1d, 82650-65-5; **1e**, 82650-66-6; **2** (R^1 = 4-MeC_6H_4, R^2 = Me, R^3 = *i*-Pr), 94518-47-5; **2** (R^1 = R^2 = Ph, R^3 = *i*-Pr), 94518-50-0; **2** (R^1 = $Ph_2C(CN)$, R^2 = CH_2Ph, R^3 = *i*-Pr), 94518-52-2; **2** (R^1 = $Ph_2C(CN)$, R^2 = Ph, R^3 = *i*-Pr), 94518-53-3; **2** (R^1 = $Ph_2C(CN)$, R^2 = Me, R^3 = *i*-Pr), 94518-54-4; **2** (R^1 = $Ph_2C(CN)$, R^2 = Me, R^3 = Ph_2CH), 94518-56-6; **3c**, 65739-14-2; **3j**, 94518-57-7; **3k**, 82650-31-5; **3l**, 94518-58-8; **3p**, 94518-59-9; **4**, 94518-60-2; **5**, 94518-61-3; **6**, 94518-62-4; **7**, 94518-63-5; **8**, 94518-64-6; **9**, 90496-26-7; **10c**, 94518-65-7; **10d**, 94518-66-8; **10g**, 94518-67-9; **10i**, 94518-68-0; **10j**, 94518-69-1; **10k**, 94518-70-4; (*E*)-**11a**, 94518-71-5; (*Z*)-**11a**, 94518-72-6; (*E*)-**11b**, 94518-73-7; (*Z*)-**11b**, 94518-74-8; **11j**, 94518-75-9; **12i**, 94518-76-0; **12o**, 94518-77-1; **12p**, 94518-78-2; **13c**, 94518-79-3; **13d**, 94518-80-6; **13e**, 94518-81-7; **13f**, 94518-82-8; **13g**, 94518-83-9; **13l**, 94518-84-0; **13m**, 94518-85-1; **13n**, 94518-86-2; **14c**, 94518-87-3; **14d**, 94518-88-4; **14e**, 94518-89-5; **14f**, 94518-90-8; **14g**, 94518-91-9; **14h**, 94518-92-0; **15**, 94518-93-1; **16**, 94518-94-2; **17**, 94518-95-3; **18**, 94518-96-4; **19**, 94518-97-5; **20**, 94518-98-6; **21**, 94518-99-7; **22**, 94519-00-3; **23**, 94519-01-4; **24**, 94519-02-5; **25**, 94519-03-6; **26**, 94519-04-7; **27**, 94519-05-8; **28**, 94519-06-9; **29**, 94519-07-0; **30**, 94519-08-1; **31**, 94519-09-2; **32**, 94519-10-5; **33**, 94519-11-6; **34**, 94519-12-7; **35**, 94519-13-8; **36**, 94519-14-9; **37**, 94519-15-0; **38**, 94519-16-1; **39**, 94519-17-2; **40**, 94519-18-3; *i*-PrNC, 598-45-8; Ph_2CHNC, 3128-85-6; 2,6-$Me_2C_6H_3NC$, 2769-71-3; *t*-BuNC, 7188-38-7.

A Nitrile Oxide Based Entry to 2,3-Dihydropyran-4-ones. Synthesis of a Protected Version of "Compactin Lactone" in Racemic and Optically Active Forms

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Received September 10, 1984

The use of nitrile oxides bearing a masked β-oxo group as β-hydroxy-3-oxopropionylating agents for the vicinal functionalization of olefins is described. The β-hydroxy ketones revealed on hydrogenation of the initially formed 1,3-dipolar cycloaddition products undergo zinc triflate promoted cyclocondensation to 2,3-dihydropyran-4-ones, useful carbohydrate building blocks. The application of this chemistry to the preparation of a protected form of "compactin lactone" is detailed.

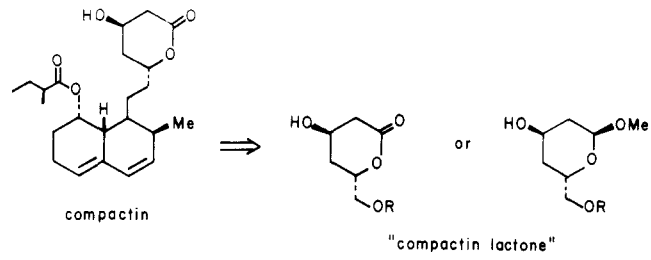
The de novo synthesis of carbohydrates and carbohydrate-related materials has long been of interest to many investigators.[1] While the Diels–Alder reaction of carbonyl dienophiles with oxygenated dienes has proven popular both in the past and the present,[1,2] it does have in spite of its successes some obvious shortcomings.

In further pursing our interests in this area[3] we have had the occasion to develop a 1,3-dipolar cycloaddition based entry to the important carbohydrate building blocks, the 2,3-dihydropyran-4-ones. The evolution of this work in the context of developing a synthesis approach to a protected form of compactin lactone is detailed herein.

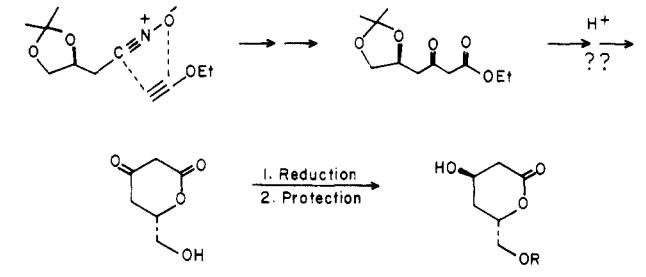
Synthesis of Compactin Lactone, Preliminary Studies

In devising an approach to compactin lactone (this lactone and a protected version of it are shown in Scheme I), we focused initially on the strategy shown in Scheme II. (*R*)-2,3-Isopropylideneglyceraldehyde[4] was transformed to the nitro compound **2** via a Henry reaction/reduction sequence,[5] and **2** reacted with phenyl isocyanate/triethylamine in the presence of ethoxyacetylene[3d] to yield isoxazole **3** (Scheme III). While hydrogenation delivered the β-keto ester **4** cleanly, subsequent *p*-toluenesulfonic acid treatment of this intermediate led either to a complicated mixture of products containing some of the diol **5** (MeOH, room temperature) or to the furan **6** as a mixture of methyl and ethyl esters by dehydrative cyclization. None of the desired cyclized lactone was observed. Additionally, attempts to either protect or to reduce the ketone group of **4** and then to effect cyclization were disappointing.

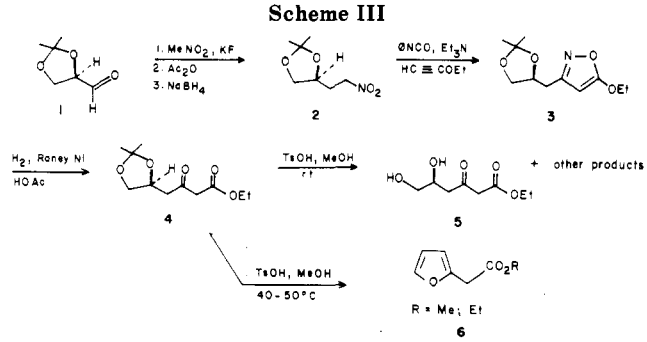
Scheme I



Scheme II



Scheme III



Furthermore, the nitrile oxide derived from **2** was added to vinyl bromide[6] to form the isoxazole **7**. The acetonide

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‡ Andrew Mellon Predoctoral Fellow of the University of Pittsburgh, 1982–1984.

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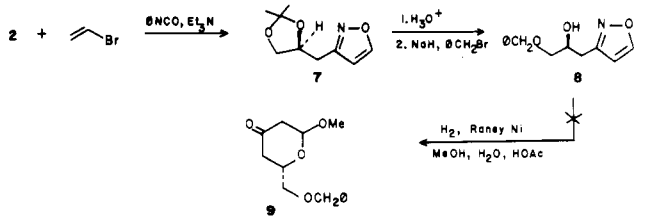
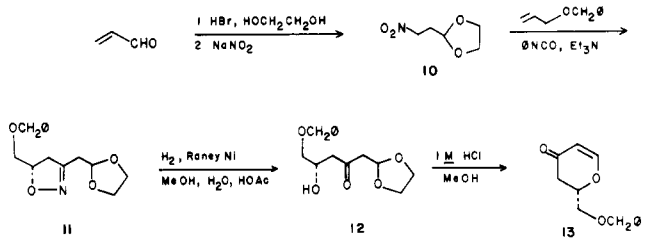
Scheme IV



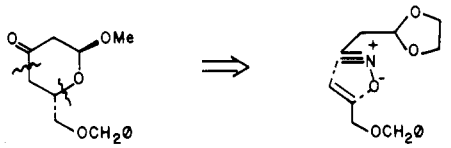
Scheme V



was then cleaved and the primary alcohol benzylated (Scheme IV). It was our hope that hydrogenation of this isoxazole in methanol would lead to the methoxypyranone **9** via the intermediate β-keto aldehyde (or hydroxymethylene ketone). Unfortunately, none of the desired product was formed. The precise reasons for this failure were not ascertained since a more efficient dissection was soon found.

Synthesis of Racemic 17

The new dissection revealed below is related to the foregoing synthesis strategy in that we have again chosen to pass through a β-keto aldehyde intermediate. However, this time the aldehyde group is protected as its 1,3-dioxolane, and it is built into the nitrile oxide component rather than emerging from the dipolarophile after union with the nitrile oxide. Such a dissection rests upon the well-documented ability of α-alkoxypyrans to serve as masked lactone equivalents.[7]



The nitro compound **10** required to test this strategy was prepared by condensation of acrolein with ethylene glycol in the presence of anhydrous hydrogen bromide,[8] followed by treatment of the resulting bromo acetal with either sodium nitrite[9] or a halogen/nitro anion-exchange resin.[10]

Reaction of this nitro compound with allyl benzyl ether under the Mukaiyama conditions[11] gave isoxazoline **11** in 85% yield (Scheme V). Hydrogenation of the isoxazoline using Raney nickel[12] then provided the dioxolane-masked β-keto aldehyde **12**. Cyclization of **12** with 1 M methanolic hydrogen chloride yielded the pyranone **13** in low yield. The structure of this material was confirmed by spectral analysis and, furthermore, by the similarity of its ^{1}H NMR spectrum to that reported for the same pyrone prepared by a Diels–Alder route.[2f]

In order to optimize the cyclization yield, **12** was stirred with Dowex-50W acidic ion exchange resin in methanol at room temperature for 2 days to afford the two isomeric trimethoxy compounds **14** and **15** (Scheme VI). These could be separated by careful flash column chromatography. The more polar fraction (minor isomer) was identified as **14** and the less polar fraction (major isomer) as **15**. The distinction between these isomers was made by comparison of the chemical shift and coupling data for their anomeric protons. For **14**, the anomeric proton assumes an equatorial position (δ 4.88, d, J = 3 Hz) and is 0.4 ppm more downfield than the anomeric proton of **15** (δ 4.48, dd, J = 10, 2 Hz).[13] The anomeric proton of **15** thus occupies an axial position in line with its large axial–axial and small axial–equatorial coupling constants.

Equilibration of either pure **14** or **15** in methanol with a catalytic amount of p-TsOH gave a mixture of **14** and **15** in a 1:2.6 ratio. Apparently, the equilibrium is tipped in favor of **15** due to the ability of the destabilizing 1,3-diaxial interaction to override to a large degree the anomeric effect.[13]

Deketalization of **14** with Dowex-50W resin in acetone afforded **9** in quantitative yield. L-Selectride (Aldrich) reduction in THF followed by acetylation gave glycoside **16** whose ^{1}H NMR spectrum matched closely that reported by Danishefsky.[2f] Deketalization of **15** followed by reduction gave, on the other hand, a diastereomeric mixture of alcohols **18**. It thus became desirable to generate **9** or **14** stereospecifically.

When **12** was treated with the Lewis acid zinc triflate,[14] a catalyst previously found by us to be effective in keying internal ketone condensations with pyrroles,[15] the pyrone **13** was obtained cleanly and in high yield. Thus, the zinc triflate promoted reaction appears to constitute a useful approach to dihydro-4*H*-pyran-4-ones. Additional examples are presented in the final sections of this paper.

On following the procedure reported by Danishefsky,[2f] the conversion of **13** to **14** proved unsatisfactory. A mixture of **9**, **14** (predominant product after 2 h), and **15** was generated which proved tedious to separate by chromatography. Interestingly, the anomer **19** of **9** was not detected (^{1}H NMR, <3%) in the reaction mixture. TLC monitoring of the reaction indicated that **9** was the first major product to be formed. Thus, it would appear reasonable to suppose that the reaction sequence leading to **9**, **14**, and **15** should be **13** → **9** → **14** → **15** as shown in Scheme VII. The stereochemistry of the first step cor-

(1) Jones, J. K. N.; Szarek, W. A. In "The Total Synthesis of Natural Products", ApSimon, J., Ed., Wiley: New York, 1973; Vol. 1, pp 1–80. Hamer, J.; Turner, J. A. In "1,4-Cycloaddition Reactions"; Hamer, J., Ed.; Academic Press: New York, 1967; pp 205–215.

(2) (a) Kubler, D. G. *J. Org. Chem.* **1962**, *27*, 1435. (b) Harris, J. F. U.S. Paten 3136786, 1964. (c) Schmidt, R. R.; Wagner, A. *Tetrahedron Lett.* **1983**, *24*, 4661. (d) David, S.; Eustache, J.; Lubineau, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1795. (e) Achmatowicz, O.; Zamojski, A. *Rocz. Chem.* **1961**, *35*, 1251. (f) Danishefsky, S.; Kerwin, J. F.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358.

(3) (a) Kozikowski, A. P.; Ames, A. *J. Am. Chem. Soc.* **1981**, *103*, 3923. (b) Kozikowski, A. P.; Schmiesing, R. J.; Sorgi, K. L. *Ibid.* **1980**, *102*, 6577. (c) Kozikowski, A. P.; Sorgi, K. L. *Tetrahedron Lett.* **1982**, *23*, *2281*; 1983, *24*, 1563. (d) Kozikowski, A. P.; Goldstein, S. *J. Org. Chem.* **1983**, *48*, 1139. (e) Kozikowski, A. P.; Ghosh, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 5788.

(4) Baer, E.; Fischer, H. O. L. *J. Biol. Chem.* **1934**, *128*, 463.

(5) Wollenberg, R. H.; Miller, S. J. *Tetrahedron Lett.* **1978**, 3219.

(6) Weygand, C.; Bauer, E. *Liebigs Ann. Chem.* **1927**, *459*, 123.

(7) Prugh, J. D.; Deana, A. A. *Tetrahedron Lett.* **1982**, *23*, 281.

(8) Büchi, G.; Wuest, W. *J. Org. Chem.* **1969**, *3*, 1122. Smith, A. B., III; Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4015.

(9) Kornblum, N.; Larson, H. O.; Blackwood, R. K.; Mooberry, D. P.; Oliveto, E. P.; Graham, G. E. *J. Am. Chem. Soc.* **1956**, *78*, 1497.

(10) Gelbard, G.; Colonna, S. *Synthesis* **1977**, 113.

(11) Mukaiyama, T.; Hoshino, T. *J. Am. Chem. Soc.* **1960**, *82*, 5339.

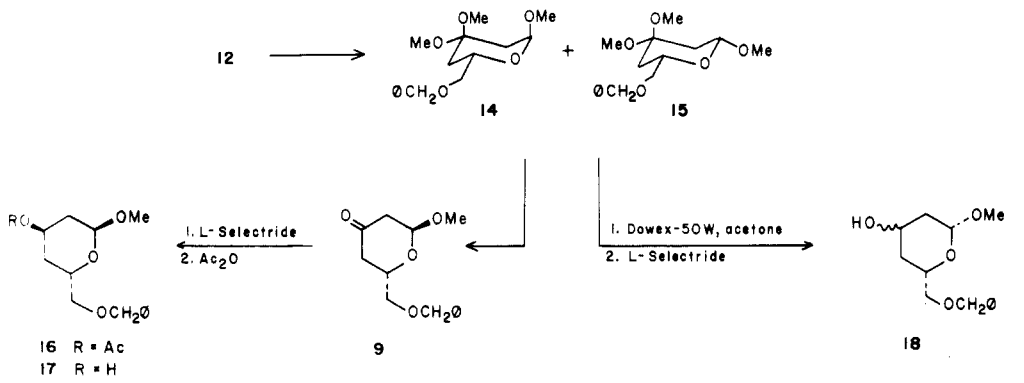
(12) Wollenberg, R. H.; Goldstein, J. E. *Synthesis* **1980**, 757.

(13) Stoddart, J. F. "Stereochemistry of Carbohydrates", Wiley-Interscience: New York, 1971.

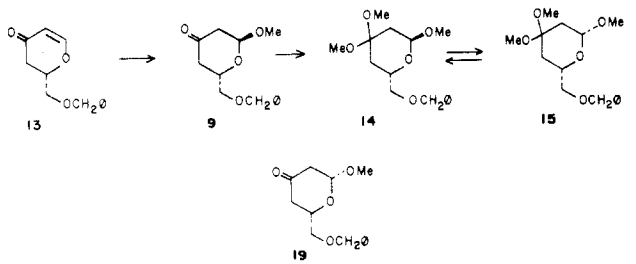
(14) Zinc triflate is conveniently prepared from zinc carbonate or zinc oxide and triflic acid. Also, see: Corey, E. J.; Shimoji, K. *Tetrahedron Lett.* **1983**, *24*, 169.

(15) Kozikowski, A. P.; Li, C. S.; Scripko, J. G.; Cheng, X.-M., manuscript submitted.

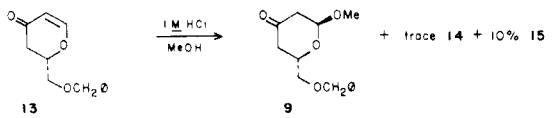
Scheme VI



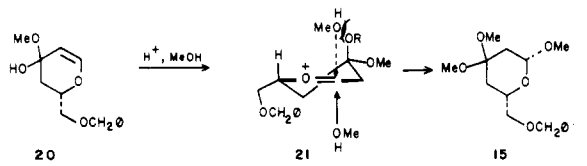
Scheme VII



Scheme VIII



Scheme IX



responds to addition via the stereochemically favored quasi-axial mode starting from the sofa conformation of **13** with the (benzyloxy)methyl group in a quasi-equatorial position.[16] Since **9** was believed to be formed as the major primary product in this sequence, it was thought that by quenching the reaction mixture before further conversions took place **9** might be isolated as the major product. Indeed, when a solution of **13** in methanol was added to 1 M methanolic hydrogen chloride (prepared by mixing concentrated aqueous hydrogen chloride and methanol) and the resulting mixture stirred at room temperature for 15 min, **9** was obtained in 79% yield on quenching with saturated sodium bicarbonate. The trimethoxy compounds were formed only as minor products in this case (Scheme VIII).

The amount of **15** (10%) formed relative to **14** (trace) may in this instance have some bearing on 1,2- vs. 1,4-addition to **13**. In early trials, using 0.2 M HCl in methanol, product isolation after 2 h still revealed that **14** was the major product. Apparently, the ketalization of **9** occurs at a faster rate than the anomerization of **14**. For a greater anomerization rate, the thermodynamic product **15** should predominate over **14** during any stage of the reaction profile. The excess of **15** present at the early stage of the 1 M HCl reaction may thus come about from **13** via a different reaction pathway, and one possibility might be the initial 1,2-addition of methanol to **13**. The hemiketal so generated (or the dimethoxy compound derived from it) would then undergo addition of methanol by way of its oxonium ion **21** in an equatorial mode in order to avoid the development of a serious 1,3-diaxial interaction with OR via the axial addition pathway (Scheme IX). Alternatively, and more likely, the presence of **15** may simply reflect the rapid ketalization of any of **19** formed by initial equatorial addition of methanol to **13**. Additional studies will be required to sort out these possibilities.

Synthesis of Optically Active 17

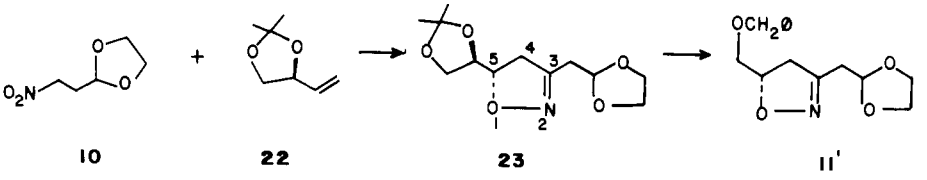
Since an efficient route to **17** was developed, our efforts now turned to a synthesis of this lactone fragment in chiral form. Previously we had shown that the addition of nitrile oxides to the D-glyceraldehyde-derived olefin **22** proceeds in an "antiperiplanar" sense.[3e] The use of this olefin instead of allyl benzyl ether as the dipolarophile in the [3 + 2] reaction with the nitrile oxide from **10** (Scheme X) might thus provide predominantly the isoxazoline **23** of correct absolute stereochemistry at C-5 (of the isoxazoline ring). Scission of the extra carbon atom from **23** would then give the required skeleton in optically active form.

On reacting the nitro compound **10** with the olefin **22** in the presence of phenyl isocyanate and a catalytic amount of triethylamine (Scheme XI), the "anti" product **23** and the "syn" product **24** were obtained in a 4:1 ratio.[17] After chromatographic separation, **23** was deprotected by Dowex-50W acidic ion exchange resin in methanol to yield the diol **25** which in turn was converted to **26** by an oxidative cleavage/reduction sequence. Optially active **11′** was then generated by reacting **26** with sodium hydride and benzyl bromide. Following the established procedures, **11′** was converted to **17′** and this intermediate further transformed to the known product **29**, a compound prepared previously from tri-*O*-acetyl-D-glucal, in order to compare optical rotations. This latter reaction sequence is shown in Scheme XII. The hydroxyl group of **17′** was protected as its *tert*-butyldiphenylsilyl ether, the benzyl group removed by hydrogenolysis, and the alcohol **28** equilibrated with *p*-toluenesulfonic acid in methanol. The optical rotation of the major isomer **29** of this equilibration experiment ($[\alpha]^{24}_D$ −11.3°) was virtually identical with that reported by Falck ($[\alpha]^{24}_D$ −11.2°).[18]

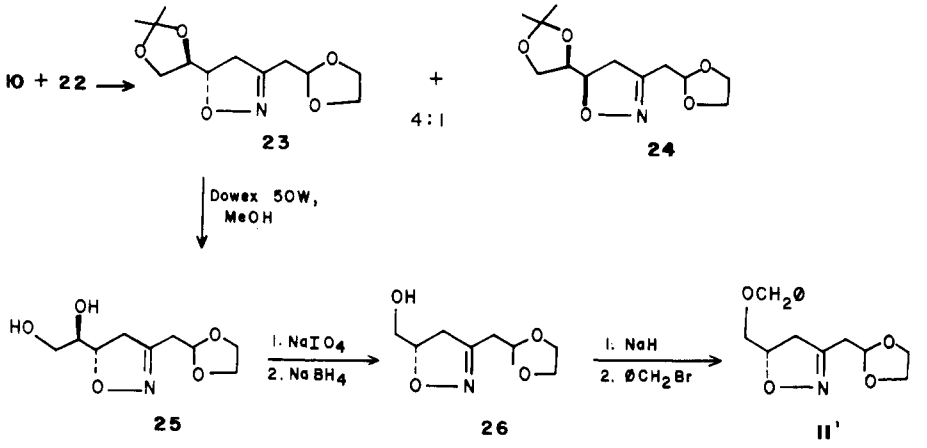
(16) Goering, H. L.; Josephson, R. R. *J. Am. Chem. Soc.* **1962**, *84*, 2779. Stevenson, T. T.; Stenkamp, R. E.; Jensen, L. H.; Cochran, T. G.; Shafizadeh, F.; Furneaux, R. H. *Carbohydr. Res.* **1981**, *90*, 319. This preference for quasi-axial addition presumably reflects both conformational energetics and the kinetic anomeric effect. For a discussion of the latter, see: Kirby, A. J. "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen" Springer-Verlag: New York, 1983.

(17) The isomer which corresponds to addition by way of our previously suggested antiperiplanar transition state is termied the "anti" product, while the other minor isomer coming from a different transition state is designated as the "syn" isomer.

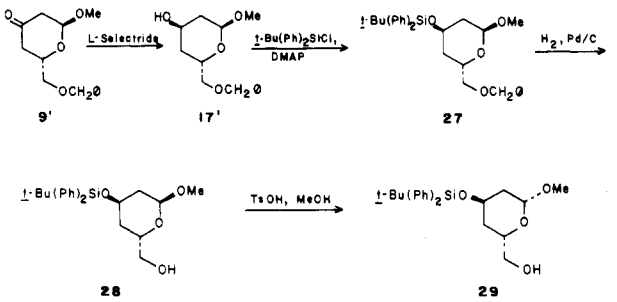
Scheme X



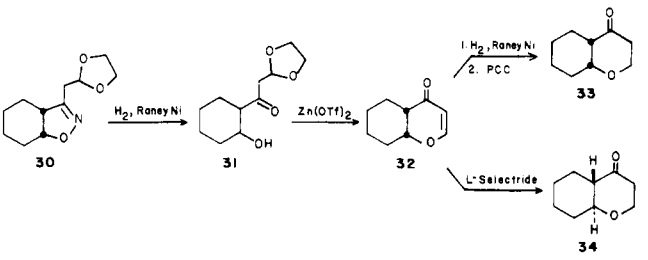
Scheme XI



Scheme XII



Scheme XIII



Other Examples of the Zinc Triflate Assisted Dihydro-4*H*-pyran-4-one Synthesis

The use of the nitrile oxide of **10** in the construction of a ring-fused pyranone is illustrated by its reaction with cyclohexene. Hydrogenation of the intermediate isoxazoline **30** and zinc triflate treatment of the β-hydroxy ketone afforded **32** (Scheme XIII). The cis nature of the ring fusion of **32** was rigorously confirmed by converting it to the known octahydrobenzopyran-4-one **33**[19] by Raney nickel hydrogenation followed by PCC oxidation. Interestingly, it was found that L-Selectride reduction of **32** occurred exclusively via the 1,4-addition mode to deliver the trans-fused pyranone **34**. Since the functionality present in **32** can be manipulated in a variety of stereopredictable ways, the present methodology should find use in the construction of ring-fused carbohydrates.

To construct a pyranone substituted at its 6-position, one need only to start with the appropriately substituted nitro compound bearing a masked ketone rather than a masked aldehyde component. For example, the nitro compound **35**, available from 2-(2-bromoethyl)-2-methyl-1,3-dioxolane,[20] was reacted with the *tert*-butyldimethylsilyl ether **36a** of 1-penten-3-ol in the presence of phenyl isocyanate and triethylamine to afford a 2:1 mixture of **37** and **38** (Scheme XIV). The diastereoselectivity observed in this cycloaddition reaction is considerably less than that found for the *tert*-butyldimethylsilyl ether of 3-buten-2-ol[21] and may reflect the smaller steric difference between the (non-hydrogen) allylic substituents. Hydrogenation and zinc triflate promoted cyclization then provided the disubstituted pyranone **39a**. Likewise, the benzyl ether of 1-penten-3-ol was transformed with comparable diastereoselectivity to **39b** (~2:1 mixture).

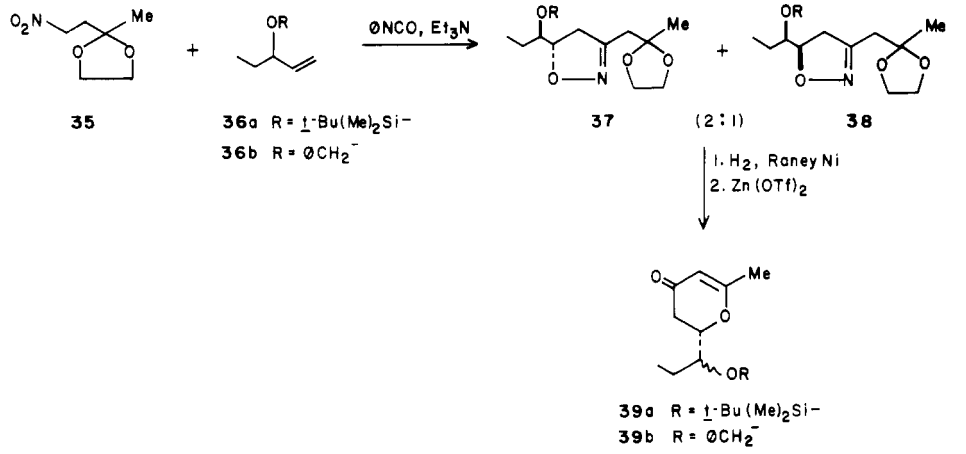
We have also shown that the nitrile oxide chemistry can be used to access 2,5-disubstituted pyran-4-ones (Scheme XV). The nitro compound **40**, available from 3-bromo-2-methylpropionaldehyde ethylene acetal,[22] was reacted with methyl 2,2-dimethyl-3-butenoate (**41**), and the ester group of the intermediate isoxazoline was reduced and benzylated to provide **42**. Hydrogenolysis and zinc triflate promoted cyclization yielded **43**.

An Approach to Spiroketals

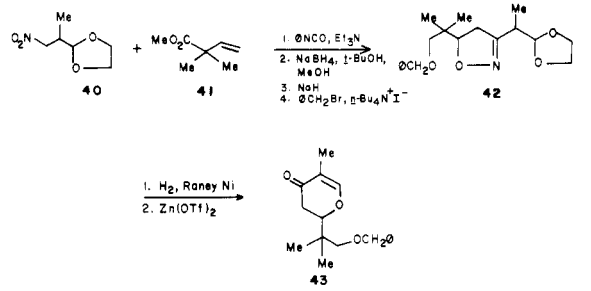
The generation of a nitrile oxide related to that prepared from **10** but bearing the β-oxygen functionality in the alcohol rather than the carbonyl oxidation state was deemed valuable in the development of a [3 + 2] based approach to spiroketals. To test this notion, the nitrile oxide prepared from the THP derivative of 3-nitropropanol[23] **44** was reacted (Scheme XVI) with the olefinic

(18) Yang, Y. L.; Falck, J. R. *Tetrahedron Lett.* **1982**, *23*, 4305.
(19) Hirsch, J. A.; Schwartzkopf, G. *J. Org. Chem.* **1974**, *39*, 2040.
(20) This bromide was prepared from methyl vinyl ketone, hydrogen bromide, and ethylene glycol by using the same procedure as described by Büchi (ref 8) for the conversion of acrolein to 3-bromopropionaldehyde ethylene acetal. The bromide was further converted to its nitro derivative by use of an anion-exchange resin (IRA-900, NO_2^- form, ref 10).
(21) Kozikowski, A. P.; Ghosh, A. K. *J. Org. Chem.* **1984**, *49*, 2762.
(22) This nitro compound was prepared from methacrolein by the same route as outlined in ref 20.

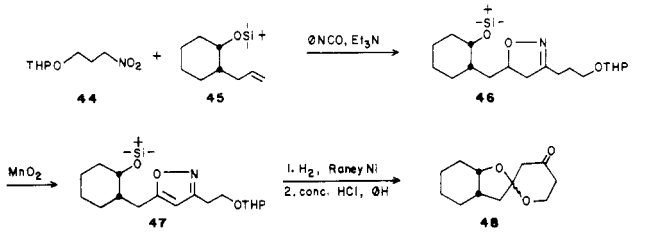
Scheme XIV



Scheme XV



Scheme XVI

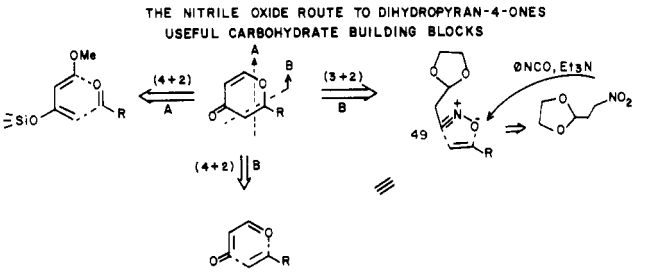


silyl ether **45**, and the intermediate isoxazoline **46** was oxidized to the isoxazole **47**.[24] Hydrogenation and acid-catalyzed cyclization provided **48** as a mixture of diastereomers (5:1 by ^{1}H NMR analysis, major isomer unassigned).[25] The application of the same methodology to naturally occurring products such as phyllanthoside should be feasible and certainly stereochemically more predictable.[26]

Conclusion

Previously, we have reported on the use of nitrile oxides bearing an α-oxygen substituent(s) for the vicinal functionalization (β-hydroxy cyanation and β-hydroxy carboxylation) of alkenes.[27] In contrast, the oxygen functionality in **49** resides β to the nitrile oxide group, thus permitting it to function as a β-hydroxy-3-oxopropionylating agent. As displayed in Scheme XVII (path B), **49** does furnish the same type of product as would

Scheme XVII



result formally from the [4 + 2] reaction of the inaccessible formyl ketene with an alkene.[29] The nitrile oxide **49** and its analogues thus offer a new and flexible entry to dihydropyran-4-ones, useful carbohydrate building blocks.

Experimental Section[28]

Nitro Compound 2. A mixture of 3.5 g (27 mmol) of aldehyde 1,[4] 10 mL of nitromethane, and 300 mg (0.2 equiv) of anhydrous potassium fluoride in 50 mL of anhydrous 2-propanol was stirred at room temperature overnight. The 2-propanol was removed by rotary evaporation and the residue was diluted with ether. The resulting mixture was filtered to remove potassium fluoride, and the filtrate was concentrated to afford 4.8 g of a colorless oily residue.

To a solution of above product and 3 g (29 mmol) of acetic anhydride in 40 mL of ether was added 100 mg (0.8 mmol) of 4-(dimethylamino)pyridine. The mixture was stirred at room temperature for 2 h, washed with a cold saturated sodium chloride solution, dried with anhydrous $MgSO_4$, and concentrated to yield a yellow oil.

The yellow oil was dissolved in 10 mL of ethanol and added dropwise to a stirred suspension of 2.8 g (74 mmol) of sodium borohydride in 50 mL of ethanol at ice-bath temperature. The mixture was further stirred for 1 h and then poured into 45 mL of a 20% aqueous solution of acetic acid and urea at 0 °C. After being stirred for 15 min, the mixture was saturated with sodium chloride and extracted with ethyl acetate (2×). The combined

(23) This nitro compound was prepared from the THP ether of commercially available 3-bromopropanol by use of an anion-exchange resin (IRA-900, NO_2^- form, ref 10).

(24) Barco, A.; Benetti, S.; Pollini, G. P. *Synthesis* **1977**, 837.

(25) Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauve, T.; Saunders, J. K. *Can. J. Chem.* **1981**, *59*, 1105.

(26) For syntheses of phyllanthocin, see: Collum, D. B.; McGuirk, P. R. *J. Am. Chem. Soc.* **1982**, *104*, 4496. Williams, D. R.; Sit, S.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 2949.

(27) Kozikowski, A. P.; Kitagawa, Y.; Springer, J. P. *J. Chem. Soc., Chem. Commun.* **1983**, 1460.

(28) Infrared spectra were obtained on a Perkin-Elmer Model 247 spectrophotometer or a Beckman Acculab 4 spectrophotometer and were calibrated to a polystyrene absorption at 1602 cm^{-1} (6.43 μm). ^{1}H NMR spectra were recorded at 60 MHz (Varian EM-360 or T-60 A), 90 MHz (Varian EM-390), or at 300 MHz (Brüker WH-300) in the solvent noted. Chemical shifts (δ) are reported in ppm downfield from Me_4Si as an internal reference (1% or 0.05% for FT). Low-resolution mass spectra were obtained on a LKB-9000 instrument operating at 15 or 70 eV ionization potential unless otherwise noted. High-resolution mass spectra were determined on a Varian MAT CH-5DF instrument by peak matching. Optical rotations were determined on a Perkin-Elmer Model 241 polarimeter. Thin-layer chromatography was performed on Merck silica gel 60 F-254 (0.25 mm, precoated on glass or 0.2-mm precoated on aluminum).

(29) For a preparation of acetylketene, see: Sato, M.; Ogasawara, H.; Yoshizumi, E.; Kato, T. *Heterocycles* **1982**, *17*, 297.

extracts were washed with water, dried over anhydrous $MgSO_4$, and evaporated.

The residue was distilled to afford 3.4 g (72%) of the nitro compound **2** as a colorless liquid: bp 88–90 °C (1 mm); IR (thin film) 2940, 1560, 1430, 1370, 1220, 1150, 1085, 1050, 980, 850, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.54 (t, 2 H, J = 7.3 Hz), 4.2 (m, 1 H), 4.12 (dd, 1 H, J = 8.1, 6.1 Hz), 3.60 (dd, 1 H, J = 8.1, 6.1 Hz), 2.40–2.05 (m, 2 H), 1.42 (s, 3 H), 1.34 (s, 3 H); mass spectrum (70 eV), m/z 160 ($M^+ - CH_3$); $[\alpha]^{24}_D$ −16.2° (c 0.73, $CHCl_3$); exact mass calcd for $C_7H_{13}NO_4 - CH_3$ 160.0609, found 160.0610.

5-Ethoxy-3-[(4*S*)-(2,2-dimethyl-1,3-dioxolan-4-yl)-methyl]isoxazole (3). A mixture of 0.6 g (3.4 mmol) of nitro compound **2**, 1.6 mL of phenyl isocyanate, 0.6 g (6.8 mmol) of ethoxyacetylene, and a catalytic amount of triethylamine in 10 mL of benzene was stirred at room temperature for 12 h. Water was then added, and the mixture was stirred for 8 h and filtered. The precipitate was washed with benzene, and the organic layer was separated, dried ($MgSO_4$), and concentrated to give a yellow liquid. The crude product was chromatographed over silica gel with hexanes–ethyl acetate (3:1) as eluent to furnish 0.6 g (77%) of **3** as a colorless liquid: IR (thin film) 2940, 1630, 1525, 1470, 1400, 1320, 1260, 1185, 1095, 900, 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.15 (s, 1 H), 4.40 (quintet, 1 H, J = 6.27 Hz), 4.23 (q, 2 H, J = 7.07 Hz), 4.10 (dd, 1 H, J = 8.29, 6.06 Hz), 3.67 (dd, 1 H, J = 8.29, 6.67 H), 2.88 (dd, 1 H, J = 14.75, 6.27 Hz), 2.78 (dd, 1 H, J = 14.75, 6.27 Hz), 1.45 (t, 3 H, J = 7.07 Hz), 1.44 (s, 3 H), 1.37 (s, 3 H); mass spectrum (70 eV), m/z 227 (M^+), 212 ($M^+ - CH_3$); $[\alpha]^{24}_D$ +0.3° (c 0.725, $CHCl_3$); exact mass calcd for $C_{11}H_{17}NO_4$ 227.1161, found 227.1158.

β-Keto Ester 4. A mixture of 0.6 g (2.6 mmol) of **3**, 1 mL of acetic acid, and a catalytic amount of Raney nickel in 50 mL of EtOH–H_2O (4:1) was hydrogenated under a hydrogen atmosphere (balloon) for 12 h. The catalyst was removed by filtration through Celite. The filtrate was neutralized by the addition of saturated sodium bicarbonate and concentrated by rotary evaporation. The resulting residue was diluted with 10 mL of water, saturated with sodium chloride, and then extracted with ethyl acetate (3×). The combined extracts were dried ($MgSO_4$) and evaporated to give a yellow liquid. Chromatography over silica gel with hexanes–ethyl acetate (3:1) yielded 0.42 g (70%) of **4** as a colorless liquid: IR (thin film) 3570, 2940,1725, 1665, 1625, 1560, 1515, 1450, 1370, 1160, 1040, 840, 790, 760, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.48 (m, 1 H), 4.20 (q, 2 H, J = 7.07 Hz), 4.19 (dd, 1 H, J = 8.49, 6.06 Hz), 3.57 (dd, 1 H, J = 8.49, 6.67 Hz), 3.49 (s, 1.7 H), 3.00 (dd, 1 H, J = 17.07, 6.06 Hz), 2.75 (dd, 1 H, J = 17.07, 6.87 Hz), 1.41 (s, 3 H), 1.35 (s, 3 H), 1.29 (t, 3 H, J = 7.07 Hz); mass spectrum (70 eV), m/z 215 ($M^+ - CH_3$); $[\alpha]^{25}_D$ −0.9° (c 1.43, $CHCl_3$); exact mass calcd for $C_{11}H_{18}O_5 - CH_3$ 215.0923, found 215.0920.

Attempted Cyclization of 4. A mixture of 20 mg (0.086 mmol) of β-keto ester **4** and a catalytic amount of *p*-toluenesulfonic acid in 2 mL of methanol was stirred at 40–50 °C for 1 h. A saturated solution of sodium bicarbonate was added, and the resulting mixture was extracted with ethyl acetate (3×). The combined ethyl acetate extracts were washed with saturated sodium chloride, dried over magnesium sulfate, and concentrated. The crude product was chromatographed on silica gel with hexanes–ethyl acetate (3:1) as eluent to afford furan **6** as a mixture of the methyl and ethyl esters: IR (thin film) 2940, 1770, 1650, 1540, 1470, 1330, 1240, 1180, 740, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (br s, 1 H), 6.34 (br s, 1 H), 6.22 (d, 1 H, J = 3.0 Hz), 4.19 (q, CH_2 of CO_2 Et, J = 7.1 Hz), 3.73 (s, CH_3 of CO_2CH_3), 3.70 (s, CH_2CO_2R of methyl ester), 3.68 (s, CH_2CO_2R of ethyl ester), 1.27 (t, CH_3 of OEt); mass spectrum (70 ev), m/z 154 (M^+ for ethyl ester), 140 (M^+ for methyl ester).

3-[(4*S*)-(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]isoxazole (7). A mixture of 400 mg (2.28 mmol) of nitro compound **2**, 5 mL of vinyl bromide, 1 mL of phenyl isocyanate, and 0.7 mL of triethylamine was stirred at room temperature for 24 h. An additional 0.5 mL of phenyl isocyanate was added after 12 h. This mixture was worked up in the same fashion as described for **3**. Chromatography of the crude product over silica gel with hexanes–ethyl acetate (3:1) as eluent afforded 310 mg (75%) of **7** as a pale yellow liquid: IR (thin film) 2900, 1650, 1510, 1450,1390, 1365, 1320, 1185, 1125, 1090, 1040, 865, 790, 765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.35 (d, 1 H, J = 1.7 Hz), 6.32 (d, 1 H, J = 1.7 Hz), 4.43 (m, 1 H), 4.12 (dd, 1 H, J = 8.3, 6.1 Hz), 3.68 (dd, 1 H, J = 8.3, 6.7 Hz), 3.03 (dd, 1 H, J = 15.0, 6.3 Hz), 2.96 (dd, 1 H, J = 15.0, 6.3 Hz), 1.43 (s, 3 H), 1.37 (s, 3 H); mass spectrum (70 eV), m/z 168 ($M^+ - CH_3$); $[\alpha]^{24}_D$ +2.9° (c 0.55, $CHCl_3$); exact mass calcd for $C_9H_{13}NO_3 - CH_3$ 168.0661, found 168.0662.

Isoxazole 8. A mixture of 100 mg (0.55 mmol) of **7** and 10 mg of Dowex-50W resin in 5 mL of methanol was stirred at room temperature for 2 h. The mixture was then filtered to remove the resin and evaporated to furnish the free diol as a pale yellow oil: ^1H NMR ($CDCl_3$) δ 8.36 (d, 1 H, J = 1.7 Hz), 6.32 (d, 1 H, J = 1.7 Hz), 4.12 (m, 1 H), 3.75 (dd, 1 H, J = 11.1, 3.4 Hz), 3.58 (dd, 1 H, J = 11.1, 5.1 Hz), 2.90 (m, 2 H).

A solution of the dihydroxy compound in 0.5 mL of dimethyl sulfoxide was added to a solution of 29 mg (0.63 mmol) of 50% NaH in 5 mL of dimethyl sulfoxide. The mixture was stirred at room temperature for 30 min. Benzyl chloride (100 mg, 0.82 mmol) was added, and the mixture was stirred for an additional 3 h. Water was added, and the resulting mixture was extracted with ether (3×). The combined etheral extracts were washed with saturated sodium chloride, dried ($MgSO_4$), and concentrated to give a pale yellow oil. Chromatography over silica gel with hexanes–ethyl acetate (1:1) as eluent afforded three fractions. The least polar fraction was the dibenzylated product. The most polar fraction was the mono-*o*-benzyl ether formed from the secondary alcohol. The intermediate fraction was the monobenzylated isoxazole **8**: IR (thin film) 3390, 2860, 1650, 1560, 1440, 1410, 1110, 790, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.35 (d, 1 H, J = 1.7 Hz), 7.46 (m, 5 H), 6.32 (d, 1 H, J = 1.7 Hz), 4.58 (s, 2 H), 4.20 (m, 1 H), 3.56 (dd, 1 H, J = 9.5, 3.8 Hz), 3.45 (dd, 1 H, J = 9.5, 6.9 Hz), 2.95 (dd, 1 H, J = 15.1, 5.3 Hz), 2.89 (dd, 1 H, J = 15.1, 7.5 Hz); mass spectrum (70 eV), m/z 233 (M^+); exact mass calcd for $C_{13}H_{15}NO_3$ 233.1054, found 233.1052.

(5*RS*)-5-[(Phenylmethoxy)methyl]-3-[(1,3-dioxolan-2-yl)methyl]-4,5-dihydroisoxazole (11). A mixture of 0.9 g (6.1 mmol) of nitro compound **10**, 1.8 g (12.2 mmol) of allyl benzyl ether, 2.9 g (24 mmol) of phenyl isocyanate, and a catalytic amount of triethylamine in 40 mL of benzene was stirred at room temperature overnight. Water was then added, and the mixture was stirred for 8 h and filtered. The precipitate was washed with benzene, and the organic layer was separated, dried ($MgSO_4$), and concentrated to give a yellow oily residue. Chromatography on silica gel with hexanes–ethyl acetate (1:1) gave 1.45 g (85%) of **11** as pale yellow oil which solidified on refrigeration. The spectral data for **11** and the experimental procedures for the conversion of **11** to **17** are the same as reported for the optically active series (**11′** → **17′**).

(5*S*)-5-[(4*R*)-(2,2-Dimethyl-1,3-dioxolan-4-yl)]-3-[(1,3-dioxolan-2-yl)methyl]-4,5-dihydroisoxazole (23). To a mixture of 0.50 g (3.9 mmol) of **22**,[3e] 1.15 g (7.8 mmol) of **10**, and 3.7 g (31 mmol) of phenyl isocyanate in 20 mL of dry benzene at room temperature was added 0.1 mL of triethylamine. The resulting mixture was stirred for 12 h. Water was then added and the mixture was stirred for 8 h and filtered. The organic layer was separated, dried ($MgSO_4$), and concentrated to give a yellow oily residue. The ^1H NMR of the crude product showed two diastereomers in a 79:21 ratio. Chromatography on silica gel with hexanes–ethyl acetate (1:1) as eluent afforded **23**, contaminated with the nitrile oxide dimer, as the major product and 0.14 g (14%) of pure **24** as the minor isomer. Minor isomer: IR (thin film) 2870, 1620, 1370, 1210, 1130, 1065, 940, 880, 850, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.06 (t, 1 H, J = 4.7 H), 4.65 (ddd, 1 H, J = 10.9, 7.7, 5.0 Hz), 4.25 (dt, 1 H, J = 6.4, 5.0 Hz), 4.10–3.79 (m, 6 H), 3.07 (dd, 1 H, J = 17.6, 10.9 Hz), 2.92 (dd, 1 H, J = 17.6, 7.7 Hz), 2.75 (d, 2 H, J = 4.7 Hz), 1.44 (s, 3 H), 1.36 (s, 3 H); mass spectrum (70 eV), m/z 257 (M^+); $[\alpha]^{24}_D$ −44.7° (c 1.250, $CHCl_3$); exact mass calcd for $C_{12}H_{19}NO_5$ 257.1263, found 257.1264.

Pure **23** was prepared by deprotection (Dowex-50X, MeOH) of the acetonide group, purification by chromatography (silica gel, 10:1 $CHCl_3$–MeOH), reprotection [Amberlyst-15, $(CH_3)_2C(OMe)_2$] and chromatography (silica gel, 1:1 hexane–ethyl acetate): IR (thin film) 2870, 1620, 1370, 1210, 1130, 1060, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.07 (t, 1 H, J = 4.7 Hz), 4.50 (ddd, 1 H, J = 10.3, 7.26 , 6.67 Hz), 4.00 (m, 7 H), 3.13 (dd, 1 H, J = 17.6, 10.3 Hz), 3.02 (dd, 1 H, J = 17.6, 6.7 Hz), 2.74 (d, 2 H, J = 4.7 Hz), 1.42 (s, 3 H), 1.35 (s, 3 H); mass spectrum (70 eV), m/z 257 (M^+); $[\alpha]^{24}_D$ +61.4° (c 1.025, $CHCl_3$); exact mass calcd for $C_{12}H_{19}NO_5$ 257.1263, found 257.1263.

(5*S*)-5-[(1*R*)-1,2-Dihydroxyethyl]-3-[(1,3-dioxolan-2-yl)-methyl]-4,5-dihydroisoxazole (25). A mixture of 0.80 g (~75% pure, 2.33 mmol) of **23** and 100 mg of Dowex-50W resin in 40 mL of methanol was stirred at room temperature for 2 h. The reaction mixture was filtered and concentrated to afford a pale yellow oil which was chromatographed on silica gel with chloroform–methanol (10:1) to yield 0.20 g of the nitrile oxide dimer (less polar fraction) and 0.50 g (100%) of **25**: IR (thin film) 3400, 2920, 1600, 1380, 1200, 1130, 1020, 940, 880, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.08 (t, 1 H, J = 4.7 Hz), 4.57 (ddd, 1 H, J = 10.7, 8.1, 5.1 Hz), 4.02–3.60 (m, 7 H), 3.13 (dd, 1 H, J = 17.6, 8.1 Hz), 3.02 (dd, 1 H, J = 17.6, 10.7 Hz), 2.74 (d, 2 H, J = 4.7 Hz); mass spectrum (70 eV), m/z 217 (M^+); $[\alpha]^{24}_D$ +57.4° (*c* 2.64, $CHCl_3$); exact mass calcd for $C_9H_{15}NO_5$ 217.0950, found 217.0947.

(5*S*)-5-(Hydroxymethyl)-3-[(1,3-dioxolan-2-yl)methyl]-4,5-dihydroisoxazole (26). To a solution of 120 mg (0.55 mmol) of diol **25** in 15 mL of MeOH–H_2O (3:1) was added 3 mL (0.69 mmol) of sodium periodate in water (0.23 M). After being stirred at room temperature for 15 min, the mixture was filtered through Celite. The filtrate was added to a suspension of 210 mg (5.5 mmol) of sodium borohydride in 15 mL of methanol at ice-bath temperature over a period of 15 min. The mixture was stirred at that temperature for 30 min, and then 0.5 mL of acetic acid was added dropwise to destroy the excess reagent. The methanol was removed by rotary evaporation, and the residue was diluted with 10 mL of water and extracted twice with ethyl acetate. The combined extracts were dried over anhydrous magnesium sulfate and concentrated to give an oily residue. Chromatography over silica gel with chloroform–methanol (20:1) as eluent afforded 62 mg (60%) of **26** as a colorless oil: IR (thin film) 3495, 2905, 1630, 1400, 1230, 1135, 1040, 950, 890, 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.08 (t, 1 H, J = 4.7 Hz), 4.70 (m, 1 H), 4.05–3.87 (m, 4 H), 3.76 (dd, 1 H, J = 12.1, 3.2 Hz), 3.57 (dd, 1 H, J = 12.1, 4.8 Hz), 3.07 (dd, 1 H, J = 17.4, 10.7 Hz), 2.93 (dd, 1 H, J = 17.4, 7.7 Hz), 2.74 (d, 2 H, J = 4.7 Hz); mass spectrum (70 eV), m/z 187 (M^+); $[\alpha]^{24}_D$ +68.1° (*c* 0.565, $CHCl_3$); exact mass calcd for $C_8H_{13}NO_4$ 187.0845, found 187.0827.

(5*S*)-5-[(Phenylmethoxy)methyl]-3-[(1,3-dioxolan-2-yl)-methyl]-4,5-dihydroisoxazole (11′). Into a 10-mL, round-bottomed flask with side arm was placed 18.5 mg (0.38 mmol) of 50% sodium hydride. The flask was flushed with nitrogen, and the sodium hydride was activated by washing with pentane twice and then with tetrahydrofuran once. To a suspension of the activated sodium hydride in 3 mL of tetrahydrofuran was added 60 mg (0.32 mmol) of **26** in 0.5 mL of tetrahydrofuran at ice-bath temperature. The mixture was stirred for 1 h and 82 mg (0.48 mmol) of benzyl bromide and a catalytic amount of tetra-*n*-butylammonium iodide was added. The resulting mixture was stirred at room temperature for 4 h. Water was added, and the solvent was removed by rotary evaporation. The residue was diluted with 10 mL of water and extracted twice with ethyl acetate. The combined extracts were dried ($MgSO_4$) and concentrated to afford a yellow oil. Chromatography over silica gel with hexanes–ethyl acetate (1:1) as eluent gave 71 mg (80%) of **11′** as a pale yellow oil: IR (thin film) 2870, 1600, 1450, 1355, 1205, 1135, 1030, 945, 885, 825, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.05 (t, 1 H, J = 4.7 Hz), 4.75 (m, 1 H), 4.58 (s, 2 H), 4.00–3.83 (m, 4 H), 3.59 (dd, 1 H, J = 10.3, 5.3 Hz), 3.54 (dd, 1 H, J = 10.3, 4.8 Hz), 3.07 (dd, 1 H, J = 17.4, 10.7 Hz), 2.91 (dd, 1 H, J = 17.4, 7.5 Hz), 2.73 (d, 2 H, J = 4.7 Hz); mass spectrum (70 eV), m/z 277 (M^+); $[\alpha]^{24}_D$ +45.7° (*c* 0.435, $CHCl_3$).

β-Hydroxy Ketone 12′. A mixture of 65 mg (0.23 mmol) of **11′**, 56 mg (0.94 mmol) of acetic acid, and a catalytic amount of Raney nickel in 10 mL of MeOH–H_2O (10:1) was hydrogenated under a hydrogen atmosphere (balloon) for 1.5 h. The catalyst was removed by filtration through Celite. The filtrate was neutralized by the addition of saturated sodium bicarbonate (ca. 1 mL) and concentrated by rotary evaporation. The residue was diluted with 5 mL of water and extracted with ethyl acetate 3 times. The combined extracts were dried ($MgSO_4$) and evaporated to leave an oil. Chromatography over silica gel with hexanes–ethyl acetate as eluent (1:3) afforded 52 mg (80%) of **12′** as a colorless oil: IR (thin film) 3520, 2870, 1720, 1450, 1385, 1125, 1020, 945, 870, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.22 (t, 1 H, J = 5.1 Hz), 4.56 (s, 2 H), 4.30 (m, 1 H), 4.00–3.85 (m, 4 H), 3.48 (m, 2 H), 2.83 (d, 2 H, J = 5.1 Hz), 2.71 (m, 2 H); mass spectrum, m/z (M^+ – 1), 262 (M^+ – H_2O); $[\alpha]^{24}_D$ –11.6° (*c* 0.545, $CHCl_3$); exact mass calcd for $C_{15}H_{20}O_5$ – H_2O 262.1205, found 262.1205.

(2*S*)-2,3-Dihydro-2-[(phenylmethoxy)methyl]-4*H*-pyran-4-one (13′). To a suspension of 130 mg (0.36 mmol) of zinc triflate in 5 mL of methylene chloride was added a solution of 50 mg (0.18 mmol) of **12′** in 1 mL of methylene chloride. The reaction mixture was stirred at room temperature for 15 min and then 3 mL of saturated $NaHCO_3$ were added. The mixture was diluted with 5 mL of water and extracted with methylene chloride twice. The combined extracts were dried ($MgSO_4$) and concentrated to afford a yellow oil. Chromatography over silica gel with hexanes–ethyl acetate (1:1) as eluent gave 33 mg (85%) of **13′** as a colorless oil: IR (thin film) 2870, 1670, 1590, 1390, 1270, 1220, 1100, 1020, 910, 790, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (m, 6 H), 5.43 (d, 1 H, J = 6.1 Hz), 4.62 (m, 3 H), 3.71 (m, 2 H), 2.75 (dd, 1 H, J = 16.8, 14.1 Hz), 2.41 (dd, 1 H, J = 16.8, 3.6 Hz); mass spectrum (70 eV), m/z 218 (M^+); $[\alpha]^{24}_D$ +75.8° (*c* 0.455, $CHCl_3$); exact mass calcd for $C_{13}H_{14}O_3$ 219.0943, found 218.0942.

(2*S*,6*S*)-Tetrahydro-2-methoxy-6-[(phenylmethoxy)-methyl]-4*H*-pyran-4-one (9′). The appropriate amount of concentrated aqueous hydrogen chloride was mixed with methanol to give a ~1 M hydrogen chloride solution. To 10 mL of that solution was added a solution of 85 mg (0.39 mmol) of **13′** in 0.5 mL of methanol. The mixture was stirred at room temperature for 15 min and then quenched with a saturated sodium bicarbonate solution. The methanol was removed by rotary evaporation, and the residue was diluted with 10 mL of water and extracted with ethyl acetate 3 times. The combined extracts were dried ($MgSO_4$) and evaporated to give a yellow oil. Chromatography over silica gel with hexanes–ethyl acetate (2.5:1) afforded 11 mg (10%) of **15′** (R_f 0.36) as a colorless oil, a small amount of **14′** (R_f 0.32), and 77 mg (79%) of **9′** (R_f 0.18) as a colorless oil. **9′**: IR (thin film) 2890, 1730, 1450, 1355, 1285, 1210, 1110, 1040, 970, 790, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.18 (d, 1 H, J = 3.8 Hz), 4.62 (AB q, 2 H, J = 12.1 Hz, ν_{AB} = 12.75 Hz), 4.20 (m, 1 H), 3.64 (dd, 1 H, J = 10.5, 3.4 Hz), 3.56 (dd, 1 H, J = 10.5, 4.9 Hz), 3.37 (s, 3 H), 2.70–2.33 (m, 4 H); mass spectrum (15 eV), m/z 250 (M^+), 218 (M^+ – CH_4O); $[\alpha]^{24}_D$ +48.5° (*c* 0.540, $CHCl_3$); exact mass calcd for $C_{14}H_{18}O_4$ – CH_4O 218.0943, found 218.0944.

Methyl 2,4-Dideoxy-6-*O*-(phenylmethyl)-α-D-*erythro*-hexopyranoside (17′). To a solution of 70 mg (0.28 mmol) of **9′** in 5 mL of tetrahydrofuran cooled to –78 °C was added 350 μL (0.35 mmol) of 1 M L-Selectride (Aldrich) in tetrahydrofuran. The mixture was stirred at that temperature for 1 h and then slowly warmed to 0 °C. Water was carefully added to destroy the excess reagent. The mixture was extracted with ethyl acetate 3 times. The combined extracts were dried over anhydrous magnesium sulfate and evaporated to give an oily residue. Chromatography over silica gel with hexanes–ethyl acetate (1:1) as eluent afforded 53 mg (75%) of **17′** as a colorless oil: IR (thin film) 3570, 2940, 1450, 1365, 1190, 1100, 1040, 785, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 4.92 (d, 1 H, J = 2.8 Hz), 4.60 (s, 2 H), 4.24 (m, 1 H), 4.10 (m, 1 H), 3.55 (m, 2 H), 3.41 (s, 3 H), 1.97–1.64 (m, 4 H); mass spectrum (70 eV), m/z 252 (M^+), 220 (M^+ – CH_4O); $[\alpha]^{24}_D$ +47.1° (*c* 0.595, $CHCl_3$); exact mass calcd for $C_{14}H_{20}O_4$ – CH_4O 220.1099, found 220.1100.

Methyl 3-*O*-(*tert*-Butyldiphenylsilyl)-2,4-dideoxy-6-*O*-(phenylmethyl)-α-D-*erythro*-hexopyranoside (27). A mixture of 50 mg (0.20 mmol) of **17**, 66 mg (0.24 mmol) of *tert*-butylchlorodiphenylsilane and 50 mg (0.40 mmol) of 4-(dimethylamino)pyridine in 1 mL of dimethylformamide was stirred at 70–80 °C for 12 h. After cooling, the mixture was diluted with 10 mL of water and extracted with ether (3×). The combined etheral extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated to give a yellow oil. The crude product was chromatographed over silica gel with hexanes–ethyl acetate (15:1) as eluent to give **27**, in nearly quantitative yield: IR (thin film) 2900, 1960, 1885, 1820, 1465, 1425, 1350, 1190, 1105, 1035, 820, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.78–7.62 (m, 4 H), 7.45–7.22 (m, 11 H), 4.76 (d, 1 H, J = 3.4 Hz), 4.58 (s, 2 H), 4.46 (m, 1 H), 4.16 (m, 1 H), 3.48 (m, 2 H), 3.40 (s, 3 H), 1.80–1.54 (m, 4 H), 1.06 (s, 9 H); $[\alpha]^{24}_D$ +21.6° (*c* 0.51, $CHCl_3$).

Methyl 3-*O*-(*tert*-Butyldiphenylsilyl)-2,4-dideoxy-α-D-*erythro*-hexopyranoside (28). A mixture of 50 mg (0.10 mmol)

of **27** and a catalytic amount of 10% palladium on charcoal in 5 mL of methanol was hydrogenated under a hydrogen atmosphere (balloon) for 24 h. The catalyst was removed by filtration. Evaporation of the solvent and chromatography of the residue over silica gel with hexanes–ethyl acetate (4:1) yielded 37 mg (90%) of **28**: IR (thin film) 3450, 2940, 1960, 1885, 1820, 1420, 1350, 1200, 1110, 1035, 970, 945, 830, 745, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.73–7.70 (m, 4 H), 7.67–7.33 (m, 6 H), 4.74 (d, 1 H, J = 3.4 Hz), 4.35 (m, 1 H), 4.16 (m, 1 H), 3.64–3.45 (m, 2 H), 3.39 (s, 3 H), 1.92–1.48 (m, 4 H), 1.07 (s, 9 H); mass spectrum (70 eV), m/z 343 ($M^+ - 57$); $[\alpha]^{24}_D$ +26.7° (c 0.045, $CHCl_3$); exact mass calcd for $C_{23}H_{32}O_4Si - C_4H_9$ 343.1365, found 343.1366.

Methyl 3-*O*-(*tert*-Butyldiphenylsilyl)-2,4-dideoxy-β-D-*erythro*-hexopyranoside (29). A solution of 20 mg (0.05 mmol) of **28** and a catalytic amount of *p*-toluenesulfonic acid in 5 mL of methanol was stirred at room temperature for 2 days. The solvent was evaporated, and the residue was chromatographed over silica gel with hexanes–ethyl acetate (4:1) as eluent to give 18 mg (90%) of **29**: IR (thin film) 3450, 2940, 1420, 1205, 1180, 1140, 1105, 1030, 935, 890, 820, 740, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.66–7.62 (m, 4 H), 7.47–7.35 (m, 6 H), 4.90 (dd, 1 H, J = 9.7, 2.0 Hz), 4.31 (m, 1 H), 4.17 (m, 1 H), 3.65–3.39 (m, 2 H), 3.54 (s, 3 H), 2.07 (m, 1 H), 1.82 (m, 1 H), 1.43–1.34 (m, 2 H), 1.09 (s, 9 H); mass spectrum (70 eV), m/z 343 ($M^+ - 57$); $[\alpha]^{24}_D$ –11.3° (c 0.195, $CHCl_3$); exact mass calcd for $C_{23}H_{32}O_4Si - C_4H_9$ 343.1366, found 343.1365.

Isoxazoline 30. This compound was prepared in the same manner as described for **11** by using cyclohexene (4 mL) and 200 mg (1.36 mmol) of **10**. The crude product was purified by silica gel chromatography with ethyl acetate–hexanes (2:1) as eluent to afford 172 mg (60%) of **30** as a pale yellow oil: IR (thin film) 2940, 1740, 1600, 1410, 1130, 1040, 945, 890, 830, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.12 (t, 1 H, J = 5.0 Hz), 4.40 (m, 1 H), 4.06–3.82 (m, 4 H), 2.95 (q, 1 H, J = 7.5 Hz), 2.84 (dd, 1 H, J = 15.0, 3.8 Hz), 2.58 (dd, 1, J = 15.0, 4.5 Hz), 2.06–1.20 (m, 8 H); mass spectrum (70 eV), m/z 211 (M^+); exact mass calcd for $C_{11}H_{17}NO_3$ 211.1208, found 211.1209.

β-Hydroxy Ketone 31. Isoxazoline **30** (211 mg, 1 mmol) was hydrogenated in the same fashion as described for **11′** to afford 150 mg (70%) of pure **31** as a colorless oil after chromatography on silica gel with hexanes–ethyl acetate (1.5:1) as solvent: IR (thin film) 3510, 2940, 1695, 1390, 1125, 1030, 970, 915, 890, 850, 835, 790 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.25 (t, 1 H, J = 5.0 Hz), 4.28 (m, 1 H), 4.00–3.85 (m, 4 H), 3.14 (m, 1 H), 2.90 (dd, 1 H, J = 15.8, 5.4 Hz), 2.82 (dd, 1 H, J = 15.8, 5.0 Hz), 2.51 (qd, 1 H, J = 10.7, 2.2 Hz), 1.93–1.20 (m, 7 H); mass spectrum (70 eV), m/z 214 (M^+).

Dihydro-4*H*-pyran-4-one 32. This compound was prepared from 220 mg (1.03 mmol) of **31** in a fashion identical with that described for the transformation of **12′** to **13′**. The crude product was chromatographed on silica gel with hexanes–ethyl acetate (3:1) to yield 110 mg (70%) of **32** as a colorless oil: IR (thin film) 2940, 1665, 1600, 1440, 1400, 1280, 1260, 1210, 1050, 990, 940, 810, 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (d, 1 H, J = 6.1 Hz), 5.34 (dd, 1 H, J = 6.1, 1.0 Hz), 4.53 (m, 1 H), 2.30 (ddd, 1 H, J = 11.7, 4.4, 3.6 Hz), 2.10 (m, 1 H), 1.80–1.20 (m, 7 H); mass spectrum (70 eV), m/z 152 (M^+); exact mass calcd for $C_9H_{12}O_2$ 152.0836, found 152.0837.

Compounds **37–43** were likewise prepared by procedures identical with those described for the preparation of **11**, **12′**, and **13′**. Spectral data for compounds **39a**, **39b**, and **43** follow.

39a (major isomer): IR (thin film) 2940, 1665, 1610, 1390, 1240, 1090, 1005, 965, 835, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.30 (s, 1 H), 4.31 (td, 1 H, J = 14.4, 3.2 Hz), 3.95 (m, 1 H), 2.71 (dd, 1 H, J = 17.0, 14.8 Hz), 2.43 (dd, 1 H, J = 17.0, 3.2 Hz), 2.00 (s, 3 H), 1.48 (m, 2 H), 0.94 (t, 3 H, J = 7.5 Hz), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); mass spectrum (70 eV), m/z 285 ($M^+ + 1$), 269 ($M^+ - CH_3$), 227 ($M^+ - C_4H_9$); exact mass calcd for $C_{15}H_{28}O_3Si - CH_3$ 269.1573, found 269.1572.

39b (major isomer): IR (thin film) 2940, 1665, 1610, 1390, 1325, 1235, 1085, 1030, 950, 930, 890, 810, 740, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (m 5 H), 5.33 (s, 1 H), 4.67 (AB q, 2 H, J = 11.6 Hz, ν_{AB} = 13.5 Hz), 4.41 (td, 1 H, J = 14.1, 3.6 Hz), 3.68 (ddd, 1 H, J = 6.3, 4.9, 3.8 Hz), 2.70 (dd, 1 H, J = 16.8, 14.1 Hz), 2.41 (ddd, 1 H, J = 16.8, 3.6, 1.0 Hz), 2.01 (d, 3 H, J = 0.4 Hz), 1.80–1.50 (m, 2 H), 0.98 (t, 3 H, J = 7.4 Hz); mass spectrum (70 eV), m/z 202 ($M^+ - C_3H_6O$), 169 ($M^+ - C_7H_7$); exact mass calcd for $C_{16}H_{20}O_3 - C_1H_6O$ 202.0994, found 202.0995.

43: IR (thin film) 2940, 1665, 1725, 1450, 1370, 1295, 1165, 1085, 1025, 965, 920, 850, 735, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.30 (m, 6 H), 4.50 (m, 2 H), 4.35 (dd, 1 H, J = 14.0, 3.9 Hz), 3.30 (AB q, 2 H, J = 8.7 Hz, ν_{AB} = 38.4 Hz), 2.57 (dd, 1 H, J = 15.6, 14.0 Hz), 2.40 (dd, 1 H, J = 15.6, 3.9 Hz), 1.68 (s, 3 H), 1.03 (s, 3 H), 0.96 (s, 3 H); mass spectrum (70 eV), m/z 274 (M^+); exact mass calcd for $C_{17}H_{22}O_3$ 274.1569, found 274.1566.

Isoxazole 47. A mixture of 340 mg (0.8 mmol) of isoxazoline **46** and 2 g (23 mmol) of manganese dioxide in 20 mL of dry benzene was refluxed overnight. The water formed was removed by means of a Dean–Stark trap. After filtration, the crude product was chromatographed on silica gel with hexanes–ethyl acetate (3:1) to afford 170 mg (50%) of **47** as a pale yellow oil: IR (thin film) 2940, 1602, 1440, 1250, 1135, 1120, 1075, 1030, 1020, 905, 835, 805, 775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.91 (s, 1 H), 4.63 (br s, 1 H), 4.02–3.48 (m, 5 H), 2.94 (t, 2 H, J = 6.8 Hz), 2.77 (dd, 1 H, J = 15.0, 6.3 Hz), 2.57 (dd, 1 H, J = 15.0, 8.3 Hz), 1.88–1.15 (m, 15 H), 0.94 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); mass spectrum (70 eV), m/z 423 (M^+), 366 ($M^+ - C_4H_9$).

Spiro Compound 48. Isoxazole **47** (35 mg, 0.083 mmol) was hydrogenated in the same fashion as described for **11′**. The crude product was chromatographed with hexanes–ethyl acetate (2:1) to give 20 mg (57%) of the enamino ketone as a pale yellow oil: IR (thin film) 2940, 1625, 1525, 1440, 1340, 1250, 1135, 1115, 1075, 1060, 1035, 1020, 835, 805, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.72 (br s, 1 H), 5.74 (br s, 1 H), 5.0 (s, 1 H), 4.62 (br s, 1 H), 3.99–3.45 (m, 5 H), 2.41 (t, 2 H, J = 5.7 Hz), 2.31 (dd, 1 H, J = 14.8, 5.7 Hz), 2.15 (dd, 1 H, J = 14.8, 8.3 Hz), 2.00–1.18 (m, 15 H), 0.91 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); mass spectrum (70 eV), m/z 368 ($M^+ - C_4H_9$), 284 ($M^+ - C_4H_9 - C_5H_9O$); exact mass calcd for $C_{23}H_{43}NO_4Si - C_4H_9$ 368.2257, found 368.2256.

To a solution of 20 mg (0.047 mmol) of the hydrogenated product in 2 mL of benzene at room temperature was added 6 drops of 6 M hydrochloric acid. The mixture was stirred for 30 min, then quenched with saturated sodium bicarbonate, and extracted with benzene. The combined extracts were dried ($MgSO_4$) and evaporated to give a yellow oil. The crude product was chromatographed over silica gel with hexanes–ethyl acetate (3:1) to afford 3.0 mg (30% based on the enamino ketone, or 17% based on **47**) of **48** as a pale yellow oil: IR (thin film) 2940, 1725, 1340, 1325, 1310, 1260, 1155, 1065, 1015, 975, 950, 880, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.27–3.89 (m, 3 H), 2.79–2.45 (m, 3 H), 2.37–2.23 (m, 2 H), 2.20–1.80 (m, 2 H), 1.75–1.15 (m, 8 H); mass spectrum (70 eV), m/z 210 (M^+); exact mass calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1257.

Acknowledgment. We are indebted to the National Institutes of Health (Grant No. HL20579) for their generous support of these investigations. We thank Mr. Arun K. Ghosh for the preparation of compound **43**.

Registry No. **1**, 15186-48-8; **2**, 94370-97-5; **3**, 94370-98-6; **4**, 94370-99-7; **5**, 94371-00-3; **6** (R = Me), 4915-22-4; **6** (R = Et), 4915-21-3; **7**, 94404-07-6; **8**, 94371-01-4; 8 (diol), 94371-29-6; (±)-**9**, 80127-51-1; **9′**, 94480-26-9; **10**, 82891-99-4; (±)-**11**, 94371-02-5; **11′**, 94480-27-0; (±)-**12**, 94371-03-6; **12′**, 94480-28-1; (±)-**13**, 80127-39-5; **13′**, 94480-29-2; (±)-**14**, 80127-49-7; (±)-**15**, 80127-50-0; **15′**, 94480-30-5; DL-**16**, 80127-53-3; DL-**17**, 80127-52-2; **17′**, 94371-04-7; DL-*erythro*-**18**, 94371-05-8; DL-*threo*-**18**, 94371-06-9; **22**, 62214-38-4; **23**, 90344-31-3; **24**, 90344-32-4; **25**, 94371-07-0; **26**, 94371-08-1; **27**, 94371-09-2; **28**, 86030-95-7; **29**, 86030-94-6; (±)-**30**, 94371-10-5; (±)-**31**, 94371-11-6; (±)-**32**, 94371-12-7; (±)-**34**, 94371-13-8; **35**, 79958-77-3; (±)-**36a**, 94371-14-9; (±)-**36b**, 94371-15-0; (±)-**37a**, 94371-16-1; (±)-**37b**, 94371-17-2; (±)-**38a**, 94371-18-3; (±)-**38b**, 94371-19-4; (±)-(*R**,*R**)-**39a**, 94371-20-7; (±)-(*R**,*S**)-**39a**, 94371-31-0; (±)-(*R**,*R**)-**39b**, 94371-21-8; (±)-(*R**,*S**)-**39b**, 94371-32-1; (±)-**40**, 94371-22-9; **41**, 19757-86-9; **42**, 94371-23-0; (±)-**43**, 94371-24-1; **46**, 94371-25-2; (±)-**47**, 94371-26-3; (±)-**47** (enamino ketone deriv), 94371-30-9; (±)-**48** (isomer 1), 94371-27-4; (±)-**48** (isomer 2), 94480-31-6; $HO(CH_2)_2OH$, 107-21-1; CH_2=C-HCHO, 107-02-8; $MeNO_2$, 75-52-5; HC≡COEt, 927-80-0; CH_2=CHBr, 593-60-2; CH_2=$CHCH_2OCH_2C_6H_5$, 14593-43-2; 2,2-dimethyl-α-(nitromethyl)-1,3-dioxolane-4-methanol, 94371-28-5; (4*S*)-2,2-dimethyl-4-(2-nitrovinyl)-1,3-dioxolane, 81893-44-9; cyclohexene, 110-83-8; 2-(2-bromoethyl)-1,3-dioxolane, 18742-02-4.