1,12-Dimethoxy-8-ethyl-10-hydroxy-7,8,9,10-tetrahydro-6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (20). A procedure similar to those described by McGee and Confalone[5f] starting from 11 and using SeO_2 in diglyme at 200 °C for 30 min was followed. However, a 60% yield of alcohol **20** (and 25% recovery of **11**) was obtained instead of the corresponding selenic ester.[5f] Mp and ^1H and ^{13}C NMR spectra of alcohol **20** are identical with those of that derived from SeO_2–AcOH oxidation or LDA·HMPA–MoOPH hydroxylation: mp 212–214 °C; IR (CH_2Cl_2) 3400, 1710; ^1H NMR 8.03 (dd, J = 8, 1 Hz, 1 H, C-4 H), 7.48 (t, J = 8 Hz, 1 H, C-3 H), 7.1 (s, 1 H, C-11 H), 6.98 (dd, J = 8, 1 Hz, 1 H, C-2 H), 5.09 (br s, 1 H, CHO), 3.99 (s, 3 H, OMe), 3.97 (s, 3 H, OMe), 2.96 (dd, J = 18, 3 Hz, 1 H), 2.2 (br d, J = 13 Hz, 1 H), 2.06 (m, 1 H), 1.9 (m, 1 H), 1.2 (m, 3 H), 1.06 (t, J = 7 Hz, 3 H, Me); ^{13}C NMR 162 (s, CO), 156.78 (s), 153.7 (s), 145.76 (s), 139.8 (s), 137.7 (s), 127.67 (d), 125.1 (s), 121.9 (s), 118.14 (s), 114.67 (d), 109.01 (d), 99.49 (d), 63.84 (d, CO), 56.96 (q, OMe), 56.58 (q, OMe), 36.99 (t), 30.62 (d), 29.17 (t), 28.91 (t), 11.23 (q); FAB MS m/e 355, 354 (M^+), 353, 246, 185, 154, 137, 93. Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.37; H, 6.01.

1,12-Dimethoxy-8-ethyl-10-oxo-7,8,9,10-tetrahydro-6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (21). A procedure similar to those described for the oxidation of alcohol **16** with PCC was followed. Starting from 0.235 g (0.66 mmol) of alcohol **16**, 0.187 g (80% yield) of **21** was isolated as red orange solids: mp 161–163 °C; IR (CH_2Cl_2) 2950, 2920, 2850, 1698 (s, CO), 1680, 1585, 1555, 1383, 1080; ^1H NMR 8.19 (s, 1 H, C-11 H), 8.12 (d, J = 8 Hz, 1 H, C-4 H), 7.52 (t, J = 8 Hz, 1 H, C-3 H), 7.03 (d, J = 8 Hz, 1 H, C-2 H), 4.02 (s, 3 H, OMe), 3.99 (s, 3 H, OMe), 3.2 (dd, J = 19, 4 Hz, 1 H), 2.84 (dd, J = 16, 4 Hz, 1 H), 2.47 (m, 2 H), 2.19 (m, 1 H, C-8 H), 1.58 (quintet, J = 7 Hz, 2 H, CH_2), 1.03 (t, J = 7 Hz, 3 H, Me); ^{13}C NMR 200.29 (s, C-10), 161.82 (s, C-6), 156.57 (s), 153.88 (s), 144.01 (s), 136.79 (s), 135.27 (s), 127.69 (d), 126.06 (s), 118.25 (s), 114.63 (d), 112.0 (s), 109.26 (d), 100.98 (d), 56.54 (q, OMe), 46.09 (q, OMe), 35.57 (2 C, t, C-7, 9), 30.86 (d), 28.48 (t), 10.9 (q); FAB MS m/e 353, 352 (M^+), 338, 246, 185, 154, 137, 93. Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72. Found: C, 71.61; H, 6.03.

8-Ethyl-1,10,12-trimethoxy-6*H*-benzo[*d*]naphtho[1,2-*b*]-pyran-6-one (1). A procedure similar to that described by McGee and Confalone[5f] using trimethyl orthoformate–*p*-TsOH and then DDQ was followed; an 89% yield of **1** (yellow crystals) was obtained from ketone **21**: mp 241–243 °C; IR (CH_2Cl_2) 3040, 2960, 2950, 2840, 1706 (s, CO), 1605, 1580, 1380, 1125, 1120; ^1H NMR 8.42 (s, 1 H, C-11 H), 8.22 (d, J = 8 Hz, 1 H, C-4 H), 7.98 (d, J = 1 Hz, C-7 H), 7.51 (t, J = 8 Hz, 1 H, C-3 H), 7.18 (d, J = 1 Hz, 1 H, C-9 H), 6.99 (d, J = 8 Hz, 1 H, C-2 H), 4.09 (s, 3 H, OMe), 4.04 (s, 3 H, OMe), 4.01 (s, 3 H, OMe), 2.79 (q, J = 7 Hz, 2 H, CH_2), 1.34 (t, J = 7 Hz, 3 H, Me); ^{13}C NMR 161.55 (s, CO), 157.31 (s), 156.66 (s), 152.81 (s), 146.02 (s), 140.55 (s), 127.15 (d), 126.5 (s), 123.3 (s), 122.21 (s), 121.56 (d), 117.52 (s), 117.08 (d), 114.86 (d), 113.73 (s), 107.98 (d), 104.43 (d), 56.75 (q, OMe), 56.52 (q, OMe), 56.23 (q, OMe), 28.93 (t), 15.1 (q, Me); EI MS m/e 364 (M^+), 277, 197, 196. Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.39; H, 5.87.

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Supplementary Material Available: Spectral data for compounds **4**, **6**, and **7** (1 page). Ordering information is given on any current masthead page.

Synthesis of Annulated Furanoses by Free-Radical Cyclization of Haloalkenes Derived from Diacetone Glucose

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In the last years the synthesis of carbocycles from carbohydrates has attracted considerable interest.[1] The free-radical route is an extremely efficient strategy for the cyclization of carbohydrate derivatives.[2] Some authors have recently advanced and demonstrated the merits of performing the free-radical cyclization without disturbing the anomeric center.[3] Following this idea, Fraser-Reid and co-workers have developed the concept and synthetic applications of annulated furanoses.[4] The publication of two recent reports[5,6] on the synthesis of new annulated furanoses prompts us to disclose our recent results on this subject.[7]

We describe here the synthesis and free radical cyclization of the chiral radical precursors **2–7** (Scheme I). These compounds can be obtained from readily available diacetone glucose **1**. They are conveniently functionalized to yield, after 6-exo[8] free-radical cyclization,[9] annulated furanoses. In these compounds, the carbocycle is trans fused at carbons C3 and C4 of the sugar moiety and the substitution in the ring can be modified by changing the type of acceptor in the intramolecular free-radical cyclization. In this process a new stereocenter can be formed and the sugar provides an ideal chiral template for achieving a good diastereoselection.[10] In addition, annulated furanoses are useful chiral polyfunctional building blocks for further development.[11]

With this scenario in mind we have synthesized and cyclized the radical precursors **2–7** (Scheme I).

The aldehyde **2** has been designed in view of the ability of aldehydes to function as acceptors.[12] We have synthesized it from 3-*C*-(carbomethoxymethyl)-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose[13] by first bromination and then reduction (DIBAH, toluene, −78 °C) of the resulting compound. The cyclization of compound **2** under typical conditions (see Experimental Section) did not yield the expected products; we obtained in turn the uncyclized compounds **8** and **9** (Scheme II). Compound **8** showed in the ^1H NMR spectrum signals at δ 1.21 (d, J = 6.7 Hz) and 1.14 (d, J = 6.7 Hz) for the methyls attached to C3/C5; H5 appears at δ 4.01 (dq, $J_{5,4}$ = 3.1 Hz, $J_{5,6}$ = 6.7 Hz). Compound **9** showed in the ^1H NMR spectrum signals at δ 9.79 (*H*COR) and 5.40 (OC*H*(OH)R), 1.29 (d, J = 6.2 Hz) and 1.23 (d, J = 6.5 Hz) corresponding to the methyl (C6), in the open or hemiacetalic form. Product **8** probably arises by intramolecular 1,7-hydrogen transfer,[14] decarbonylation, and hydrogen trapping. The absence of cyclized products in this case is surprising in view of some recent results.[15] This also proves that the success of the aldehyde as acceptor in free-radical cyclizations is very dependent on the structure.

Oxime ethers are known as more reliable acceptors.[16] So, the radical precursor **3** has been obtained from compound **2** (Scheme I) by the routine method (*O*-benzylhydroxylamine hydrochloride, pyridine, methylene chlo-

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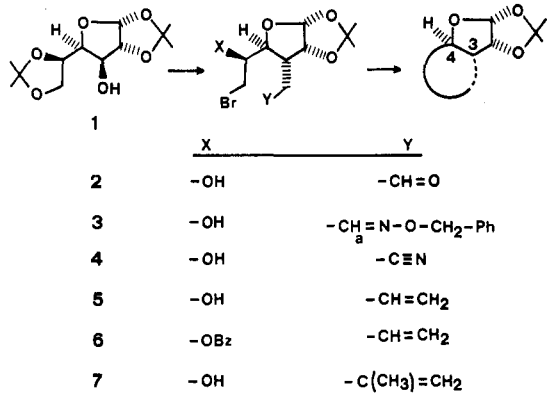
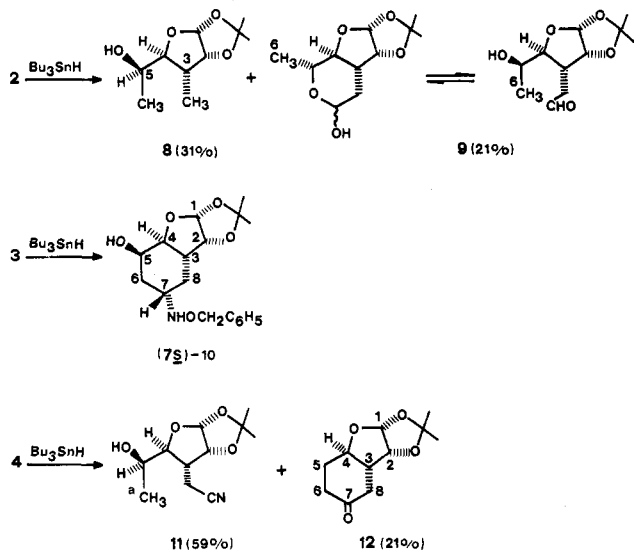
Scheme I

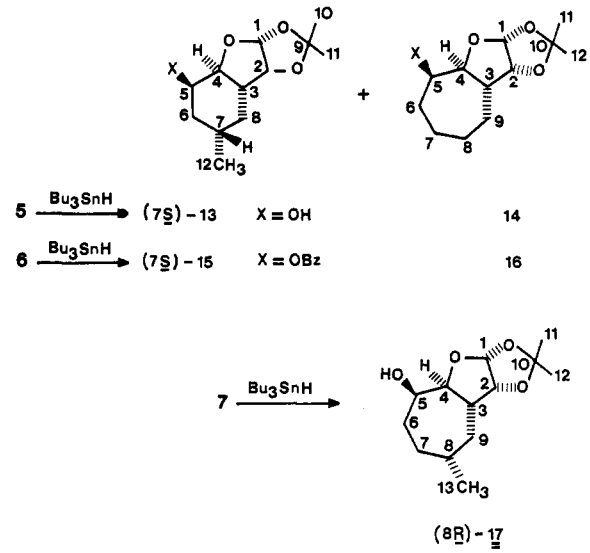


Scheme II



ride); after chromatography we could obtain pure **3** syn isomer and a mixture of **3** syn (δH_a 7.55 (t, J = 5.2 Hz)) + anti (δH_a 6.90 (t, J = 5.3 Hz)) isomers (1:1). The free-radical cyclization of compound **3** gave a complex reaction mixture; after careful flash chromatography[17] we could isolate pure the major (7*S*)-**10** isomer (Scheme II) and a mixture of (7*S*)-**10** and its 7*R* isomer in poor overall yield (30%). We could also detect other, more polar, probably carbohydrate dimers, incompletely identified. The ratio of products (7*S*)-**10**:(7*R*)-**10** = 90:10 was found to be independent of the starting material (pure **3** syn or (1:1) **3** syn + anti), and could be determined by integration of the signals for H7 in the ^{1}H NMR spectrum of the crude mixtures; the major isomer (7*S*)-**10** showed δ H7 3.30 (tt, $J_{7,6ax} = J_{7,8ax}$ = 11.8 Hz and $J_{7,6eq} = J_{7,8eq}$ = 4.3 Hz); the minor isomer (7*S*)-**10** showed δ H7 3.47 as a complex multiplet. In spite of the low yield obtained in the synthesis of this inosamine,[18] to our knowledge this is the first example of a 6-exo free-radical cyclization on a oxime ether as acceptor.

Scheme III



In our general project, the cyclization of compound **4** (Scheme I) leading to a cyclohexanone was of interest. This radical precursor has been synthesized by bromination of 3-*C*-(cyanomethyl)-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose.[19] The attempted free-radical cyclization of compound **4** gave the uncyclized product **11** (δCH_3-a 1.30 (d, J = 6.2 Hz); IR (CN) 2255 cm^{-1}) and the annulated furanose **12** (Scheme II). The structure of this compound was determined by its analytical and spectroscopic data: the combustion analysis and the mass spectrum established a molecular formula $C_{11}H_{16}O_4$; the IR spectrum showed no hydroxyl absorption and a carbonyl band at 1715 cm^{-1}; the ^{1}H NMR spectrum showed signals for H1, H2, and H4 at

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low field; the resonance for H_5COH was absent, appearing as complex signals at high field for protons H5, H6, and H8. Compound **12** probably arises by dehydratation of the cyclized β-hydroxyimine,[20] 1,4-hydride addition,[21] and hydrolysis of the imine. The low ability of nitriles as acceptors has also been reported.[22]

Compounds **5–7** were designed in order to synthesize carbon-chain-substituted annulated furanoses; it was also an opportunity in order to evaluate the 6-exo/7-endo ratio in the products obtained in the cyclization of these radical precursors.

Compounds **5** and **6** (Scheme I) were obtained from 3-*C*-(carbomethoxymethyl)-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[13] and compound **7** (Scheme I) from 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuran-3-ulose[13] following standard methodologies (see supplementary material). The cyclization of compound **5** gave cleanly a mixture of compounds **13** (33%) and **14** (44%) (Scheme III); after careful and repeated flash chromatography[17] we could isolate pure the major (7*S*)-**13** isomer and **14**. The ratio (7*S*)-**13** and its former (7*R*)-**13**, 70:30, was determined in the ^{1}H NMR spectrum of the crude reaction mixture, integrating the signals corresponding to the methyls of the isopropylidene group ((7*S*)-**13**: δ 1.52, 1.32; (7*R*)-**13**: δ 1.54, 1.34). The absolute stereochemistry at C7 in the major **13** isomer has been established by careful analysis fo the ^{1}H NMR spectrum and selective decoupling experiments: H7 δ 2.10–1.80, appears as a multiplet with vicinal coupling constants $J_{7,6ax} = J_{7,8ax} =$ 12.2 Hz, only compatible with 7-*S* in a chair conformation for the cyclohexane ring.

The cyclization of compound **6** gave the annulated furanoses **15** (34%) and **16** (46%) (Scheme III). Unfortunately, we could not determine the ratio of isomers in compound **15** by ^{1}H NMR analysis. After purification we could obtain pure compound **16** and the major isomer (7*S*)-**15**, whose ^{1}H NMR spectrum showed H7 δ 2.15 (multiplet) with vicinal coupling constants $J_{7,8ax} = 13.1$ Hz, $J_{7,6ax} = 12.0$ Hz, $J_{7,6eq} = J_{7,8eq} = 3.6$ Hz; this is only compatible with 7*S* as absolute configuration as in compound (7*S*)-**13**. This assignment was finally confirmed by X-ray diffraction analysis (supplementary material).

The unusual 7-endo/6-exo ratio observed in the free radical cyclization of compounds **5** and **6** has been also observed in related haloalkenes[10] and is probably due to the ring strain in the 6-*exo* products.

The radical precursor **7** (Scheme I) gave, in addition to other more polar compounds of unknown structure, the 7-*endo* product **17** (Scheme III) in 25% yield and a ratio of isomers at C-8, 72:28; after purification we could obtain pure the major 8*R* isomer that showed in the ^{1}H NMR spectrum H8 δ 1.50 ($J_{8,9ax} = 11.4$ Hz and $J_{8,9eq} = 5.0$ Hz), only compatible with this absolute configuration at C8 in a favored chairlike conformation.

In summary, we have synthesized a series of polyfunctionalized carbocycles, in enantiomerically pure form, moderate yield, and good diastereoselectivity via free-radical cyclization of suitable intermediates derived from diacetone glucose.

Experimental Section

General Procedures. Melting points were determined in a Kofler apparatus and are uncorrected. The ^{1}H NMR coupling constants were verified by homonuclear decoupling experiments. The progress of all reactions was monitored by thin-layer chromatography (TLC), which was performed on aluminium plates precoated with silica gel HF-254 (0.2-mm layers) containing a fluorescent indicator (Merck, 5539). Detection was by UV (254 nm), followed by charring with sulfuric acid spray or with a solution of ammonium molybdate (VI) tetrahydrate (12.5 g) and cerium sulfate hydrate (5.0 g) in 10% aqueous sulfuric acid (500 mL). Flash chromatography was performed by using Kiesegel 60 (230–400 mesh, Merck) silica gel, and petroleum ether/ethyl acetate mixtures as eluent.

Standard Procedure for Free-Radical Cyclization. The bromide (15 mmol) in dry benzene (750 mL, 0.02 M), at reflux, under argon was treated with tributyltin hydride (22 mmol) and AIBN in dry benzene (0.8 M) by dropwise addition via syringe pump in 16 h. The reaction mixture was cooled and the solvent evaporated. The residue was dissolved in ether, 10% aqueous potassium fluoride solution was added, and the mixture was stirred 18 h. The organic phase was separated, dried, and evaporated. Flash chromatography of the residue gave the product.

Free-Radical Cyclization of Compound 2. Compound **2** (219 mg, 0.7 mmol) was submitted to cyclization according to the standard procedure. Flash chromatography (hexane/ethyl acetate (4:1)) gave compound **8** (45 mg, 31%) as an oil [$[\alpha]^{25}_D$ +23.2° (*c* 1.7, $CHCl_3$); IR (neat) 3600–3200 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (d, $J_{1,2} = 3.7$ Hz, 1 H, H1), 4.55 (t, $J_{2,1} = 3.7$ Hz, 1 H, H2), 4.01 (dq, $J_{5,6} = 6.6$ Hz, $J_{5,4} = 3.1$ Hz, 1 H, H5), 3.80 (dd, $J_{4,5} =$ 3.1 Hz, $J_{4,3} = 10.0$ Hz, 1 H, H4), 2.1 (m, 1 H, H3), 2.0 (d, 1 H, O*H*), 1.51 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.21 (d, $J = 6.7$ Hz, 3 H, CH_3-6 or CH_3-5), 1.14 (d, $J = 6.8$ Hz, 3 H, CH_3-5 or CH_3-6). Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.23; H, 8.60.] and compound **9** (35 mg, 21%) as an oil: IR (film) 3600–3200, 1730, cm^{-1}. The ^{1}H NMR spectrum is complex due to the presence of the open and hemiacetalic forms: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (s, 1H, C*H*O), 5.90 (d, $J = 3.4$ Hz, 1 H, H1), 5.83 (d, $J_{1,2} = 3.5$ Hz, 1 H, H1), 5.80 (d, $J_{1,2} = 3.8$ Hz, 1 H, H1), 5.40 (m, 1 H, C*H*OHO), 4.71, 4.64, 4.61 (t, 1 H, H2), 4.08, 3.89 (m, H5), 3.78, 3.60 (dd, 1 H, H4), 2.47 (m, 1 H, H3), 1.51, 1.49 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.29 (d, $J = 6.2$ Hz, 3 H, CH_3-6), 1.23 (d, $J = 6.5$ Hz, 3 H, CH_3-6); MS *m*/*z* 215 (M^+ – 15, 25). Anal. Calcd for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88. Found: C, 57.67; H, 7.87.

Cyclization of Compound 3. Compound **3** (97 mg, 0.23 mmol) was cyclized by the standard procedure to give, after flash chromatography (hexane/ethyl acetate (4:1)) compounds (7*S*)-**10** (18 mg) and (7*S*)-**10** + (7*R*)-**10** (6 mg); total yield 30%. (7*S*)-**10**: oil; $[\alpha]^{25}_D$ +25.2° (*c* 2.4, $CHCl_3$); IR (film) 3600–3300 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.27 (5H, aromatic), 5.76 (d, $J_{1,2} = 3.6$ Hz, 1 H, H1), 4.62 (s, –OCH_2O), 4.52 (t, $J_{1,2} = J_{2,3} = 3.6$ Hz, 1 H, H2), 4.30 (m, 1 H, H5), 3.65 (dd, $J_{4,3} = 11.0$ Hz, $J_{4,5} = 2.4$ Hz, 1 H, H4), 3.30 (tt, $J_{7,6ax} = J_{7,8ax} = 11.8$ Hz, $J_{7,6eq} = J_{7,8eq} =$ 4.3 Hz, 1 H, H7), 2.15–1.95 (m, 4 H, H3, H6(eq), H8(eq), O*H*), 1.40–1.25 (m, 2 H, H6(ax), H8(ax)), 1.44 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3); MS *m*/*z* 320 (M^+ – 15, 3). Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.38; H, 7.36; N, 3.98.

Cyclization of Product 4. Compound **4** (243 mg, 0.79 mmol) was cyclized according to the standard procedure to give, after flash chromatography (hexane/ethyl acetate (4:1)), compound **11** (108 mg, 59%) and compound **12** (23 mg, 12%). **11**: mp 56–59 °C; $[\alpha]^{25}_D$ +87° (*c* 3.1, $CHCl_3$); IR (KBr) 3540, 2255 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.87 (d, $J_{1,2} = 3.6$ Hz, 1 H, H1), 4.78 (t, $J_{2,1} = 3.6$ Hz, 1 H, H2), 4.00–3.65 (m, 2 H, H4, H5), 2.75 (m, 2 H, CH_2–CN), 2.50–2.10 (m, 1 H, H3), 2.00 (s, O*H*), 1.55 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.30 (d, $J = 6.2$ Hz, 3 H, CH_3CHOH–); MS *m*/*z* 212 (M^+ – 15, 56), 182 (28), 152 (18), 124 (47), 96 (27), 83 (16), 59 (100), 43 (84). Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.13; H, 7.54; N, 6.16. Found: C, 57.97; H, 7.70; N, 6.01. **12**: mp 94–100 °C; $[\alpha]^{25}_D$ –10° (*c* 0.32, $CHCl_3$); IR (KBr) 2995, 2980, 2940, 2915, 2880, 1715, 1465, 1425, 1390, 1210, 1100, 875 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.57 (d, $J_{1,2} = 3.6$ Hz, 1 H, H1), 3.82 (t, $J_{1,2} = J_{2,3} =$ 3.6 Hz, 1 H, H2), 3.81 (dt, $J_{3,4} = 11.0$ Hz, $J_{4,5} = 4.1$ Hz, 1 H, H4), 2.32 (m, 1 H, H6(eq)), 2.11 (dd, $J_{8ax,8eq} = 15.8$ Hz, $J_{8eq,3} =$ 5.1 Hz, H8(eq)), 1.84 (m, 1 H, H3), 1.70–1.56 (dd, $J_{8ax,8eq} = 15.8$ Hz, $J_{8ax,3} = 13.2$ Hz, $J_{6ax,5ax} = 11.7$ Hz, $J_{6ax,5eq} = 5.1$ Hz, H6(ax)), 1.20 (m, H5(eq), 1.10–1.00 (m, H5(ax)), 1.43 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3); MS *m*/*z* 197 (M^+ – 15, 100), 155 (80), 137 (50), 109

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(40), 95 (38), 85 (70), 59 (25). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.60; H, 7.73.

Cyclization of Compound 5. Compound **5** (185 mg, 0.6 mmol) was cyclized according to the standard procedure. Flash chromatography (hexane/ethyl acetate (4:1)) gave compound **13** (45 mg, 33%) and compound **14** (59 mg, 44%). After recrystallization from hexane we obtained pure the major (7*S*)-**13** isomer: mp 106–108 °C; $[\alpha]^{25}_D$ +7.5° (*c* 0.48, $CHCl_3$); IR (KBr) 3595 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table I, supplementary material); MS *m/z* 213 (M^+ – 15, 100). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.39; H, 8.57. **14**: mp 42–44 °C; $[\alpha]^{25}_D$ –3.2° (*c* 3.4, $CHCl_3$); IR (KBr) 3500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table II, supplementary material); MS *m/z* 213 (M^+ – 15, 100). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.98; H, 8.79.

Cyclization of Compound 6. Compound **6** (232 mg, 0.56 mmol), was cyclized according to the standard procedure. Flash chromatography (hexane/ethyl acetate (19:1)) gave compound **15** (63 mg, 34%) and compound **16** (83 mg, 46%). After recrystallization from hexane we obtained pure the major (7*S*)-**15** isomer: 109–111 °C; $[\alpha]^{25}_D$ –4° (*c* 1.0 $CHCl_3$); IR (KBr) 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (See Table I, supplementary material); MS *m/z* 317 (M^+ – 15, 20), 105 (100). Anal. Calcd for $C_{19}H_{24}O_5$: C, 72.12; H, 7.65. Found: C, 71.25; H, 7.49. **16**: mp 76–78 °C; $[\alpha]^{25}_D$ –37° (*c* 0.4 $CHCl_3$); IR (KBr) 1725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) (see Table II, supplementary material); MS *m/z* 332 (2), 105 (100). Anal. Calcd for $C_{19}H_{24}O_5$: C, 72.12; H, 7.65. Found: C: 72.37; H, 7.67.

Cyclization of Compound 7. Compound **7** (214 mg, 0.66 mmol) was cyclized according to the standard procedure to give after flash chromatography (hexane/ethyl acetate (9:1)) compound **17** (30 mg, 18% (25% taking into account the recovered starting material **7**)). After crystallization we could obtain major (8*R*)-**17** isomer: mp 99–101 °C; $[\alpha]^{25}_D$ +4° (*c* 0.3, $CHCl_3$); IR (KBr) 3500 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) (see Table II; supplementary material); MS *m/z* 227 (M^+ – 15, 100). Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.03; H, 9.47.

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Supplementary Material Available: Schemes IV–VI, synthetic procedures and spectral data of the intermediates in the synthesis of compounds **2–7**, ^1H NMR data for compounds (7*S*)-**13**, (7*S*)-**15**, **14**, **16**, and **17**, ORTEP representation of compound (7*S*)-**15**, and the rest of the crystallographic data (32 pages). Ordering information is given on any current masthead page.

Addition of Triphenylphosphonium Salts to Aldehydes. Remarkable Counter Ion Effects on Phosphorus Proton Couplings

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As part of a program aimed at developing synthetic methods based on divalent germanium and divalent tin,[1] we had the opportunity to examine the chemistry of triphenylphosphonium salts **1**. Phosphonium salt **1a**, a precursor to dichloro- or bisamidogermylenes, can be obtained in nearly quantitative yield by the addition of tributyltin hydride[2] to an ethereal solution of germanium tetrachloride and triphenylphosphine (eq 1).[3] Tin and zinc analogues **1b**, **1c** can also be prepared in high yield.[3]

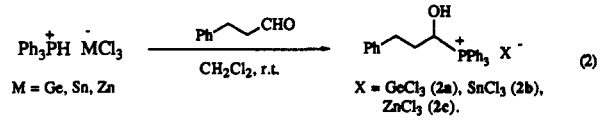
$$Ph_3P + GeCl_4 \xrightarrow[Et_2O,\ rt]{nBu_3SnH} Ph_3\overset{+}{P}H\ \overset{-}{M}Cl_3 \qquad (1)$$

1a, M = Ge
b, M = Sn
c, M = Zn

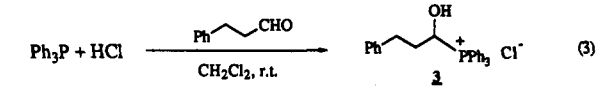
We were interested in preparing 1-hydroxytrichlorogermanes via the addition of **1a** to aldehydes. This approach was based on work by Mironov that had shown that 1-hydroxytrichlorogermanes could be prepared by the addition of $HGeCl_3$ to aldehydes.[4] In our system it was not clear whether the triphenylphosphine would compete with the germanate anion for addition to the carbonyl carbon.

Recent work by Lee and Trogler showed that a variety of 1-hydroxy phosphonium salts could be prepared in high yield by the addition of an anhydrous acid to acetone, acetaldehyde, or benzaldehyde in the presence of PMe_3 or PEt_3.[5] However, no reaction was observed with triphenylphosphine.[5] Interestingly, Anders et al. prepared 1-hydroxy triphenylphosphonium tetrafluoroborate salts from triphenylphosphine, benzaldehyde or acetaldehyde, and tetrafluoroboric acid.[6] In addition, triphenylphosphonium tetrafluoroborate reacts with thiodienes to give thioallylphosphonium tetrafluoroborates[7] and triphenylphosphonium bromide[8] adds to enol ethers to give 1-alkoxy phosphonium bromides.[9] Thus, whether triphenylphosphine would add to an aldehyde or whether it could compete against trichlorogermanate or trichlorostannate was unclear.

When **1a–c** were added to hydrocinnamaldehyde, 1-hydroxy triphenylphosphonium salts **2a–c** were obtained irrespective of the counterion (eq 2). We similarly pre-



(2)



(3)

pared phosphonium salt **3** from triphenylphosphine, hydrogen chloride, and hydrocinnamaldehyde without incident (eq 3).[10] Thus, triphenylphosphine readily adds to aldehydes under anhydrous acidic conditions and it is more nucleophilic than trichlorogermanate, trichlorostannate, or chloride anions.

Due to significant differences in the ^1H NMR and IR spectra of compounds **2** and **3** (see below) their structures were determined based on the following information: (i) the spectra for **2a–c** were very similar, (ii) $^-ZnCl_3$ is not a nucleophile, unlike $^-GeCl_3$ or $^-SnCl_3$, and thus it cannot add to an aldehyde, (iii) there were no observable tin satellite peaks in the ^1H NMR spectra for the C_1-H proton

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