# Model Studies of the Synthesis of the A Ring of Gibberellic Acid[1]

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Abstract: A method for the synthesis of the A ring of gibberellic acid is described. The first of the two sequences described leads to the A ring of tetrahydrogibberellic acid. Treatment of ethyl 2-(2-oxocyclopentyl)propionate (1) with homoallyl magnesium bromide leads to 1-(3-butenyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane which upon oxidation with osmium tetraoxide and sodium periodate gives 1-(3-oxopropyl)-2-oxa-3-oxo-4-methylbicyclo-[3.3.0]octane (3). Cyclization of 3 with potassium *tert*-butoxide affords a mixture of the axial and equatorial hydroxy epimers 2-carboxyl-2-methyl-3,6-dihydroxybicyclo[4.3.0]nonane-2,6-lactone in 60% yield. The configurations of the two products were established by equilibration experiments in which the equatorial alcohol predominated by a ratio of 10:1 which was the ratio found in the cyclization reaction. The second sequence leading to the A ring model compound with the double bond in place begins with the condensation of 1 with the lithium salt of propargylaldehyde dimethyl acetal to give 1-(3,3-dimethoxypropynyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]-octane (7). Hydrolysis of the acetal moiety of 7 followed by partial reduction of the triple bond afforded 1-(3-oxo-1-*cis*-propenyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (9) which was cyclized by potassium *tert*-butoxide to give the equatorial epimer (the unnatural configuration) of 2-carboxy-2-methyl-3,6-dihydroxybicyclo[4.3.0]non-4-ene-2,6-lactone (10). The configuration of the hydroxyl group was inverted by an oxidation–reduction sequence which afforded only the axial alcohol.
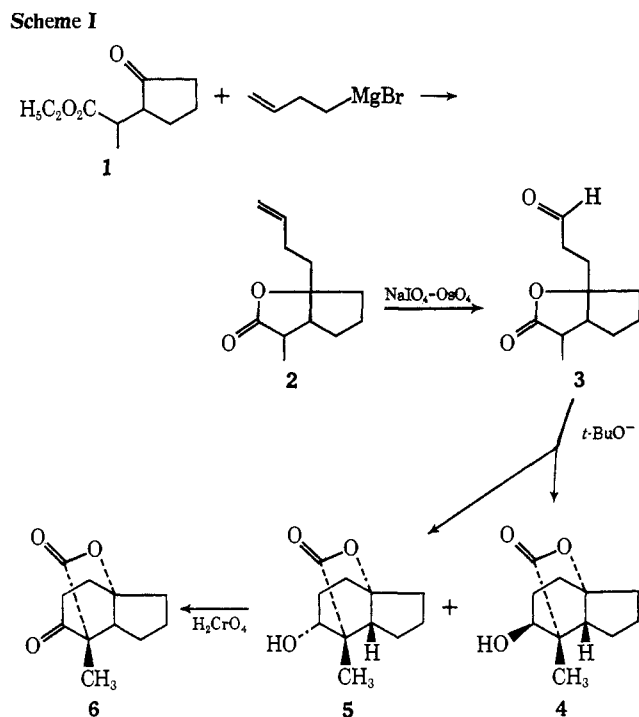
A great deal of effort has been devoted to the synthesis of the gibberellins over the past 15 years. Although certain of the gibberellins have been synthesized,[2,3] gibberellic acid itself has been very elusive.
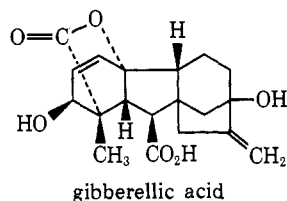
gibberellic acid

A major challenge in the synthesis of gibberellic acid is the construction of the lactone and A ring portion of the molecule which is sensitive to both acid and base. Since the report of a portion of the present work[4] two other quite different approaches have been developed.[5,6] This paper presents an approach to this synthetic problem in which the lactone ring is constructed prior to the completion of the carbocyclic portion of the A ring. This approach was suggested by the facile epimerization of the A ring hydroxyl group of tetrahydrogibberellic acid which probably takes place by a retroaldol–aldol condensation sequence.[7]

The synthesis of the saturated A ring compound is outlined in Scheme I.

All of the steps proceed in reasonable yields and the final cyclization produces the epimeric alcohols in 60% yield. The equatorial alcohol predominates in the

(1) The authors gratefully acknowledge financial support from the National Science Foundation.

(2) K. Mori, M. Shiozaki, N. Itaya, M. Matsui, and Y. Sumiki, *Tetrahedron*, 25, 1293 (1969).

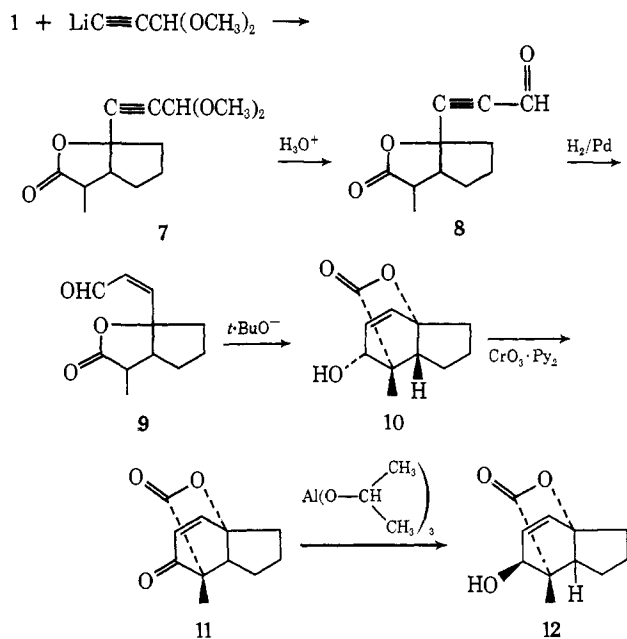(3) W. Nagata, T. Wakabayashi, M. Narisada, Y. Hayase, and S. Kamata, *J. Amer. Chem. Soc.*, 93, 5740 (1971).

(4) L. J. Dolby and R. J. Milligan, *J. Amer. Chem. Soc.*, 88, 4536 (1966).

(5) M. D. Bachi, J. W. Epstein, Y. Herzberg·Minzly, and H. J. E. Loewenthal, *J. Org. Chem.*, 34, 126 (1969).

(6) E. J. Corey, T. M. Brennan, and R. L. Carney, *J. Amer. Chem. Soc.*, 93, 7316 (1971).

(7) B. E. Cross, J. F. Grove, and A. Morrison, *J. Chem. Soc.*, 2498 (1961).

Scheme I

product by a ratio of about 10:1. Independent equilibration experiments show that this is the equilibrium mixture and secure the stereochemistry of the two products. Oxidation of the hydroxyl group affords the corresponding keto lactone (6) which was reduced with aluminum isopropoxide to give the axial alcohol in 38% yield.

The second sequence resulting in the A ring model compound with the double bond in place is outlined in Scheme II.

The keto ester 1 was treated with the lithium salt of 3,3-dimethoxypropyne to give a mixture of lactone 7 and uncyclized ester alcohols. The mixture was hydrolyzed to the acids with sodium hydroxide. Acidification of the hydrolysis mixture led to relactonization and gave

Scheme II

1 + LiC≡CCH(OCH₃)₂ ⟶

crude **7** from which the unlactonized hydroxy acids could be separated either by extraction or by filtration through Florisil. In initial experiments, only a small excess of acetylene was used, and the yield of **7** was only 15%. Use of a twofold excess of the anion of 3,3-dimethoxypropyne increased the yield to 25%. It is worth noting that **7** isolated in this manner consisted of a single methyl epimer as shown by its pmr spectrum. It would appear that the other C-1 epimer did not lactonize when the hydrolysis mixture was acidified. No attempt was made to find conditions under which the other epimer of lactone **7** would also be produced, but it seems reasonable to assume that the yield of **7** could be significantly increased if this were done.

After some experimentation, convenient conditions for hydrolysis of the acetal function of **7** were developed. Treatment of acetal lactone **7** with perchloric acid in aqueous dioxane for 24 hr at room temperature resulted in 93% hydrolysis by pmr measurements and gave the lactone aldehyde **8** in 76% yield. Prolonged reaction times did not result in complete hydrolysis of the acetal and it appears that equilibrium between **7** and **8** is reached after about 24 hr under the reaction conditions. The small amount of acetal remaining in the aldehyde lactone **8** did not interfere with subsequent transformations.

Partial hydrogenation of **8** using Lindlar catalyst yielded **9**. Due to the ease with which the cis double bond isomerized to the trans configuration, no attempt was made to accurately determine the yield. It was assumed that all material was recovered after the hydrogenation. The hydrogenation was followed by hydrogen uptake in early stages of the reaction. Although very little overreduction occurred as long as **8** remained, **9** could also be reduced. Hence, the final stages of the reduction were monitored by pmr analysis of aliquots. Upon careful hydrogenation, a mixture of aldehydes could be obtained containing 88% of **9**, 6% of the trans isomer, and 3% each of the acetylenic and saturated aldehydes (**8**, **3**), in addition to acetal remaining from the previous reaction. Although on one occasion the hydrogenation mixture was stored for 5 days

at −20° with little isomerization, in general, the mixture was used as soon as possible.

The aldol closure of the A ring was carried out by filtering crude **9** in tetrahydrofuran through molecular sieves into a solution of potassium *tert*-butoxide in *tert*-butyl alcohol and tetrahydrofuran at 0°, and stirring at this temperature for 10 min. Since the product is sensitive to both acid and aqueous base, the reaction was run under strictly anhydrous conditions and quenched with glacial acetic acid before the addition of water for the isolation. The dark brown oil obtained after work-up was filtered through Florisil to remove the polar and resinous impurities. A 75% yield of crude material was obtained, the majority of which appeared to be the desired cyclized material **10**. Only one hydroxyl epimer appears to have been formed. Purification, which was accompanied by large losses, gave pure **10** in 17% yield.

The stereochemistry of **10** was established by catalytic reduction of the double bond which gave the equatorial saturated hydroxy lactone **5**. Although this served as proof of the stereochemistry of **10** and demonstrated the usefulness of this approach, it indicated that the cyclization produced the undesired stereochemistry for the hydroxyl group. The gibberellic acid stereochemistry was produced by an oxidation–reduction sequence. Oxidation of **10** with chromium trioxide–pyridine complex in dichloromethane[8] led to the unsaturated ketone **11** in good yield. The ketone was reduced with aluminum isopropoxide to the desired axial alcohol, **12**, uncontaminated by the equatorial epimer.

The pmr spectra of **10** and **12** are rather interesting. In the spectrum of gibberellic acid, the olefinic proton at C-4 is a slightly broadened doublet, while the C-3 olefinic proton is a doublet of doublets, being split by both the C-4 and the C-2 protons. In **10**, the olefinic protons are doublets of doublets, both being split by the allylic carbinyl proton as well as by each other. The splitting in **12**, however, is almost identical with that in gibberellic acid. These observations served as further proof both of the structures of **10** and **12** and of their configurations at the carbinyl carbon.

The overall sequence for the synthesis for the lactone and A ring system has been shown to work in a model system. The approach is straightforward, using a relatively simple precursor, and generates the lactone and A ring system in four steps. Although the cyclization of the A ring in the model system yielded only the undesired equatorial alcohol, the cyclization may well produce the desired axial alcohol as well when applied to the synthesis of gibberellic acid.

Experimental Section[9]

1-(3-Butenyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (2). A Grignard reagent was prepared in the usual manner by adding a

(8) R. Ratcliffe and R. Roderhorst, *J. Org. Chem.*, **35**, 4000 (1970).

(9) All melting points are reported uncorrected. Infrared spectra were recorded on a Beckman IR-7 infrared spectrophotometer. Proton magnetic resonance spectra were recorded at 100 MHz on Varian Models HA-100 and XL-100 pmr spectrometers. The chemical shift values are expressed in δ values (ppm) relative to tetramethylsilane internal standard. In the presentation of the pmr spectra the following notations are used: b = broad, dist = distorted, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Ultraviolet spectra were recorded on a Cary Model 15 recording spectrophotometer. The mass spectra were obtained with a Consolidated Electrodynamics Corporation Model 21-110 double focus mass spectrometer equipped with a direct inlet system. Combustion analyses were performed by Dr.

solution of 4-bromo-1-butene (40.5 g, 0.30 mol) in ether (125 ml) to magnesium turnings (8.1 g, 0.33 g-atom) and ether (50 ml). The resulting solution was cooled to 0° and 36.8 g (0.20 mol) of keto ester **1**, prepared as previously described,[10] was added. After stirring at room temperature for 6 hr the reaction mixture was treated with 20 g of ammonium chloride in 250 ml of water. The layers were separated and the aqueous portion was extracted with three 100-ml portions of benzene-ether (1:1). The solvent was removed and distilled to yield 25.4 g of material, bp 110–138° (6 mm), which was stored overnight in 1.7 N sodium hydroxide-aqueous methanol (140 ml). The hydroxy acids were isolated in the usual manner and distilled to yield 23.3 g of material which was taken up in ether and washed with 10% aqueous sodium carbonate. The dried ether solution was concentrated and distilled to yield 19.3 g (50%) of lactones, bp 95–103° (0.5 mm). Vapor phase chromatography (10% FFAP on Chromosorb W at 138°, 5 ft × 0.25 in.) showed two methyl epimers in the ratio of 9:1. The major epimer showed pmr (CDCl$_3$) 1.33 (d, 3, J = 6.5 Hz) and the minor epimer showed 1.18 (d, 3, J = 6.5 Hz). Both epimers exhibited peaks for a terminal double bond in the region 4.80–6.38. Both isomers show the expected infrared absorptions (CCl$_4$): 1780 and 1640 cm^{-1}.

Anal. Calcd for C$_{12}$H$_{18}$O$_2$: C, 74.19; H, 9.34. Found: C, 74.02; H, 9.22.

1-(3-Oxopropyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (3). To a stirred solution of water (25 ml) and tetrahydrofuran (75 ml) was added 4.8 g (0.025 mol) of **2** followed by a solution of 0.065 g (0.0002 mol) of osmium tetraoxide in 0.5 ml of tetrahydrofuran. Finely ground sodium metaperiodate (11.2 g) was then added during 1 hr and the solution was stirred for an additional 2 hr. The sodium iodate was filtered and the solution was extracted with ether. The combined ether extracts were washed with two small portions of dilute aqueous hydrogen sulfide, aqueous sodium bicarbonate, and water in succession. Removal of the ether and short path distillation afforded 2.88 g of almost pure **3** as a mixture of epimers. The two epimers were separated by glpc (10% FFAP on Chromosorb W at 200°, 5 ft × 0.25 in.). The mixture of epimers showed absorption maxima in the infrared at 2760, 1780, and 1725 cm^{-1}.

Anal. Calcd for C$_{11}$H$_{16}$O$_3$: C, 67.32; H, 8.22. Found: C, 67.10; H, 8.17.

2-Carboxy-2-methyl-3,6α-dihydroxybicyclo[4.3.0]nonane-2α,6α-lactone (4, 5). To 25 ml of freshly prepared 1 N potassium *tert*-butoxide in *tert*-butyl alcohol was added 3.81 g (0.019 mol) of aldehyde 3 in 5 ml of *tert*-butyl alcohol. The solution was heated under reflux for 2 hr, cooled, poured into 100 ml of an ice-water slush containing 0.036 mol of hydrogen chloride, and immediately extracted with three 75-ml portions of ether. The extracts were combined, washed with saturated aqueous sodium bicarbonate solution, dried over anhydrous magnesium sulfate, and concentrated to yield 3.1 g of material. Chromatography of this material over 100 g of Florisil afforded 0.094 g of the axial alcohol **4** eluted with 8% ether-benzene. The pure axial alcohol showed mp 78.5–79.5° after crystallization from ether and sublimation; pmr (CDCl$_3$) 3.4–3.9 (m, 1, C*H*OH), 2.55 (s, 1, OH), 1.3–2.3 (m, 10), 1.15 (s, 3, CH$_3$); ir $\bar{\nu}_{max}^{CCl_4}$ 3600 and 1780 cm^{-1}.

Anal. Calcd for C$_{11}$H$_{16}$O$_3$: C, 67.32; H, 8.22. Found: C, 67.08; H, 8.26.

Elution with 16% ether-benzene afforded 2.21 g of the equatorial epimer **5** which could not be crystallized. The material showed: pmr (CDCl$_3$) 3.4–3.9 (m, 1, C*H*OH), 2.55 (s, 1, OH), 1.3–2.3 (m, 10), 1.13 (s, 3, CH$_3$); ir $\bar{\nu}_{max}^{CCl_4}$ 3600 and 1780 cm^{-1}. The combined yield of alcohols was 60%.

Anal. Calcd for C$_{11}$H$_{16}$O$_3$: C, 67.32; H, 8.22. Found: C, 66.91; H, 8.25.

Equilibration of the Equatorial and Axial Epimers of 2-Carboxy-2-methyl-3,6α-dihydroxybicyclo[4.3.0]nonane-2α,6α-lactone. To 3 ml of 1 N potassium *tert*-butoxide in *tert*-butyl alcohol was added 43.6 mg of alcohol **5**. The solution was stored for 4 hr, then it was poured into 12 ml of an ice-water slush containing hydrochloric

acid. The aqueous mixture was extracted with ether, dried, and concentrated. The residue was taken up in carbon tetrachloride and analyzed by glpc (¹⁄₈ in. × 1 m column of 10% FFAP on Chromosorb W at 180°) using β-acetoxynaphthalene as an internal standard with the appropriate calibrations. The results indicated an equatorial/axial ratio of 11:1.

A similar experiment using the pure axial epimer **4** gave an equatorial/axial ratio of 10:1. The recovery of alcohols for both experiments was *ca.* 70%.

2-Carboxy-2-methyl-3-oxo-6-hydroxybicyclo[4.3.0]nonane-3α,6α-lactone. A sample of alcohol **5** (0.242 g) was oxidized by the method of Brown and Garg[11] to yield 0.197 g (82%) of ketone **6** which crystallized on standing: mp 45–47°; pmr (CDCl$_3$) 1.7–2.9 (m, 11) and 1.25 (s, 3); ir $\bar{\nu}_{max}^{CCl_4}$ 1780 and 1725 cm^{-1}.

Anal. Calcd for C$_{11}$H$_{14}$O$_3$: C, 68.02; H, 7.27. Found: C, 67.85; H, 7.27.

The 2,4-dinitrophenylhydrazone showed mp 222–223° dec after two crystallizations from ethanol–ethyl acetate.

Anal. Calcd for C$_{17}$H$_{18}$N$_4$O$_6$: C, 54.54; H, 4.85. Found: C, 54.63; H, 4.71.

Aluminum Isopropoxide Reduction of Ketone 6. In a 25-ml flask, fitted with a reflux condenser, was dissolved the saturated ketone **6** (151 mg, 0.78 mmol) in 2-propanol (10 ml) containing aluminum isopropoxide (1.0 g, 5 mmol). The solution was refluxed for 3 hr. Concentrated hydrochloric acid (1.5 ml) was added, and the resulting solution was poured into ethyl acetate (20 ml) and water (5 ml). The mixture was partitioned, and the organic layer washed with water (5 ml) and saturated aqueous sodium sulfate (two 5-ml portions). The organic layer was dried and concentrated to give yellow oil (176 mg). The oil was chromatographed on Florisil (15 g) to give, in order of elution, the starting ketone **6** (17 mg, 11%), the saturated axial alcohol **4** (57 mg, 38%), and the equatorial alcohol **5** (52 mg, 34%).

1-(3,3-Dimethoxypropynyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (7). In a dry 500-ml flask equipped with a serum cap, an addition funnel, and a magnetic stirrer was dissolved 3,3-dimethoxy-propyne (30 ml, 28 g, 0.28 mol) in dry, freshly distilled tetrahydrofuran (150 ml). The solution was cooled to −70° and 1.6 M butyl-lithium in hexane (150 ml, 0.24 mol) was added with a syringe. The solution was stirred 10 min at −70°, during which time a white precipitate formed. On warming the solution to 0°, and stirring for 30 min, the precipitate dissolved. A solution of methyl 2-(2-oxocyclopentyl)propionate (1) (21.2 g, 0.125 mol) in tetrahydrofuran (25 ml) was then added, and resulting solution was stirred at 0° for 30 min. Acetic acid (20 ml) and water (25 ml) were added. The mixture was partitioned and the aqueous layer was diluted with water (40 ml), acidified to pH 1 with concentrated hydrochloric acid, and extracted with ether (two 15-ml portions).

The ether extracts were combined with the original organic layer and concentrated; the residue was dissolved in methanol (150 ml). Fifty per cent aqueous sodium hydroxide (38 g) was added to the methanol solution and the resulting solution stored 24 hr at room temperature. Most of the methanol was removed at reduced pressure, the residue was redissolved in water (125 ml) and the solution was extracted with ether (four 40-ml portions). The aqueous solution was then cooled in an ice bath and acidified with 6 N hydrochloric acid (100 ml). The ice bath was removed and the mixture stirred for 30 min. The mixture was extracted with ether (three 60-ml portions), and the combined ether extracts were washed with 0.5 M aqueous sodium bicarbonate (four 50-ml portions). The ether was evaporated to give crude **7** (13.3 g). Filtration through Florisil (200 g) gave pure lactone acetal **7** as an oil (7.38 g, 25%): ir $\bar{\nu}_{max}^{CCl_4}$ 2245 and 1785 cm^{-1}; pmr (CDCl$_3$) 1.44 (d, 3 H, J = 7.5 Hz), 1.6–2.8 (m), 3.38 (s, 6 H), 5.21 (s, 1 H). The analytical sample was prepared by preparative glpc (0.25 in. × 5 ft column of 10% FFAP on Chromosorb W at 220°).

Anal. Calcd for C$_{13}$H$_{18}$O$_4$: C, 65.52; H, 7.60. Found: C, 65.88; H, 7.70.

1-(3-Oxopropynyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (8). In a 250-ml flask was dissolved lactone acetal **7** (6.21 g, 26.1 mmol) in dioxane (100 ml) and treated with 60% perchloric acid (40 g) and water (13.3 g). The resulting solution was stored in the dark at room temperature for 24 hr. The solution was then poured into a mixture of water (60 ml) and benzene (250 ml). The organic layer was separated, and the aqueous layer was extracted with benzene (three 50-ml portions). The combined organic layers

Susan Rottschaefer, Department of Chemistry, University of Oregon, Eugene, Oregon. All solvents and reagents used were commercial reagent grade, and were used without further purification unless otherwise specified. Organic solutions were dried by filtration through anhydrous sodium sulfate and were concentrated by rotary evaporation at reduced pressure. All compounds are racemic modifications. The nomenclature is for the enantiomorph shown in the discussion for convenience in representing the relative stereochemistry.

(10) L. D. Bergel'son and A. N. Grigoryan, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 282 (1966).

(11) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

were washed with water (10 ml) and 0.5 M aqueous sodium bicarbonate (two 50-ml portions), dried, and evaporated to give the lactone aldehyde **8** (4.20 g) which contained 7% of the starting lactone acetal **7** by pmr analysis. Hence the yield of **8** was 3.82 g (19.9 mmol, 76%): ir $\bar{\nu}_{max}^{CCl_4}$ 2200, 1790, and 1675 cm^{-1}; pmr (CDCl$_3$) 1.41 (d, 3 H, J = 7 Hz), 1.5–2.9 (m), 9.30 (s, 1 H).

Lactone aldehyde **8** formed a 2,4-dinitrophenylhydrazone, mp 153–155°.

Anal. Calcd for C$_{17}$H$_{16}$N$_4$O$_6$: C, 54.84; H, 4.33. Found: C, 55.09; H, 4.61.

1-(3-Oxo-1-*cis*-propenyl)-2-oxa-3-oxo-4-methylbicyclo[3.3.0]octane (9). Lactone aldehyde **8** (4.20 g of 93% pure material; 3.82 g, 19.9 mmol of **8**) was dissolved in benzene (125 ml), and Lindlar catalyst (0.30 g) was added. The mixture was hydrogenated at atmospheric pressure until 425 ml of hydrogen had been taken up, at which point pmr analysis indicated that the reaction mixture consisted of, in addition to unhydrolyzed acetal **7** from the previous reaction, four aldehydes. These were the desired *cis*-ethylene aldehyde **9**, the trans isomer, the saturated aldehyde **3**, and the starting aldehyde **8**, comprising 88, 6, 3, and 3%, respectively, of the total aldehydes. Spectral data for **9** are: ir $\bar{\nu}_{max}^{CCl_4}$ 1785, 1695, 1635 cm^{-1}; pmr (CDCl$_3$) 1.31 (d, 3 H, J = 7.5 Hz), 1.5–2.9 (m), 5.92 (d of d, 1 H, J = 8 Hz, 12 Hz), 6.50 (d, 1 H, J = 12 Hz), 10.35 (d, 1 H, J = 8 Hz).

The ethylene aldehyde **9** formed a 2,4-dinitrophenylhydrazone, mp 172–174°.

Anal. Calcd for C$_{17}$H$_{18}$N$_4$O$_6$: C, 54.54; H, 4.85; N, 14.97. Found: C, 54.53; H, 4.81; N, 15.06.

The hydrogenation mixture was filtered free from catalyst, concentrated, and used directly in the next reaction.

2α-Carboxy-2β-methyl-3α,6α-dihydroxybicyclo[4.3.0]non-4-ene-2α,6α-lactone (10) In a dry, nitrogen-purged 100-ml flask, equipped with an addition funnel packed with 4A molecular sieves, a serum cap, and a magnetic stirrer, was placed dry, freshly distilled tetrahydrofuran (25 ml). A 0.66 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol (30 ml, 20 mmol) was added with a syringe, and the solution was cooled to 0°. Crude *cis*-ethylene aldehyde **9** (82% pure, from the hydrogenation of 4.20 g of 93% pure **10**; 3.45 g, 17.5 mmol), dissolved in dry tetrahydrofuran (25 ml), was filtered through 4A molecular sieves into the potassium *tert*-butoxide solution over a 2-min period. The mixture was stirred at 0° for an additional 10 min, during which time the mixture became dark brown. Acetic acid (2 ml) was added to the reaction mixture, which was then poured into benzene (125 ml). This mixture was washed with water (25 ml) and 0.5 M aqueous sodium bicarbonate (three 25-ml portions). The washings were extracted with benzene (25 ml). The combined benzene solutions were dried and evaporated to give a dark brown oil.

The dark brown oil was filtered through Florisil (40 g), eluting with 10% ethyl acetate in chloroform (800 ml). Concentration of the eluate yielded the crude **10** (3.1 g, 74% weight recovery) from which oily crystals (0.7 g) were obtained. Chromatography of the mother liquors on Florisil (30 g) gave material which yielded more crystalline material (0.30 g). The crystals were sublimed (100°, 1 Torr) and crystallized from ether to give pure **10** (0.59 g, 3.0 mmol, 17.5% yield from **9**; mp 99–101°; ir $\bar{\nu}_{max}^{CCl_4}$ 3570, 3450, 1770 cm^{-1}; pmr (CDCl$_3$) 1.37 (s, 1 H), 1.5–2.1 (m, 5 H), 1.96 (d, 1 H, J = 10 Hz), 2.30 (m, 2 H), 4.23 (d of d of d, 1 H, J = 10 Hz, 2 Hz, 3 Hz), 5.85 (d of d, 1 H, J = 9 Hz, 3 Hz), 6.35 (d of d, 1 H, J = 9 Hz, 2 Hz).

Anal. Calcd for C$_{11}$H$_{14}$O$_3$: C, 68.02; H, 7.27. Found: C, 67.81; H, 7.17.

Hydrogenation of Unsaturated Hydroxy Lactone 10. A sample of the alcohol (52.4 mg) in ethyl acetate (10 ml) was hydrogenated over 5% rhodium-on-alumina (26.6 mg) until hydrogen uptake ceased (3 hr). The solution was filtered through Celite to give the crude hydroxy lactone **5**. Chromatography over Florisil afforded pure **5** as an oil (29.5 mg, 56%) identical with the material obtained previously.

2α-Carboxy-2β-methyl-3-oxo-6α-hydroxybicyclo[4.3.0]non-4-ene-2α,6α-lactone (11). In a 25-ml flask with a magnetic stirrer was placed chromium trioxide (320 mg, 3.2 mmol) and dichloromethane (10 ml). Pyridine (0.49 g, 6.2 mmol) was added to the stirred suspension, and stirring continued for 30 min to give a red solution and a black precipitate. The cyclic alcohol **10** (49.0 mg, 0.25 mmol), dissolved in dichloromethane (1 ml), was added, and a brown precipitate immediately formed. The mixture was stirred for 45 min after the addition. The dichloromethane solution was decanted, and the tarry residue was washed with dichloromethane (two 4-ml portions). The dichloromethane solution and washings were filtered through Florisil (1 g). The yellow eluate was concentrated, redissolved in benzene (10 ml), and washed with 1 N hydrochloric acid (five 2-ml portions). The benzene solution was dried and evaporated to give the ketone **11** (44.3 mg) as a yellow oil. Chromatography on Florisil (1 g) gave pure ketone **11** (32.3 mg, 67% yield). Sublimation gave crystals; mp 57–59°; uv (methanol) λ_{max} 231 (ϵ 6600); ir $\bar{\nu}_{max}^{CCl_4}$ 1787 and 1698 cm^{-1}; pmr (CDCl$_3$) 1.35 (s, 3 H), 1.5–2.8 (m, 6 H), 2.94 (m, 1 H), 6.03 (d, 1 H, J = 9.5 Hz), 7.41 (d, 1 H, J = 9.5 Hz).

Anal. Calcd for C$_{11}$H$_{12}$O$_3$: C, 68.74; H, 6.29. Found: C, 68.83; H, 6.31.

2α-Carboxy-2β-methyl-3β,6α-dihydroxybicyclo[4.3.0]non-4-ene-2α,6α-lactone (12). The unsaturated cyclic ketone **11** (185 mg, 0.96 mmol) was placed in a 25-ml flask equipped with a 10-cm Vigreux column. 2-Propanol (10 ml) containing aluminum iso-propoxide (1.0 g, 5 mmol) was added. The solution was heated in a hot water bath at 80° for 20 min, then refluxed on a steam bath for 30 min, during which time a few drops of liquid distilled.

The solution was then cooled to room temperature, and acetic acid (1.0 ml) was added. The solution was poured into a mixture of saturated aqueous potassium sodium tartrate (10 ml), benzene (10 ml), and ethyl acetate (10 ml). A copious precipitate formed, which was redissolved by the addition of solid sodium bicarbonate. The aqueous layer was separated and extracted with 1:1 benzene-ethyl acetate (10 ml). The combined organic layers were washed with 0.5 M aqueous sodium bicarbonate (two 10-ml portions), dried, and concentrated to yield an oil containing the axial cyclic alcohol **12** and polar material; none of the equatorial alcohol **10** could be detected by tlc. The oil was chromatographed on Florisil (5 g), and gave **11** (84 mg, 0.43 mmol, 45% yield), which was sublimed to give crystals: mp 73–76°; ir $\bar{\nu}_{max}^{CCl_4}$ 3620, 3480, 1777, 1762 (sh) cm^{-1}; pmr (CDCl$_3$) 1.29 (s, 1 H), 1.4–2.4 (m), 2.64 (m, 1 H), 3.02 (br s, 1 H), 4.17 (m, 1 H), 5.86 (d of d, 1 H, J = 9.5 Hz, 3.5 Hz), 6.42 (d, 1 H, J = 9.5 Hz).

Anal. Calcd for C$_{11}$H$_{14}$O$_3$: C 68.02; H, 7.27. Found: C, 67.75; H, 7.40.