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REGIOSELECTIVE MANIPULATION OF HYDROXYL GROUPS VIA ORGANOTIN DERIVATIVES

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INTRODUCTION

The need for selective functionalization and chemical manipulation of OH groups in alcohols in particular and polyols in general is an acknowledged feature of everyday laboratory operations in organic chemistry. The first aspect is manifested mainly in the temporary protection of OH groups during a synthetic sequence in which a substrate in question contains such a function. Indeed, reagents for the protection of OH groups occupy an important cornerstone in the arsenal of reagents available to the organic chemist.[1] Newer types and useful modifications of existing ones continually enter into reaction schemes. The second feature, involving selective chemical modification such as oxidation, reduction, dehydration, etc. has also commanded interest among the practitioners of organic synthetic methodology. Suffice it to survey the number of oxidation methods that emerge in the chemical literature every year.[2]

In spite of the apparent plethora of options available to the organic chemist to deal with the OH group, the problems that arise are far from simple, particularly in dealing with polyfunctional molecules and in multistep syntheses, where the delicate balance of maintaining compatibility in a particular chemical step, and anticipating success in others further along the synthetic pathway becomes somewhat tenuous. The uneventful outcome of a synthesis may thus depend on the choice of protecting groups.

The reactivity of an OH group can be predicted to some extent based on kinetic and thermodynamic criteria.[3] For example, it is well known that an equatorial OH group in a 6-membered ring system can be acylated preferentially in the presence of secondary axial partners. Likewise, a primary OH group may be protected by selective acylation or etherification in the presence of several other secondary OH groups in the molecule. Oxidation is another process where some selectivity can be achieved, in catalytic processes for example.[4] In general however, these processes may not be efficient and recourse is made to prior functionalization, followed by generation of the desired OH group for further transformation. This may involve several steps before the desired transformation can be effected.

The purpose of this article is to demonstrate the utility of organotin derivatives of alcohols in regioselective manipulations involving indirect acylation, alkylation and oxidation. Other aspects of organotin derivatives involved in the formation of macrocyclic lactones and lactams will also be discussed. With regard to alcohols and polyols, we will discuss trialkyltin alkoxides (type I, Fig. 1) and dialkylstannylenes (type II, Fig. 1) with applications in the field of carbohydrates, nucleosides, polyols

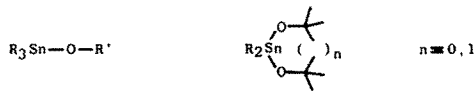


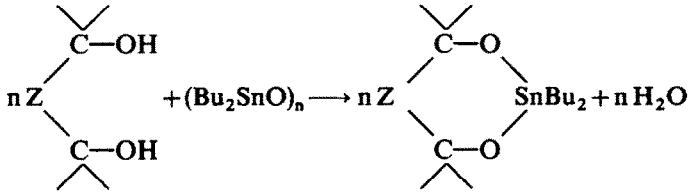
Fig. 1.

and selected natural products. Some early developments of these methods have been reviewed by Pereyre and Pommier.[5]

Tributylstannyl ethers are easily prepared by refluxing a mixture of an alcohol with an equivalent quantity of hexabutyldistannoxane, in benzene or toluene with azeotropic removal of water (Eq. 1):

$$2\,R^1R^2R^3COH + (Bu_3Sn)_2O \rightarrow 2\,R^1R^2R^3{-}O{-}SnBu_3 + H_2O \qquad (1)$$

Dibutylstannylenes may be prepared in the same way with polymeric dibutyltin oxide[6] (Eq. 2):



(2)

Stannylenes may also be prepared at fairly high dilutions (1%) in refluxing methanol,[7] where the soluble methyl ether $CH_3O{-}SnBu_2{-}O{-}SnBu_2{-}OCH_3$,[8,9] is perhaps the reactive species. However, there are some indications that if some ester functions are present in the starting molecule, they may be methanolyzed under such conditions.[10,11]

For subsequent utilization in synthetic transformations such as acylation, etc., both types of derivatives may be used *in situ*, or transferred to another solvent after evaporation of their solution. No special precautions, such as a nitrogen atmosphere, or rigid exclusion of moisture are necessary, although tributylstannyl ethers appear more sensitive than stannylenes to traces of water. Their formation is practically quantitative, and more extensive purification is seldom, if ever needed.

Structural aspects

The ^{119}Sn NMR chemical shifts for a series of tri-n-butylin alkoxides suggest that they are monomeric tetrahedral species, even in the neat liquid at room temperature. However, they may be self-associated at 80 K[12] and indeed, trialkyltin methoxide,[13] as well as the parent hydroxide[14] are self-associated in the solid state into linear chain polymers in which the tin atom is pentacoordinate bipyramidal (Fig. 2).

The degree of association of alkoxides R_3SnOR' may depend on the nature and type of the R and R_1 groups. For example, an X-ray structure determination of tetrachloro-1,4-bis(triethylstannoxy)benzene[15] shows the existence of discrete molecules with near tetrahedral tin atom geometries.

Alternatively, if some atoms with ligand properties are present in the alkoxide moiety, a monomeric structure with pentacoordinate tin may be achieved by chelation.[16] This may have significance in the regioselectivity of the reactions of triols and higher polyols. Preliminary information on the solid state constitution of the stannylene of 1,3-propanediol was disclosed in 1973.[16a] The first X-ray structure determination of a stannylene derivative in the solid state was that of the 2,3-O-dibutylstannylene derivative **1** of methyl 4,6-O-benzylidene-α-D-glucopyranoside where a dimeric structure was seen[17] (Fig. 3). Each of the tin atoms is in the center of a trigonal bypyramid with the butyl groups occupying two equatorial positions. One of the O-atoms is in the apical position and the other in the equatorial position. The two monomeric structures in the unit are joined by a parallelogram

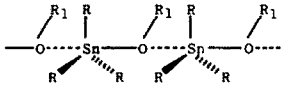


Fig. 2.

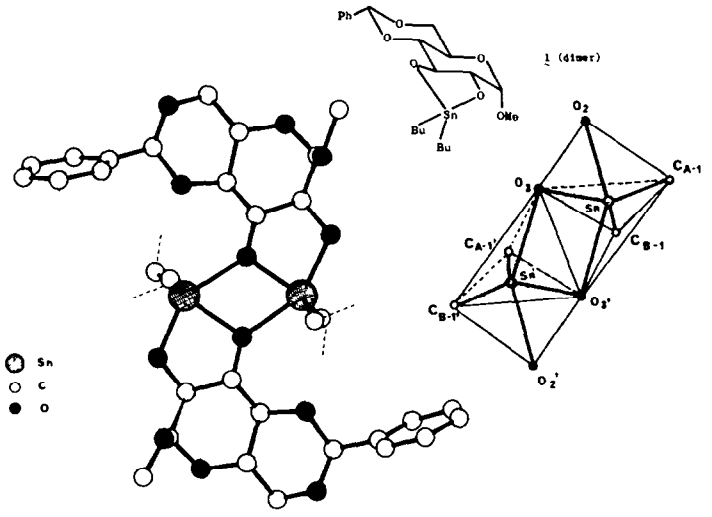


Fig. 3.

involving Sn_2O_2 which has a pseudo C_2 axis of symmetry. This leads to a dissymmetry with regard to the O-atoms in the dioxastannacyclopentane ring. One O-atom is tricoordinated and occupies an apical position with regard to one Sn atom and an equatorial position with regard to the other. The other O-atom of the glycol unit is dicoordinated and apical. There are no apparent distortions resulting from such an arrangement.

The only other solid state structure of a carbohydrate stannylene which has been reported so far is that of methyl 4,6-O-benzylidene-2,3-O-dibutylstannylene-α-D-mannopyranoside, which crystallizes as a pentamer (Fig. 4, for simplicity, only the ring structures are shown).[18] Dioxastannacyclopentane units are clearly recognizable, with an average intramolecular 2.07 Å Sn—O bond length. The association of these units involves Sn—O bonds which appear weaker, especially when they connect oxygen to hexacoordinate tin (average 2.47 Å). It is our opinion that because of these weaker bonds, the pentamer may be considered as the association of two external dimers with C_2 symmetry to a central monomeric unit. Dissolving this pentamer in benzene gives rise to several oligomeric species, as evidenced by a complex ^{119}Sn NMR spectrum. Such an atypical behaviour may be general for α-D-mannosides, and may have some consequences on their reactions, which are less straightforward than those of the stannylenes considered above.

The fourth and last reported structure is that of the simple stannylene derivative of 1,2-ethanediol.[18a] The molecule is an infinite ribbon coordination polymer, with 6-coordinate tin. The dibutylstannylene derivative of 1,3-propanediol forms a similar infinite polymer.[16a] Again, dioxastannacyclopentane-(cyclohexane) units are recognizable with short Sn—O bonds. The association of such units by an Sn_2O_2 parallelogram, with O—Sn bonds which are either short (to a 5-coordinate tin atom) or long (to a 6-coordinate one), is a common feature of the four known structures.

Mössbauer studies in the solid state of stannylene derivatives of glycols show values which lie within the range found for the trigonal bipyramidal *cis*-R_2SnX_3 type compounds.[12] The same conclusion was reached for the derivative of adenosine.[19]

Studies of stannylene derivatives in the liquid and gaseous phase also indicate the existence of

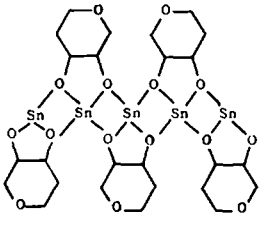


Fig. 4.

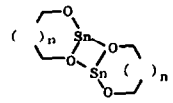


Fig. 5.

dimeric forms. Smith[12] had observed upfield chemical shift values for ^{119}Sn in a series of stannylenes in the range of 100–200 ppm regardless of ring size (ex. 5, 6 or 7). This can be attributed to a change in higher coordination state as would be expected of the dimeric structures in chloroform (Fig. 5). More recently, ^{119}Sn NMR studies on stannylenes derived from chiral diols have provided further insight into their structures.[20] Thus for the stannylenes derived from methyl 4,6-O-benzylidene-α-D-glucopyranoside (Fig. 3), 1,2-O-isopropylidene-3-O-methyl-α-D-glucofuranose, benzyl 2,6-di-O-benzyl-β-D-galactopyranoside, benzyl 2,3-di-O-benzyl-β-D-glucopyranoside, a single peak (3 Hz at half width) was observed at 125–180 ppm at 24°, indicating that there was an element of symmetry (C_2 axis as in Fig. 3). For dialkyltin dialkoxides $R_2SnOR'_2$, which are acyclic analogs of stannylenes, variable temperature NMR shows an equilibrium between the monomeric and dimeric form.[12] No such equilibrium could be observed for stannylenes in non-polar solvents. Finally geminal ^{119}Sn—^{117}Sn coupling observed in the ^{119}Sn spectrum of the stannylene shown in Fig. 3 can only be interpreted in the light of a square Sn_2O_2 structure as present in a dimer.[21] The sharp Sn peak broadens in more polar solvents such as pyridine, or DMF which indicates an interaction with the solvent.[20] Of course, if other species are present in rapid equilibrium, they would result in broadened signals and possibly escape detection.

The relatively high boiling point of the stannylene of 1,3-propanediol (b.p. 182–186°/0–3 mmHg) may well indicate an associated vapor at that pressure.[16a] The dimeric state exists in the gas phase for stannylene of *cis*- and *trans*-cyclohexane 1,2-diol and adenosine as evidenced by field desorption mass spectroscopy.[22] So far, no physical evidence has been found for the existence of stannylenes with tetracoordinate tin in 10-membered rings, as first suggested on the basis of molecular weight estimations.[6]

Stereoelectronic consequences of the Sn—O *bond—nucleophilic enhancement of the oxygen atom*

As previously discussed ^{119}Sn NMR and mass spectrometric studies of chiral carbohydrate-derived stannylenes suggest that they are dimeric in all physical states, except perhaps in polar solvents. Stannylene derivatives, as well as trialkyl tin alkoxides undergo regioselective acylation, alkylation and oxidation as it will be discussed in the coming sections of this article. The precise origin of the regioselectivity is not known. However the hypothesis can be advanced that one of two oxygens involved in the stannylene ring is more nucleophilic than the other. Invoking the dimeric structure (Fig. 6) may provide a plausible explanation.[19]

Within one monomeric unit of the dimer, the apically bound O-atoms (O^1 and $O^{1'}$) are regioselectively acylated and alkylated. These are the O-atoms *not* involved in the Sn_2O_2 parallelogram. Such nucleophilic enhancement may be the result of electron channelling from the Sn atom toward the apically bound O-atoms resulting in preferential activation and bond rupture at the expense of the equatorially oriented and electronically less enriched O-atoms (O^2 and $O^{2'}$ in Fig. 3). In fact it has been claimed, on the basis of ^{35}Cl-NQR experiments that tin was a much more effective transmitter of electronic displacements than carbon.[23] Furthermore, O-atoms O^2 and $O^{2'}$ (Fig. 6) are relatively protected by threefold coordination. This interpretation agrees with the known, exclusive benzoylation of the *equatorial* oxygen on C-2 of the *gluco* stannylene of Fig. 3. In non-polar solvents the *manno* stannylene of Fig. 4 is benzoylated preferentially on the *axial* oxygen on C-2.[18] While only *two*

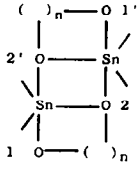


Fig. 6.

such positions appear activated in the pentamer, decomposition to two C_2 dimers by severance of four weak bonds in solution would expose two more. Likewise, with the stannylenes of methyl 6-chloro-6-deoxy-α-D-mannopyranoside, 1,2-O-isopropylidene-β-D-fructopyranose and methyl β-D-arabinopyranoside, each of which contains a vicinal axial-equatorial pair of stannylated oxygens, esterification in non-polar solvents takes place preferentially at the axial oxygen.[18] Thus, it would appear that the origin of the regioselectivity is inherent in the constitution of the dimer, and does not depend on the orientation (axial or equatorial) of the OH groups in the parent 6-membered rings.

The question is also raised regarding which O-atom of a diol will preferentially bind apically in stannylene formation, hence undergo acylation, etc. This may be the more electronegative one, as it is known that in trigonal bipyramid complexes, electronegative ligands are more stable when occupying apical positions.[24] Conversion to a stannylene may thus accentuate small electronegativity differences between the two oxygen atoms of a diol, although steric factors may also play an important role. In the case of stannylenes involving a diol from a primary and secondary alcohols, reaction takes place at the oxygen atom of the primary carbon.

In spite of these arguments, we cannot predict the existence of dimeric structures in the transition states of such reactions. All electrophilic attacks reported so far involve polar reagents or solvents and the extent of dissociation to monomeric stannylenes may be appreciable. The dissymmetric nature of the two apically disposed oxygen atoms may persist however in an intermediate coordinated to the reagent, the solvent or the catalyst. Polar solvents, which are unavoidable for uncatalysed allylation (benzylation, etc.) may decrease or alter the regioselectivity. For instance, benzoylation of the *manno* derivative of Fig. 4 in the presence of N-methylimidazole gave exclusively the equatorial ester, demonstrating a dramatic reversal of regioselectivity.[18]

The stannylenation of poly-hydroxylated compounds such as oligosaccharides is a new and exciting extension of the method.[25] Because of the dimeric nature of stannylenes, it should be realized that, except for quite unusual, tailor-made structures, polystannylenation of tetrols, or higher polyols should give polymeric chains of monomer units linked by Sn_2O_2 double bridges. However, in practice one may encounter overwhelming site-specific monoalkylation through the intermediacy of a stannylene derivative. For instance, methyl β-lactoside, with seven free OH groups gives a 70% yield of the 3′-O-allyl ether **81** (Fig. 26), the rest being starting material.[25] Such selectivity is unparalleled in other chemical processes and is somewhat reminiscent of enzymatic specificity. Although practically any diol can be easily converted into the corresponding stannylene, it seems that given a choice, the Sn atom may be very particular in its selection of a pair of O-atoms in a given polyol. Competitive experiments with mixtures of *cis* and *trans* diols have indicated so far, a preference, sometimes overwhelmingly so, for vicinal *trans* (diequatorial) diols in a 6-membered ring, in spite of intuitive predictions to the contrary. Thus, the unique selectivity observed in these reactions appears to be the consequence of a cascade of effects—first the selection of a particular diol system by the Sn atom, and then the placing of one of the two O-atoms of this diol to a reactive apical position, possibly as a result of an intrinsic manifestation of a subtle difference between them. A multinuclear (^{119}Sn, ^{13}C, ^{1}H) NMR study of the site of di- and tributylstannylation in carbohydrates has been reported.[25a]

Regioselective esterification and alkylation via O-*stannyl ethers*

The synthetic applications of trialkyltin ethers manifest themselves most remarkably in the case of polyols such as carbohydrates. Probably the first example of preparative utility of alkoxy trialkyltin ethers in carbohydrate chemistry was shown by Moffatt *et al.*[26] Thus, direct sulfamoylation of the adenosine derivative **2** with sulfamoyl chloride gave low yields. However, conversion to the 5′-O-tributyltin ether **3**, followed by sulfamoylation gave the desired 5′-sulfamate **4** in high yield (Fig. 7).

2

3, R = $SnBu_3$
4, R = SO_2NH_2

Fig. 7.

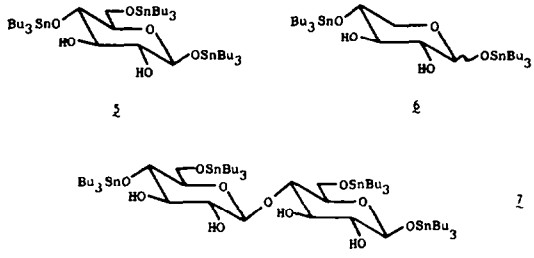


Fig. 8.

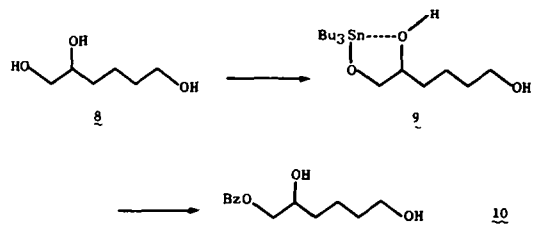


Fig. 9.

An interesting case of regioselective O-stannylation can be found in the treatment of various unsubstituted carbohydrates with bis(tributyltin) oxide.[27] The OH groups at 1,4 and 6 are the most reactive (Fig. 8), and the corresponding tributyltin ethers (**5**–**7**) are distillable liquids which are reasonably stable. Ogawa and Matsui[28,29] have reported elegant studies on the regioselective tributylstannylation of polyols, and their subsequent acylation or alkylation based on the nucleophilic enhancement of the O-atoms. Model reactions with a hexane triol **8** showed that it could be converted into the tributyltin ether **9** with one equivalent of bis(tributyltin)oxide (Fig. 9). Subsequent treatment with benzoyl chloride gave the primary monobenzoate **10** in 67% yield. The regioselective benzoylation can be explained based on the formation of a coordinated tributyltin ether. It should be noted that acylation takes place with the acyl halide *in the absence of added base.*

Stannylation of methyl α-D-glucopyranoside **11** with bis(tributyltin) oxide and subsequent treatment with three equivalents of benzoyl chloride gave an 82% yield of the 2,6-di-O-benzoyl **13** and 18% of the 2,3,6-tri-O-benzoyl derivative. Again, a coordinated intermediate **12** can be invoked to explain the preferential acylation at O-2.

Under the same conditions, methyl α-D-mannopyranoside **14** and methyl β-D-galactopyranoside **17** gave the corresponding 3,6-di-O-benzoyl derivatives **16** and **19** respectively (Fig. 10). On the other

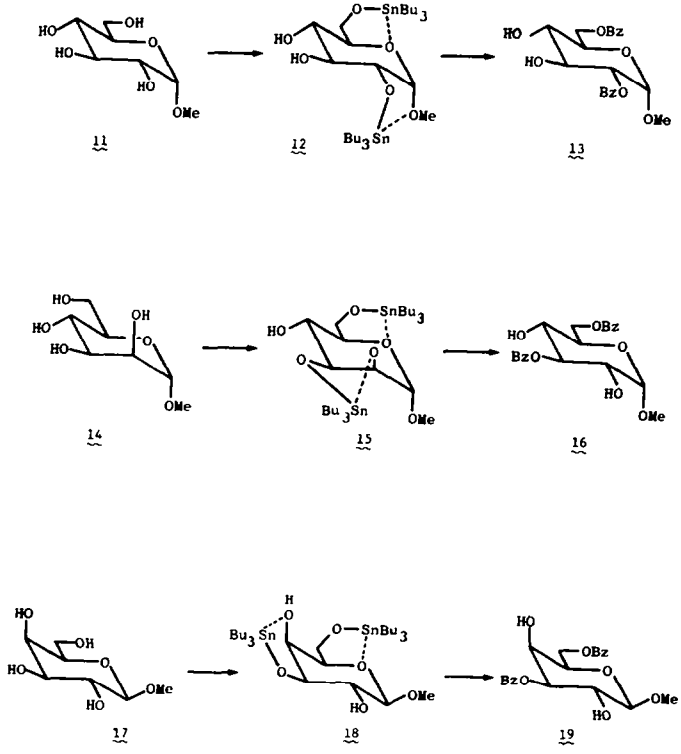


Fig. 10.

hand, methyl α-D-galactopyranoside **20** gave a mixture consisting of mono-, di- and tribenzoates of which the 2,3,6-tri-O-benzoyl derivative **23** (41%) and the 2,6-di-O-benzoyl derivative **24** (10%) are shown in Fig. 11. Several partially benzoylated disaccharides **25–27** could also be prepared via regioselective stannylation followed by benzoylation.

Thus, in all the examples shown above, regioselective stannylation took place to produce a coordinated O-tributyltin ether in which the oxygen atom is more nucleophilic than the original OH group. Acylation was found to take place preponderantly at that ether oxygen.

While the acylation of tributylstannyl ethers is a very fast reaction at room temperature in any solvent, alkylation is extremely slow, even with the reactive allyl or benzyl bromide. One reported technique involved the use of extended periods of heating, up to 8 days, at 88–85° under argon, with the neat halide as solvent.[30–32] Thus, stannylation of methyl α-D-glucopyranoside **11** with 1.5 equivalents of bis(tributyltin)oxide and subsequent treatment of the partially stannylated intermediates with benzyl bromide at 80°, gave the corresponding 3,6-,2,6-,4,6-dibenzyl ethers, and the 6-monobenzyl ether in yields of 4.5, 30, 6 and 48%. Alkylation with allyl bromide also gave a mixture of di- and monoallyl ethers. Interestingly, tritylation of the stannylated intermediate derived from **11** with trityl chloride 65° gave the 3,4,6-tritrityl and 2,6-ditrityl ethers in 37 and 53% yields respectively. The significant proportion of O-tritylation at secondary hydroxyl groups by this procedure is noteworthy.[31]

Based on the preferential benzoylation of the stannylated intermediate derived from methyl β-D-galactopyranoside **17** at O-3 and O-6, it was expected that benzylation would follow the same course. Indeed benzylation at 85° for 3 days with benzyl bromide gave the 3,5-dibenzyl ether and the 6-monobenzyl ether in yields of 48 and 24% respectively. Allylation was also effected in a similar manner. Tritylation led to the crystalline 2,6-ditrityl ether in 71% yield.[32]

A milder technique was introduced by Veyrières, who found that these alkylations are catalyzed by quaternary ammonium halides (0.1–0.3 molar equivalent).[33] In their presence, good to excellent yields are achieved in less than two days with 0.1 M solutions of the tributylstannyl ethers in toluene at 80°. In this way benzyl 2-acetamido-3-O-benzyl-2-deoxy-α-D-glucopyranoside **28** was specifically benzylated at the primary position to give derivative **29** in 86% yield (Fig. 12).[33] Benzyl 6-O-trityl-α-D-mannopyranoside gave mainly the 3-O-allyl ether (62%) **31** together with some 2-O-allyl ether (15%).[34] Practically quantitative yields were later reported when this technique was used for the preparation of the 3,6-di-O-benzyl ether **32**,[35] and in the specific benzylation at the primary position of allyl 2,3-di-O-benzyl-α-D-glucopyranoside.[36] Higher molar proportions of catalyst notably reduce the reaction

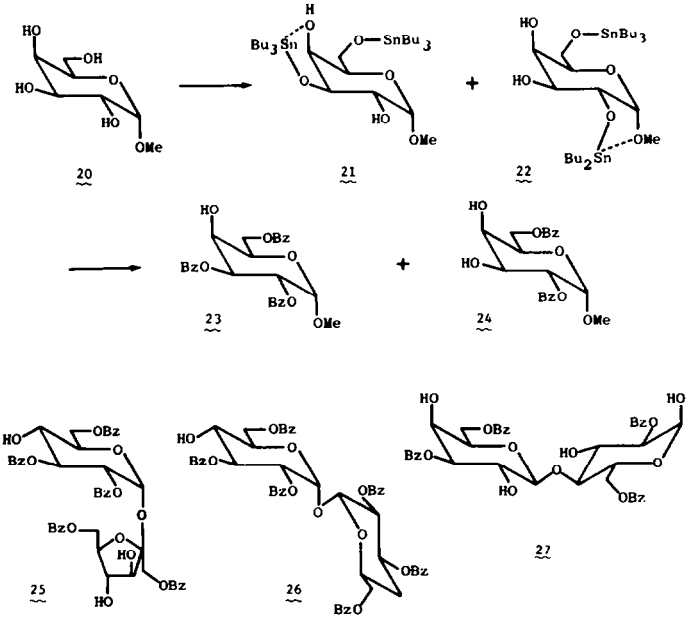
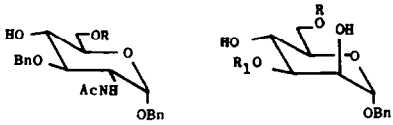


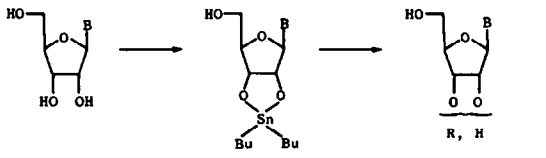
Fig. 11.



28, R = H
29, R = Bn

30, R = Tr; R_1 = H
31, R = Tr; R_1 = allyl
32, R_1R_1 = Bn

Fig. 12.



B = uracilyl
= cytosinyl
= adenylyl

R = acyl, alkyl
etc.

Fig. 13.

times. It should also be noted that preferentially substituted benzyl and allyl ethers of carbohydrates have great utility in the synthesis of oligosaccharides.

Pursuing initial findings by Avela and Holmbom,[37] Eby and Schuerch[38] have effected regioselective allylation and benzylation of selected carbohydrate derivatives by treatment with sodium hydride and anhydrous copper (II) chloride in a solvent such as dimethoxyethane or oxolane, followed by the alkyl halide and heating. Greater than 85% of monoalkylated products were produced with reasonable to high regioselectivity. In most cases, the substrates contained vicinal or 1,3-diol systems.

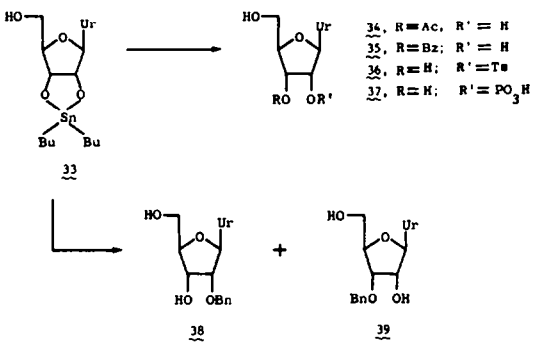
Regioselective esterification and alkylation via O-stannylene acetals

In a pace-setting publication, Moffatt *et al.*[7] demonstrated the utility of O-stannylene acetals in regioselective acylation and alkylation of nucleosides. Thus, β-D-ribofuranosyl nucleosides, when treated with an equimolar amount of dibutyltin oxide in methanol resulted in the formation of the corresponding 2',3'-O-stannylene derivatives in good yields. Several were obtained in crystalline form (Fig. 13).

Upon treatment of 2',3'-O-(stannylene)uridine **33** with acetyl chloride and triethylamine in methanol, a major product identified as 3'-O-acetyluridine **34** (R = Ac) was formed (69%) (Fig. 14). The other product was the 2'-O-acetate, but remarkably no 5'-O-acetate derivative was formed.

Utilizing the same procedure, it was possible to prepare other 3-substituted esters of uridine in high yields (Fig. 14). However, tosylation of **33** led to the 2'-O-*p*-toluenesulfonyl derivative **36** in good yield. From this result it can be concluded that the preponderance of the 3'-carboxylate esters was a result of a kinetic acylation at O-2' followed by acyl migration to O-3', a process which is well known in this series.[39] Since it is generally accepted that sulfonyl esters are not prone to such migration, the isolation of the 2'-ester in this case is understandable. Moreover, these experiments indicate the strong preference for reaction at the O-2' site in such stannylenes. Attempts to benzylate the stannylene derivative **33** led to a 1 : 1 mixture of the 2' and 3'-O-benzyl derivatives, **38** and **39** in a combined yield of 65%. The same results were obtained upon methylation. *p*-Methoxybenzylation gave a 21% yield of the 2'-O-*p*-methoxybenzyl ether.[39a]

Benzoylation of 2',3'-O-(stannylene)cytidine **40** gave an 87% yield of the 3'-benzoate **41**, but acetylation gave a 3 : 1 mixture of the 3'- and 2'-acetates. As in the case of the uridine derivative, it was possible to effect phosphorylation with phosphorus oxychloride to isolate a crystalline mixture of 2'- and 3'-phosphates **42** in 73% yield (Fig. 15).



34, R=Ac, R' = H
35, R=Bz; R' = H
36, R=H; R'=Ts
37, R=H; R'= PO_3H

Fig. 14.

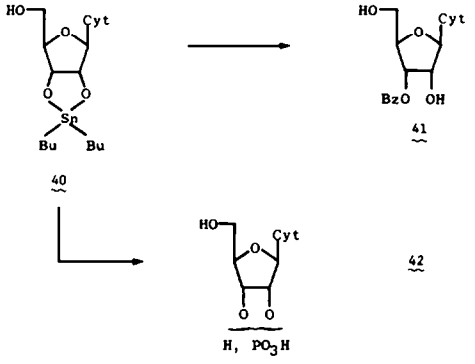


Fig. 15.

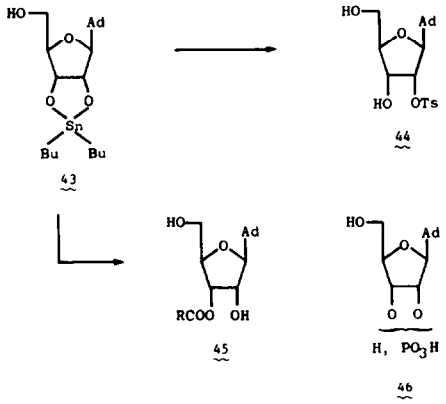


Fig. 16.

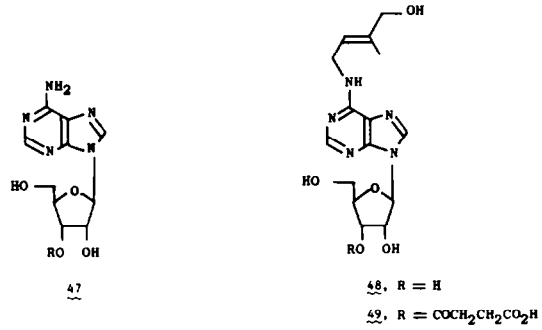


Fig. 17.

Experiments with 2',3'-O-(stannylene)adenosine **43** were also highly successful in producing the carboxylate esters at 3'- (ex. **45**) and a 2'-*p*-toluenesulfonate **44**. As in the case of the pyrimidine nucleosides, phosphorylation produced a 2:3 mixture of adenosine 2'- and 3'-phosphates **46** in 78% yield.

It might be of interest at this point to comment on the possible modes of reactivity of such stannylene derivatives. We had previously discussed a stereochemical rationale for the enhancement of nucleophilicity of an oxygen atom attached to tin. In stannylenes there exist two such oxygens, hence two options for preferential reactivity (example, Fig. 15). It may be that the O-2' oxygen in particular benefits from a privileged apical orientation hence a higher reactivity compared to the O-3' oxygen which would be equatorially oriented in the presumed Sn_2O_2 parallelogram involving a dimeric structure. Unfortunately, X-ray data are not available for the 2',3'-O-(stannylene)-nucleosides, which would lend some support to this hypothesis, based on David's original results[20] and the four-center transition state model of Bloodworth and Davies.[40] The possibility also exists that the preferential acylations and alkylations are the results of equilibrium concentrations of ionic species in which the O-2' or O-3' oxygens of the stannylene are the anionic intramolecular counterparts to positively charged dibutyltin alkoxy appendages. Partial ionic character has been invoked in related cases.[41]

Further examples of regioselective benzoylations, tosylations and thiophosphorylation of the stannylenes of ribonucleosides have been reported.[42] The stannylene of adenosine, **43** was inert to succinic anhydride in pyridine but reacted smoothly in the presence of tetrabutylammonium bromide, to give a 93% yield of the 3'-(acid succinate) **47**. This technique was successful with three cytokinin plant hormones. For instance, *trans*-zeatine **48** (a tetrol) was esterified to the 3'-(acid succinate) **49** (Fig. 17), a useful derivative for the elaboration of an immunoassay technique.[43]

Concurrent with the studies of Moffatt *et al.*, and based on previous experiments on the formation of stannylenes,[6] David and Thieffry[44] reported on the formation and properties of carbohydrate stannylenes. In a subsequent publication, David *et al.*[45] demonstrated the feasibility of regioselective monobenzylation of *cis*-diol derived from galactose. Thus, treatment of the 3,4-O-(stannylene) derived from **50** with benzyl bromide in DMF at 100° gave after chromatography a 66% yield of **51** (Fig. 18). It is of interest to note that attempted selective benzylation of **50** directly (sodium hydride method) gave a mixture of four products from which the monobenzylated components were isolated in a combined yield of 60% yield. Preferential attack at O-4 has been observed in other cases.[46] Access to equatorially disposed benzyl ethers in such systems, via the intermediacy of *cis*-O-stannylene derivatives is of preparative significance.

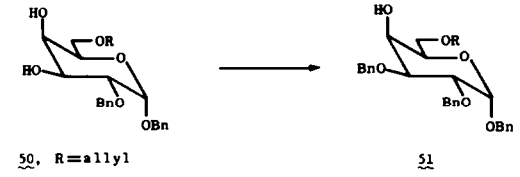


Fig. 18.

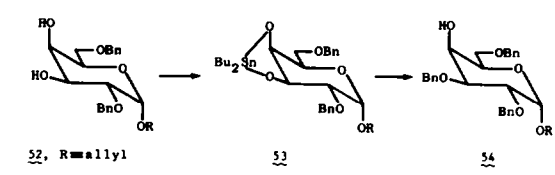
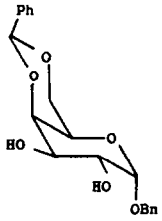
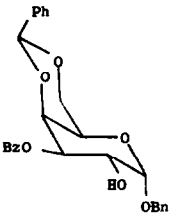


Fig. 19.

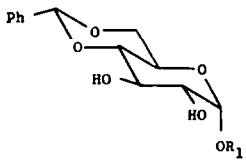


55

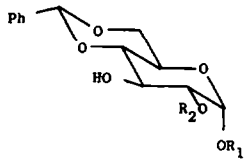


56

Fig. 20.



57, R_1 = Me
58, R_1 = Bn



59, R_1 = Me, R_2 = Bz
60, R_1 = Me; R_2 = Ts, etc
61, R_1 = Bn; R_2 = Bn

Fig. 21

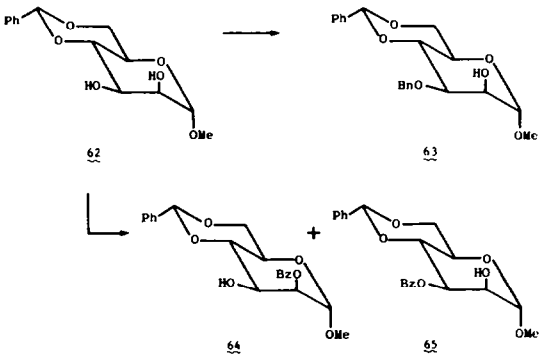
In independent studies, Nashed and Anderson[47] demonstrated the preparative utility of O-stannylene derivatives for the selective acylation and alkylation of hexopyranose derivatives. High regioselective benzoylation, benzylation, allylation and methylation could be achieved in the case of the stannylene **53** (Fig. 19). Subsequent work in this series has made it possible to prepare preferentially substituted D-galactopyranosides for the purposes of oligosaccharide synthesis.[48–50]

Alkyl D-galactopyranosides with a free, 3,4-*cis*-diol system react only at the 3-position. On the other hand, the stannylene of the 2,3-diequatorial *trans*-diol system in the benzylidene derivative **55** was benzoylated also exclusively at the 3-position to give **56** in 93% yield (Fig. 20).[51]

The reaction of methyl 4,6-O-benzylidene-α-D-glucopyranoside **57** in methanol gave a stannylene for which a monomeric structure, with chelation of the tin to the anomeric oxygen was suggested.[52] However, from its m.p., this stannylene appears identical with the dimeric derivative formerly prepared in benzene.[44] The situation is quite different from that of the more flexible tributylstannyl ethers such as **12** (Fig. 10). Treatment with benzoyl chloride or *p*-toluenesulfonyl chloride gave the corresponding 2-esters **59** and **60** respectively in high yield (Fig. 21). The reactions of the same stannylene with methyl iodide[49] or benzyl bromide[53] were less selective, however the stannylene from the corresponding benzyl glucoside **58** was benzylated exclusively at position 2 to give the benzyl ether **61** in 77% yield.[53]

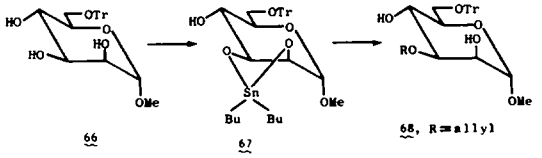
The preferential esterification at O-2 of alkyl-α-D-hexopyranosides in the absence of steric effects has been known for some time and rationalized on the basis of a greater kinetic acidity of the hydroxyl group.[54] However, the enhanced reactivity at O-2 in the stannylene of **57** is readily explained on the basis of stereoelectronic effects associated with is dimeric structure **1** (Fig. 3).

Other utilizations of glucopyranoside stannylenes have been reported.[51] In the methyl 4,6-O-benzylidene-D-mannopyranoside series, **62**, selective benzylation could be achieved via the corresponding O-stannylene derivative to give **63** (Fig. 22). However, benzoylation led to the axial benzoate **64** as the major product.[47] These anomalies are now readily explained by the complex nature of the stannylene (Fig. 4). Varma and Schuerch[56] reported a regioselective allylation of the equatorial OH group at C-3 in methyl 6-O-trityl α-D-mannopyranoside **66** to give **68** (Fig. 23). It was not necessary to go through the 4,6-O-benzylidene derivative, since regioselective stannylation was effective with the



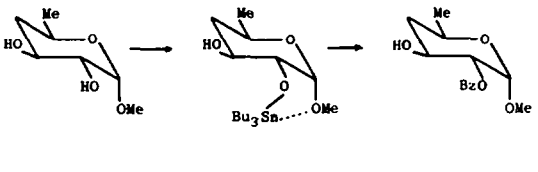
62 63 64 65

Fig. 22.



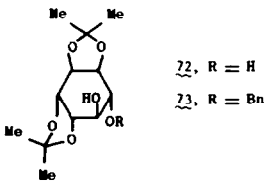
66 67 68, R=allyl

Fig. 23.



69 70 71

Fig. 24.



72, R = H
73, R = Bn

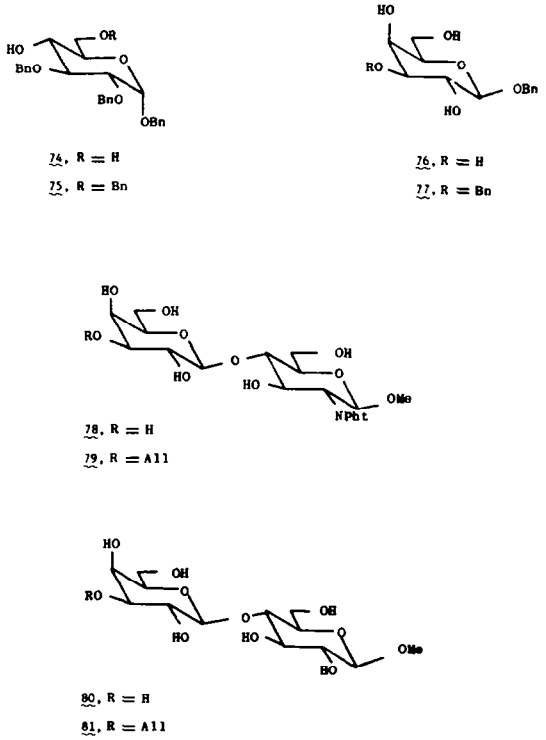
Fig. 25.

triol system present in **66**. In fact, it has been possible to allylate the 3-OH group directly (42%), starting with the stannylene derivative formed from the reaction of methyl α-D-mannopyranoside.[57] The related methyl α-L-rhamnopyranoside was benzylated at the 3-position in 50% yield.[58]

Regioselective benzoylation of the equatorial OH group in **69** was achieved via the 2,3-O-stannylene derivative **70** to give the benzoate **71** in 94% yield (Fig. 24).[59] It should be noted that **71** could be prepared by direct selective benzoylation with N-benzoylimidazole, but the yield was only 30%.[60] This once again reflects the great utility of stannylenes in preferential esterification. Highly regioselective benzoylation[61] or toluenesulfonylation[62] at the primary position of hexofuranose derivatives with a free 5,6-diol system have also been reported.

Nashed and Anderson also showed the extension of regioselective equatorial alkylation in the case of *cis*-O-stannylene derivative of a *myo*-inositol derivative.[47] The stannylene derivative of another inositol, 1,2:5,6-di-O-isopropylidene-L-inositol, **72** (Fig. 25) gave a 95% yield of the 3-O-benzyl derivative **73** when alkylated with benzyl bromide in a 1:1 benzene–DMF mixture.[63] Compound **73** is a useful starting material in the synthesis of (−)-kasuganobiosamine.[64]

All the allylations and benzylations of stannylene derivatives reported above have been conducted in polar solvents, mostly DMF, for there is no appreciable transformation in non-polar media. However, it was found that these reactions proceed smoothly in benzene or toluene solution in the presence of quaternary ammonium halides. Thus benzylation of benzyl 2,3-di-O-benzyl-α-D-glucopyranoside **74** (Fig. 26) gave the 6-O-benzyl ether **75** in 80% yield, while the reaction in N,N-dimethylformamide has no preparative value.[65] These conditions were also tested on benzyl β-D-



74, R = H
75, R = Bn

76, R = H
77, R = Bn

78, R = H
79, R = All

80, R = H
81, R = All

Fig. 26.

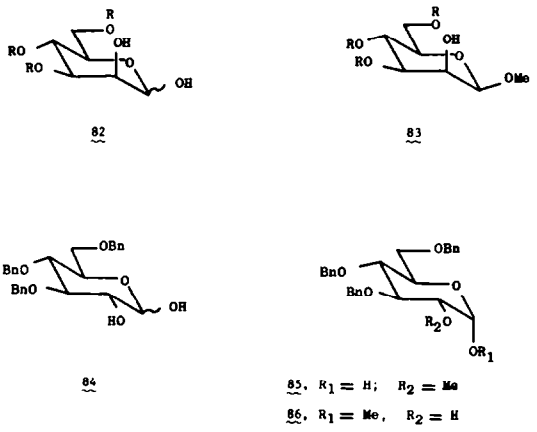


Fig. 27.

galactopyranoside and ten partially protected derivatives, with good regioselectivity in nine cases. Interestingly, the tetrol **76** gave exclusively the 3-O-benzyl ether **77** in 67% yield, the rest being starting material.[65] This suggested to test the method on polyols with an even greater number of free hydroxy groups. With the stannylene derivative of methyl 2-deoxy-2-phthalimido-β-lactoside **78**, allylation was again selective, but not complete, giving the 3'-O-allyl ether **79** in 56% yield. As a consequence, two cycles of stannylation-catalyzed allylation were used with methyl β-lactoside **80**. In spite of the presence of no less than seven free hydroxyl groups in compound **80**, the 3-O-allyl ether was isolated in crystalline form without recourse to chromatography in 70% yield as the only product of substitution.[25] Possibly the upper limit of the range of applicability of this method to highly hydroxylated molecules has not yet been reached. Compounds **79** and **81** are useful starting materials for glycolipid synthesis. Selective monobenzylation of methyl α-L-rhamnopyranoside in the presence of tin(II) chloride has been reported.[65a]

O *and* S-*Glycosides*

The preparation of alkyl glycosides from alkyl halides has been very seldom, if ever, considered so far, because the alkaline conditions necessary for the traditional activation of the anomeric oxygen are highly destructive of reducing sugars. Di- and tributyltin ethers which are highly nucleophilic, and yet neutral derivatives of hydroxyl functions should allow to explore this unusual pathway. Thus the methylation of the stannylene derivative of 3,4,6-tri-O-allyl-D-mannose **82** (Fig. 27) gave a 88% yield of the β-D-mannoside **83**,[66] the parallel sequence from 3,4,6-tri-O-benzyl-D-glucose **84** mainly gave the reducing 2-O-methyl ether **85** and little of the α-D-glucoside **86**.[57] Likewise, benzyl 3,5-di-O-benzyl-α-D-ribofuranoside may be prepared in 83% yield from 3,5-di-O-benzyl-D-ribose.[67]

The other route to glycosides involves the action of glycosylating reagents on tributyltin ethers and

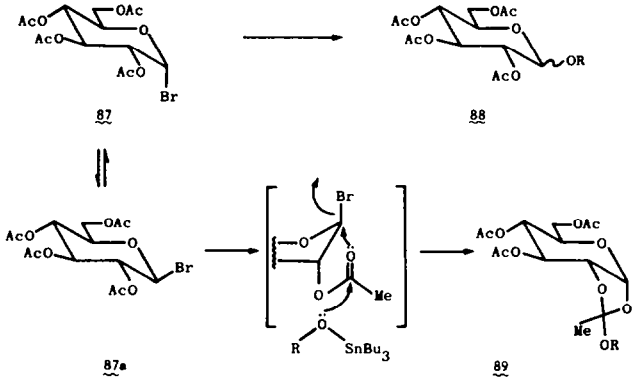


Fig. 28.

thioethers.[68] Per-O-acetyl-α-D-glucopyranosyl bromide **87** (Fig. 28) reacted with a range of tributyltin ethers, in the presence of $SnCl_4$ to give per-O-acetylated D-glycosides, **88** with variable anomeric configuration (Table 1). On the other hand, in the presence of quaternary ammonium halides, preliminary anomerization to the β-bromide **87a** led finally to the orthoesters **89** (Table 2).[68] Complex orthoester derivatives can be prepared by this procedure[68a] (Fig. 29). Another route to O-glycosides involved the per-O-acetyl glucosamine derivative **90** (Fig. 30), which reacted with tributyltin ethers in the presence of $SnCl_4$ to give good yields of the β-D-glucosides **91** and **92**. Under the same conditions, tributyltin thioethers gave the S-glycosides, **93–95**.[69–71] These glycosidations were also catalyzed by trimethylsilyl triflate.[72] Benzylated galactopyranosyl halides cannot give orthoesters. Following a systematic investigation of their reactions with galactose-derived stannylenes in a variety of conditions, it was concluded that this kind of activation brought no improvement, except when the condensation was run in dichloromethane in the presence of tetrabutylammonium iodide.[73] A 70% yield of protected α-D-galactopyranose-[1 → 3]-D-galactose was obtained in this way.

Synthesis of large ring lactones

Esters may be prepared from mixtures of glycols and benzoic acid by heating in the presence of dibutyltin oxide.[74] This method of esterification proved extremely valuable in the synthesis of macrocyclic lactones and lactams, which were obtained in good to excellent yields by refluxing solution of ω-hydroxycarboxylic acids, or ω-aminocarboxylic acids in mesitylene or with 10% (mol-equiv) di-n-butyltin oxide, using a Dean–Stark apparatus for the continuous removal of water (Table 3).[75] The

Table 1. Formation of acetylated glucopyranosides (Fig. 28)

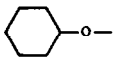
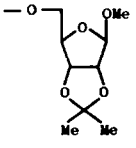
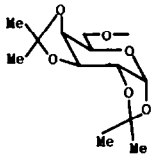
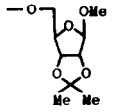
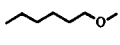
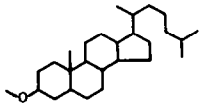
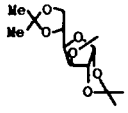
RO—	Yield
MeO–	86% β-
PhO–	89% β-
BnO–	52% β-
	47% α-
	32% α-
	37% β-

Table 2. Formation of acetylated D-glucopyranose-1,2-orthoesters (Fig. 28)

RO—	Yield
	82%
	93%
	77%
	77%
	80%
	84%
PhO–	
	90% (53% conversion)

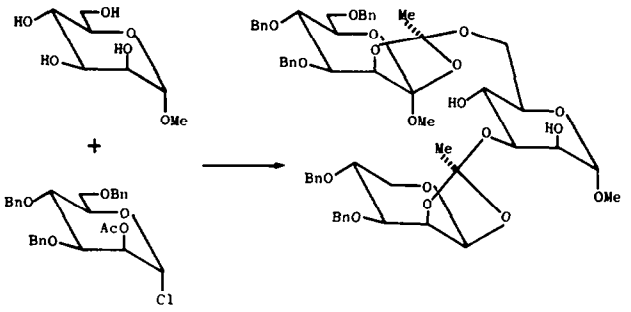


Fig. 29.

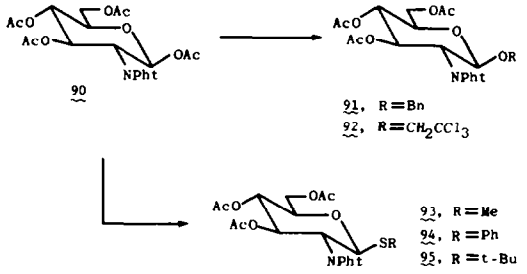
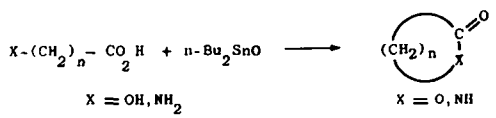


Fig. 30.

suggested mechanism (Fig. 31) first postulates the esterification of dibutyltin oxide by the alcoholic function of the hydroxy acid. However, owing to the strong complexing ability of tin^{IV} derivatives when the Sn atom is linked to two O-atoms, consecutive chelation by the carboxyl, to give B, is possible, and should be followed by elimination of water to give the (covalent) alkoxydialkyltin carboxylate C. In intermediate C, the nucleophilic and electrophilic partners are held in close proximity, and reaction occurs with the elimination of dibutyltin oxide. This mechanism also accounts for the relative inefficiency of bis(tributyltin) oxide in this reaction, the driving force for the formation of complexes such as A being much lower with trialkyltin derivatives. This mechanism meets with Mandolini's

Table 3.



X	n	Solvent*	Reaction time (hr)†	Monolide or lactam %	Diolide %‡
O	7	M	3.5	0	20
O	10	M	19	5	
O	11	M	21	22	
O	14	M	23	43	
O	15	M	19	60	
NH	3	X	12	95	
NH	4	X	12	95	
NH	5	X	12	95	

* M = mesitylene, x = xylene.

† Reflux temperature.

‡ See E. J. Corey and K. C. Nicolaou, *J. Am. Chem. Soc.* **96**, 5614 (1974) for another method which reports monolides and diolides in the same series.

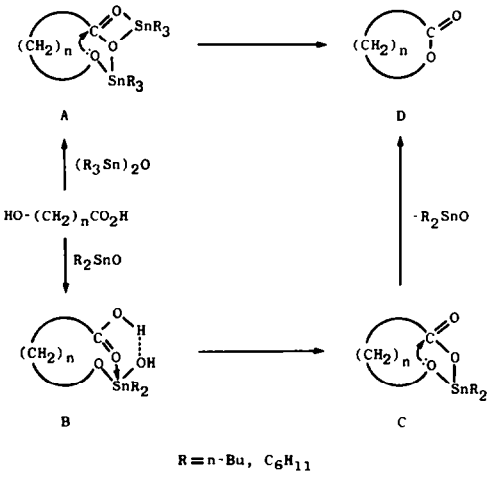


Fig. 31.

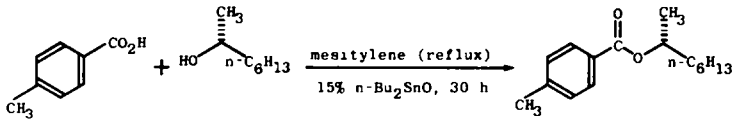


Fig. 32.

molarity criterion[76] for a true template mechanism. There is no severance of the alcoholic C—O bond in these esterifications, and it was found that (−)-2-octanol could be converted to the paratoluate without racemization by this method (Fig. 32).

Direct lactonization of the corresponding hydroxy seco-acid or some activated derivative thereof is often the key step in the synthesis of natural macrolides. The new, tin-mediated, template-driven esterification process reported above has proved efficient for such ring-closures. To ensure shorter reaction periods at high temperature with the sensitive substrates, stoichiometric rather than catalytic quantities of dibutyltin oxide were used.[77] In this way, ricinelaidic acid **96** (Fig. 33) was converted to the 13-membered ring lactone **97**. The potent antimicrobial agent ingramycine, **99**, a 14-membered lactone, was prepared in 30% yield from the hydroxy acid **98** (Fig. 34).

The per-tetrahydropyranyl ether **101** (Fig. 35) of the potent antibiotic nodusmicine smoothly undergoes hydrolysis to give protected seco-acid **100** in 88% yield. Lactonization back into **101** was best effected using stoichiometric amounts of dimethyltin oxide in 9.3% yield. This is not a high yield, but the problem is fraught with difficulties. Ten-membered macrolides are among the most difficult to prepare through cyclization techniques and the pro-lactone forming hydroxyl group is severely sterically hindred.

The hydroxy acids **102** and **103** (Fig. 36) are readily available from a common precursor. Tin mediated dilactonization gave diolides **104** and **105**, in 34 and 15% respective yields, which are among

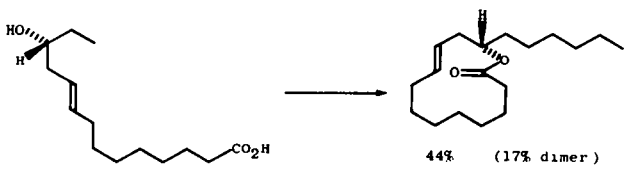
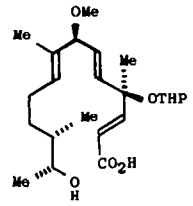
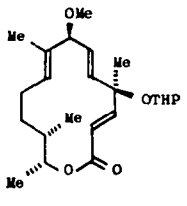


Fig. 33.

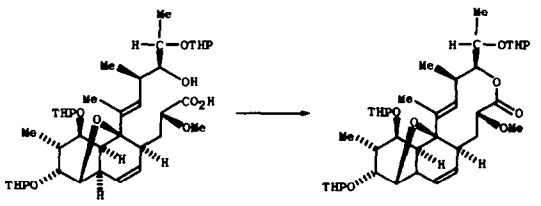


98



99

Fig. 34.



100 101

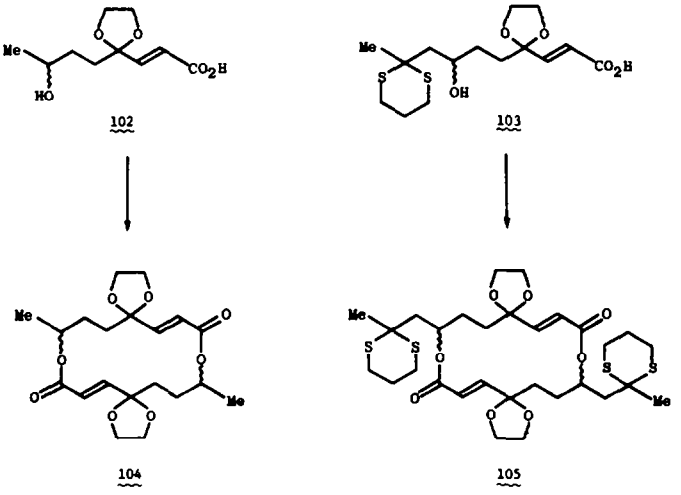
Fig. 35.

the best reported for this reaction. The competitive reaction in both cases is a kinetically favoured internal Michael-type of addition of the OH group across the conjugated double bond. Diolides **104** and **105** are intermediates in the syntheses of the fungicide (−)-pyrenophorine and the antibiotic (−)-vermiculine, respectively.

5, 6 and 7-Membered lactams are easily prepared by tin mediated cyclization in nearly quantitative yield. For example, by this process, the bridged lactam **107** was prepared directly from **106** in 77% yield (Fig. 37). This is in sharp contrast to the 2% yield reported in the literature for this compound.[77a]

Following a different approach, Shanzer and his associates have prepared a collection of macrocyclic polylactones by heating stannylenes with bifunctional diacid derivatives. For example, α,ω-dicarboxylic acid chlorides give the corresponding tetralactones represented by expression **108** in good yield, as shown in Fig. 38.[78]

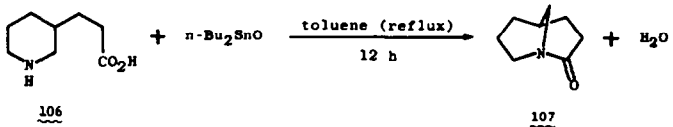
In the same type of reactions, the stannylene of D-diethyl tartrate gave a macrocyclic ring **109** noteworthy for its C_2 axis, a feature which is also found in the products arising from the reaction of N-(trifluoracetyl)glutamic and N-(trifluoroacetyl) aspartic anhydrides on the stannylene of 1,2-ethanediol.[79] On the other hand, reaction of α,ω-*bis*-isocyanates led to the cyclic, n + 8-membered, *bis*-carbamates **110**.[80] A completely different reaction occurred when a mixture of β-propiolactone and the stannylene of 1,2-ethanediol was refluxed in chloroform solution, yielding a range of cyclic polylactones (Fig. 40).[81]



102 103

104 105

Fig. 36.



106 107

Fig. 37.

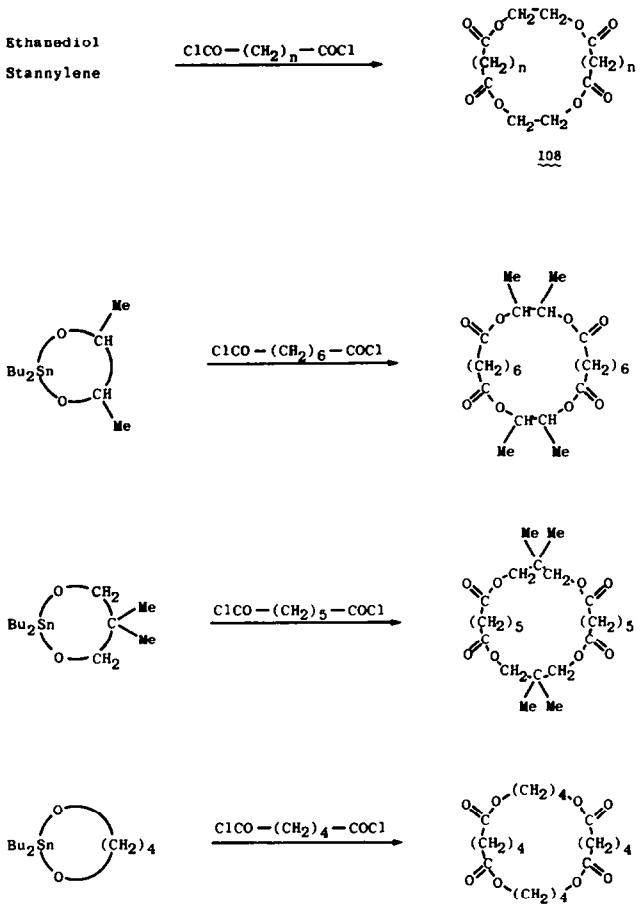


Fig. 38.

The covalent 8-membered ring structure for the stannylene of 1,2-ethanediol considered by Shanzer *et al.* does not seem compatible with the ^{119}Sn NMR measurements of Smith *et al.*[12] even if allowances were made for "noncovalent transannular interactions".[79] Strictly covalent (associated) 5-membered units are manifest in the known solid-state structures in this series.[17,22] Shanzer *et al.*[81a] have prepared diastereomeric organotin complexes derived from asymmetric diols and have utilized them as a method for optical enrichment of diols.

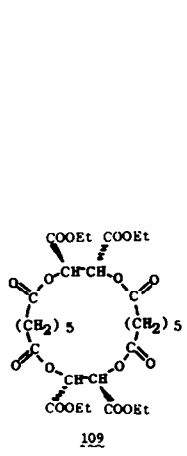
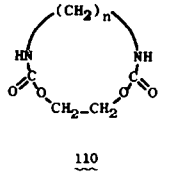


Fig. 39.



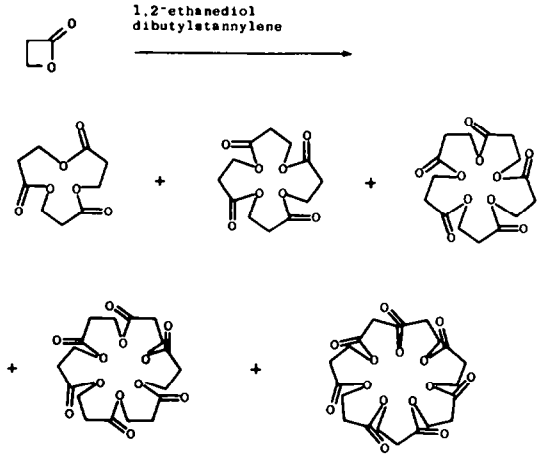


Fig. 40.

Oxidation

Stannylenes are oxidized to keto-alcohols by dropwise addition of bromine in dichloromethane. The reaction proceeds at room temperature at the speed of a titration.[82] The ketone function appears to be chelated to the tin in the medium (ν_{CO} 1685 cm^{-1}). Thus the stannylene derivatives of *cis* and *trans*-cycloheptanediol **111** (Fig. 41) are oxidized quantitatively to the hydroxy-ketone **112**. Good to excellent yields have also been reported in the oxidation by this method of four other *bis*-secondary diols, but an interesting feature of the reaction lies in the possibility to oxidize tertiary–secondary glycols. Thus, the stannylenes of 1,2-diphenylpropane-1,2-diol, **113**, *trans*-1-methylcyclohexane-1,2-diol **115** and *trans*-1-phenyl-cyclohexane-1,2-diol **116** were oxidized to the corresponding ketones, **114**, **117** and **118**, in 67, 96 and 73% respective yields, the rest being starting material.[83] Classical reagents often effect predominating C—C bond cleavage on such substrates. When extended to unsymmetrical diols, the reaction proved to be highly regioselective.[84] The three α-D-*xylo*-hexopyranose-4-ulosides **119**, **120** and **121** were obtained by the bromine oxidation of the pyranoside diols, methyl 2-O-methyl-6-O-trityl-α-D-glucopyranoside, benzyl 2,3-di-O-benzyl-α-D-glucopyranoside and benzyl 2,6-di-O-benzyl-α-D-galactopyranoside in yields of 72, 87 and 75% respectively. While the yield of **123** from 1,2-isopropylidene-3-O-methyl-α-D-glucofuranose was only 48%, the highly crystalline ketone **112** was obtained in 72% yield from benzyl 4,6-O-benzylidene-α-D-galactopyranoside. Ketonic sugars are useful intermediates for labeling, configurational inversion and functionalization.

In enterobacteria (and possibly in all prokaryotic cells), the immediate precursor of the five-carbon chain of the thiazole of thiamine is a five-carbon sugar, 1-deoxy-D-*threo*-pentulose, or, more likely, a derived phosphate.[85] This novel sugar was conveniently prepared in the labeled form **127** (Fig. 42) by the bromine oxidation of the mixed stannylene derivatives of the easily prepared epimeric mixture of **124** and **125**. This gave only one ketone, **126** which was deprotected to the free sugar **127**.[86]

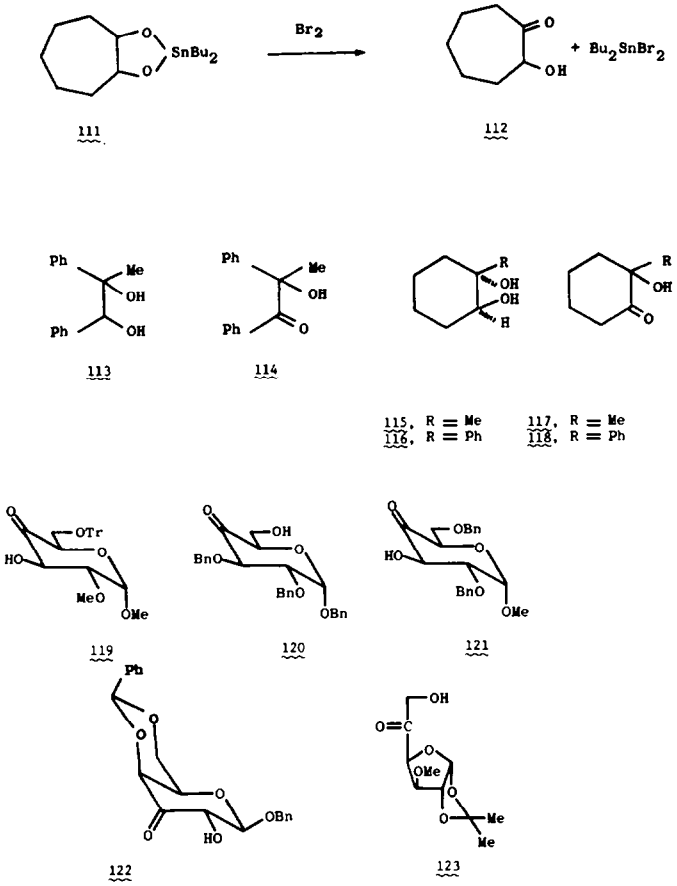
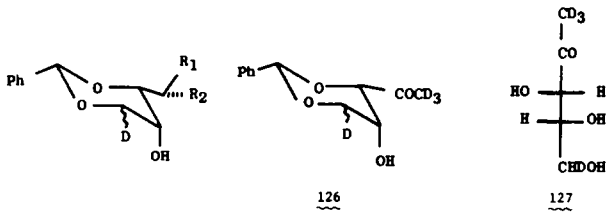


Fig. 41.



126 127

124, $R_1 = OH$; $R_2 = CD_3$

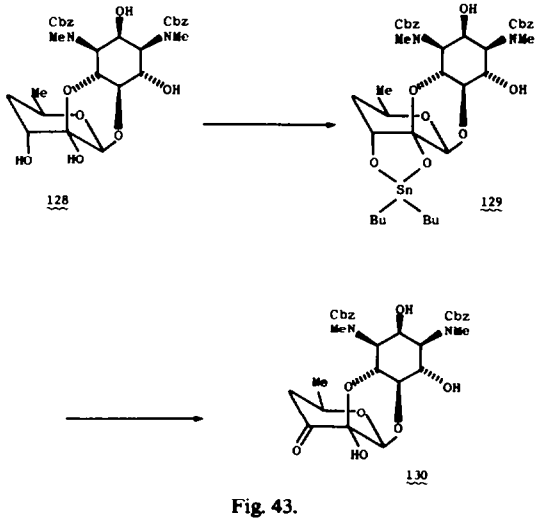
125, $R_1 = CD_3$; $R_2 = OH$

Fig. 42.

A crucial transformation in the total synthesis of spectinomycin[57] was based on the oxidative ring-opening of the stannylene derivative **129** to give **130**, a direct chemical precursor to the antibiotic (Fig. 43). This key step was inherent in the original strategy, which sought to create the *cis*-diol orientation found in the N,N'-[(benzyloxy)carbonyl] dihydrospectinomycin derivative **128**, hence the corresponding stannylene **129**. The same oxidation could also be achieved by sequential treatment of **128** with bis(tributyltin)oxide and N-bromosuccinimide. In this case, presumably, oxidation takes place via an intermediate O-stannyl ether which may derive further stabilization by coordination with the *cis*-disposed equatorial tertiary OH group. Oxidations on simple models were known,[82,87] since brominolysis of the tributylstannyl ethers of allylic, benzylic and secondary alcohols, in the presence of triethyltin methoxide as proton captor, gave the corresponding carbonyl derivatives[87] (Table 4). The use of nitrosonium tetrafluoroborate as the oxidant has been also reported.[88]

Miscellaneous

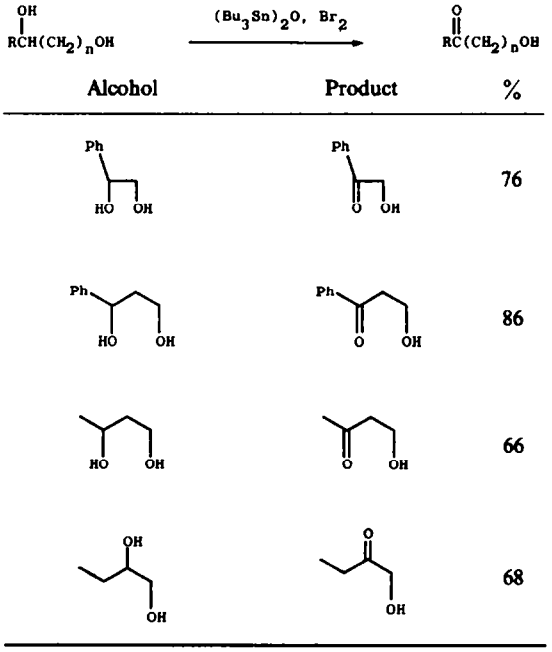
Glycol-splitting reagents act in the same way on the corresponding stannylenes, and at comparable rate.[89] The examples shown in Table 5 appear to be the first of this type of oxidative cleavage with a substrate other than a diol. The possibility to achieve glycol cleavage under strictly aprotic conditions should be interesting in mechanistic studies, since reaction rates are known to be markedly pH-dependent. The reaction may also be of preparative significance, in those cases where the evolution of



128 129 130

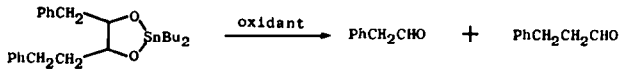
Fig. 43.

Table 4. Selective oxidation of hydroxyl groups in diols[87]



Alcohol	Product	%
		76
		86
		66
		68

Table 5. Oxidation of the dibutylstannylene of DL-erythro-1,5-diphenylpentane-2,3-diol by glycol-splitting reagents*



Oxidant	Equiv.	Temperature (°)	Time	$PhCH_2CHO$ (%)	$PhCH_2CH_2CHO$ (%)
Bu_4NIO_4	1	RT	5 min	82	99
$Pb(OAc)_4$	1	RT	5 min	85	91
$PhI(OAc)_2$	1	RT	5 min	†	98
$Ph_3Bi(OAc)_2$[90]	1.5	40	2 hr	66	90

* In CH_2Cl_2 solution.
† Interference from PhI.

acetic acid in the reaction medium is to be avoided. For instance, the best preparation of 2,4-O-benzylidene-D-threose was found to be the oxidation of the dibutylstannylene of 1,3-O-benzylidene-D-arabitol with (diacetoxyiodo)-benzene in benzene.[86]

Stannylenes react under mild conditions with phenyl isothiocyanate to give quantitative yields of iminocarbonates, with the elimination of dibutylstannyl sulfide, possibly *via* a 7-membered ring intermediate.[91]

REFERENCES

[1] T. W. Greene, *Protective Groups in Organic Synthesis*. Wiley, New York (1981).
[2] See for example, A. H. Haines, *Chem. Ind.* 883 (1976); H. Tamioka and K. Oshima, *Tetrahedron Lett.* **23**, 539 (1982); T. L. Gilchrist and D. Tuddenham, *J. Chem. Soc. Chem. Commun.* 657 (1981); S. Hanessian, D. H. Wong and M. Therien, *Synthesis* 394 (1981); E. Santianello and P. Ferraboschi, *Synth. Commun.* **10**, 75 (1980); A. Cornelis and P. Laszlo, *Synthesis* 849 (1980); R. V. Stevens, K. T. Chapman and N. N. Weller, *J. Org. Chem.* **45**, 2030 (1980); G. A. Olah, Y. D. Vankar and M. Arvanghi, *Synthesis* 141 (1980); A. J. Mancuso, D. S. Brownfain and D. Swern, *J. Org. Chem.* **44**, 4148 (1979); D. H. R. Barton, J. P. Kitchin and W. B. Motherwell, *J. Chem. Soc. Chem. Commun.* 1099 (1978).
[3] A. H. Haines, *Adv. Carbohydr. Chem. Biochem.* **33**, 11 (1976).
[4] K. Heyns and H. Paulsen, *Adv. Carbohydr. Chem.* **17**, 169 (1962).
[5] M. Pereyre and J. C. Pommier, *New Applications of Organometallic Reagents in Organic Synthesis* (Edited by D. Seyferth), p. 161. Elsevier, Amsterdam (1976).
[6] W. J. Considine, *J. Organomet. Chem.* **5**, 263 (1966).
[7] D. Wagner, J. Verheyden and J. G. Moffatt, *J. Org. Chem.* **39**, 24 (1974).
[8] A. G. Davies, P. R. Palan, unpublished work quoted in ref. 9, p. 160; P. R. Palan, Ph.D. Thesis, London (1967).
[9] A. G. Davies, *Organotin Compounds* (Edited by A. K. Sawyer), Vol. I, Chapter 4. Marcel Dekker, New York (1971).
[10] T. L. Chwang, *J. Carbohydr. Nucl.* **7**, 159 (1980).
[11] J. M. Vatèle and S. David, unpublished observation.
[12] P. J. Smith, R. F. M. White and L. J. Smith, *J. Organomet. Chem.* **40**, 341 (1972).
[13] A. M. Domingos and G. M. Sheldrick, *Acta Crystallogr.* **B30**, 519 (1974).
[14] N. Kasa, K. Yasuda and R. Okawara, *J. Organomet. Chem.* **3**, 172 (1965).
[15] P. J. Wheatley, *J. Chem. Soc.* 5027 (1961).
[16] P. G. Harrison, *Adv. Chem. Ser.* **157**, 258 (1976).
[16a] J. C. Pommier, E. Mendes, J. Valade and J. Housty, *J. Organomet. Chem.* **55**, C19 (1973).
[17] S. David, C. Pascard and M. Cesario, *Nouveau J. Chim.* **3**, 63 (1979).
[18] C. W. Holzapfel, J. M. Koekemoer, C. F. Marais, G. J. Kruger and J. A. Pretorius, *S. Afr. J. Chem.* **35**, 80 (1982).
[18a] A. G. Davies, H. M. Dawes, M. B. Hursthouse and A. J. Price (private communication, to be published).
[19] L. Pellerito, G. Ruisi, R. Barbieri and M. T. La Siudia, *Inorg. Chim. Acta* **21**, 33 (1977).
[20] S. David, A. Thieffry and A. Forchioni, *Tetrahedron Lett.* 2647 (1961).
[21] J. Y. Lallemand, unpublished results.
[22] J. Defaye, unpublished results.
[23] V. P. Feshin, L. S. Romanenko, M. G. Voronkof, G. V. Dolgushin and P. A. Nikitin, *J. Mol. Struct.* **83**, 325 (1982).
[24] R. Hoffmann, J. H. Howell and E. L. Muetterties, *J. Am. Chem. Soc.* **94**, 3047 (1972).
[25] J. Alais, A. Maranduba and A. Veyrières, *Tetrahedron Lett.* 2383 (1983).
[25a] S. J. Blunden, P. J. Smith, P. J. Beynon and D. G. Gillies, *Carbohydr. Res.* **88**, 9 (1981).
[26] I. D. Jenkins, J. P. H. Verheyden and J. G. Moffatt, *J. Am. Chem. Soc.* **93**, 4323 (1971).
[27] A. J. Crowe and P. J. Smith, *J. Organomet. Chem.* **110**, C57 (1976).
[28] T. Ogawa and M. Matsui, *Carbohydr. Res.* **56**, C1 (1977).
[29] T. Ogawa and M. Matsui, *Tetrahedron* **37**, 2263 (1981).
[30] T. Ogawa, S. Nakabayashi and K. Sasajima, *Carbohydr. Res.* **96**, 29 (1981).
[31] T. Ogawa, Y. Takahashi and M. Matsui, *Carbohydr. Res.* **102**, 207 (1982).
[32] T. Ogawa, T. Nukada and M. Matsui, *Carbohydr. Res.* **101**, 263 (1982).
[33] A. Veyrières, *J. Chem. Soc. Perkin Trans. I* 1626 (1981).
[34] J. Alais and A. Veyrières, *J. Chem. Soc. Perkin Trans. I* 377 (1981).

[35] J. Arnap, H. Baumann, H. Lönn, J. Lönngren, H. Nyman and M. Ottoson, *Acta Chem. Scand.* **B37**, 329 (1983).
[36] F. Sugawara, H. Nakayama and T. Ogawa, *Carbohydr. Res.* **108**, C5 (1982).
[37] E. Avela and B. Holmbom, *Acta Acad. Aboeneis* **B31**, No. 14 (1971).
[38] R. Eby and C. Schuerch, *Carbohydr. Res.* **100**, C41 (1982).
[39] R. S. Tipson, *Adv. Carbohydr. Chem.* **8**, 107 (1953); D. H. Ball and F. W. Parrish, *Ibid.* **23**, 233 (1968); **24**, 139 (1969).
[39a] H. Takaku, K. Kamaike and H. Tsuchiya, *J. Org. Chem.* **49**, 51 (1984).
[40] A. J. Bloodworth and A. G. Davies, *J. Chem. Soc.* 5238 (1965).
[41] J. Lorberth and M. R. Kula, *Chem. Ber.* **97**, 3444 (1964).
[42] M. Ikehara and T. Maruyama, *Tetrahedron* **31**, 1369 (1975); *Nuc. Acids Res.* **1**, 1351 (1974); A. Holy and P. Kois, *Coll. Czech. Chem. Commun.* **45**, 2817 (1980); J. B. Chattopadhyaya, *Tetrahedron Lett.* 4113 (1980); T. Kato and J. Zemlicka, *J. Org. Chem.* **45**, 4006 (1980); I. Rosenberg and A. Holy, *Coll. Czech. Chem. Commun.* **44**, 3327 (1979); R. Langanathan and D. Larwood, *Tetrahedron Lett.* 4341 (1978); M. Y. Karpesky, L. N. Beigelman, S. N. Mikhailov, N. S. Padyukova and J. Smart, *Coll. Czech. Chem. Commun.* **47**, 156 (1982).
[43] S. David, G. de Sennyey and B. Sotta, *Tetrahedron Lett.* 1817 (1982).
[44] S. David and A. Thieffry, *C.R. Acad. Sci. Paris Sér. C* **279**, 1045 (1974).
[45] C. Augé, S. David and A. Veyrières, *J. Chem. Soc. Chem. Commun.* 375 (1976).
[46] H. M. Flowers, *Carbohydr. Res.* **39**, 245 (1975) and refs therein.
[47] M. A. Nashed and L. Anderson, *Tetrahedron Lett.* 3503 (1976); M. A. Nashed and L. Anderson, *Carbohydr. Res.* **56**, 419 (1977); M. A. Nashed, *Ibid.* **60**, 200 (1978).
[48] M. A. Nashed and L. Anderson, *Carbohydr. Res.* **56**, 325 (1977).
[49] C. W. Slife, M. A. Nashed and L. Anderson, *Carbohydr. Res.* **93**, 219 (1981).
[50] M. A. Nashed, M. S. Chowdhary and L. Anderson, *Carbohydr. Res.* **102**, 99 (1982).
[51] S. David and A. Thieffry, *J. Chem. Soc. Perkin Trans. I* 1568 (1979).
[52] R. M. Munavu and H. H. Szmant, *J. Org. Chem.* **41**, 1832 (1976).
[53] T. Ogawa and T. Kaburagi, *Carbohydr. Res.* **103**, 53 (1982).
[54] J. M. Sugihara, *Adv. Carbohydr. Chem.* **8**, 1 (1953).
[55] V. G. Box, *Heterocycles* **20**, 677 (1983).
[56] A. J. Varma and C. Schuerch, *J. Org. Chem.* **46**, 799 (1981).
[57] V. K. Srivastava and C. Schuerch, *Tetrahedron Lett.* 3269 (1979).
[58] S. S. Rana, J. J. Barlow and K. L. Matta, *Carbohydr. Res.* **85**, 313 (1980); N. Hong, M. Funabashi and J. Yoshimura, *Ibid.* **96**, 21 (1981).
[59] S. Hanessian and R. Roy, *J. Am. Chem. Soc.* **101**, 5839 (1979); *J. Antibiotics* **32**, Suppl. S-73 (1979).
[60] J. S. Brimacombe, J. Mishell and C. W. Smith, *J. Chem. Soc. Perkin Trans. I* 682 (1975).
[61] S. David and G. De Sennyey, *Carbohydr. Res.* **77**, 79 (1979).
[62] J. Thiem and H. P. Wessel, *Tetrahedron Lett.* 3571 (1980).
[63] S. David and A. Lubineau, unpublished experiment.
[64] S. David and A. Lubineau, *Nouveau J. Chim.* **1**, 375 (1977).
[65] S. David, A. Thieffry and A. Veyrières, *J. Chem. Soc. Perkin Trans. I* 1796 (1981).
[65a] R. Toman, J. Rosik and M. Zikmund, *Carbohydr. Res.* **103**, 165 (1982).
[66] E. S. H. El Ashry and C. Schuerch, *Carbohydr. Res.* **105**, 33 (1982).
[67] T. L. Su, R. S. Klein and J. J. Fox, *J. Org. Chem.* **47**, 1506 (1982).
[68] T. Ogawa and M. Matsui, *Carbohydr. Res.* **51**, C13 (1976); T. Ogawa, K. Katano, K. Sasajima and M. Matsui, *Tetrahedron* **37**, 2779 (1081).
[68a] T. Ogawa, K. Katano and M. Matsui, *Carbohydr. Res.* **64**, C3 (1978).
[69] T. Ogawa, S. W. Nakabayashi and K. Sasajima, *Carbohydr. Res.* **95**, 308 (1981).
[70] T. Ogawa, S. Nakabayashi and K. Sasajima, *Carbohydr. Res.* **96**, 26 (1981).
[71] T. Ogawa and S. Nakabayashi, *Carbohydr. Res.* **97**, 81 (1981).
[72] T. Ogawa, K. Beppu and S. Nakabayashi, *Carbohydr. Res.* **98**, C6 (1981).
[73] C. Augé and A. Veyrières, *J. Chem. Soc. Perkin Trans. I* 1825 (1979).
[74] O. M. O. Habib and J. Malek, *Coll. Czech. Chem. Commun.* **41**, 2724 (1976); L. Nondek and J. Malek, *Makromol. Chem.* **178**, 2211 (1977); *Coll. Czech. Chem. Commun.* **43**, 424 (1978).
[75] K. Steliou, A. Szcygielska-Nowosielska, A. Favre, M. A. Poupart and S. Hanessian, *J. Am. Chem. Soc.* **192**, 7578 (1980).
[76] C. Galli and L. Mandolini, *J. Chem. Soc. Chem. Commun.* 251 (1982).
[77] K. Steliou and M. A. Poupart, *J. Am. Chem. Soc.* **105**, 7130 (1983).
[77a] H. K. Hall, Jr., R. G. Shaw and A. Deutschmann, *J. Org. Chem.* **45**, 3722 (1980).
[78] A. Shanzer, N. Mayer-Shochet, F. Frolow and D. Rabinovich, *J. Org. Chem.* **46**, 4662 (1981).
[78a] For a recent review, see, A. Shanzer, *Acc. Chem. Res.* **16**, 60 (1983).
[79] A. Shanzer, J. Libman, H. Gottlieb and F. Frolow and D. Rabinovich, *J. Org. Chem.* **46**, 4662 (1981).
[80] A. Shanzer, N. Sochet, D. Rabinovich, F. Frolow, *Angew. Chem. Int. Ed. Engl.* **19**, 326 (1980).
[81] A. Shanzer, J. Libman and F. Frolow, *J. Am. Chem. Soc.* **103**, 7339 (1981).
[81a] A. Shanzer, J. Libman and H. Gottlieb, *J. Org. Chem.* **48**, 4612 (1983).
[82] S. David, *C.R. Acad. Sci. Paris Sér. C* **278**, 1051 (1974).
[83] S. David and A. Thieffry, unpublished experiments.
[84] S. David and A. Thieffry, *J. Chem. Soc. Perkin Trans. I* 1568 (1979).
[85] S. David, B. Estramareix, J. C. Fischer and M. Thérisod, *J. Am. Chem. Soc.* **103**, 7341 (1981).
[86] S. David, B. Estramareix, J. C. Fischer and M. Thérisod, *J. Chem. Soc. Perkin Trans. I* 2131 (1982).
[87] K. Saigo, A. Morikawa and T. Mukaiyama, *Chem. Lett.* 145 (1975); *Bull. Chem. Soc. Jpn.* **49**, 1656 (1976); see also Y. Ueno and M. Okawara, *Tetrahedron Lett.* 4597 (1976).
[88] G. A. Olah and T. L. Ho, *Synthesis* 609 (1976).
[89] S. David and A. Thieffry, *Tetrahedron Lett.* 2885 (1981).
[90] D. H. R. Barton, D. J. Lester, W. B. Motherwell and T. Barros-Papoula, *J. Chem. Soc. Chem. Commun.* 705 (1979).
[91] S. Sakai, H. Nümi, Y. Kobayashi and Y. Ishii, *Bull. Chem. Soc. Jpn.* **50**, 3271 (1977).