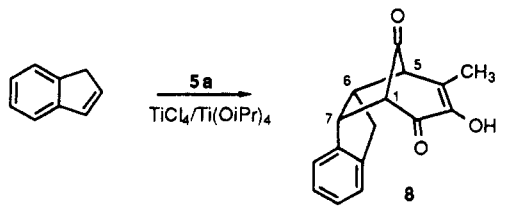

evident from a J_{H1-H7} of 6–7 Hz and the lack of a measurable coupling constant between H5 and H6.[6f] In the indene adduct 8, an endo orientation is indicated by J_{H1-H7} and J_{H5-H6} of 8–9 Hz. The structures of 2 and 3 have been reported previously.[4]

The mechanism(s) of the reactions remains to be firmly established;[4b,7] however, the rationale presented here is a useful guide for the design of experiments and reaction conditions to control the various reaction manifolds available to styrenes and quinones. In addition, since the quinones and styrenes are readily available and the reactions are stereoselective, this new methodology should be valuable for the efficient and stereoselective preparation of a number of different naturally occurring carbocyclic and heterocyclic systems.

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Supplementary Material Available: Representative experimental procedures for the preparation of **4a/b** and **8**, including complete physical and spectral data; ^1H and ^{13}C NMR spectra of **4a/b** and **8**; full crystallographic data and an ORTEP representation of **4a** (24 pages). Ordering information is given on any current masthead page.

Direct Preparation of 2-Deoxy-D-glucopyranosides from Glucals without Ferrier Rearrangement

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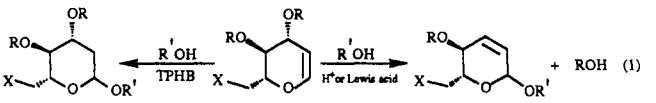
Summary: An efficient catalytic procedure for the preparation of 2-deoxyglucosides from glucals without allylic or Ferrier rearrangement using triphenylphosphine hydrobromide and a wide variety of hydroxylic nucleophiles is described.

2-Deoxyglycosides are versatile synthetic intermediates[1] as well as common structural units in many biologically significant substances.[2] Their preparation by electrophilic glycosylation[3] of hydroxylic donors with readily available glycals[4] is complicated in many instances by the proclivity of the cyclic enol toward allylic rearrangement resulting in 2,3-unsaturated glycosides (eq 1). This is commonly



known as the Ferrier reaction[5] and is most prevalent when the C(3)-hydroxyl is derivatized or under the influence of Lewis acid catalysts.[6]

Although several procedures have been introduced recently to circumvent rearrangement, they generally involve introduction of an auxiliary derived from a toxic, expensive, or difficult to handle reagent.[7] By necessity, one or more further steps are required to remove or transpose the auxiliary. Herein, we describe an efficient catalytic procedure using triphenylphosphine hydrobromide (TPHB) for the preparation of 2-deoxyglucosides directly from substituted glucals and a wide selection of hydroxylic nucleophiles. We have reported previously that stoichiometric amounts of TPHB add to enol ethers to give α-

(1) For example: Falck, J. R.; Lumin, S.; Yadagiri, P.; Shin, D.-S. *Adv. Prost. Throm. Leuk. Res.* **1989**, *19*, 635–638. Lumin, S.; Falck, J. R. *Tetrahedron Lett.* **1990**, *31*, 2971–2974.

(2) Williams, N. R.; Wander, J. D. In *The Carbohydrates*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. 1B, p 761. Gould, R. F. *Deoxy Sugars*; American Chemical Society: Washington, D.C., 1968.

(3) For alternative approaches to 2-deoxyglycosides, see: (a) Kahne, D.; Yang, D.; Lim, J. J.; Miller, R.; Paguaga, E. *J. Am. Chem. Soc.* **1988**, *110*, 8716–8717. (b) Michalska, M.; Borowiecka, M. *J. Carbohydr. Chem.* **1983**, *2*, 99. (c) Tavecchia, P.; Trumtel, M.; Veyrieres, A.; Sinay, P. *Tetrahedron Lett.* **1989**, *30*, 2533. (d) Crich, D.; Ritchie, T. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 945–954. (e) Giese, B.; Gilges, S.; Groninger, K. S.; Lamberth, C.; Witzel, T. *Liebigs Ann. Chem.* **1988**, 615–617. (f) Catelani, G.; Colonna, F.; Rollin, P. *Gazz. Chim. Ital.* **1989**, *119*, 389–393.

(4) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48–61. Wittman, M. D.; Halcomb, R. L.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1979–1981.

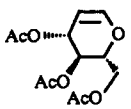
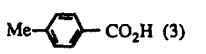
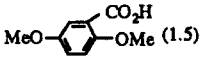
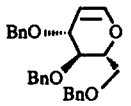
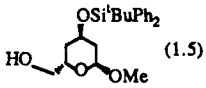
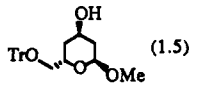
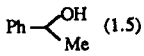
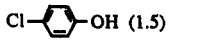
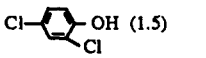
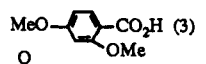
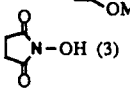
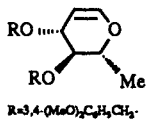
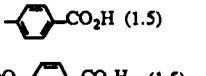
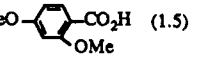
(5) Ferrier, R. J. *Adv. Carbohydr. Chem. Biochem.* **1969**, *24*, 199–266. Ferrier, R. J.; Prasad, N. *J. Chem. Soc. C* **1969**, 570.

(6) Descotes, G.; Martin, J.-C. *Carbohydr. Res.* **1977**, *56*, 168–172. Grynkiewicz, G.: Priebe, W.; Zamojski, A. *Ibid.* **1979**, *68*, 33–41. Hadfield, A. F.; Sartorelli, A. C. *Ibid.* **1982**, *101*, 197–208. Lundt, I.; Pedersen, C. *Acta Chem. Scand.* **1970**, *24*, 240–246.

(7) For recent examples, see: Ramesh, S.; Kaila, N.; Grewal, G.; Franck, R. W. *J. Org. Chem.* **1990**, *55*, 5–7 and references cited therein. Also: Bock, K.; Lundt, I.; Pedersen, C. *Carbohydr. Res.* **1984**, *130*, 125–134.

0022-3263/90/1955-5812$02.50/0

Table I. Triphenylphosphine Hydrobromide Catalyzed O-Glycosylation

entry	glucal	nucleophile (equiv)	anomer,[a] α/β	yield,[b] %
1		EtOH (3)	78/22	88
2		 (3)	95/5	78
3		cholesterol (3)	>95/5	82
4		*tert*-BuOH (1.5)	>95/5	66
5		PhOH (2)	88/12	67
6		 (3)	94/6	55
7		 (1.5)	80/20	60
8		 (1.5)	>95/5	60
9		 (1.5)	>95/5	58
10		MeOH (1.5)	70/30	87
11		 (1.5)	>95/5	80[c]
12		PhOH (1.5)	94/6	58
13		 (1.5)	88/12	70
14		 (1.5)	65/35	50
15		CH_3CO_2H (1.5)	92/8	71
16		$ClCH_2CO_2H$ (1.5)	>95/5	60
17		 (3)	79/21	68
18		 (3)	>95/5	80
19	 R=3,4-(MeO)$_2$C$_6$H$_3$CH$_2$-	EtOH (3)	85/15	53
20		PhOH (1.5)	90/10	55
21		CH_3CO_2H (1.5)	91/9	70
22		 (1.5)	92/8	40
23		 (1.5)	82/18	25

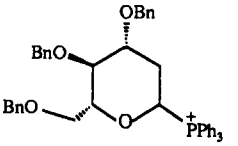
[a] Ratio determined[4f] by $^1H/^{13}C$ NMR. [b] Isolated yield of chromatographically and spectrally homogeneous material. [c] Obtained as a chromatographically separable diastereomeric mixture.

alkoxytriphenylphosphonium salts.[8]

In a typical procedure, the glucal (2 mmol) and hydroxylic nucleophile (1.5–3.0 equiv) are combined with a catalytic amount (5 mol %) of TPHB in anhydrous dichloromethane (10 mL) at ambient temperature. After 1–3 h, the reaction mixture is washed with saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo, and the residue is purified by flash SiO_2 chromatography.

The results obtained with three representative glucals, viz., 3,4,6-tri-*O*-acetyl-D-glucal, 3,4,6-tri-*O*-benzyl-D-glucal,[9] and 3,4-di-*O*-(3,4-dimethoxybenzyl)-6-deoxy-D-glucal, are summarized in Table I. Primary (entries 1, 2, 10, and 19), secondary (entries 3 and 11), and tertiary (entry 4) alcohols as well as phenols (entries 5, 12–14, and 20) and carboxylic acids (entries 6, 7, 15–17, and 21–23) afford moderate to good yields of 2-deoxy-D-glucopyranosides. Sensitive functionalities including cyclic acetal, acetonide, acetate, α-chloroacetate, silyl, benzyl, and trityl ethers are well tolerated under the mild reaction conditions. The method shows promise for the preparation of polysaccharides[10] (entries 8 and 9) and glycolipids[11] (entries 2 and 3). Condensation with *N*-hydroxysuccinimide (entry 18) provides access to a reactive but little utilized class of glycosylating agents.[12] Since time course studies during the reaction revealed little (±5%) variation in the anomeric ratio in the products, the predominance[4f] in all cases of the α-anomer probably reflects kinetic rather than thermodynamic factors.

In contrast with classical Bronsted and Lewis acids, e.g., hydrochloric and hydrofluoric acids, $BF_3{\cdot}Et_2O$, Amberlyst H-15 resin, and *p*-toluenesulfonic acid, all of which catalyze Ferrier rearrangement, TPHB appears unique in its ability to specifically promote direct addition of oxygen nucleophiles to glucals. This possibly can be attributed to protonation of the softer β-enolic carbon by TPHB in preference to the harder C(3)-oxygen center.[13] The reaction does not appear to involve a C(1)-phosphonium intermediate since independently prepared[8] **1** fails to exchange with alcohols under the reaction conditions.



1

On the basis of the above results and current investigations, we anticipate that TPHB and related reagents will find additional applications where specificity and mild conditions are required.

Acknowledgment. Supported financially by the Robert A. Welch Foundation (I-782), NATO (RG 85/0026), and the NIH (GM36465). A student fellowship to V.B. was provided by the Association pour la Recherche sur le Cancer.

Supplementary Material Available: Analytical and spectral data for *O*-glucosides from entries 3–6, 19, 20, 22, and 23 (5 pages). Ordering information is given on any current masthead page.

(8) Ousset, J. B.; Mioskowski, C.; Yang, Y.-L.; Falck, J. R. *Tetrahedron Lett.* **1984**, *25*, 5903–5906.

(9) 3,4,6-Tri-*O*-benzyl-D-glucal was prepared from commercial 3,4,6-triacetyl-D-glucal according to: Blackburne, I. D.; Fredericks, P. M.; Guthrie, R. D. *Aust. J. Chem.* **1976**, *29*, 381. 3,4-Bis-*O*-(3,4-dimethoxybenzyl)-6-deoxy-D-glucal was obtained from the same starting material by the sequence: (a) NaOMe, MeOH, 0 °C, 12 h (90%); (b) (i) TsCl, py, 0 °C, 72 h, (ii) Ac_2O, 0 °C, 4 h, (65%); (c) $LiAlH_4$, Et_2O, 24 °C, 5 h (60%); (d) KH, 3,4-$(MeO)_2C_6H_3CH_2Br$, THF, 45 °C, 20 h (65%).

(10) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–173.

(11) Reviere, M.; Fournie, J. J.; Puzo, G. *J. Biol. Chem.* **1987**, *262*, 14879–14884. Alexakis, M. N. *Trends Pharm. Sci.* **1987**, *8*, 10.

(12) Abe, K.; Sato, T.; Nakamura, N.; Sakan, T. *Chem. Lett.* **1977**, 817–818.

(13) Pearson, R. G. *Coord. Chem. Rev.* **1990**, *100*, 403–425.