a small AB q appeared at 5.36 and 5.50, $J$ = 13.0 Hz; IR (neat) 3385 (br O–H), 1635 (C=O), 1579, 1304, 1274, 1012, 873, 748, 723, 694 cm$^{-1}$; MS (EI), $m/e$ (rel intensity) 262 ($M^+$, 97), 245 (44), 244 (100), 215 (66), 128 (35), 127 (42), 105 (37), 77 (76); HRMS found 262.0994, calcd for $C_{18}H_{14}O_2$ 262.0998.

**1,3-Dihydro-1-hydroxy-1-phenylnaphtho[1,2-*c*]furan (80) [1-Benzoyl-2-naphthalenemethanol (81)].** This tautomeric mixture was prepared from **28** by using the method described for the preparation of **76**/**77**. The $^1$H NMR spectrum showed the product to be a tautomeric mixture of 54% **81** and 46% **80**: $^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 1.95 (br s, 1 H, exchanges with $D_2O$), 4.64 (s, 2 H chain), 5.36 and 5.45 (AB q, $J$ = 13.1 Hz, 2 H ring), 7.21–7.66 (m, 11 H); IR (neat) 3419 (br O–H), 1662 (C=O), 1025, 813, 763, 699 cm$^{-1}$; MS (EI), $m/e$ (rel intensity) 262 ($M^+$, 59), 245 (40), 244 (100), 215 (67), 185 (33), 127 (28), 105 (30), 77 (46); HRMS found 262.0994, calcd for $C_{18}H_{14}O_2$ 262.0993.

**Acknowledgment.** This work could not have been completed without the generous support of several people following the untimely death of research director Dr. James G. Smith in 1985. We thank Dr. D. A. Brodie, Dean of Science, and Drs. A. J. Carty, R. G. Woolford, R. Rodrigo, and G. Lajoie, Department of Chemistry, University of Waterloo, for financial and moral support. We also thank Mrs. J. H. Venne for her assistance with much of the NMR work and Dr. Richard Smith and co-workers at the McMaster Regional Centre for Mass Spectrometry (funded by a major installation grant from the Natural Science and Engineering Research Council of Canada) for their work.

**Registry No.** **8**, 38399-19-8; **11**, 18982-54-2; **12**, 114468-79-0; **14**, 37806-17-0; **15**, 26904-03-0; **16**, 114468-80-3; **17**, 114529-97-4; **18**, 31790-95-1; **20**, 114468-81-4; **21**, 114468-82-5; **22**, 114468-83-6; **23**, 114530-85-7; **24**, 114468-84-7; **25**, 114468-85-8; **26**, 114529-98-5; **27**, 114468-86-9; **28**, 114468-87-0; **29**, 76635-70-6; **30**, 114468-88-1; **31**, 114468-89-2; **32**, 114468-90-5; **33**, 86853-93-2; **34**, 114468-91-6; **35**, 114529-99-6; **36**, 114468-92-7; **38**, 114468-93-8; **39**, 114468-94-9; **40**, 114468-95-0; **41**, 3378-82-3; **42**, 114468-96-1; **43**, 114468-97-2; **45**, 114468-99-4; **46A**, 114469-00-0; **46B**, 25308-63-8; **47A**, 114469-01-1; **47B**, 5345-98-2; **48**, 89005-09-4; **49A**, 114530-00-6; **49B**, 114468-75-6; **49C**, 114468-76-7; **49D**, 114578-93-7; **50A**, 114530-01-7; **50B**, 114468-77-8; **50C**, 114468-78-9; **50D**, 114529-96-3; **51**, 103668-59-3; **52**, 114469-02-2; *cis*-**53**, 114468-98-3; *trans*-**53**, 114469-03-3; **54**, 103668-60-6; **55**, 114469-04-4; **56**, 114469-05-5; **58**, 114469-06-6; **59**, 114530-02-8; **60**, 114469-07-7; **61**, 114469-08-8; **62**, 114469-09-9; **64**, 114469-10-2; **65**, 114469-11-3; **68**, 114469-12-4; **69**, 114469-13-5; **76**, 114469-14-6; **77**, 100560-58-5; **78**, 114469-15-7; **79**, 114469-16-8; **80**, 114469-17-9; **81**, 114469-18-0; MA, 108-31-6; PhCN, 100-47-0; $CH_2$=$CHCO_2CH_3$, 96-33-3; PhCHO, 100-52-7; 1,4-naphthoquinone, 130-15-4; 1,4-benzoquinone, 106-51-4; 2-naphthaldehyde, 66-99-9.

# Synthesis of a Structurally Modified Glycal. (–)-(2*R*,4*S*)-2-Methyl-2-vinyl-4-(benzyloxy)-3,4-dihydro-2*H*-pyran

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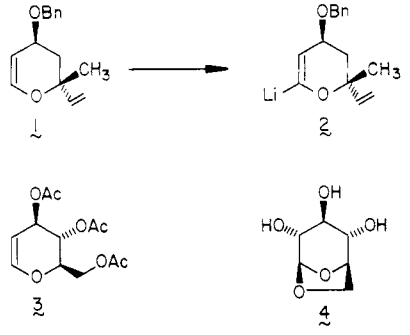
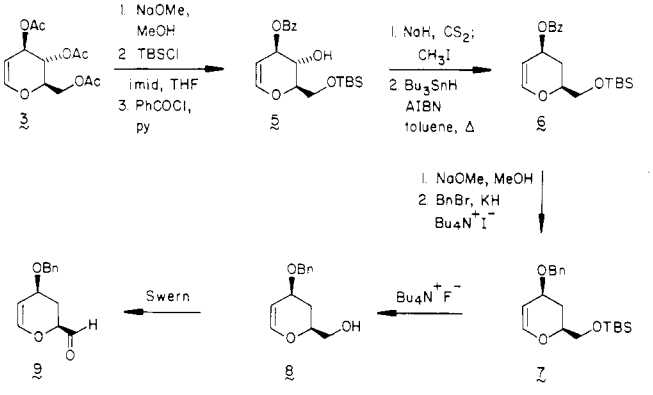
A synthetic procedure for the transformation of levoglucosan (**4**) to (–)-(2*R*,4*S*)-2-methyl-2-vinyl-4-(benzyloxy)-3,4-dihydro-2*H*-pyran (**1**) in 11 steps is described. The scheme relies on selective deoxygenation of the pair of $\alpha$-hydroxyl groups, blocking of the $\beta$-hydroxyl, and formation of ester **16**. The presence of the carboxylate group allows for stereocontrolled methylation of the enolate anion, conversion of ester to vinyl, and ultimate eliminative removal of the methoxyl substituent in methyl glycoside **25**. This key transformation takes advantage of regioselective acetal cleavage by trimethylsilyl iodide and in situ dehydroiodination of the product so formed with hexamethyldisilazane. Certain unsuccessful attempts to form the $\alpha$-lithio anion of **1** are also discussed.

In connection with a convergent synthesis of forskolin projected to utilize oxyanionic Cope rearrangement chemistry subsequent to a kinetic resolution,[1] a quantity of optically pure **1** was required as a prelude to its metalation as in **2**. The stereocontrolled C-5 alkylation of glycosides




**Scheme I**




or glycals appears to be a fundamental problem in the carbohydrate area that has not yet been meaningfully investigated. To us, the stereochemical correspondence at C-2 between **1** and tri-*O*-acetyl-D-glucal (**3**)[3a] as well as

(1) Oplinger, J. A.; Paquette, L. A. *Tetrahedron Lett.* **1987**, *28*, 5441.

0022-3263/88/1953-2953$01.50/0 

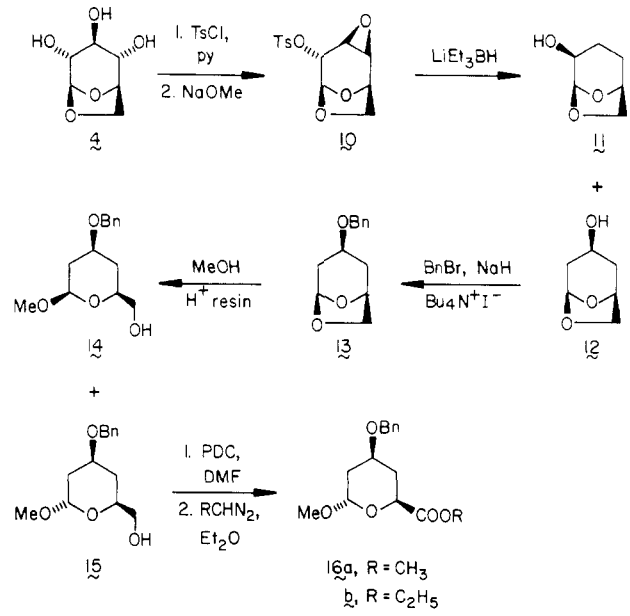
levoglucosan (4)[3b] suggested that one or both of these readily available carbohydrate derivatives could serve as practical starting materials. The following experiments were undertaken to evaluate their feasibility as precursors.

The first approach began with the conversion of **3** to **5** along the lines adopted by Ireland[4] in the early stages of his tirandamycic acid synthesis (Scheme I). Early attempts at reductive removal of the C-3 hydroxyl group focused on lithium triethylborohydride reduction of the derived tosylate. When this protocol and that recommended by Prugh and Deana ($NaBH_4$, DMSO, 80 °C)[5] did not deliver **6**, **5** was transformed instead into its xanthate, and deoxygenation was effected under free radical conditions.[6] Significantly, the "standard" conditions for xanthate formation (NaH in refluxing THF followed by introduction of $CS_2$) failed, perhaps because of rapid silyl migration.[7] However, recourse to carbon disulfide as solvent successfully eliminated this competing reaction, these conditions leading to the xanthate in quite respectable yield. Reductive deoxygenation proved most efficient (72%) when performed with 5 equiv of the tin hydride reagent in toluene at 110 °C for 1.5 h.

Ester hydrolysis with sodium methoxide in methanol and subsequent O-benzylation[4] proceeded in a straightforward manner to provide dihydropyran **7**. Arrival at the desired aldehyde **9** was achieved by desilylation of **7** and Swern oxidation of the resulting alcohol **8**. However, all attempts to C-methylate the *tert*-butyl imine[8] of **9** failed to give any recognizable product and caused abandonment of this approach to **1**.

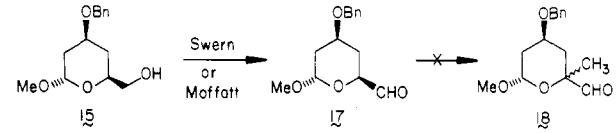
The second approach (Scheme II) began with the ditosylation of **4** and regioselective cyclization in the presence of sodium methoxide to provide epoxide **10**.[9] Treatment of the crystalline epoxide **10** with lithium triethylborohydride furnished in >95% yield a 1:6 mixture of **11** and **12**,[10] the separation of which could be achieved by flash chromatography. (Separation was more efficiently effected as their benzyl ethers, however.) Benzylation of the predominant isomer (**12**) and exposure of **13** to acidic ion exchange resin in methanol[11] led to an approximate 1:5 mixture of the $\beta$- and $\alpha$-methyl glycosides **14** and **15**. The major component, obtained in pure condition by chromatography on silica gel, was oxidized with 4 equiv of pyridinium dichromate.[12] Direct esterification of the carboxylic acid so produced with diazomethane or diazoethane produced **16a** and **16b**, respectively.

**Scheme II**



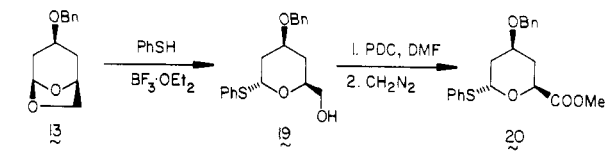

**16a**, R = $CH_3$
**b**, R = $C_2H_5$

The conversion to these esters was implemented following our total inability to alkylate aldehyde **17** with methyl iodide. Oxidation of **15** to **17** was best achieved




under modified Swern (88%)[13] or Moffatt conditions (90%),[14] with anhydrous workup proving essential to success in either case. Of the numerous conditions examined for transforming **17** to **18** (for example, KH, THF, then $CH_3I$;[15] *t*-$BuNH_2$, $C_2H_5MgBr$, $CH_3I$;[8] $NaNH_2$, KO-*t*-Bu, DME, $CH_3I$;[16] KOH (6 equiv), DME, $CH_3I$, 25 °C[17]), no evidence was gained for the formation of C-alkylated product, although in some cases minor amounts of O-methylated material was detected.

The peculiarities associated with **9** and **17** were not entirely restricted to aldehydes. Thus, methyl ester **20**, prepared from 1,6-anhydro compound **13** by Lewis acid catalyzed ring opening in the presence of thiophenol,[18] oxidation of the single alcohol so produced, and esterification, was likewise not successfully methylated under any of the conditions that were attempted.




Fortunately, these complications did not present themselves with either **16a** or **16b**. Both esters were readily alkylated under standard conditions to deliver a 5:1 mixture of **21** and **22** (Scheme III). Following reduction of either pair of esters with diisobutylaluminum hydride in ether at −78 °C, aldehydes **23** and **24** were obtained and

(2) The divergence in the numbering schemes utilized by carbohydrate chemists for glycals and by *Chemical Abstracts* for dihydropyrans can prove exasperating. Hereafter in this paper, only the latter system is employed for consistency.

(3) (a) Commercially available from the Aldrich Chemical Co., Milwaukee, WI, and the Pfanstiehl Laboratories, Waukegan, IL. (b) Available from the pyrolysis of corn starch: Ward, R. B. *Methods Carbohydr. Chem.* **1963**, *2*, 394.

(4) Ireland, R. E.; Wuts, P. G. M.; Ernst, B. *J. Am. Chem. Soc.* **1981**, *103*, 3205.

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

(6) (a) For a review dealing with the radical deoxygenation of alcohols, see: Hartwig, W. *Tetrahedron* **1983**, *39*, 2609. (b) For the deoxygenation of xanthates, consult: Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

(7) A similar chemical event has been mentioned in a review of mevinic acid synthesis: Heathcock, C. H.; Rosen, T. *Tetrahedron* **1986**, *42*, 4909.

(8) Buchi, G.; Powell, J. E., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 3126.

(9) Cerny, M.; Kalvoda, L.; Pacak, J. *Collect Czech. Chem. Commun.* **1967**, *33*, 1143.

(10) Kelly, A. G.; Roberts, J. S. *Carbohydr. Res.* **1979**, *77*, 231.

(11) Kelly, A. G.; Roberts, J. S. *J. Chem. Soc., Chem. Commun.* **1980**, 228.

(12) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, *20*, 399.

(13) Mancuso, A. J.; Huang, S. L.; Swern, D. J. *J. Org. Chem.* **1978**, *43*, 2480.

(14) Pfitzner, K. W.; Moffatt, J. G. *J. Am. Chem. Soc.* **1965**, *87*, 5661.

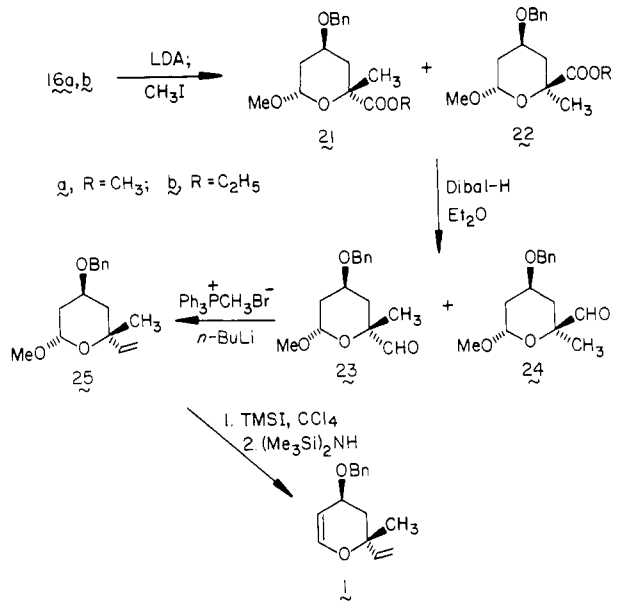
(15) Groenewegan, P.; Kallenberg, H.; Van der Gen, A. *Tetrahedron Lett.* **1978**, *19*, 49.

(16) Carre, M. C.; Ndebeka, G.; Riondel, A.; Bourgasser, P.; Caubere, P. *Tetrahedron Lett.* **1984**, *25*, 1551.

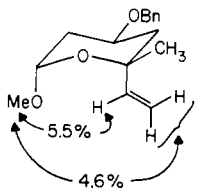
(17) Artaud, I.; Torossian, G.; Viout, P. *Tetrahedron* **1985**, *41*, 5031.

(18) Boehme, F. *Chem. Ztg.* **1972**, *96*, 37.

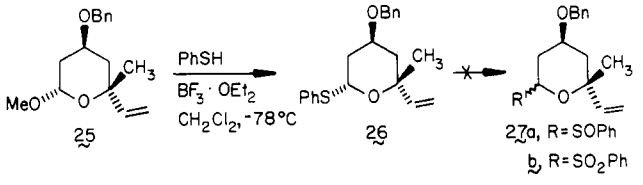
**Scheme III**



separated chromatographically. Proper stereochemical differentiation of these epimers was realized by subjecting the major constituent to Wittig methylenation. Difference NOE experiments were performed on **25**. Double irradiation of the methyl ether singlet produced enhancements of 5.5 and 4.6% for the vinyl protons as indicated in the illustration. The quaternary methyl singlet was not at all affected.



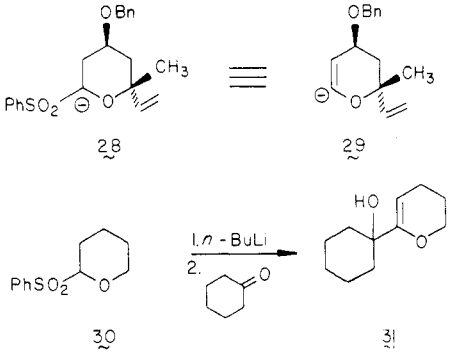
With **25** in hand, the stage was now set for conversion to title compound **1**. In principle, conversion to sulfoxide **27a** would provide an opportunity for subsequent thermal



elimination. To this end, the conversion of methyl glycoside **25** to **26** was first pursued. This transformation was easily accomplished in 97% yield through use of thiophenol and boron trifluoride etherate in dichloromethane at −78 °C. The single stereoisomer isolated has been tentatively assigned the $\alpha$ configuration. However, attempts to achieve sulfoxide formation failed to produce a characterizable product. Degradation was chiefly operational in these reactions, possibly stemming from accelerated ionization at C-6.

As a consequence of these difficulties, an alternate route based on the elimination of methanol from **25** was given attention. After considerable experimentation it was uncovered that trimethylsilyl iodide acts on **25** in carbon tetrachloride at −20 °C to effect regiocontrolled ether cleavage. Addition of hexamethyldisilazane 10 min later reproducibly provided **1** in 67% yield.

The metalation of vinyl ethers has generated considerable recent interest because of numerous successful applications in organic synthesis.[19] We have not found it possible to achieve direct conversion of **1** to its $\alpha$-lithio derivative, or even to prepare a trialkyltin intermediate.[20] In the belief that the benzyl blocking group may be a possible source of the problem, an investigation was mounted to gain access to sulfone **27b**. The intent was to increase substantially the acidity of H-6 (see **28**), while at



the same time taking advantage of the synthon relationship between **28** and **29**. Ley and his co-workers have detailed the efficacy with which the anion of **30** condenses with carbonyl compounds to give dihydropyranyl addition products by spontaneous elimination of benzenesulfinic acid.[21] Since all methods to prepare **27b** met with degradation problems similar to those encountered in the earlier sulfoxide work, it would appear that the additional substituents in **27** so activate the tetrahydropyran ring that ionization at C-6 operates too readily.[22]

In summary, a synthetic route to **1** has been developed. Although 2-carboxaldehyde intermediates have proven too sensitive for proper $\alpha$-alkylation, carboxylate esters serve as conveniently available, reactive substrates. The approach outlined here is presented as a utilitarian synthetic entry to little known 2,2-disubstituted glycals.

## Experimental Section

**(−)-(2R,3R,4R)-2-(((*tert*-Butyldimethylsilyl)oxy)-methyl)-3-hydroxy-4-(benzoyloxy)-3,4-dihydro-2H-pyran (5).** A solution of **3** (20 g, 73.4 mmol) in 100 mL of methanol was treated with methanolic sodium methoxide (1.0 mL of 2.0 M), magnetically stirred at 25 °C for 3 h, and concentrated. Rapid elution of the residue through a short column of silica gel (elution with 30% acetone in ether) left 10.8 g (99%) of the triol as a flaky white solid.

This material was taken up into dry dimethylformamide (100 mL) and treated successively with imidazole (10.99 g, 162 mmol) and *tert*-butyldimethylsilyl chloride (12.2 g, 80.8 mmol). The reaction mixture was stirred at 25 °C for 12 h, diluted with ether (400 mL), and washed with water (2 × 150 mL) and copper(II) sulfate solution (2×). The combined aqueous layers were reextracted with ether, and the total organic solution was dried and concentrated. The resulting oil was purified by silica gel chromatography to give 18.0 g (94%) of monosilyl ether as a clear colorless oil homogeneous by TLC analysis: IR (neat, $cm^{-1}$) 3350, 2960, 2935, 2890, 2865, 1650, 1488, 1472, 1367, 1261, 1240, 1110, 1060, 945, 880, 840, 783, 760; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 6.27 (dd, $J$ = 6.06, 1.7 Hz, 1 H), 4.68 (dd, $J$ = 6.07, 1.8 Hz, 1 H), 4.27

(19) Review: Leaver, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943.
(20) (a) Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E. *J. Chem. Soc., Chem. Commun.* **1986**, 925. (b) Hanessian, S.; Martin, M.; Desai, R. C. *Ibid.* **1986**, 926. (c) Lesimple, P.; Beau, J.-M.; Jaurand, G.; Sinay, P. *Tetrahedron Lett.* **1986**, *27*, 6201.
(21) (a) Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985**, *26*, 535. (b) Ley, S. V.; Lygo, B.; Sternfeld, F.; Wonnacott, A. *Tetrahedron* **1986**, *42*, 4333.
(22) Following completion of this work, there appeared a report [Boechman, R. K., Jr.; Charette, A. B.; Asberom, T.; Johnston, B. H. *J. Am. Chem. Soc.* **1987**, *109*, 7553] of similar difficulties in achieving deprotonation of a substituted glycal.

(m, 1 H), 3.8 (m, 5 H), 0.89 (s, 9 H), 0.08 (s, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 144.07, 102.47, 77.17, 71.49, 69.42, 63.44, 25.86, 18.30, −5.33, −5.41 ppm; $[\alpha]^{25}_D$ +1.29° (*c* 2.48, $CHCl_3$).

Anal. Calcd for $C_{12}H_{24}O_4Si$: C, 55.35; H, 9.29. Found: C, 55.86; H, 9.40.

To a cold (−35 °C), magnetically stirred solution of the preceding diol (7.55 g, 29.0 mmol) in 50 mL of dry pyridine were added 4-(dimethylamino)pyridine (354 mg) and then benzoyl chloride (3.48 mL, 30 mmol) neat via syringe. The reaction mixture was allowed to warm to 0 °C during 3 h and subsequently to 25 °C over 9 h prior to pouring into ether (200 mL). This solution was washed with water (2 × 100 mL) and copper(II) sulfate solution (2 × 100 mL). The combined aqueous washings were back-extracted with ether (2 × 50 mL), and the total organic solution was dried and concentrated. The residue was purified by chromatography (silica gel, elution with 10% ether in petroleum ether) to provide 8.1 g (77%) of **5** as a clear colorless oil homogeneous by TLC analysis: IR (neat, $cm^{-1}$) 3615, 3466, 2956, 2931, 2886, 2856, 1714, 1647, 1602, 1472, 1464, 1451, 1317, 1269, 1170, 1106, 1028, 839, 705; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05 (m, 2 H), 7.55 (m, 1 H), 7.42 (m, 2 H), 6.47 (dd, *J* = 6.1, 1.3 Hz, 1 H), 5.54 (dt, *J* = 6.57, 1.77 Hz, 1 H), 4.82 (dd, *J* = 6.07, 2.58 Hz, 1 H), 4.14 (t, *J* = 7.9 Hz, 1 H), 3.95 (m, 3 H), 3.54 (s, 1 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.10 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 167.31, 146.10, 133.13, 129.82, 129.72, 128.28, 98.74, 77.99, 73.38, 68.15, 62.63, 25.85, 18.31, −5.38, −5.41 ppm; $[\alpha]^{25}_D$ −73.6° (*c* 5.78, $CHCl_3$).

Anal. Calcd for $C_{19}H_{28}O_5Si$: C, 62.61; H, 7.74. Found: C, 62.76; H, 7.95.

**(−)-(2*S*,4*S*)-2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-(benzoyloxy)-3,4-dihydro-2*H*-pyran (6).** To a magnetically stirred suspension of sodium hydride (216 mg of 97%, 8.7 mmol) in 25 mL of carbon disulfide was added a solution of **5** (1.59 g, 4.30 mmol) in 3 mL of the same solvent. After 4 h, neat methyl iodide (1.36 mL, 21.8 mmol) was introduced via syringe. The reaction mixture was stirred for 12 h before dilution with ether and washing with water and ammonium chloride solution. Following drying and solvent evaporation, the residue was purified by chromatography (silica gel, elution with 10–30% ether in petroleum ether) to give 1.68 g (87%, 98% based on recovered **5**) of xanthate as a clear colorless oil homogeneous by TLC analysis: IR (neat, $cm^{-1}$) 2950, 2926, 2861, 1724, 1648, 1473, 1464, 1454, 1384, 1318, 1266, 1206, 1106, 1071, 1027, 1008, 977, 841, 781, 718; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 2 H), 7.55 (m, 1 H), 7.22 (m, 2 H), 6.55 (dd, *J* = 6.18, 1.06 Hz, 1 H), 6.34 (t, *J* = 5.3 Hz, 1 H), 5.59 (m, 1 H), 5.02 (m, 1 H), 4.39 (m, 1 H), 3.95 (m, 2 H), 2.55 (s, 3 H), 0.90 (s, 9 Hz), 0.08 (s, 3 H), 0.07 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 214.55, 165.57, 146.16, 133.13, 129.86, 129.80, 128.34, 97.86, 76.24, 75.12, 66.69, 60.95, 25.86, 18.32, −5.29, −5.37 ppm; MS *m*/*z* ($M^+ - C(CH_3)_3$) calcd 397.0500, obsd 397.0527; $[\alpha]^{25}_D$ −145.8° (*c* 1.72, $CHCl_3$).

Anal. Calcd for $C_{21}H_{30}O_5S_2Si$: C, 55.48; H, 6.65. Found: C, 55.67; H, 6.84.

To a magnetically stirred solution of 2.63 g (5.94 mmol) of the xanthate and ca. 20 mg of AIBN in 15 mL of anhydrous toluene was added 8.0 mL (29.72 mmol) of tri-*n*-butyltin hydride. The resulting solution was stirred at the reflux temperature for 1.5 h. The reaction contents were cooled, concentrated in vacuo, and flushed rapidly through a short column of silica gel. Following elution with petroleum ether to remove higher $R_f$ byproducts, use of 5% anhydrous ether in petroleum ether effected elution of **6** (1.5 g, 72%) as a clear, colorless oil. Although stable for short periods of time on "wet" silica gel, **6** rapidly decomposes to base-line material on dry silica gel as witnessed by spotting a TLC plate and allowing only 60 s before developing; none of the initially spotted material was seen: IR ($CHCl_3$, $cm^{-1}$) 3060, 2950, 2855, 1720, 1638, 1598, 1580, 1467, 1458, 1446, 1385, 1355, 1310, 1265, 1235, 1172, 1105, 1065, 1022, 1000, 958, 920, 845, 775, 710, 685, 665; $^1$H NMR (300 MHz, $CDCl_3$) δ 8.05–8.02 (m, 2 H), 7.58–7.52 (m 1 H), 7.46–7.40 (m, 2 H), 6.50 (d, *J* = 6 Hz, 1 H), 5.66–5.60 (m, 1 H), 4.90 (ddd, *J* = 6.2, 2.7, 1.0 Hz, 1 H), 4.20–4.12 (m, 1 H), 3.82 (AB of ABX, Δν = 34.1 Hz, $J_{AB}$ = 10.8 Hz, $J_{AX}$ = 5.7 Hz, $J_{BX}$ = 5.1 Hz), 2.41–2.30 (m, 1 H), 2.05–1.95 (m, 1 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.075 (s, 3 H); MS *m*/*z* ($M^+ - C(CH_3)_3$) calcd 291.1052, obsd 291.1045; $[\alpha]^{25}_D$ −74.8° (*c* 1.73, $CHCl_3$).

Anal. Calcd for $C_{19}H_{28}O_4Si$: C, 65.48; H. 8.10. Found: C, 65.29; H, 8.11.

**(−)-(2*S*,4*S*)-2-(((*tert*-Butyldimethylsilyl)oxy)methyl)-4-(benzyloxy)-3,4-dihydro-2*H*-pyran (7).** A magnetically stirred solution of **6** (1.50 g, 4.30 mmol) in 20 mL of absolute methanol was treated with methanolic sodium methoxide (0.3 mL of 2.0 M, 0.6 mmol). After 18 h at room temperature, the solution was concentrated, diluted with ether, and quenched with saturated ammonium chloride solution. The organic phase was dried and concentrated to leave an oil which was purified by silica gel chromatography (elution with 20–40% ether in petroluem ether). There was isolated 660 mg (62%) of alcohol as a homogeneous colorless oil: IR (neat, $cm^{-1}$) 3600–3100, 2955, 2930, 2860, 1643, 1475, 1465, 1393, 1366, 1261, 1239, 1145, 1110, 1033, 1013, 964, 945, 927, 845, 785; $^1$H NMR (300 MHz, $CDCl_3$) δ 6.35 (d, *J* = 6.2 Hz, 1 H), 4.76 (ddd, *J* = 6.2, 2.8, 1.3 Hz, 1 H), 4.35 (br s, 1 H), 4.02 (m, 1 H), 3.74 (m, 2 H), 2.24 (m, 2 H), 1.72 (m, 1 H), 0.9 (s, 9 H), 0.07 (s, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 144.85, 105.05, 74.63, 65.63, 61.76, 34.93, 25.92, 25.89, 25.85, 18.36, −5.32, −5.38 ppm; MS *m*/*z* ($M^+ - C(CH_3)_3$) calcd 187.0790, obsd 187.0802; $[\alpha]^{25}_D$ + 5.23° (*c* 1.72, $CHCl_3$).

Anal. Calcd for $C_{12}H_{24}O_3Si$: C, 58.97; H, 9.90. Found: C, 59.04; H, 9.95.

A magnetically stirred suspension of dry, oil-free potassium hydride (20 mg, 0.5 mmol) in 1 mL of dry tetrahydrofuran was treated with the above alcohol (70 mg, 0.286 mmol) in 1 mL of the same solvent. After 15 min, benzyl bromide (47 μL, 0.43 mmol) was added followed by 4 mg of tetra-*n*-butylammonium iodide. The mixture was stirred at 25 °C for 12 h, colled to 0 °C, and treated slowly with saturated ammonium chloride solution (5 mL). The product was extracted into ether, this solution was dried and concentrated, and the residual oil was purified by silica gel chromatography (elution with 2% ether in petroleum ether). There was isolated 70 mg (74%) of **7** as a colorless oil homogeneous by TLC; IR (neat, $cm^{-1}$) 3060, 3030, 2955, 2925, 2855, 1640, 1495, 1471, 1461, 1452, 1378, 1360, 1250, 1238, 1130, 1098, 1030, 840, 780, 737, 700; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.38–7.26 (m, 5 H), 6.40 (dd, *J* = 6.2, 1.0 Hz, 1 H), 4.87 (m, 1 H), 4.57 (s, 2 H), 4.22 (m, 1 H), 4.0 (m, 1 H), 3.76 (AB of ABX, Δν = 38.2 Hz, $J_{AB}$ = 8.7 Hz, $J_{AX}$ = 5.4 Hz, $J_{BX}$ = 5.1 Hz), 2.23–2.15 (m, 1 H), 1.86–1.75 (m, 1 H), 0.91 (s, 9 H), 0.08 (s, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 145.13, 138.65, 129.48, 128.34, 127.58, 102.52, 75.29, 69.82, 68.98, 65.34, 30.94, 25.94, 18.41, −5.28 ppm; MS *m*/*z* ($M^+ - C(CH_3)_3$) calcd 277.1260, obsd 277.1264; $[\alpha]^{25}_D$ −16.45° (*c* 0.98, $CHCl_3$).

Anal. Calcd for $C_{19}H_{30}O_3Si$: C, 68.22; H, 9.04. Found: C, 68.43; H, 9.11.

**(−)-(2*S*,4*S*)-2-(Hydroxymethyl)-4-(benzyloxy)-3,4-dihydro-2*H*-pyran (8).** To a cold (0 °C), magnetically stirred solution of **7** (526 mg, 1.57 mmol) in 6 mL of anhydrous tetrahydrofuran was added 3.14 mL (3.14 mmol) of 1.0 M tetra-*n*-butylammonium fluoride solution in tetrahydrofuran. The reaction mixture was warmed to 25 °C, stirred for 2 h, treated with 10 mL of aqueous ammonium chloride solution, and extracted several times with 4:1 ether–dichloromethane. The combined organic layers were dried and concentrated. The crude product was purified by silica gel chromatography (elution with 50% ether in petroleum ether) to give 315 mg (91%) of **8** as a clear, colorless oil: IR (neat, $cm^{-1}$) 3410, 3060, 3030, 2920, 2860, 1675, 1492, 1450, 1395, 1348, 1320, 1235, 1030, 1070, 1025, 822, 735, 700; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5 H), 6.41 (dd, *J* = 6.35, 0.95 Hz, 1 H), 4.90 (ddd, *J* = 6.3, 2.8, 1.1 Hz, 1 H), 4.54 (AB q, δν = 16.1 Hz, $J_{AB}$ = 11.8 Hz, 2 H), 4.19–4.12 (m, 1 H), 4.12–4.05 (m, 1 H), 3.7 (br s, 2 H), 2.52 (br s, 1 H), 2.10 (m, 1 H), 1.88 (m, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 144.97, 138.22, 128.32, 127.53, 102.05, 74.54, 69.80, 67.90, 64.41, 30.14 ppm; MS *m*/*z* ($M^+$) calcd 220.1099, obsd 220.1101; $[\alpha]^{25}_D$ −48.47° (*c* 2.98, $CHCl_3$).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.66; H, 7.48.

**(−)-(2*S*,4*S*)-4-(Benzyloxy)-3,4-dihydro-2*H*-pyran-2-carboxaldehyde (9).** To a cold (−45 °C), magnetically stirred solution of 0.143 mL (1.6 mmol) of oxalyl chloride in 10 mL of anhydrous dichloromethane was slowly added dropwise 0.243 mL (3.42 mmol) of anhydrous dimethyl sulfoxide. After 30 min, a solution of 315 mg (1.43 mmol) of **8** in 3 mL of anhydrous dichloromethane was introduced. The reaction mixture was stirred for 2 h at −45 °C, at which point 1.00 mL (7.17 mmol) of triethylamine was added, the cold bath was removed, and warming to ambient temperature was allowed to occur over 30 min. Water

(20 mL) was added, followed by dilution with ether (30 mL). The organic phase was washed with water (2 × 10 mL) and 10 mL of copper(II) sulfate solution, and the combined aqueous solutions were extracted into ether–dichloromethane (3×). The combined organic layers were dried and concentrated, and the resulting crude oil was purified by silica gel chromatography (rapid elution with 50% ether in petroleum ether) to yield 240 mg (77%) of **9** as a colorless oil: IR (neat, $cm^{-1}$) 3440, 3060, 3015, 2925, 2850, 1730, 1635, 1492, 1450, 1425, 1400, 1380, 1320, 1242, 1085, 1065, 960, 900, 735, 700; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.7 (d, $J$ = 0.73 Hz, 1 H), 7.37–7.26 (m, 5 H), 6.6 (d, $J$ = 6.3 Hz, 1 H), 5.1–5.06 (m, 1 H), 4.5–4.45 (m, 1 H), 4.45 (s, 2 H), 3.93 (dd, $J$ = 8.5, 3.6 Hz, 1 H), 2.5–2.42 (m, 1 H), 2.22–2.13 (m, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 200.38, 144.97, 137.98, 128.32, 127.60, 127.53, 102.34, 77.04, 69.27, 64.47, 28.91 ppm; MS $m/z$ ($M^+$ − CHO) calcd 189.0916, obsd 189.0917; $[\alpha]^{25}_D$ −15.3° ($c$ 1.98, $CHCl_3$).

**Benzylation of 12.** To a magnetically stirred suspension of sodium hydride (242 mg of 97%, 9.8 mmol) in 10 mL of dry tetrahydrofuran was added 1.07 g (7.53 mmol) of **12** as a solution in 2 mL of THF. The suspension was stirred at reflux for 3 h before being cooled to 25 °C and treated with benzyl bromide (1.06 mL, 9.8 mmol). Following the addition of tetra-*n*-butylammonium iodide (20 mg), the mixture was stirred at the reflux temperature for several hours, cooled to 0 °C, and quenched slowly with saturated ammonium chloride solution. The product was extracted into dichloromethane (5×), and the combined organics were dried and concentrated. The residue was purified chromatographically (silica gel, elution with 20% ether in petroleum ether) to give 1.48 g (89%) of **13** as a colorless oil; IR (neat, $cm^{-1}$) 3060, 3030, 2950, 2920, 2885, 1493, 1472, 1451, 1397, 1370, 1331, 1328, 1260, 1258, 1192, 1175, 1126, 1090, 1068, 1022, 991, 952, 907, 888, 866, 818, 740, 700; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.35–7.25 (m, 5 H), 5.57 (s, 1 H), 4.52 (AB q, $\Delta\nu$ = 23.3 Hz, $J_{AB}$ = 12.2 Hz, 2 H), 4.49 (m, 1 H), 4.36 (d, $J$ = 6.4 Hz, 1 H), 3.73 (m, 2 H), 2.17–1.80 (series of m, 4 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 138.57, 128.19, 127.22 (2 C), 100.08, 71.53, 70.35, 69.66, 67.65, 35.15, 33.85 ppm; MS molecular ion too fleeting to be mass measured; $[\alpha]^{25}_D$ −59.5° ($c$ 1.14, $CHCl_3$).

Anal. Calcd for $C_{13}H_{16}O$: C, 70.89; H, 7.32. Found: C, 70.95; H, 7.40.

**Preparation of Methyl Glycosides 14 and 15.** To a magnetically stirred solution of **13** (5.2 g, 23.6 mmol) in 70 mL of absolute methanol was added 5.8 g of Bio-Rad $H^+$ exchange resin ($H_2SO_4$). The suspension was stirred rapidly at 25 °C for 18 h, filtered, and concentrated. Partial separation of the epimers was effected by silica gel chromatography. Elution with 30, 50, and 80% ether in petroleum ether in gradient fashion provided 3.85 g of the oily $\alpha$ anomer **15** and 2.0 g of a nearly 1:1 mixture of $\alpha$ and $\beta$ isomers (total yield of 5.85 g (98%) of a 4.9:1 mixture of **15** and **14**). Repetitive silica gel chromatography provided pure 14 as well.

For **14**: IR (neat, $cm^{-1}$) 3590, 3420, 3000, 2855, 2835, 1490, 1446, 1383, 1352, 1270, 1160, 1100, 1060, 1028, 995, 938, 895, 871, 843; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.35–7.25 (m, 5 H), 4.54 (s, 2 H), 4.32 (dd, $J$ = 9.8, 2.0 Hz, 1 H), 3.67–3.56 (m, 3 H), 3.50 (s, 3 H), 3.49–3.41 (m, 1 H), 2.34 (br s, 1 H), 2.3–2.2 (m, 1 H), 1.98–1.90 (m, 1 H), 1.49–1.26 (m, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 138.20, 128.34, 127.56, 127.45, 101.42, 72.99, 72.71, 69.77, 65.44, 56.37, 37.88, 33.22 ppm; MS $m/z$ ($M^+$ − 1) calcd 251.1283, obsd 251.1327; $[\alpha]^{25}_D$ −13.6° ($c$ 2.8, $CHCl_3$).

For **15**: IR (neat, $cm^{-1}$) 3440, 3160, 3120, 2930, 2830, 1493, 1450, 1360, 1300, 1260, 1198, 1168, 1120, 1050, 980, 930, 912, 868, 850, 800, 740, 700; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.36–7.24 (m, 5 H), 4.89 (d, $J$ = 3.0 Hz, 1 H), 4.54 (s, 2 H), 3.96–3.76 (dm, 2 H), 3.65–3.53 (m, 2 H), 3.32 (s, 3 H), 2.39 (br s, 1 H), 2.23–2.16 (m, 1 H), 2.01–1.95 (m, 1 H), 1.57 (ddd, $J$ = 15.0, 11.4, 3.6 Hz, 1 H), 1.38 (dd, $J$ = 23.5, 11.9 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 138.52, 128.26, 127.41, 127.38, 99.16, 70.53, 69.81, 68.48, 65.67, 54.50, 36.47, 33.61 ppm; MS $m/z$ ($M^+$) calcd 252.1361, obsd 252.1419; $[\alpha]^{25}_D$ +112.6° ($c$ 2.63, $CHCl_3$).

Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.74; H, 8.02.

**(+)-(2S,4S,6S)-Methyl 2-Methoxy-4-(benzyloxy)tetrahydropyran-6-carboxylate (16a).** To a magnetically stirred solution of pyridinium dichromate (3.58 g, 9.51 mmol) in 6 mL of dry dimethylformamide was added a solution of **15** (600 mg, 2.38 mmol) in 4 mL of the same solvent. The dark-colored reaction mixture was stirred at room temperature for 18 h, poured into 70 mL of water, and extracted six times with ether–dichloromethane (3:1, 170-mL total). The combined extracts were dried and concentrated and the oily acid was directly esterified with ethereal diazomethane at 0 °C. The dried reaction mixture was evaporated to leave an oil that was purified by silica gel chromatography. There were isolated 460 mg (69%) of **16a** and 90 mg of a mixture of unreacted **15** and **16a**.

For **16a**: IR (neat, $cm^{-1}$) 3080, 3050, 3020, 2950, 2930, 2900, 1753, 1490, 1450, 1435, 1390, 1342, 1268, 1198, 1165, 1125, 1105, 1040, 970, 905, 858, 828, 740, 700; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.33–7.23 (m, 5 H), 4.97 (d, $J$ = 1.6 Hz, 1 H), 4.51 (AB q, $J$ = 17.1, 11.8 Hz, 2 H), 4.31 (dd, $J$ = 12.0, 2.6 Hz, 1 H), 3.93–3.84 (m, 1 H), 3.74 (s, 3 H), 3.32 (s, 3 H), 2.39 (ddd, $J$ = 12.4, 4.3, 2.1 Hz, 1 H), 2.12 (ddd, $J$ = 12.75, 3.8, 1.6 Hz, 1 H), 1.67–1.53 (m, 2 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 171.27, 138.22, 128.25, 127.47, 127.40, 99.32, 70.02, 69.87, 67.30, 58.32, 54.98, 52.06, 36.02, 34.46 ppm; MS $m/z$ ($M^+$) calcd 280.1311, obsd 280.1292.

**(+)-(2S,4S,6S)-Ethyl 2-Methoxy-4-(benzyloxy)tetrahydropyran-6-carboxylate (16b).** Oxidation of 1.35 g (5.35 mmol) of **15** with 8.05 g (21.4 mmol) of pyridinium dichromate in the predescribed manner and subsequent esterification with diazoethane at 0 °C afforded an oily product. Silica gel chromatography (elution with 25% ether in petroleum ether) afforded 1.13 g (72%) of **16b** as a clear, colorless oil and 250 mg of a mixture of unreacted **15** and **16b**.

For **16**: IR (neat, $cm^{-1}$) 3060, 3025, 2960, 2930, 2835, 1750, 1492, 1448, 1362, 1345, 1268, 1200, 1165, 1125, 1104, 1038, 968, 901, 855, 738, 699; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.33–7.24 (m, 5 H), 5.0 (d, $J$ = 1.2 Hz, 1 H), 4.55 (AB q, $J$ = 15.5, 11.6 Hz, 2 H), 4.32 (dd, $J$ = 12.0, 2.6 Hz, 1 H), 4.23 (q, $J$ = 7.0 Hz, 2 H), 3.98–3.87 (m, 1 H), 3.35 (s, 3 H), 2.40 (dm, $J$ = 12.4 Hz, 1 H), 2.15 (dm, $J$ = 12.8 Hz, 1 H), 1.70–1.55 (m, 2 H), 1.29 (t, $J$ = 7.0 Hz, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 170.99, 138.34, 128.34, 127.53, 127.45, 99.41, 70.23, 69.97, 67.45, 61.15, 55.11, 36.10, 34.62, 14.14 ppm; MS $m/z$ ($M^+$ − $C_2H_5O$) calcd 263.1283, obsd 263.1261; $[\alpha]^{25}_D$ +100.28° ($c$ 2.46, $CHCl_3$).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.09; H, 7.89.

**Oxidation of 15. A. Swern Conditions.** To a cold (−60 °C)8 magnetically stirred solution of 0.47 mL (5.4 mmol) of oxalyl chloride in 10 mL of anhydrous dichloromethane was added 0.80 mL (11.3 mmol) of anhydrous dimethyl sulfoxide in 5 mL of the same solvent. The reaction mixture was stirred at −60 °C for 1 h, at which point 1.19 g (4.72 mmol) of **15** dissolved in 5 mL of anhydrous dichloromethane was introduced. After 2 h at −60 °C, 3.3 mL (23.7 mmol) of triethylamine was added, producing a white precipitate. An additional 18 mL of anhydrous dichloromethane was added at this time in order to facilitate stirring. The mixture was warmed to ambient temperature over 2 h, stirred for an additional 6 h, and diluted with 50 mL of anhydrous ether. After filtration to remove solids, the concentrated filtrate was purified by silica gel chromatography (rapid elution with 50–80% anhydrous ether in petroleum ether) to provide 1.04 g (88%) of **17** as a viscous oil: $^{13}C$ NMR (75 MHz, $CDCl_3$) 200.41, 138.23, 128.41, 127.63, 127.52, 99.48, 76.64, 72.99, 70.05, 55.12, 36.43, 32.16 ppm; MS $m/z$ ($M^+$ − CHO) calcd 221.1177, obsd 221.1174.

**B. Moffatt Conditions.** To a magnetically stirred solution of 96 mg (0.38 mmol) of **15** in 2 mL of dimethyl sulfoxide and 2 mL of benzene was added 81 mg (0.42 mmol) of pyridinium trifluoroacetate followed by 235 mg (1.14 mmol) of dicyclohexylcarbodiimide. The reaction mixture was stirred at 25 °C for 18 h, diluted with 5 mL of diethyl ether, and treated with 144 mg (1.14 mmol) of oxalic acid dihydrate and 2 mL of absolute methanol. After 30 min of stirring, the solids were separated by filtration and the filtrate was concentrated. The residue was taken up in diethyl ether and again filtered and concentrated to provide a crude, oily product which was purified by silica gel chromatography (rapid elution using 50–80% diethyl ether in petroleum ether). There was isolated 91 mg (90%) of **17**, identical with the product of part A.

**(+)-(2S,4S,6R)-2-(Hydroxymethyl)-4-(benzyloxy)-6-(phenylthio)tetrahydropyran (19).** To a cold (−78 °C), magnetically stirred solution of **13** (540 mg, 12.3 mmol) and thiophenol (1.26 mL, 12.3 mmol) in 10 mL of dry tetrahydrofuran was added

0.9 mL (7.35 mmol) of boron trifluoride etherate. The resulting solution was stirred for 4 h at −78 °C and allowed to warm to 25 °C during 30 min. Following the addition of water (30 mL) and ether (50 mL), the aqueous phase was extracted several times with ether. The combined organic layers were dried and concentrated, and the residue was subjected to silica gel chromatography (elution with 20–50% ether in petroleum ether). There was isolated 710 mg (88%) of **19**: mp 74–75 °C (from ether–petroleum ether); IR ($CHCl_3$, $cm^{-1}$) 3595, 3002, 2978, 2925, 2875, 1582, 1480, 1453, 1443, 1438, 1382, 1362, 1350, 1292, 1220, 1163, 1110, 1027, 1012, 960, 948, 910, 842, 695; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.50–7.23 (m, 10 H), 5.73 (d, $J$ = 5.4 Hz, 1 H), 4.59 (m, 2 H), 4.57–4.3 (m, 1 H), 3.95 (tt, $J$ = 11.2, 4.5 Hz, 1 H), 3.67–3.55 (m, 2 H), 2.46–2.39 (m, 1 H), 2.10–1.89 (m, 3 H), 1.46 (dd, $J$ = 23.4, 11.9 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 138.28, 134.69, 131.71, 128.90, 128.39, 127.61, 127.53, 127.26, 84.54, 71.03, 69.97, 69.52, 65.55, 37.20, 33.96 ppm; MS $m/z$ ($M^+ - SC_6H_5$) calcd 221.1178, obsd 221.1207; $[\alpha]^{25}_D$ +248° ($c$ 1.20, $CHCl_3$).

Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 69.16; H, 6.83.

**(+)-(2*S*,4*S*,6*R*)-Methyl 4-(Benzyloxy)-6-(phenylthio)-tetrahydropyran-2-carboxylate (20).** A magnetically stirred solution of **19** (116 mg, 0.35 mmol) in 1.5 mL of dimethylformamide was treated with 528 mg (1.4 mmol) of pyridinium dichromate. The orange solution was stirred at 25 °C for 18 h, poured into water (10 mL), and extracted with ether (6×). The combined extracts were dried and concentrated to leave an oily residue which was esterified without purification. The oil was taken up in 10 mL of ether and treated (at 0 °C) with an ethereal solution of diazomethane and stirred with warming to ambient temperature over 30 min. Anhydrous magnesium sulfate was carefully added and the mixture was filtered and concentrated. The crude product was purified by silica gel chromatography to yield 66 mg (52%) of **20** as a colorless oil: IR (neat, $cm^{-1}$) 3055, 3025, 2945, 2920, 2860, 1740, 1580, 1492, 1478, 1450, 1435, 1360, 1268, 1208, 1165, 1090, 1025, 955, 860, 740, 695; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.55–7.17 (m, 10 H), 5.84 (t, $J$ = 4.3 Hz, 1 H), 4.80 (dd, $J$ = 9.8, 3.4 Hz, 1 H), 4.53 (AB q, $\Delta\nu$ = 18.8 Hz, $J_{AB}$ = 11.3 Hz, 2 H), 3.88 (m, 1 H), 3.70 (s, 3 H), 2.36 (m, 1 H), 2.23 (m, 1 H), 2.06 (m, 1 H), 1.82 (dt, $J$ = 12.9, 9.6 Hz, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 171.09, 137.98, 134.56, 130.49, 128.78, 128.28, 127.53, 127.33, 126.85, 82.73, 70.50, 69.97, 68.72, 52.02, 36.63, 33.76 ppm; MS molecular ion too fleeting to be mass measured; $[\alpha]^{25}_D$ +138.4° ($c$ 0.85, $CHCl_3$).

Anal. Calcd for $C_{20}H_{22}O_4S$: C, 67.02; H, 6.19. Found: C, 66.99; H, 6.21.

**Methylation of 16a.** A cold (0 °C), magnetically stirred solution of diisopropylamine (1.82 mL, 13.0 mmol) in 15 mL of anhydrous tetrahydrofuran was treated with $n$-butyllithium (8.17 mL of 1.55 M, 12.67 mmol) in hexanes and stirred for 20 min before being cooled to −78 °C. Ester **16a** (2.95 g, 10,53 mmol) as a solution in the same solvent (10 mL) was added dropwise over 5 min. After 1 h at −78 °C, methyl iodide (3.3 mL, 53 mmol) was introduced via syringe and stirring was maintained for 30 min before the reaction mixture was warmed to 25 °C and treated with saturated ammonium chloride solution. The products were extracted into ether (3 × 20 mL), dried, and concentrated. Chromatography of the residual oil on silica gel afforded **21** and **22** (ratio 5:1) as an inseparable mixture of epimers (2.74 g, 88%).

**Methylation of 16b.** Reaction of **16b** (1.10 g, 3.74 mmol) with 4.7 mmol of LDA and then with 1.16 mL (18.7 mmol) of methyl iodide in the manner described above afforded 880 mg (77%) of a 5:1 mixture of **21b** and **22b** as a clear, colorless oil following silica gel chromatography. Flash chromatography of this material using peak-shaving techniques provided a sample of pure **21b**: IR (neat, $cm^{-1}$) 3085, 3060, 3025, 2975, 2930, 2835, 1728, 1492, 1450, 1362, 1345, 1295, 1257, 1195, 1178, 1130, 1105, 1070, 1045, 981, 951, 898, 870, 850, 768, 738, 699; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.36–7.24 (m, 5 H), 4.85 (dd, $J$ = 3.6, 1.5 Hz, 1 H), 4.58 (AB q, $\Delta\nu$ = 18.1 Hz, $J_{AB}$ = 9.7 Hz, 2 H), 4.30–4.19 (m, 1 H), 4.14–3.97 (m, 2 H), 3.36 (s, 3 H), 2.74 (ddd, $J$ = 12.7, 4.2, 2.1 Hz, 1 H), 2.15 (dm, $J$ = 12.7 Hz, 1 H), 1.66–13.1 (m, 2 H)8, 1.43 (s, 3 H), 1.26 (t, $J$ = 7.2 Hz, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 174.06, 138.73, 128.30, 127.55, 127.43, 101.16, 74.65, 70.08, 68.19, 60.82, 56.84, 39.53, 36.78, 28.16, 13.92 ppm; MS $m/z$ ($M^+ - OCH_3$) calcd 277.1440, obsd 277.1428; $[\alpha]^{25}_D$ −51° ($c$ 1.25, $CHCl_3$).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 66.09; H, 7.89.

**Reduction of 21a/22a.** To a cold (−78 °C), magnetically stirred solution of the **21a/22a** mixture (1.05 g, 3.57 mmol) in anhydrous ether (20 mL) was added 10.7 mL of Dibal-H solution in hexanes (1.0 M, 10.7 mmol). The reaction mixture was stirred at −78 °C for 3 h, treated with 1.5 mL of absolute methanol, and poured into a mixture of sodium potassium tartrate solution (60 mL) and ether (40 mL). The organic phase was separated, washed with an additional 40 mL of tartrate solution, dried, and concentrated. The residue was separated into its two components by silica gel chromatography (elution with 20% ether in petroleum ether) to give 540 mg of **23** and 260 mg of a mixture of **23** and **24**. Rechromatography furnished 130 mg of each aldehyde (71% of **23** and 14% of **24**).

For **23**: IR (neat, $cm^{-1}$) 3080, 3060, 3020, 2920, 2830, 2695, 1722, 1492, 1450, 1363, 1345, 1312, 1272, 1238, 1190, 1150, 1120, 1048, 970, 920, 864, 795, 735, 700; $^1H$ NMR (300 Hz, $CDCl_3$) $\delta$ 9.37 (d, $J$ = 1.9 Hz, 1 H), 7.36–7.22 (m, 5 H), 4.88 (dd, $J$ = 3.3, 1.4 Hz, 1 H), 4.54 (AB q, $\Delta\nu$ = 22.5 Hz, $J_{AB}$ = 11.5 Hz, 2 H), 3.84–3.73 (m, 1 H), 3.44 (s, 3 H), 2.69 (ddd, $J$ = 12.7, 4.5, 2.1 Hz, 1 H), 2.16–2.08 (m, 1 H), 1.61–1.50 (m, 1 H)8 1.38–1.21 (m, 1 H), 1.22 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 202.10, 138.55, 128.28, 127.53, 127.44, 100.99, 79.39, 70.16, 67.70, 56.57, 36.54, 36.33, 22.99 ppm; MS $m/z$ ($M^+$ − CHO) calcd 235.1334, obsd 235, 1349; $[\alpha]^{25}_D$ +42.21° ($c$ 1.45, $CHCl_3$).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.45; H, 7.69.

For **24**: IR (neat, $cm^{-1}$) 3080, 3060, 3020, 2970, 2930, 2860, 2790, 1732, 1492, 1450, 1365, 1345, 1295, 1262, 1195, 1120, 1042, 1008, 990, 915, 860, 735, 699; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 9.66 (s, 1 H), 7.36–7.23 (m, 5 H), 5.03 (dd, $J$ = 8.1, 2.7 Hz, 1 H), 4.44 (AB q, $\Delta\nu$ = 31.5 Hz, $J_{AB}$ = 11.8 Hz, 2 H), 3.91 (m, 1 H), 3.54 (s, 3 H), 2.27 (ddd, $J$ = 14.0, 4.8, 1.24 Hz, 1 H), 2.0–1.92 (m, 1 H), 1.67–1.52 (m, 2 H), 1.31 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 202.42, 138.00, 128.33, 127.54, 127.41, 97.33, 79.42, 70.57, 70.12, 56.09, 35.82, 35.07, 23.53 ppm; MS $m/z$ ($M^+$) calcd 264.1361, obsd 264.1414.

**(+)-(2*R*,4*S*,6*S*)-2-Methyl-2-vinyl-4-(benzyloxy)-6-methoxytetrahydropyran (25).** To a cold (0 °C), magnetically stirred suspension of methyltriphenylphosphonium bromide (1.55 g, 4.33 mmol) in dry tetrahydrofuran (15 mL) was added $n$-butyllithium in hexanes (2.77 mL of 1.55 M, 4.30 mmol). The reaction mixture was stirred for 30 min, cooled to −78 °C, and treated with a solution of **23** (955 mg, 3.61 mmol) in 5 mL of tetrahydrofuran. After 10 min, the solution was warmed to ambient temperature, stirred for 10 min, and treated with saturated ammonium chloride solution. The aqueous phase was extracted with ether (2 × 20 mL), and the combined oragnic layers were dried and concentrated. The residue was purified by silica gel chromatography (elution with 10% ether in petroleum ether) and provided 822 mg (87%) of **25** as a colorless oil homogeneous by TLC: IR (neat, $cm^{-1}$) 3080, 3060, 3020, 2930, 1490, 1449, 1408, 1360, 1345, 1310, 1270, 1195, 1112, 1090, 1070, 1050, 1028, 975, 948, 918, 863, 735, 698; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.34–7.24 (m, 5 H), 6.0 (dd, $J$ = 17.8, 11.1 Hz, 1 H), 5.04–4.88 (m, 3 H), 4.55 (s, 2 H), 4.02–3.92 (m, 1 H), 3.37 (s, 3 H), 2.29–2.23 (m, 1 H), 2.15–2.07 (m, 1 H), 1.71–1.52 (m, 2 H), 1.33 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) 144.85, 138.73, 128.31, 127.46, 110.56, 99.72, 75.49, 70.10, 69.17, 55.42, 40.25, 36.64, 29.28 ppm; MS $m/z$ ($M^+$) calcd 262.1569, obsd 262.1546; $[\alpha]^{25}_D$ +69.96° ($c$ 2.35, $CHCl_3$).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.22; H, 8.44.

**(−)-(2*R*,4*S*)-2-Methyl-2-vinyl-4-(benzyloxy)-3,4-dihydro-2*H*-pyran (1).** A cold (−25 °C), magnetically stirred solution of **25** (42 mg, 0.16 mmol) in 1.5 mL of carbon tetrachloride was treated with trimethylsilyl iodide (32 μL, 0.224 mmol), followed 5 min later by hexamethyldisilazane (51 μL, 0.24 mmol). The reaction mixture was stirred for 10 min at −20 °C, quenched with saturated sodium bicarbonate solution, and diluted with ether. The aqueous phase was extracted once with ether, and the combined organic layers were dried and concentrated. The residue was chromatographically purified (silica gel, elution with 5–10% ether in petroleum ether) to furnish 24.9 mg (67%) of **1** as a colorless oil: IR ($CHCl_3$, $cm^{-1}$) 3090, 3060, 3000, 2980, 2930, 2860, 1636, 1492, 1450, 1405, 1371, 1348, 1320, 1240, 1130, 1105, 1095, 1068, 1028, 928, 868; $^1H$ NMR (300 MHz, $CHCl_3$) $\delta$ 7.34–7.24 (m,

5 H), 6.38 (dd, $J$ = 6.4, 1.4 Hz, 1 H), 5.78 (dd, $J$ = 17.3, 10.8 Hz, 1 H), 5.17 (dd, $J$ = 17.3, 1.1 Hz, 1 H), 5.06 (dd, $J$ = 10.7, 1.1 Hz, 1 H), 4.88 (ddd, $J$ = 6.4, 2.6, 1.3 Hz, 1 H), 4.54 (AB q, $\Delta\nu$ = 15.8 Hz, $J_{AB}$ = 11.85 Hz, 2 H), 3.96 (m, 1 H), 2.10 (ddd, $J$ = 13.4, 6.0, 1.2 Hz, 1 H), 1.87 (dd, $J$ = 13.3, 8.0 Hz, 1 H), 1.39 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 143.75, 140.83, 138.72, 128.33, 127.52, 127.46, 112.99, 101.20, 77.22, 69.91, 68.07, 38.27, 26.95 ppm; MS $m/z$ ($M^+$) calcd 230.1307, obsd 230.1300; $[\alpha]^{25}_D$ −142.3° ($c$ 0.61, $CHCl_3$).

**(−)-(2*R*,4*S*,6*R*)-2-Methyl-2-vinyl-4-(benzyloxy)-6-(phenylthio)tetrahydropyran (26).** A cold (−78 °C), magnetically stirred solution of **25** (230 mg, 0.88 mmol) in 3 mL of dichloromethane was treated with thiophenol (103 μL, 1 mmol) followed by boron trifluoride etherate (0.16 mL, 1.3 mmol). After 1 h at −78 °C, the reaction mixture was quenched with cold, saturated sodium bicarbonate solution (10 mL) and extracted with ether (3 × 10 mL). The combined organic phases were dried and concentrated, and the residue was purified by silica gel chromatography (elution with 10% ether in petroleum ether). There was isolated 290 mg (97%) of **26** as a clear, colorless oil homogeneous by TLC: IR (neat, cm$^{-1}$) 3055, 3030, 2970, 2945, 2920, 2860, 1580, 1493, 1478, 1450, 1438, 1410, 1358, 1310, 1210, 1182, 1150, 1125, 1070, 1040, 1025, 970, 928, 878, 806, 740, 695; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.55–7.49 (m, 2 H), 7.35–7.21 (m, 8 H), 5.66 (dd, $J$ = 17.8, 11.1 Hz, 1 H), 5.08 (d, $J$ = 11.1 Hz, 1 H), 4.93 (d, $J$ = 17.8 Hz, 1 H), 4.83 (dd, $J$ = 12.0, 2.05 Hz, 1 H), 4.52 (AB q, $\Delta\nu$ = 17.6 Hz, $J_{AB}$ = 11.8 Hz, 2 H), 3.65 (m, 1 H), 2.35–2.20 (series of m, 2 H), 1.62–1.40 (m, 2 H), 1.33 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) 141.67, 138.36, 133.85, 132.25, 128.59, 128.34, 127.56, 127.51, 127.48, 127.39, 115.42, 78.56, 71.91, 69.89, 39.81, 37.96, 31.04 ppm; MS $m/z$ ($M^+$ − SPh) calcd 232.1462, obsd 232.1462; $[\alpha]^{25}_D$ −57.4° ($c$ 1.25, $CHCl_3$).

Anal. Calcd for $C_{21}H_{24}O_2S$: C, 74.08; H, 7.10. Found: C, 74.32; H, 7.10.

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# Action of Alkylmagnesium and Alkyllithium Reagents on Some Quaternary Hydrazonium Salts[1]

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Benzophenone *N*-methyl-*N*,*N*-pentane-1,5-diylhydrazonium iodide (**1a**) and its *p*,*p*′-dichloro and *p*,*p*′-dimethoxy analogues undergo loss of $CH_3I$ in boiling ethyl ether or THF, but the fluoroborates are stable. The complexes formed from **1** and Grignard reagents do not undergo incorporation of deuterium when they are hydrolyzed with $D_2O$. When **1** and analogues are treated with propyl- and decylmagnesium bromide, the corresponding alkane, alkene, and bialkyl are produced, facts that imply formation of alkyl radicals by a single-electron-transfer process. With all alkyl Grignard reagents studied, the overwhelming reaction is reductive cleavage of the N,N bond to form imines unsubstituted on nitrogen; no *N*-alkyl imines were detected. Small amounts of 1,1-diarylalkylamines, formed by addition of R′MgX to the azomethine carbon, were formed in some instances, and *tert*-butylmagnesium chloride formed about 2% of benzhydrylamine in reaction with **1a**. Sodium cyanide reacted with the tetrafluoroborate analogue of **1a** to form acetonitrile by demethylation; neither addition nor reduction was detected. Sodium azide behaved analogously.

The thin stream of literature on quaternary hydrazonium compounds since the first report[2] in 1957 has been mostly concerned with their use as intermediates in synthesis of azirines, an analogue of the Neber rearrangement. Their stereochemistry has been studied by Arseniyadis, Laurent, and Mison,[3] who also showed[4] that reaction of Grignard reagents with quaternary hydrazonium iodides having a hydrogen α to the azomethine carbon is an efficient method for synthesis of aziridines (a second equivalent of RMgX adds to the azirine first formed). They observed that the direction of ring closure with hydrazonium salts derived from unsymmetrical ketones was independent of the stereochemistry about the C=N double bond, and that it occurred highly preferentially to the least hindered α-position, regardless of the relative acidities of the α-hydrogens. Yields were mostly high, and the only competing reaction reported was dealkylation at the quaternary nitrogen to form a dialkylhydrazone (in general, products other than aziridines were not determined, even for those cases in which the yields of aziridine were very low).

In contrast, quaternary benzophenone hydrazonium salts (**1**), which have no α-hydrogens, have been shown by Smith and Tan[5] to react with Grignard reagents through an intermediate of unknown composition (**2**?), formed with evolution of heat, which proceeds to a mixture of products resulting from at least three competing reactions (eq 1–3),

$$\underset{\textbf{1a–f}}{Ar_2C{=}\overset{+}{N}{-}NR_3I^-} + R'MgX \rightarrow [\textbf{2}?] \xrightarrow{\Delta} \underset{\textbf{3}}{Ar_2C{=}NMgX} + R_3N + R'{-}R' \quad (1)$$

**1a**, Ar = Ph, $R_3$ = $CH_3$ and $(CH_2)_5$

**1b**, Ar = *p*-$CH_3C_6H_4$, $R_3$ = $CH_3$ and $(CH_2)_5$

**1c**, Ar = *p*-$ClC_6H_4$, $R_3$ = $CH_3$ and $(CH_2)_5$

**1d**, Ar = Ph, R = $CH_3$

**1e**, Ar = Ph, $R_3$ = $C_2H_5$ and $(CH_2)_5$

**1f**, Ar = *p*-$CH_3OC_6H_4$, $R_3$ = $CH_3$ and $(CH_2)_5$

(1) From the doctoral dissertation of C. R. Messing.
(2) Smith, P. A. S.; Most, E. E., Jr. *J. Org. Chem.* **11957**, *22*, 358.
(3) Arseniyadis, S.; Laurent, A.; Mison, P. *Bull. Soc. Chim. Fr.* **1980**, *II*, 233.
(4) Arseniyadis, S.; Laurent, A.; Mison, P. *Bull. Soc. Chim. Fr.* **1980**, II, 246.
(5) Smith, P. A. S.; Tan, H. H. *J. Org. Chem.* **1967**, *32*, 2586.

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