General Procedure. Diisobutylaluminum hydride (1.0 M, hexanes) was added portionwise to a 0.3 M toluene solution of the unsaturated lactone (7.0 mmol) cooled to −78 °C (dry ice–CH_3OH bath) until TLC analysis judged the reaction complete. It was then poured into a rapidly stirred mixture of ice (25 g) and acetic acid (7 mL). Chloroform (50 mL) was added and the two-phase system stirred vigorously for 10 min. Another 100-mL portion of chloroform was added and vigorous stirring continued until two distinct layers formed when the stirring was halted (typically 30–60 min). The layers were separated, and the organic layer was washed with bicarbonate (2 × 100 mL) and brine (75 mL). Drying and removal of the solvents afforded a colorless oil which was used without purification.

The crude lactol and triethylsilane (1.22 g, 10.5 mmol) in dichloromethane (25 mL) were cooled under nitrogen. Dropwise addition of boron trifluoride etherate (0.95 mL, 7.7 mmol) gave a solution which was stirred until TLC indicated that no lactol was present and then quenched by addition of ca. 10 mL of aqueous bicarbonate. The cooling bath was removed and the solution allowed to warm to room temperature with vigorous stirring. After the mixture was transferred to a separatory funnel, ether (100 mL) was added and the whole washed with bicarbonate (20 mL) and brine (20 mL). Drying and removal of the solvents afforded an oil which was chromatographed (silica gel, hexanes–EtOAc).

1: IR (film) 2070, 3040, 2930, 2830, 1490, 1455, 1380, 1120, 750, 695 cm^{-1}; NMR ($CDCl_3$) δ 1.74 (m, 3 H), 2.20 (m, 4 H), 4.34 (m, 2 H), 4.55 (dd, J = 5, 9 Hz), 5.52 (m, 1 H), 7.40 (s, 5 H).

2: IR (film) 2980, 2895, 1065; NMR ($CDCl_3$) δ 1.52–2.42 (m, 4 H), 3.70–4.18 (m, 2 H), 4.68–4.94 (m, 1 H), 7.03–7.30 (m, 5 H); ^{13}C NMR 143.315, 128.146, 126.954, 125.492, 80.527, 68.446, 34.534, 25.919. The boiling point [105–107 °C (15 mmHg)] was identical with the literature[13] boiling point.

3 (R = CN): mp 75–76 °C; IR (film) 2980, 2880, 2205, 1120 cm^{-1}; 100-MHz NMR ($CDCl_3$) δ 0.10 (s, 6 H), 0.91 (s, 9 H), 1.72 (br s, 3 H), 1.8–2.0 (m, 4 H), 2.07 (t, J = 2 Hz, 3 H), 3.57, 3.70 (AB q, J = 10 Hz, 2 H), 4.15 (m, 3 H), 5.44 (m, 1 H); high-resolution mass spectrum for $C_{15}H_{22}O_2NSI$ (P − 57) requires m/e 276.15103, found m/e 276.14199.

4 (R = SPh): IR (film) 3035, 2970, 2940, 2870, 1685, 1480, 1445, 1260, 1105, 1070, 740, 690 cm^{-1}; 100-MHz NMR ($CDCl_3$) δ 0.06 (s, 6 H), 0.92 (s, 9 H), 1.75 (m, 3 H), 1.90 (m, 4 H), 1.97 (t, 3 H, J = 2 Hz), 3.60 and 3.80 (AB q, 2 H, J = 10 Hz), 4.07 (m, 2 H), 4.30 (m, 1 H), 5.47 (m, 1 H).

5 (R = H): IR (film) 2980, 2970, 2870, 1110 cm^{-1}; 100-MHz NMR ($CDCl_3$) δ 0.10 (s, 6 H), 0.90 (s, 9 H), 1.7–2.0 (m, 10 H), 3.50 and 3.72 (AB q, 2 H, J = 10 Hz), 4.02 (q, J = 2.5 Hz, 2 H), 4.20 (m, 1 H), 5.44 (m, 2 H); 90-MHz ^{13}C NMR ($CDCl_3$) δ 18.314, 23.135, 25.579, 25.898, 27.523, 41.124, 62.469, 65.511, 70.917, 121.353, 123.412, 134.517, 139.014; high-resolution mass spectrum for $C_{18}H_{32}O_2Si$ requires m/e 308.21717, found 308.21645.

7: IR (film) 3460, 2970, 2920, 1730, 1205; NMR ($CDCl_3$) δ 0.82–0.97 (m, 3 H), 1.60 (br s, 3 H), 1.73–2.63 (m, 5 H), 2.87 (br s, 1 H, OH), 3.30–3.82 (m, 6 H), 3.91–4.11 (m, 1 H), 5.14–5.43 (m, 1 H); mass spectrum for $C_{13}H_{20}O_4$ requires m/e 240.1361, found m/e 240.1369.

8 (R = H): NMR ($CDCl_3$) 1.31 (s, 3 H), 1.44 (m, 2 H), 1.80–2.48 (envelope, 7 H), 2.98 (m, 1 H), 3.40 (m, 3 H), 3.74 (m, 3 H), 4.60 (s, 2 H), 7.34 (s, 5 H); ^{13}C NMR ($CDCl_3$) 21.718, 22.433, 29.003, 30.954, 35.636, 41.099, 52.544, 53.324, 70.882, 71.857, 72.117, 73.548, 73.743, 82.782, 127.849, 128.434, 136.823, 213.039; IR ($CHCl_3$) 3400, 3040, 3005, 2980, 2880, 1700, 1450, 1090, 1050 cm^{-1}. Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83. Found: C, 70.14; H, 8.05.

9 (R = $COCH_3$): NMR ($CDCl_3$) 1.24 (s, 3 H), 1.34 (m, 2 H), 1.86 (m, 2 H), 2.02 (s, 3 H), 2.14 (s, 3 H), 2.18–2.66 (envelope, 5 H), 3.02 (dd, 1 H, J = 7, 12 Hz), 3.50 (m, 4 H), 4.52 (s, 2 H), 4.84 (d, 1 H, J = 6 Hz), 5.02 (m, 1 H), 7.34 (s, 5 H); ^{13}C NMR ($CDCl_3$) 21.133, 21.263, 22.108, 24.126, 25.752, 28.418, 35.831, 41.944, 50.723, 51.178, 70.101, 71.987, 73.223, 73.808, 73.938, 82.522, 127.784, 128.434, 138.124, 169.404, 169.794, 209.788; IR (film) 3040, 2980, 2880, 1735, 1710, 1450, 1370, 1230, 1100, 1040, 1010, 940, 860, 735, 695 cm^{-1}. Anal. Calcd for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26. Found: C, 67.52; H, 7.31.

(13) Loewen, P. C.; Makhubu, L. P.; Brown, R. K. *Can. J. Chem.* **1972**, *50*, 1502.

Acknowledgment. We thank the National Institutes of Health (CA 23663) for generous financial support.

Registry No. 1, 60335-71-9; 2, 16133-83-8; 3, 77256-27-0; 4, 77256-28-1; 5, 77256-29-2; 6, 87-41-2; 7, 77256-30-5; 8, 77256-31-6; 9, 77256-32-7; 5,6-dihydro-4-methyl-6-phenyl-2*H*-pyran-2-one, 29643-79-6; dihydro-5-phenyl-2(3*H*)-furanone, 1008-76-0; *cis*-3-cyano-4,7-dimethyl-4a-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4a,5,6,8a-tetrahydrobenzopyran-2-one, 77256-33-8; *cis*-4,7-dimethyl-4a-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-(phenylthio)-4a,5,6,8a-tetrahydrobenzopyran-2-one, 77256-34-9; *cis*-4,7-dimethyl-4a-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4a,5,6,8a-tetrahydrobenzopyran-2-one, 77256-35-0; 3-hydroxy-1-(3*H*)-isobenzofuranone, 16859-59-9; methyl 4,7-dimethyl-3,4,4a,5,8,8a-hexahydro-3-hydroxy-2-oxo-4a-benzopyrancarboxylate, 77256-36-1; hexahydro-1,4,9-trihydroxy-3-methyl-10-[2-(phenylmethoxy)ethyl]-1*H*-3,9a-methano-2-benzoxepin-6(7*H*)-one, 77256-37-2; 1,4,9-tris(acetyloxy)hexahydro-3-methyl-10-[2-(phenylmethoxy)ethyl]-1*H*-3,9a-methano-2-benzoxepin-6(7*H*)-one, 77256-38-3.

p-Methoxyacetophenone Dimethyl Ketal and α,*p*-Dimethoxystyrene. Efficient and Useful Reagents for 1,2- and 1,3-Diol Protection†

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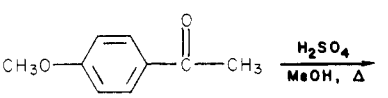
Received December 2, 1980

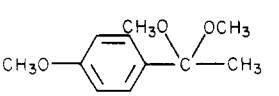
The use of carbohydrates as chiral templates in syntheses of complex natural products continues to attract an increasing amount of attention.[1] Selective derivatization of these optically pure building blocks plays a major role both in total synthesis and in the preparation of novel analogues of sugar-containing natural products (e.g., anthraquinones, aureolides, aminoglycosides, etc.).[2]

A key feature in most synthetic schemes involves control of the polyhydroxyl functionality present in the starting sugar. Need for the selective manipulation of these groups has led to a variety of 1,2- and 1,3-diol protecting groups,[3] perhaps the most common being acetals derived from benzaldehyde.[4,5] These derivatives, however, oftentimes require fairly strong (aqueous) acid for hydrolysis[6] or large quantities of an expensive hydrogenation catalyst[7] to effect cleavage. Hence, it was felt that an alternative protection/deprotection procedure which avoids these somewhat limiting conditions yet is highly efficient, rapid, and mild would be particularly useful. We now report our results from a study in this area which provide new methodology for a mild, nonaqueous 1,2- and 1,3-diol protection/deprotection sequence.

Conversion of *p*-methoxyacetophenone (**1**) to its dimethyl ketal **2** was readily performed in 81% distilled



1



2

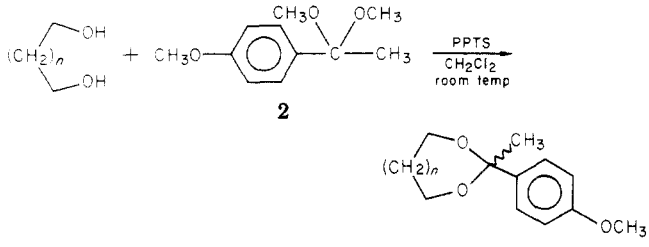
yield, using concentrated H_2SO_4 in MeOH at room tem-

† Dedicated to Professor Harry H. Wasserman on the occasion of his sixtieth birthday.

‡ Recipient of an American Cancer Society Junior Faculty Research Award, 1981–1983.

0022-3263/81/1946-2419$01.25/0

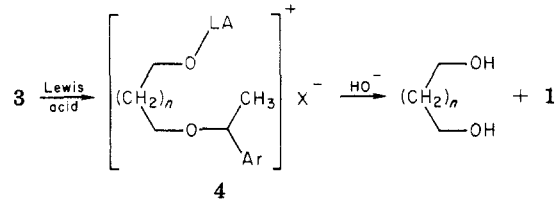
perature for 24 h. Treatment of a variety of 1,2- or 1,3-diols with **2** (5–10 equiv) in CH_2Cl_2 (0.5 M) at room temperature for ca. 2–3 h in the presence of PPTS[8] (2 equiv) leads to derivatives **3** (method A) in high yields (Table I). Use of other acid catalysts (e.g., TsOH, $ZnCl_2$, IR-120 resin) gave inferior results. Most protected diols were further derivatized (Table I) as benzyl or naphthyl[9] ethers or benzoyl esters by using standard conditions.



Interestingly, while this protecting group introduces a new chiral center, we have observed, in many cases studied, a strong preference for the formation of a major isomer. While the unequivocal assignment of relative stereochemistry was not made, the observation of a product distribution was determined on the basis of both NMR and HPLC[10] analyses. Ratios for each derivative examined are listed in Table II.

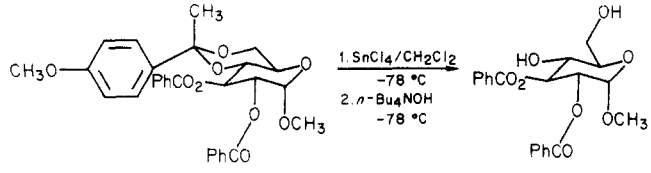
The synthetically useful saccharide α-methylglucoside (entry 2) formed a single product in high yield upon reaction with **2**, analogous stereochemically (i.e., with the phenyl ring presumably in the equatorial position)[11] to that observed with benzylidene acetals. Likewise, arabinose, as its α-methyl derivative at C-1 (entry 4), efficiently gave a single new compound under the reaction conditions.

In choosing **2**, it was anticipated that simple exposure of **3** to a Lewis acid (LA) should, following workup, effect cleavage,[12] due to the strong stabilizing nature of the functional groups located on the incipient carbocation (i.e., **4**). Quenching with soluble hydroxide ion (see Experimental Section) should return the diol, as illustrated below.



This was, indeed, the case, as reaction of derivatized carbohydrates (Table I) with excess $SnCl_4$ in CH_2Cl_2 at −78 °C for 20 min, followed by quenching at −78 °C with *n*-Bu_4NOH (in CH_2Cl_2) and workup afforded products in 89–96% isolated yields.

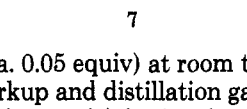
For example, α-methylglucoside **5** gave diol diester **6** in 96% yield. Use of these exceedingly mild conditions for



short but sufficient periods of time did not affect the ester functions. Substitution of "wet" THF for hydroxide, however, was unacceptable and led to complex reaction mixtures. Chromatographic separation of the desired product(s) from *p*-methoxyacetophenone was trivial based on the large difference in relative polarity.

For reasons which we cannot explain at this time, ribonic acid γ-lactone derivative **13**, protected as either its *tert*-butyldiphenylsilyl ether[13] or phenyl carbonate, did not react with $SnCl_4$ at −78 °C. Raising the temperature to −45 °C, 0 °C, or even room temperature led to only traces of the anticipated diol. All other carbohydrates studied, however, gave the expected products in quite good yields.

In an effort to decrease both the time of reaction and amount of 2 necessary to form acetals **3**, we have prepared α,*p*-dimethoxystyrene (**7**).[14] Stirring 1 in MeOH con-



taining H_2SO_4 (ca. 0.05 equiv) at room temperature for 24 h followed by workup and distillation gave **7** in 61% yield. Substitution of **7** (1.5 equiv) for **2**, using a catalytic amount of PPTS (method B), likewise afforded derivatives in excellent yields (see Table I).

Hence, α-methylglucoside (entry 2), an L-rhamnose derivative (entry 3), β-methylriboside (entry 5), ribonic acid

(1) (a) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159. (b) Fraser-Reid, B. *Ibid.* **1975**, *8*, 192.

(2) Remers, W. A., "The Chemistry of Antitumor Antibiotics"; Wiley: New York, 1979; Vol. I.

(3) Representative examples include the following. (a) Tetraisopropyldisoloxane: Markiewiez, W. T. *J. Chem. Res. (S)* **1979**, 24. (b) Ortho ester: Reese, C. B. *Tetrahedron* **1978**, *34*, 3151. (c) Butylidene: Yuceer, L. *Carbohydr. Res.* **1977**, *56*, 87. (d) Cycloheptylidene: Van Heeswijk, W. A. R.; Goedhart, J. B.; Vliegenthart, J. F. G. *Ibid.* **1977**, *58*, 337. (e) Trichloroethylidene: Yuceer, L. *Ibid.* **1977**, *56*, 87. (f) Cyclic carbonates: Kutney, J. P.; Ratcliff, A. H. *Synth. Commun.* **1975**, 47. (g) Dibutylstannylene: Wagner, D.; Verheyden, J. P. H.; Moffatt, J. G. *J. Org. Chem.* **1974**, *39*, 24. (h) 1-(Dimethylamino)ethylidene: Hanessian, S.; Moralioglu, E. *Can. J. Chem.* **1972**, *50*, 233. (i) *o*-Nitrobenzylidene: Collins, P. M.; Oparaeche, N. N. *J. Chem. Soc., Chem. Commun.* **1972**, 532. (j) Dimethoxymethylidene: Niaz, G. R.; Reese, C. B. *Ibid.* **1969**, 552. (k) Dimethylsilylene: Kelly, R. W. *Tetrahedron Lett.* **1969**, 967. (l) Cyclopentylidene: Hampton, A.; Fratantoni, J. C.; Carroll, P. M.; Wang, S. C. *J. Am. Chem. Soc.* **1965**, *87*, 5481. (m) 4-(Dimethylamino)-benzylidene: Cramer, F.; Saenger, W.; Scheit, K. H.; Tennigkeit, J. **1965**, *683*, 199. (n) Cyclohexylidene: Gardi, R.; Vitali, R.; Ercoli, A. *J. Org. Chem.* **1962**, *27*, 668.

(4) For a general discussion on the uses of benzylidene acetals in carbohydrate chemistry, see: Horton, D.; Weckerle, W. In "Synthetic Methods for Carbohydrates"; El Khadem, H. S., Ed.; American Chemical Society: Washington, D.C., 1976; pp 22–35.

(5) Acetals derived from acetophenone have been prepared and subsequently cleaved by using protic acid at room temperature over 3 days: Evans, M.E.; Parrish, F. W.; Long, L. *Carbohydr. Res.* **1967**, *3*, 453.

(6) Representative cases include the following. (a) Chrysanthemumdicarboxylic acids: Fitzsimmons, B. J.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1979**, *101*, 6123. (b) Multistriatin: Sum, P. E.; Weiler, L. *Can. J. Chem.* **1978**, *56*, 2700. (c) Thromboxanes: Ohrui, H.; Emoto, S. *Agric. Biol. Chem.* **1977**, *41*, 1773.

(7) See, for example: Hanessian, S.; Rancourt, G. *Pure Appl. Chem.* **1977**, *49*, 1201.

(8) Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

(9) Tavssig, P. R.; Miller, G. B.; Storms, P. W. *J. Org. Chem.* **1965**, **30**, 3122.

(10) HPLC was performed on a Waters M-6000 liquid chromatograph using varying percentages (0.25–3%) of 2-propanol in heptane and a μPorasil column.

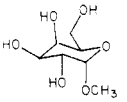
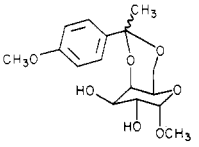
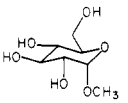
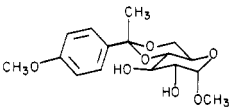
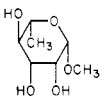
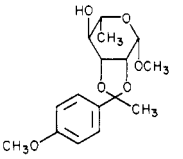
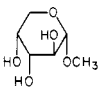
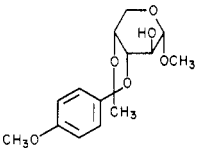
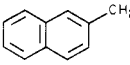
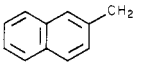
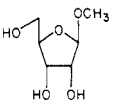
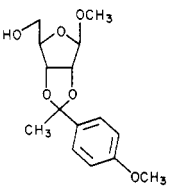
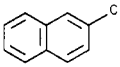
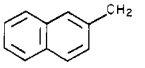
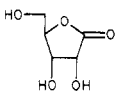
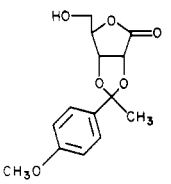
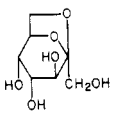
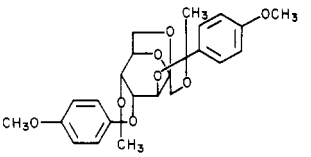
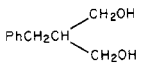
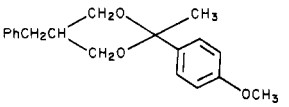
(11) For a review on carbohydrate cyclic acetal formation, see: Clode, D. M. *Chem. Rev.* **1979**, *79*, 491.

(12) Boron trichloride is known to effect cleavage of sugar acetals, including benzylidene groups, in 55–85% yields. However, it is nonselective in that several other processes (e.g., methyl ether cleavage) take place under the reaction conditions: Bonner, T. G.; Bourne, E. J.; McNally, S. *J. Chem. Soc.* **1960**, 2929; Bonner, T. G.; Saville, N. M. *Ibid.* **1960**, 2851.

(13) Hanessian, S.; Lavallee, P. *Can. J. Chem.* **1975**, *53*, 2975.

(14) Loudon, G. M.; Smith, C. K.; Zimmerman, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 465.

Table I. Protection, Derivatization, and Deprotection of Polyhydroxy-Containing Compounds

entry	starting material	protection product(s) (%)[a]	method[b]	derivatization (%)[a,c]	deprotection (%)[a]
1		 8	(93) A A	PhCO (73) $PhCH_2$ (83)	PhCO (95) $PhCH_2$ (94)
2		 9	(97) A (94) B	PhCO (58) $PhCH_2$ (85)	PhCO (96) $PhCH_3$ (93)
3		 10	(89) B	$PhCH_2$ (74)	$PhCH_2$ (90)
4		 11	(95) A	 (69)	 (90)
5		 12	(97) B	 (88)	 (89)
6		 13	(100) A (96) B	$Ph_2(t\text{-Bu})Si$ (97) PhOC(O) (62)	d
7			(84) B		e
8	 15	 16	(82) B		e

[a] All yields are for isolated, chromatographically pure products. [b] Method A, using ketal 2; method B, via enol ether 7; see text. [c] Unoptimized yields. [d] See text. [e] Not attempted.

γ-lactone (entry 6), sedoheptulosan (entry 7), and a non-carbohydrate-related 1,3-diol (entry 8) all afforded protected materials in 82–97% yields. Within experimental error, use of either 2 or 7 gave essentially identical results in terms of efficiency (compare entries 2 and 6). Sedoheptulosan reacted to form a bis derivative 14, which is believed to be a combination of a C-2, C-7 trans-fused 6,6-bicyclic moiety, as well as the cis-fused C-3,C-4 5,6-bicyclic system.

In summary, *p*-methoxyacetophenone, an inexpensive, readily available material has been converted into two reactive reagents (i.e., 2 and 7), each of which can serve as a 1,2- and 1,3-diol protecting group precursor. Protection generally occurs fairly rapidly and in high yields at ambient temperature. Deprotection takes place under conditions where many functional groups are unaffected and may be among the mildest conditions available for protected diol cleavage.

Experimental Section

General Procedures. Melting and boiling points are not corrected. IR spectra were recorded on a Perkin-Elmer 283

Table II. Isomer Ratios of Acetals Using 2 or 7

entry	acetal	ratio
1	8	3:1
2	9	1:0
3	10	5:3
4	11	1:0
5	12	4:1
6	13	10:1
7	14	2:1:1:1
8	16	3:1

infrared spectrophotometer. NMR spectra were taken on a Varian T-60 or FT-80 spectrometer; chemical shifts were measured downfield from Me_4Si as an internal standard. Analytical thin-layer chromatography was performed on Merck silica gel 60 F-254. Column chromatography was carried out with Merck silica gel 60 (70–230 mesh).

Materials. Stannic chloride was distilled under reduced pressure and stored under argon at room temperature. Tetra-*n*-butylammonium hydroxide in methanol (Eastman) was concentrated in vacuo and redissolved in methylene chloride prior to use. Arabinose, ribose, and ribonic acid γ-lactone were purchased from the Aldrich Chemical Company. Methyl α-D-arabinoside,[15] methyl β-D-riboside,[16] and methyl α-L-rhamnoside[17] were prepared by literature procedures. Methyl glucopyranoside, methyl galactopyranoside, and sedoheptulosan were available from Pfanstiehl Laboratories, Waukegan, IL. Diol **15** was prepared by LAH reduction of diethyl 2-benzylmalonate.

***p*-Methoxyacetophenone Dimethyl Ketal, 2.** *p*-Methoxyacetophenone (23 g, 0.15 mol) and trimethyl orthoformate (40 mL, 0.36 mol) were dissolved in 80 mL of absolute methanol at room temperature. To this solution were added 8 drops of concentrated H_2SO_4 and, following a 12-h period, the reaction was quenched with triethylamine until slightly basic. Concentration in vacuo gave a residue which was distilled from ca. 10 g of IR-45 ion-exchange resin ($RNH_3^+OH^-$) at 74 °C (1 mm), giving 24.3 g (81%) of the desired ketal; NMR (CCl_4) δ 7.21 (d, 2 H, J = 8 Hz), 6.78 (d, 2 H, J = 8 Hz), 3.75 (s, 3 H), 3.0 (s, 6 H), 1.4 (s, 3 H).

α,*p*-Dimethoxystyrene, 7. *p*-Methoxyacetophenone (11.9 g, 79.3 mmol) and trimethyl orthoformate (20 mL, 0.18 mol) were dissolved in 40 mL of absolute methanol at room temperature. Four drops of concentrated H_2SO_4 were added and the mixture was stirred for 26 h. Triethylamine was then used, dropwise, to effect neutralization. Concentration in vacuo followed by distillation under reduced pressure [bp 87–89 °C (0.15 mm)] afforded 9.5 g (61%) of enol ether **7**; NMR (CCl_4) δ 7.41 (d, 2 H, J = 8 Hz), 6.88 (d, 2 H, J = 8 Hz), 4.45 (d, 1 H, J = 3 Hz), 4.0 (d, 1 H, J = 3 Hz), 3.70 (s, 3 H).

Representative Procedure for Diol Protection Using 2. Methyl 4,6-*O*-[(4-Methoxyphenyl)ethylidene]-α-D-glucopyranoside, 9. A mixture of 118.6 mg (0.613 mmol) of methyl α-D-glucopyranoside and 1.13 mL (6.1 mmol) of ketal **2** in 2 mL of CH_2Cl_2 was treated with 350 mg (1.4 equiv) of pyridinium tosylate. The solution was stirred for 3 h at room temperature under Ar. The mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with ether. The combined extracts were washed with H_2O and brine and dried over anhydrous Na_2SO_4. Filtration followed by concentration in vacuo gave a residue which was filtered through a column of silica gel with Et_2O. There was obtained 198.5 mg (98%) of the desired material as a white crystalline solid: mp 136–140 °C (Et_2O); $[\alpha]^{25}_D$ +120° (c 1.65, $CHCl_3$); R_f 0.13 (Et_2O); NMR ($CDCl_3$, partial) δ 7.42 (d, 2 H, J = 9 Hz), 6.85 (d, 2 H, J = 9 Hz), 3.81 (s, 3 H), 3.41 (s, 3 H), 1.54 (s, 3 H); IR ($CHCl_3$) 3440, 1220, 840 cm^{-1}; mass spectrum, m/e (relative abundance) 326 (11, M^+), 311 (54), 151 (28), 150 (8), 135 (100), 77 (6), 43 (41). Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.92; H, 6.80. Found: C, 58.68; H, 6.64.

Methyl 4,6-*O*-[(4-methoxyphenyl)ethylidene]-α-D-galactopyranoside, 8: R_f 0.07 (Et_2O, major isomer), 0.11 (Et_2O, minor isomer); NMR ($CDCl_3$, partial) δ 7.39 (d, 2 H, J = 9 Hz), 6.86 (d, 2 H, J = 9 Hz), 3.81 (s, 3 H), 3.38 (s, 3 H), 1.60 (minor isomer, s), 1.56 (major isomer, s); IR ($CHCl_3$) 3440, 3010, 1600, 1245, 1220, 830 cm^{-1}; mass spectrum, m/e (relative abundance) 326 (6, M^+), 311 (51), 151 (18), 150 (16), 135 (100), 77 (14), 43 (45). Anal. Calcd for $C_{16}H_{22}O_7$: C, 58.87; H, 6.80. Found: C, 59.00; H, 6.61.

Methyl 2,3-*O*-[(4-methoxyphenyl)ethylidene]-α-L-rhamnopyranoside, 10: R_f 0.26 (1:1 Et_2O—C_5H_{12}); NMR ($CDCl_3$, partial) δ 7.47 (d, 2 H, J = 8 Hz), 6.86 (d, 2 H, J = 8 Hz), 4.97 (s, 1 H), 3.82 (s, 3 H), 3.47 (s, 3 H), 1.62 (s, 3 H), 1.22 (d, 3 H, J = 6 Hz); IR ($CHCl_3$) 3460, 3010, 1620, 1510, 1250, 1080, 835 cm^{-1}; mass spectrum, m/e (relative abundance) 310 (1, M^+), 295 (6), 281 (13), 151 (13), 150 (20), 135 (100), 107 (13), 92 (13), 77 (27), 43 (40). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.96; H, 7.15. Found: C, 61.86, H, 6.85.

Representative Prodcedure for Diol Protection Using 7. Methyl 2,3-*O*-[(4-Methoxyphenyl)ethylidene]-β-D-ribofuranoside, 12. To a solution of 179.6 mg (1.10 mmol) of methyl β-D-ribofuranoside and 0.50 mL (3.0 mmol) of **7** in 3 mL of CH_2Cl_2 was added a catalytic amount (~10 mg) of pyridinium tosylate. The mixture was stirred at room temperature for 0.5 h under Ar, quenched by addition to saturated aqueous $NaHCO_3$, worked up, and purified as described in the case above. There was obtained 315.8 mg (97%) of the protected sugar as a clear oil: R_f 0.33 (Et_2O, Minor isomer), 0.22 (Et_2O, major isomer); NMR ($CDCl_3$, partial) δ 7.55 (d, 2 H, J = 10 Hz), 6.90 (d, 2 H, J = 10 Hz), 3.81 (s, 3 H), 3.55 (s, 3 H), 1.6 (s, 3 H); IR (neat) 3440, 1250, 842 cm^{-1}; mass spectrum, m/e (relative abundance) 296 (1, M^+), 281 (46), 249 (17), 135 (100), 77 (13), 43 (34); mol wt calcd for $C_{15}H_{20}O_6$ 296.1260, found 296.1263.

Methyl 3,5-*O*-[(4-methoxyphenyl)ethylidene]-α-D-arabinopyranoside, 11: $[\alpha]^{25}_D$ −20.1° (c 0.80, $CHCl_3$); R_f 0.38 (Et_2O); NMR ($CDCl_3$, partial) δ 7.43 (d, 2 H, J = 9 Hz), 6.80 (d, 2 H, J = 9 Hz), 4.54 (d, 1 H, J = 4 Hz), 3.82 (s, 3 H), 3.45 (s, 3 H), 1.70 (s, 3 H); IR ($CHCl_3$) 3420, 3010, 1610, 1220 cm^{-1}; mass spectrum, m/e (relative abundance) 281 (26, M^+), 135 (100), 86 (28), 84 (46), 43 (80); mol wt calcd for $C_{15}H_{20}O_6$ 296.1260, found 296.1240.

2,3-*O*-[(4-Methoxyphenyl)ethylidene]ribonic acid γ-lactone, 13: R_f 0.30 (Et_2O); NMR (Me_2SO, partial) δ 7.44 (d, 2 H, J = 9 Hz), 6.95 (d, 2 H, J = 9 Hz), 3.81 (s, 3 H), 1.67 (s, 3 H); IR ($CHCl_3$) 3500, 1780, 1600, 1220, 840 cm^{-1}; mass spectrum, m/e (relative abundance) 280 (4, M^+), 265 (14), 163 (15), 150 (20), 135 (100), 77 (35), 43 (22). Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.98; H, 5.76. Found: C, 60.07; H, 5.51.

2,7:3,4-Di-*O*-[(4-methoxyphenyl)ethylidene]sedoheptulosan, 14: R_f 0.16 (1:1 Et_2O–C_5H_{12}); NMR ($CDCl_3$, partial) δ 7.01 (m, 8 H), 3.80 (s, 6 H), 1.7 (s, 3 H), 1.5 (s, 3 H); IR ($CHCl_3$) 3000, 1610, 1240, 1220, 1080, 830 cm^{-1}; mass spectrum, m/e (relative abundance) 456 (8, M^+), 441 (19), 187 (27), 135 (100), 57 (63), 43 (58), 41 (38). Anal. Calcd for $C_{25}H_{28}O_8$: C, 65.76; H, 6.19. Found: C, 65.79; H, 6.16.

***p*-Methoxyacetophenone 2-benzyl-1,3-propylene ketal, 16:** R_f 0.79 (1:1 Et_2O–C_5H_{12}); NMR ($CDCl_3$, partial) δ 7.76 (d, 2 H, J = 9 Hz), 7.20 (m, 5 H), 6.75 (d, 2 H, J = 9 Hz), 3.77 (s, 3 H), 1.61 (s, minor isomer), 1.50 (s, major isomer); IR ($CHCl_3$) 1340, 1275, 1030 cm^{-1}; mass spectrum, m/e (relative abundance) 298 (1, M^+), 283 (47), 135 (100), 131 (68), 91 (53), 77 (19). Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.54; H, 7.43. Found: C, 76.35; H, 7.15.

Typical Procedure for Cleavage of Protected diols with Stannic Chloride. Methyl 2,3-Di-*O*-benzyl-α-D-glucopyranoside. A solution of 92.3 mg (0.182 mmol) of methyl 2,3-di-*O*-benzyl-4,6-*O*-[(4-methoxyphenyl)ethylidine]-α-D-glucopyranoside in 3 mL of CH_2Cl_2 was cooled to −78 °C under a blanket of Ar. $SnCl_4$ (0.5 mL, 4.2 mmol) was added dropwise to the well-stirred solution, affording an orange-colored reaction mixture. After 20 min at this temperature, the mixture was quenched with excess n-Bu_4NOH dissolved in CH_2Cl_2. The resulting colorless mixture was poured into saturated aqueous $NaHCO_3$, extracted with Et_2O, and treated further as described in the examples above. A white crystalline solid was thus obtained:

(15) Prepared according to: Bishop, C. T.; Cooper, F. P. *Can. J. Chem.* **1963**, *41*, 2743; mp 133–135 °C (lit.[18] mp 131 °C).

(16) Prepared as described in ref 15. Further proof of structure for the protected material (i.e., **12**) was obtained by comparison with the known isopropylidene analogue: Leonard, N. J.; Carraway, K. L. *J. Heterocycl. Chem.* **1966**, *3*, 485.

(17) Fischer, E. *Chem. Ber.* **1894**, *27*, 2985.

(18) Bell, D. J.; Lorber, J. *J. Chem. Soc.* **1940**, 453.

63.1 mg (93%); mp 73–74 °C (lit.[18] mp 75–76 °C); $[\alpha]^{25}_D$ +18.2° (c 0.98, $CHCl_3$) (lit.[18] $[\alpha]^{18}_D$ +18.8°); R_f 0.25 (Et_2O); NMR ($CDCl_3$, partial) δ 7.25 (s, 10 H), 4.56 (m, 4 H), 3.31 (s, 3 H); IR ($CHCl_3$) 3400, 1220, 750, 680 cm^{-1}; mass spectrum, m/e (relative abundance) 374 (1, M^+), 283 (7), 253 (4), 121 (5), 92 (7), 91 (100); mol wt calcd for $C_{21}H_{26}O_6$ 374.1729, found 374.1716.

Acknowledgment. Financial support from the Chemistry Department, UCSB, the Committee on Research of the University of California, the Research Corporation, and the American Cancer Society is gratefully acknowledged. Initial work on the development of reagents **2** and **7** arose during work by B.H.L. on the total synthesis of (−)-*N*-methylmaysenine in the laboratories of Professor E. J. Corey at Harvard University. We also thank Dr. H. Webb for recording the mass spectral data.

Registry No. 1, 100-06-1; 2, 27150-99-8; 7, 51440-56-3; 8 (isomer 1), 77397-48-9; 8 (isomer 2), 77397-50-3; 9, 77397-49-0; 10 (isomer 1), 77270-37-2; 10 (isomer 2), 77270-42-9; 11, 77270-38-3; 12 (isomer 1), 77270-39-4; 12 (isomer 2), 77270-43-0; 13 (isomer 1), 77270-40-7; 13 (isomer 2), 77270-44-1; 14 (isomer 1), 77341-11-8; 14 (isomer 2), 77270-45-2; 14 (isomer 3), 77340-67-1; 14 (isomer 4), 77340-68-2; 15, 2612-30-8; *cis*-16, 77270-41-8; *trans*-16, 77270-46-3.

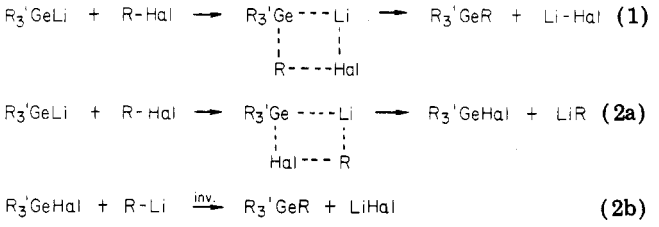
Communications

Organogermyl Anion Chemistry: Free-Radical Involvement in Reactions with Alkyl Bromides

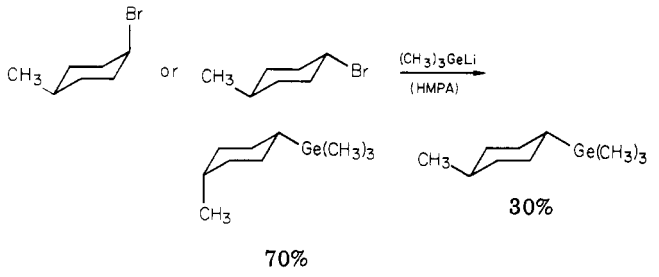
Summary: The importance of free-radical pathways in substitution reactions of secondary bromides with R_3GeLi (R = CH_3, C_6H_5) reagents is indicated strongly by determinations of product stereochemistry in cyclohexyl systems and cyclization of the 6-hepten-2-yl moiety to yield [(2-methylcyclopentyl)methyl]germanes, with the appropriate cis/trans ratio. Appropriate comparisons are made with the corresponding organotinlithium reagents.

Sir: Although considerable information has accumulated regarding the reactions of organostannyl alkalis (R_3SnM) with alkyl halides,[1-11] the mechanistic picture for the corresponding organogermyl derivatives is unclear.[7] Some years ago, Eaborn, Hill, and Simpson[12] examined some reactions of optically active [ethyl(1-naphthyl)phenylgermyl]lithium with simple alkyl, allyl, and benzyl halides and identified systems proceeding with predominant retention at germanium (alkyl bromides and chlorides) or predominant inversion (alkyl iodides and benzyl bromide). No stereochemical information at carbon was available but the following sequences were suggested for the predominant retentive (eq 1) and invertive processes (eq 2).

In view of the potential importance of these reactions for forming C–Ge bonds, we have conducted further examination of some (R_3GeLi; alkyl bromide) systems which permit mechanistic conclusions and provide interesting comparisons with the corresponding organostannyl systems.



Reaction of either *cis*-[7] or *trans*-4-methylcyclohexyl bromide with $(CH_3)_3GeLi$[7] provided the same 70:30 mixture of cis and trans germanes. This apparently complete stereoequilibration indicates that a single-step four-center process (eq 1) is unimportant but could be consistent with electron-transfer and free-radical processes.[13] To investigate this possibility further, certain reactions were conducted with the primary 6-bromo-1-hexene and the secondary 6-bromo-1-heptene, the free radicals from which (loss of Br·) are known to cyclize rapidly to yield cyclopentylmethyl and (2-methylcyclopentyl)methyl products, respectively.[14,15]



With the above primary bromide, none of the reagents $(CH_3)_3SnLi$, $(CH_3)_2(C_6H_5)SnLi$, $CH_3(C_6H_5)_2SnLi$, $(C_6H_5)_3SnLi$, $(CH_3)_3GeLi$, and $(C_6H_5)_3GeLi$ provided rearranged cyclopentylmethyl product, and the S_N2 pathway is presumably the important one.[3,10,16] However, with the secondary bromide (lowered "S_N2" reactivity at the more

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(7) W. Kitching, H. Olszowy, and J. Waugh, *J. Org. Chem.*, **43**, 898 (1978).
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(13) It is interesting to note that whereas $(CH_3)_3GeLi$ (HMPA) provides a 70:30 cis/trans mixture of germanes from either 4-methylcyclohexylbromide, $(CH_3)_3SnLi$ (either THF or HMPA) leads to an ca. 30:70 cis/trans mixture of stannanes. This reversal in distribution indicates important differences in the transition states for abstraction of $(CH_3)_3Ge$ and $(CH_3)_3Sn$ by the 4-methylcyclohexyl radical. For a general discussion see F. R. Jensen, L. H. Gale, and J. E. Rodgers, *J. Am. Chem. Soc.*, **90**, 5793 (1968).
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