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Generation and Reactivity of an Unstabilized Carbohydrate Phosphorane

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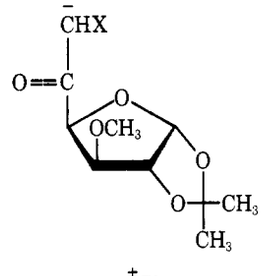
Generation of the ylide of methyl 5-deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-β-D-ribofuranoside iodide (**2a**) is described. Treatment of the ylide with aldehydes affords good yields of olefinic products of the α-L-*lyxo* configuration, resulting from epimerization of the ylide prior to reaction. Ketones do not react cleanly with the ylide. Addition of a proton source to the ylide under appropriate conditions allows the formation of good yields of a self-condensation product **14**.

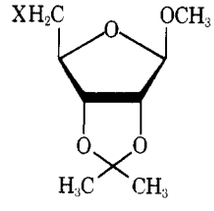
The Wittig reaction has been extensively utilized as a method of chain extension in the carbohydrate field.[1] Both aldehydo and keto sugars have proven amenable to the action of stabilized as well as unstabilized phosphorus ylides, and many unique and interesting chain-extended and branched-chain carbohydrates have been synthesized in this manner. The concept of reversing the roles of the two partners in the Wittig reaction, that is, the combination of a carbohydrate ylide and an aliphatic or aromatic carbonyl compound, has received only scant attention. Zhdanov[2,3] has generated the stabilized carbohydrate-containing phosphorane **1a** as well



1a, X = $\overset{+}{P}Ph_3$
1b, X = $\overset{+}{S}(CH_3)CH_2Ph$

as one other carbonyl-stabilized example. Both phosphoranes have very low reactivity, as would be expected, and only condense with a few activated aromatic aldehydes (*p*-nitro- and *o*-hydroxybenzaldehyde). Recently, an analogous stabilized carbohydrate sulfur ylide **1b** has been prepared and found to react with acrolein and acrylonitrile.[4] To further explore the potential of unstabilized carbohydrate ylides, we have examined the generation and reactivity of the ylide derived from methyl 5-deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-β-D-ribofuranoside iodide (**2a**). Though phosphorus-containing carbohydrates have been well studied,[5] the only examples of triphenylphosphonium salts appear to be those employed as leaving groups in studies on the synthesis of α-glycosides.[6,7]

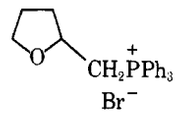
The major obstacle in the use of an unstabilized carbohydrate phosphorane is the presence of a leaving group β to the phosphorus in the vast majority of carbohydrates. Generation of the phosphorane might then be rapidly followed by elimination to form a vinylphosphonium salt. In principle, this problem can be approached through experimental manipulations (solvents, temperature) as well as by decreasing the ability of the β substituent to leave. The selection of **2a**, with



2a, X = $\overset{+}{P}Ph_3I^-$
2b, X = I
2c, X = OH
2d, X = OTs

the β substituent additionally attached through the carbon chain, should provide a particularly favorable case, since intramolecular closure to regenerate the ylide should be possible.

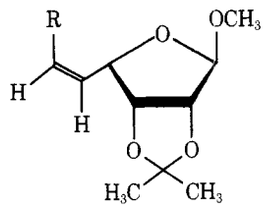
Precedent for this reversible β elimination is found in the ylide generated from tetrahydrofurfuryltriphenylphosphonium bromide (**3**), which will condense with carbonyl compounds to produce alkenyltetrahydrofurans.[8]



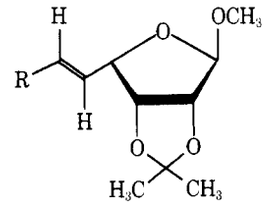
3

The synthesis of **2a** was accomplished in over 80% yield by treatment of methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (**2b**)[9,10] with triphenylphosphine in sulfolane at 110 °C for several days. A number of other conditions were examined for this unexpectedly difficult transformation,[11] with only the above conditions providing **2a** of acceptable yield and purity. The NMR spectrum is somewhat unusual in that H-3 (or H-2), a doublet, is shifted downfield to δ 5.56, presumably residing in the deshielding region of an aromatic ring. Additionally, the chemical-shift difference between the isopropylidene methyls is only 0.10 ppm, quite narrow, and much different from any other compounds in this study. Phosphorus decoupling combined with proton decoupling at 100 MHz allowed assignment of the resonances of **2a**.

Generation of the red-brown ylide of **2a** was carried out in 2:1 THF–HMPA at −50 °C under nitrogen by the addition of 1 equiv of *n*-butyllithium. As an initial look at the reactivity of the ylide, condensation with benzaldehyde at −50 °C provided a 79% yield of two isomeric, olefinic products, readily separable by preparative TLC.[12] These compounds proved to be not of the anticipated β-D-ribo configuration, but were rather the cis and trans isomers **4a** and **5a** of the α-L-*lyxo*

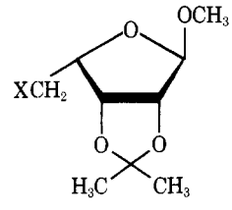


4a, R = Ph–
4b, R = pClPh–
4c, R = pCH$_3$OPh–



5a, R = Ph–
5b, R = pClPh–
5c, R = pCH$_3$OPh–

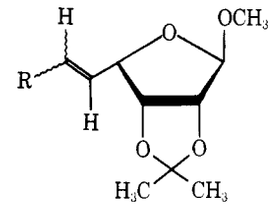
configuration. Since in principle four configurational variants are possible (β-D-*ribo*, α-D-*ribo*, β-L-*lyxo*, α-L-*lyxo*), the assignments were confirmed in several ways. The trans nature of H-1 and H-2 was clear from the sharp H-1 singlet for both **4a** and **5a**. It was not possible to clearly distinguish β-D-*ribo* and α-L-*lyxo* spectroscopically, so we resorted to chemical methods to clarify the configuration at C-4. Catalytic reduction (H_2,Pd/C) of **4a** and **5a** both afforded the same compound, indicating that they both had the same configuration at C-4. Ozonolysis followed by reductive workup ($LiAlH_4$)[13] also gave the same alcohol **6a** from both **4a** and **5a**. Compari-



6a, X = OH
6b, X = OTs
6c, X = $\overset{+}{P}Ph_3I^-$

son of this alcohol with methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (**2c**) by TLC, ^{1}H NMR, and ^{13}C NMR clearly showed it to be a different compound. Methyl 2,3-*O*-isopropylidene-α-L-lyxofuranoside (**6a**) was independently synthesized by a recent method[14] and shown to be identical to the product of ozonolysis–reduction by spectral and TLC comparison. As a final check, the mixture melting point of the *p*-toluenesulfonate derivative **6b** from both routes was undepressed (a mixture melting point of **2d** with **6b** derived from **2a** showed a marked depression). Compounds of other configurations were not detected in the Wittig reaction. The cis isomer **4a** ($J_{5,6}$ = 11 Hz) was isolated in 48% yield, with the trans isomer **5a** ($J_{5,6}$ = 16 Hz) making up the other 31%. *p*-Chlorobenzaldehyde and *p*-methoxybenzaldehyde were found to react similarly to afford 79% yields, in both cases, of a mixture of the cis (**4b, c**) and trans (**5b, c**) isomers of the α-L-*lyxo* configuration.[15]

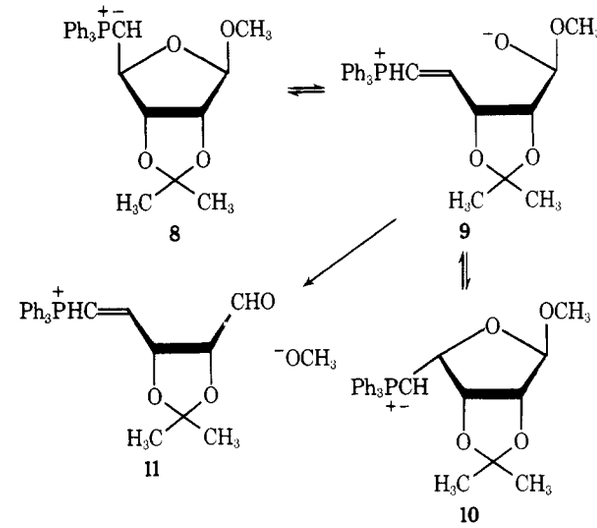
Examination of several representative aliphatic aldehydes also demonstrated their ability to react with the ylide of **2a**. Treatment of the ylide at −50 °C with 3-phenylpropionaldehyde, butanal, and pentanal, afforded the products **7a–c**



7a, R = PhCH$_2$CH$_2$–
7b, R = CH$_3$CH$_2$CH$_2$
7c, R = CH$_3$(CH$_2$)$_3$–

in yields of 85, 66, and 65%, respectively. In all three cases only a single isomer of the α-L-*lyxo* configuration was produced.[15] The cis or trans nature of the double bond in these cases could not be unequivocally established.

That the α-L-*lyxo* products are formed in all instances of condensation with aldehydes indicates that equilibration of the β-D-*ribo* ylide to the α-L-*lyxo* ylide through an open-chain structure (**8** ⇄ **9** ⇄ **10**) must be occurring. This equilibration



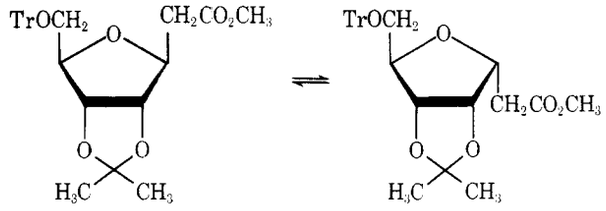
8 **9**

11

10

must occur very rapidly, since the aldehyde is added shortly (within several minutes) after the *n*-BuLi is added. Interestingly, under the standard conditions of the reaction the open-chain compound **9** closes back to an ylide rather than lose methoxide to form the open-chain aldehyde **11**. Isolation of the epimerized phosphonium salt **6c** proved to be possible if the ylide was generated in pure THF and then quenched with an excess of Dowex 50 (H^+) ion-exchange resin. After 1 min or so, TLC studies showed no **2a**, but only **6c**. If the ylide is generated at −78 °C and a TLC taken immediately, some **2a** is still present, though epimerization is still very rapid at

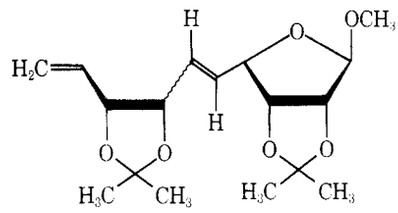
this temperature. A somewhat analogous epimerization through an open-chain structure also takes place between compounds **12** and **13.**[16] In this case, the equilibrium lies



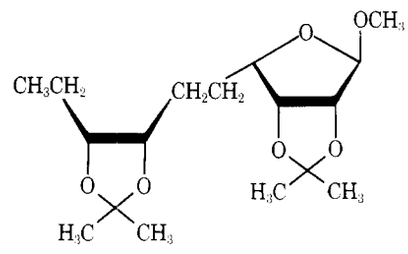
12 Tr = trityl **13**

unexpectedly far on the side of **13.** That **10,** with the configurations at C-2, C-3, and C-4 all *cis,* is the major epimer upon equilibration is also somewhat surprising.

The behavior of the ylide of **2a** also was examined with respect to ketones. Employing conditions similar to those of the aldehyde cases, it was found for all compounds examined (acetone, 2-butanone, 2-pentanone, ethylvinyl ketone, cyclohexanone, and acetophenone) that a complex mixture of products was formed. The major product (20–25%) in all of these reactions was identified as **14,** with the disubstituted double-bond configuration still in doubt. The proton NMR of **14** shows four distinct isopropylidene methyl resonances



14

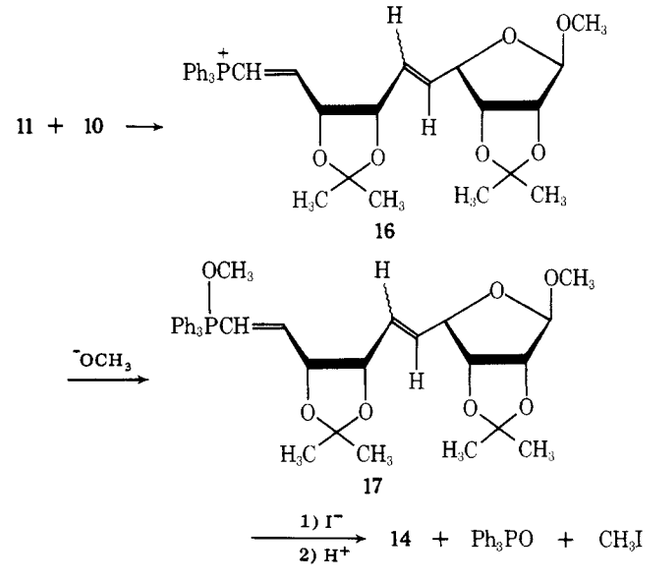


15

as well as only one methoxyl resonance. Catalytic hydrogenation produced a compound with all the expected resonances for **15,** including a newly formed methyl triplet at δ 0.98. In addition, ozonolysis–reduction of **14** afforded the α-L-*lyxo* alcohol **6a,** confirming the configuration at C-4. Formation of **14** must be the result of condensation of the vinyl phosphonium aldehyde **11** with the ylide **10** followed by loss of the phosphorus moiety. This self-condensation product can be formed in 64% yield if the ylide generated in 2:1 THF–HMPA is simply quenched with an excess of Dowex 50 (H^+). The other isolated product (94%) is triphenylphosphine oxide. One possible mechanism is shown in Scheme I. After condensation to afford the salt **16,** both methoxide (0.5 equiv) and iodide (1.0 equiv) are present. Attack by methoxide at phosphorus would give the pentavalent phosphorus intermediate **17.** Iodide attack on the methoxyl carbon would result in the formation, after protonation, of **14,** triphenylphosphine oxide, and methyl iodide. Gas chromatographic analysis of the crude reaction mixture indicates the presence of methyl iodide.[17] Ample literature precedent exists for this type of attack on phosphorus in other systems,[18] and a related cleavage of a vinyltriphenylphosphonium salt with methoxide has also been carried out.[19]

To summarize, it is possible to generate the ylide **10** and carry out high-yield condensations with aldehydes, but not

Scheme I



with ketones. The reactivity of the ylide is apparently lessened by steric constraints about C-5, seen not only in the difficulty of formation of **2a,** but also in the scope of reactivity of the ylide. The intramolecular attachment of the β-leaving group of **2a** enables the opening and reclosure to the furanoside to occur readily, keeping the general structural features intact. Our results indicate that the generation of anionic centers on other carbohydrates may be feasible with appropriate design of the molecule.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting-point apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer 467 grating infrared spectrophotometer. ^1H NMR spectra were measured with Varian A-60A or EM-360 instruments, and ^{13}C NMR spectra with a Bruker WP 80; chemical shifts in $CDCl_3$ are expressed in parts per million downfield from internal tetramethylsilane. Decoupling experiments on phosphonium salts **2a** and **6c** were carried out on a Varian HA-100 spectrometer. Ozone was generated with a Welsbach Ozonator T-408. Microanalysis was done by Galbraith Laboratories, Inc. The mass spectrum was recorded with an AEI-MS9 spectrometer at 70 eV.

Tetrahydrofuran (THF) was dried by distillation from sodium and benzophenone. Hexamethylphosphoric triamide (HMPA) was dried by distillation from calcium hydride. Tetramethylene sulfone was dried by distillation from KOH.

Methyl 5-Deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-β-D-ribofuranoside Iodide (2a). A solution of 4.0 g (13 mmol) of methyl 5-deoxy-5-iodo-2,3-*O*-isopropylidene-β-D-ribofuranoside (**2b**)[9,10] and 3.67 g (14 mmol) of triphenylphosphine in 4.5 mL of tetramethylene sulfone was heated at 110 °C for 64 h. The yellow solution was diluted with 80 mL of chloroform followed by ~700 mL of ether. The mixture was cooled to −78 °C to ensure complete precipitation of the salt, which was then filtered and washed with ether, affording 6.16 g (84%) of colorless crystals. Recrystallization from ethyl acetate–methanol provided analytically pure material: mp 177.5–179 °C; IR (KBr) 3050, 2990, 2930, 2830, 2775, 1589, 1487, 1441, 1385, 1108 cm^{-1}; NMR (100 MHz) δ 7.61–8.09 (m, 15, ArH), 5.56 and 4.78 (2 d, 2, J = 6 Hz, H_2, H_3), 4.83 (s, 1, H_1), 4.45–5.0 (m, 2, H_5, H_5'), 3.47–3.85 (m, 1, H_4), 2.87 (s, 3, OCH_3), 1.27 and 1.37 [2 s, 6, $C(CH_3)_2$]. Phosphorus decoupling simplified H_4 (dd, $J_{4,5}$ = 10 Hz, $J_{4,5'}$ = 12 Hz), H_5, and $H_{5'}$. Irradiation of H_2 collapsed H_3 to a singlet, and vice versa.

Anal. Calcd for $C_{27}H_{30}IO_4P$: C, 56.25; H, 5.24. Found: C, 56.48; H, 4.99.

General Procedure for Generation of the Ylide and its Condensation with Aldehydes. A solution of 360 mg (0.625 mmol) of phosphonium salt **2a** in 3 mL of 2:1 THF–HMPA was cooled to −50 °C, and *n*-BuLi (0.625 mmol) was added via syringe. After several minutes, a solution of the aldehyde (0.75 mmol) in 0.5 mL of THF was added to the red-brown ylide via syringe, and the solution was allowed to warm up to −10 °C over 45 min. Petroleum ether (38–56 °C) was

added, followed by extraction with H_2O, aqueous $NaHSO_3$, and H_2O. Isolation of the products was accomplished by preparative TLC with an ether–petroleum ether eluant. These same relative amounts were used for larger scale runs as well.

Methyl (*E*)- and (*Z*)-5,6-Dideoxy-2,3-*O*-isopropylidene-6-phenyl-α-L-*lyxo*-hex-5-enofuranoside (4a and 5a). Condensation of **2a** (2.16 g, 3.75 mmol) with benzaldehyde afforded 818 mg (79%) of a mixture of **4a** and **5a**, after separation by preparative TLC.

4a (48%): mp 58.5–60 °C; IR (KBr) 3085, 3045, 2995, 2945, 2925, 2845, 1645, 1600, 1577, 1497, 1455, 1380, 1218, 1105 cm^{-1}; NMR δ 7.33 (s, 5, ArH), 6.84 (d, 1, J = 11.5 Hz, H_6, A of ABX), 5.79–6.17 (m, 1, H_5, B of ABX), 4.95 (s, 1, H_1), 4.53–4.90 (m, 3, H_2, H_3, H_4), 3.35 (s, 1, OCH_3), 1.35 and 1.53 [2 s, 6, $C(CH_3)_2$].

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29. Found: C, 69.60; H, 7.16.

5a (31%): mp 65.5–67 °C; IR (KBr) 3028, 2988, 2925, 2892, 2836, 1655, 1598, 1578, 1494, 1453, 1382, 1214, 1105 cm^{-1}; NMR δ 7.37 (m, 5, ArH), 6.77 (d, 1, J = 15.5 Hz, H_6, A of ABX), 6.13–6.50 (m, 1, H_5, B of ABX), 4.95 (s, 1, H_1), 4.47–4.82 (m, 3, H_2, H_3, H_4), 3.38 (s, 1, OCH_3), 1.33 and 1.51 [2 s, 6, $C(CH_3)_2$].

Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29. Found: C, 69.88, H, 7.23.

Methyl (*E*)- and (*Z*)-6-(*p*-Chlorophenyl)-5,6-dideoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hex-5-enofuranoside (4b and 5b). Condensation of **2a** (576 mg, 1.0 mmol) with *p*-chlorobenzaldehyde afforded a total of 245 mg (79%) of **4b** and **5b** after separation by preparative TLC.

4b (29%): mp 58–59.5 °C; IR (KBr) 3005, 2995, 2940, 2905, 2832, 1654, 1593, 1490, 1382, 1218, 1100 cm^{-1}; NMR δ 7.25 (s, 4, ArH), 6.71 (d, 1, J = 11 Hz, H_6, A of ABX), 5.73–6.1 (m, 1, H_5, B of ABX), 4.91 (s, 1, H_1), 4.47–4.77 (m, 3, H_2, H_3, H_4), 3.35 (s, 3, OCH_3), 1.33 and 1.52 [2 s, 6, $C(CH_3)_2$].

Anal. Calcd for $C_{16}H_{19}ClO_4$: C, 61.83; H, 6.16. Found: C, 62.01; H, 6.30.

5b (50%): mp 70.5–72 °C; IR (KBr) 3072, 3045, 3028, 2990, 2978, 2960, 2930, 2895, 2835, 1655, 1592, 1495, 1375, 1105 cm^{-1}; NMR δ 7.30 (s, 4, ArH), 6.68 (d, 1, J = 15.5 Hz, H_6, A of ABX), 6.05–6.43 (m, 1, H_5, B of ABX), 4.92 (s, 1, H_1), 4.42–4.77 (m, 3, H_2, H_3, H_4), 3.37 (s, 3, OCH_3), 1.31 and 1.49 [2 s, 6, $C(CH_3)_2$].

Anal. Calcd for $C_{16}H_{19}ClO_4$: C, 61.83; H, 6.16. Found: C, 62.11; H, 6.32.

Methyl (*E*)- and (*Z*)-5,6-Dideoxy-2,3-*O*-isopropylidene-6-(*p*-methoxyphenyl)-α-L-*lyxo*-hex-5-enofuranoside (4c and 5c). Condensation of **2a** (1.728 g, 3.0 mmol) with *p*-methoxybenzaldehyde affords 727 mg (79%) of a **4c** and **5c** mixture (an oil), which is partially separable: IR (mixture, neat) 3040, 2990, 2935, 2840, 1645 (br), 1608, 1513, 1387, 1378, 1260, 1103 cm^{-1}; NMR (**4c**) δ 7.07 (m, 4, ArH), 6.78 (d, 1, J = 11.5 Hz, H_6, A of ABX), 5.68–6.02 (m, 1, H_5, B of ABX), 4.95 (s, 1, H_1), 4.53–4.92 (m, 3, H_2, H_3, H_4), 3.83 (s, 3, $ArOCH_3$), 3.38 (s, 3, OCH_3), 1.35 and 1.53 [2 s, 6, $C(CH_3)_2$]; NMR (**5c**) δ 7.07 (m, 4, ArH), 6.66 (d, 1, J = 15.5 Hz, H_6, A of ABX), 5.96–6.34 (m, 1, H_5, B of ABX), 4.90 (s, 1, H_1), 4.39–4.75 (m, 3, H_2, H_3, H_4), 3.80 (s, 3, $ArOCH_3$), 3.37 (s, 3, OCH_3), 1.32 and 1.50 [2 s, 6, $C(CH_3)_3$].

Anal. (mixture) Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.23. Found: C, 66.29; H, 7.16.

Methyl 5,6,7,8-Tetradeoxy-2,3-*O*-isopropylidene-8-phenyl-α-L-*lyxo*-hept-5-enofuranoside (7a). Condensation of **2a** (360 mg, 0.625 mmol) with 3-phenylpropionaldehyde affords 161 mg (85%) of one oily isomer: IR (neat) 3085, 3065, 3030, 2990, 2935, 2860, 2835, 1686, 1603, 1498, 1456, 1383, 1375, 1100 cm^{-1}; NMR δ 7.18 (s, 5, ArH), 5.42–5.98 (m, 2, H_5, H_6), 4.83 (s, 1, H_1), 4.15–4.67 (m, 3, H_2, H_3, H_4), 3.28 (s, 3, OCH_3), 2.25–2.93 [m, 4, $-(CH_2)_2-$], 1.28 and 1.44 [2 s, 6, $C(CH_3)_2$].

Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 71.05; H, 8.00.

Methyl 5,6,7,8,9-Pentadeoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-non-5-enofuranoside (7b). Condensation of **2a** (1.077 g, 1.87 mmol) with butyraldehyde affords 300 mg (66%) of one oily isomer: IR (neat) 3035, 2990, 2958, 2935, 2875, 2835, 1660, 1463, 1387, 1377, 1216, 1109 cm^{-1}; NMR δ 5.47–6.02 (m, 2, H_5, H_6), 4.92 (s, 1, H_1), 4.58–4.85 (m, 3, H_2, H_3, H_4), 3.33 (s, 3, OCH_3), 1.92–2.38 (m, 2, allylic CH_2), ca. 1.48 (m, partially hidden, 2, $CH_2CH_2CH_3$), 1.33 and 1.48 [2 s, 6, $C(CH_3)_2$], 0.93 (t, 3, J = 6 Hz, CH_2CH_3).

Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.43; H, 9.15. Found: C, 64.59; H, 9.19.

Methyl 5,6,7,8,9,10-Hexadeoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-dec-5-enofuranoside (7c). Condensation of **2a** (360 mg, 0.625 mmol) with *n*-pentanal affords 104 mg (65%) of one oily isomer: IR (neat) 3040, 2990, 2955, 2935, 2878, 2865, 2835, 1661, 1471, 1462, 1387, 1377, 1216, 1107 cm^{-1}; NMR δ 5.43–6.0 (m, 2, H_5, H_6), 4.90 (s, 1, H_1), 4.49–4.86 (m, 3, H_2, H_3, H_4), 3.37 (s, 3, OCH_3), 1.89–2.52 (m, 2, allylic CH_2), 1.41 (m, partially hidden, 4, $-CH_2CH_2CH_3$), 1.33 and 1.48 [2, s, 6, $C(CH_3)_2$], 0.91 (t, 3, J = 6 Hz, CH_2CH_3).

Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.59; H, 9.44. Found: C, 65.75; H, 9.55.

Epimerization of 2a. Formation of Methyl 5-Deoxy-2,3-*O*-isopropylidene-5-(triphenylphosphonio)-α-L-lyxofuranoside Iodide (6c). To a solution of 360 mg (0.625 mmol) of phosphonium salt **2a** in 7 mL of THF at −40 °C was added 0.7 mmol of *n*-BuLi. After 3 min an excess of Dowex 50 (H^+) was added with stirring. The resin was filtered off and washed with THF, and the filtrate was evaporated to dryness. Purification by preparative TLC (elution with 95:5 CH_2Cl_2–CH_3OH) gave 184 mg (51%) of the colorless epimerized semisolid salt: IR (KBr) 3053, 2990, 2935, 2868, 2835, 1587, 1488, 1450, 1388, 1098, 1013 cm^{-1}; NMR (100 MHz) δ 7.44–8.06 (m, 15, ArH), 5.10 (m, 1, H_3), 4.75 (s, 1, H_1), 4.53 (d, 1, J = 6 Hz, H_2), 4.44–4.93 (m, 2, partially hidden, H_5, $H_{5'}$), 3.61–3.90 (m, 1, H_4), 2.64 (s, 3, OCH_3), 1.32 and 1.51 [2, s, 6, $C(CH_3)_2$]. Phosphorus decoupling (100 MHz) simplified H_3 (dd, $J_{2,3}$ = 6 Hz, $J_{3,4}$ = 3 Hz), H_4, H_5, and $H_{5'}$.

Self-condensation of Ylide 10. Production of Methyl 5,6,9,10-Tetradeoxy-2,3:7,8-di-*O*-isopropylidene-D-*glycero*-β-D-*gulo*-deca-5,9-dienofuranoside (14). To a solution of 360 mg (0.625 mmol) of phosphonium salt **2a** in 3 mL of 2:1 THF–HMPA at −50 °C under nitrogen was added 0.726 mmol of *n*-BuLi. After 3 min, 0.5 g of Dowex 50 (H^+) was added, the solution gradually lightening to a pale yellow. The solution was warmed to −10 °C, benzene added, and the resin filtered off and washed. The organic layer was washed with H_2O, dried, and concentrated. Purification was accomplished by preparative TLC (elution with 3:1 petroleum ether–ether) to afford 65 mg (64%) of a colorless oil: IR (neat) 3085, 3050, 2990, 2935, 2835, 1646, 1607, 1597, 1457, 1378 cm^{-1}; ^1H NMR δ 4.45–6.12 (m, 10, H_{2-9}, H_{10}, $H_{10'}$), 4.85 (s, 1, H_1), 3.33 (s, 3, OCH_3), 1.29, 1.40, 1.45, 1.50 [4 s, 12, 2 $C(CH_3)_2$]; ^{13}C NMR (multiplicity in off resonance decoupling measurement) δ 25.0, 25.6, 26.2, 28.1 [4 q, 2 $C(CH_3)_2$], 54.7 (q, OCH_3), 74.9, 75.5, 79.9, 81.3 (4 d, C_2, C_3, C_7, C_8), 85.3 (d, C_4), 107.4 (d, C_1), 109.0, 112.6 [2, s, 2 $C(CH_3)_2$], 117.9 (t, CH_2=CH), 127.2, 130.9, 134.3 (3 d, 3 CH=).

Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.79; H, 7.92.

Hydrogenation of 14. Formation of Methyl 5,6,9,10-Tetradeoxy-2,3:7,8-di-*O*-isopropylidene-D-*glycero*-β-D-*gulo*-decofuranoside (15). A mixture of 80 mg of **14** (0.245 mmol) and 10 mg of 10% Pd/C in 4 mL of ethanol was hydrogenated (Parr shaker) at 2 atm for several hours. The catalyst was filtered off and washed with ethanol. Removal of solvent was followed by purification by preparative TLC (elution with 4:1 petroleum ether–ether) afforded 58 mg (72%) of oily **15**: NMR δ 4.83 (s, 1, H_1), 4.45–4.69 (m, 2, H_2, H_3), 3.78–4.25 (m, 3, H_4, H_7, H_8), 3.31 (s, 3, OCH_3), 1.68 (m, partially hidden, 6, 3 CH_2), 1.30, 1.33, 1.46 [3 s, 12, $2C(CH_3)_2$], 0.98 (t, 3, CH_3CH_2); mass spectrum calcd m/e 330.2042; found m/e 330.2048.

General Procedure for Ozonolysis–Reduction of 4a–4c, 5a–5c, 7a–7c, and 14. Formation of Methyl 2,3-*O*-Isopropylidene-α-L-lyxofuranoside (6a). Ozone was passed through a hexane solution of the olefinic carbohydrate derivative for 5 min at 0 °C; nitrogen gas was then passed through, and an excess of an ethereal solution of $LiAlH_4$ was added at −30 °C. The solution was warmed to RT, heated at reflux 1 h, and worked up by addition of H_2O to quench the excess $LiAlH_4$ followed by dilution with ether and extraction. The organic layer was dried and concentrated, and the alcohol **6a**[14] was separated by preparative TLC (elution with 1:2 petroleum ether–ether): ^{13}C NMR δ 24.7, 26.0 [$C(CH_3)_2$], 54.7 (OCH_3), 61.0 (C_5), 79.6, 80.3, 85.3 (C_2, C_3, C_4), 107.2 (C_1), 112.8 [$C(CH_3)_2$]. For comparison purposes: ^{13}C NMR (**2c**) δ 24.7, 26.3 [$C(CH_3)_2$], 55.4 (OCH_3), 64.0 (C_5), 81.4, 85.7, 88.3 (C_2, C_3, C_4), 110.0 (C_1), 112.1 [$C(CH_3)_2$]. Specific assignments for C_2, C_3, and C_4 in both cases are not known.

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Registry No.—**2a**, 63559-65-5; **2b**, 38838-06-1; **4a**, 63599-66-6; **4b**, 63599-67-7; **4c**, 63599-68-8; **5a**, 63599-69-9; **5b**, 63599-70-2; **5c**, 63599-71-3; **6a**, 5531-21-5; **6c**, 63599-72-4; **7a**, 63599-73-5; **7b**, 63599-74-6; **7c**, 63599-75-7; **10** ylide, 63599-76-8; **10** unchanged, 63599-77-9; **14**, 63599-78-0; **15**, 63599-79-1; triphenylphosphine, 603-35-0; benzaldehyde, 100-52-7; *p*-chlorobenzaldehyde, 104-88-1; *p*-methoxybenzaldehyde, 123-11-5; 3-phenylpropionaldehyde, 104-53-0; butyraldehyde, 123-72-8; pentanal, 110-62-3.

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Organoboranes. 23. Reaction of Organolithium and Grignard Reagents with α-Bromoalkylboronate Esters. A Convenient, Essentially Quantitative Procedure for the Synthesis of Tertiary Alkyl-, Benzyl-, Propargyl-, and Stereospecific Allylboranes

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Treatment of trimethylene α-bromoalkylboronate esters in ether at −78 °C with a wide variety of organolithium and Grignard reagents results in an essentially quantitative replacement of the α-bromine substituent by the corresponding organic group. Simple distillation provides, in high yield and purity, many novel, highly substituted organoboronate esters not available via hydroboration.

Organoboronate esters, $RB(OR')_2$, are becoming increasingly important as intermediates in organic synthesis. For example, their reaction with lithium aluminum hydride, $LiAlH_4$, or aluminum hydride, AlH_3, provides essentially quantitative yields of the corresponding monoalkylboranes, RBH_2.[2] Their reaction with Grignard reagents provides a route to mixed trialkylboranes.[3] In addition, organoboronate esters can make more efficient use of the boron-bound alkyl groups in certain synthetic transformations involving organoboranes where the utilization of only one alkyl group is inherent in the reaction. In these particular cases, only one-half of the alkyl groups, R, in dialkylborinates, R_2BOR', and only one-third of the alkyl groups in trialkylboranes, R_3B, would be utilized.[4-6] This would seriously limit the synthetic utility of the reaction if the alkyl group was derived from a valuable intermediate. The promising synthetic potential of organoboronate esters in such situations has recently been demonstrated by D. A. Evans.[4] It was shown that in stereospecific olefin syntheses leading to prostaglandins the use of organoboronate esters can overcome the inefficient utilization of the alkyl group in trialkylboranes.

Perhaps the most convenient route to organoboronate esters is via hydroboration of olefins and acetylenes with catecholborane[7] or dihaloboranes[8] followed by esterification (eq 1).

$$X_2BH + CH_2{=}CHR \rightarrow X_2BCH_2CH_2R \qquad (1)$$

Hydroboration of olefins followed by subsequent redistribution of the trialkylboranes with boron halides[9] or borate esters[10] also provides a facile route to alkylboronate esters (eq 2).

$$BH_3 + 3CH{=}CHR \longrightarrow B(CH_2CH_2R)_3 \xrightarrow{2BX_3} 3X_2BCH_2CH_2R \qquad (2)$$

However, certain organoboronate esters cannot be obtained directly by hydroboration due to the remarkable regioselectivity inherent in the hydroboration reaction.[6] Hydroboration of terminal olefins places the boron predominantly at the terminal carbon. Hydroboration of 1-substituted cycloalkenes places the boron nearly exclusively at the 2 position. While this exceptional regioselectivity has important implications in organoborane chemistry, it precludes, with few exceptions,[6,11] the synthesis of tertiary organoboranes by direct hydroboration (eq 3 and 4).

Furthermore, certain groups, such as methyl, alkynyl, benzyl, propargyl, and many allyl, cannot be attached to boron through the hydroboration reaction.

A great deal of progress has been made in the synthesis of "mixed" trialkylboranes possessing groups not available via simple hydroboration.[12-15] However, the synthesis of organoborate esters of this class is quite limited.[16]