pure oxygenated α-methylene lactone **14** (27 mg, 100%).

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Registry No.—**4,** 26054-46-6; **5,** 54911-58-9; **6,** 54911-59-0; **7,** 54911-60-3; **8,** 54911-61-4; **10,** 34896-02-1; **11,** 54911-62-5; **12,** 54911-63-6; **13,** 54911-64-7; **14,** 54911-65-8; 2-hydroxy-5-tetrahydropyranyloxycyclopentylacetic acid α-methylhydroxy lactone, 54911-66-9; 2-hydroxy-5-tetrahydropyranyloxycyclopentylacetic acid α-methylhydroxymesylate lactone, 54911-67-0; 2-hydroxy-6-tetrahydropyranyloxycyclohexylacetic acid α-methylhydroxy lactone, 54911-68-1; 2-hydroxy-6-tetrahydropyranyloxycyclohexylacetic acid α-methylhydroxymesylate lactone, 54911-69-2.

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(11) We have observed that tetrahydropyranyl ethers can be efficiently cleaved in pyridine with either methanesulfonic acid (i) or *p*-toluenesulfonic acid (ii). For example, treatment of **13** with i (2.0 equiv) in pyridine for 6 hr at 135° results in a 91% yield of **12.** Utilization of ii under identical conditions affords **12** in 82% yield. Heating in pyridine for 6 hr at 135° without added i or ii results in complete recovery of starting material. We have also found that **13** can be quantitatively cleaved with a catalytic amount of pyridinium *p*-toluenesulfonate in absolute ethanol at 55° for 3 hr.
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Reaction of Benzoins with Hexamethylphosphoric Triamide. A Convenient Synthesis of 2,3,5,6-Tetraarylpyridines[1]

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In the course of our investigation[2] on the reaction between hexamethylphosphoric triamide (HMPT) and benzyl alcohols to give *N,N*-dimethylbenzylamines, we treated benzoin (**1a**) with HMPT in an attempt to prepare the corresponding α-dimethylaminodeoxybenzoin (**2**). After a 30-min reflux, the solution was subjected to a water work-up and an 18% yield of 2,3,5,6-tetraphenylpyridine (**3a**) was isolated (Scheme I). The identity of the product was verified by comparison with a sample prepared by the published method.[3]

The reaction of benzoin with ammonium acetate in acetic acid to give 2,3,5,6-tetraphenylpyrazine is well known,[4a] but the conversion of benzoins to substituted pyridines requires the incorporation at the 4 position of one additional carbon atom whose source is not immediately apparent, although a related reaction of simple ketones has been the

Scheme I