

Organoselenium Chemistry: Stereoselective Conversion of Glycals into Anomeric Spiro-orthoesters using a Glycosyloxyselenation–Oxidation Elimination Sequence

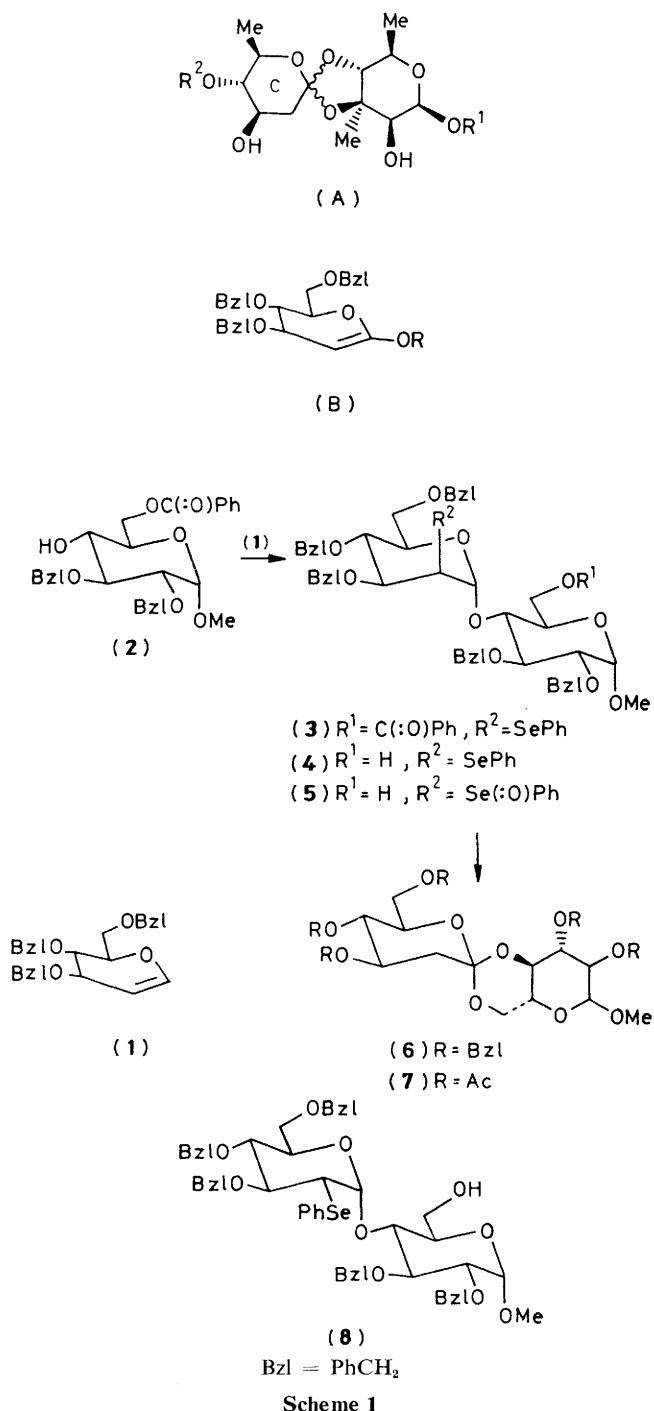
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Glycosyloxyselenation of tri-*O*-benzyl-*D*-glucal followed by oxidation and regiospecific *syn*-elimination of the resulting selenoxide offers, *via* an *in situ* generated keten acetal, a new method for the stereoselective construction of spiro-orthoesters associated with carbohydrate residues, as found in the orthosomycins.

The orthosomycins are members of a new family of antibiotic and their structures include one or two unique spiro-orthoester

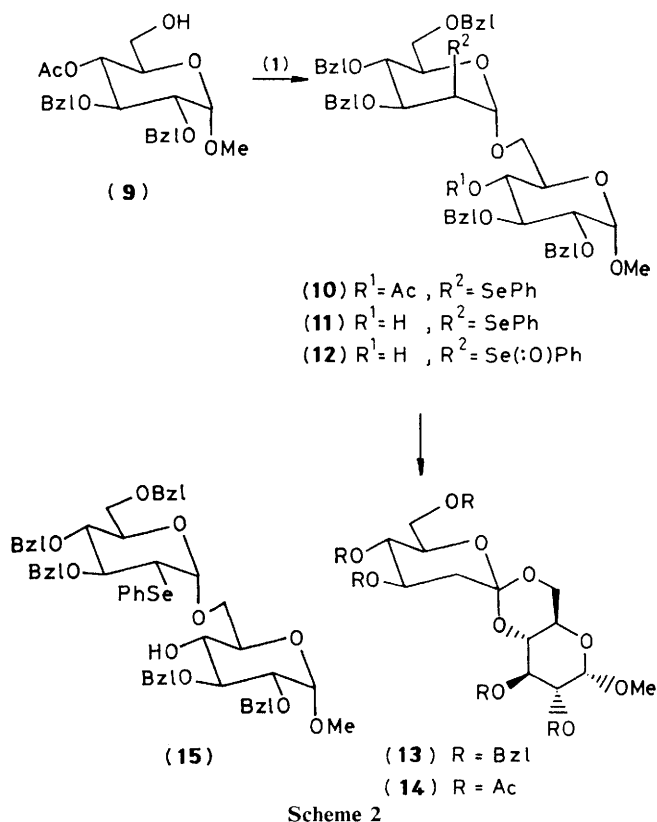
linkages associated with carbohydrate residues.¹ One example is found in flambamycin,² where the two sugar moieties *c* and



D are joined as in structure (A).[†] We now report the first synthesis of model 'anomeric spiro-orthoesters,' where the C-residue is a 2-deoxy-sugar, as found in many orthosomycins.[‡] Other approaches, where the C-unit is D-glucopyranose, have recently appeared.⁴

[†] In structure (A) the absolute configuration at C-3 of the carbohydrate residue C has been corrected according to the suggestion of Bock *et al.*³

[‡] For simplicity, we shall use the name 'anomeric spiro-orthoesters' for such orthoesters in which the anomeric centre of a monosaccharide is the spiro-carbon atom.



Reaction of tri-*O*-benzyl-D-glucal (1) with methyl 6-*O*-benzoyl-2,3-di-*O*-benzyl- α -D-glucopyranoside (2)⁵ provided mainly the α -linked disaccharide (3) (65%), $[\alpha]_D + 41^\circ$,[§] using the glycosyloxyselenation procedure previously reported by us,⁶ except that work-up was done after 2 days at room temperature (Scheme 1). Minor amounts of the β -glycoside also formed will not be considered further here. Debenzoylation (sodium methoxide in methanol) provided the disaccharide (4) (95%), $[\alpha]_D + 33^\circ$. Subsequent oxidation of (4) using sodium periodate (1.5 equiv.) in methanol-water (20°C; 1 h) quantitatively afforded the selenoxide (5) as a mixture of easily interconvertible diastereoisomers at selenium.⁷ Because *syn*-elimination of this selenoxide, away from the two oxygen atoms, is not possible for stereochemical reasons, we expected that it would proceed regiospecifically under forcing conditions⁸ towards the anomeric centre to provide a transient and reactive keten acetal of the type (B). Intramolecular reaction of the hydroxy-group should result in a spiro-orthoester.⁹ On refluxing the mixture of diastereoisomeric selenoxides (5) in pentyl vinyl ether¹⁰ in the presence of di-isopropylamine (20 equiv.) for 2 h, as a result of stereoelectronic control,¹¹ the orthoester (6) was indeed obtained (61.5%), $[\alpha]_D + 47^\circ$. The reaction was stereospecific, as the orthoester (13) could not be detected in the reaction mixture. The disaccharide (8) (19.5%), $[\alpha]_D - 5^\circ$, was isolated as the major by-product, tentatively the result of a stereospecific reduction of a seleno-Pummerer intermediate. Pentyl vinyl ether is a rational solvent for this fragmentation, since it is a scavenger of phenyl selenenic acid,¹² and has an appropriate boiling point (118°C) to initiate the required *syn*-elimination. Debenzoylation of (6) (Na, NH₃, 1,2-dimethoxyethane) followed by acetylation (Ac₂O in

[§] All new compounds had satisfactory microanalytical and spectral properties. Optical rotations were measured for solutions in chloroform at 20°C.

pyridine) gave the crystalline orthoester (**7**) (77%), m.p. 78–80 °C (from di-isopropyl ether–light petroleum), $[\alpha]_D + 107^\circ$.

A similar sequence (Scheme 2) with methyl 4-*O*-acetyl-2,3-di-*O*-benzyl- α -D-glucopyranoside (**9**)¹³ provided successively the α -linked disaccharide (**10**) (75.5%), $[\alpha]_D + 41^\circ$, the deacetylated compound (**11**) (95%), m.p. 90–92 °C (from ethyl acetate–hexane), $[\alpha]_D + 40^\circ$, a mixture of the diastereoisomeric selenoxides (**12**) (99%), one of them obtained in crystalline form, m.p. 165–166 °C (from methanol–water), $[\alpha]_D + 13^\circ$, and finally the orthoester (**13**) (45%), $[\alpha]_D + 9^\circ$. The orthoester (**6**) (16%) and the disaccharide (**15**) (5%), $[\alpha]_D - 7^\circ$, were isolated as by-products.

Debenzylation of (**13**) (Na, NH₃, 1,2-dimethoxyethane) followed by acetylation (Ac₂O–pyridine) gave the crystalline orthoester (**14**) (85%), m.p. 156 °C (from di-isopropyl ether), $[\alpha]_D + 66^\circ$. A single-crystal X-ray diffraction study[¶] was performed¹⁴ on the acetate (**14**) and confirmed the absolute configuration assigned to the spiro-orthoesters.

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¶ This diffraction study showed that the 1,3-dioxan ring of the acetate (**14**) adopts a boat conformation, which may explain the lack of complete selectivity in the formation of the spiro-orthoester.

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