dry nitrogen before use. GLC analysis were carried out on a Varian 3700 gas chromatograph equipped with a 10-m fused-silica capillary column coated with OV-101 liquid phase. Peak integrations were performed on a Hewlett-Packard 3390A integrator. ^1H and ^{13}C NMR spectra were recorded on Varian EM-360 (60 MHz in ^1H) and Varian CFT-20 (20 MHz in ^{13}C) NMR spectrometers, respectively. IR spectra were taken on a Beckman IR-8 spectrometer. Mass spectra were obtained on a Finnigan 4021 instrument. Elemental analyses were performed by Galbraith Laboratories, Inc. of Knoxville, TN.

Materials. The preparation of *B*-methoxy-9-borabicyclo-[3.3.1]nonane and purification of BF_3·OEt_2 were described elsewhere.[7] *tert*-Butyllithium in pentane was obtained from Alfa. 1-(Trimethylsilyl)propyne was purchased from Petrarch. 1-(Trimethylsilyl)-1-hexyne was prepared as described earlier.[8] Imines were prepared by reacting various primary amines with aldehydes and ketones[5] and stored under nitrogen after distillation. Basic alumina of grade II–III was obtained from Merck.

Condensation of Imine with 1. The following procedure for the reaction between 1 and imine derived from benzaldehyde and *n*-propylamine (entry 1) is representative. The organoborane 1 (10 mmol) was prepared as described previously.[4] To the reaction flask was then added via syringe 1.60 mL (1.47 g, 10 mmol) of imine derived from benzaldehyde and *n*-propylamine at room temperature. After stirring for 50 h, 4 mL of 3 N NaOH and 3.5 mL of 30% H_2O_2 were introduced dropwise at 0 °C. The organic layer was then separated and extracted with 4 N HCl (3 × 25 mL). The combined extracts were neutralized with aqueous sodium bicarbonate solution. The neutralized solution was then extracted with ether. The combined extracts were dried over anhydrous sodium sulfate. After removing of solvent at reduced pressure, the red oily residue was column chromatographed on basic alumina using petroleum ether and petroleum ether–ether (95:5) as eluents. Distillation on a short-path distilling head afforded 1.944 g (75% yield) of 4-phenyl-4-(*n*-propylamino)-3-(trimethylsilyl)-1,2-butadiene as a pale yellow liquid: bp 96 °C (5×10^{-3} torr); IR (neat) 3350 (w), 1930 (s, C=C=C), 1450 (m), 1245 (s), 830 (s), 750 (m), 690 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4 (s, 5 H), 4.75 (d, 2 H, J = 3 Hz), 4.65 (t, 1 H, J = 3 Hz), 2.45 (t, 2 H), 2.05 (br, 1 H), 1.55 (m, 2 H), 0.9 (t, 3 H), −0.05 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 207.8, 143.4, 128.1, 127.8, 127.1, 99.8, 71.7, 62.2, 49.7, 23.2, 11.9, −1.2. Anal. Calcd for $C_{16}H_{25}NSi$: C, 74.06; H, 9.71; N, 5.40. Found: C, 74.08; H, 9.48; N, 5.38.

4-Phenyl-4-(phenylamino)-3-(trimethylsilyl)-1,2-butadiene Hydrochloride (entry 3). The reaction was carried out as in the earlier case except that the imine (1.81 g, 10 mmol) derived from benzaldehyde and aniline was first dissolved in 5 mL of THF and then transferred via cannula to the reaction flask containing 10 mmol of organoborane 1. The crude product was isolated as the hydrochloride of 4-phenyl-4-(phenylamino)-3-(trimethylsilyl)-1,2-butadiene and further recrystallized from acetone to afford 2.052 g (62%) of an analytically pure sample as pale yellow needles: mp 168–169 °C; IR (KBr) 3000–2500 (br), 1935 (s, C=C=C), 1400 (s), 1250 (s), 835 (s), 750 (m), 690 (s) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.72 (br, s, 10 H), 5.35 (d, 2 H, J = 2 Hz), 5.2 (t, 1 H, J = 2 Hz), 0.12 (s, 9 H); ^{13}C NMR (Me_2SO-d_6) δ 208.2, 142.6, 139.4, 128.9, 128.3, 128.2, 128.0, 121.4, 117.8, 97.0, 73.7, 59.8, −1.3; mass spectrum, m/e (relative intensity) 294 (M·HCl − Cl^-, 10), 201 (10), 182 (100), 150 (14), 128 (10), 104 (32), 77 (43), 73 (50). Anal. Calcd for $C_{19}H_{23}NSi$·HCl: C, 69.17; H, 7.33; N, 4.25. Found: C, 69.36; H, 7.41; N, 4.20.

Condensation of Imine with 2. The following procedure for the condensation between 2 and imine derived from benzaldehyde and *n*-propylamine (entry 7) is representative. The organoborane 2 (10 mmol) was prepared as described previously.[4] After cooling to −78 °C, the imine (1.60 mL, 1.47 g, 10 mmol) dissolved in 5 mL of THF was transferred by cannula into the reaction flask. The reaction mixture was kept at −78 °C for 1 h and then allowed to warm to room temperature and stirred overnight. After the usual workup as described earlier, the product was isolated by column chromatography on basic alumina using petroleum ether and petroleum ether–ether mixture (95:5) as eluents. A pale yellow liquid 2.514 g (83%) of 1-phenyl-1-(*n*-propylamino)-2-(trimethylsilyl)-2,3-heptadiene was obtained. The product had the following: IR (neat) 3350 (w), 1940 (s, C=C=C), 1450 (s), 1245 (s), 835 (s), 750 (m), 695 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (s, 5 H), 5.1 (dt, 1 H, J = 2, 7 Hz), 4.2 (d, 1 H, J = 2 Hz), 2.7–2.35 (m, 2 H), 2.35–1.85 (m, 2 H), 1.8 (s, 1 H), 1.8–1.2 (m, 4 H), 1.2–1.08 (m, 6 H), −0.05 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 204.9, 141.8, 128.5, 128.2, 127.5, 99.7, 89.3, 62.6, 49.4, 30.9, 23.3, 22.3, 14.0, 11.8, −1.0. Anal. Calcd for $C_{19}H_{31}NSi$: C, 75.68; H, 10.36; N, 4.64. Found: C, 75.13; H, 10.76; N, 4.64.

4-(Cyclohexylamino)-5-methyl-1-(trimethylsilyl)-3-propyl-1-hexyne (entry 11): colorless liquid, 2.642 g (86%); IR (neat) 2170 (s, C≡C), 1450 (s), 1380 (s), 1250 (s), 860 (s), 835 (s), 755 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.8–2.3 (br, 2 H), 2.3–1.2 (br, 17 H), 1.2–0.8 (m, 9 H), 0.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 109.4, 108.7, 86.9, 66.7, 61.8, 55.5, 55.1, 36.6, 36.1, 35.2, 34.4, 34.3, 33.8, 33.6, 33.5, 32.8, 32.0, 28.3, 27.4, 26.4, 25.8, 25.2, 25.1, 23.6, 22.8, 22.3, 21.2, 21.1, 20.1, 19.8, 19.0, 14.0, 0.4, 0.2. The ^{13}C NMR spectrum indicated the presence of both erythro and threo isomers. Anal. Calcd for $C_{19}H_{37}NSi$: C, 74.19; H, 12.13; N, 4.55. Found: C, 74.06; H, 12.09; N, 4.20.

1-(Trimethylsilyl)-3-[1-(phenylamino)cyclohexyl]-1-hexyne (entry 12): colorless liquid, 2.156 g (66%); IR (neat) 3450 (w), 2170 (s, C≡C), 1600 (s), 1495 (s), 1450 (m), 1320 (m), 1280 (m), 1250 (s), 1155 (m), 995 (m), 870 (s), 835 (s), 750 (s), 690 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35–7.0 (m, 2 H), 6.95–6.6 (m, 3 H), 3.5 (s, 1 H), 2.8 (br, 1 H), 2.2–1.1 (br, 14 H), 0.9 (br, 3 H), 0.15 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.2, 128.8, 118.0, 116.9, 109.1, 87.5, 58.3, 41.1, 33.1, 32.4, 30.5, 26.0, 21.6, 21.3, 13.8, 0.2. Anal. Calcd for $C_{21}H_{33}NSi$: C, 77.00; H, 10.16; N, 4.28. Found: C, 76.88; H, 10.21; N, 4.14.

Acknowledgment. Financial support of this research by the National Science Foundation is greatfully acknowledged.

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A New Synthesis of 3-*n*-Butyl-4-bromo-5(*Z*)-(bromomethylidene)-2-(5*H*)-furanone, a Naturally Occurring Fimbrolide from *Delisia fimbriata* (Bonnemaisoniaceae)

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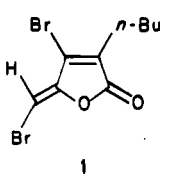
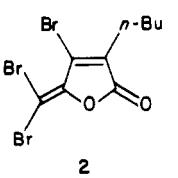
We have reported previously that lithium (*E*)-β-bromo-β-lithioacrylates react with electrophilic reagents such as carbonyl compounds[1] or acid anhydrides[2] to give the corresponding β-bromo- or β-bromo-γ-hydroxybutenolides after acidification. We now report the application of this methodology to a new synthesis of the dibromobutenolide 1 which is a member of a novel class



1



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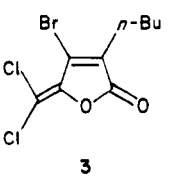

3

of halogenated antibiotics isolated from the red seaweed *Delisea fimbriata* (Bonnemaisonaceae).[3-5] An attempt was

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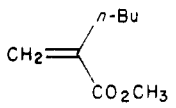
also made to prepare the tribromo compound **2**, which is also a naturally occurring fimbrolide.[3,4] This was unsuccessful, but the related bromo dichloro compound **3** was produced.

The starting material for the synthesis of **1** and **3** was methyl 2-*n*-butylpropenoate (**4**) which was prepared by the method of Hoffman and Jurgen.[6] Addition of bromine to this α,β-unsaturated ester gave the α,β-dibromo derivative **5a**, which was converted into the (*E*)-bromo ester **6a** by dehydrobromination and transesterification with sodium isopropoxide in isopropyl alcohol. Hydrolysis of **6a** with potassium hydroxide in aqueous ethyl alcohol afforded (*E*)-3-bromo-2-*n*-butylpropenoic acid (**6b**) in ~40% yield from ester **4**. The ^{1}H NMR spectrum of the compound exhibited a singlet at δ 7.62 for the C-3 hydrogen atom. This is consistent with the structural assignment since the corresponding 2-methyl compound **6c**[7a] showed a singlet at δ 7.71 while the *Z* isomer of **6c** exhibited a singlet at δ 6.74. In addition, the subsequent reactions of **6b** support the structural assignment.



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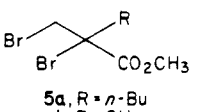
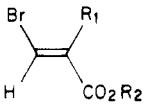


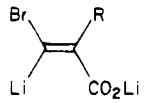
5a, R = *n*-Bu
b, R = CH_3



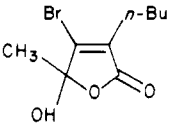
6a, R_1 = *n*-Bu; R_2 = *i*-Pr
b, R_1 = *n*-Bu; R_2 = H
c, R_1 = CH_3; R_2 = H

The dehydrobromination of dibromo ester **5a** proved to be unexpectedly difficult. When it was treated with potassium or sodium hydroxide in aqueous tetrahydrofuran (THF) or ethyl alcohol under conditions that allowed the smooth conversion of the related 2-methyl compound **5b** into the corresponding acid **6c**,[8] less than 10% of **6a** was formed and the major product of the reaction appeared to be derived from substitution of the C-3 bromine atom by hydroxide ion. Likewise, treatment of **5a** with sodium methoxide in methyl alcohol led largely to substitution rather than elimination. Also, then **5a** was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in methylene chloride or potassium *tert*-butoxide in *tert*-butyl alcohol at room temperature, largely unchanged starting material was recovered. Apparently, the 2-*n*-butyl group in **5a** causes an unusual amount of steric hindrance toward abstraction of the C-3 proton by certain bases, and of the bases tried isopropoxide ion was the only one with the appropriate combination of basicity and steric requirements to allow the dehydrobromination process to occur relatively easily.

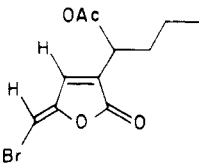
Treatment of bromo acid **6b** with 2 equiv of *n*-butyllithium in THF at −78 °C provided the β-lithio carboxylate **7a** which upon reaction with acetic anhydride yielded after acidification the γ-hydroxybutenolide **8** in 50% yield. Conversion of compound **8** into **1** was accomplished along the lines described by Kosuki, Monden, and Ochi for the synthesis of the debromoacetoxyfimbrolide **9**.[9] Thus,



7a, R = *n*-Bu
b, R = CH_3



8



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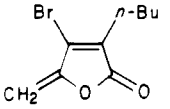
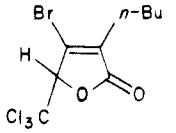


10

dehydration of **8** with phosphorus pentoxide in benzene gave the γ-methylidene derivative **10** in 87% yield. Addition of bromine to **10** followed by dehydrobromination of the adduct with DBU in methylene chloride gave **1** in 95% yield. This material showed identical ^{1}H NMR and IR spectral properties to those reported by Beechan and Sims.[5,10]

Our original plan for the synthesis of the tribromofimbrolide **2** involved the reaction of the β-lithio carboxylate **7a** with tribromoacetaldehyde to form a γ-(tribromomethyl)-β-bromo butenolide followed by elimination of one mole of hydrogen bromine to generate the γ-dibromomethylidene group. However, this approach was abandoned when it was shown that reaction of the related vinyllithium compound **7b** with tribromoacetaldehyde occurred with attack of the vinyl carbanion at a bromine atom to yield 2-methyl-3,3-dibromopropenoic acid[11] rather than addition to the carbonyl group.[12] Reagent **7a** was found to undergo addition to the carbonyl group of trichloroacetaldehyde to yield the γ-(trichloromethyl)butenolide **11**. Dehydrochlorination of **11** with DBU gave



11

the dichlorobromo compound **3** in 78% yield. We had hoped to convert **3** into the naturally occurring tribromo compound **2** by reaction with bromide ion to effect exchange of the chlorine atoms.[13] However, when **3** was treated with excess lithium bromide in dimethylformamide (DMF) or potassium bromide and 18-crown-6 in benzene or the recently reported dilithium tetrabromonickellate(II) reagent[14] only a trace of material containing two bromine atoms and no product containing three bromine atoms was produced according to MS/GC analysis of the reaction mixture. Possibly, the greater strength of the sp^2 carbon–chlorine bond than the sp^2 carbon–bromine bond prevents the exchange process from being favorable.

Experimental Section

Melting points were determined with a Fisher-Johns hotstage and are uncorrected. The IR spectra were determined with Perkin-Elmer Model 457 or Model 1420 spectrometers and absorptions are reported in cm^{-1}. The ^{1}H NMR spectra were de-

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(4) For the isolation of other fimbrolides closely related to **1**, see: Pettus, J. A., Jr.; Wing, R. M.; Sims, J. J. *Tetrahedron Lett.* **1977**, 41.
(5) For the first synthesis of **1** by oxidation/dehydration of dibrominated 2-butyllevulinic acid with sulfuric acid, see: Beechan, C. M.; Sims, J. J. *Tetrahedron Lett.* **1979**, 1649.
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termined at 60 MHz with a Varian Associates Model T-60 or EM-360 spectrometer or at 300 MHz with a Bruker Model WM-300 NMR Spectrometer. The ^{13}C spectra were determined at 75 MHz with a Bruker Model WM-300 or at 50 MHz with a Nicolet Model 293-A NMR spectrometer The mass spectra were obtained with Hitachi Perkin Elmer Model RMU-7, Hitachi RMU-6M or Varian MAT 1125 spectrometers with a 70 electron volt source. GC/MS spectra were obtained with a Hewlett Packard Model 5985 chromatograph on a DB-1 (eq SE-30) column. Microanalyses were performed by Atlantic Microlabs, Inc., Atlanta, Georgia.

(*E*)-3-Bromo-2-*n*-butylpropenoic Acid. To a solution of methyl *n*-butylacrylate (**4**), 7.10 g (0.05 mol), prepared according to the reported procedures,[6] in 50 mL of acetic acid at 0 °C was added dropwise with stirring, 8.11 g (0.05 mol) of bromine. The resulting red-brown solution was stirred at 25 °C for an additional 3 h. Then 25 mL of H_2O was added and the mixture was extracted with 3 × 25 mL of pentane. The combined pentane extracts were washed with 2 × 25 mL of saturated aqueous $NaHSO_3$ solution until the bromine color was discharged. After an additional washing with 25 mL of saturated aqueous NaCl solution, the organic extract was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo. The residual oil was distilled (bp 86.0–88.0 °C, 1.5 torr) to give the clean dibromo derivative **5a**, 13.59 g (90%), which had the following spectral data: ^1H NMR (CCl_4) δ 3.75 (3 H, s), 2.10 (2 H, m), 1.45 (4 H, m), 0.98 (3 H, t, J = 6 Hz); MS, m/e 300, 302, 304. Dehydrobromination of compound **5a** was carried out as follows: sodium, 0.82 g (0.04 mol), was dissolved in 400 mL of *i*-PrOH at reflux. The solution was then cooled to 25 °C and the dibromo ester **5a**, 12.00 g (0.04 mol), was added. The mixture was stirred at 25 °C for 18 h. The isopropyl alcohol was then removed in vacuo and the resulting white emulsion was taken up in 20 mL of water. The aqueous phase was extracted with 2 × 25 mL of ether, dried over anhydrous $MgSO_4$ and concentrated in vacuo. This allowed the isolation of crude isopropyl (*E*)-3-bromo-2-*n*-butylacrylate (**6a**), 5.01 g (50%): ^1H NMR (CCl_4) δ 7.30 (1 H, s), 5.00 (1 H, br m), 2.45 (2 H, t, J = 8 Hz), 1.32 (10 H, m), 1.00 (3 H, t, J = 5 Hz).

Without further purification, compound **6a**, 5.01 g (0.02 mol), was dissolved in a 3:1 mixture by volume of 95% ethanol and H_2O, respectively. The mixture was stirred at 25 °C for 48 h. Then most of the ethanol was removed on the rotary evaporator and the residual aqueous solution was acidified with 15% hydrochloric acid and extracted with 3 × 10 mL of ether. The combined ethereal extracts were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo led to the isolation of 3.31 g (80%) of crude (*E*)-3-bromo-2-*n*-butylpropenoic acid (**6b**). Distillation (bp 109.0–110.0 °C (0.5 torr)) afforded analytically pure bromo acid **6b** as a colorless oil. The spectral data for compound **6b** were as follows: ^1H NMR (CCl_4) δ 7.62 (1 H, s), 2.49 (2 H, t, J = 8 Hz), 1.45 (4 H, m), 0.98 (3 H, t, J = 5 Hz), 12.30 (1 H, br s, CO_2H); MS, m/e 207, 209. Anal. Calcd for $C_7H_{11}BrO_2$: C, 40.60; H, 5.35. Found: C, 40.75, H, 5.36.

5-Hydroxy-5-methyl-4-bromo-3-*n*-butyl-2(5*H*)-furanone (8). To a solution of 2.07 g (10.0 mmol) of bromo acid **6b** in 200 mL of dry THF at −78 °C was added dropwise with stirring under nitrogen 8.0 mL (20.0 mmol) of 2.50 M *n*-butyllithium. The reaction mixture was stirred for 3 h at −78 °C and the vinyllithium reagent **7a** thus generated was then added dropwise to a solution of 1.50 g (15.0 mmol) of acetic anydride in 20 mL of dry THF at −78 °C. The mixture was stirred for 3 h at −78 °C and allowed to warm to room temperature. Water (50 mL) was added and the layers were separated. The organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo. The aqueous layer was acidified with 15% hydrochloric acid and then extracted with 2 × 25 mL of ether. These combined ethereal extracts were dried over anhydrous $MgSO_4$ and then concentrated in vacuo. The ^1H NMR spectrum of the crude material indicated that the butenolide product was distributed between the basic and neutral fractions. The combined yields of product was 1.31 g (50%). Preparative thin-layer chromatography on silica gel with 30:70 ethyl acetate/hexane elution gave analytically pure material. The spectral data for hydroxybutenolide **8** were as follows: IR (CCl_4) 3380, 2945, 1778, 1660, 1250, 1100, 700 cm^{-1}; ^1H NMR (CCl_4) δ 5.31 (1 H, br, s), δ 2.22 (2 H, t, J = 1.0 Hz), 1.50 (3 H, s), 1.30 (4 H, m), 0.93 (3 H, t, J = 6 Hz). Anal. Calcd C, 43.39; H, 5.26. Found: C, 43.62; H, 5.35.

5-Methylene-4-bromo-3-*n*-butyl-2(5*H*)-furanone (10). A solution of 0.50 g (2.0 mmol) of butenolide **8** in 55.0 g of a 10:1 by weight mixture of benzene and P_2O_5 was refluxed under nitrogen for 2 h. After cooling to room temperature, 30 mL of H_2O was added and the phases were separated. The organic phase was dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to obtain the γ-methylene-β-bromobutenolide **10**, 0.40 g (87%): ^1H NMR (CCl_4) δ 5.10 (1 H, d, J = 1 Hz), 5.00 (1 H, d, J = 1 Hz), 2.35 (2 H, t, J = 7 Hz), 1.31 (4 H, m), 0.95 (3 H, t, J = 6 Hz).

3-*n*-Butyl-4-bromo-5(*Z*)-(bromomethylidene)-2(5*H*)-furanone (1). Without further purification, compound **10**, 0.40 g (1.7 mmol), obtained above, was treated with 0.329 g (2.0 mmol) of bromine in 25 mL CH_2Cl_2 in the presence of a small amount of hydroquinone at −5 °C. The mixture was stirred for 2 h while being allowed to warm up to room temperature and then was washed with 10 mL of saturated aqueous $NaHSO_3$ solution to remove excess bromine. The organic phase was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The residual oil was taken up in 25 mL of CH_2Cl_2 and the resulting solution was cooled to −10 °C. Then, DBU (0.45 g, 3.0 mmol) was added. After being stirred for 30 min, the reation mixture was washed with 10 mL of 15% hydrochloric acid and dried over anhydrous $MgSO_4$, and solvent was removed in vacuo to obtain fimbrolide **1**, 0.43 g (95%), after chromatography on a silica gel column (5% EtOAc in hexane): IR (CCl_4) 2960, 1792, 1615, 1261, 1100, 1020 cm^{-1}; ^1H NMR (CCl_4) δ 6.20 (1 H, s), 240 (3 H, t, J = 6 Hz), 1.35 (4 H, m), 0.98 (3 H, t, J = 6 Hz). These spectral properties were identical with those reported by Beechan and Sims.[5,10]

5-(Trichloromethyl)-4-bromo-3-*n*-butyl-2(5*H*)-furanone (11). To a solution of bromo acid **6b** (2.07 g, 10.0 mmol) in 200 mL of dry THF at −78 °C was added dropwise with stirring under nitrogen 8.0 mL (20.0 mmol) of 2.50 M *n*-butyllithium in hexane. The reaction mixture was stirred for 3 h at −78 °C. Trichloroacetaldehyde,[15] 2.50 g (15.0 mmol), was dissolved in 20 mL of dry THF and added via a syringe to the reaction mixture. The mixture was kept at −78 °C while stirring was continued an additional 2 h and then the solution was allowed to warm up to room temperature over a 1-h period. Twenty milliliters of H_2O was added and the layers were separated. The organic phase was washed with additional 20 mL of H_2O. The combined basic fractions were acidified with 15% hydrochloric acid and then extracted with 2 × 20 mL of ether. The combined ethereal extracts were washed with 20 mL of saturated aqueous NaCl solution and dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo followed by chromatography of the residue on silica gel with 5% EtOAc in hexane as the elution solvent gave compound **11**, 2.35 g (70%). Sublimation (40 °C, 1.5 torr) of the crude solid provided analytically pure material: mp 39.0–40.0 °C; IR (CCl_4) 2945, 2870, 1792, 1695, 1645, 1250, 1070, 648 cm^{-1}; ^1H NMR (CCl_4) δ 5.30 (1 H, s), 2.49 (2 H, t, J = 6 Hz), 1.55 (4 H, m) 1.01 (3 H, t, J = 5 Hz). Anal. Calcd for $C_9H_{10}BrCl_3O_2$: C, 32.13; H, 3.00. Found: C, 32.24; H, 3.01.

Dehydrochlorination of Compound 11. A solution of 1.01 g (3.0 mmol) of butenolide **11** in 50 mL of dry CH_2Cl_2 was cooled to −20 °C and DBU, 0.60 g (3.3 mmol), was added. The mixture was stirred at −10 °C for 30 min and then washed with 2 × 10 mL of 15% hydrochloric acid. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo to yield 0.72 g (78%) of the γ-(dichloromethylene)-β-bromobutenolide **3** after chromatography on silica gel with 5% EtOAc in hexane elution. Hickman distillation (145 °C, bath temperature, 1.0 torr) afforded an analytically pure sample: IR (CCl_4) 2920, 2905, 1763, 1015, 940 cm^{-1}; ^1H NMR (CCl_4) δ 2.45 (2 H, t, J = 6 Hz), 1.52 (4 H, m), 1.00 (3 H, t, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 162.9, 142.8, 137.0, 126.6, 111.5, 28.8, 25.4, 22.3, 13.7; GC/MS, m/e 298, 300, 302, 304. Anal. Calcd for $C_9H_9BrCl_2O_2$: C, 36.04; H, 3.04. Found: C, 36.24; H, 3.04.

Registry No. **1**, 63025-35-4; **3**, 96129-51-0; **4**, 3070-68-6; **5a**,

(15) Trichloroacetaldehyde was prepared by shaking chloral hydrate with 4 times its weight of concentrated H_2SO_4 in a separatory funnel. The layers were separated and the crude aldehyde was distilled under nitrogen, bp 94.0–95.0 °C (760 torr), to obtain the clean material in 64% yield; ^1H NMR (CCl_4) δ 11.40 (1 H, s). Stecher, P. G., Ed. "Merck Index", 8th ed.; Merck: Rahway, NJ, 1968; p 1067.

96129-52-1; **6a**, 96129-53-2; **6b**, 96129-54-3; **7a**, 96129-55-4; **7b**, 77130-01-9; **8**, 96150-65-1; **10**, 96129-57-6; **11**, 96150-66-2; trichloroacetaldehyde, 75-87-6; tribromoacetaldehyde, 115-17-3; 2-methyl-3,3-dibromopropenoic acid, 1578-22-9.

Application of the Swern Oxidation to the Manipulation of Highly Reactive Carbonyl Compounds†,[1]

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In the course of synthetic studies toward the polyether ionophore antibiotics, we encountered several aldehydes and ketones which were inductively destabilized by strongly electronegative substituents toward hydration and decomposition.[3] Here we report that the direct addition of nucleophilic reagents to crude Swern oxidation[4] mixtures can circumvent the deleterious side reactions characteristic of highly reactive carbonyl compounds.

The Swern oxidation is anhydrous, proceeds rapidly at low temperature, and produces relatively innocuous byproducts: carbon monoxide, carbon dioxide, dimethyl sulfide, and triethylamine hydrochloride.[5] Thus, while other oxidation methods led to the formation of an intractable 2-ketofuranoside hydrate,[6] Swern oxidation of the alcohol **1** (Scheme I) in THF gave the ketone **2** nearly quantitatively, and addition of 5 equiv of methylmagnesium bromide provide the branched-chain carbohydrate[7] **3** as a single diastereomer in 85% yield.

The aldehyde **5** was also prone to hydration and decomposition and could not be isolated in good yield, even in an impure state. In this case, addition of methyl (triphenylphosphoranylidene)acetate to the crude Swern oxidation mixture provided a remarkable 98% yield of the unsaturated esters **6**.

Aliphatic α-keto aldehydes are another class of hyperreactive carbonyl compounds, and, as a consequence of their propensity toward hydration, polymerization, and air oxidation,[8] they have seen little use in organic synthesis.[9,10] Addition of methyl (triphenylphosphoranylidene)acetate to the crude Swern oxidation of 1,2-octanediol quenched the bright yellow color characteristic of hexylglyoxal[10] instantaneously at −78 °C, and the Wittig condensation product **9**[11] was isolated in 90% yield. This constitutes a simple new method for the synthesis[12] of the γ-oxygenated crotonates found in several natural products.[13]

As an even more demanding test of this protocol, we selected the hitherto unknown parent acylsilane, (trimethylsilyl)formaldehyde. In this instance, Swern oxidation of (trimethylsilyl)methanol[14] was carried out entirely at −78 °C, and the addition of trimethylamine was followed 5 min later by the addition of ethyl 2-(triphenylphosphoranylidene)propionate. The solution was then allowed to warm to room temperature, and the novel silicon compound **12** was isolated by chromatography in 54% yield.[15] Since the addition of the Wittig reagent to a crude reaction mixture which had been allowed to warm to 0 °C produced no condensation product, we infer that polymerization occurs quite rapidly. However, the low-temperature viability of monomeric (trimethylsilyl)formaldehyde suggests new possibilities for the incorporation of silicon into organic molecules.[16,17]

† Contribution No. 7086.

Experimental Section

Melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 90 MHz. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0 ppm) as an internal standard. Data are reported as follows: chemical shift (multiplicity, integrated intensity, coupling constants, assigment). Optical rotations were measured in 1-dm cells of 1-mL capacity. Chloroform, when used as a solvent for optical rotations, was filtered through neutral alumina (activity I) immediately prior to use. Analytical thin-layer chromatography (TLC) was conducted on 2.5 × 10 cm precoated TLC plates: layer thickness 0.25 cm. Silica gel columns for chromatography utilized 70–230-mesh ASTM. Reaction solvents and liquid reagents were purified by distillation or drying shortly before use. All other reactants and solvents were reagent grade unless described otherwise. Reaction were run under an argon atmosphere arranged with a mercury bubbler so that the system could be alternatively evacuated and filled with argon and left under a positive pressure. Reported temperatures were measured externally. Syringes and reaction flasks were dried at least 12 h in an oven (120–140 °C) and cooled in a desiccator over anhydrous $CaSO_4$ prior to use. If feasible, reaction flasks were also flame-dried in vacuo.

Allyl 3,5-*O*-(1-Methylethylidene)-2-*C*-methyl-D-lyxofuranoside (3). To a stirred solution of 67 μL (0.77 mmol) of oxalyl chloride in 2.0 mL of THF at −78 °C was added 57 μL (0.81 mmol) of dimethyl sulfoxide. The solution was allowed to warm to −35 °C for 3 min and was then recooled to −78 °C. A solution of 169 mg (0.734 mmol) of the alcohol **1** in 1.0 mL of THF was then added to the reaction mixture. The resulting solution was allowed to warm to −35 °C and after 15 min was treated with 0.51 mL (3.7 mmol) of triethylamine. The reaction mixture was allowed to warm briefly to room temperature and was then recooled to

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