Conversion of Homoallylic Alcohols with Alkene Protection to the Corresponding Methyl Ketones

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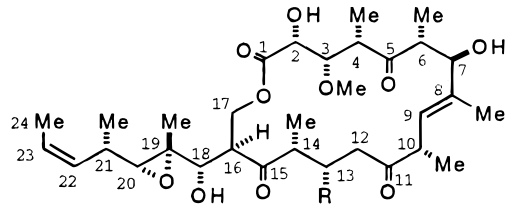
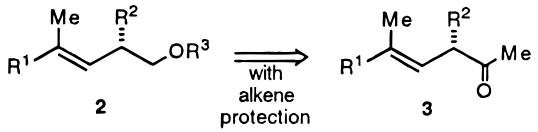
In the course of a total synthesis of the potent cytotoxic agents tedanolide **1a** and 13-deoxy-tedanolide **1b**,[2] a good method was needed to carry out two specific transformations, namely, a reversible protection of the alkene of the homoallylic alcohol system **2** and the conversion of the homoallylic alcohol or ether into the methyl ketone **3**.



1a R = OH
1b R = H

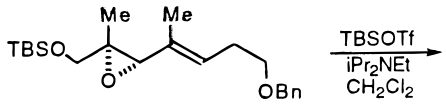


2 **3**

Accordingly, it was necessary to protect the alkene functionality in order to permit the application of a "non-aldol aldol" process,[3] thereby avoiding certain problems associated with allylic epoxide rearrangements.[4] For example, when the oxirane **4** was treated with a silyl triflate in the presence of base, the major product obtained was the ketone **6** arising from cleavage of the allylic oxirane C−O bond rather than the expected non-aldol aldol product **5**, which would have been formed by cleavage of the tertiary oxirane C−O bond. To prevent this undesirable rearrangement (to give **6** instead of **5**), the alkene had to be protected. Herein we describe our successful attempt at protecting the alkene of **2** coupled with selective oxidation, reductive ring opening, and final conversion to the methyl ketone **3**.

Table 1. Formation of 3 from 2 via Intermediates 7, 8, and 9

				yields (%)			
compd	R^1	R^2	R^3	**7**	**8**	**9**	**3**
a	Me	Me	H	60	93	86	67
b	Me	Ph	H	86	82	87	66
c	Me	H	H	48	82	76	
d	CH_2OTBS	Me	Bn	64	88	70	52
e	CH_2OTBS	Me	H	86			



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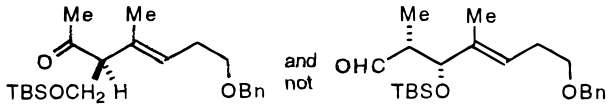
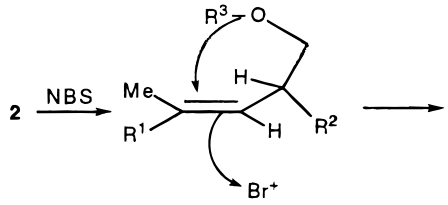
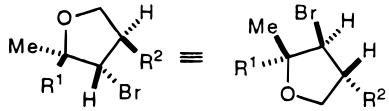


6 **5**

Cyclization of either the homoallylic alcohols or the corresponding benzyl ethers **2a**−**f** to the bromotetrahydrofurans **7a**−**f** was carried out (Table 1) by treatment with *N*-bromosuccinimide (NBS) in dichloromethane to give only one diastereomer of the desired products.[5,6] This

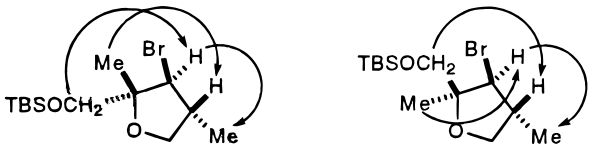


I



7 **7**

diastereoselectivity can be explained by postulating that bromination proceeds via addition of the positive bromine to the bottom face of the alkene in conformation **I** with the hydrogen "inside" with concomitant attack of the oxygen on the top face (with loss of a proton or benzyl cation)[7] to give **7**. The stereochemistry of the products was proven rigorously for compounds **7d** and **7f** by NOESY experiments (correlations shown below) and has been assigned by analogy for **7a**−**c**.



7d **7f**

(1) UCLA President's Fellow, 1994−1998. Awardee of Excellence for First Year Graduate Study Award, 1995.

(2) (a) Fusetani, N.; Sugawara, T.; Matsunaga, S.; Hirota, H. *J. Org. Chem.* **1991**, *56*, 4971. (b) Schmitz, F. J.; Gunasekera, S. P.; Yalamanchili, G.; Hossain, M. B.; van der Helm, D. *J. Am. Chem. Soc.* **1984**, *106*, 7251.

(3) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1993**, *115*, 12208.

(4) (a) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1995**, *117*, 7379. (b) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1997**, *119*, 12150. (c) Jung, M. E.; Anderson, K. L. *Tetrahedron Lett.* **1997**, *38*, 2605.

(5) For a good review of cyclizations of this type, see: Harding, K. E.; Tiner, T. H. Electrophilic Heteroatom Cyclizations. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 4, Chapter 1.9, p 363.

(6) For an example of this less common 5-endo cyclization, see: Mihailovic, M. Lj.; Marinkovic, D. *J. Serb. Chem. Soc.* **1985**, *50*, 5.

(7) For examples of the loss of an alkyl cation in electrophilic cyclizations, see: (a) Parker, K. A.; O'Fee, R. *J. Am. Chem. Soc.* **1983**, *105*, 654. (b) Rychnovsky, S. D.; Bartlett, P. A. *J. Am. Chem. Soc.* **1981**, *103*, 3963. (c) See also ref 5.

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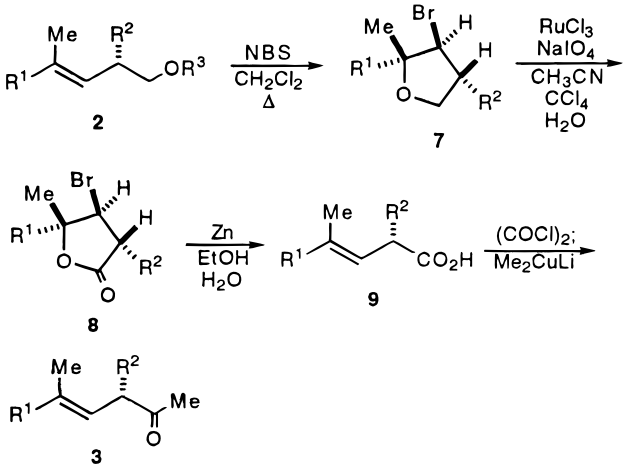
Having protected the alkene as a bromo ether, further transformations of the R^1 group were possible. To regenerate the alkene and eventually to prepare the desired methyl ketone, we decided to oxidize the tetrahydrofurans **7** to the lactones **8**. This was accomplished using $RuCl_3$ and $NaIO_4$[8] in the preferred mixed solvent system[9] to give 82−93% yields of the desired lactones. Reductive ring opening was then effected with zinc dust in aqueous ethanol to give the alkenoic acids **9** in 70−87% yield. Simple reduction of the bromotetrahydrofurans **7** to regenerate the homoallylic alcohols was unsuccessful with zinc or a variety of other reducing agents, although it was cleanly carried out with *tert*-butyllithium. Finally, the acids **9**, on treatment with lithium dimethylcuprate, were converted to the methyl ketones via their crude acid chlorides (prepared by reaction with oxalyl chloride) to give **3** in 52−67% yield.



We have thus shown that bromoetherification of homoallylic alcohols and ethers occurs diastereoselectively to give bromotetrahydrofurans (where the alkene functionality has been protected), which are cleanly oxidized to the lactones, reduced to the alkenoic acids, and converted into the desired methyl ketones. Further work on the "non-aldol aldol" process and the synthesis of the tedanolides will be reported in due course.[10]

Experimental Section

General Methods. All reactions were carried out under argon with the exclusion of moisture. Reagents were purchased from commercial sources and used without further purification unless otherwise specified. The following solvents and reagents were distilled from the indicated agent under argon: tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl; dichloromethane, benzene, and toluene from calcium hydride; triethylamine from calcium hydride. Flash column chromatography was carried out in the indicated solvent system on 230−400 mesh silica gel. The proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 200 and 500 MHz, and the carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 50 and 125 MHz. Spectra were taken in the indicated solvent at ambient temperature, and the chemical shifts are reported in parts per million relative to the solvent used. The infrared (IR) spectra were recorded on a Fourier transform IR spectrometer.

General Procedure for the Preparation of the 3-Pentenoic Acids, 9. Excess zinc dust was suspended in ethanol containing a small amount of water. The zinc suspension was treated with a solution of lactone **8** (0.4−1.0 mmol) in ethanol (4 mL). The mixture was refluxed for 5 h and cooled to room temperature. Insoluble particles were filtered through Celite. The filtrate was concentrated in vacuo and extracted with diethyl ether (2 × 20 mL). The organic phase was extracted with 10% Na_2CO_3 (2 × 20 mL), followed by acidification with cold concentrated HCl and subsequent extraction with diethyl ether (4 × 50 mL). The organic phases were washed with brine (30 mL), dried over $MgSO_4$, and vacuum concentrated to give the 3-pentenoic acid **9**.

2,4-Dimethyl-3-pentenoic acid, 9a. Zinc dust (3.14 g, 48 mmol) and **8a** (191 mg, 1.0 mmol) gave 110 mg (86%) of the known carboxylic acid **9a**. The spectroscopic data for **9a** matched that reported in the literature.[11]

4-Methyl-2-phenyl-3-pentenoic Acid, 9b. Zinc dust (4.71 g, 72 mmol) and lactone **8b** (380 mg, 1.50 mmol) gave 249 mg (87%) of carboxylic acid **9b**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.40 (5H, m), 5.53 (1H, dm, J = 9.4 Hz), 4.49 (1H, d, J = 9.4 Hz), 1.67 (3H, d, J = 1.1 Hz), 1.59 (3H, d, J = 1.3 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 179.16, 138.87, 135.71, 128.70, 127.90, 127.20, 121.39, 50.42, 25.86, 25.74. IR (neat): 3500−3100 (br), 2978, 2928, 2856, 1736, 1456, 1116 cm^{-1}.

4-Methyl-3-pentenoic Acid, 9c. Zinc dust (1.30 g, 19.8 mmol) and lactone **8c** (80 mg, 0.414 mmol) gave 36 mg (76%) of the known carboxylic acid **9c**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 10.59 (1H, bs), 5.21 (1H, tm, J = 7.1 Hz), 2.98 (2H, d, J = 7.2 Hz), 1.67 (3H, s), 1.56 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 178.85, 136.12, 115.11, 33.53, 25.56, 25.24. IR (neat): 3450−3100 (br), 2968, 2924, 1708, 1414, 1302, 1221, 1155 cm^{-1}.

(3*E*)-2,4-Dimethyl-5-[((1,1-dimethylethyl)dimethylsilyl)-oxy]-3-pentenoic Acid, 9d. Zinc dust (3.14 g, 48 mmol) and lactone **8d** (300 mg, 0.89 mmol) gave 160 mg (70%) of carboxylic acid **9d**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 5.38 (1H, dm, J = 9.4 Hz), 3.97 (2H, s), 3.33 (1H, m), 1.59 (3H, d, J = 1.1 Hz), 1.19 (3H, d, J = 7.0 Hz), 0.94 (9H, s), 0.02 (6H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 181.23, 137.27, 122.72, 67.96, 38.33, 25.89, 18.37, 17.63, 13.58 (two high-field carbons not recorded). IR (neat): 2939, 2893, 2860, 1713, 1464, 1253, 1082, 815, 777 cm^{-1}.

General Procedure for the Conversion of the Acid 9 into the 4-Hexen-2-one, 3. A solution of the acid **9** (0.5−1 mmol) in methylene chloride was treated with a 2 M oxalyl chloride solution in methylene chloride. After the mixture had stirred for 4 h at room temperature, it was concentrated under vacuum to produce the crude acid chloride, which was dissolved in THF and added at −78 °C to a THF solution of lithium dimethylcuprate, previously prepared by addition of 1 M methyllithium (2 equiv) to a suspension of copper(I) iodide (1 equiv) in THF at 0 °C and stirred at room temperature for 10 min. After the THF solution had stirred for 1 h, the reaction was quenched by the sequential addition of methanol and saturated NH_4Cl at −78 °C. The organic phase was removed under vacuum. The remaining aqueous phase was extracted with diethyl ether, dried over $MgSO_4$, and purified by flash column chromatography (silica gel, 50% diethyl ether:hexanes) to give the enone **3**.

3,5-Dimethyl-4-hexen-2-one, 3a. The acid **9a** (100 mg, 0.780 mmol) gave 66 mg (67%) of the known enone **3a**. The spectroscopic data for **3a** matched that reported in the literature.[12]

5-Methyl-3-phenyl-4-hexen-2-one, 3b. The acid **9b** (200 mg, 1.05 mmol) gave 130 mg (66%) of compound **3b**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.25 (5H, m), 5.62 (1H, dm, J = 9.4 Hz), 4.52 (1H, d, J = 9.4 Hz), 2.08 (3H, s), 1.76 (3H, d, J = 0.9 Hz), 1.69 (3H, d, J = 1.3 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 207.14, 139.26, 135.43, 128.85, 128.05, 127.01, 121.53, 58.82, 28.27, 25.98, 18.24. IR (neat): 2972, 2914, 2860, 1716, 1601, 1493, 1354, 1155, 750, 700 cm^{-1}.

(8) Smith, A. B., III; Scarborough, R. M. *Synth. Commun.* **1980**, *10*, 205.

(9) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(10) (a) Jung, M. E.; Lee, W. S. Manuscript submitted for publication. (b) Jung, M. E.; Marquez, R. Manuscript submitted for publication.

(11) Henin, F.; Mortezaei, R.; Muzart, J.; Pete, J.-P.; Piva, O. *Tetrahedron* **1989**, *45*, 6171.

(12) Van der Weerdt, A. J. A.; Cerfontain, H. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1357.

3,5-Dimethyl-6-hydroxy-4-hexen-2-one, 3d. The acid **9d** (130 mg, 0.503 mmol) gave 37 mg (52%) of compound **3d**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 5.30 (1H, dm, J = 9.7 Hz), 3.98 (2H, s), 3.38 (1H, m), 2.08 (3H, s), 1.68 (3H, d, J = 1.2 Hz), 1.10 (3H, d, J = 6.3 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 209.98, 137.65, 124.49, 68.15, 46.59, 27.97, 16.46, 14.02. IR (neat): 3427, 2974, 2930, 2872, 1709, 1456, 1356 cm^{-1}.

General Procedure for the Formation of the 3-Bromotetrahydrofurans, 7. The 3-penten-1-ol **2** (1 equiv) was dissolved in anhydrous methylene chloride. *N*-Bromosuccinimide (NBS, 2 equiv) was added, and the mixture was refluxed in the dark for 8 h. The solvent was evaporated, pentane was added, and the suspension was filtered. The filtrate was concentrated under vacuum. It was flash column chromatographed (silica gel, 20% diethyl ether:hexanes) to yield the bromotetrahydrofuran **7**.

***trans*-3-Bromo-2,2,4-trimethyltetrahydrofuran, 7a.** 2,4-Dimethyl-3-penten-1-ol, **2a** (400 mg, 3.50 mmol), gave 406 mg (60%) of compound **7a**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.95 (1H, app t, J = 8.5 Hz), 3.42 (1H, d, J = 8.7 Hz), 3.32 (1H, t, J = 8.7 Hz), 2.45 (1H, m), 1.25 (3H, s), 1.22 (3H, s), 1.09 (3H, d, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 82.21, 70.96, 62.25, 41.99, 26.19, 23.98, 15.40. IR (neat): 2974, 2934, 2876, 1593, 1458, 1388, 1136, 1028, 804, 699 cm^{-1}.

***trans*-3-Bromo-2,2-dimethyl-4-phenyltetrahydrofuran, 7b.** 4-Methyl-2-phenyl-3-penten-1-ol, **2b** (1.4 g, 7.95 mmol), gave 1.75 g (86%) of compound **7b**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.30 (5H, m), 4.24 (1H, app t, J = 9.1 Hz), 3.92 (1H, d, J = 10.3 Hz), 3.88 (1H, app t, J = 8.7 Hz), 3.65 (1H, m), 1.42 (3H, s), 1.41 (3H, s). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 138.86, 128.72, 127.34, 82.87, 71.31, 62.00, 53.46, 25.87, 23.35 (one low field carbon unresolved). IR (neat): 2976, 2930, 2878, 1601, 1369, 1136, 1032, 698 cm^{-1}.

3-Bromo-2,2-dimethyltetrahydrofuran, 7c. 4-Methyl-3-penten-1-ol, **2c** (250 mg, 2.50 mmol), gave 216 mg (48%) of the known bromo furan compound **7c**. The spectroscopic data for **7c** matched that reported in the literature.[6]

***trans*-3-Bromo-2,4-dimethyl-2-[((1,1-dimethylethyl)dimethylsilyl)oxy]methyltetrahydrofuran, 7d.** (3*E*)-2,4-Dimethyl[((1,1-dimethylethyl)dimethylsilyl)oxy]-5-(phenylmethoxy)-2-pentene, **2d** (1.00 g, 2.99 mmol), was dissolved in anhydrous methylene chloride (80 mL). NBS (1.05 g, 5.98 mmol) was added, and the mixture was refluxed in the dark for 5 days. The solvent was evaporated, pentane (25 mL) was added, and the suspension was filtered. The filtrate was concentrated under vacuum. It was flash column chromatographed (silica gel, 2.5% diethyl ether: hexanes) to yield 620 mg (64%) of compound **7d**. The spectroscopic data for this compound matched that of the optically active compound prepared from **2e** as described below.

(2*R*,3*S*,4*R*)-3-Bromo-2,4-dimethyl-2-[((1,1-dimethylethyl)-dimethylsilyl)oxy]methyltetrahydrofuran, 7d. (3*E*,2*S*)-2,4-Dimethyl-5-[((1,1-dimethylethyl)dimethylsilyl)oxy]pent-3-en-1-ol, **2e** (124.4 mg, 0.546 mmol), was dissolved in anhydrous methylene chloride (18 mL). After addition of NBS (214 mg, 1.20 mmol), the mixture was refluxed in the dark for 1.5 h. Water was added, and the layers were separated, with subsequent washing of the aqueous layer with methylene chloride (15 mL). Combining of the organic layers, followed by drying ($MgSO_4$), concentration under vacuum, and flash column chromatography (silica gel, 4% ethyl acetate in hexanes), yielded 146.7 mg (88%) of compound **7d**: $[\alpha]^{25}_D = -12.88°$ (*c* 0.73 in $CHCl_3$). ^{1}H NMR (C_6D_6, 500 MHz) δ: 4.07 (1H, d, J = 10.7 Hz), 3.69 (1H, app t, J = 8.1 Hz), 3.54 (1H, d, J = 10.8 Hz), 3.52 (1H, d, J = 10.8 Hz), 3.18 (1H, dd, J = 10.0, 8.3 Hz), 2.26 (1H, m), 1.26 (3H, s), 0.96 (9H, s), 0.84 (3H, d, J = 6.52 Hz), 0.07 (3H, s), 0.06 (3H, s). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 84.19, 72.09, 66.60, 56.32, 42.13, 25.76, 21.64, 18.15, 14.08, −5.46, −5.64. IR (neat): 2957, 2930, 2856, 1460, 1381, 1251, 1103, 1037, 925, 837, 814, 777 cm^{-1}.

(2*S*,3*S*,4*R*)-3-Bromo-2,4-dimethyl-2-[((1,1-dimethylethyl)-dimethylsilyl)oxy]methyltetrahydrofuran, 7f. By an analogous procedure, (3*Z*,2*S*)-2,4-dimethyl-5-[((1,1-dimethylethyl)-dimethylsilyl)oxy]pent-3-en-1-ol, **2f** (42.7 mg, 0.187 mmol), yielded 49 mg (86%) of compound **7f**: $[\alpha]^{25}_D = -36.74°$ (*c* 1.87 in $CHCl_3$). ^{1}H NMR ($CHCl_3$, 500 MHz) δ: 4.11 (1H, app t, J = 8.3 Hz), 3.81 (1H, d, J = 10.7 Hz), 3.58 (1H, d, J = 10.7 Hz), 3.52 (1H, d, J = 10.4 Hz), 3.41 (1H, dd, J = 8.5, 8.2 Hz), 2.82 (1H, m), 1.20 (3H, s), 1.09 (3H, d, J = 6.7 Hz), 0.90 (9H, s), 0.07 (3H, s), 0.06 (3H, s). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 83.71, 72.73, 68.39, 60.90, 42.33, 25.76, 21.65, 18.13, 15.50, −5.66 (2C's). IR (neat): 2959, 2930, 2858, 1471, 1462, 1361, 1251, 1109, 1032, 942, 839, 777 cm^{-1}.

General Procedure for the Formation of the 4-Bromodihydrofuran-2(3*H*)-ones, 8. A mixture of the 3-bromotetrahydrofuran **7** (1 equiv), $RuCl_3 \cdot H_2O$ (0.55 equiv), and $NaIO_4$ (8 equiv) in a solvent mixture of 1:1:1.5 carbon tetrachloride, acetonitrile, and water was stirred at room temperature for 14 h. The reaction mixture was treated with 2-propanol and was stirred vigorously for an additional 1 h. The mixture was extracted with methylene chloride. The combined organic phases were dried over $MgSO_4$. After evaporation of the solvent, diethyl ether was added and the suspension was filtered through Celite. The solvent was removed under vacuum to produce a crystalline solid which, upon washing with cold pentane, yielded the bromolactones **8**.

***trans*-4-Bromodihydro-3,5,5-trimethylfuran-2(3*H*)-one, 8a.** 3-Bromo-2,2,4-trimethyltetrahydrofuran, **7a** (130 mg, 0.67 mmol), yielded 120 mg (93%) of compound **8a**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.76 (1H, d, J = 11.7 Hz), 2.80 (1H, dd, J = 11.7, 6.9 Hz), 1.44 (6H, bs), 1.28 (3H, d, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 174.38, 84.47, 56.36, 43.60, 26.00, 23.63, 12.41. IR (neat): 3057, 2986, 1780, 1265, 1109, 738, 704 cm^{-1}.

***trans*-4-Bromodihydro-5,5-dimethyl-3-phenylfuran-2-(3*H*)-one, 8b.** 3-Bromo-2,2-dimethyl-4-phenyltetrahydrofuran, **7b** (1.70 g, 6.66 mmol), yielded 1.38 g (82%) of compound **8b**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.30 (5H, m), 4.20 (1H, d, J = 11.9 Hz), 4.01 (1H, d, J = 11.9 Hz), 1.61 (3H, s), 1.58 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 162.20, 133.39, 129.03, 128.55, 128.44, 84.65, 57.06, 55.00, 26.10, 24.06. IR (neat): 2959, 2924, 2853, 1753, 1456, 1375, 1259, 1095, 734, 698 cm^{-1}.

4-Bromodihydro-5,5-dimethylfuran-2(3*H*)-one, 8c. 3-Bromo-2,2-dimethyltetrahydrofuran, **7c** (650 mg, 3.63 mmol), yielded 574 mg (82%) of compound **8c**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 4.28 (1H, t, J = 7.4 Hz), 3.16 (1H, dd, J = 18.1, 7.5 Hz), 2.87 (1H, dd, J = 18.1, 7.3 Hz), 1.59 (3H, s), 1.49 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 173.50, 86.35, 49.62, 39.83, 25.88, 25.29. IR (neat): 2984, 2928, 2855, 1786, 1464, 1275, 1122, 611 cm^{-1}.

(3*R*,4*S*,5*R*)-4-Bromodihydro-3,5-dimethyl-5-[((1,1-dimethylethyl)dimethylsilyl)oxy]methylfuran-2(3*H*)one, 8d. (2*R*,3*S*,4*R*)-3-Bromo-2,4-dimethyl-2-[((1,1-dimethylethyl)dimethylsilyl)oxy]methyltetrahydrofuran, **7d** (350 mg, 1.083 mmol), yielded 320 mg (88%) of compound **8d**. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 4.26 (1H, d, J = 11.6 Hz), 3.68 (1H, d, J = 11.7 Hz), 3.57 (1H, d, J = 11.7 Hz), 2.77 (1H, m), 1.34 (3H, s), 1.26 (3H, d, J = 7.0 Hz), 0.82 (9H, s), 0.07 (3H, s), 0.06 (3H, s).^{13}C NMR ($CDCl_3$, 50 MHz) δ: 174.29, 86.03, 64.60, 49.34, 43.55, 25.73, 19.78, 18.17, 12.48, (two high-field carbons not recorded). IR (neat): 2955, 2885, 2858, 1788, 1461, 1311, 1120, 949, 839, 779, 613 cm^{-1}.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of all new compounds and the NOESY data for compounds **7d** and **7f** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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