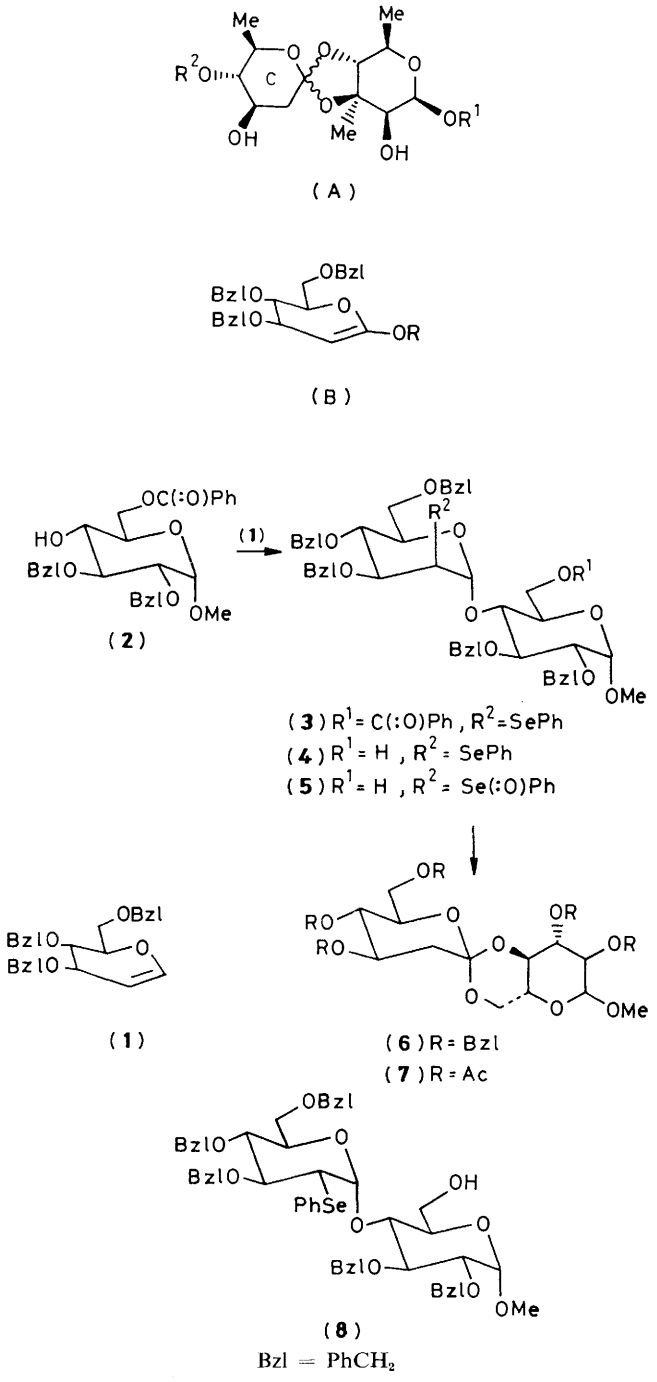
Organoselenium Chemistry: Stereoselective Conversion of Glycals into Anomeric Spiro-orthoesters using a Glycosyloxyselenation–Oxidation Elimination Sequence

Guy Jaurand, Jean-Marie Beau, and Pierre Sinaÿ*

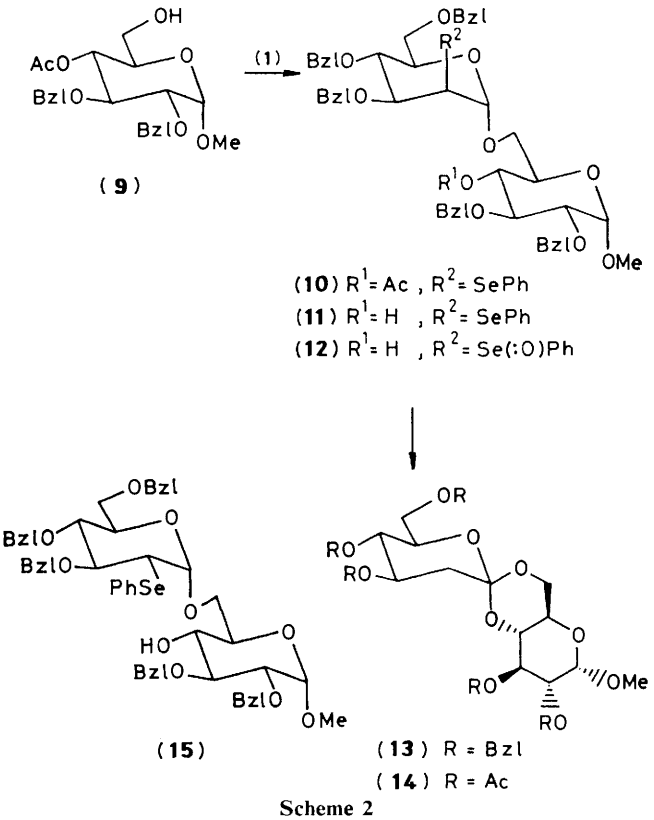
Laboratoire de Biochimie Structurale, E.R.A. 739, U.E.R. de Sciences Fondamentales et Appliquées, 45046 Orléans Cédex, France

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



Scheme 1



Scheme 2

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]

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°,§ 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°. 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 conditions[8] 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 ether[10] 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°. The reaction was stereospecific, as the orthoester (**13**) could not be detected in the reaction mixture. The disaccharide (**8**) (19.5%), $[\alpha]_D$ − 5°, 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. Debenzylation of (**6**) (Na, NH_3, 1,2-dimethoxyethane) followed by acetylation (Ac_2O in

† 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.

§ 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°.

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°, the deacetylated compound (**11**) (95%), m.p. 90—92 °C (from ethyl acetate–hexane), $[\alpha]_D$ + 40°, 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°, and finally the orthoester (**13**) (45%), $[\alpha]_D$ + 9°. The orthoester (**6**) (16%) and the disaccharide (**15**) (5%), $[\alpha]_D$ −7°, were isolated as by-products.

Debenzylation of (**13**) (Na, NH_3, 1,2-dimethoxyethane) followed by acetylation (Ac_2O–pyridine) gave the crystalline orthoester (**14**) (85%), m.p. 156 °C (from di-isopropyl ether), $[\alpha]_D$ + 66°. A single-crystal *X*-ray diffraction study¶ was performed[14] 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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