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Levoglucosenone: the properties, reactions, and use in fine organic synthesis

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Abstract. The review deals with the synthesis, structure, chemical properties, and use of 1,6-anhydro-3,4-dideoxy-β-D-pyranosen-2-one (levoglucosenone) in the synthesis of natural products. The bibliography includes 67 referencces.

I. Introduction

Levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-pyranosen-2-one) is a sugar enone obtained in the acid-catalysed pyrolysis of cellulose and related materials which has attracted the attention of investigators by the unique nature of its structure and as a means for the introduction of chiral centres in the stereospecific synthesis of natural products. The 6,8-dioxabicyclo[3.2.1]octane skeleton, an enone system, and a highly activated keto-group and an acetal centre are combined in the structure of levoglucosenone. The effective facial differentiation of the attack by the reactants, induced by the 1,6-anhydro-bridge, as well as the coordinating and 'cooperative' effects of the 'chelate' acetal oxygen atoms ensure ease of occurrence and the high regio- and stereo-selectivity of the majority of the reactions involving levoglucosenone. Levoglucosenone is 'self-protected' in the form of an internal acetal, is thermally stable, and distils without appreciable decomposition. It forms readily dimeric and oligomeric condensation products and under certain conditions can generate highly reactive oxidopyrylium ylides. Levoglucosenone has proved useful as an effective Michael acceptor and as a powerful dienophile in Diels–Alder reactions, in dipolar cycloaddition, etc.

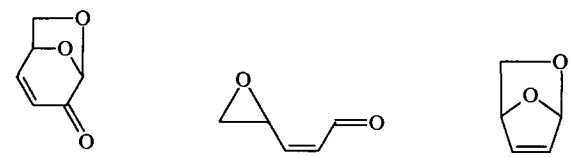
Although levoglucosenone has been known for more than 20 years,[1] it has still found only limited applications in organic synthesis. This is apparently associated with certain difficulties in the synthesis, purification, and handling of this compound and also with the lack of reviews on this topic. We hope that the data presented in this review will stimulate research by Russian chemists in this field.

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II. The synthesis, structure, and mechanism of the formation of levoglucosenone

Since the 1970s, the attention of investigators has been directed to the study of the structure, mechanism of the formation, and the properties of levoglucosenone **1**, which is one of the principal volatile products of the acid-catalysed thermolysis of cellulose and related carbohydrates.[1] Other empirical and structural formulae were initially attributed erroneously to this compound; 4,5-epoxy-2(*Z*)-pentenal ($C_5H_6O_2$) **2**,[2] 1,5-anhydro-2,3-deoxy-β-D-pent-2-enofuranose ($C_5H_6O_2$) **3**,[3] etc. The principal difficulties in the determination of the structure **1** were associated with the incorrect interpretation of mass-spectrometric data; the *m/z* 98 peak, corresponding to the formula $C_5H_6O_2$, was assumed to be due to a molecular ion.



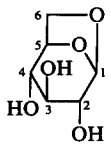
1 **2** **3**

Having investigated by NMR, UV, and IR spectroscopy as well as mass spectrometry and osmometry the products of the thermolysis of cellulose obtained under analogous conditions, Halpern et al.[4] concluded that it has the molecular formula $C_6H_6O_3$ and is 1,6-anhydro-3,4-dideoxy-β-D-pyranosen-2-one **1**, which was given the trivial name levoglucosenone.

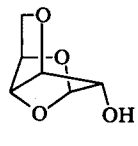
The structure of levoglucosenone was subsequently confirmed and adopted also by other investigators.[5–10] In particular, the exact mass of the molecular ion was determined[11] in 1985 as 126.0327, which corresponds to the empirical formula $C_6H_6O_3$, with the aid of chromatograph-linked mass spectrometry using both electron impact and chemical ionisation. The ion with *m/z* 98.0381 proved to be secondary and was produced as a result of fragmentation of levoglucosenone with ejection of CO. On the basis of ^1H and ^{13}C NMR spectroscopic data, it was also established that the six-membered ring of levoglucosenone has the envelope conformation.[12]

The pyrolysis of cellulose is a complex process, which leads to various products depending on the conditions.[13–18] Thus pyrolysis in vacuo (300–500 °C) affords a high yield of levoglucosan — 1.6-anhydro-β-D-glucopyranone **4**; at atmospheric pressure, levoglucosenone **1** and 1.4:3,6-dianhydro-β-D-glucopyranose **5** are formed as a result of the combination of

the reactions involving transglycosylation and dehydration of the D-glucose residues of cellulose.[17] The rapid removal of levoglucosan and other anhydrosugars prevents their further transformations into oligosaccharides, their decomposition into other volatile components, and salt formation. The presence of an acid catalyst promotes dehydration and charring accompanied by the formation of levoglucosenone, other unsaturated compounds, and carbon.[18]



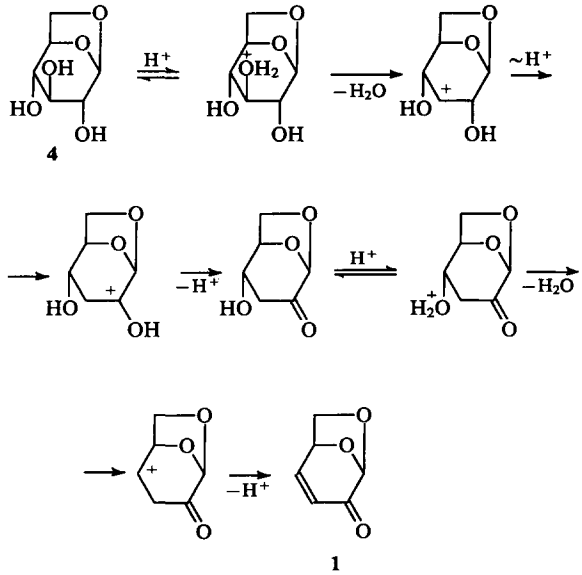
4



5

Studies of the influence of reaction conditions on the yield of levoglucosenone[17-21] led to the discovery of the optimum process parameters: 300 °C, atmospheric pressure, and 1% phosphoric acid concentration.

A mechanism has been proposed for acid-catalysed isotypical thermal decomposition reactions of cellulose, D-glucose, and levoglucosenone.[22] The C(1) and C(5) chiral centres of levoglucosan **5** are not involved in the transformations but the levoglucosenone obtained from the optically active levoglucosan $\{[\alpha]_D^{25} = -55°, c = 0.5, H_2O\}$ is chiral $\{[\alpha]_D^{25} = -52.7°, c = 1.0, CHCl_3\}$.

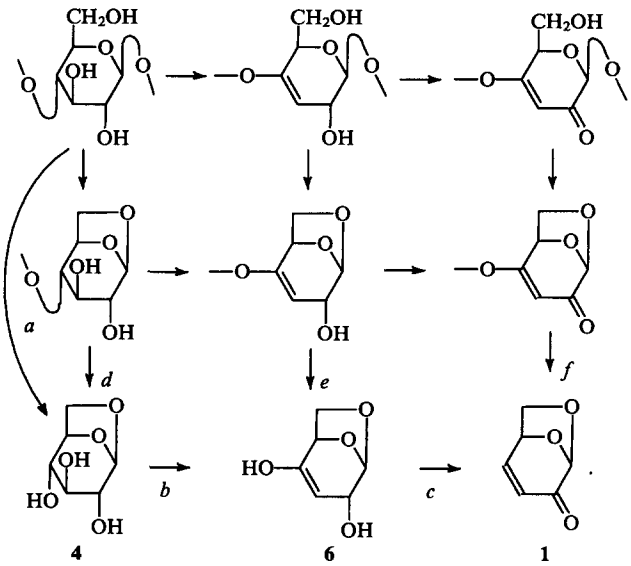


1

The third stage of the proposed mechanism, involving a 1,2-hydride shift from the C(2) atom to the carbenium centre C(3) and the formation of a more stable hydroxycarbenium ion, is the most important. The alternative 1,2-hydride shift leading to a hydroxycarbenium ion at C(4) apparently does not occur, since the corresponding levoglucosenone isomer was not found in the pyrolysate.[23]

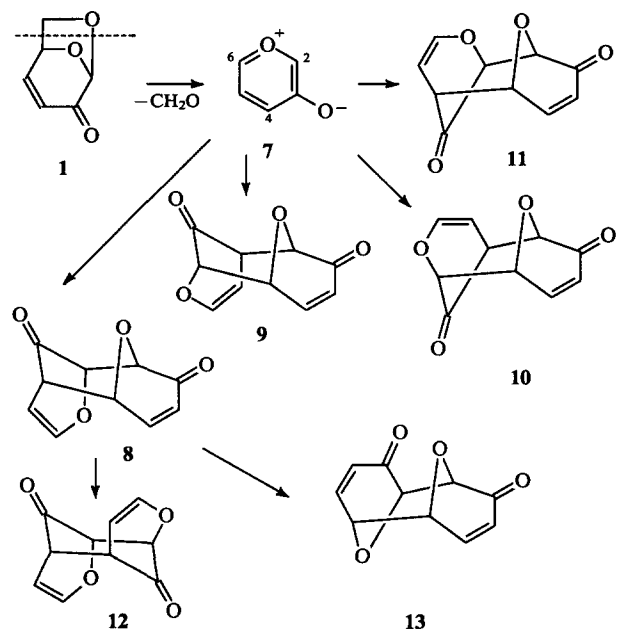
The method involving pyrolysis at the Curie point was used subsequently to identify the primary products of the decomposition of cellulose and related compounds.[7] In this procedure, the specimen was heated briefly to a fixed temperature under an inert carrier gas atmosphere. As a result of the relatively low temperature, the reactions of the primary products were ruled out. The pyrolysis mechanism (top right) was proposed.[7]

Compounds **1**, **4**, and **6** can be formed not only via routes *a*, *b*, or *c* but also via polymeric anhydro- and deoxy-sugar units (stages *d*–*f*). However, direct evidence for this has not yet been obtained.



4 6 1

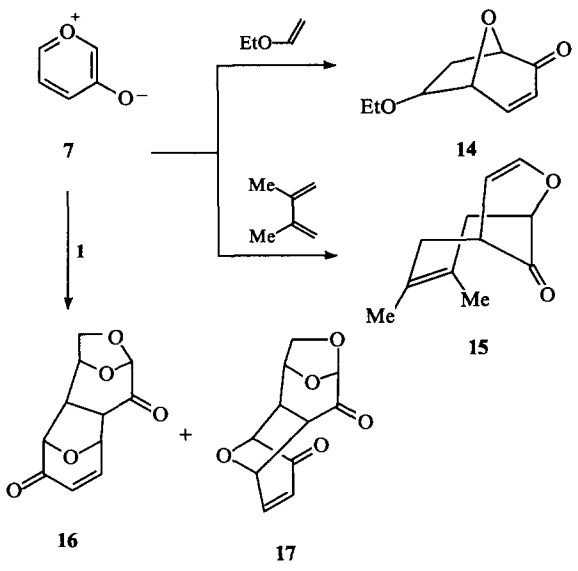
Levoglucosenone can undergo pyrolytic deformylation, affording the 3-oxidopyrylium intermediate **7**.[25] The highly reactive ylide **7** readily dimerises via a [6π + 4π] mechanism to form four regioisomeric adducts — the *endo*-compounds **8** and **9** and the *exo*-compounds **10** and **11** respectively. The situation is complicated by the fact that each of these adducts undergoes allyl rearrangements in its turn, affording two new dimers in each case. Thus the dimers for the primary adduct **8** are the bisvinyl ether **12** and the bisenone **13**.



1 7 11 9 10 8 12 13

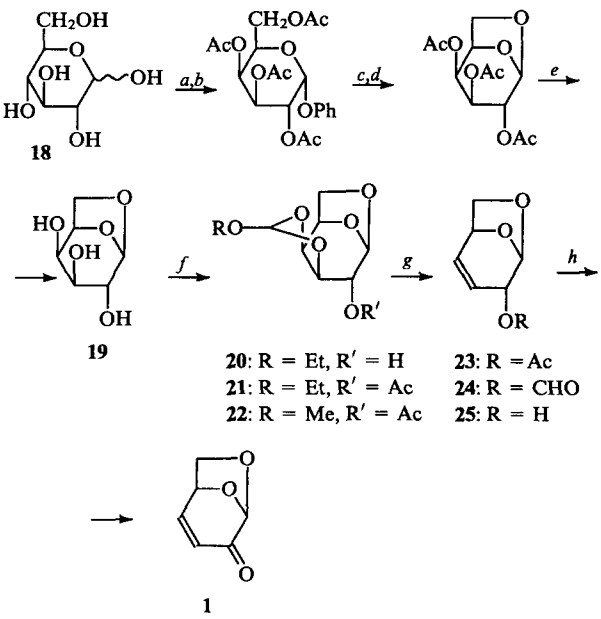
In thermal cycloaddition reactions, the 3-oxidopyrylium derivative **7** behaves both as a 4π-electron system (addition of ethyl vinyl ether and the formation of the bicyclic enone **14**) and as a 6π-electron component (addition in the 2- and 4-positions in the reaction with 2,3-dimethylbutadiene and the formation of the bicyclic vinyl ether **15**). In addition, the ylide **7** enters into a [4π + 2π]-cycloaddition reaction with levoglucosenone, affording the adducts **16** and **17**.

Thus the 3-oxidopyrylium intermediate **7** can condense with itself, with alkenes, and with dienes in electrocyclic reactions permitted by thermal conditions. All these factors are responsible for the diversity of the pyrolysis products.



III. Chemical syntheses of levoglucosenone

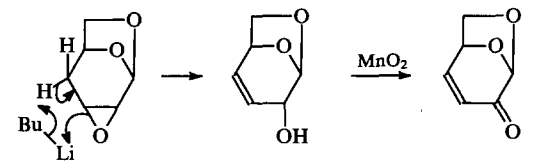
The synthesis of levoglucosenone from D-galactose **18** has been described.[26]



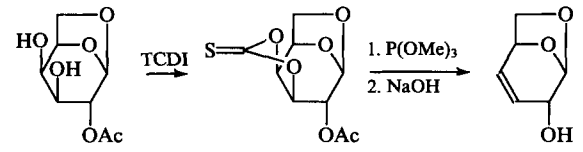
(*a*) AcONa–Ac_2O; (*b*) H^+, PhOH; (*c*) NaOH–H_2O; (*d*) Ac_2O, Py; (*e*) NaOMe; (*f*) $(RO)_3CH$, H^+, DMF; (*g*) Ac_2O, Cat; (*h*) MnO_2.

1,6-Anhydro-β-D-galactopyranose **19**, obtained from D-galactose, was mixed with 4 equivalents of triethyl orthoformate in solution in *N*,*N*-dimethylformamide in the presence of catalytic amounts of H_2SO_4 and was allowed to stand for 12 h. After appropriate treatment of the reaction mixture, the 3,4-ethoxyacetal of 1,6-anhydro-β-D-galactopyranose **20** was isolated in 95% yield. In the key reductive decarboxylation stage, the ethoxyacetal **20** or its acetyl derivatives **21** and **22** were refluxed in solution in acetic anhydride containing the catalyst. The highest yield of 2-acetyl-1,6-anhydro-3,4-dideoxy-β-D-*erythro*-hex-3-enopyranose **23** (in the absence of Ac_2O, the corresponding 2-formyl derivative **24** may be formed) was achieved when an aqueous solution of zirconium oxide was used (the yield of the alkene **23** was 88%). In the concluding stage, levoglucosenone was obtained as a result of the allylic oxidation of compound **25** by MnO_2.

Köll et al.[27] developed a scheme for the synthesis of levoglucosenone the key stage of which is the rearrangement of the epoxide **26**[28] to the allyl alcohol **25**.



The same workers proposed a more practical route to the enone **1** starting with the groundnut galactomannan. Pyrolysis of this polysaccharide followed by acetonation affords a monoisopropylidene derivative of 1,6-anhydro-β-D-galactopyranose. Its acetylation and treatment with aqueous acid lead to compound **27**. The crystalline thionocarbonate **28** was obtained from the latter by reaction with *N*,*N*′-thiocarbonyldiimidazole (TCDI) in boiling 2-butanone. On heating compound **28** with trimethyl phosphite for many hours and on treatment with alkali, the allyl alcohol **25** is produced.



A method for the synthesis of levoglucosenone from glucose has been described.[29] The reaction is carried out in dimethylformamide at 70–120 °C in the presence of concentrated H_2SO_4.

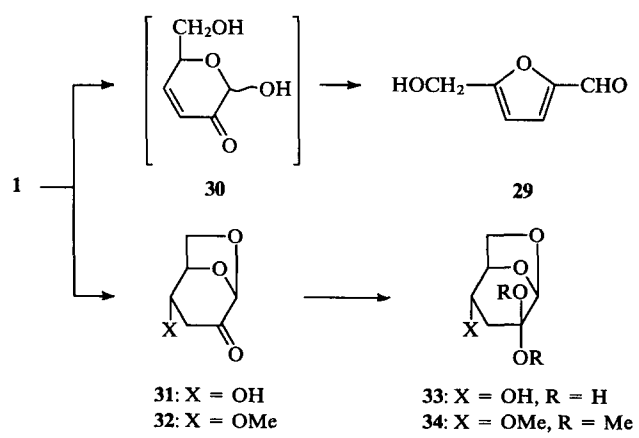
We may note that none of the methods of synthesis of levoglucosenone listed above can compete with the pyrolysis of cellulose, which remains the most economical and effective method for its preparation despite disadvantages such as the low yield of the product and the need to work with relatively large volumes of solid cellulose materials.

IV. Reactions of levoglucosenone and its derivatives

1. Acid- and base-catalysed reactions of levoglucosenone

Levoglucosenone has three reaction centres: the carbon–carbon double bond, the keto-group, and the glycosidic anhydro-linkage. Depending on the process conditions, each of these groups can react selectively.

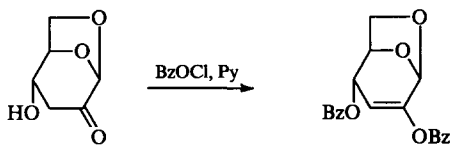
When levoglucosenone is heated with aqueous solutions of inorganic acids, 5-hydroxymethylfurfural **29** is formed.[17] This entails the initial rupture of the 1,6-anhydro-linkage of levoglucosenone and the formation of 3,4-dideoxy-D-*glycero*-hex-3-enopyranos-2-ylose **30**, which is in fact an intermediate in the acid-catalysed dehydration of hexoses to the furfural **29**.



Heating of levoglucosenone in aqueous acetic acid affords an intermediate resulting from the addition of water of the double bond — 1,6-anhydro-3-deoxy-D-*erythro*-hexopyranos-2-ylose **31**. Compound **31** can be readily separated from levoglucosenone **1** by extracting the latter with chloroform. The high solubility of compound **31** in water is due to the hydration of the keto-group and the formation of the *gem*-diol **33**, which has been confirmed by ^{1}H NMR spectroscopy.

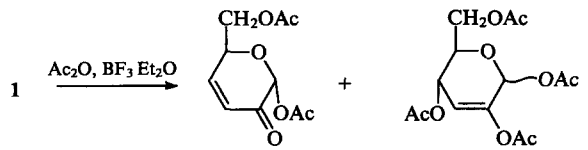
The acid-catalysed addition of methanol to the double bond of levoglucosenone using the MeOH–HCl system initially affords 4-*O*-methyl-2-ylose **32**, which is then rapidly converted into the dimethyl acetal **34** in an almost quantitative yield. Hydrolysis of compound **34** again leads to 4-*O*-methyl-2-ylose **32**.

The attempts to benzoylate the 4-hydroxy-group in compound **31** by benzoyl chloride in pyridine led to 1,6-anhydro-2,4-di-*O*-benzoyl-3-deoxy-β-D-*erythro*-hex-2-enopyranose **35** (via stages involving the successive enolisation and benzoylation of the keto-group).



31 **35**

The 1,6-anhydride ring of levoglucosenone is readily opened under acetolysis conditions in the presence of $BF_3.Et_2O$ as catalyst, which leads to the diacetate **36**. The anomeric tetraacetates **37** and **38** are formed in smaller amounts as a result of the exhaustive acetylation of the enone.



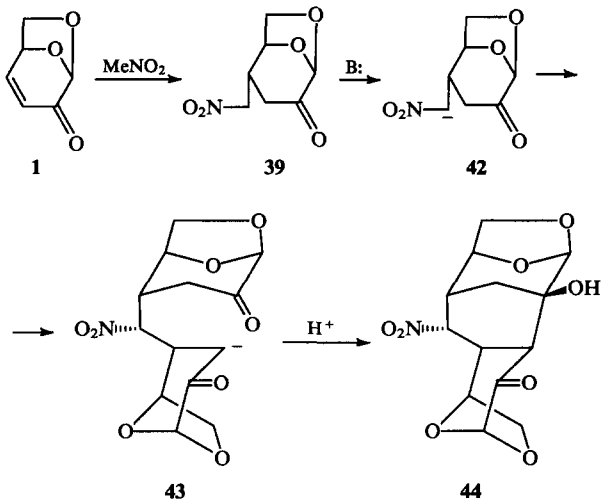
36 **37(α), 38(β)**

Reactions involving addition to the 3,4-double bond of levoglucosenone are also catalysed by bases. In the presence of small amounts of triethylamine, levoglucosenone affords satisfactory yields of the adducts **31** and **32** in water and anhydrous methanol respectively.

2. Michael addition

The reactions in which levoglucosenone serves as a Michael acceptor merit special attention.[30–33] Treatment of levoglucosenone with an excess of nitromethane in the presence of catalytic amounts of tetramethylguanidine gave rise to a mixture of two isomeric 2:1 adducts in an overall yield of 98%.[30] The reaction involves the initial 1,4-addition to the enone [the nitronate anion $^-CH_2NO_2$ adds to the C(4) atom of levoglucosenone from the side opposite to that of the 1,6-anhydro-bridge]; the subsequent base (B)-catalysed addition of a second nitromethane molecule to the carbonyl group of compound **39** leads to the formation of the diadducts **40** and **41** in proportions of 10:1.

When the reaction is carried out with an excess of levoglucosenone, 1:2 adducts are formed. The proposed mechanism of the formation of compound **44** represents the Michael addition of the nitromethyl anion **42** to levoglucosenone accompanied by the intramolecular aldol condensation of the intermediate diketone **43**. The high yield of the product **44** (95%) shows that each of the reaction stages is highly selective and that in each case the attack on the nucleophilic centre is directed exclusively to the *exo*-position.

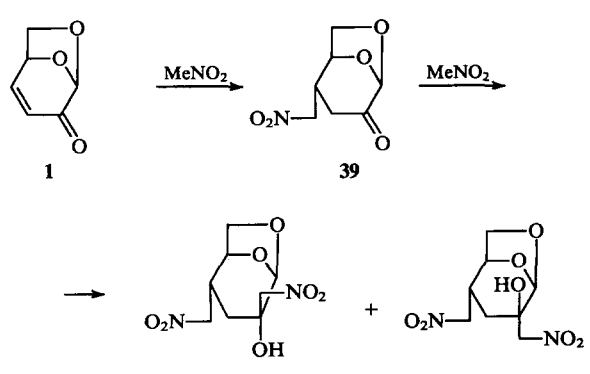


1 **39** **42**

43 **44**

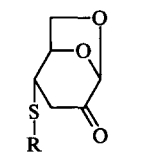
1,6-Anhydro-4-butylthio-3-deoxy-β-D-hexopyranos-2-ylose **45** has been obtained in a quantitative yield by the addition of butane-1-thiol to levoglucosenone.[31] Steric hindrance generated by the 1,6-anhydro-bridge interferes so much with equatorial attack on the thiol that the axial sulfide is formed exclusively. Other thiols behave similarly, affording the adducts **46–51**.

The same workers investigated the possibility of cross-coupling two levoglucosenone molecules via dithiols. Ethane-1,2-dithiol was chosen as the binding component, its reaction with levoglucosenone affording two products. The structure of one of them (compound **52**), obtained in 47% yield, was established by spectroscopic methods. The other reaction product could not be identified because of its instability (the compound decomposed rapidly at room temperature and it was shown by thin-layer chromatography that it afforded highly polar secondary products). Its ^{1}H and ^{13}C NMR spectra indicated the presence of three levoglucosenone molecules in its structure. The monoadduct was not detected.



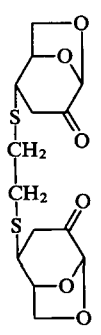
1 **39**

40 **41**



45: R = $(CH_2)_3CH_3$
46: R = $(CH_2)_5CH_3$
47: R = $(CH_2)_9CH_3$
48: R = $(CH_2)_{11}CH_3$
49: R = $CH_2CH(CH_3)_2$
50: R = $C(CH_3)_3$

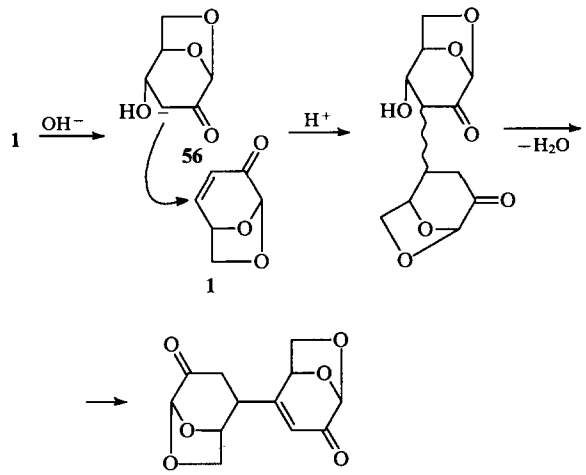
51: R = 



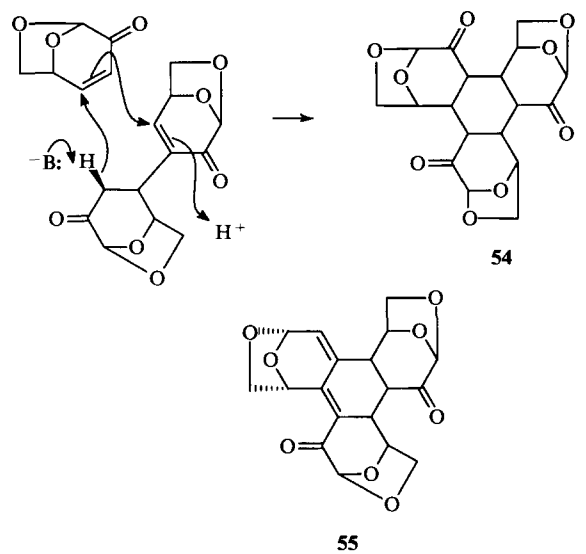
52

Heating levoglucosenone in aqueous triethylamine gives three principal oligomers: the dimer **53**, the saturated trimer **54**, and the unsaturated trimer **55**.[32]

The mechanism of the dimerisation of levoglucosenone is presented below. The base-catalysed hydration of compound **1** leads to the α-keto-stabilised carbanion **56**, which attacks a second levoglucosenone molecule in the *exo*-position. Subsequent dehydration affords the dimer **53**.

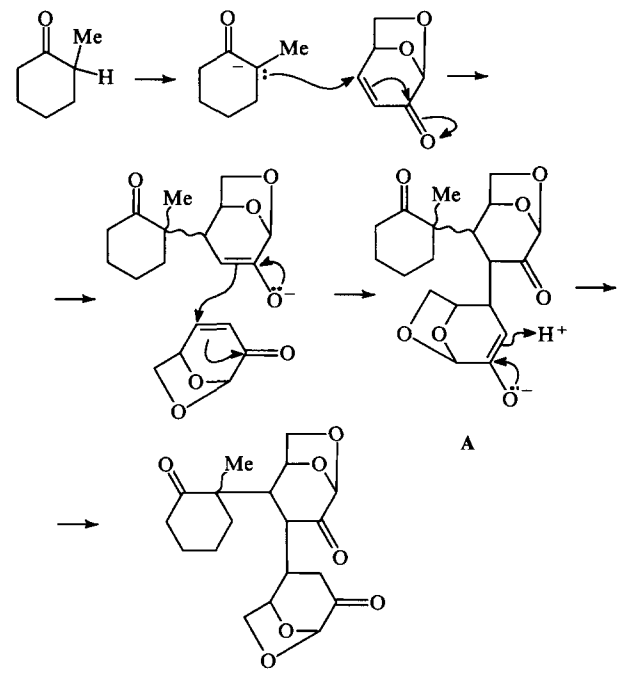


The mechanism of formation of the trimer **54** involves the condensation of three levoglucosenone molecules. The intramolecular condensation of the α-keto-stabilised carbanion **56** with a molecule of compound **1** is then accompanied by intramolecular cyclisation.

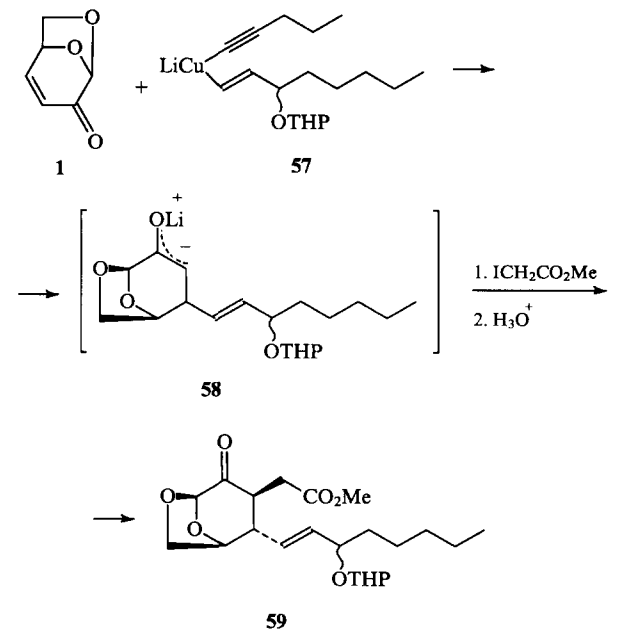


The formation of the alkene trimer **55** from compound **1** in aqueous triethylamine proceeds mainly via a similar mechanism. The crystal structures of the cyclic levoglucosenone trimers have been confirmed by X-ray diffraction.[33]

The Michael additions of diethyl malonate, ethyl cyanoacetate, 2-nitropropane, and 2-methylcyclohexanone to levoglucosenone using various catalysts have also been investigated.[34] The reaction of levoglucosenone with 2-methylcyclohexanone was carried out in *tert*-butyl alcohol in the presence of equimolar amounts of potassium *tert*-butoxide. The structure **A** was attributed to the product on the basis of spectroscopic data.

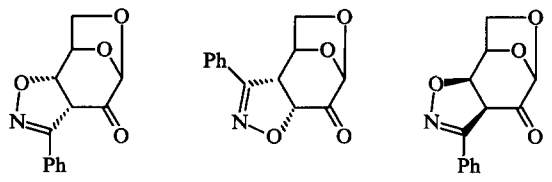


In order to obtain thromboxane-like structures, a study was made[35] of the coupled 1,4-addition of the racemic cuprate reagent **57** to levoglucosenone with subsequent alkylation of the intermediate enolate **58** by ethyl iodoacetate. The 'triple convergent coupling' sequence achieved ultimately led to compound **59** in 35% yield.

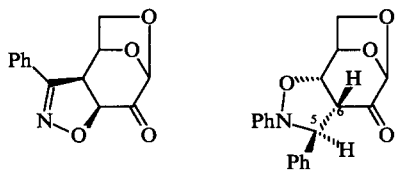


3. 1,3-Dipolar cycloaddition reactions

Levoglucosenone readily enters into cycloaddition reactions with benzonitrile oxide ($PhC{\equiv}N^{+}-O^{-}$) and with *C*,*N*-diphenylnitrone [$PhCH=N^{+}(Ph)-O^{-}$].[36] It was shown that, of the four possible adducts of levoglucosenone with benzonitrile oxide (the two *endo*-isomers **60** and **61** obtained when 1,3-dipolarophile is attacked from the side opposite to that of the 1,6-anhydro-bridge and the two alternative *exo*-isomers **62** and **63**), the *endo*-adduct **60** (yield 71%) and trace amounts (0.6%) of the *exo*-isomer **62** are formed.



60 61 62



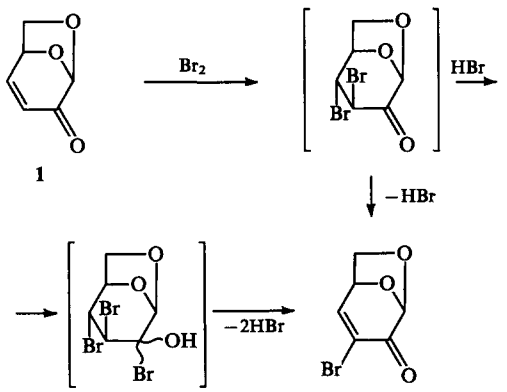
63 64

In the case of the *C,N*-diphenylnitrone, there is a possibility of the formation of eight adducts: the *exo*- and *endo*-isomers for each pair of regioisomers. However, refluxing of levoglucosenone with *C,N*-diphenylnitrone in toluene afforded only one 1 : 1 adduct in 68% yield. The absence of an appreciable Overhauser effect (< 2%) between the H(5) and H(6) protons is evidence in support of the *endo*-structure **64**, which was subsequently confirmed by X-ray diffraction. Thus the reaction also proved to be regio- and stereo-specific.

4. Bromination of levoglucosenone

The crystalline monobromo-derivative **65**, characterised by spectroscopic methods, has been obtained by brominating levoglucosenone with two equivalents of Br_2 in $CHCl_3$ and the subsequent removal of excess bromine by washing the organic phase with sodium hydroxide.[37]

The change in the type of treatment, i.e. the removal of the excess bromine by evacuation at 20 °C, led to the unstable crystalline tribromo-derivative **66**. In all probability, this anomalous course of the reaction is caused either by the presence in the reaction mass of HBr, formed owing to the presence of moisture in bromine, or by the radical reaction between bromine and chloroform. On heating in the solution, compound **66** splits off two HBr molecules, affording 3-bromolevoglucosenone **65**.

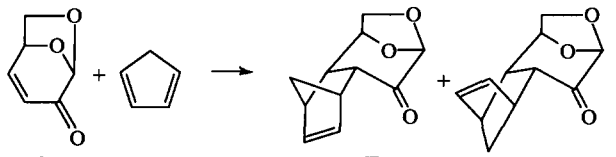


1 66 65

5. Levoglucosenone in the Diels–Alder reaction

The Diels–Alder reaction of levoglucosenone with cyclopentadiene, carried out in an excess of boiling dicyclopentadiene, affords a 47.8% yield of the crystalline adduct **67** and insignificant amounts of an unidentified carbohydrate.[38] Other investigators[39,40] carried out the reaction in boiling chlorobenzene and isolated the syrupy isomer **68** (in 16.5% yield) in addition to the crystalline compound **67** (in 65% yield).

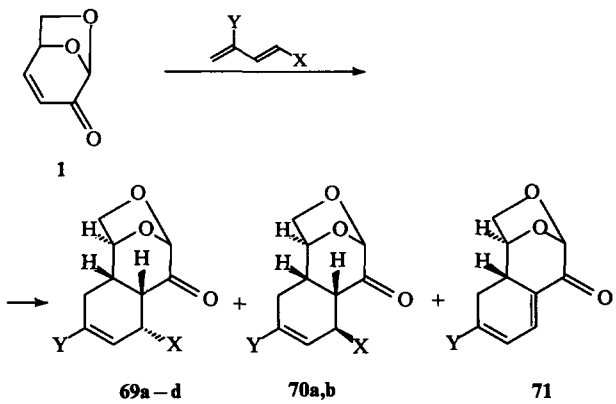
The structure of the adducts follows from spectroscopic data. Thus the absence of an appreciable interaction between H(4) and H(5) indicated by the ^1H NMR spectra of compounds **67** and **68** is evidence that these protons are diequatorial (the β-D-*ribo*-configuration) and that both adducts are formed when the diene is attacked 'from below'. The main adduct **67** is an *endo*-alkene (established with the aid of X-ray diffraction of the transformed product), while the minor adduct **68** is an *exo*-alkene (the configuration relative to the norbornene fragment is indicated).



1 67 68

The $ZnCl_2$-catalysed low-temperature Diels–Alder reaction of the above components, which makes it possible to obtain compound **67** in 75% yield without an admixture of the second isomer, is preparatively preferable.[41]

Subsequently various derivatives of cyclopentadiene, buta-1,3-diene, hexa-1,3-diene, and furan were tried as the diene component in the [4 + 2]-cycloaddition reactions of levoglucosenone.[38–40,42] In particular, in connection with the development of approaches to the synthesis of the indole alkaloid reserpine,[42] a study was made of the reaction of levoglucosenone with substituted buta-1,3-dienes. Unsubstituted buta-1,3-diene afforded a 98% yield of the adduct **69a**. In the case of 1-acetoxybuta-1,3-diene, the product of the elimination reaction **71** was formed together with the main product **69b** (in proportions of 3 : 1), whilst prolonged heating led to compound **71** as the only product formed in a quantitative yield. The reaction of levoglucosenone with 1-trimethylsiloxybuta-1,3-diene led to the formation of a mixture of the *endo*- and *exo*-adducts **69** and **70** in proportions of 2 : 1 in a 91% overall yield. the introduction of 5-benzyloxy-2-methoxypenta-1,3-diene, necessary for the formation of the basic reserpine synthons, into the reaction led to a stereoisomeric mixture of products in an overall yield of 38%.



1 69a–d 70a,b 71

Y = H: X = H (**a**), OAc (**b**), $OSiMe_3$ (**c**); Y = OMe, X = CH_2OCH_2Ph (**d**).

Y = H, X = $OSiMe_3$ (**a**); Y = OMe, X = CH_2OCH_2Ph (**b**)

Y = H, X = OAc (**a**); Y = OMe, X = CH_2OCH_2Ph (**b**).

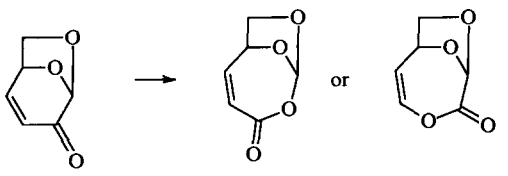
X	Y	Product ratios			Yield (%)
		69	**70**	**71**	
H	H	1	0	0	98
OAc	H	3	0	1	83
OAc	H	0	0	1	100
$OSiMe_3$	H	2	1	0	91
CH_2OCH_2Ph	OMe	1	1	1	38

6. The oxidation reactions of levoglucosenone and some of its derivatives

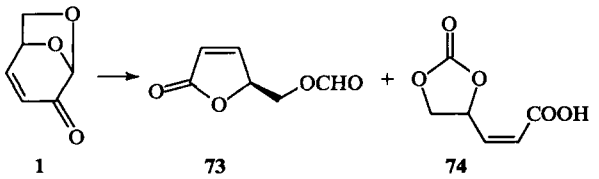
The unsaturated γ-lactone (*S*)-5-hydroxypent-2-en-4-olide **72**, containing one chiral centre, has found extensive applications in the manufacture of various medicinal drugs (burseran and isostegan), the antibiotic lasalocid A,[43] pheromones, aromatisers for whisky and cognac,[44] and also preparations suppressing the growth of the AIDS virus.[45]

In contrast to the approaches to the synthesis of the lactones **72** proposed previously and based on expensive and multistage syntheses using D-ribose and L-glutamic acid as the starting materials, the method developed by Koshi et al.[46] is extremely convenient and simple. The lactone **72** is obtained in one stage by oxidising levoglucosenone with *m*-chloroperbenzoic acid (MCPBA) by the Baeyer–Villiger method.

Shafizadeh and Furneaux,[17] who investigated the oxidation of levoglucosenone by *m*-chloroperbenzoic acid, demonstrated on the basis of spectroscopic data that the product of this reaction is either compound **A** or compound **B**, the formation of the enol-lactone **B** being most probable.



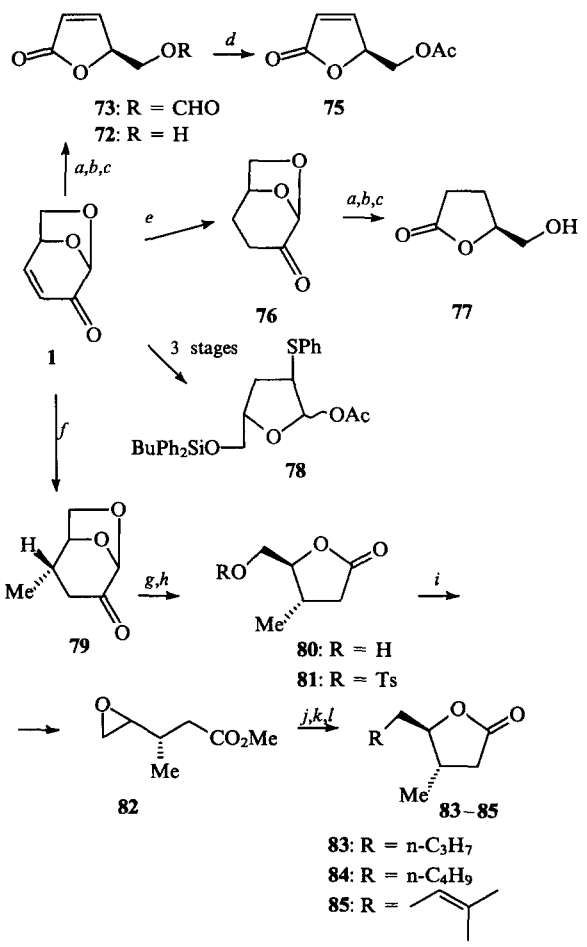
However, a more correct study of the oxidation reaction carried out by Koshi et al.,[46] established that the main reaction product is the formate **73** (yield 59%), while the cyclic carbonate **74** is a side product (yield 16%).



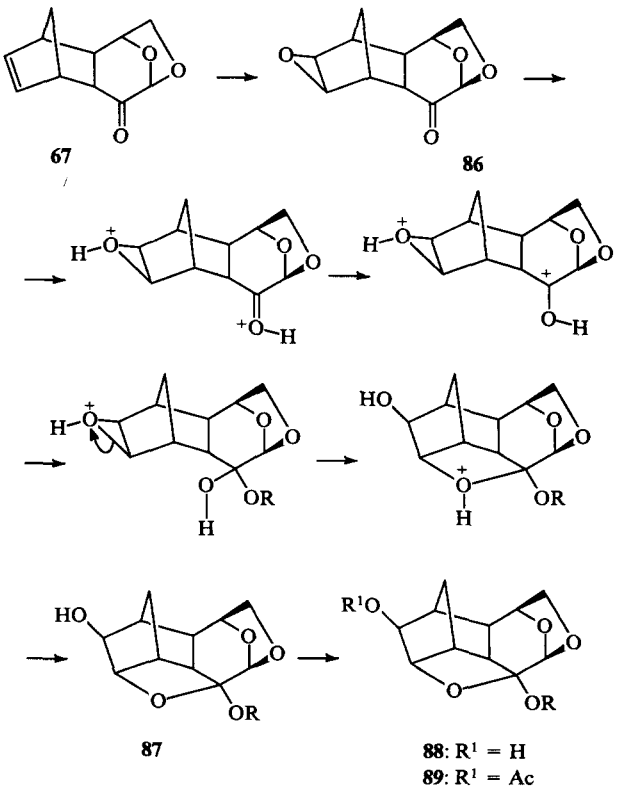
Subsequently peracetic acid was used to avoid oxidative rearrangements as side processes. After methanolysis and acetylation, the acetate **75** was synthesised as a result in 65% yield relative to levoglucosenone. (*S*)-5-Hydroxypentan-4-olide **77**[46,47] as well as 2-α-phenylthio-2,3-dideoxyribose **78** were obtained similarly from dihydrolevoglucosenone **76**.[48]

3,4-Dibsubstituted γ-lactones have been synthesised by the same procedure.[44] The methyl ketone **79** was oxidised to the lactone **80** and tosylated, the key epoxide **82** being obtained after the treatment of the tosylate **81** with alkali. The regioselective opening of the epoxide ring in compound **82** by means of appropriate cuprate reagents led to the 4-substituted γ-lactones **83**–**85**.

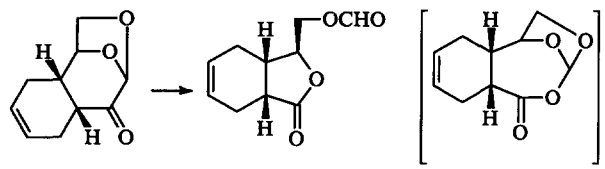
The oxidation of the principal cyclic [4 + 2]-adduct of levoglucosenone and cyclopentadiene **67** by *m*-chloroperbenzoic acid has been investigated.[43] The reaction afforded the *exo*-epoxide **86** in 86% yield. Its stereochemistry was elucidated by means of chemical reactions. Thus the hydrolysis of compound **86** does not entail the formation of a nonclassical ion characteristic of the norbornyl epoxide. Instead intramolecular cyclisation takes place and leads to the pentacyclic product **87**. Chemical proof of the involvement of the carbonyl group at the C(2) atom in the acid-catalysed solvolysis of compound **86** has been obtained by changing the solvent (water replaced by methanol). In order to determine the position of the hydroxy-group, compound **88** was acetylated. The spectra of the resulting acetate **89** indicated unambiguously that the hydroxy-group is at the C(9) atom while the methoxy-group is at the C(2) atom in compound **88**.



(*a*) AcOOH, AcOH; (*b*) Me_2S; (*c*) MeOH–HCl, 45 °C; (*d*) AcCl, Py, CH_2Cl_2; (*e*) H_2, Pd/C; (*f*) Me_2CuLi; (*g*) AcOOH, AcOH; (*h*) *p*-TsCl, Py; (*i*) K_2CO_3, MeOH; (*j*) Pr^n_2CuLi; (*k*) Bu^n_2CuLi; (*l*) $Me_2C{=}CHMgBr{-}CuBr$.



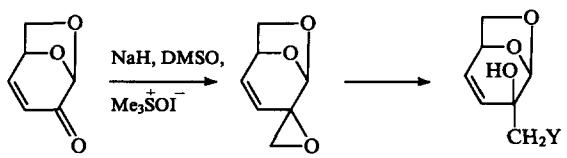
The Baeyer–Villiger oxidation of the tricyclic ketone **69a** afforded a high yield of the formyloxy-γ-lactone **90** with a *cis*-junction.[50] It was postulated that the formation of the formate is associated with the acid-catalysed rearrangement of the intermediate mixed inner orthoester **91**.



69a **90** **91**

7. Reactions involving the keto-group of levoglucosenone

In the course of the nucleophilic attack on the carbonyl group, the 1,6-anhydro-bridge of levoglucosenone exercises steric control, directing the approach of the reagent 'from below' the plane of the pyranose ring. Thus the interaction of the levoglucosenone with Cory's reagent, obtained by the reaction of NaH with $Me_3S^+OI^-$ in dimethyl sulfoxide, afforded a 50% yield of the epoxide **92**, which is obtained exclusively as a result of the *endo*-attack on the bulky reactant from the side of the levoglucosenone less shielded by the 1,6-anhydro-bridge.[51,52]



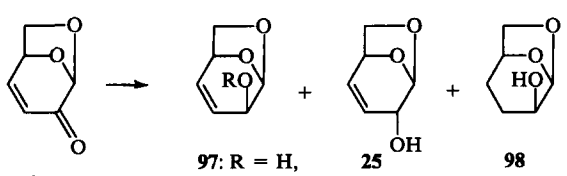
1 **92** **93–96**

Y = OH (**93**), H (**94**), N_3 (**95**), NH_2 (**96**).

Alkaline hydrolysis of the epoxide **92** by aqueous NaOH leads to the crystalline diol **93** in 71% yield. X-Ray diffraction of the specimen confirmed the structure **93** and hence also the structure of the epoxide **92**. Next the derivative **94** was obtained from the epoxide **92** by reduction with $LiAlH_4$, while azidolysis gave rise to the azide **95**, the reduction of which with $LiAlH_4$ led to the crystalline aminoalcohol **96**.

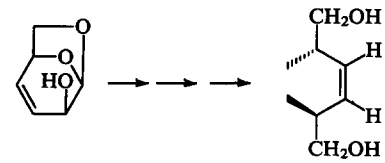
Thus the opening of the ring in the spiroepoxide **92** takes place entirely regiospecifically via an S_N2 mechanism.

It has been shown[13,27,53] that the double bond of levoglucosenone can be selectively hydrogenated. On the other hand, the reduction of the keto-group by $NaBH_4$ affords the allyl alcohols **97** and **25** as the main products, although the formation of minor unsaturated alcohols of type **98** is also possible depending on the reaction conditions.



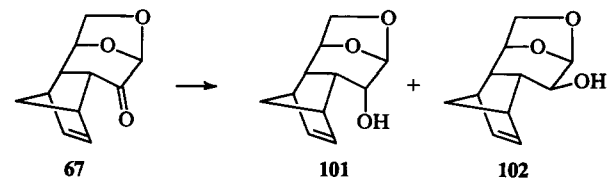
1 **97**: R = H, **99**: R = Ts. **25** **98**

On the basis of preliminary data obtained in Shafizadeh's laboratory,[13] the D-*erythro*-configuration (compound **25**) was attributed incorrectly to the product of the reduction of levoglucosenone by $LiAlH_4$. Subsequently the product was characterised as the D-*threo*-isomer **97** by comparing the alcohol obtained and its tosylate with authentic specimens[53,54] and also by the stereospecific conversion into (*Z*)-3,4-dideoxy-D-*threo*-hex-3-enitol **100**[17] with a known absolute configuration.

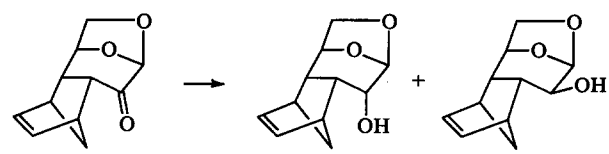


97 **100**

The reduction of the adduct **67** by sodium tetrahydroborate in 95% ethanol at 25 °C led to a mixture of the *endo*-alcohol **101** and the *exo*-alcohol **102** in 53% and 39% yields respectively.



67 **101** **102**



68 **103** **104**

Similarly the reduction of the minor adduct **68** with $NaBH_4$ afforded a mixture of the *exo*-alcohol **103** (yield 74%) and the less polar *endo*-alcohol **104** (yield 22%), the structures of which were established by spectroscopic methods. Axial attack on the *endo*-alkene **67** by the BH_4^- anion is more difficult, since in this case the carbonyl group occupies the *syn*-position relative to the bicyclo[2.2.1]hept-2-ene system.

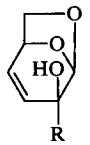
It had been reported earlier[13] that 1,2-adducts were obtained by the reaction of levoglucosenone with methylmagnesium iodide: 1,6-anhydro-3,4-dideoxy-2-*C*-methyl-β-D-*erythro*-hex-3-enopyranose **105** in 56% yield, its C(2)-epimer (1,6-anhydro-3,4-dideoxy-2-*C*-methyl-β-D-*threo*-hex-3-enopyranose **106**) in 6% yield, and the 1,4-adduct (1,6-anhydro-3,4-dideoxy-4-*C*-methyl-β-D-*erythro*-hexopyranos-2-ylose **79**) in 6% yield. When the reaction was carried out in the presence of Bu_3PCuI at −78 °C, the 1,4-adduct **79** was formed exclusively. The small spin–spin coupling constant between the H(4) and H(5) atoms obtained from the ^1H NMR spectrum of the adduct **79** indicated the *erythro*-configuration of the chiral centres. However, subsequently this claim was recognised as erroneous and, by analogy with the hydride reduction reaction, the D-*threo*-configuration was assigned to the main product of the Grignard reaction of levoglucosenone with methylmagnesium iodide.[17]



105: R^1 = Me, R^2 = OH. **106**: R^1 = OH, R^2 = Me. **79**

In order to attach long hydrocarbon chains, the reactions of levoglucosenone with tetradecyl- and octadecyl-magnesium bromides were carried out. Despite the fact that the target products **107** and **108** were obtained in 20% and 11% yields, the main products proved to be higher hydrocarbons formed via the

Wurtz reaction; the replacement of the Grignard reagent by alkyllithium reagents in order to suppress side reactions did not lead to the desired results.



107: R = $(CH_2)_{13}CH_3$;
108: R = $(CH_2)_{17}CH_3$.

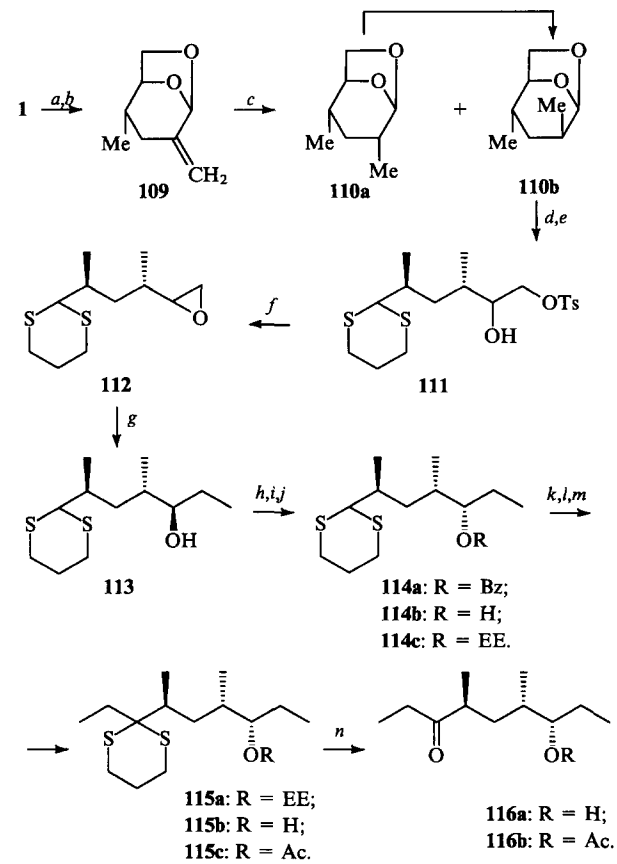
V. The use of levoglucosenone in the synthesis of natural products

The employment of sugars in the total syntheses of natural products has attracted the attention of investigators by the ready availability of the starting material with chiral centres and the universality of the approach, which are ensured by the diversity of the monomeric carbohydrates with a known configuration of the chiral centres. In contrast to other monosaccharides, levoglucosenone, which is a 1,6-anhydro-sugar, has a greater synthetic potential in view of its unusual structure and the conformational rigidity of the molecule. The characteristic features and advantages of levoglucosenone, noted in the Introduction and in the previous sections, were subsequently demonstrated on specific examples.

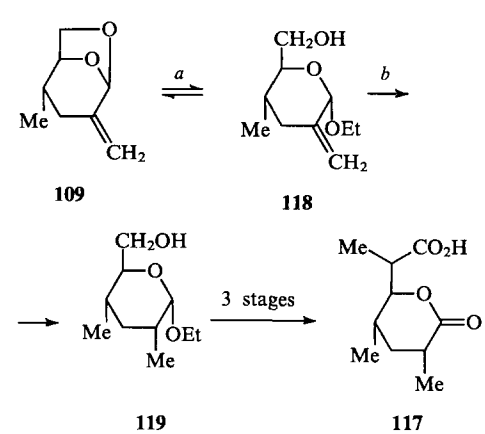
The stereoselective synthesis of serricornine, which is a sex pheromone of the tobacco beetle (*Lasioderma serricorne*—a pest on tobacco leaves), has been described.[55] Levoglucosenone was used as the starting material, its 1,6-anhydro bridge controlling unambiguously the stereoselective introduction of the methyl group at the C(4) atom. After the methylenation of the keto-group and hydrogenation of compound **109** in the presence of Pd/C, the 2,4-dimethyl derivatives **110a** and **110b** were obtained in proportions of 4:1. Compound **110b** (95% diastereoisomeric purity) was converted into the dithiane **111** and was then tosylated and the epoxide **112** was obtained after treatment with alkali. The epoxide reacted smoothly with 5 equiv. of Me_2CuLi in diethyl ether, affording the alcohol **113**. In order to obtain the alcohol having the desired configuration, Mitsunoba's method was used, the benzoate **114a** being hydrolysed to the alcohol **114b**. Compound **114b** was converted into acetylserricornine **116b** by a standard procedure: via stages involving the alkylation of dithiane, the replacement of the protecting group, and the hydrolysis of the dithiane **115c** with the aid of the $HgCl_2-CaCO_3$–aqueous MeCN system. The deacylated product **116a** exhibited the expected biological activity.

The *exo*-methylene derivative **109** proved to be a convenient starting material in the synthesis of the chiral synthon for the Prelog–Djerassi lactonoacid **117**.[56] Heating of the allyl glycoside **109** with trifluoroacetic acid in ethanol afforded an equilibrium mixture of compound **109** and the transglycosylation product **118**, isolated chromatographically. The stereoselective hydrogenation of the α-anomer **118** on a platinum catalyst led to ethyl 2,3,4-trideoxy-2,4-dimethyl-α-*ribo*-hexopyranoside **119** and its C(2) epimer in proportions of 6:1. Spectroscopic data confirmed the identity of compound **119** and of the key intermediate used in the synthesis of the Prelog–Djerassi lactonoacid. The method proposed makes it possible to reduce significantly the number of stages in the synthesis of the target lactone.

Pyranonaphthoquinones are compounds containing the naphtho[2,3-*c*]pyran ring system, which exhibit fungicidal, antibacterial, and anticancer activities. The fungal metabolite nanomycin A, altersolanol A, and the anthracycline antibiotic β-rhodomycinone are the best known representatives of these compounds.

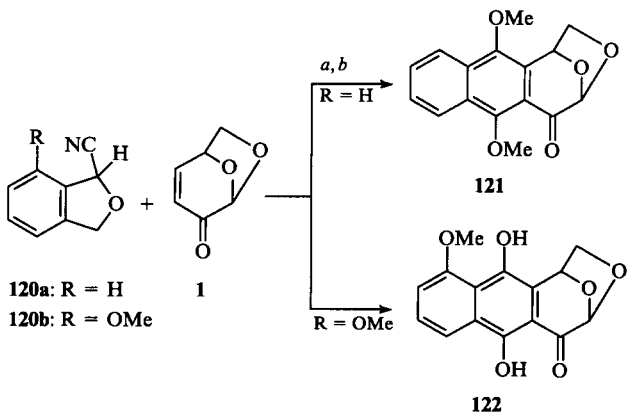


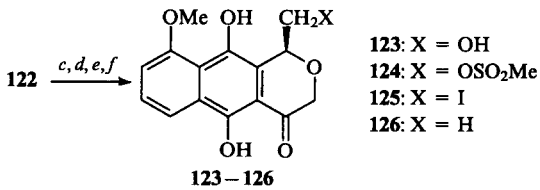
(*a*) Me_2CuLi, Et_2O; (*b*) Ph_3PCH_2, Et_2O; (*c*) H_2, Pd/C; (*d*) $HS(CH_2)_3SH$, $BF_3.Et_2O$, CH_2Cl_2; (*e*) *p*-TsCl, Py; (*f*) KOH, MeOH; (*g*) Me_2CuLi, Et_2O; (*h*) Ph_3P, BzOH, Et_2O; (*i*) KOH, MeOH; (*j*) EVE (EtOCH=CH_2), *p*-TsOH, CH_2Cl_2; (*k*) BuLi, TMEDA ($Me_2NCH_2CH_2NMe_2$), THF–EtI; (*l*) *p*-TsOH, EtOH; (*m*) Ac_2O, Py; (*n*) $HgCl_2$, $CaCO_3$, MeCN.



(*a*) 0.5% CF_3COOH–EtOH, 50 °C; (*b*) H_2, PtO_2, Et_2O.

The development of a new method for the construction of the rings of the naphthopyran ring system, which constitutes the central component of the above antibiotics, has been reported.[57] Levoglucosenone, which has the same stereochemistry as the dihydropyran fragments of the above antibiotics, was condensed with cyanotetrahydroisobenzofuran **120a**, affording an unstable naphthohydroquinone derivative, which was converted by methylation into compound **121** in 40% yield.





(*a*) $MeSCH_2Li$; (*b*) $Me_2SO_4.OH^-$; (*c*) Zn–Cu; (*d*) $MeSO_2Cl$; (*e*) NaI; (*f*) Zn–Cu.

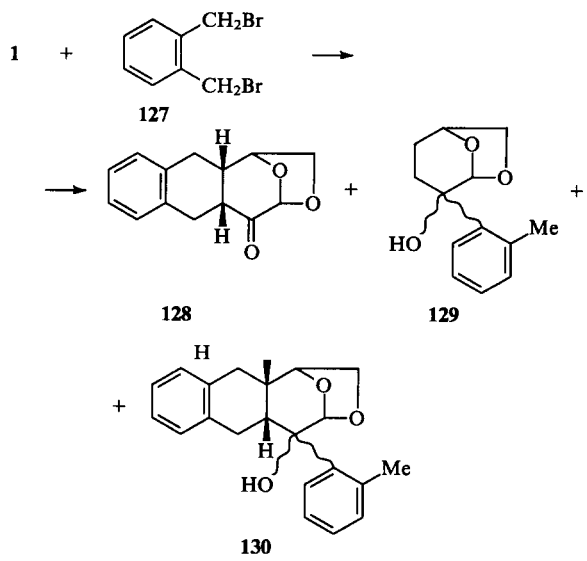
On the other hand, the reaction of compound **120b** with levoglucosenone gave rise to the stable crystalline naphthohydroquinone **122** in 65% yield. Its ring was subjected to reductive opening by the Zn–Cu couple in tetrahydrofuran. Having synthesised the chiral unit **123**, it was possible to construct in two stages the ring system of naphtho[2,3-*c*]pyran-5,10-quinones.

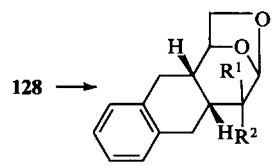
After several unsuccessful attempts to remove the primary hydroxy-group from compound **123**, the latter was converted via the methanesulfonate **124** into the iodide **125** and the required compound **126** was obtained by treatment with the Zn–Cu couple in moist THF. It is also noteworthy that the attachment of the lactone ring opened an easy route to calafungin, while the synthesis of the enantiomers **123–126** provided a short pathway to intermediates for the synthesis of nanomycin and its analogues. Overall, the sequence of reactions described above constitutes a promising method of synthesis of a series of substituted derivatives **123–126**, the hydroxyphthalides required for the synthesis of compound **120** being readily available.

It has been observed [57,58] that the interaction of levoglucosenone with the dibromo-derivative **127** in 1,4-dioxane in the presence of zinc powder in an ultrasonic bath affords compounds **128–130** in 53%, 3%, and 14% yields respectively.

The ^1H and ^{13}C NMR spectra of the main product **128** agree with the structure ascribed to it. The reduction of the ketone **128** with sodium tetrahydroborate leads to the epimeric alcohols **131** and **132**, which were isolated in 35% and 50% yields respectively. They were characterised as the acetates **133** and **134**; the H(4) and H(4a) atoms in compounds **131** and **133** are axial (according to ^1H NMR data), so that the compounds have the D-*altro*-configuration established by the *exo*-addition of the reagent to the double bond.

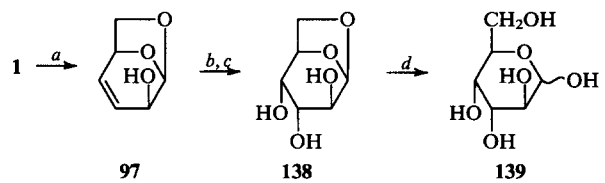
Compound **128** — a potential synthetic precursor of a series of representatives of pyranonaphthoquinone antibiotics — has been obtained by the Barton deoxygenation via the alcohols **131** and **132** and their thionocarbonates **135** and **136**. The side products **129** and **130** are believed tentatively to be formed from compound **127** via the Reformatskii reaction with participation of an organozinc intermediate, which attacks the carbonyl groups of the main product and levoglucosenone.





D-Altrose **139** is a rare sugar, for the preparation of which there is no readily available natural raw material. All the known syntheses of this compound consist of many stages. The method of synthesis of D-altrose via D-altrosan — 1,6-anhydro-β-D-altropyranose **138** — proposed by Chew and Ferrier [59] includes three stages and the overall yield is 29.1%.

1,6-Anhydro-3,4-dideoxy-β-D-*threo*-hex-3-enopyranose **97** has been synthesised from levoglucosenone by reduction using a standard method. [60] The *cis*-dihydroxylation of the double bond of the pyranose **97** by the OsO_4–*N*-methyl-morpholine *N*-oxide system proceeds stereoselectively, affording D-altrosan **138** in 86% yield; when stoichiometric amounts of $KMnO_4$ were used for the oxidation, the yield of the triol **138** was only 32.7%. Acid hydrolysis of compound **138** leads to D-altrose **139**.



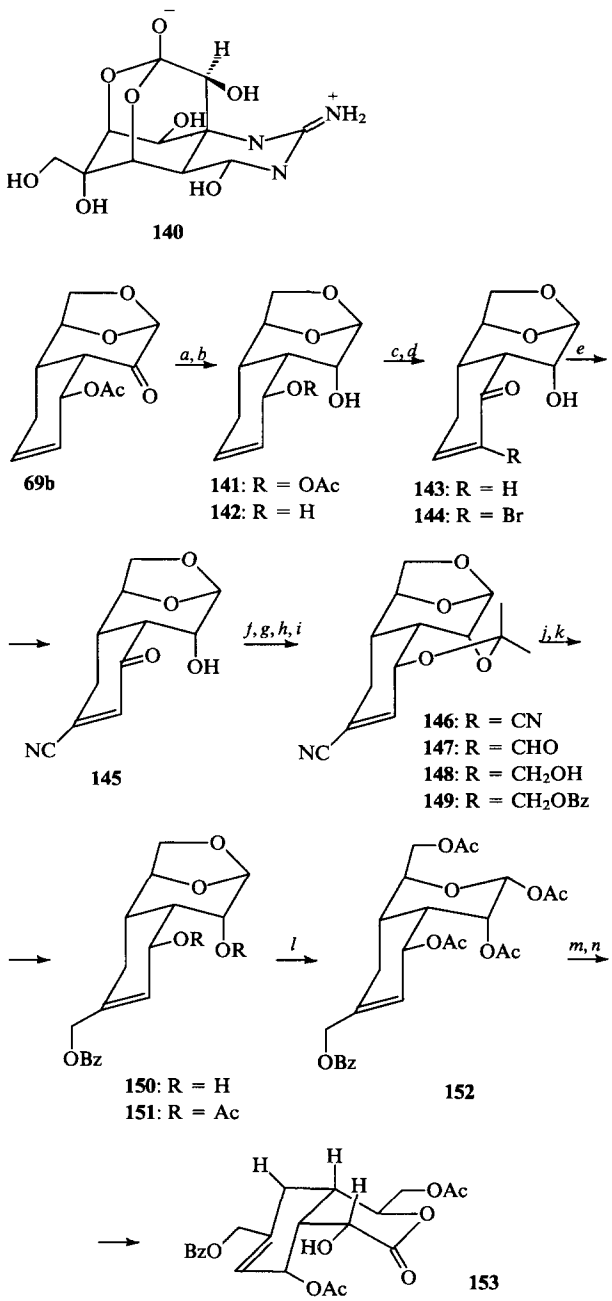
(*a*) $LiAlH_4$; (*b*) OsO_4–*N*-methylmorpholine *N*-oxide, Me_2CO, H_2O; (*c*) Na_2SO_3; (*d*) HCl–1,4-dioxane.

The same investigators obtained D-allosan and D-allose in six stages from levoglucosenone in 45% and 30% yields respectively. [61,62]

The key aspect of the approach to the synthesis of tetrodotoxin **140**, one of the best known of the food toxins, is the stage involving formation of the structure of the chiral cyclohexane via cycloaddition of acetoxybutadiene to the chiral dienophile — levoglucosenone. [63]

For this purpose, adduct **69b** was transformed into enone **143** via compounds **141** and **142**. The bromo-derivative **144** was obtained from the enone **143** by reaction with 1 equiv. of bromine in dichloromethane and subsequent treatment with triethylamine.

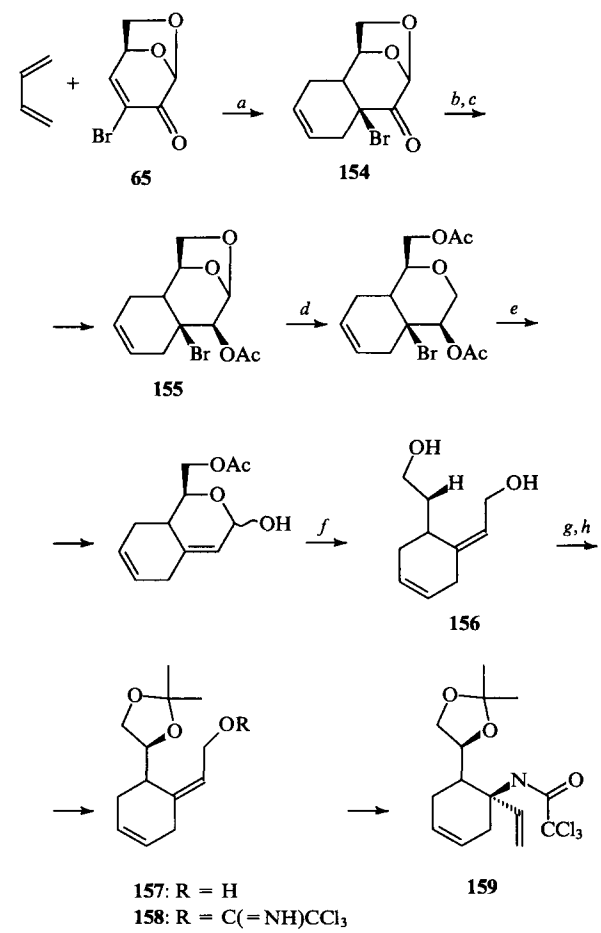
The addition of 2 equiv. of KCN at room temperature in the presence of ammonium chloride to the bromo-derivative **144** afforded the crystalline compound **145**. The reduction of the keto-group in compound **145** with sodium tetrahydroborate and protection of the diol group by 2,2-dimethoxypropane in camphorsulfonic acid (CSA) led to the acetonide **146**. Next followed the two-stage reduction of the nitrile group to the hydroxymethyl group via the aldehyde **147**. The alcohol **148** obtained was converted into the benzoate **149** and after acid hydrolysis the diacetate **151** was obtained from the diol **150**. The tricyclic compound **151** was solvolysed in the trifluoroacetic acid–acetic anhydride system. The yield of compound **152** was 96%.



(*a*) $NaBH_4$; (*b*) NaOMe; (*c*) MnO_2; (*d*) Br_2, CH_2Cl_2, Et_3N; (*e*) KCN–NH_4Cl; (*f*) $NaBH_4$, $Me_2C(OMe)_2$, CSA; (*g*) Bu^i_2AlH (DIBAL-H); (*h*) $LiAlH_4$; (*i*) BzCl–Py; (*j*) AcOH–THF–H_2O; (*k*) Ac_2O–Py; (*l*) Ac_2O–CF_3COOH; (*m*) $NH_2NH_2 \cdot H_2O$–DMF; (*n*) Jones reagent.

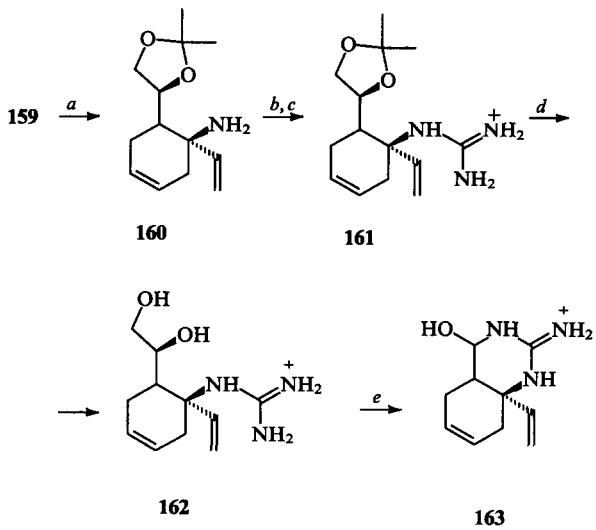
Acid hydrolysis of the anomeric acetate gave rise to the corresponding hemiacetal in a maximum yield of 70%, but this was accompanied by the formation of a side product. The hydrolytic stage was optimised by employing hydrazine (1.2 equiv. of $NH_2NH_2.H_2O$ in DMF at 60 °C). Oxidation of the hemiacetal by the Jones reagent completes the stage involving the formation of the cyclohexane unit **153**, into which suitable functional groups have been introduced.

The guanidine-containing part of tetrodotoxin was synthesised from the bromoketone **154**.[64] By opening the 1,6-anhydro-bridge and subsequent treatment with $NaBH_4$, the bromohydrin acetate **155** was transformed into the triol **156** and further into the *exo*-allyl alcohol **157**. The latter was treated with trichloroacetonitrile and NaH, the imide **158** formed was heated for 12 h in xylene, and the trichloroamidate **159** was obtained as a result of the successful Overman rearrangement.



(*a*) 110 °C, 12 h; (*b*) $NaBH_4$–MeOH; (*c*) Ac_2O, Py; (*d*) CF_3COOH, AcOH; (*e*) Zn–Cu; (*f*) $LiAlH_4$–THF; (*g*) $Me_2C(OMe)_2$, CSA; (*h*) Cl_3CCN, NaH, Et_2O; (*i*) 110 °C, 12 h.

The subsequent stages involved the hydrolysis of the trichloroacetamide group of compound **159** and the successive treatment of the amine **160** with bromocyanogen and ammonia, which led to the formation of the guanidine **161**. Next the acetonide protecting group was hydrolysed with trifluoroacetic acid, the glycol **162** was cleaved with periodic acid, and the guanidine derivative **163** was obtained in a satisfactory yield. Thus the optically active model tetrodoxin units **153** and **163** were synthesised from levoglucosenone.

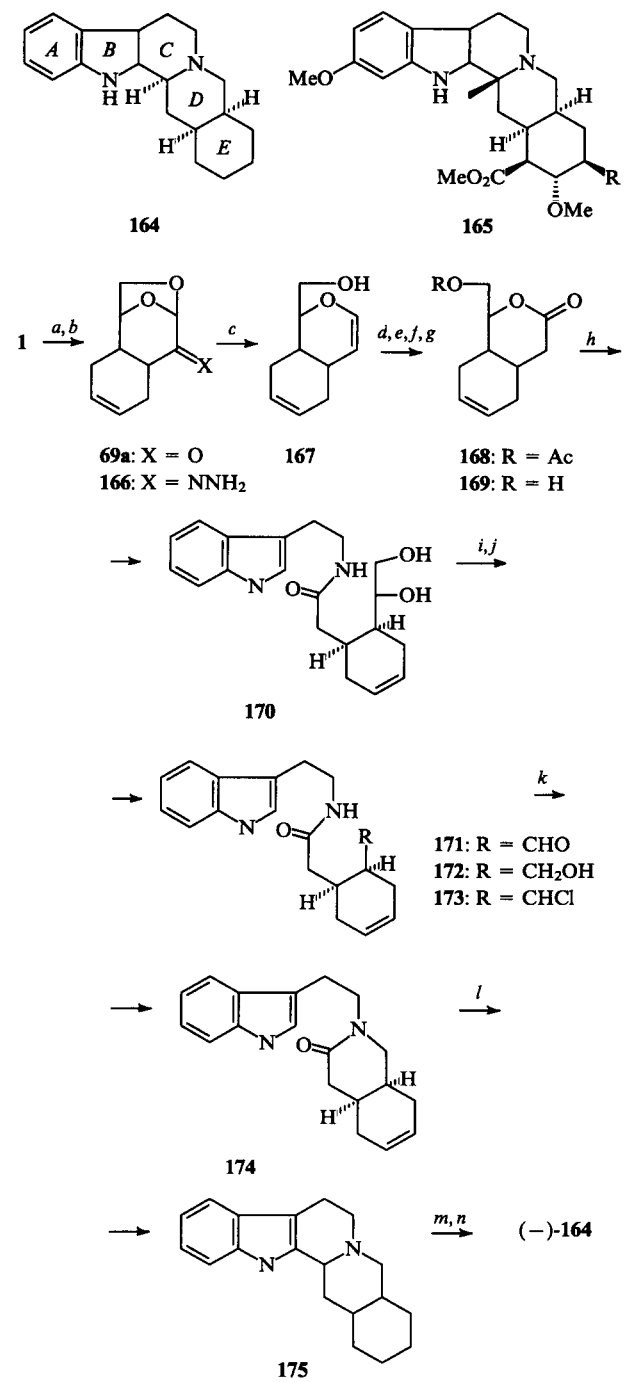


(*a*) KOH, EtOH, 50 °C; (*b*) BrCN–$NaHCO_3$; (*c*) NH_3, 100 °C; (*d*) CF_3COOH; (*e*) HIO_4.

The syntheses of the related optically active alkaloids alloyohimbane **164** and reserpine **165** from levoglucosenone have been described.[65] The crystalline Diels–Alder adduct of levoglucosenone with buta-1,3-diene **69a** was converted into the hydrazone **166**, the treatment of which with NaH in dimethyl sulfoxide (DMSO) afforded the vinyl ether **167**. Next followed stages involving acetylation, hydrolysis, and oxidation with the Jones reagent. The lactone **168** obtained was treated with MeONa in MeOH and compound **169** was heated with three equivalents of tryptamine in a 6:11 tetrahydrofuran–ethyldiisopropyl amine mixture. The glycol **170** produced was cleaved with HIO_4 to the aldehyde **171**. The reduction of the latter with $NaBH_4$ in methanol afforded the amidoalcohol **172**. The alcohol **172** was then converted by standard methods into the chloro-derivative **173**. Since compound **173** proved to be unstable, it was rapidly introduced into the reaction with lithium bis(trimethylsilyl)amide and the lactone **174** was obtained. In the concluding stage, cyclisation was achieved by heating compound **174** with $POCl_3$ and reduction of compound **175** with tetrahydroborate led to the target compound **164**.

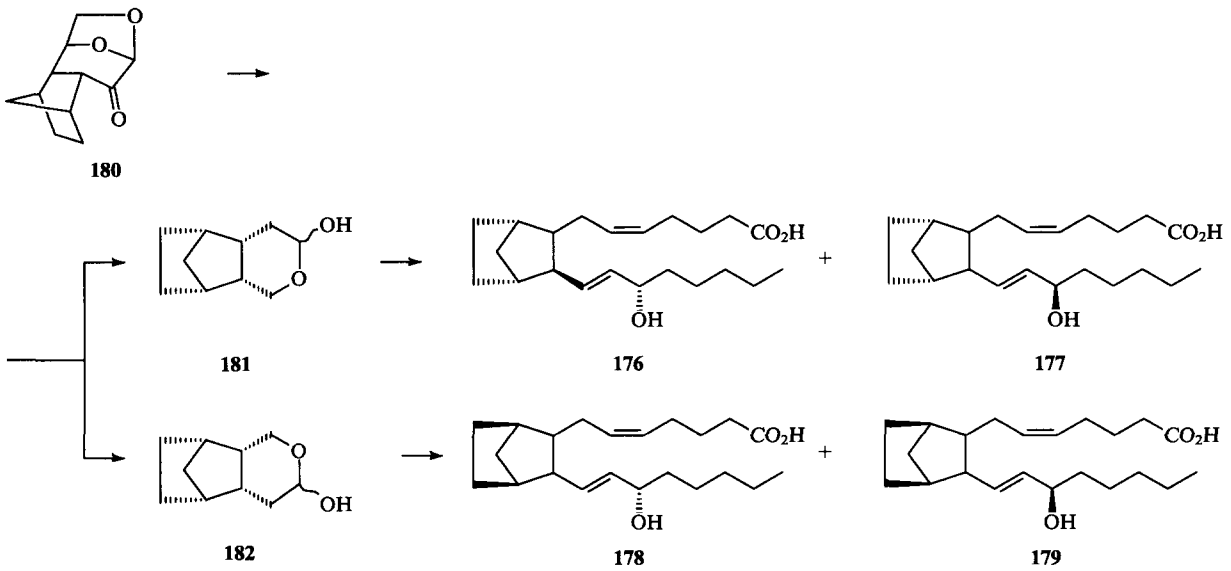
The enantiodivergent approach to the synthesis of the 9,11-ethano-analogues of the prostaglandin *endo*-peroxides (PGH_2) **176–179**, developed on the basis of the single chiral unit **180**, ensures a rational synthesis of the structures of both key enantiomeric precursors of the target compounds — the lactols **181** and **182** (see Scheme 1).[66,67]

The synthesis of nat-9,11-ethano-PGH_2 **176** and of its (15*R*)-diastereoisomer **177** is presented in Scheme 2. As can be seen from the latter, the transition **180** → **181** requires deoxygenation at the C(1) atom and the cleavage of the C(8)–C(9) bond in compound **180**. For this purpose, the ketone **180** was introduced into the Baeyer–Villiger reaction and the intermediate formate **183** was obtained in a high yield. It was hydrolysed to the alcohol **184**. The subsequent methanesulfonation, bromination (giving rise to compounds **185** and **186**), and then dehydrobromination with zinc



(*a*) $CH_2=CH-CH=CH_2$, 140 °C; (*b*) $NH_2NH_2 \cdot H_2O$, Et_3N; (*c*) NaH, DMSO; (*d*) Ac_2O–Py; (*e*) HCl–THF; (*f*) Jones reagent, 0 °C; (*g*) NaOMe–MeOH; (*h*) tryptamine, Pr^i_2EtN, THF; (*i*) HIO_4; (*j*) $NaBH_4$; (*k*) Ph_3P, CCl_4–LiN(SMe_3); (*l*) $POCl_3$, 100 °C; (*m*) $NaBH_4$; (*n*) H_2, Pd/C.

Scheme 1

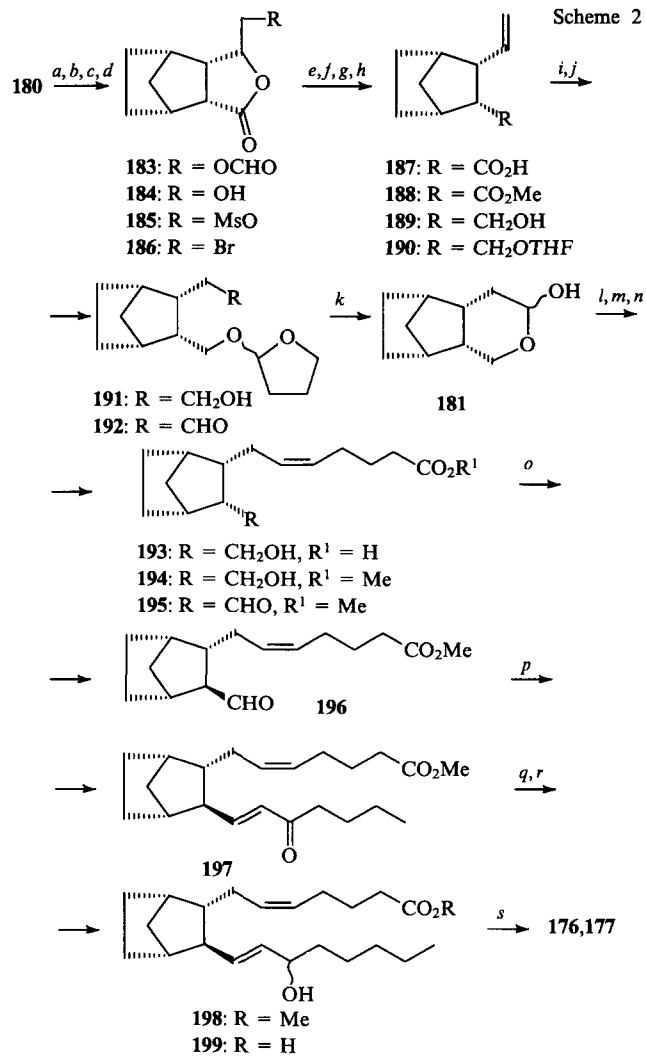


in Pr^iOH-H_2O led to the acid **187**. The latter was converted into the methyl ester **188** and treated with $LiAlH_4$ to form the alcohol **189**. After blocking the hydroxy-group in compound **189** by formation of the tetrahydrofuryl ether, the terminal double bond in compound **190** was functionalised with the aid of 9-borabicyclo[3.3.1]nonane (9-BBN) and the resulting diastereoisomeric mixture of alcohols **191** was oxidised with the Collins reagent and the acetal **192** was deblocked to form the lactol **181**. In view of its lability, the lactol **181** was converted, without purification, into an alkene by treatment with a phosphorane reagent and the alkene **193** was converted into the stable hydroxyacid **194** [the content of the 2'-(*Z*)-isomer was ~95%]. After methylation and oxidation by the P_2O_5-DMSO system, the hydroxyacid **194** afforded the *cis*-aldehyde **195**, which isomerises smoothly to the *exo*-aldehyde **196** on refluxing in toluene containing 1,5-diazabicyclo-[5.4.0]-undec-5-ene (DBU). Next the enone **197** was synthesised by the reaction of the aldehyde **196** with dimethyl 2-oxoheptylphosphonate under the conditions of the Wittig–Horner reaction. In the concluding stages, tetrahydroborate reduction of the enone **197** and hydrolysis of the ester **198** afforded a mixture of the 15α,β-epimeric alcohols **199** in proportions of ~1 : 1, which were separated by high performance liquid chromatography (HPLC).

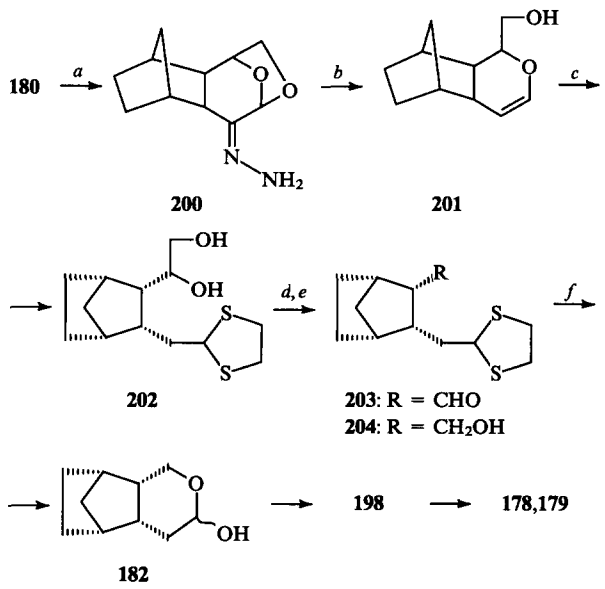
The synthesis of ent-9,11-ethano-PGH_2 **178** and of its (15*S*)-diastereoisomer **179** requires the C(8)-deoxygenation of the ketone **180**, which was achieved by the Huang–Minlon method. The conversion of the ketone **180** into the hydrazone **200** and then into the unsaturated ether **201** was achieved with an overall yield of 50% (see over). The following stages involved the conversion of compound **201** into the dithioacetal **202**, the cleavage of its diol group by $Pb(OAc)_4$, the reduction of the resulting *cis*-aldehyde **204** with sodium tetrahydroborate, and the Hg^{2+}-induced hydrolysis of the mercaptal **204** to the lactol **182**, which was transformed into the enone ent-**198** and further into substances of the ent-series **178** and **179**, as had been done in the case of compound **181**.

Thus the data presented demonstrate the extensive possibilities for the employment of levoglucosenone as a chiral precursor in the complex stereospecific synthesis of natural products and their analogues.

Scheme 2



(*a*) AcO_2H, $AcOH-H_2O$; (*b*) $MeOH-MeONa$; (*c*) $MsCl-NEt_3$, CH_2Cl_2; (*d*) $LiBr-Me_2CO$; (*e*) Zn, Pr^iOH-H_2O, ultrasound; (*f*) CH_2N_2; (*g*) $LiAlH_4$; (*h*) THF, H^+; (*i*) 1.1 equiv. of 9-BBN, H_2O_2-NaOH; (*j*) $CrO_3 \cdot 2Py$; (*k*) 10% HCl–dioxane; (*l*) $Ph_3P=CH(CH_2)_3CO_2Na$; (*m*) CH_2N_2; (*n*) P_2O_5– DMSO, CH_2Cl_2; (*o*) PhMe, 10% DBU, Δ; (*p*) $(MeO)_2POCH_2COC_5H_{11}$, 50% $NaOH-CH_2Cl_2$, $BnNEt_3Cl-Cat$; (*q*) $NaBH_4$, MeOH; (*r*) NaOH, $MeOH-H_2O$; (*s*) HPLC.



(*a*) NH_2NH_2. H_2O, 95 % Et_3N; (*b*) KOH–HOCH=CHOH; (*c*) $HSCH_2$.CH_2SH, BF_3.Et_2O; (*d*) $Pb(OAc)_4$, CH_2Cl_2, −40 °C; (*e*) $NaBH_4$, MeOH; (*f*) HgO–BF_3.Et_2O, THF.

References

1. Y Tsuchiya, K Sumi *J. Appl. Polym. Sci.* **14** 2003 (1970)
2. L K M Lam, D P C Fung, I Tsuchiya, K Sumi *J. Appl. Polym. Sci.* **17** 391 (1973)
3. A E Lipsca, G E McCasland *J. Appl. Polym. Sci.* **150** 419 (1976)
4. Y Halpern, R Riffer, A Broido *J. Org. Chem.* **38** 204 (1973)
5. F Shafizadeh, P P S Chin *Carbohydr. Res.* **46** 149 (1976)
6. A Broido, M Evett, C C Hodges *Carbohydr. Res.* **44** 267 (1975)
7. A Ohnishi, K Kato, E Takagi *Polym. J.* 7 431 (1975)
8. US P. 480 107; *Ref. Zh. Khim.* 20 P 14 (1976)
9. F Wodly *J. Appl. Polym. Sci.* **15** 835 (1971)
10. G E Domburg, I Yu Berzinya, I Z Kirshbaum, M P Gavars *Khim. Drev.* **6** 105 (1978)
11. Y Halpern, J P Hoppech *J. Org. Chem.* **50** 1556 (1985)
12. G E Domburg, I Yu Berzinya, Z L Kupche *Khim. Drev.* 3 99 (1980)
13. F Shafizadeh, P P S Chin *Carbohydr. Res.* **58** 79 (1977)
14. F Shafizadeh, P P S Chin *Carbohydr. Res.* **46** 149 (1976)
15. A G Bradbury, F Shafizadeh, R H Furneaux, T G Cochran *J. Appl. Polym. Sci.* **23** 3271 (1979)
16. F Shafizadeh, A G Bradbury *J. Appl. Polym. Sci.* **23** 1431 (1979)
17. F Shafizadeh, R H Furneaux *Carbohydr. Res.* **71** 169 (1979)
18. F Shafizadeh, Y Z Lai, C R McIntyre *J. Appl. Polym. Sci.* **22** 1183 (1978)
19. F Shafizadeh, P P S Chin *Synth. Methods Carbohydr.* **39** 179 (1976)
20. P Köll, J Metzger *Angew. Chem.* **90** 802 (1978)
21. J J Miller, R Saunders *Fuel* **66** 123 (1987)
22. Y Halpern, R Riffer, A Broido *J. Org. Chem.* **38** 204 (1973)
23. R H Furneaux, G J Gainsford *Carbohydr. Res.* **146** 113 (1986)
24. K Kato, H Komorita *Agric. Biol. Chem.* **32** 21 (1968)
25. R H Furneaux, J M Mason, I J Miller *J. Chem. Soc., Perkin Trans. 1* 1923 (1984)
26. M Shibagaki, K Takahashi, H Kuno, I Honda, H Matsushita *Chem. Lett.* 307 (1990)
27. P Köll, T Shultek, R-W Rennecke *Chem. Ber.* **109** 337 (1976)
28. M Cerny, V Gut, J Pacak *Collect. Czech. Chem. Commun.* **26** 2542 (1961)
29. Russian P.1 710 563; *Ref. Zh. Khim.*19 O 115 (1992)
30. A C Forsyth *Tetrahedron Lett.* **30** 993 (1989)
31. M G Essig *Carbohydr. Res.* **156** 225 (1986)
32. F Shafizadeh, R H Furneaux *Carbohydr. Res.* **100** 303 (1982)
33. T T Stevenson, R E Stenkamp, L H Jensen, F Shafizadeh, R H Furneaux *Carbohydr. Res.* **104** 11 (1982)
34. F Shafizadeh, D D Ward, D Pang *Carbohydr. Res.* **102** 217 (1982)
35. G A Tolstikov, F A Valeev, A A Gareev, L M Khalilov, M S Miftakhov *Zh. Org. Khim.* **27** 565 (1991)
36. A J Blake, A C Forsyth, R M Paton *J. Chem. Soc., Chem. Commun.* 440 (1988)
37. D D Ward, F Shafizadeh *Carbohydr. Res.* **93** 284 (1981)
38. D D Ward, F Shafizadeh *Carbohydr. Res.* **95** 155 (1981)
39. P Bhat, D Horton *Carbohydr. Res.* **122** 189 (1983)
40. F Shafizadeh, M G Essig *Carbohydr. Res.* **114** 71 (1983)
41. G A Tolstikov, F A Valeev, I N Gaisina, L V Spirikhin, M S Miftakhov *Zh. Org. Khim.* **28** 2072 (1992)
42. M Isobe, N Fukami, T Nishikava *Heterocycles* **25** 521 (1987)
43. Jpn. P 411 403; *Chem. Abstr.* **114** 185 135m (1989)
44. E Takashi, M Katsuya, Y Hajime, K Koseki, H Kawakami, H Matsushita *Heterocycles* **31** 1585 (1990)
45. H Kawakami, T Ebata, K Koseki, K Statsumoto, H Matsushita, Y Naoi, K Itoh *Heterocycles* **31** 2041 (1990)
46. K Koshi, E Takashi, H Kawakami, H Matsushita, Y Naoi, K Itoh *Heterocycles* **31** 423 (1990)
47. Jpn. P. 418 925; *Chem. Abstr.* **115** 8 564a (1991)
48. H Kawakami, T Ebata, K Koseki, H Matsushita, Y Naoi, K Itoh *Chem. Lett.* 1459 (1990)
49. M G Essig, F Shafizadeh *Carbohydr. Res.* **127** 235 (1984)
50. F A Valeev, I N Gaisina, M S Miftakhov, G A Tolstikov *Zh. Org. Khim* **29** 105 (1993)
51. Y Gelas-Mialhe *Carbohydr. Res.* **199** 243 (1990)
52. Y Gelas-Mialhe, J Gelas, D Avenel, R Brahmi *Heterocycles* **24** 931 (1986)
53. J S Brimacombe, F Hunedy, L C N Tucker *Carbohydr. Res.* **60** C11 (1978)
54. J Pecka, M Cerny *Collect. Czech. Chem. Commun.* **43** 1720 (1978)
55. M Mori, T Chuman, K Kato *Tetrahedron Lett.* **23** 4593 (1982)
56. M Mori, T Chuman, K Kato *Carbohydr. Res.* **129** 73 (1984)
57. J N Freskos, J S Swenton *J. Chem. Soc., Chem. Commun.* 658 (1985)
58. S Chew, R J Ferrier *J. Chem. Soc. Chem. Commun.* 911 (1984)
59. S Chew, R J Ferrier *Carbohydr. Res.* **174** 161 (1988)
60. K Matsumoto, T Ebata, K Koseki, H Kawakami, H Matsushita *Bull. Chem. Soc. Jpn.* **64** 2309 (1991)
61. K Matsumoto, K Ebata, K Koseki *Heterocycles* **32** 2225 (1991)
62. K Matsumoto, K Ebata, K Koseki *Chem. Eng. News* **69** 36 (1991)
63. M Isobe, T Nishikawa, S Pikul, T Goto *Tetrahedron Lett.* **28** 6485 (1987)
64. M Isobe, Y Fukuda, T Nishikawa, Ph Chabert, T Kawai, T Goto *Tetrahedron Lett.* **31** 3327 (1990)
65. M Isobe, N Fukami, T Goto *Chem. Lett.* 71 (1985)
66. G A Tolstikov, F A Valeev, I N Gaisina, L V Spirikhin, M S Miftakhov *Zh. Org. Khim.* **28** 2072 (1992)
67. M S Miftakhov, F A Valeev, I N Gaisina, O V Shitikova, V R Sultanmuratova, G A Tolstikov *Zh. Org. Khim.* **29** 1122 (1993)