Vitamin C and isovitamin C derived chemistry. 3. Chiral butenolides via efficient 2,3-didehydroxylations of L-gulono-, D-mannono-, and D-ribono-1,4-lactones

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Efficient, operationally simple procedures for preparing the chiral butenolides \(3a, \ 4a, \ 15a, b, \) and \(16a-d\) from the commercial L-ascorbic acid (L-\( \text{threo-hex-2-enono-1,4-lactone} \) and D-\( \text{ascorbic acid (D-\text{erythro-hex-2-enono-1,4-lactone} \) are described. The concept centers on the novel \( \text{NaHSO}_3 \)-induced regiospecific trans-\(\beta\)-bromo-\(\alpha\)-acetoxy elimination of the readily accessible \(\text{O-acetylated bromodeoxyaldono-1,4-lactones 10a,b} \) to compounds \(13a, b\). These, on decacytetylation and treatment of the resulting bromohydrins \(16a, b\) with \(\text{Ag}_2\text{O} \), afford the enantiomerically pure epoxides \(16c, d\) and thence, in boiling water, the corresponding diols \(3a, \ 4a\) and \(15a, b\). In a similar manner \(\text{NaHSO}_3 \) causes the \(\text{D-ribono-1,4-lactone-derived bromo-acetoxy mixture 17a, b} \) to undergo elimination to the corresponding butenolides \(18a, b\), which, on subsequent hydrolysis and chromatographic purification, has given compound \(1a\) in 48% overall yield.

**Introduction**

Enantiomerically pure 4-substituted \(\alpha, \beta\)-unsaturated and saturated \(\gamma\)-lactones occur widely in nature, i.e., as flavor components and as constituents of insect and mammalian pheromonal systems.\(^1\) Butyrolactones are often found annelated onto lignan frameworks.\(^2\) The biological activity of \(\text{L-ascorbic acid (vitamin C) is due mainly to the 2,3-diol functionality on the butenolide system.}^3\) Publications describing the preparation of some of these molecules have illustrated the potential of simple butenolides as chiral synthons in natural product syntheses. Compounds \(1a-d\) and \(2\) have been particularly useful in this respect and have served in the construction of \(\text{(+)- and (-)-eldanolid,}^6\) \(\text{the antileukemic lignans }^5\text{ (+)-trans-bursarier,}^5\text{ (-)-isostegane,}^5\text{ (+)- and (-)-steganacin,}^5\) \(\text{the flavor components and as constituents of insect and mammalian pheromonal systems.}^5\) Butyrolactones are often found annelated onto lignan frameworks.\(^2\) In mammalian pheromonal systems,\(^3\) \(\text{Butyrolactones are often found annelated onto lignan frameworks.}^2\) These, on deacetylation and treatment of the resulting bromohydrins \(16a, b\) with \(\text{Ag}_2\text{O} \), afford the enantiomerically pure epoxides \(16c, d\) and thence, in boiling water, the corresponding diols \(3a, \ 4a\) and \(15a, b\). In a similar manner \(\text{NaHSO}_3 \) causes the \(\text{D-ribono-1,4-lactone-derived bromo-acetoxy mixture 17a, b} \) to undergo elimination to the corresponding butenolides \(18a, b\), which, on subsequent hydrolysis and chromatographic purification, has given compound \(1a\) in 48% overall yield.

Considerable effort has been expended on preparing butenolide chirons from chiral and nonchiral sources. When starting with nonchiral materials asymmetry has been introduced via (a) resolution of intermediates

\[ \text{(1)} \quad \text{For useful compilations of some naturally occurring } \gamma\text{-lactones, see:} \]

\[ \text{(a) Ravid, U.; Silverstein, R. M.; Smith, L. R. J. Tetrahedron 1978, 34, 1449.} \]

\[ \text{(b) Cardelich, J.; Font, J.; Ortuño, R. M. J. Heterocycl. Chem. 1984, 21, 227.} \]

\[ \text{(2) Ward, R. S. Chem. Soc. Rev. 1982, 11, 75.} \]

\[ \text{(3) Selb, P. A.; Tolbert, B. M. Ascorbic Acid: Chemistry, Metabolism, and Uses; Advances in Chemistry 200; American Chemical Society: Washington, DC, 1982.} \]


\[ \text{(5) (a) Mann, J.; Thomas, A. J. Chem. Soc., Perkin Trans. 1 1986, 873.} \]

\[ \text{(b) Drew, M. G. B.; Mann, J.; Thomas, A. J. Chem. Soc., Perkin Trans. 2 1986, 2278.} \]

\[ \text{(c) Mann, J.; Thomas, A. J. Chem. Soc., Perkin Trans. 1 1986, 2287.} \]


\[ \text{(7) (a) Tomioka, K.; Seto, F.; Koga, K. Heterocycles 1982, 32, 171.} \]


\[ \text{(a) Drew, M. G. B.; Mann, J.; Thomas, A. J. Chem. Soc., Perkin Trans. 2 1986, 2278.} \]

\[ \text{(b) Mann, J.; Thomas, A. J. Chem. Soc., Perkin Trans. 1 1986, 2287.} \]


\[ \text{(b) Vigneron, J. P.; Meric, R.; Larchevêque, M.; Debal, A.; Kunesch, G.; Zgäetti, P.; Gallois, M. Tetrahedron 1984, 40, 3521.} \]


resulting in the formation of unequal amounts of two diastereomeric \( \beta \)-sulfanyl \( \gamma \)-lactones; their separation and subsequent pyrolysis then gave enantiomerically pure 4-substituted butenolides.\(^{11a}\) Optically active (\( R \))- and (\( S \))-4-octyl- and (\( R \))- and (\( S \))-4-tridecylbutenolides were prepared via the reaction of the diamines of chiral N-monom substituted 3-(phenylsulfonyl)propionamides with aldehydes.\(^{11b}\)

Syntheses of chiral butenolides from naturally occurring materials are illustrated by the following examples. (\( \alpha \))-Eldanolide has been obtained from (\( \alpha \))-\( \delta \)-pinene by a route featuring a cyclobutyl-cyclopentylmethyl-homoallyl cation rearrangement.\(^{12}\) A procedure starting from l-glutamic acid has given carboxylic acid lactone 5a with complete retention of configuration.\(^{13}\) This was reduced to the carbinol 5b\(^ {13} \) and then converted into ethers 5c,d. Introduction of the C-2-C-3 double bond was then achieved via the C-2 phenylselenation and the subsequent NaI\(_{04}\)-induced PhSeOH elimination to give 1b,c BaPb.

Introduction of the C-2-C-3 double bond was then achieved via the C-2 phenylselenation and the subsequent NaI\(_{04}\)-induced PhSeOH elimination to give 1b,c BaPb.

Various approaches to chiral butenolides from carbohydrates via formal C-2-C-3 dihydroxylation\(^{14}\) of aldon o-1,4-lactones have been reported. D-Ribono-1,4-lactone and its derivatives have provided 1a-c by pyrolysis of the cyclic orthofromates 6a,b,c\(^ {16a,b} \) Raney nickel desulfurization transformed the corresponding thionocarbonates 6d,e\(^ {16} \) and 6e\(^ {g} \) into 1c and 1d, respectively. The 6-O-benzyl ether of the homologous hex-2-eno no-1,4-lactone 3e was afforded by lactonizing the olefination product produced from 4-O-benzyl-2,3-O-isopropylidene-\( \beta \)-threose and Ph\(_{2}\)CHCOOEt.\(^ {8}\) Recently butenolides 1a, 1c, and 1d were obtained from \( \alpha \)-mannotiol via an analogous approach\(^ {17a} \) or via the intermediate dehydration of a 2-deoxy-\( \alpha \)-ribono-1,4-lactone derivative.\(^ {17b} \)

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butenolides to racemization at C-4 or elimination at C-4-C-5 is well documented. A brief study of the behavior of 11b under mildly basic conditions and in various solvent systems was, therefore, undertaken; the reactions were monitored by TLC and NMR. A two-phase system of ether–aqueous NaHCO₃ led to mixtures of 11b, 12a, and 13b. Treatment of 11b with aqueous NaOAc produced only an E/Z mixture of 12a. The substrate 11b was unaffected by aqueous PbCO₃·Pb(OH)₂ at room temperature but gave a mixture of products on heating.

Attention was thereafter shifted toward the preparation of 13b from 10b directly. This decision was based partly on an observation that 14 was transformed quantitatively into butenolide 15 via a NaHSO₃-mediated trans-ACOH elimination (eq 1), suggesting that the butenolide is stable to the action of NaHSO₃.

The effect of NaHSO₃ on the C-2 epimeric bromolactone 10b was therefore examined. The reaction, conducted in 87.5% aqueous propan-2-ol at room temperature proceeded sluggishly but produced, most gratifyingly, after 100 h, in quantitative yield the thermally unstable, oily, unsaturated γ-lactone 13b, which was characterized spectrally. The method was extended subsequently and required compound 10a. This was prepared from L-gulono-1,4-lactone and HBr-AcOH in the manner described for 10b. Similarly, lactone 10a when treated with NaHSO₃ in 90% aqueous methanol at room temperature afforded crystallizable butenolide 15a in high yield after 100 h (Scheme II).

The NaHSO₃-mediated elimination of 10a,b merits further comment. Whereas β-eliminations involving halogen and a hetero group are not uncommon, there seems to be no precedent for NaHSO₃ bringing about such a transformation. This would be substantiated by the stability of the 5-bromo-6-acetoxy groups of 13a,b and 15 toward the reagent. The fact that NaHSO₃ does cause 10a,b to undergo a trans-β-bromo-acetoxy elimination may either reflect the enhanced electrophilicity of halogens located α to the carbonyl or the actual participation of the carbonyl group in facilitating the process. Although aldehydes and some ketones are known to give crystalline addition compounds with NaHSO₃, no comparable adducts have apparently been derived from esters or lactones, albeit that [2,2′-bifuran]-5,5′-dione is claimed to yield adducts with NaHSO₃. The interaction in solution of NaHSO₃ with the lactone carbonyl may therefore not be precluded. An additional aspect to be considered concerns the conformational–configurational relationships of the reactive species participating in the process. Spectral studies of lactones in solution have suggested them to exist as equilibrium mixtures of two envelope forms, E₁ and E₂, with the substituents occupying pseudoequatorial and axial positions.

These data also showed decreases in the H-2 and H-3 coupling constants on going from axial–axial to axial–equatorial and equatorial–equatorial orientations, the respective values being 10 ± 3, 6 ± 3, and 2 ± 2 Hz. The spectrum of 10b shows no evidence of coupling between H-2 and H-3; these protons are assumed to be equatorially disposed. The C-2 bromo and C-3 acetoxy groups would then be trans-diaxially oriented with the most bulky C-4 substituent adopting an equatorial position (I). If the carbonyl group is intimately involved through complex formation, reversible attack of NaHSO₃ on the Si face of the C=O of this conformer would be nonproductive, whereas complexation from the Re face would leave the reagent suitably positioned for initiating an antiperiplanar β-bromo-acetoxy elimination to provide 13b. Compounds 10a,b, in contrast, exhibit an H-2–H-3 coupling constant of ca. 5 Hz. This is higher than would be expected for an equatorial–equatorial coupling but is insufficient

* (a) NaI, acetone, CF₃CO₂H; (b) aqueous NaOAc; (c) NaHCO₃ in H₂O-Et₂O; (d) NaHSO₃; aqueous alcohol.

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(27) For eliminations of the type

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\text{CH}_3\text{CO} \rightarrow \text{C} = \text{O} \]

see among others; the following. (a) X = COOR or OTos: Cristol, S. J.; Rademacher, L. E. J. Am. Chem. Soc. 1959, 81, 1600. Also ref 19. (b) X = NBr: Gurien, H. J. Org. Chem. 1963, 28, 878 (c) X = SR: Amstutz, E. D. J. Org. Chem. 1944, 9, 310. The reactions are generally brought about by Zn, Mg, or Na.

to account for an axial-axial one. These data may be accommodated by assuming the presence at room temperature of two readily interconvertible conformers I and II. Structure II, with two of its three bulky substituents being directed equatorially, might be more stable than I; its elimination to 13a would, however, require a prior equilibrium shift to I (Figure 1).

Some reagents resembling NaHSO₃ but unlikely to participate in C=O complexation, such as Na₂SO₄, sodium hydrogen oxalate, Na₂HPO₃, or the reducing agent NaH₂PO₃, failed to bring about the conversions of 10a,b to 13a,b under the cited reaction conditions. Aqueous NaH₂PO₃ caused partial decarboxylation and fully eliminated products resulted from treatment with aqueous NaHCO₃ alone or in combination with NaH₂PO₃. The substrates were also inert toward the action of sodium iodide in aqueous methanol but did undergo elimination in acetone. Altogether, the regio- and stereoselective NaHSO₃-induced elimination may well occur via a concerted, ionic E2 mechanism, be it with or without direct carbonyl participation.

Variations in the reaction conditions indicated the need for at least 3 equiv of NaHSO₃ (eq 2).

Optimal results were, in practice, attained on using 4 equiv of reagent. The reaction rate was shown to be critically pH dependent and adversely affected by an accumulation of the produced acidic components: the formation of SO₂ was established by passing N₂ through the reaction medium and observing the discoloration of aqueous KMnO₄ by the effluent gases. This aspect was considered to be of great importance and the NaHSO₃-promoted eliminations were subsequently conducted in a NaHCO₃-buffered system at pH ~6. This resulted in a 50-fold increase in the reaction rate, producing 13a,b cleanly, efficiently, and quantitatively after 2 h rather than 100 h. The system NaHSO₃-Na₂SO₃ (1:2), being equivalent to the NaHSO₃-NaHCO₃ (3:2) mixture, served equally well to bring about the elimination and was thereafter chosen for preparing the butenolides.

In principle the aforementioned dibromo-D-mannono-lactone 14, obtained in one step from the very cheap calcium D-gluconate, could also represent a good precursor for butenolide 13b and hence for diol 4a, provided that S₂O₂ inversion at C-2 could be realized in high yield. Treatment of 14 with NaI in acetone (neutral conditions) at room temperature yielded a 4:1 mixture of 2-bromobutenolide 15 and the desired product 13b. The former derives from trans 2-H-3-OAc elimination, as observed with methanolic NaHSO₃, and the latter from S₂O₂ inversion with iodide and subsequent trans 2-1-3-OAc elimination. Since elimination proceeded faster than substitution, 14 was no longer considered as a practical precursor for 4a. Conversely reaction of 2-deoxy derivative 11 with NaHSO₃-Na₂SO₃ (1:2), as described for dibromo diacetates 10a,b, gave after 100 h only limited amounts of butenolide 13b, together with substantial amounts of starting material, indicating that both acidity and steric factors may well contribute to the formation of 15 or 13b.

The documented instability of chiral butenolides toward basic, nucleophile agents (addition to or opening of the ring system, deprotonation at C-4 followed by expulsion of a C-5 leaving group with loss of chirality or by reprotontation with loss of chiral integrity) imposes considerable restrictions for achieving the seemingly straightforward conversions of 13a,b to 3a and 4a. Conditions for conducting these transformations under mild, neutral or slightly acidic circumstances were therefore devised. Heating compounds 13a,b under reflux in acidic MeOH produced deacetylated materials in addition to considerable amounts of the diene 12a. When the hydrolyses were conducted at 5 °C for 48 h, however, high yields of the bromohydrins 16a,b were obtained. These, on heating in boiling water, slowly produced mixtures of unidentified materials. The need for milder reaction conditions suggested the use of aqueous Ag₂O (Ag"OH") for a silver ion assisted epoxide formation and also for neutralizing the HBr produced. An ice-cold aqueous solution of 15b was consequently treated with slightly less than 1 equiv of Ag₂O giving an oily product in high yield. This was essentially devoid of OH functions and was characterized spectrally as the epoxide 16d, contaminated with traces of the diene 12b. The product was stable to silica gel chromatography and vacuum distillation. Its sensitivity to base was, however, convincingly demonstrated during an NMR-monitored experiment in which the addition of 0.1 equiv of Et₄N to a 0.5 M solution of 16d in CDCl₃ produced more than 50% of 12b within 1 min. The reaction of bromohydrin 16a with Ag₂O, in the manner described for 16b, produced the crystalline epoxide 16c. The structurally related 5,6-anhydro-~-ascorbic acid has shown to be the reactive intermediate in the formation of 6-substituted L-ascorbic acid derivatives from the corresponding 6-bromo compound. Attempts to isolate the intermediate epoxide were unsuccessful owing to the rapid autohydrolysis to L-ascorbic acid. Epoxides are known to undergo ring opening preponderantly at the least hindered site under neutral or basic conditions. Whereas the epoxides 16c,d had been unaffected by water at room temperature, the action of boiling water brought about their exclusive conversion to the previously described diols 3a and 4a. In contrast with Ag₂O, an aqueous suspension of Cu₂O, at or below room temperature, is unable to induce epoxide formation from bromohydrin 16a. Heating under reflux for 2 days, however, led to the direct production of the compound 3a in less than 40% yield. The formation of the epoxide is clearly slower than its ring opening to the diol.

The reaction conditions for preparing compounds 3a and 4a on a large scale were ultimately optimized and reduced to their simplest terms. The O-acetylated dibromo dideoxy 1,4-lactones 10a,b were obtained from vitamin and isovitamin C in two steps on a 2-mol scale in 75% and 40% yield. Ag₂O has also brought about the conversion of 2-bromo-3-hydroxy-1-indanone to 2,3-epoxyindanone: Undheim, K.; Nilsen, B. P. Acta Chem. Scand., Ser. B 1976, 30, 503.


(21) Synthetically useful reactions of epoxides have been reviewed in depth: Gorzynski Smith, J. Synthesis 1984, 629.
overall yields by treating the respective hydrogenation products with HBr-AcOH. The subsequent NaHSO₃-
Na₂SO₃-promoted elimination of 0.2 mol of 10a gave 13a, which, without purification, was desiccated to bromo-
hydrin 16a in 85% yield on treatment with 1 M HCl in MeOH. Compound 3a resulted on hydrolysis of the in-
termediately produced (Ag₂O-H₂O) epoxide 16c in 65% overall yield from 10a. The C-5 epimeric diol 4a was
obtained similarly in 69% overall yield from 10b on a 0.2-mol scale without purification of the oily intermediates
13b, 16b, and 16d.

The methodology was subsequently extended to include a three-step synthesis of 1a from D-ribono-1,4-lactone, not
requiring purification of any of the intermediates.29 Treatment of the lactone with 33% HBr in AcOH gave an oily
6/1 mixture of 17a,b.34 This material in i-PrOH produced, on stirring with aqueous NaHSO₃-Na₂SO₃ for
3 h at room temperature, an oil consisting of 18a,b in a similar ratio. Subsequent hydrolysis (MeOH-HCl) then
furnished mainly 1a contaminated with minor amounts of the corresponding bromide 18b. Column chromato-
graphy afforded essentially pure, oily 1a in 48% overall yield, which, on Kugelrohr distillation, gave material
solidifying at room temperature (Scheme III). The product yielded the triphenylmethyl ether 13b, 16d, 17a,b,
FOUND: C, 31.3; H, 3.1. 5-O-Acetyl-6-bromo-2,3,6-trideoxy-3-threo-hex-2-enono-1,4-lactone (13a). A stirred suspension of compound 16a (77.6 g, 0.20 mol) in methanol-water (9:1, 210 mL) was treated with NaHSO₃ (80.8 g, 0.20 mol) and then portionwise with Na₂SO₃ (50.4 g, 0.40 mol) at a rate that did not cause the temperature to exceed 27.5 °C. The mixture was then allowed to stir for 3 h, whereupon 1 M HCl (600 mL) and dichloromethane (750 mL) were added. The aqueous phase was separated and reextracted with dichloromethane (3 × 250 mL). The combined extracts were washed with water (500 mL), dried (MgSO₄), and concentrated in vacuo to give an oil (69 g, ~100%), which solidified on storage at 0 °C. The 1H NMR spectrum of the crude product indicated that it was the essentially pure butenolide 13a. Trituration of this material with diisopropyl ether gave analytical material (~50%): mp 42.5–43 °C; 1H NMR (CDCl₃) δ 2.07 s, 3 H), 3.59 (dd, J = 11 and 6 Hz, 1 H), 3.68 (dd, J = 11 and 6.5 Hz, 1 H), 5.32 (dd, J = 6.5 and 3 Hz, 1 H), 5.47 (t, J = 1.5 and 3 Hz, 1 H), 6.19 (dd, J = 6.5 and 1.5 Hz, 1 H), 7.46 (dd, J = 6 and 1.5 Hz, 1 H). Anal. Calc'd for C₁₉H₁₇BrO₆ (MW 388.02): C, 30.94; H, 3.12. Found: C, 31.3; H, 3.1.

Concluding Remarks

In spite of their potential as chiral building blocks, the use of large amounts of optically active butenolides in
synthesis has been limited owing to difficulties in their preparation. The present route offers a novel and opera-
tionally simple way for producing the chironos 1a, 3a, 4a, 10a,b, 13a,b, and 16a–d from the relatively inexpensive,
industrially produced L-ascorbic and D-isoascorbic acids or from moderately priced D-ribono-1,4-lactone.

The approach involves high-yield processes conducted in water or alcohol mostly at ambient temperatures and may well

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(35) The reactivity of 19 and its congeners is under current investigation.
in water (200 mL) at 0 °C was treated with moist, neutral, and freshly prepared Ag2O (0.25 mol). The mixture was maintained at this temperature for 4 h, when HBr (45%, 1 mL) was added and the precipitated AgBr was removed by filtration and washed with dichloromethane (500 mL). The filtrate and washings were mixed thoroughly with vigorous stirring and separated. The aqueous phase was extracted exhaustively with dichloromethane (5 × 200 mL), and the combined organic phases were dried (MgSO4) and concentrated in vacuo below 30 °C to give an oily residue (31.5 g, 99%). This material crystallized on storage at 0 °C and was shown to be essentially pure by a sample recrystallized from ethyl acetate analytically pure 16c (72%) needles: mp 48-49 °C; [α]D -79° (c 1.01, water); IR (KBr, cm⁻¹): vmax 3600 (OH, secondary), 3400 (OH, primary), 1765 (C=O, lactone), 1700 (C=O, acetates); 'H NMR (CDCl₃, 300 MHz) δ 2.10 (s, 3 H), 3.69 (d, J = 6 and 1.75 Hz, 1 H), 7.72 (dd, J = 6 and 1.75 Hz, 1 H). Anal. Found: C, 50.0; H, 5.6.

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (14). A stirred suspension of compound 10b (18.5 g, 0.10 mol) in methanol-water (9:1, 360 mL) was treated with NaHSO3 (10.4 g, 0.10 mol), followed by the portionwise addition of Na2S03 (25.2 g, 0.20 mol) and copper(1) oxide (1.42 g, 10 mmol) and stirred suspension of compound 10b (38.8 g, 0.10 mol) in methanol-water (7:1, 200 mL), and the combined organic phases were dried (MgSO4) and concentrated in vacuo below 30 °C to give an oily residue (35 g, 95%).

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (15) was obtained as a white solid, mp 92-93 °C; [α]D -186° (c 1.01, water); IR (KBr, cm⁻¹): vmax 3400 (OH, secondary), 3320 (OH, primary), 1760 (C=O, lactone), 1700 (C=O, acetates); 'H NMR (CDCl₃, 300 MHz) δ 2.14 (s, 3 H), 3.63 (d, J = 6 and 1.75 Hz, 1 H), 7.72 (dd, J = 6 and 1.75 Hz, 1 H). Anal. Found: C, 50.0; H, 5.6.

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (16). A stirred suspension of compound 10b (18.5 g, 0.10 mol) in methanol-water (9:1, 360 mL) was treated with NaHSO3 (10.4 g, 0.10 mol), followed by the portionwise addition of Na2S03 (25.2 g, 0.20 mol) and copper(1) oxide (1.42 g, 10 mmol) and stirred suspension of compound 10b (38.8 g, 0.10 mol) in methanol-water (7:1, 200 mL), and the combined organic phases were dried (MgSO4) and concentrated in vacuo below 30 °C to give an oily residue (35 g, 95%).

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (17). A stirred suspension of compound 10b (18.5 g, 0.10 mol) in methanol-water (9:1, 360 mL) was treated with NaHSO3 (10.4 g, 0.10 mol), followed by the portionwise addition of Na2S03 (25.2 g, 0.20 mol) and copper(1) oxide (1.42 g, 10 mmol) and stirred suspension of compound 10b (38.8 g, 0.10 mol) in methanol-water (7:1, 200 mL), and the combined organic phases were dried (MgSO4) and concentrated in vacuo below 30 °C to give an oily residue (35 g, 95%).

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (18). A stirred suspension of compound 10b (18.5 g, 0.10 mol) in methanol-water (9:1, 360 mL) was treated with NaHSO3 (10.4 g, 0.10 mol), followed by the portionwise addition of Na2S03 (25.2 g, 0.20 mol) and copper(1) oxide (1.42 g, 10 mmol) and stirred suspension of compound 10b (38.8 g, 0.10 mol) in methanol-water (7:1, 200 mL), and the combined organic phases were dried (MgSO4) and concentrated in vacuo below 30 °C to give an oily residue (35 g, 95%).

2,3-DIDEOXY-2-ACETOXY-2-ENONO-1,4-LACTONE (19). A stirred suspension of the dibromo lactone 10a (3.88 g, 10 mmol) in 96% aqueous propan-2-ol (20 mL), which was 0.5 M with respect to HBr, was heated under reflux for 2 h. Propan-2-ol and other volatile material were then removed slowly by distillation, with continuous replenishment of the propan-2-ol (6 mL/h). After a total period of 8 h, the mixture was concentrated in vacuo to give a residue (2.25 g), which was chromatographed (dichloromethane-ethyl acetate, 3:1), and yielded (1H NMR) pure compound 19 as an oil (1.21 g, 54%). The addition of chloroform-disopropyl ether (1:1) induced crystal
The reactions of a variety of ester and lactone enolates with methyldiphenylchlorosilane were studied. The C- versus O-silylation, leading to α-silyl ester or lactone and silyl ketene acetals, respectively, was studied as a function of the structure of the ester or lactone and the reaction conditions. It was found that all simple acetylates are C-silylated irrespective of the steric demands of the alcohol portion of the ester. Esters that are monosubstituted in the α-position are cleanly C-silylated with the notable exceptions of ethyl phenylacetate and ethyl phenoxacacetate, both of which give mixtures of C- and O-silylations. The α,α-disubstituted esters give only O-silylation, but the α,α-substituted α-silyl esters are readily prepared by the alkylation of the appropriate monosubstituted α-silylated ester. The reaction of the lithium enolate of ethyl acetate and tert-buty1 acetate with (S)-(−)-1-naphthylmethy1chlorosilane showed the reaction to occur with inversion of configuration at silicon. Methylation of tert-butyl (1-naphthylmethy1silyl)acetate gave a 91:9 mixture of diastereomeric α-silyl propionates, which could not be separated. It was found that only the γ-lactones gave C-silylation with δ-valero lactone and γ-caprolactone giving O-silylation.

The silylation of ester or lactone enolates can occur to produce the silyl ketene acetal or the α-silyl esters or lactones, all synthetically useful classes of compounds, as a result of silylation at the O- or C-termi nus of the enolate.