Russian Chemical Reviews **64** (7) 675 – 703 (1995) ©1995 Russian Academy of Sciences and Turpion Ltd

UDC 547.454

Uronic acids: synthesis and reactions

V A Timoshchuk

Contents

I.	Introduction	675
II.	Tetruronic acids	675
III.	Penturonic acids	676
IV.	Hexuronic acids	678
V.	Higher and branched uronic acids	683
VI.	Aminodeoxyuronic acids	686
VII.	Reactions of uronic acids	692
VIII.	Conclusion	701

Abstract. The review describes the methods of synthesis of uronic acids involving both the catalytic oxidation of sugars and their oxidation by nonspecific oxidants. The principal paths in the transformations of uronic acids and their derivatives, characteristic of compounds of this class, which make it possible to synthesise new compounds that are otherwise difficult to obtain are considered. The bibliography includes 217 references.

I. Introduction

By definition, the term uronic acid is applied to monosaccharides in which the primary hydroxy-group has been transformed as a result of oxidation into a carboxy group. Uronic acids are usually understood only as alduronic acids, which are derivatives of aldoses, while the preferred name for keturonic acids is ketoaldonic acids. However, in the present review the term 'uronic acids' is used in a wide sense for all polyhydroxy-compounds containing carbonyl and carboxy-groups simultaneously. The presence of the carboxy-group in the structure of uronic acids is reflected in the relative reactivities of the hydroxy-groups, in the resistance to hydrolysis of the *O*- and *N*-glycosidic bonds, and also in their tendency to undergo β-elimination, leading to the formation of unsaturated sugars, which frequently serve as valuable intermediates in the synthesis of compounds which are difficult to obtain. The chemistry of uronic acids abounds with examples of the successful employment of the carboxy-group in monosaccharides in the construction of molecules having a specified structure.

The aim of the present review is to give a systematic account and to survey the extensive and interesting data on the synthesis and reactions of uronic acids. The review summarises data on the methods of synthesis of uronic acids with different carbon chain lengths, attention being concentrated on the oxidation reactions of monosaccharide derivatives. The methods of synthesis of diverse derivatives of uronic acids, which may be of interest in experimental studies and which may serve as synthons in the synthesis of optically active noncarbon compounds, are also examined.

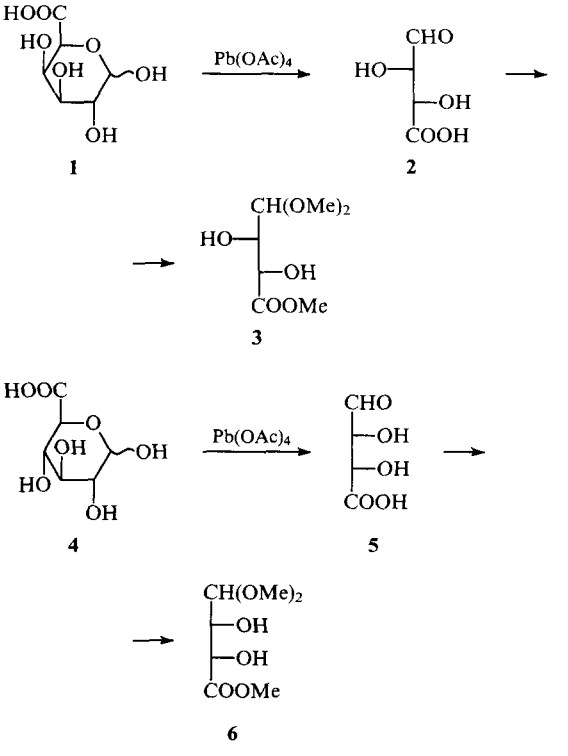
The last section of the review is devoted to numerous chemical reactions of uronic acids, which illustrate the extensive synthetic possibilities of compounds of this class.

V A Timoshchuk Radiation Chemistry Laboratory, Faculty of Chemistry, Belorussian State University, prosp. F. Skoriny 4, 220050 Minsk, Belarus. Fax (7-017) 220 82 72, Tel. (7-017) 220 67 56

Received 21 February 1995
Uspekhi Khimii **64** (7) 721 – 750 (1995); translated by A K Grzybowski

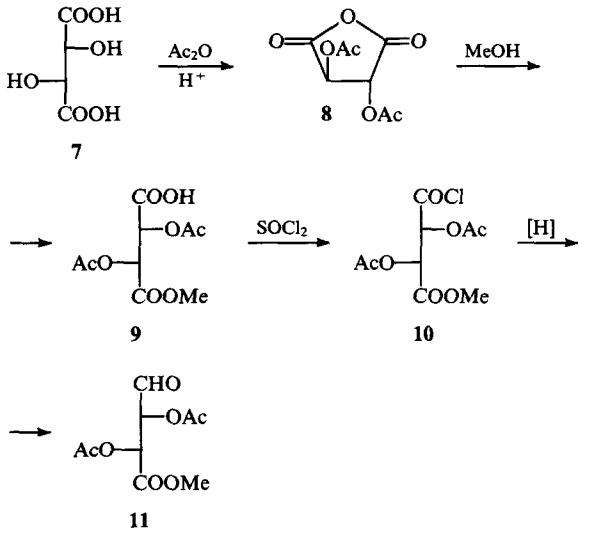
II. Tetruronic acids

D-*threo*-Tetruronic acids **2** and D-*erythro*-tetruronic acids **5** are readily formed when D-galacturonic acid **1** and D-glucuronic acid **4** are treated with two equivalents of $Pb(OAc)_4$. Tetruronic acids have been isolated and characterised as the dimethyl acetals of their methyl esters **3** and **6**.[1]

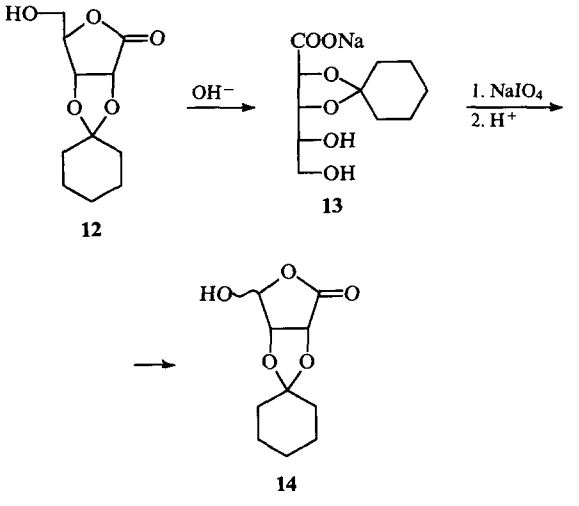


1 **2** **3** **4** **5** **6**

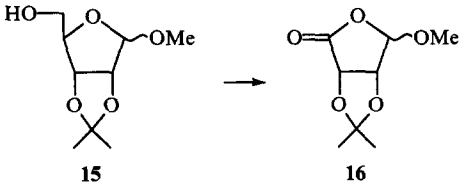
The source of L-*threo*-tetruronic acid is L-tartaric acid **7**, which is converted, as a result of treatment with acetic anhydride, into the anhydride **8**, affording the monomethyl ester **9** in methanol. The Rosenmund reduction of the acid chloride **10** leads to the methyl ester of 2,3-di-*O*-acetyl-L-*threo*-tetruronic acid **11**.[2]



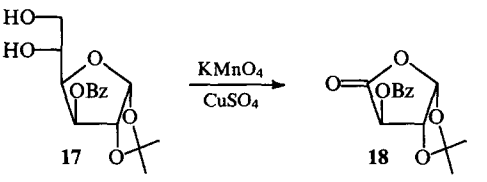
The cyclohexylidene derivative of the lactone of L-*erythro*-tetruronic acid **14** has been obtained in 93% yield by the periodate oxidation of the salt **13** formed from D-ribonolactone **12**.[3]



An unexpected result has been obtained in the oxidation of the methyl riboside **15**. Refluxing it with pyridinium chlorochromate in benzene, using a Dean–Stark procedure, leads to D-erythruronolactone **16**.[4]

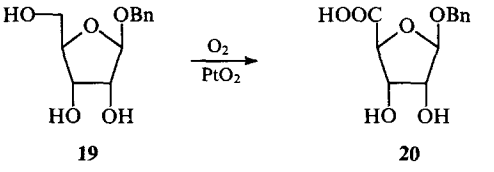


The lactone of L-*threo*-tetruronic acid **18** is formed smoothly on oxidation of 3-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose **17** by $KMnO_4$ in the presence of $CuSO_4$.[5]

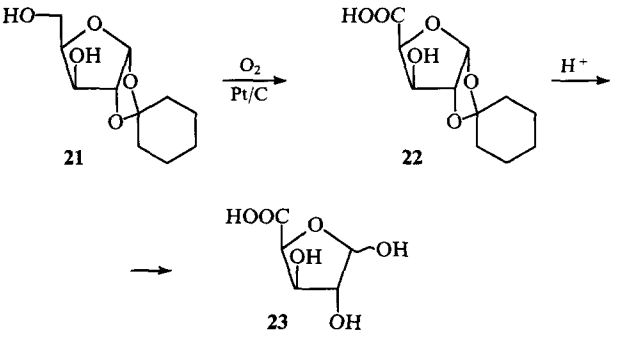


III. Penturonic acids

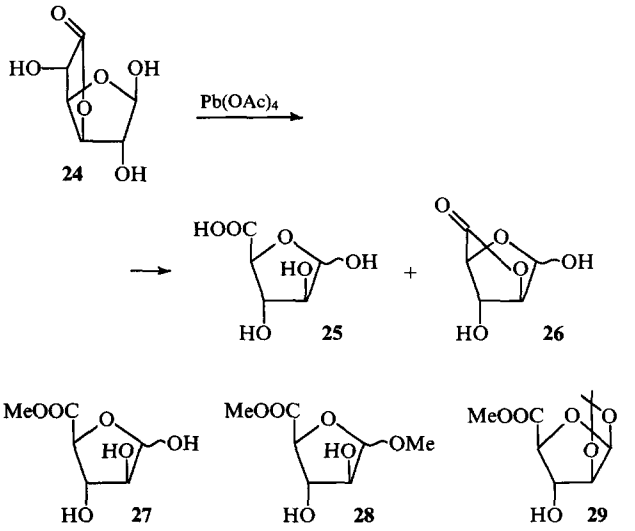
A convenient, albeit expensive and not always satisfactorily reproducible, method of synthesis of penturonic acids is the oxidation of pentofuranosides by oxygen over platinum or platinum black. The catalytic oxidation of benzyl β-D-ribofuranoside **19** over platinum black leads to the corresponding riburonide **20** in 48% yield. Oxidation by oxygen in the presence of platinum on charcoal affords a less satisfactory result (yield 13%).[6]



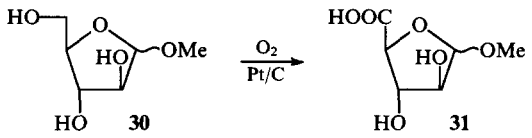
The acid **22**, the acid hydrolysis of which gives rise to D-xyluronic acid **23**, has been synthesised by the catalytic oxidation of 1,2-*O*-cyclohexylidene-α-D-xylofuranose **21**.[7]



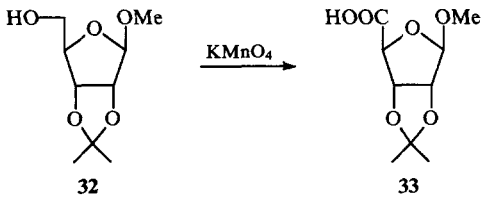
Treatment of the glucurone **24** with one equivalent of $Pb(OAc)_4$ leads to the formation of D-arabinuronic acid **25** and its lactone **26**, which has been identified as the methyl ester **27**, its glycoside **28**, and its acetal **29**.[1]



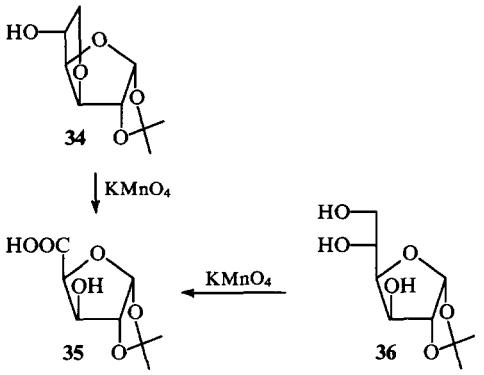
The catalytic oxidation of the arabinoside **30** to the arabinuronide **31** has been described.[8]



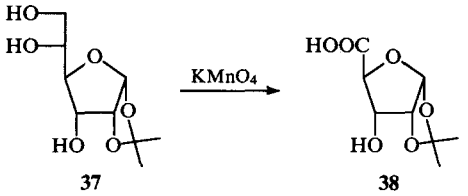
$KMnO_4$ has been used successfully for the oxidation of appropriately protected pentoses. The acetal of the methyl riboside **32** is oxidised to the acid **33** in 31% yield in an aqueous alkaline solution.[9] Acidification of the reaction mixture and rapid removal of the acid **33** formed by extraction with ether makes it possible to increase its yield to 65%.[10] Oxidation in a mixture of acetone and acetic acid leads to the formation of the acid **33** in 54% yield.[11]



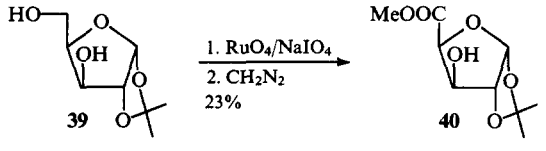
Anhydroglucofuranose **34** is oxidised by $KMnO_4$ to xyluronic acid **35**.[12]



The acid **35** is formed readily when the acetal of glucofuranose **36** is treated with $KMnO_4$. Riburonic acid **38** has been obtained from the acetal of allofuranose **37** under similar conditions.[13]

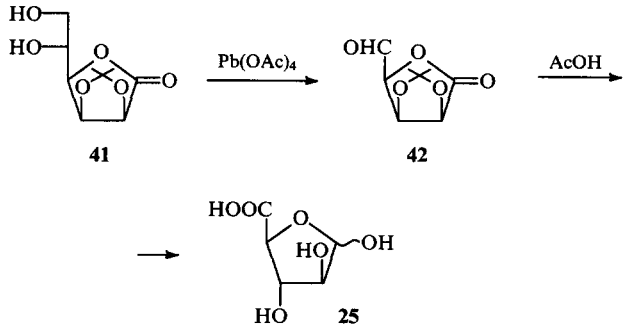


Ruthenium tetroxide in the presence of sodium metaperiodate can be used as the oxidant in the synthesis of penturonic acids. The acid **33** has been synthesised from compound **15** by this method.[14] The xyluronic acid ester **40** has been obtained by the oxidation of [the acetal of] xylofuranose **39** with subsequent esterification.[15]

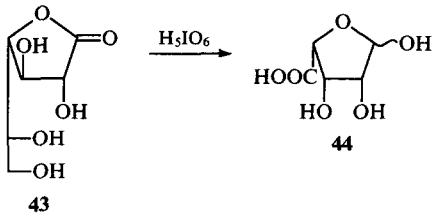


The preparation of the acid **35** by the successive oxidation of the glucofuranose acetal **36** by $Pb(OAc)_4$ and bromine in the presence of $BaCO_3$ has been described.[16]

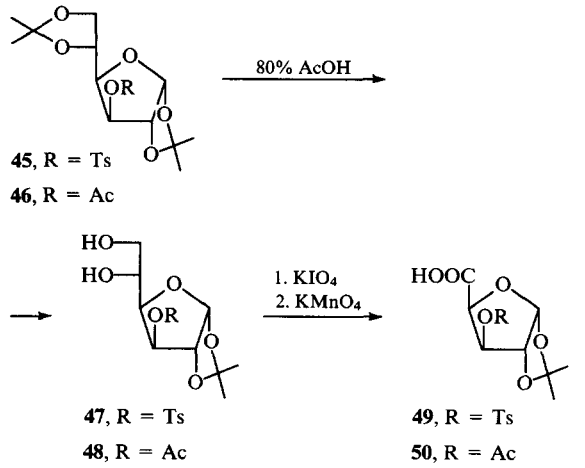
One of the sources for the synthesis of penturonic acids is glyconic acid γ-lactones. An example of such synthesis has been demonstrated by Mashida.[16] The aldehyde **42** has been obtained by oxidising the mannonolactone **41** by $Pb(OAc)_4$ and was then transformed in 10% acetic acid into arabinuronic acid **25**.



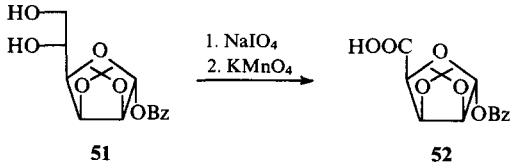
This approach has been used successfully in the synthesis of L-lyxuronic acid **44** from D-gulonolactone **43**.[17]



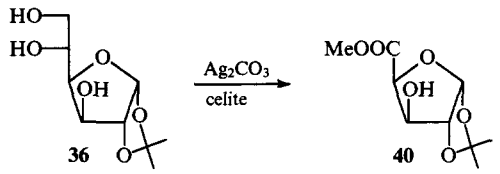
The derivatives of glucofuranose diacetals **45** and **46** are readily available starting compounds for the synthesis of penturonic acids with various substituents at C(3). The diols **47** and **48** obtained from them by mild acid hydrolysis are oxidised in succession by potassium metaperiodate and permanganate. The yield of the acids **49** and **50** is 50%.[18]

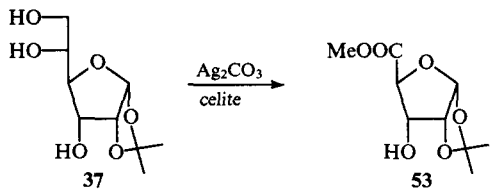


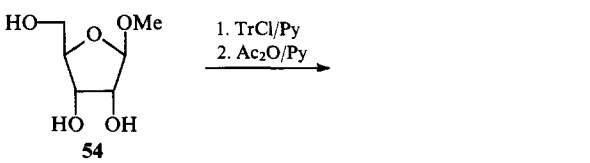
The successive oxidation of 1-*O*-benzoyl-2,3-*O*-isopropylidene-α-D-mannofuranose **51** initially with $NaIO_4$ and then $KMnO_4$ leads to the formation of the D-lyxuronic acid derivative **52**.[19]

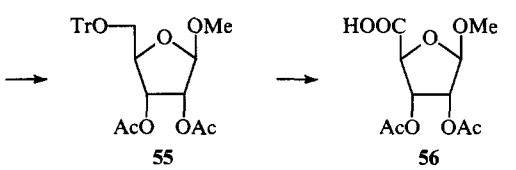


Silver carbonate on celite has been used as the oxidant for the synthesis of penturonic acids. Methyl D-xyluronate **40** and methyl D-riburonate **53** have been obtained by oxidising the hexofuranose acetals **36** and **37** in methanol.[20]



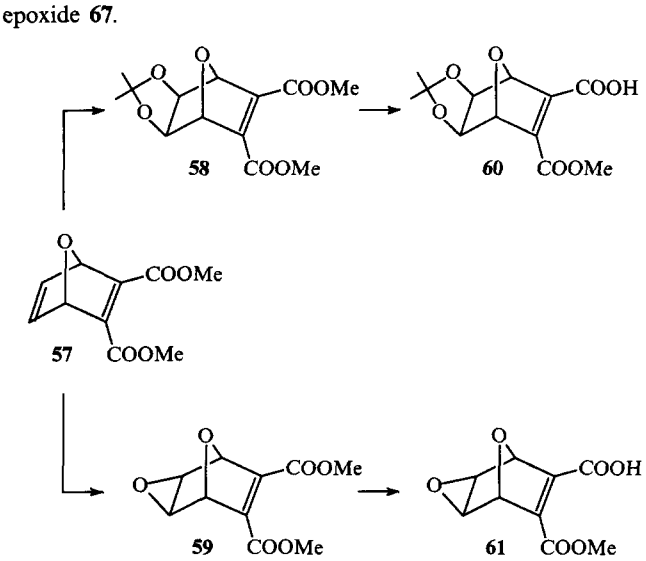


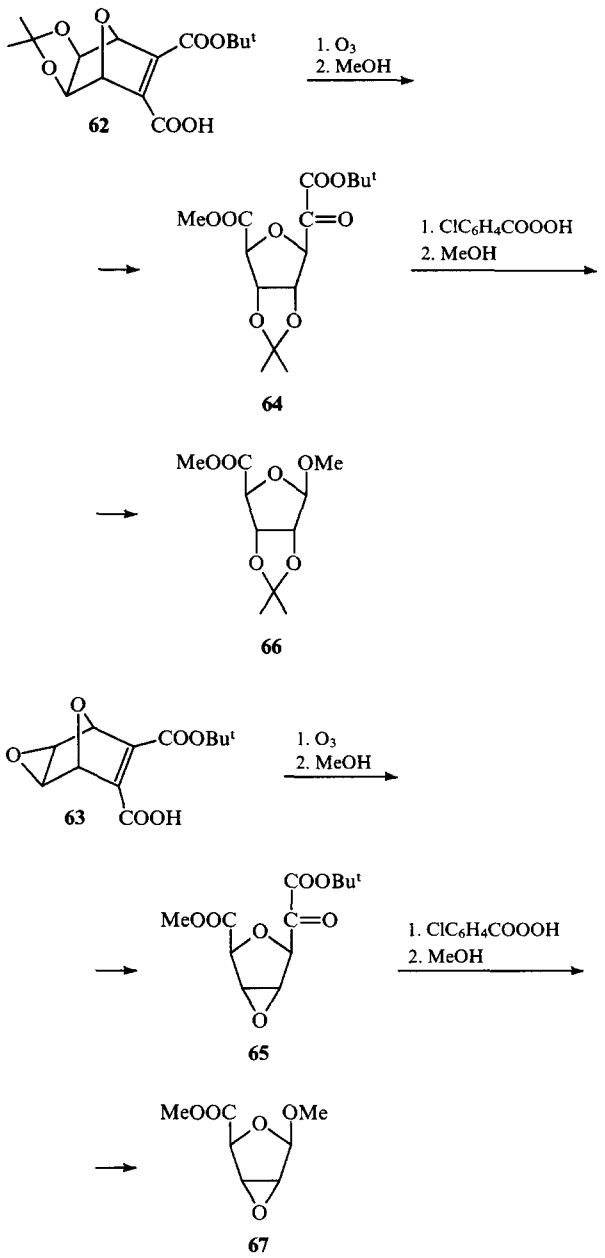




A procedure has been developed for the transformation of *O*-glycosides into *O*-glycuronides.[21] The successive tritylation and acetylation of the methyl riboside **54** afforded a fully protected derivative **55**, the oxidation of which with CrO_3 in acetone in the presence of sulfuric acid (the Jones reagent) gives rise to the D-riburonide acetate **56** in 67% yield.

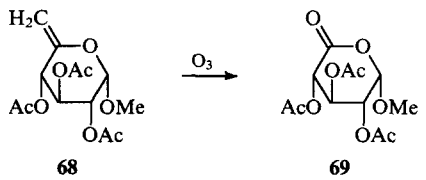
A chemical-enzymic strategy has been used in the total enantioselective synthesis of riburonides.[22] The Diels–Alder adduct **57** (the result of the condensation of furan with dimethyl ethynedicarboxylate) was transformed into the unsaturated esters **58** and **59**. Their asymmetric hydrolysis by pig liver esterase gave the half-esters **60** and **61** in fairly high optical yields. The *tert*-butyl esters **62** and **63** obtained from them were converted by ozonisation in methanol into the ketoacids **64** and **65**, the Baeyer–Villiger oxidation of which followed by methanolysis, afforded derivatives of D-riburonic acid — the acetal **66** and the epoxide **67**.





The L-enantiomer of the riburonide **66** has been obtained by the ozonolysis of the half-ester **60** and oxidation with *m*-chloroperbenzoic acid.

The conversion of the glucosene **68** into the 1,5-lactone of D-xyluronic acid **69** may serve as an example of a nontrivial and fairly general method of synthesis of penturonic acids.[23]

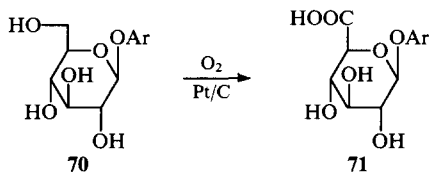


IV. Hexuronic acids

Like penturonic acids, hexuronic acids are obtained either by the catalytic oxidation of *O*-glycosides or by treating appropriately protected sugars with nonselective oxidants.

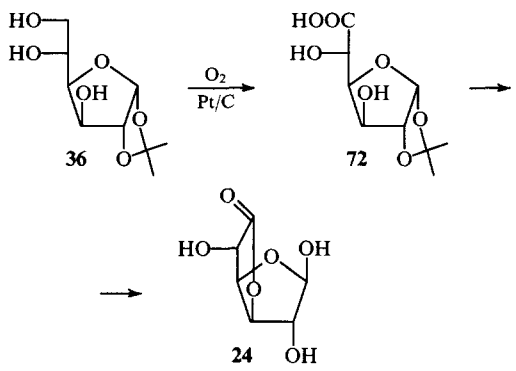
The conditions for the catalytic oxidation and the methods for the isolation and identification of alkyl *O*-glucuronides,

O-galacturonides, and *O*-mannuronides have been described.[24-26] Methyl α- and β-2-deoxyglucuronides and galacturonides have been synthesised by catalytic oxidation.[27] The methods of synthesis of phenyl and naphthyl β-D-glucuronides **71** from the corresponding aryl glycosides **70** have been described.[28,29]



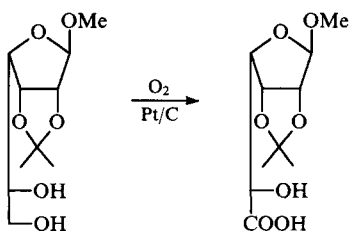
70 **71**

Derivatives of hexofuranoses can also be used for the preparation of uronic acids. Thus the oxidation of the glucofuranose acetal **36** with oxygen over platinum leads to the acid **72**, which is converted by lactone-formation into the glucurone **24** on heating in water.[30]



36 **72** **24**

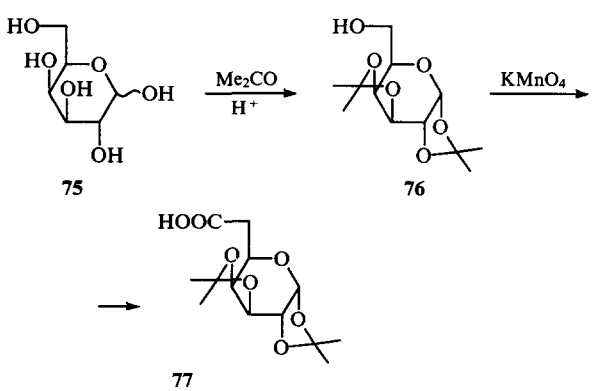
The catalytic oxidation of the D-gulofuranoside acetal **73** has been used in the synthesis of the D-guluronide **74**.[31]



73 **74**

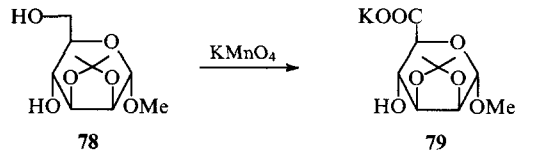
A review presenting more detailed data has been devoted to the catalytic oxidation of sugars.[32]

Appropriately protected sugars with a free primary hydroxy-group are smoothly oxidised to uronic acids by nonselective oxidants. The oxidation of the diacetal **76** obtained from D-galactose by $KMnO_4$ affords the galacturonic acid derivative **77**.[33]



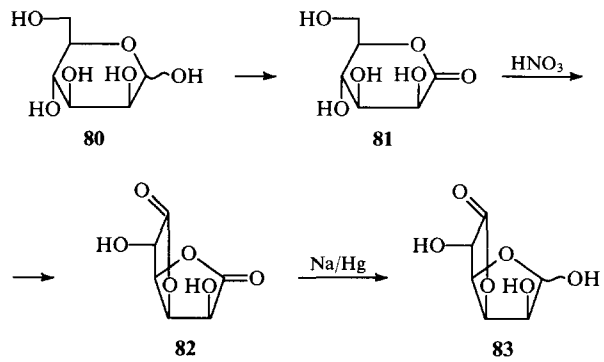
75 **76** **77**

The D-mannopyranoside acetal **78** can be oxidised by $KMnO_4$ to the acid **79** in an acceptable yield even in the presence of a free secondary hydroxy-group.[34]



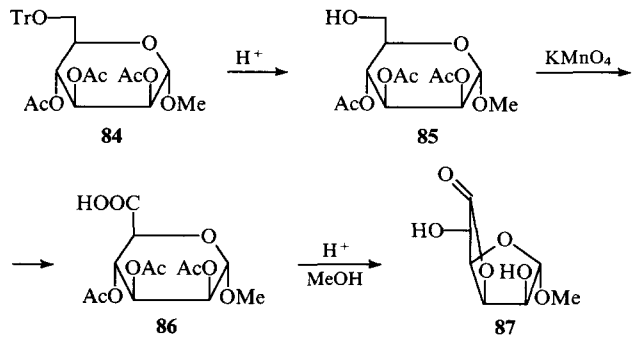
78 **79**

The electrolytic oxidation of D-mannose **80** leads to the formation of δ-mannonolactone **81**, the treatment of which with nitric acid gives rise to the dilactone of D-mannosaccharic acid **82**, while the reduction of the latter with sodium amalgam results in the formation of the 6,3-lactone of D-mannuronic acid **83**.[35]



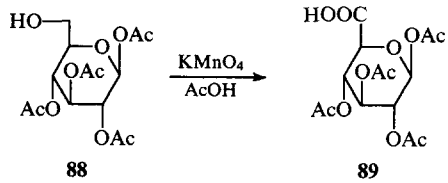
80 **81** **82** **83**

The oxidation with potassium permanganate in an acetone–acetic acid mixture of the sugar **85**, obtained from its 6-*O*-trityl precursor **84**, is yet another example of the synthesis of derivatives of D-mannuronide **86** and its lactone **87**.[36]



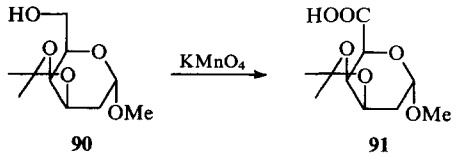
84 **85** **86** **87**

A similar synthetic scheme has been used in the oxidation of β-D-glucopyranose tetraacetate **88** to the full acetate of D-glucopyranuronic acid **89**.[37]

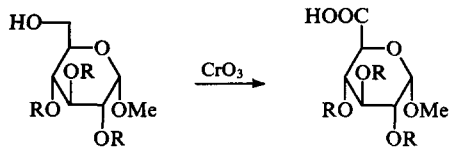


88 **89**

$KMnO_4$ has been used to oxidise the acetal of methyl 2-deoxy-α-D-galactopyranoside **90** to the acid **91**.[38]



90 **91**

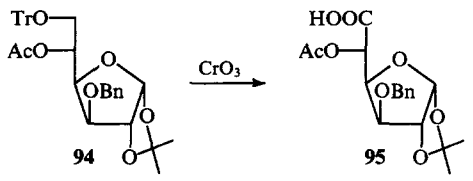


92 93

R = Me, Bn.

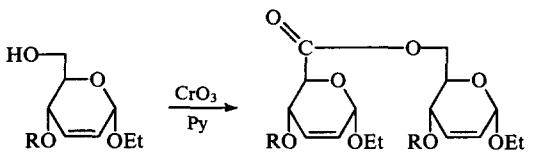
CrO_3 may be used as the oxidant in the synthesis of glucuronic acid derivatives **93** from the partly protected glucopyranosides **92**.[39,40]

A convenient method of synthesis of the D-glucofuranuronic acid derivative **95** involves the oxidation of the fully protected glucofuranose **94** by CrO_3 in acetone in the presence of sulfuric acid.[41]



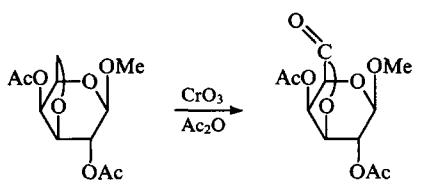
94 95

The formation of the ester **97** has been observed in the oxidation of the unsaturated sugar **96** with CrO_3 in pyridine.[42]



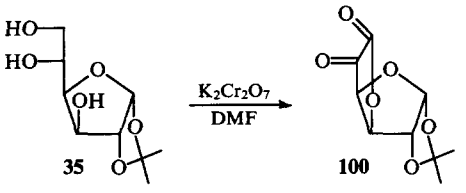
96 97

The oxidation of 3,6-anhydrogalactopyranoside **98** with CrO_3 in acetic anhydride leads to the 6,3-lactone **99**.[43]



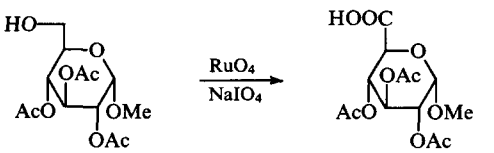
98 99

The sugar **35** can be oxidised by potassium dichromate in dimethylformamide (DMF) to the ketolactone **100**.[44]

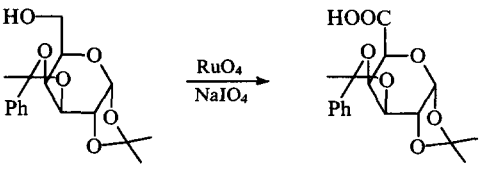


35 100

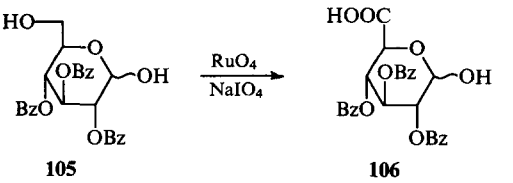
Ruthenium tetroxide together with sodium metaperiodate has found an application as the oxidant in the synthesis of hexuronic acids. The acids **103** and **104** have been obtained by this method from the sugars **101** and **102**. It has been shown for sugar **105**, with free primary and hemiacetal hydroxy-groups, that the oxidation does not involve the anomeric centre and leads to the acid **106**.[15]



101 103

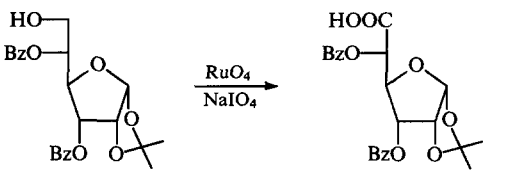


102 104



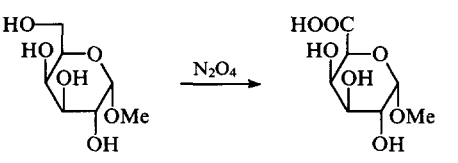
105 106

D-Allofuranose **107** is transformed into D-allofuranuronic acid **108** on oxidation with RuO_4.[45]



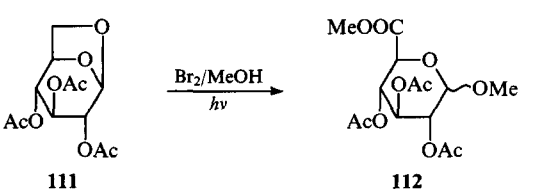
107 108

When the D-galactopyranoside **109** is treated with nitrogen(IV) oxide, the latter exhibits an oxidative selectivity, affording the D-galacturonide **110**.[46]



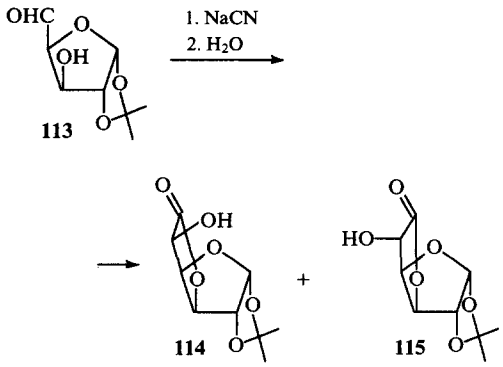
109 110

Despite the low yield, the oxidation of the levoglucosan acetate **111** with bromine on irradiation with UV light to give the ester **112** is nevertheless of interest.[47]

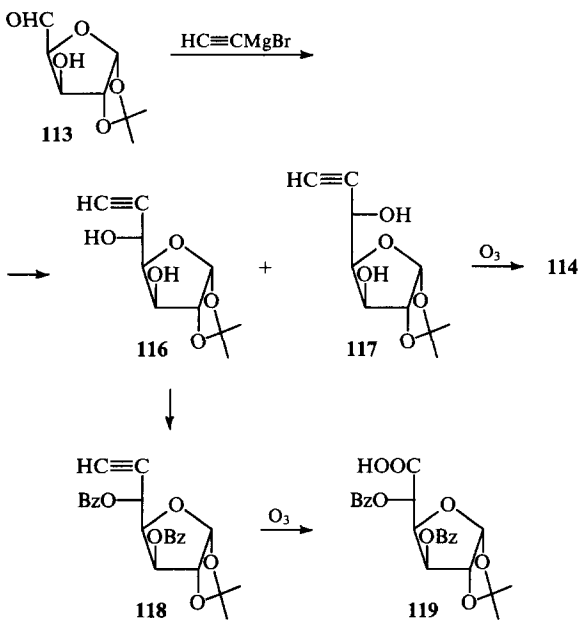


111 112

The introduction of a carboxy-group is achieved in a number of instances by the addition of nucleophiles to the aldehyde group. Two lactones — L-iduronolactone **114** and D-glucuronolactone **115** — have been obtained from 1,4-pento-dialdoxylofuranose **113** by the cyanohydrin synthesis.[48]

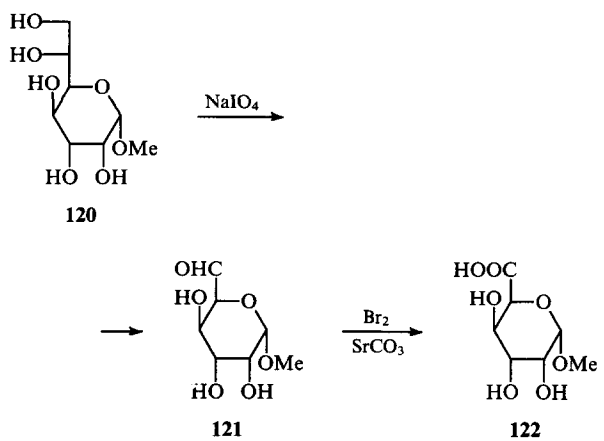


The addition of ethynylmagnesium bromide to the aldehyde **113** affords ethynyl sugars with D-gluco- and L-ido-configurations (compounds **116** and **117** respectively). The lactone **115** and the acid **119** have been obtained by the ozonolysis of compound **116** and the dibenzoate **118**.[49]

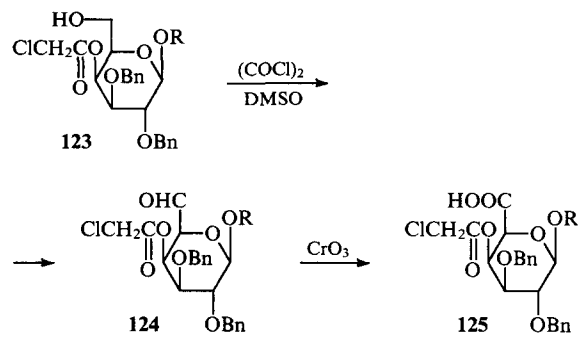


1,4-Pentodialdoribofuranose has also been used for reactions of a similar type.[50]

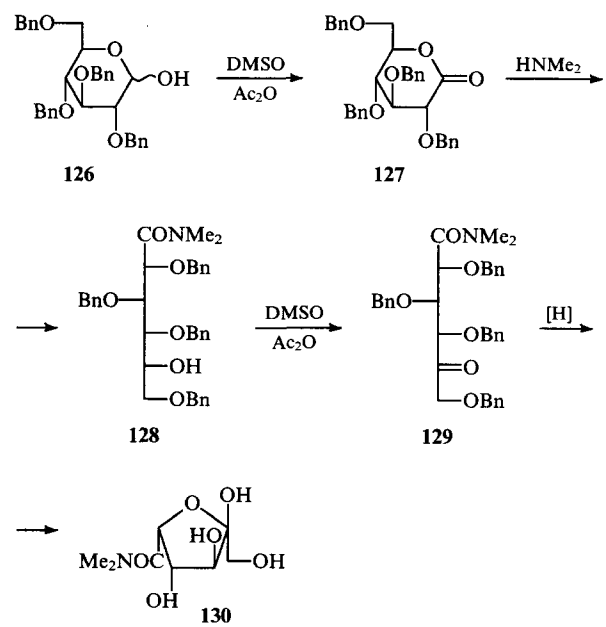
Heptopyranosides can also serve as a source of hexuronic acids. Thus oxidation of the sugar **120** (the product of the cyanohydrin synthesis from D-glucose) with sodium metaperiodate results in the formation of the aldehyde **121**, the treatment of which with bromine in the presence of strontium carbonate gives the D-guluronide **122**.[51]



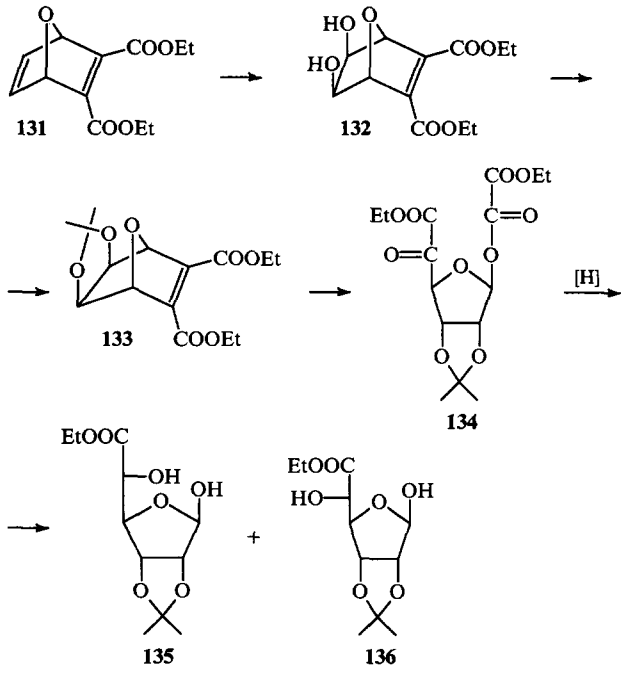
The Swern oxidation of the primary hydroxy-group in sugars to the aldehyde group followed by the conversion of the latter in one way or another into a carboxy-group constitutes yet another procedure for the preparation of uronic acids. Treatment of the galactopyranoside **123** with the dichloride of oxalic acid in dimethyl sulfoxide (DMSO) at −78 °C leads to the aldehyde **124**, the oxidation of which by the Jones reagent affords the acid **125**.[52]



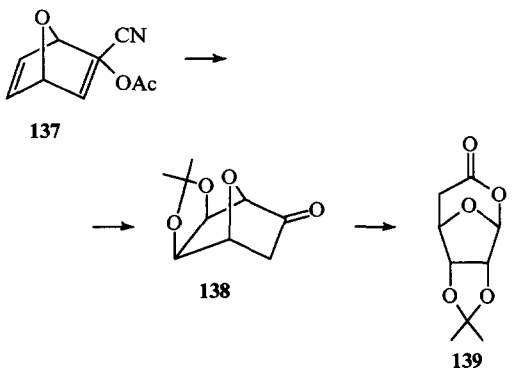
A rare example of the synthesis of uronic acids in a series of ketoses has been demonstrated by Kuzuhara and Fletcher.[53] The glucopyranose **126** with the free hemiacetal hydroxy-group was oxidised by Pfitzner–Moffatt method to the D-gluconolactone **127**. The gluconamide **128** obtained from it was oxidised by the same method to the ketone **129**. The removal of the protecting benzyl groups from the latter leads to the amide of L-sorburonic acid **130**.



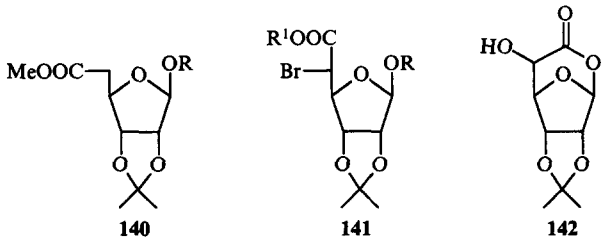
Fairly effective methods have been developed for the preparation of hexuronic acids by the diene synthesis. The total synthesis of uronic acids with the D,L-talo- and allo-configurations has been described.[54] The adduct **131**, obtained as a result of the condensation of furan with methyl ethynedicarboxylate, is oxidised by OsO_4 to the diol **132**. The ozonolysis of its acetal **133** followed by a thermal rearrangement leads to the ester of the ketoacid **134**, the hydrogenation of which over platinum affords the D,L-taluronate **135** and the D,L-alluronate **136**.



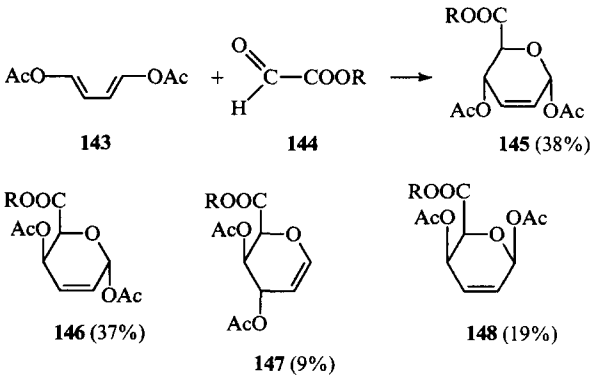
The condensation of furan with α-acetoxyacrylonitrile leads to the formation of the adduct **137**, which is transformed into the ketone **138** by successively: oxidation with OsO_4, acetal formation, and treatment with MeONa. Its oxidation with *m*-chloroperbenzoic acid leads to the acetal of 5-deoxy-D,L-ribo-hexofuranurono-6,1-lactone **139**.[55]



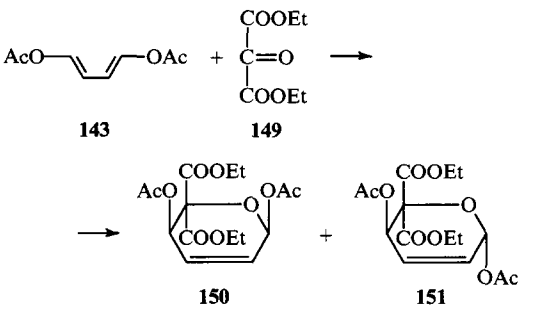
The use of cyanovinylcamphanate for the condensation makes it possible to obtain, as a result of total asymmetric synthesis, the optically active uronic acid derivatives **140**–**142**.[56–60]



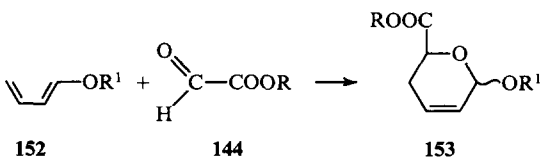
The Diels–Alder reaction between 1,4-diacetoxybuta-1,3-diene **143** and the alkyl glyoxylate **144** leads to a way of synthesising racemic unsaturated hexopyranuronic acids **145**–**147**.[61] When the reaction is carried out under mild conditions, the isomer **148** with an admixture of compound **145** (13%) is formed.



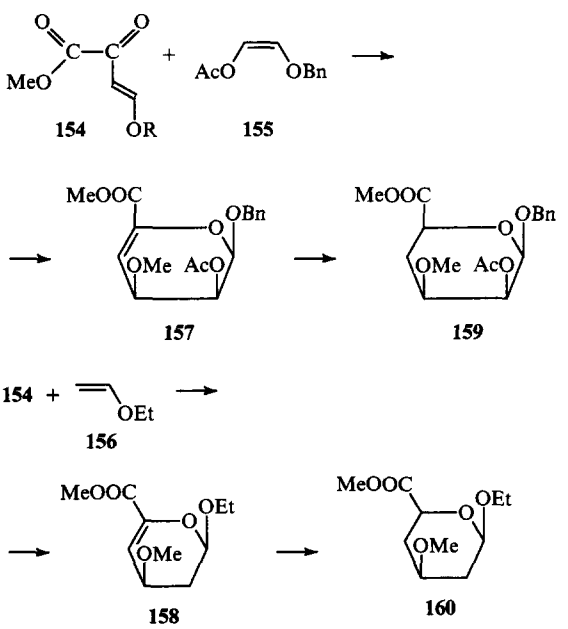
The condensation of the substituted butadiene **143** with diethyl mesoxalate **149** leads to the formation of the isomeric compounds **150** and **151**,[61] which are related to uronic acids.



The unsaturated 2,3,4-trideoxyuronides **153** are formed on condensation of the glyoxylates **144** with 1-alkoxybuta-1,3-dienes **152**.[62–64]

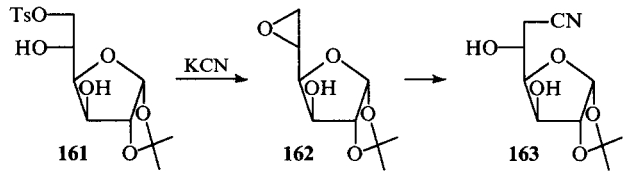


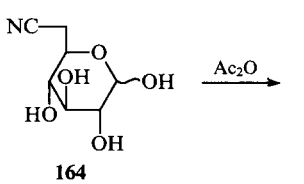
The 4-deoxy- and 2,4-dideoxy-D,L-mannopyranuronides **159** and **160** have been obtained by the hydrogenation of the Diels–Alder adducts **157** and **158** formed as a result of the condensation of compound **154** with the dienophiles **155** and **156**.[65]

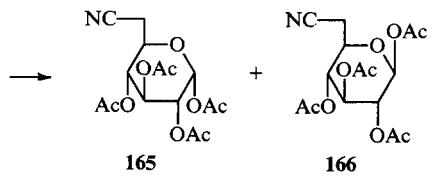


V. Higher and branched uronic acids

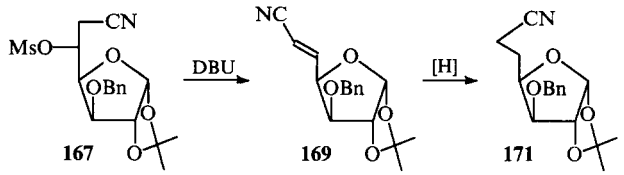
The substitution of primary tosyloxy-groups in sugars by potassium cyanide is used to obtain uronic acids with a lengthened carbon chain. It has been shown[66] that the interaction of D-glucofuranose tosylate **161** with potassium cyanide in acetone leads to the formation of the α-epoxide **162**, while the reaction in ethanol affords the nitrile **163**. The acetates of the α- and β-anomers of 6-deoxyhepturonitrile **165** and **166** have been obtained by the acid hydrolysis of the nitrile **163** and the acetylation of the D-pyranuronitrile **164** formed.

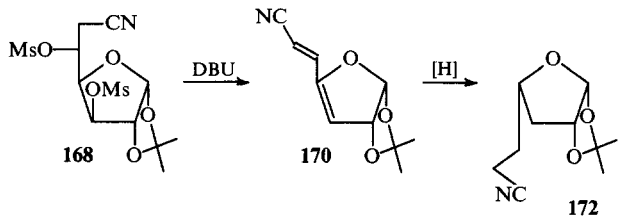






The monomethanesulfonyl derivative **167** and the di(methanesulfonyl) derivative **168** of the nitrile **163** are readily transformed on treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) into the unsaturated nitriles **169** and **170**, the reduction of which gives rise to D-dideoxyheptofuranurono-nitrile **171** and L-trideoxyheptofuranurononitrile **172**.

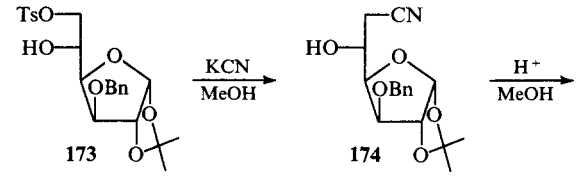


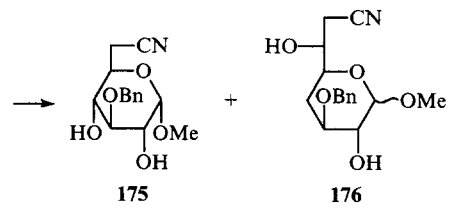


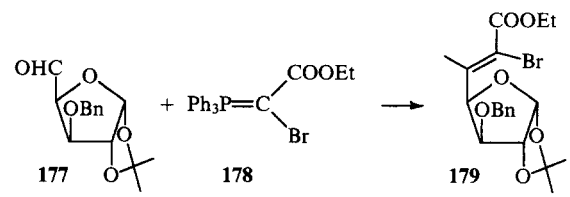
The interaction of the tosylate **173** with potassium cyanide in methanol leads to the 6-deoxyurononitrile **174**, the methanolysis of which results in the formation of the nitriles of the hexopyranuronide **175** and the hexofuranuronide **176**.[67]

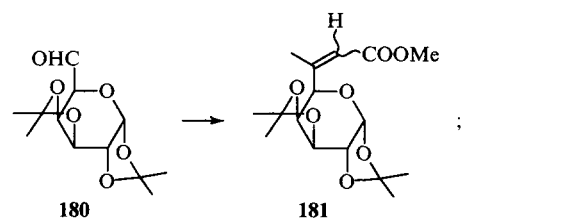
The carbon chain of sugars can be built up by several units at once with the aid of the Wittig reaction. Treatment of the aldehyde **177** with bromoethoxycarbonylmethylenetriphenylphosphorane **178** affords a satisfactory yield of the unsaturated uronic acid ester **179**.[68]

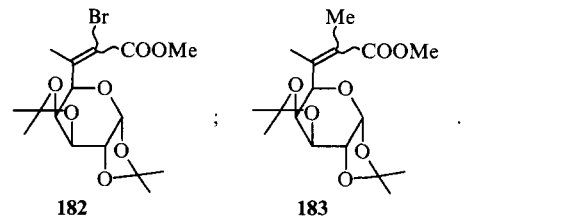
This approach has been used to obtain the analogues of lincomycin **181**–**183** from the aldehyde **180**.[69]



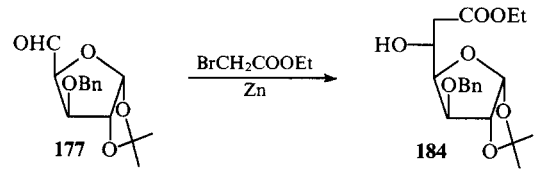








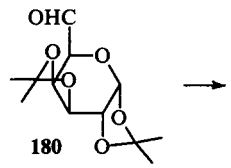
The Reformatskii reaction has been used to synthesise higher uronic acids. The condensation of the aldehyde **177** with ethyl bromoacetate and zinc gives rise to the ethyl 6-deoxyheptofuranuronate derivative **184**.[70]



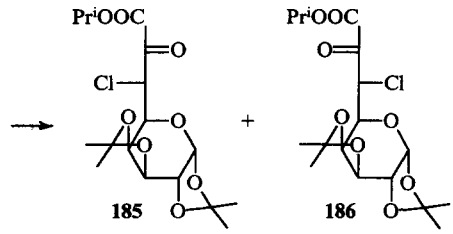
Under the conditions of the Darzens condensation, the aldehyde **180** condenses with dichloroacetic acid ester to form a diastereoisomeric mixture of glycidic esters, which are converted by treatment with $MgCl_2$ into the chlorodeoxyketouronic acid esters **185** and **186**.[71]

A method for lengthening the carbon chain of sugars with formation of uronic acids has been demonstrated.[72] It was shown that the interaction of the tosylate **187** with sodium dicarbonylcyclopentadienylferrate and then with bromine in methanol leads to the hepturonic acid ester **188**.

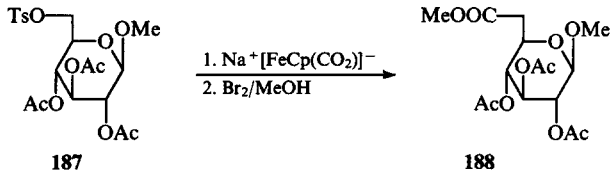
The free radical species generated from the iododeoxysugar **189** in the Zn–$FeCl_3$–NaI–Py system adds to methyl acrylate, affording the trideoxyoctofuranuronic acid ester **190**.[73]



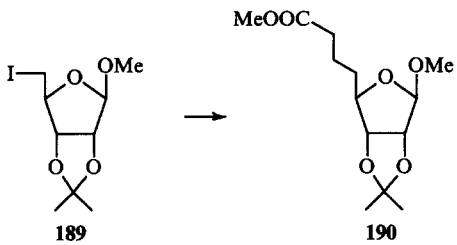
180



185 186

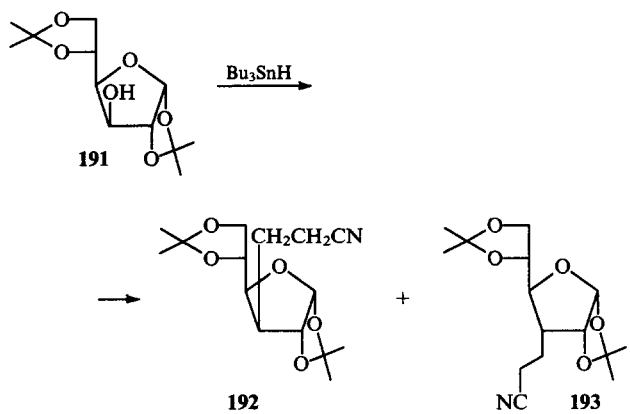


187 188



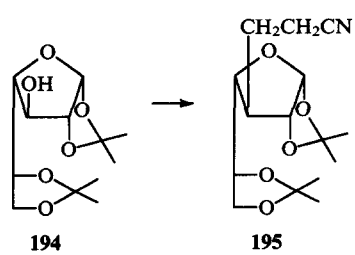
189 190

Alkyl halides form a C–C bond with electron-deficient alkenes in the presence of tributyltin hydride. It has been shown [74] that this reaction can be extended also to alcohols. The interaction of glucose diacetal **191** with acrylonitrile and tributyltin hydride results in the formation of a mixture of the isomeric uronic acid nitriles **192** and **193** branched at the C(3) carbon atom.



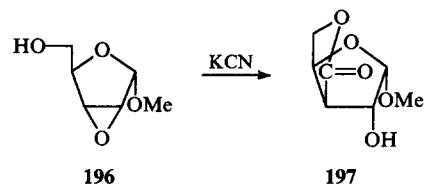
191 192 193

In contrast to the sugar **191**, the galactofuranose diacetal **194** reacts stereoselectively, giving only the nitrile **195**.

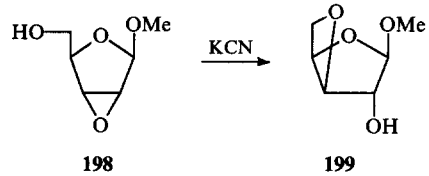


194 195

The opening of the oxirane ring on treatment with potassium cyanide can be used to obtain branched uronic acids.[75] Thus heating of 2,3-anhydro-α-D-riboside **196** in an aqueous solution of KCN gives rise to the lactone **197**. The β-D-riboside **198** is converted under these conditions into the 3,5-anhydro-β-D-riboside **199**.

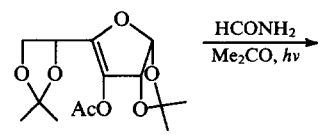


196 197

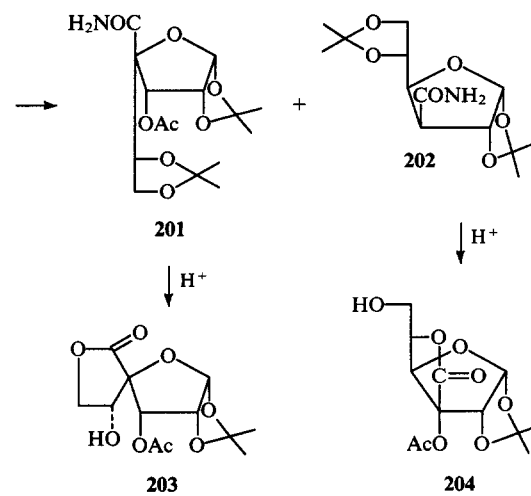


198 199

The photoamidation of the unsaturated sugar **200** leads to the formation of the two isomeric carbamoylation products **201** and **202**.[76] Mild acid hydrolysis results in the formation of the spirolactone **203** from the amide **201** and of the lactone **204** from the isomer **202**.



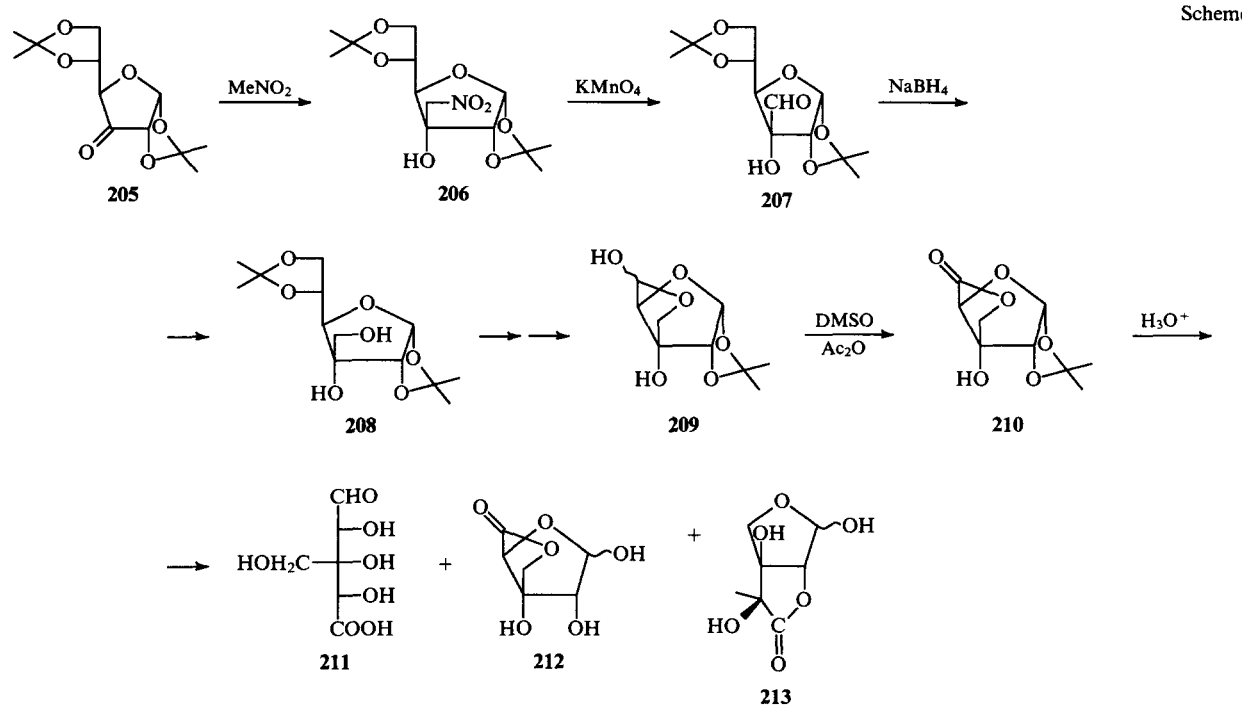
200



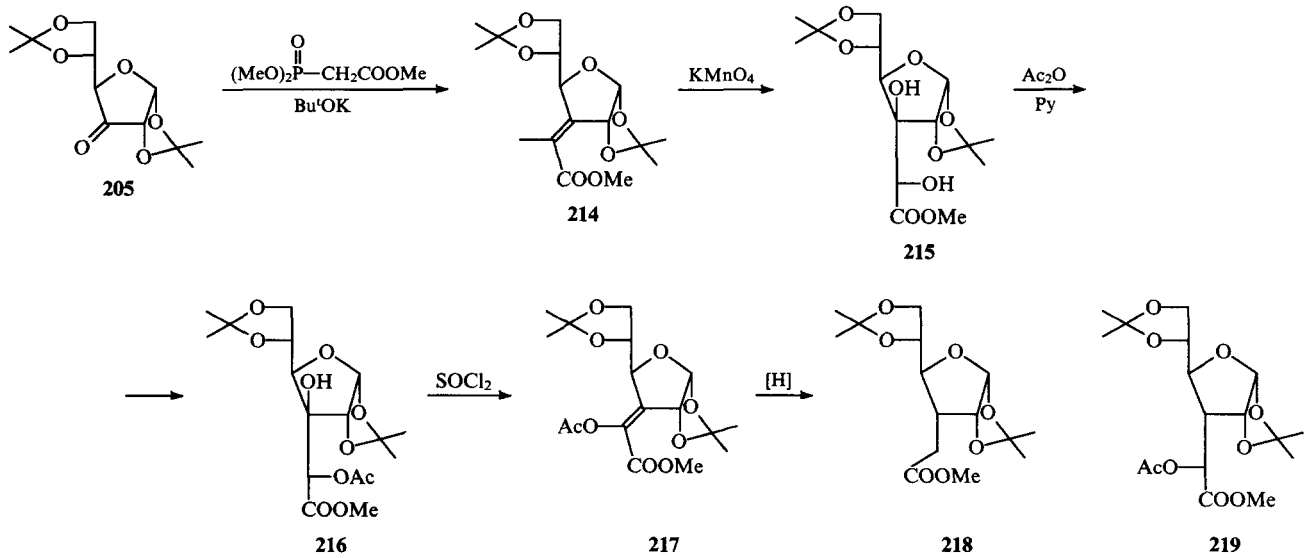
201 202 203 204

3-*C*-Hydroxymethyl-D-riburonic acid **211** has been detected in human bile as a complex of bilirubin glycosides. It was synthesised by treating the keto-derivative **205** with nitromethane and Bu^{t}OK. The Nef oxidation of the resulting nitroalcohol **206** with $KMnO_4$ led to the formation of the aldehydoalcohol **207**, which was smoothly reduced with $NaBH_4$ to the alcohol **208**. Successive acylation of the primary hydroxy-group in compound **208**, the removal of the isopropylidene protecting group, and the metaperiodate oxidation of the 5,6-diol group, and deacetylation led to the synthesis of the hemiacetal **209**. Its Pfitzner–Moffatt oxidation leads to the lactone **210**, the mild acid hydrolysis of which affords the acid **211** together with two of its isomeric lactones — **212** and **213** (Scheme 1).[77]

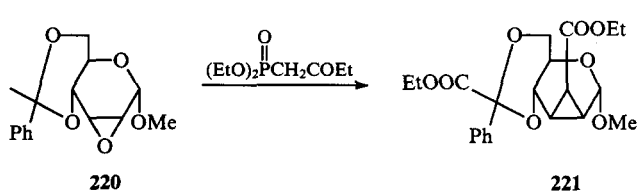
Scheme 1



Scheme 2

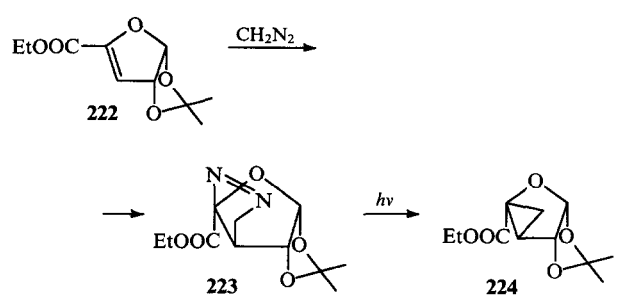


The condensation of the hexulose **205** with trimethyl phosphonoacetate in the presence of Bu'OK leads to the unsaturated ester **214**, the hydroxylation of which with $KMnO_4$ in pyridine leads stereospecifically to the diol **215**. Its monoacetate **216** is transformed on treatment with thionyl chloride in pyridine into the enol acetate **217**, the reduction of which with hydrogen over platinum in methanol affords the deoxyacid ester **218**. The hydrogenation of the enol acetate **217** over palladium in ethyl acetate produces the acetate of the ester **219** (Scheme 2).[78]

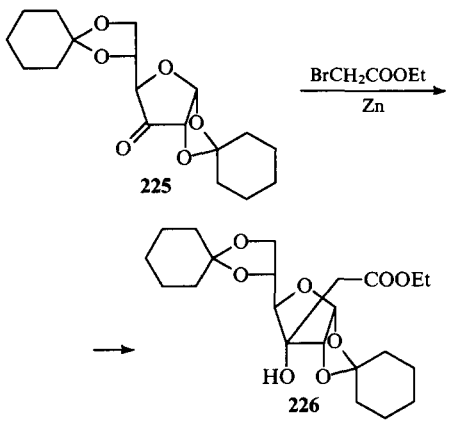


The ethyl ester of the branched uronic acid **221** has been obtained by treating the oxirane **220** with triethyl phosphonoacetate.[79]

The interaction of the eneuronate **222** with diazomethane and subsequent photolysis of the pyrazoline **223** formed give rise to the uronic acid ester **224** with a cyclopropane ring.[80]

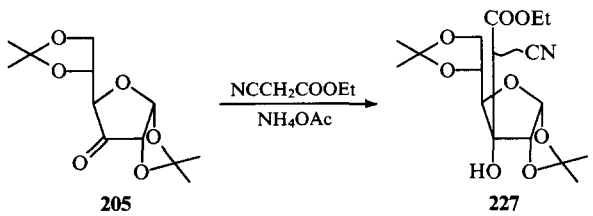


The applicability of the Reformatskii reaction in the synthesis of branched deoxyuronic acid esters has been demonstrated.[81] The condensation of the ketone **225** with ethyl bromoacetate and zinc affords the deoxyacid ester **226**.



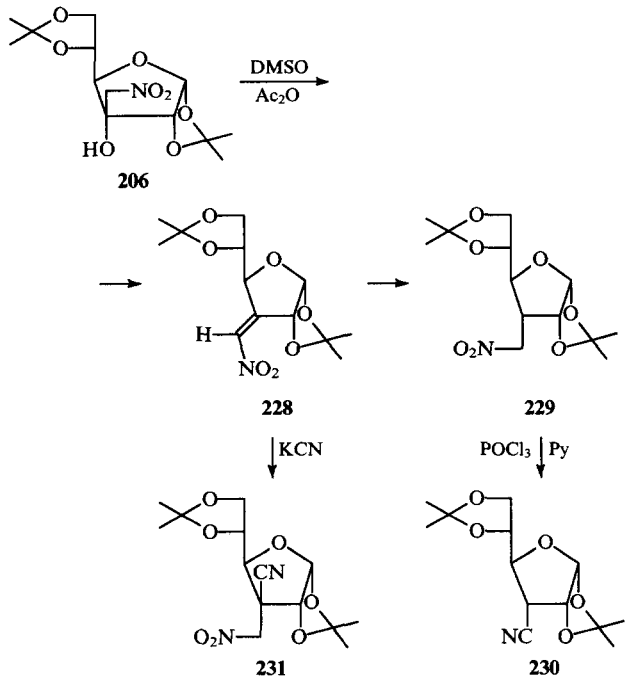
225 **226**

The Knoevenagel reaction between the carbonyl compound **205**, cyanoacetic ester, and ammonium acetate leads to the ester nitrile **227**, which gives rise to the possibility of synthesising branched uronic acids with an additional carboxy-group.[82]



205 **227**

The nitroalcohol **206**, formed as a result of the condensation of compound **205** with nitromethane, leads to extensive possibilities for the synthesis of a whole series of derivatives of branched uronic acids.[83] The dehydration of the nitroalcohol by acetic anhydride in DMSO affords the 3-*C*-methylene derivative **228**. The product of its reduction **229** is converted into the nitrile **230** on treatment with phosphoryl chloride in pyridine. The alkene **228** readily combines with potassium cyanide, giving the nitrile **231**.

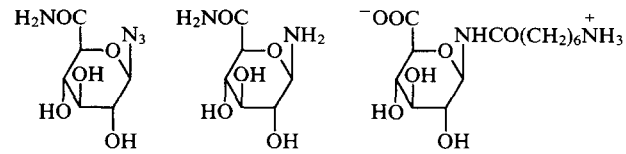


206 **228** **229** **231** **230**

VI. Aminodeoxyuronic acids

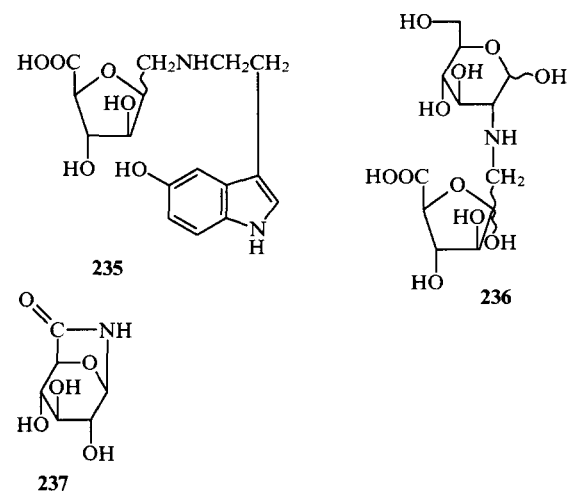
Aminodeoxyuronic acids are fairly common in nature. They have been detected in many bacterial polysaccharides and in nucleoside antibiotics.

The glycosylamines derived from uronic acids, which on the grounds of formal considerations can be considered in this section, are obtained by reducing the corresponding glycosyl azides; the latter are formed in their turn from acetylated halogenoses and sodium azide. The azide **232** and the amine **233** synthesised in this way exhibit antitumour activity.[84]



232 **233** **234**

The ω-aminoheptanoyl derivative of β-D-glucuronopyranosylamine **234** is an effective inhibitor of β-D-glucuronidase.[85] Direct treatment of uronic acids with amines is accompanied by the Amadori rearrangement. Thus the condensation of glucuronic acid with serotonin and glucosamine afforded the derivatives **235** and **236** of 1-amino-1-deoxy-D-fructuronic acid,[86,87] although the lactam **237** could be isolated on treatment with ammonia.[88]



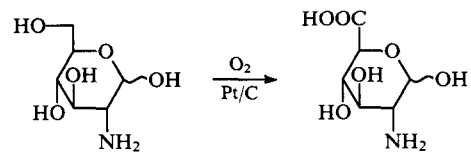
235 **236**

237

The synthesis and reactions of uronic acid nucleosides (*N*-uronides) have been considered in a review.[89]

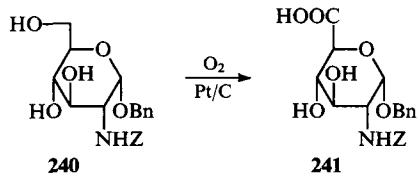
The methods of synthesis of the aminodeoxyuronic acid forming part of the composition of nucleoside antibiotics have been partly described in Suhadolnik's book.[90]

Mild oxidation by oxygen over platinum at pH 7 makes it possible to obtain 2-amino-2-deoxy-D-glucuronic acid **239** from glucosamine **238**.[91]



238 **239**

Since the free amino-group lowers the activity of the platinum catalyst, sugars with protected amino-group and hemiacetal hydroxyl are usually employed for the oxidation. The oxidation of the sugar **240** yields the acid **241**, the hydrolysis of which leads to the aminoacid **239**.[92]



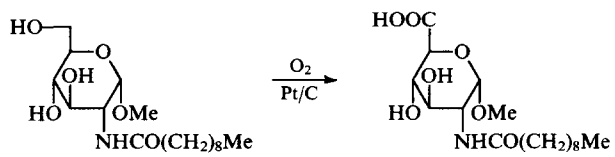
240 **241**

Z = $C_6H_5CH_2COO$.

It has been shown[93-95] that an increase in the rate of stirring of the solution leads to an appreciable improvement of the yield of the acid synthesised from the sugar **240** and its β-anomer.

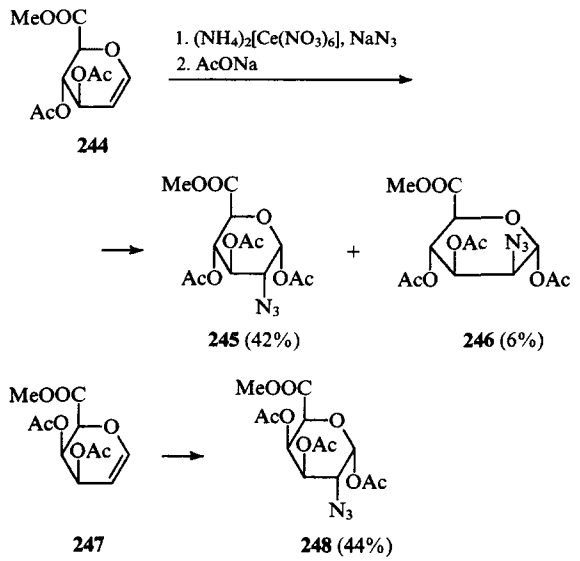
The corresponding aminouronic acids have been obtained similarly from D-galactosamine and D-mannosamine.[96-98]

Oxidation by oxygen over platinum has been used to obtain from the methyl glycoside derived from *N*-decanoyl-D-glucosamine **242** the aminodeoxyuronic acid derivative **243**, which forms part of the composition of the antibiotic aridicin.[99]



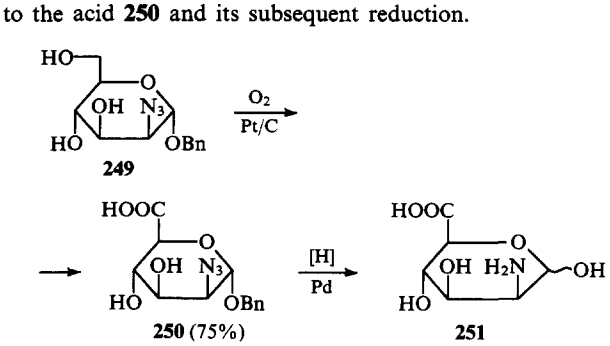
242 **243**

Another approach to the synthesis of 2-amino-2-deoxyuronic acid has been proposed.[100] It consists in the successive treatment of the glycal **244** with cerium ammonium nitrate and sodium azide and acetate, which results in the formation of the azides **245** and **246**. The azide **248** was obtained from the glycal **247**. The hydrogenolysis of the azides affords high yields of the corresponding amines.



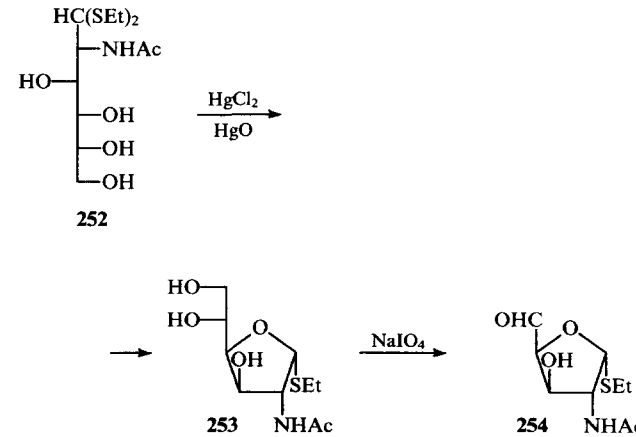
244 **245** (42%) **246** (6%) **247** **248** (44%)

An alternative scheme for the synthesis has been developed by Paulsen et al.[98] who employed catalytic oxidation of the azide **249** to the acid **250** and its subsequent reduction.



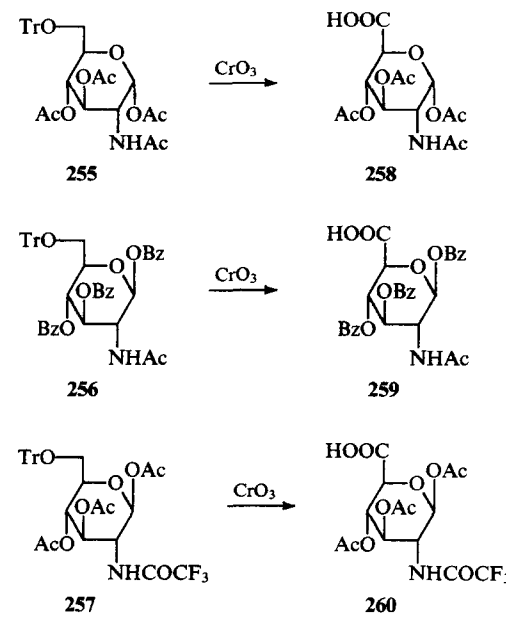
249 **250** (75%) **251**

The diethyl dithioacetal of 2-acetamido-2-deoxy-D-glucose **252** is a potential source for the synthesis of aminodeoxyuronic acids. The aldehyde **254**, obtained from the furanose **253** by periodate oxidation, may be readily converted into the corresponding acid.[101]



252 **253** **254**

It has been shown[102] that the trityl derivatives **255**, **256**, and **257** of the acylated glucosamine are readily oxidised by the Jones reagent to the corresponding aminodeoxyglucuronic acids **258**–**260**.

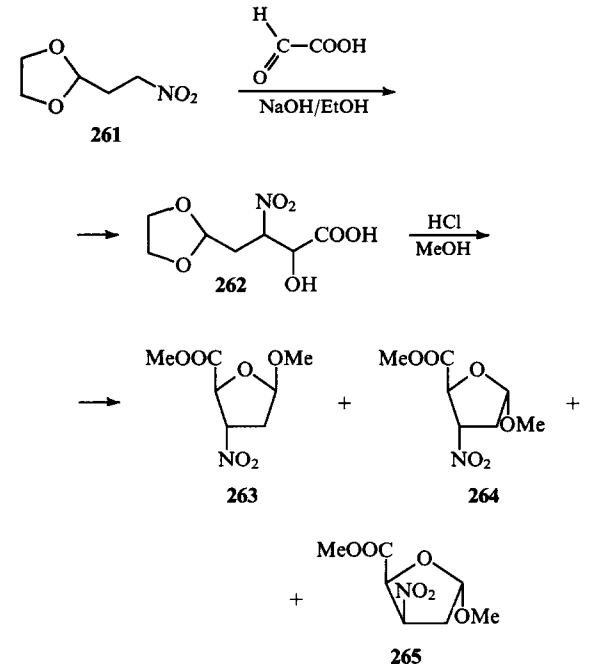


255 **258** **256** **259** **257** **260**

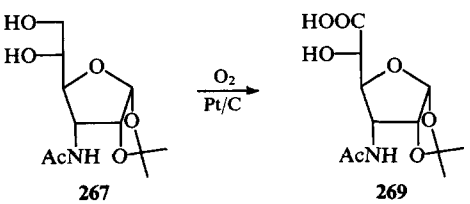
Since the nitro-group in sugars can be readily reduced, nitrodeoxyuronic acids are of definite interest. The synthesis of compounds of this type has been described. The nitroacid **262**, formed from the ethylene acetal of 3-nitropropanal **261** and glyoxylic acid, affords a mixture of the isomeric 2,3-dideoxynitro-D,L-furanuronates **263**, **264**, and **265** in HCl solution in methanol.[103]

The same authors proposed 2,3-*O*-isopropylidene-D-glyceraldehyde as the initial compound for the synthesis of 3-nitrouronic acids of this type.[104]

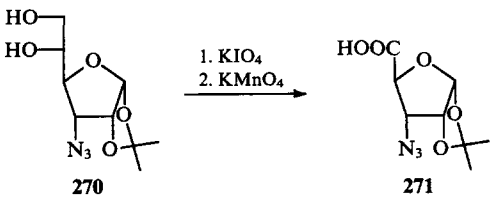
3-Acetamido-3-deoxy-α-D-ribofuranuronic acid **268** has been obtained by oxidising the pentofuranose **266** with $KMnO_4$ and by the successive treatment of the hexofuranose **267** with $NaIO_4$ and Br_2.[105]



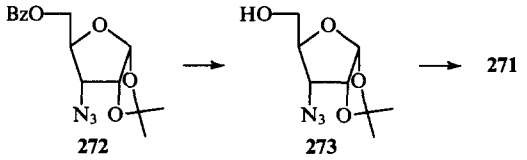
Catalytic oxidation of 3-acetamidoallofuranose **267** leads to the 3-amino-3-deoxy-D-allofuranuronic acid derivative **269**.[106,107]



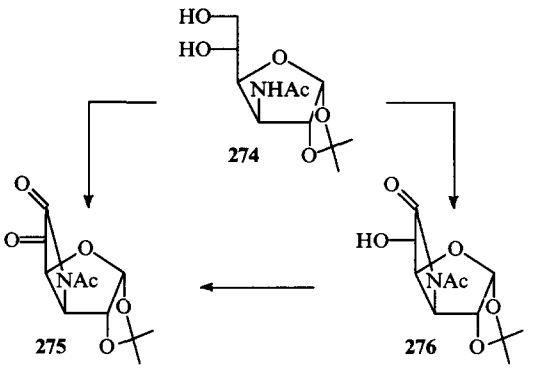
The successive oxidation of the azide **270** with KIO_4 and $KMnO_4$ leads to a satisfactory result in the synthesis of 3-azido-3-deoxyriburonic acid **271**.[108]



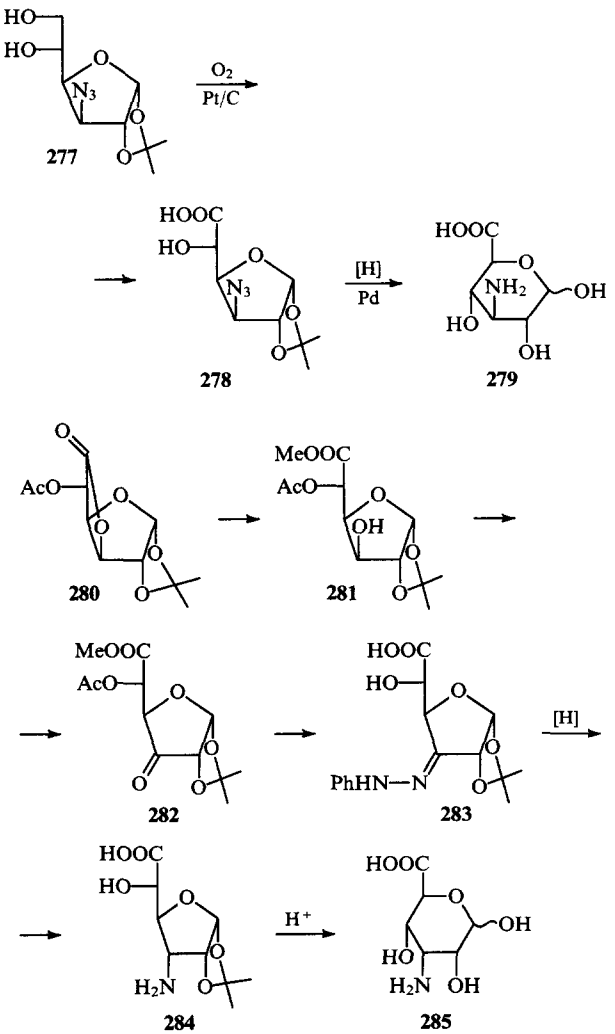
The acid **271** has been obtained by the debenzoylation of the azide **272** and the oxidation of the resulting alcohol **273** with $KMnO_4$.[109]



The oxidation of 3-acetamido-3-deoxyglucofuranose **274** with pyridinium dichromate in DMF leads to the ketolactone **275**, while oxidation with the Jones reagent affords the lactam **276**.[44]

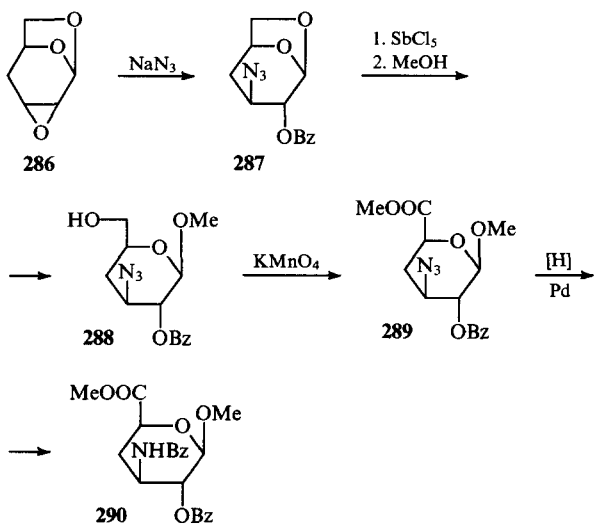


3-Amido-3-deoxyglucuronic acid **279** has been obtained from the azide **277**, which was oxidised by oxygen over platinum to the acid **278** and the product of its spontaneous hydrolysis was reduced over palladium, which led to the isolation of the required aminoacid **279**.[110]



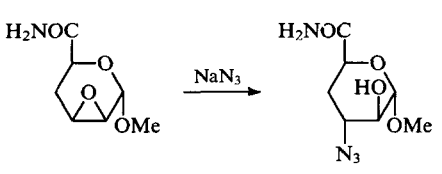
The transesterification of the lactone **280** in methanol, catalysed by an anion-exchange resin, and the oxidation of the resulting alcohol **281** with chromium trioxide in ethyl acetate lead to the ketone **282**. Its phenylhydrazone **283** is reduced by hydrogen over platinum to the aminoacid **284**, the acid hydrolysis of which affords 3-amino-3-deoxy-D-alluronic acid **285**.[111]

The ezoaminuronic acid derivative **290**, which forms part of the composition of the antibiotic ezomycin, has been obtained from the oxirane **286**, which is converted into the azide **287** on heating with sodium azide and acylation. The alcohol **288**, formed as a result of the opening of the 1,6-anhydro-ring by antimony pentachloride, is oxidised with $KMnO_4$, the acid is esterified, the ester **289** is reduced, the amino-group is benzoylated, and 3-benzamido-3,4-dideoxy-D-glucopyranuronide **290** is obtained.[112]



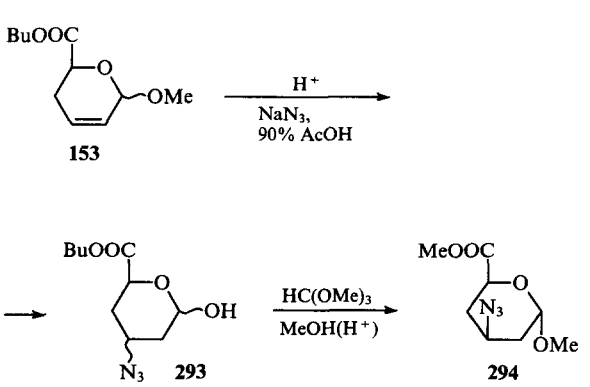
286 **287** **288** **289** **290**

The 3-azido-3,4-dideoxyuronamide **292** is formed as a result of the interaction of the oxirane **291** with sodium azide.[113]

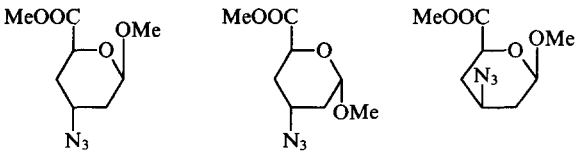


291 **292**

The unsaturated 4-deoxyuronides **153** interact with sodium azide in 90% acetic acid to form a mixture of the isomeric azides **293**, the treatment of which with orthoformic ester in methanol leads to the isomeric 3-azido-3-deoxypyranuronides **294**–**297**.[114]

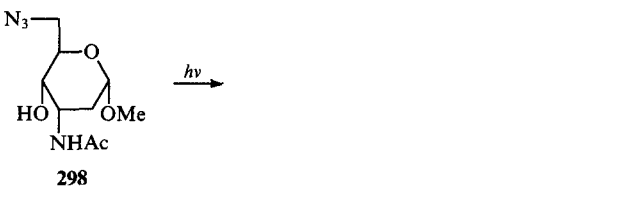


153 **293** **294**



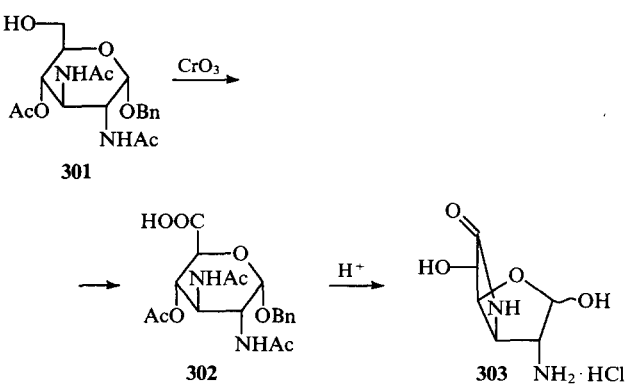
295 **296** **297**

The primary azido-group in sugars is capable of being transformed into an aldehyde as a result of photocleavage. The aldehyde **299**, obtained on UV irradiation of the azide **298**, is oxidised with bromine, esterified, and the ester of the methyl glycoside derived from 3-acetamido-2,3-dideoxy-D-allopyranuronic acid **300** is isolated.[115]



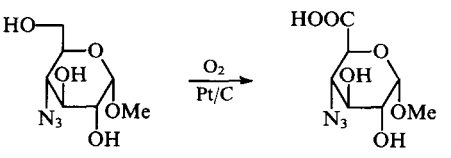
298 **299** **300**

Diaminouronic acids have been detected in certain polysaccharides. The 2,3-diacetoamidouronic acid **302** has been obtained when the α-benzyl glycoside derived from 2,3-diacetamidoglucopyranose **301** was oxidised with the Jones reagent. Hydrolysis of the acid **302** leads to the 2-amino-6,3-lactam **303**.[116]



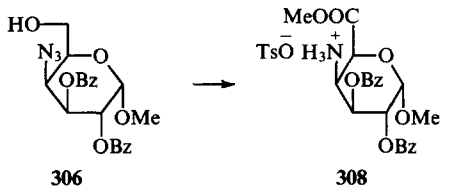
301 **302** **303**

Apart from the methods of synthesis of 4-amino-4-deoxyuronic acids (forming part of the composition of the nucleoside antibiotics gougerotin and blasticidin S) considered in Suhadolnik's review,[90] there are at least two further examples of their synthesis in the literature. It has been shown[108] that the 4-azido-4-deoxy-D-glucopyranoside **304** is smoothly oxidised by oxygen over platinum to the azidoacid **305**.

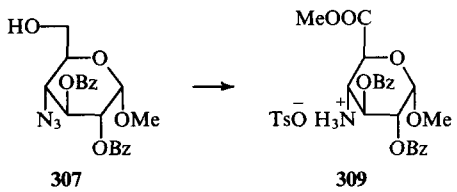


304 **305**

The oxidation of the 4-azidosugars **306** and **307** with the D-galacto- and D-gluco-configurations by $KMnO_4$ in acetone and acetic acid afforded the corresponding acids, the esterification and hydrogenolysis of which give rise to the aminodeoxyuronic acid esters **308** and **309**.[117]

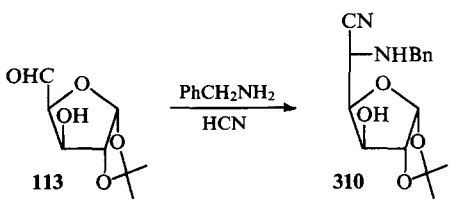


306 **308**



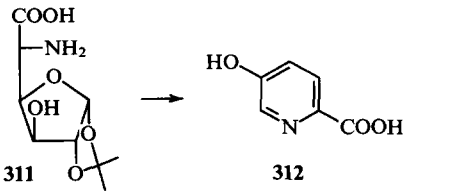
307 **309**

5-Aminodeoxyuronic acids have been detected in polyoxine antibiotics.[90] One of the first syntheses of compounds of this group described involves the addition of benzylamine and hydrocyanic acid to the aldehyde **113** with formation of 5-benzylamino-L-iduruononitrile **310**.[118]

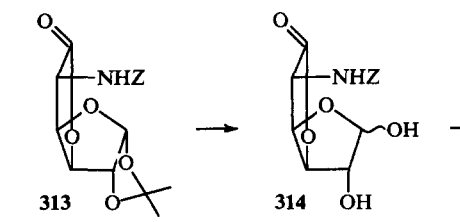


113 **310**

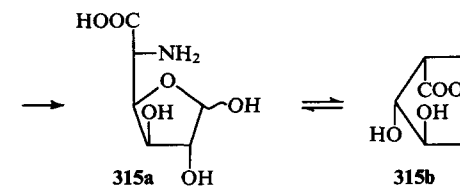
The hydrolysis of the nitrile **310** and the reductive elimination of the *N*-benzyl group over Raney nickel lead to the aminoacid **311**, the acid hydrolysis of which results in the formation of the pyridinecarboxylic acid **312**. 5-Amino-5-deoxy-L-iduronic acid has been obtained as an equilibrium mixture of the isomers **315a** and **315b** after the hydrolysis of the *N*-benzyloxycarbonyl derivative **313** and the removal of the *N*-protecting group from compound **314**.[119]



311 **312**

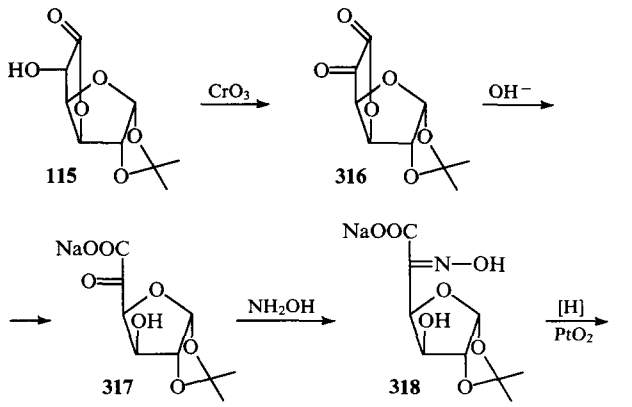


313 **314**

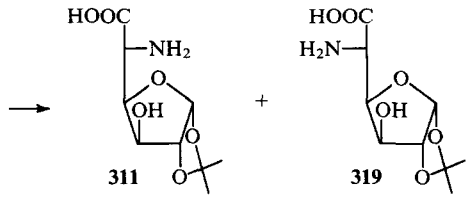


315a **315b**

L- and D-5-amino-5-deoxyidoglucofuranuronic acids (compounds **311** and **319**) have been obtained from the glucurone acetal **115** as a result of its oxidation to the ketolactone **316**, the conversion of the salt **317** into an oxime, and the reduction of the oxime **318** by hydrogen over platinum black under pressure.[120]

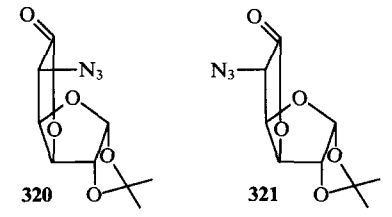


115 **316** **317** **318**



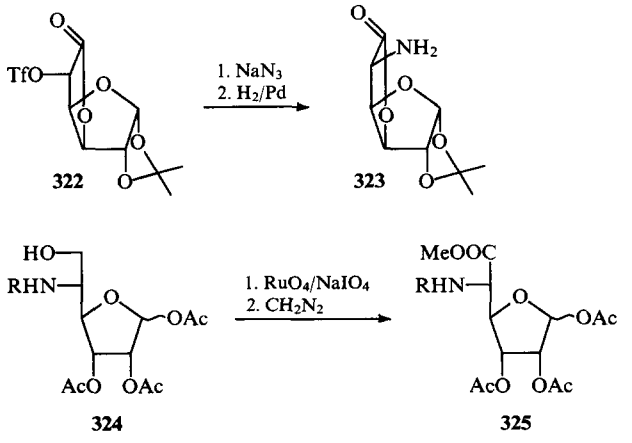
311 **319**

5-Azido-5-deoxyhexofuranuronolactones have found an application in the synthesis of 5-aminodeoxyuronic acids. The interaction of the lactone **115** with hydrazoic acid in the presence of triphenylphosphine and azodicarboxylic acid ester leads to the formation of 5-azidolactones with the L-ido- and D-idogluco-configurations (compounds **320** and **321**) in 45% and 20% yields respectively.[121]



320 **321**

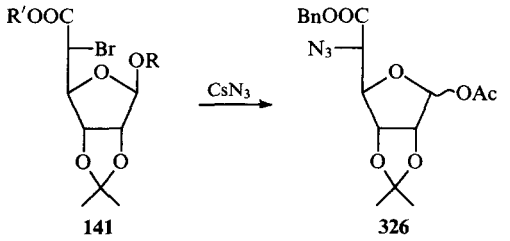
Treatment of the glucurone triflate **322** with sodium azide at −20 °C affords a satisfactory yield of the azide **320**, the reduction of which leads to the aminolactone **323**.[122]



322 **323** **324** **325**

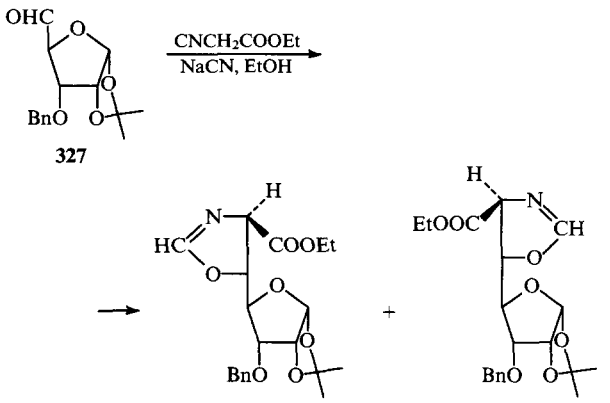
The oxidation of a derivative of the amine **324**, obtained as a result of asymmetric synthesis from the *N*-BOC-*N*,*O*-isopropylidene derivative of D-serinal and the ester of lithioethynecarboxylic acid (BOC = *tert*-butoxycarbonyl), to the aminodeoxyuronate **325** has been described.[123]

5-Azido-5-deoxy-D-allofuranuronate **326** has been obtained by the nucleophilic substitution reaction between the bromo-derivative **141** and caesium azide.[58]

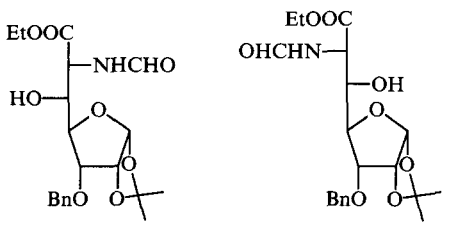


141 **326**

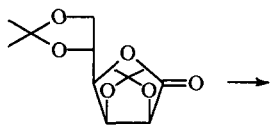
In connection with the problem of the synthesis of the structural fragments of certain antibiotics, methods have been developed for the synthesis of higher and branched amino-deoxyuronic acids. Thus treatment of the aldehyde **327** with ethyl isocyanoacetate and sodium cyanide in ethanol results in the formation of a diastereoisomeric mixture of the oxazolines **328** and **329**, the hydrolysis of which leads to the formation of isomeric 6-formamido-6-deoxyhepturonates **330** and **331**.[124]



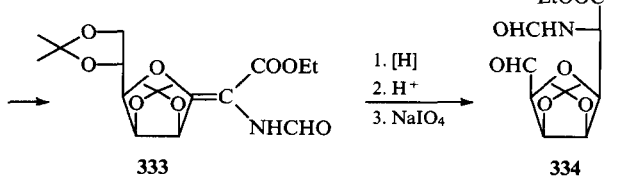
327 **328** **329**



330 **331**



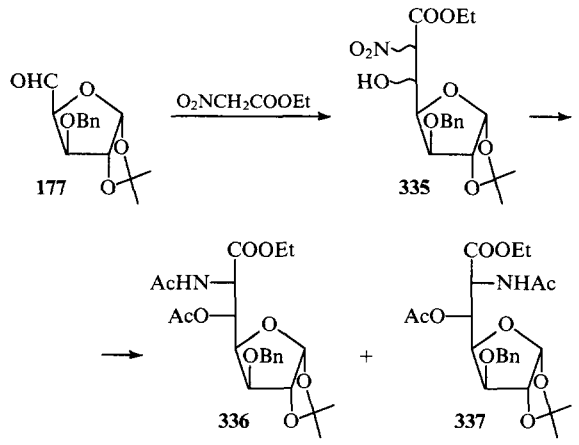
332



333 **334**

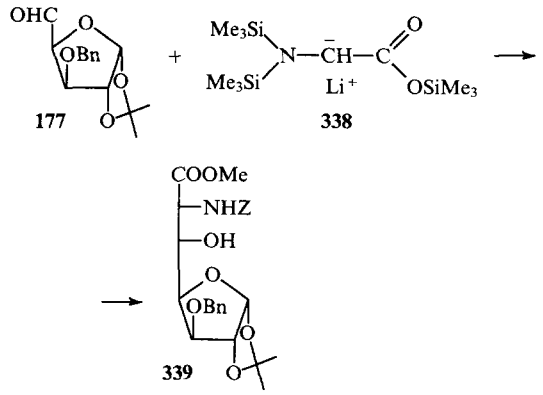
The unsaturated adduct **333**, formed from the lactone **332** and ethyl isocyanoacetate, is transformed into 6-formamido-6-deoxy-L-hepturonate **334** as a result of hydrogenation, the selective removal of one isopropylidene group, and oxidation with sodium metaperiodate.[125]

The nucleophilic addition of ethyl nitroacetate to the aldehyde **177**, the hydrogenation of the nitroester **335**, and subsequent acetylation also lead to the formation of 6-amino-6-deoxyhepturonate derivatives (compounds **336** and **337**).[126]



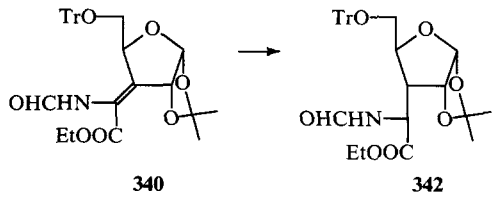
177 **335** **336** **337**

The 6-amino-6-deoxy-L-hepturonate derivative **339** was obtained in the same laboratory by adding the lithium salt of silylated glycine **338** to the aldehyde **177**.[127]

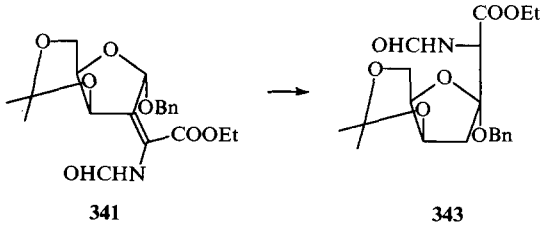


177 **338** **339**

The unsaturated esters **340** and **341**, obtained from the corresponding ketones and ethyl isocyanoacetate, are used for the synthesis of branched aminodeoxyuronic acids. The hydrogenation of compounds **340** and **341** leads to the aminoacid derivatives **342** and **343**.[128,129]

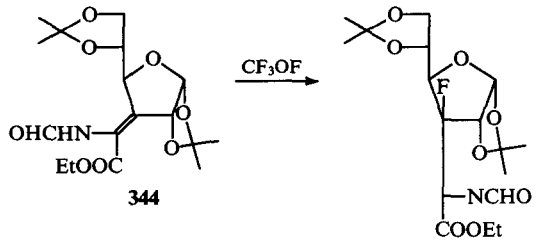


340 **342**



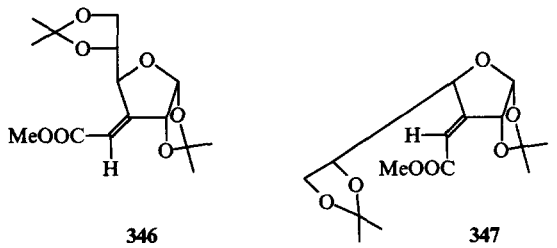
341 **343**

The fluorine-containing aminouronic acid derivative **345** is formed when the adduct **344** interacts with trifluoro-(fluorooxy)methane.[130]

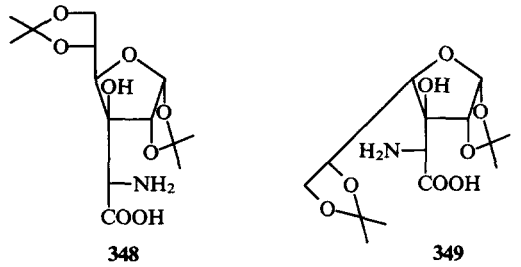


344 **345**

The unsaturated esters **346** amd **347** are converted by hydroxylation with the aid of $KMnO_4$ into branched uronic acids, which are transformed into the aminodeoxyuronic acids **348** and **349** as a result of the substitution of a hydroxyl by an amino-group.[131,132]

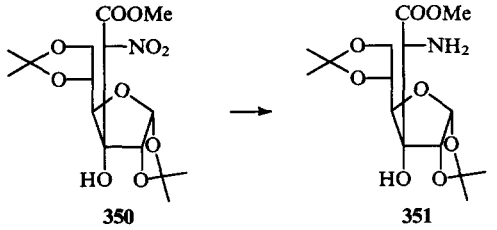


346 **347**



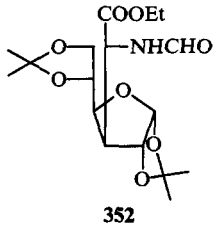
348 **349**

The addition of methyl nitroacetate to the aldehyde **205** with formation of the nitroester **350** is one of the ways of obtaining the branched aminouronate **351**.[133]



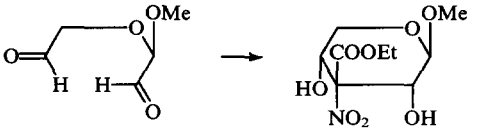
350 **351**

The aminouronate **352**, having a similar structure, has been synthesised by adding ethyl isocyanoacetate to the aldehyde **205**.[134]



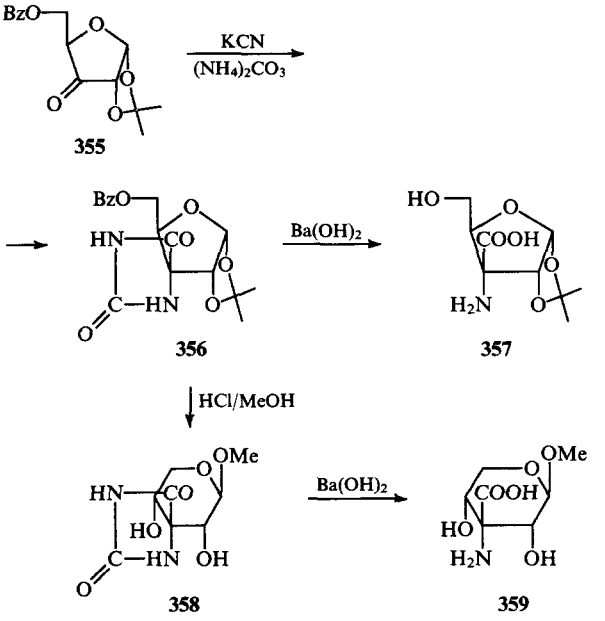
352

The ability of type **353** dialdehydes, synthesised from pyranosides, to interact with ethyl nitroacetate, forming, for example, the nitroester **354**, may serve as yet another way of synthesising branched aminouronic acids.[135]



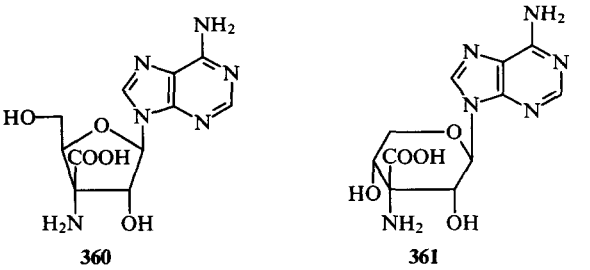
353 **354**

Another scheme for the synthesis of branched aminouronic acids involves the Bucherer conversion of the ketone **355** into the hydantoin **356**, the hydrolysis of which with $Ba(OH)_2$ leads to the aminoacid **357**, while methanolysis affords the hydantoin **358**, which is easily hydrolysed by $Ba(OH)_2$ to the aminoacid **359** with a pyranose ring.[136]



355 **356** **357** **358** **359**

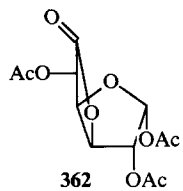
The sugars **358** and **359** obtained have been used to synthesise analogues **360** and **361** of the nucleoside antibiotic puromycin.



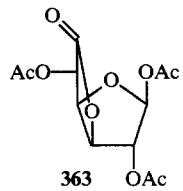
360 **361**

VII. Reactions of uronic acids

One of the most typical reactions of uronic acids is the formation of lactones. Lactones with different positions and sizes of the lactone rings are in their turn widely used for the synthesis of sugars with the necessary set of protecting groups. D-Gluco-furanurono-6,3-lactone (glucurone) **24** is formed when an aqueous solution of D-glucuronic acid is evaporated. The acetates **362** and **363** with the α- and β-anomeric configurations are synthesised by acetylating glucurone with acetic anhydride in the presence of pyridine or $ZnCl_2$.[137] Brief treatment of glucurone with boron trifluoride etherate in acetic anhydride gives the acetate **363** in 90% yield.[28]

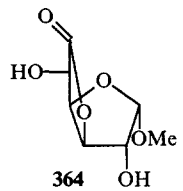


362

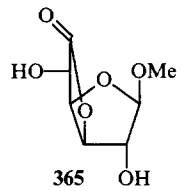


363

A convenient method of synthesis of 1,2-*O*-isopropylidene-glucurone **115** involves the refluxing of glucurone in acetone over a cation-exchange resin.[138] Treatment of glucurone with methanol and the cation-exchange resin leads to a mixture of the α- and β-D-glucofuranuronides **364** and **365**.[139]

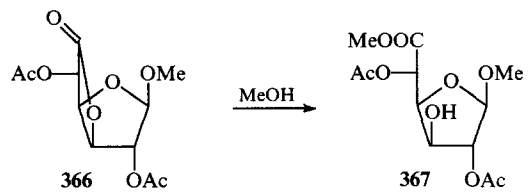


364



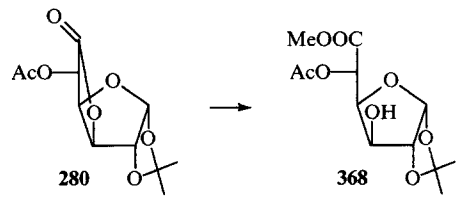
365

It has been shown that under controlled conditions the lactone **366** is deacetylated (with retention of the lactone ring) by ammonia to the lactone **365**, while refluxing in methanol converted it into the methyl ester **367**.[140]



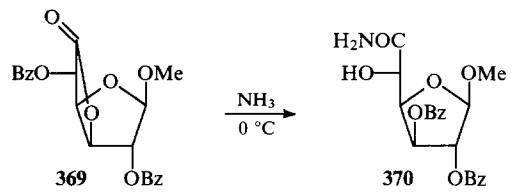
366 → **367**

The opening of the lactone rings in the lactone **280** with formation of the ester **368** is readily achieved with the aid of triethylamine or an anion-exchange resin.[141,142]



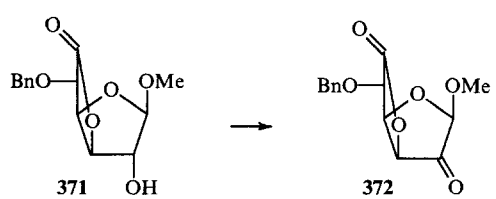
280 → **368**

On treatment of the lactone **369** with ammonia in chloroform, the benzoyl group is found to migrate from the 5-position to the 3-position with formation of the amide **370**.[143]



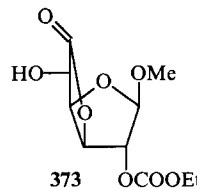
369 → **370**

The ketolactones **100** and **372** have been obtained from the lactones **115** and **371** by treatment with DMSO and acetic anhydride as well as RuO_4.[144,145]

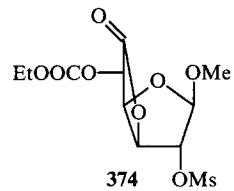


371 → **372**

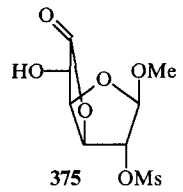
A difference between the reactivities of glucurone and its derivatives has been demonstrated.[146] Conditions were selected under which it is possible to obtain the sugars **373**–**376** protected in different ways.[146]



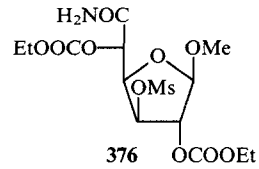
373



374



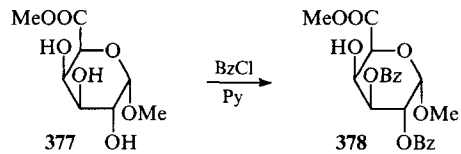
375



376

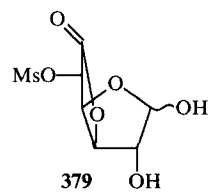
Selective acylation of glucurone and its derivatives by pivaloyl chloride in pyridine affords reaction products with different numbers of pivaloyl groups. The relative reactivities of the hydroxy-groups [OH(5) > OH(2) > OH(1)] depend to a large extent on the reaction conditions.[147]

The dibenzoate **378** can be obtained by the selective benzoylation of the galacturonide **377**.[148]

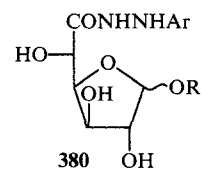


377 → **378**

The methods of synthesis of various amides and *N*-aryl-glucuronides from D-glucurone, ammonia, and aromatic amines have been described.[149] The methanesulfonate **379** was found to possess an antitumour activity,[150] while the hydrazides having the general formula **380** were found to offer protection against hepatitis.[151]

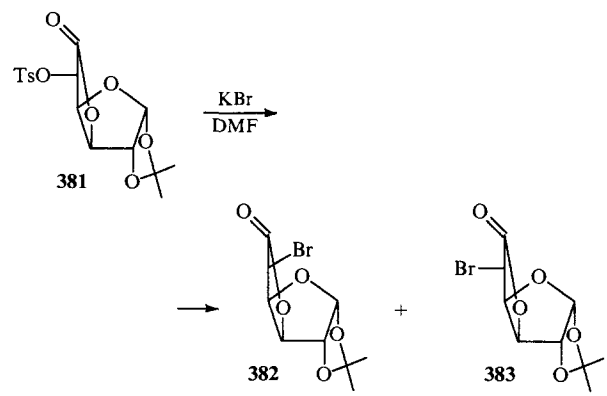


379



380

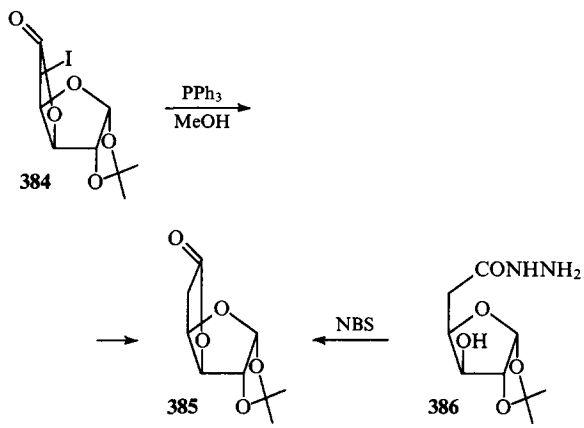
A characteristic property of glucurone derivatives is their extensive decomposition with formation of conjugated polyenes as a result of β-elimination, which competes with nucleophilic substitution at the C(5) carbon atom. Examples of reactions of this kind have been reviewed.[152]



381 → **382** + **383**

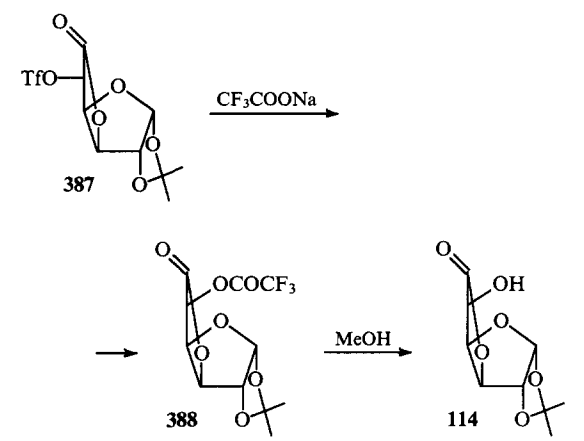
Nucleophilic substitution of the tosyl group can be achieved only with the aid of nucleophiles having a low basicity. Thus a mixture of the isomeric bromo-derivatives **382** and **383** is obtained when the tosylate **381** is heated with KBr in DMF.[153]

The interaction of the lactone **115** with triphenylphosphine iodide leads to the iodo-derivative **384** (with inversion of configuration), which is converted into 5-deoxylactone **385** on treatment with triphenylphosphine in methanol.[154]

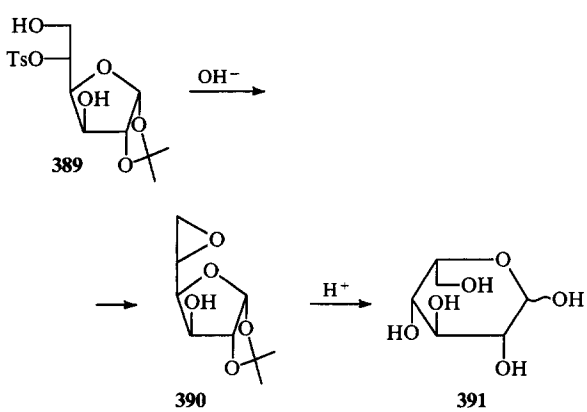


It has been observed that the tosylate **381** is readily converted into the 5-deoxysugar **386** as a result of its reaction with hydrazine.[105] Treatment of the hydrazide **386** with *N*-bromosuccinimide (NBS) leads to the 5-deoxylactone **385**.[154]

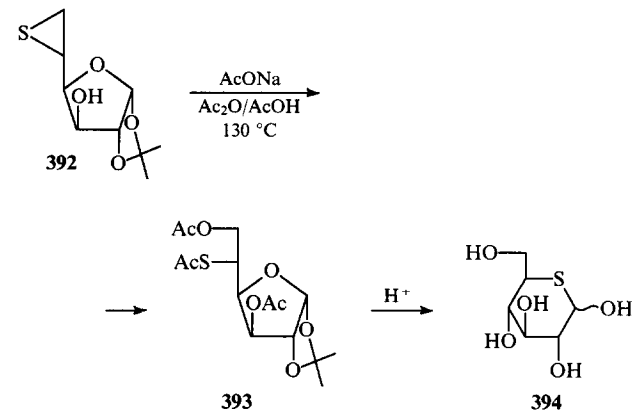
The triflate **387** is transformed under very mild conditions into the trifluoroacetate **388**, the methanolysis of which results in transition to the L-iduronolactone **114**.[155]



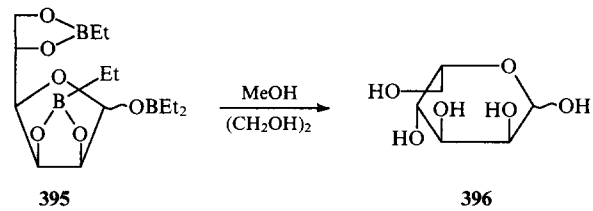
The lactone **381** is smoothly reduced by $NaBH_4$ to the alcohol **389**, from which the oxirane **390**, transformed further to L-idose **391**, is obtained on treatment with a base.[156]



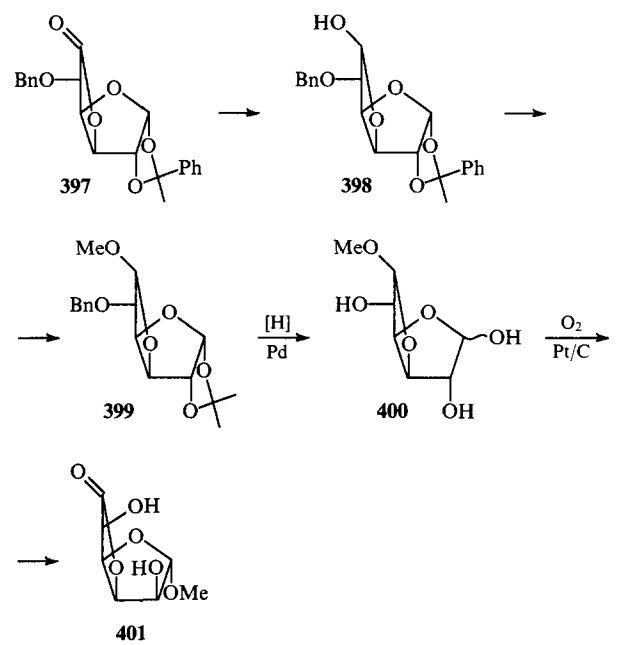
The oxirane **390** interacts with thiourea to form the thiirane **392**. Its treatment with sodium acetate in an acetate anhydride–acetic acid mixture leads to the triacetate **393** and to 5-thio-D-glucose **394** after the removal of the protecting groups.[157]



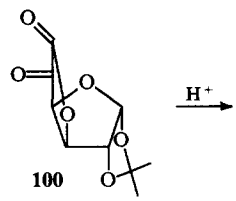
The reduction of glucurone by diethylborane takes place with formation of the borate **395**, which is readily hydrolysed to L-gulose **396**.[158]



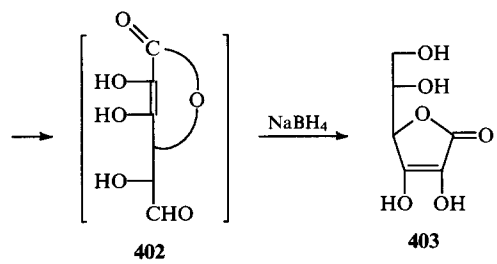
Yet another example of the transformation of the lactones into sugars which are otherwise difficult to obtain is the reduction of the D-glucuronolactone derivative **397** to the hexodialdofuranose **398**, the formation of the methyl glycoside **399**, its hydrogenolysis to the sugar **400**, and the catalytic oxidation of the latter to L-gulofuranourono-6,3-lactone **401**.[159]



Hydrolysis of the ketolactone **100** gives the aldehyde **402**, the reduction of which with $NaBH_4$ leads to L-ascorbic acid **403**.[160,161]

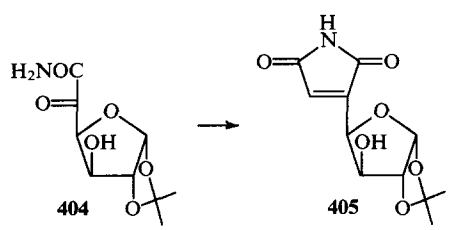


100



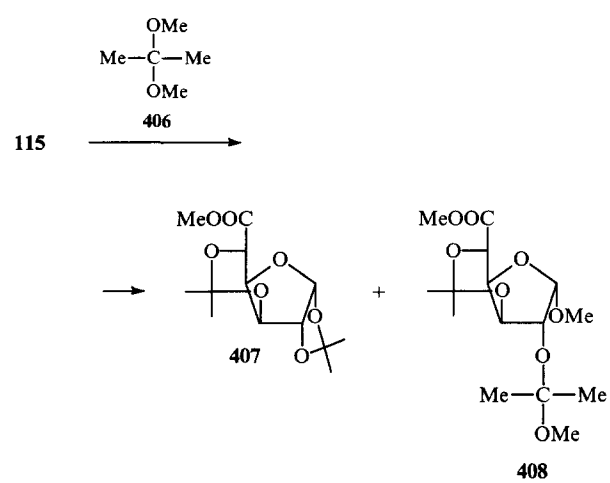
402 403

The ketoamide **404**, obtained from the lactone **100**, reacts with ethoxycarbonylmethylenetriphenylphosphorane to form the analogue of the antibiotic showdomycin **405**.[162]



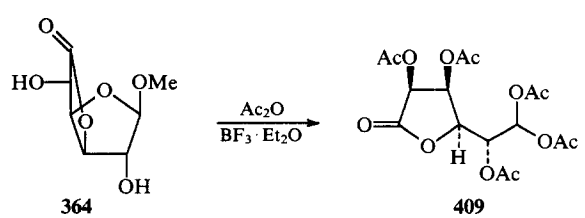
404 405

Prolonged refluxing of the lactone **115** with dimethoxypropane **406** and *p*-toluenesulfonic acid in acetone results in the formation of the diacetal **407** and the uronide **408**.[163]



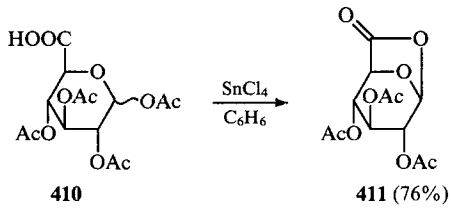
115 406 407 408

Acetolysis of the lactone **364** gives rise to the acylal **409**.[164]



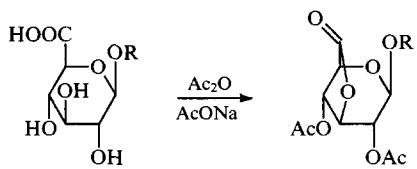
364 409

Acetylation of the sodium salt of D-glucuronic acid by acetic anhydride and *p*-toluenesulfonic acid makes it possible to obtain an anomeric mixture of the tetraacetates **410**. Its refluxing with $SnCl_4$ in benzene leads to the 6,1-lactone **411**.[165]

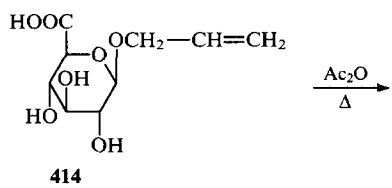


410 411 (76%)

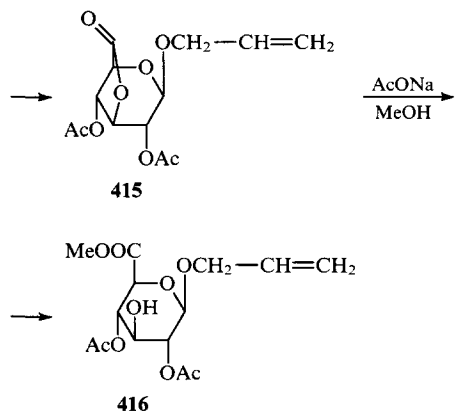
D-Glucopyranurono-6,3-lactone **413** has been obtained by treating the glucuronide **412** with sodium acetate in acetic anhydride at room temperature.[166] Brief heating of the glucuronide **414** in acetic anhydride with subsequent addition of pyridine also makes it possible to obtain the 6,3-lactone **415**, which is converted on treatment with sodium acetate in methanol into the uronate **416** with a free hydroxy-group.[167]



412 413

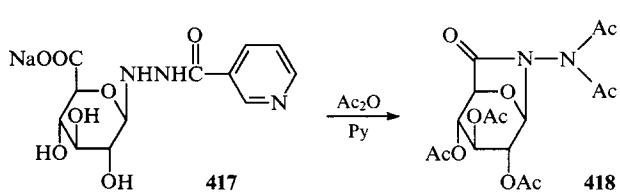


414



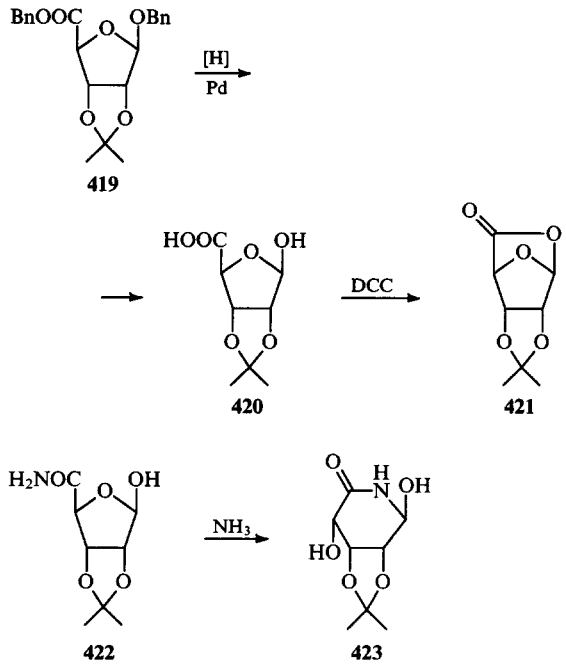
415 416

The formation of the lactam **418** has been detected after prolonged treatment of the hydrazide **417** with acetic anhydride and pyridine.[168]

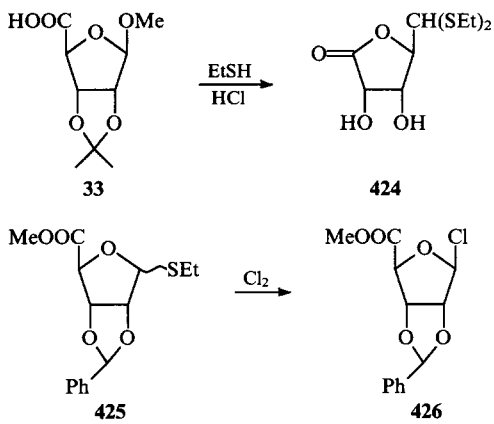


417 418

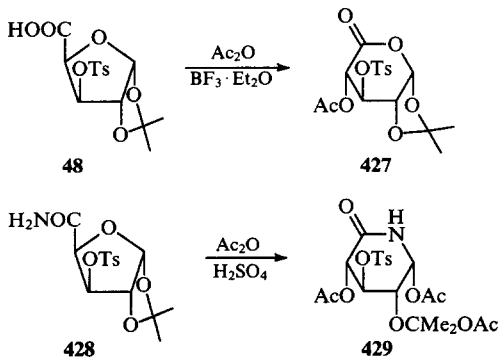
The formation of the lactones and lactams having different structures is characteristic also of penturonic acids. Thus the acid **420**, formed as a result of the hydrogenolysis of the D-riburonate **419**, can be cyclised to the 5,1-lactone **421** with the aid of dicyclohexylcarbodiimide (DCC) in ether. On treatment with ammonia, the amide **422** is converted into the lactam **423**.[169]



The acid **33** reacts with ethanethiol and concentrated HCl to form the lactone **424**. Chlorination of the ribouronate **425** obtained from compound **424** led to the synthesis of the glycosyl chloride **426** and some of its analogues.[170]

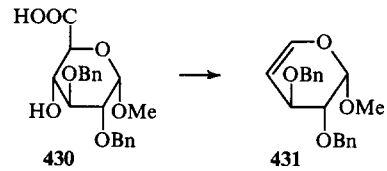


On treatment with acetic anhydride and boron trifluoride etherate, the acid **49** rearranges to the lactone **427**. Under acetolysis conditions, the amide **428** is transformed into the lactam **429**.[171,172]

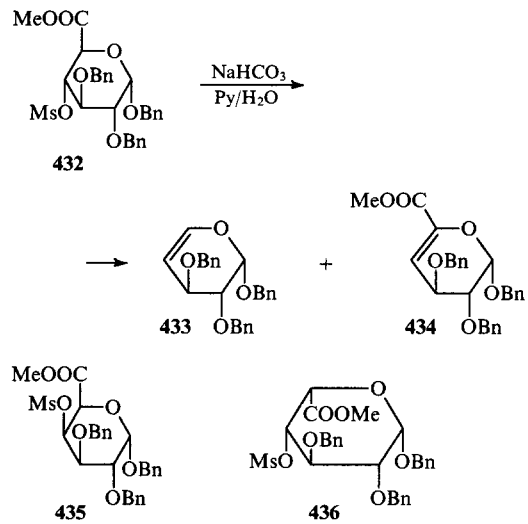


A characteristic feature of uronic acids is their ability to be converted by bases, as a result of β-elimination reactions, into unsaturated compounds, which are used in their turn in the synthesis of diverse derivatives of uronic acids. The principal characteristics and a large number of examples of β-elimination reactions have been described in a review.[173]

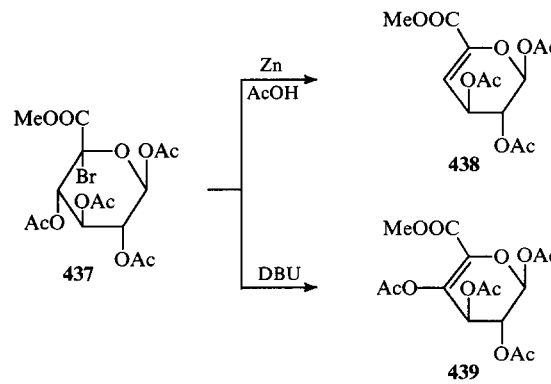
The β-elimination reaction coupled with decarboxylation merits special attention. Thus heating of the glucuronide **430** with the dineopentyl acetal of dimethylformamide leads to the formation of the unsaturated sugar **431**.[174]



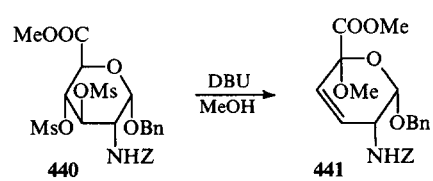
Treatment of the glucuronate **432** with sodium bicarbonate in aqueous pyridine leads to the formation of the decarboxylated sugar **433** and the eneuronate **434**. The galacturonate **435** is not decarboxylated under these conditions, giving rise only to the uronate **434**. The L-iduronate **436** is converted into the uronate **434** and a small amount of the sugar **433**.[175]



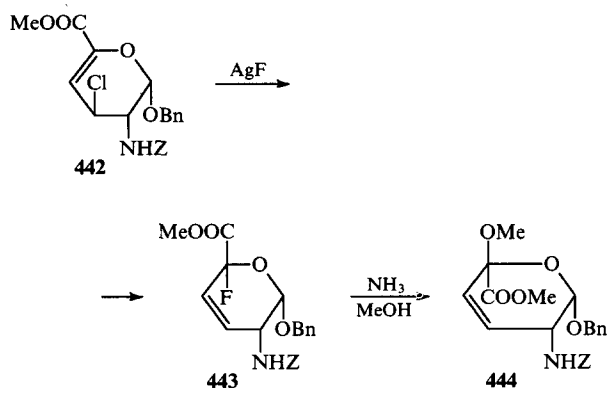
The 5-bromouronate **437** interacts with zinc in acetic acid to form the 4,5-unsaturated uronate **438**, whilst its reaction with DBU leads to its 4-acetoxy-analogue **439**.[176]



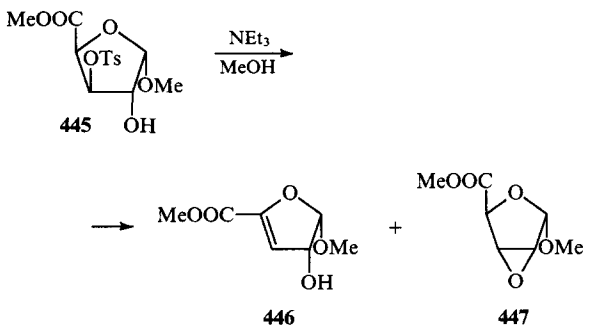
Treatment of the di(methanesulfonate) **440** with DBU in methanol led to the formation of the 3,4-unsaturated 4-methoxyuronate **441**.[177]



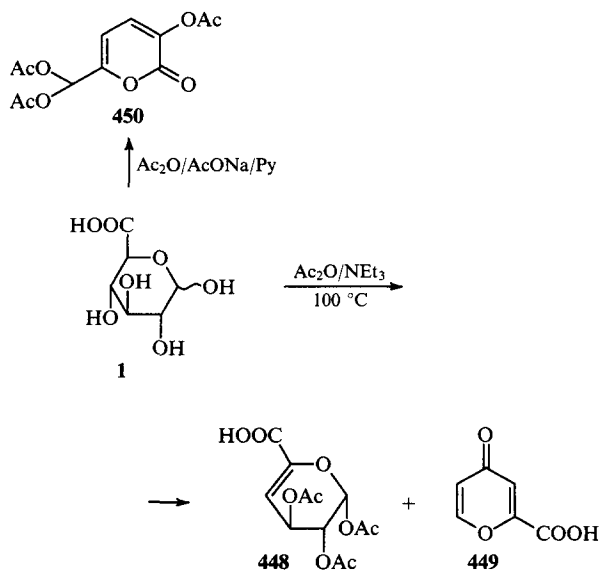
The unsaturated 3-chlorouronate **442** interacts with AgF, affording the 5-fluorouronate **443**, which is converted on treatment with ammonia in methanol into the uronate **441** and its isomer **444**.[178]



The xyluronate **445** exhibits a dual reactivity.[179,180] Its refluxing with triethylamine in methanol gives rise to the 3,4-unsaturated uronate **446** and the oxirane **447**.[21]

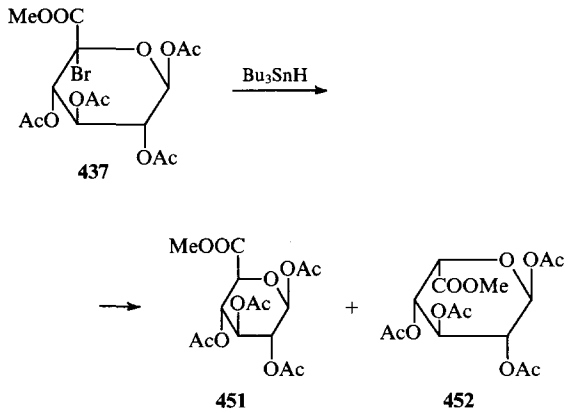


The formation of β-elimination products is observed in the interaction of free uronic acids with weak bases in acetic anhydride. When D-glucuronic acid **1** is heated with triethylamine in acetic anhydride, the 4,5-unsaturated acid **448** and coumanic acid **449** are formed. Heating of the acid **1** with pyridine in a mixture of acetic acid and its anhydride leads to the acylal of the unsaturated lactone **450**.[181]

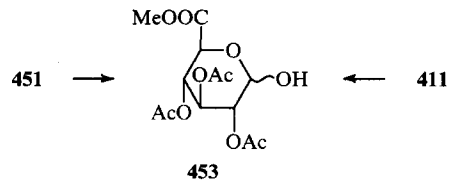


Coumanic acid **449** is formed in a satisfactory yield on heating the peracetate of D-glucuronic acid **410** with pyridine in acetic anhydride.[182]

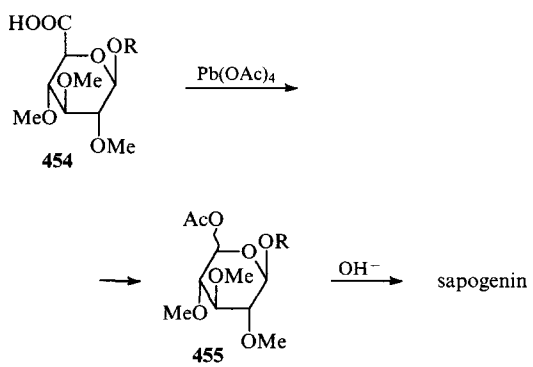
On interaction with tributyltin hydride, the 5-bromouronate **437** already mentioned is converted into a mixture of the D-glucuronate **451** and the L-iduronate **452**.[183,184]



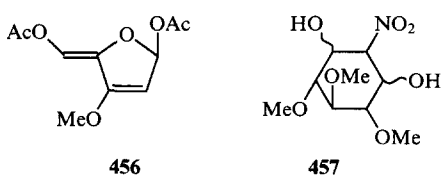
The acetate of D-glucuronic acid **453** with a hemiacetal hydroxy-group, which is of definite interest, may be obtained in two ways: by heating the peracetate **451** with Bu_3SnOMe in toluene and by treating the lactone **411** with methanol in the presence of pyridine.[165]



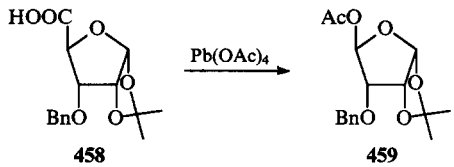
The methylated glycosides of uronic acids are decarboxylated by refluxing them with lead tetraacetate in benzene. The acetate **455** formed from the acid **454** as a result of the decarboxylation decomposes on treatment with alkali, liberating the aglycone and a product the acylation of which leads to the diene **456**.[185,186]

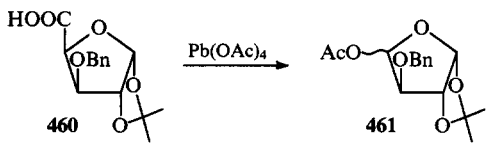


The condensation of the acetate **455** with nitromethane has found an application in the synthesis of the nitrocyclitols **457**.[187]

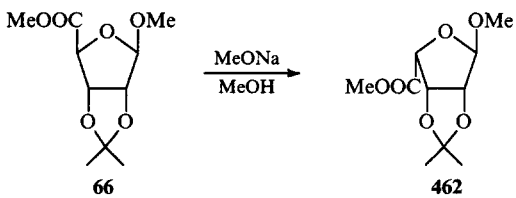


The interaction of protected riburonic and xyluronic acids (compounds **458** and **460**) with $Pb(OAc)_4$ results in the formation of the corresponding acetates **459** and **461**.[188]

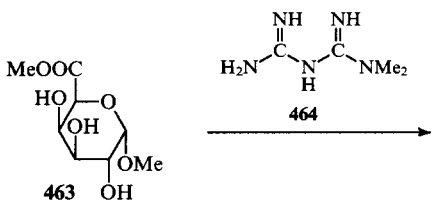


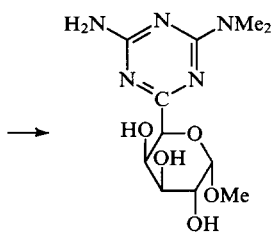


The D-riburonic acid ester **66** can be converted into the L-lyxuronic acid ester **462** by simple treatment with sodium methoxide in methanol.[11,189]

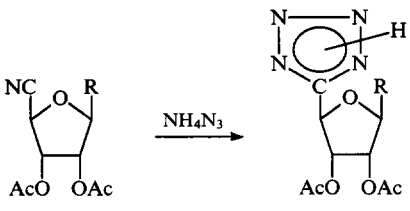


Reactions characteristic of the carboxy-group and its derivatives constitute yet another means for the modification of uronic acids. On treatment with dimethylbiguanidine **464**, the galacturonate **463** is transformed into the 5-triazine derivative of the β-L-arabinopyranoside **465**.[190]

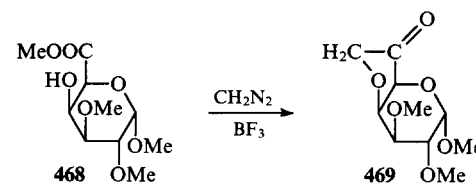




On treatment with ammonium azide, the nitrile **466** is converted into the tetrazole derivative **467**.[191]

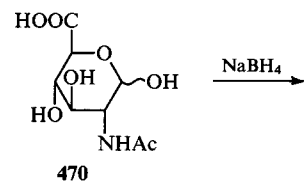


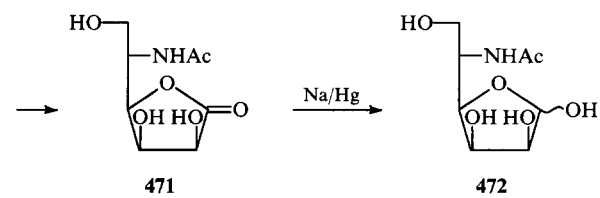
An unusual result has been obtained on treating the galacturonate **468** with diazomethane in the presence of BF_3. Together with the expected methylation product, the formation of the ketone **469** was observed.[192]

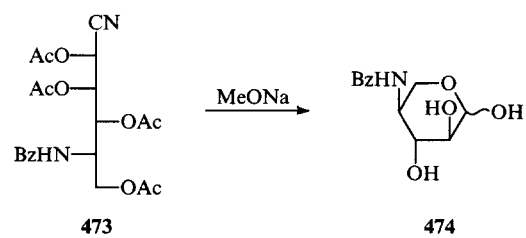


Uronic acids serve as a source of glyconolactones. L-Gulono- and L-galactono-lactones are obtained by reducing D-glucuronic and D-galacturonic acids with $NaBH_4$.[193]

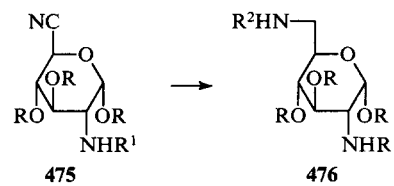
The possibility of using aminodeoxyuronic acids for the synthesis of aminosugars which are difficult to obtain has been demonstrated.[194] The lactone **471** has been obtained by reducing 2-acetamidoglucuronic acid **470**. Its reduction with sodium amalgam affords 5-acetamido-L-gulofuranose **472**. The nitrile **473**, obtained from the *N*-benzoylated lactone, is converted into 4-benzamido-L-xylopyranose **474** on treatment with sodium methoxide.







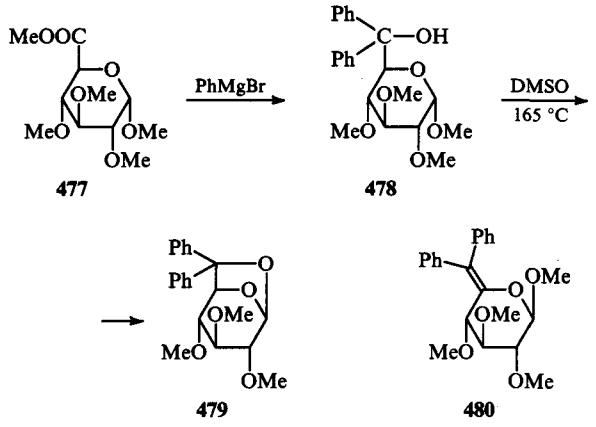
The reduction of the nitrile **475** makes it possible to synthesise the diaminosugar **476**.[195]



Treatment of the permethylated methyl α-D-glucuronide **477** with phenylmagnesium bromide gives the tertiary alcohol **478**, which is converted into the anhydrosugar **479** on heating in DMSO, whereas the corresponding β-glycoside preferentially forms the 5-enylpyranoside **480** under the same conditions.[196]

Numerous examples of the synthesis of glycuronides have been described systematically in a review.[197]

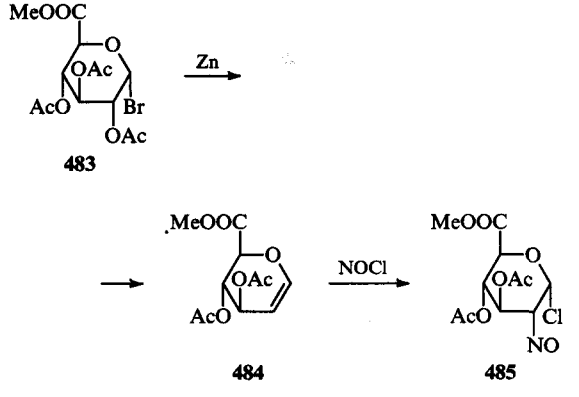
The presence of an alkoxycarbonyl group in the molecule exerts a significant influence on the stereochemical result of the reactions involving glycosylation by uronic acids, which depends in many respects on the selected reaction conditions (solvent, condensing agent, temperature). Halogenoses



[haloakylhalides? Ed.] are the most active glycosylating agents. The formation of the halo-derivatives of uronic acids is achieved with the aid of dihalomethyl methyl ether together with the employment of the traditional method. The $ZnCl_2$-catalysed reaction of the galacturonide **481** with dichloromethyl methyl ether affords the chlorosugar **482** in a satisfactory yield.[198]

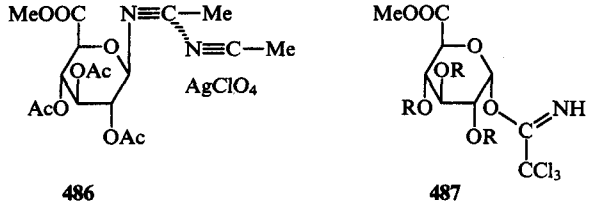


The addition of nitrosyl chloride to the glycal **484**, synthesised from the bromo-derivative **483**, leads to the chlorosugar **485** containing a nitroso-group, which is capable of being transformed further into an aminosugar.[199]

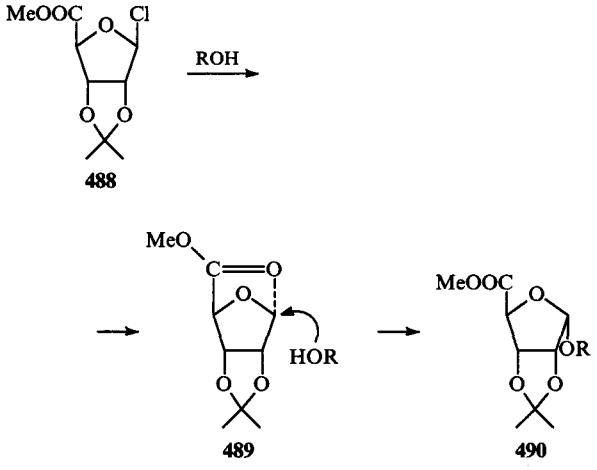


Alcohols are glycosylated by the peracetate **451** in the presence of $SnCl_4$ in dichloroethane in satisfactory yields, both α- and β-anomers being formed under these conditions.[200]

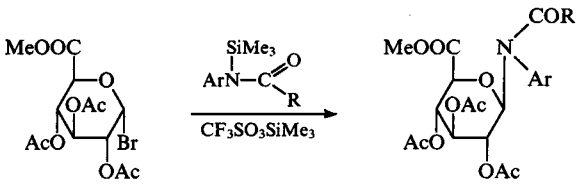
It has been shown[201] that the stereochemical specificity of the glycosylation of alcohols by the bromo-derivative **483** in acetonitrile in the presence of $AgClO_4$ is controlled by the presence in solution of type **486** conjugated compounds, which results in the preferential formation of the α-anomers. It has been suggested that trichloroacetimidates, for example compound **487**, be employed as active glycosylating agents.[202,203]



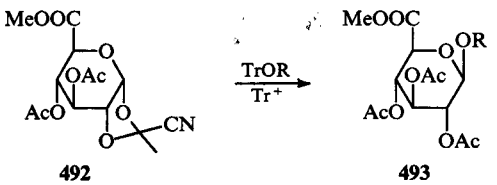
The synthesis of mainly the α-riburonide **490** from the chlorosugar **488** has been explained by the formation of the intermediate **489**, which can undergo nucleophilic attack only in the α-region.[204]



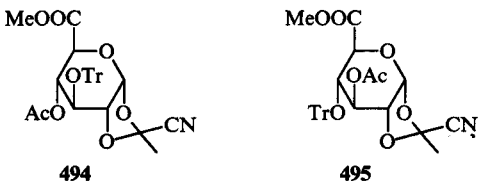
Trimethylsilyl triflate is a very effective condensing agent for the synthesis of uronides. The condensation of the bromo-derivative **483** with alcohols in its presence makes it possible to obtain glucuronides in satisfactory yields.[205] The condensation of the bromo-derivatives **483** with secondary arylamides to the *N*-glycuronides **491** has been carried out with its aid.[206]



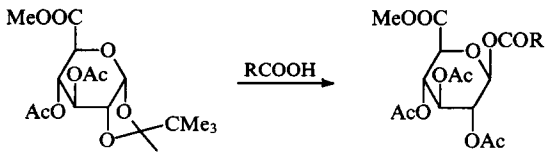
An effective method has been developed for the synthesis of the β-D-glycuronides **493**, which consists in the condensation of the cyanoethylidene derivative **492** with tritylated alcohol in the presence of a triphenylmethylium salt.[207]



In order to obtain disaccharides by this method, the cyanoethylidene derivatives of glucuronic acids **494** and **495** with the trityl group in different positions were synthesised.[208]

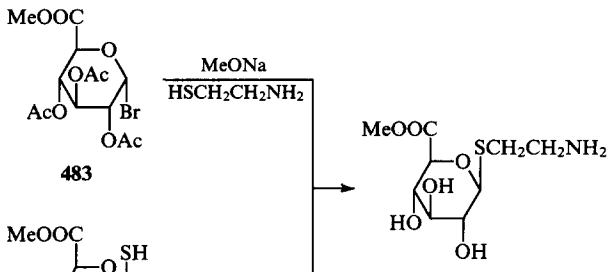


The *tert*-butoxyethylidene D-glucuronate derivative **496** is converted into the 1-*O*-acylates **497** on treatment with carboxylic acids.[209]



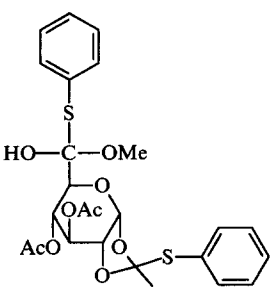
496 497

The β-*S*-alkylglucuronide **499** has been obtained by condensing the bromo-derivatives **483** with cystamine or the mercaptan **498** with 2-bromoethylamine.[210]



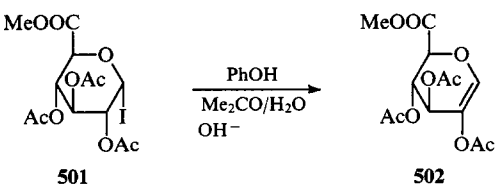
483 498 499

The glycosylation of thiophenol by D-glucopyranose pentaacetate in dichloroethane in the presence of $SnCl_4$ affords the tetraacetate of phenylthio-β-D-glucopyranoside. The 1-[2-phenylthio]orthoacetate of 3,4-di-*O*-acetyl-6-methoxy-6-phenylthio-α-D-glucopyranose **500** is formed from the acetate **451** under the same conditions.[211]



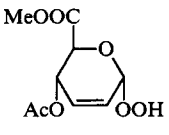
500

Instead of the expected *O*-phenylglucuronide, the glycosylation of phenol by the iodo-derivative **501** in aqueous acetone in the presence of base led to the isolation of the 2-acetoxyglycal **502** as the main reaction product.[212]



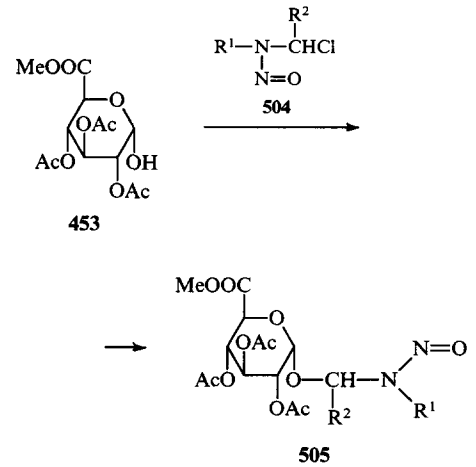
501 502

On treatment with 85% H_2O_2, the glycal **484** is converted into the hydroperoxide **503**.[213]



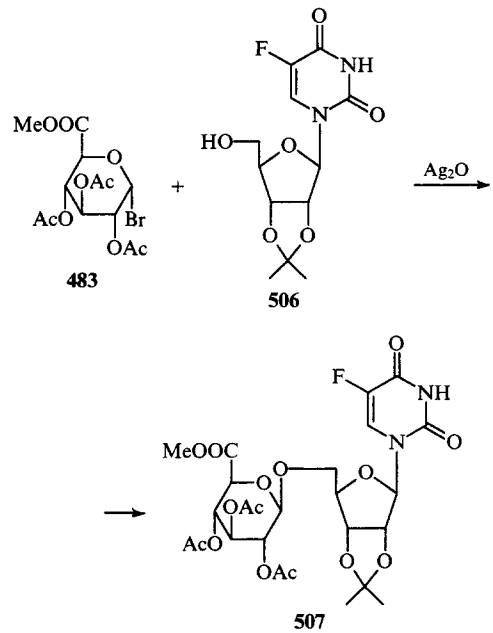
503

The glucuronate **453** condenses in pyridine with the chloroderivative of the *N*-nitrosodialkylamine **504** to the glucuronide **505**, which models the conjugates of D-glucuronic acid with nitrosoaminoalcohols formed in the organism.[214]



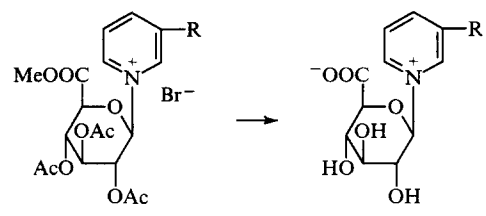
453 505

In order to synthesise the conjugate of D-glucuronic acid with 5-fluorouridine (a cytostatic agent), the bromo-derivative **483** was condensed with the 5-fluorouridine acetal **506** in the presence of Ag_2O, which led to the formation of the glucuronide **507**.[215]



483 506 507

The bromo-derivative **483** interacts with pyridines, affording the *N*-glycuronides **508**, which hydrolyse to analogues of nicotinamidoriboside **509** on treatment with bases.[216,217]



508 509

R = H, Me, $CONH_2$.

VIII. Conclusion

The data presented in the review make it possible to establish a general idea about the possibilities in the synthesis of uronic acids with a specified structure, in particular the methods for the oxidation or the conditions governing the transformation of monosaccharide derivatives.

The unique combination of functional groups in uronic acids and especially aminodeoxyuronic acids is the reason for the diversity of their chemical properties. The numerous examples of the nontrivial reactions of uronic acids described in this review should be borne in mind in planning new synthetic approaches to the preparation of chiral natural products which are difficult to obtain on a preparative scale. The broad spectrum nucleoside antibiotics, the composition of which incorporates uronic and aminodeoxyuronic acids, may serve as an example of a class of such substances which are important from the practical standpoint.[89] The syntheses of the natural representatives of this class and their structural analogues, based on the chemical reactions of uronic acids, are very important for the development of ideas concerning the biological role of uronic acid residues in the molecules of these compounds.

References

1. P A J Gorin, A S Perlin *Can. J. Chem.* **34** 693 (1956)
2. H J Lucas, W Baumgarten *J. Am. Chem. Soc.* **63** 1653 (1941)
3. D Beer, R Meuwly, A Vasella *Helv. Chim. Acta* **65** 2570 (1982)
4. Syed Mashhood Ali, K Remesh, R T Borhardt *Tetrahedron Lett.* **31** 1509 (1990)
5. S B Mandal, B Achari, P P G Dastidar *Tetrahedron Lett.* **34** 1979 (1993)
6. R K Ness, H W Diehl, H G Fletcher Jr *J. Am. Chem. Soc.* **76** 763 (1954)
7. K Heyns, J Lenz *Chem. Ber.* **94** 348 (1961)
8. Fr. P. 1 044 563 (1953)
9. E Walton, J O Rodin, C H Stammer, F W Holly, K Folkers *J. Am. Chem. Soc.* **80** 5168 (1958)
10. R R Schmidt, D Heermann, K-H Jung *Liebigs Ann. Chem.* 1856 (1974)
11. M P Kotick, D L Leland *Carbohydr. Res.* **46** 299 (1976)
12. H Ohle, H Erlbach *Chem. Ber.* **62** 2758 (1929)
13. H Weidmann, H W Oberwalder, E Wildschek, H Schwarz *Monatsh. Chem.* **103** 210 (1972)
14. A Holý, I Wotruba, E De Clercq *Collect. Czech. Chem. Commun.* **47** 1392 (1982)
15. J Šmejkal, L Kalvoda *Collect. Czech. Chem. Commun.* **38** 1981 (1973)
16. S Mashida *J. Chem. Soc. Jpn., Pure Chem. Sect.* **70** 82 (1949)
17. R K Hulyalkar, M B Perry *Can. J. Chem.* **43** 3241 (1965)
18. L N Kulinkovich, V A Timoshchuk *Zh. Obshch. Khim.* **53** 2126 (1983)
19. R R Schmidt, P Hermentin *Chem. Ber.* **112** 3616 (1979)
20. S Morgenlie *Carbohydr. Res.* **59** 73 (1977)
21. V A Timoshchuk *Zh. Org. Khim.* **28** 1512 (1992)
22. M Ohno, Y Ito, M Arita, T Shibata, K Adachi, H Sawai *Tetrahedron* **40** 145 (1984)
23. B Helferich, E Himmen *Chem. Ber.* **61** 1825 (1928)
24. C A Marsh *J. Chem. Soc.* 1578 (1952)
25. S A Barker, E J Bourne, M Stacey *Chem. Ind.* 970 (1951)
26. K Heyns, H Paulsen *Angew. Chem.* **69** 600 (1957)
27. W G Overend, F Shafizadeh, M Stacey, G Vaughan *J. Chem. Soc.* 3633 (1954)
28. K-C Tsou, A M Seligman *J. Am. Chem. Soc.* **74** 5605 (1952)
29. K-C Tsou, A M Seligman *J. Am. Chem. Soc.* **75** 1042 (1953)
30. C L Mehltretter, B H Alexander, R L Mellies, C E Rist *J. Am. Chem. Soc.* **73** 2424 (1951)
31. W A Szarek, G W Hay, D M Vyas, E R Ison, L J J Hronowski *Can. J. Chem.* **62** 671 (1984)
32. K Heyns, H Paulsen *Adv. Carbohydr. Chem.* **17** 169 (1962)
33. H M Sell, K P Link *J. Am. Chem. Soc.* **60** 1813 (1938)
34. R G Ault, W N Haworth, E L Link *J. Chem. Soc.* 517 (1935)
35. C Niemann, K P Link *J. Biol. Chem.* 407 (1933)
36. M Stacey, P J Wilson *J. Chem. Soc.* 587 (1944)
37. M Stacey *J. Chem. Soc.* 1529 (1939)
38. W G Overend, F Shafizadeh, M Stacey *J. Chem. Soc.* 1487 (1951)
39. P Kováč *Chem. Zvesti* **28** 820 (1974)
40. D Keglević, D Ljevaković *Carbohydr. Res.* **64** 319 (1978)
41. J C Jacquinet, M Petítou, P Duchanssoy, I Lederman, J Choay, G Torri, P Sinaÿ *Carbohydr. Res.* **130** 221 (1984)
42. M B Yunker, B Fraser-Reid *J. Chem. Soc., Chem. Commun.* **61** (1975)
43. A I Usov, V V Deryabin *Izv. Akad. Nauk SSSR, Ser. Khim.* 394 (1980)
44. K S Kim, W A Szarek *Carbohydr. Res.* **104** 328 (1982)
45. D Horton, C G Tindall Jr *Carbohydr. Res.* **15** 215 (1970)
46. K Maurer, G Drehfahl *Chem. Ber.* **80** 94 (1947)
47. R J Ferrier *Aust. J. Chem.* **33** 1025 (1980)
48. F Shafizadeh, M L Wolfrom *J. Am. Chem. Soc.* **77** 2568 (1955)
49. D Horton, F O Swanson *Carbohydr. Res.* **14** 159 (1970)
50. N Berg, O Kjlberg *Carbohydr. Res.* **57** 65 (1977)
51. T Anthonsen, M A E Sallam *Carbohydr. Res.* **78** 368 (1980)
52. Y Nakahara, T Ogawa *Carbohydr. Res.* **173** 306 (1988)
53. H Kuzuhara, H G Fletcher Jr *J. Org. Chem.* **32** 2535 (1967)
54. G Just, K Grozinger *Can. J. Chem.* **53** 2701 (1975)
55. R R Schmidt, C Beitzke, A K Forrest *J. Chem. Soc., Chem. Commun.* 909 (1982)
56. J Wagner, E Vieira, P Vogel *Helv. Chim. Acta* **71** 624 (1988)
57. Y Auberson, P Vogel *Angew. Chem., Int. Ed. Engl.* **28** 1498 (1989)
58. Y Auberson, P Vogel *Tetrahedron* **46** 7019 (1990)
59. D J Ager, M B East *Heterocycles* **37** 1789 (1994)
60. G M Rubottom, J M Gruber, R K Boeckman Jr, M Ramaiach, J B Medwid *Tetrahedron Lett.* **19** 4603 (1978)
61. R Angerbauer, R R Schmidt *Carbohydr. Res.* **89** 193 (1981)
62. O A Shavrygina, S M Makin *Zh. Org. Khim.* **2** 1354 (1966)
63. S M Makin, S D Yablonovskaya, O A Shavrygina, G N Pershin, N S Bogdanova *Khim.-Farm. Zh.* **10** 34 (1969)
64. J Jurczak, A Zamojski *Tetrahedron* **28** 1505 (1972)
65. D L Boger, K D Robarge *J. Org. Chem.* **53** 5793 (1988)
66. R Grewe, G Rockstroh *Chem. Ber.* **86** 536 (1953)
67. I Dijong, U Wittkötter *Chem. Ber.* **101** 1948 (1968)
68. J M J Tronchet, O R Martin, J-B Zumwald *Helv. Chim. Acta* **62** 1303 (1979)
69. J M J Tronchet, M A M Massoud *Helv. Chim. Acta* **62** 1632 (1979)
70. Yu A Zhdanov, Yu E Alekseev, Kh A Kurdanov *Zh. Obshch. Khim.* **42** 1836 (1971)
71. P Coutrot, C Grison, M Tabyaoui, S Czernecki, J-M Valery *J. Chem. Soc., Chem. Commun.* 1515 (1988)
72. H H Baer, H R Hanna *Carbohydr. Res.* **102** 169 (1982)
73. P Blanchard, A D Da Silve, M S El Kortbi, J-L Fourrey, M Robert-Géro *J. Org. Chem.* **58** 6517 (1993)
74. B Giese, J A Gonzalez-Gomes, T Witzel *Angew. Chem., Int. Ed. Engl.* **23** 69 (1984)
75. P W Austin, J G Buchanan, E M Oakes *J. Chem. Soc., Chem. Commun.* 374 (1965)
76. A Rosenthal, M Ratcliffe *Carbohydr. Res.* **54** 61 (1977)
77. W P Blackstock, C C Kuenzle, C H Eugster *Helv. Chim. Acta* **57** 1003 (1974)
78. A Rosenthal, K Shudo *J. Org. Chem.* **37** 4391 (1972)
79. W M zu Reckendorf *Chem. Ber.* **105** 673 (1972)
80. R Bonjouklian, B Ganem *Carbohydr. Res.* **76** 245 (1979)
81. Yu A Zhdanov, Yu E Alekseev, Kh A Kurdanov *Zh. Obshch. Khim.* **43** 186 (1973)
82. A Rosenthal, R H Dodd *J Carbohydr. Nucl., Nucl.* **5** 545 (1978)
83. Y Ali, D M Vyas, R C Nabinger, W A Szarek *Carbohydr. Res.* **104** 183 (1982)
84. Jpn. P. 3 017; *Chem. Abstr.* **60** 15 974g (1964)
85. R T Lee, Y C Lee *Carbohydr. Res.* **64** 302 (1978)
86. M M Vigdorchik, R P Olad'ko, N P Kostyuchenko, N N Suvorov *Zh. Org. Khim.* **10** 1256 (1974)
87. A Klemer, W Funcke *Carbohydr. Res.* **33** 313 (1974)
88. L G Revel'skaya, A N Anikeeva, S N Danilov *Zh. Obshch. Khim.* **42** 241 (1972)
89. V A Timoshchuk *Usp. Khim.* **63** 730 (1994) [*Russ. Chem. Rev.* **63** 695 (1994)]

90. R J Suhadolnik *Nucleoside Antibiotics* (New York: Wiley-Interscience, 1970)
91. K Heyns, W Koch *Chem. Ber.* **86** 110 (1953)
92. K Heyns, H Paulsen *Chem. Ber.* **88** 188 (1955)
93. H Weidmann, H K Zimmerman *Liebigs Ann. Chem.* **639** 198 (1961)
94. S M Block, P H Gross, H Weidmann, H K Zimmerman *Liebigs Ann. Chem.* **696** 209 (1966)
95. J Yoshimura, T Sato, H Ando *Bull. Chem. Soc. Jpn.* **42** 2352 (1969)
96. K Heyns, M Beck *Chem. Ber.* **90** 2443 (1957)
97. N G Kundu, J F Crawford, B Prajsnar, E J Reed, S Rosenthal *Carbohydr. Res.* **12** 225 (1970)
98. H Paulsen, J P Lorentzen, W Kutschker *Carbohydr. Res.* **136** 153 (1985)
99. P W Jeffs, G Chan, R Sitrin, N Holder, G D Roberts, C De Brosse *J. Org. Chem.* **50** 1726 (1985)
100. E Darakas, H Hultberg, K Leontein, J Lönngren *Carbohydr. Res.* **103** 176 (1982)
101. M L Wolfrom, M W Winkley *J. Org. Chem.* **31** 1169 (1966)
102. V A Timoshchuk, L N Kulinkovich *Zh. Obshch. Khim.* **58** 919 (1988)
103. T M Williams, R Grumbie, H S Mosher *J. Org. Chem.* **50** 91 (1985)
104. T M Williams, H S Mosher *Tetrahedron Lett.* **26** 6269 (1985)
105. H Ando, K Ajisaka *J. Chem. Soc. Jpn., Chem. Ind. Chem.* 1161 (1972)
106. H Ishidate, M Kimura, V Kawata *Chem. Pharm. Bull.* **11** 1083 (1963)
107. J Yoshimura, J Hashimoto, H Ando *Bull. Chem. Soc. Jpn.* **46** 1272 (1973)
108. L N Kulinkovich, V A Timoshchuk *Zh. Obshch. Khim.* **53** 2126 (1983)
109. M Yamashita, Y Kawai, I Uchida, T Komori, M Kohsaka, H Imanaka, K Sakane, H Setoi, T Teraji *Tetrahedron Lett.* **25** 4689 (1984)
110. H Paulsen, W Koebernick, E Autschbach *Chem. Ber.* **105** 1524 (1972)
111. A Tsuji, T Kinoshita, M Maeda *Chem. Pharm. Bull.* **16** 539 (1968)
112. T Ogawa, M Akatsu, M Matsui *Carbohydr. Res.* **44** 22 (1975)
113. A Banaszek, A Zamojski *Carbohydr. Res.* **51** 276 (1976)
114. M Chmielewski *Pol. J. Chem.* **54** 1197 (1980)
115. D Horton, W Weckerle, B Winter *Carbohydr. Res.* **70** 59 (1979)
116. B A Dmitriev, N A Kocharova, N K Kochetkov *Bioorg. Khim.* **8** 1234 (1982)
117. T Naka, T Hashizume *Agric. Biol. Chem.* **34** 1855 (1970)
118. H Paulsen, K Todt *Chem. Ber.* **99** 3450 (1966)
119. H Paulsen, E Mäckel *Chem. Ber.* **106** 1525 (1973)
120. K Ochi, K Okui *Chem. Pharm. Bull.* **22** 2223 (1974)
121. J Schweng, E Zbiral *Tetrahedron Lett.* **19** 119 (1978)
122. B P Bashyal, H-F Chow, L E Fellows, G W J Fleet *Tetrahedron* **43** 415 (1987)
123. P Garner, J M Park *Tetrahedron Lett.* **30** 5065 (1989)
124. K Bischofberger, A J Brink, O G De Villiers, R H Hall, A Jordaan *Carbohydr. Res.* **64** 33 (1978)
125. R H Hall, K Bischofberger, S J Eitelman, A Jordaan *J. Chem. Soc., Perkin Trans. 1* 743 (1977)
126. H Paulsen, M Brieden, V Sinnwell *Liebigs Ann. Chem.* 113 (1985)
127. H Paulsen, M Brieden, G Benz *Liebigs Ann. Chem.* 565 (1987)
128. A J Brink, A Jordaan *Carbohydr. Res.* **34** 1 (1974)
129. K Bischofberger, A J Brink, O G De Villiers, R H Hall, A Jordaan *J. Chem. Soc., Perkin Trans. 1* 1472 (1977)
130. K Bischofberger, A J Brink, A Jordaan *J. Chem. Soc., Perkin Trans. 1* 2457 (1975)
131. A Rosenthal, C M Richards, K Shudo *Carbohydr. Chem.* **27** 353 (1973)
132. A Rosenthal, C M Richards *Carbohydr. Res.* **29** 413 (1973)
133. A Rosenthal, B L Cliff *Carbohydr. Res.* **79** 63 (1980)
134. A J Brink, J Goetzer, O G De Villiers, R H Hall, A Jordaan, G J Kruger *Tetrahedron* **32** 965 (1976)
135. S Umesawa, M Kinoshita, H Yanagisawa *Asahi Garasu Kogyo Gijutsu Shoereikai Kenkya Hokoru* **16** 83 (1970)
136. H Yanagisawa, M Kinoshita, S Nakada, S Umezawa *Bull. Chem. Soc. Jpn.* **43** 246 (1970)
137. W F Goebel, F H Babers *J. Biol. Chem.* **100** 743 (1933)
138. H Weidmann *Liebigs Ann. Chem.* **679** 186 (1964)
139. E M Osman, K C Hobbs, W E Walston *J. Am. Chem. Soc.* **73** 2727 (1951)
140. W F Goebel, F H Babers *J. Biol. Chem.* **110** 707 (1935)
141. I Matsunaga, Z Tamura *Chem. Pharm. Bull.* **17** 1383 (1969)
142. A Y Chernyak, K V Antonov, N K Kochetkov, L N Padyukov, N V Tsvetkova *Carbohydr. Res.* **141** 199 (1985)
143. H Weidmann, D Wewerka, N Wolf *Monatsh. Chem.* **99** 509 (1968)
144. K Onodera, S Hirano, N Kishimura *Carbohydr. Res.* **6** 276 (1968)
145. K Dax, H Weidmann *Carbohydr. Res.* **25** 363 (1972)
146. H Weidmann, K Dax, D Wewerka *Monatsh. Chem.* **101** 1831 (1970)
147. D Keglević, D Ljevaković, S Tomić-Kulenović *Carbohydr. Res.* **92** 51 (1981)
148. P L Gill, M W Horner, L Hough, A C Richardson *Carbohydr. Res.* **17** 213 (1971)
149. J Ide *Yakugaku Zasshi* **85** 213 (1965)
150. Jpn. P. 6 812; *Chem. Abstr.* **59** 738e (1963)
151. Germ. P. 2 124 044; *Chem. Abstr.* **104** 1 525 17b (1972)
152. K Dax, H Weidmann *Adv. Carbohydr. Chem. Biochem.* **33** 189 (1976)
153. T Irimajiri, H Yoshida, T Ogata, S Inokawa *Bull. Chem. Soc. Jpn.* **43** 3242 (1970)
154. K Dax, A P Rauter, A E Stutz, H Weidmann *Liebigs Ann. Chem.* 1768 (1981)
155. R Csuk, H Honig, J Nimpf, H Weidmann *Tetrahedron Lett.* **21** 2135 (1980)
156. M Blanc-Muesser, J Defaye *Synthesis* 568 (1977)
157. H Driguez, B Henrissat *Tetrahedron Lett.* **22** 5061 (1981)
158. W V Dahlhoff, P Idelmann, R Köster *Angew. Chem., Int. Ed. Engl.* **19** 546 (1980)
159. I Macher, K Dax, H Inselsbacher, H Weidmann *Carbohydr. Res.* **77** 225 (1979)
160. J Bakke, O Theander *J. Chem. Soc., D* 175 (1971)
161. T Kitahara, T Ogawa, T Naganuma, M Matsui *Agric. Biol. Chem.* **38** 2189 (1974)
162. A P Rauter, J A Figueiredo, I M Ismael *Carbohydr. Res.* **188** 19 (1989)
163. C H Lee *Carbohydr. Res.* **22** 230 (1972)
164. H Itoh, K Aoki, T Matsumoto *Bull. Chem. Soc. Jpn.* **58** 777 (1985)
165. E M Fry *J. Am. Chem. Soc.* **77** 3915 (1955)
166. H Wagner, G Aurnhammer, H Danninger, O Seligmann, L Pallos, L Farkas *Chem. Ber.* **105** 257 (1972)
167. A Ya Chernyak, K V Antonov, N K Kochetkov *Bioorg. Khim.* **13** 958 (1987)
168. Y Takeda, T Akimoto, Y Kyogoku *Carbohydr. Res.* **106** 175 (1982)
169. R R Schmidt, K-H Jung, P Hermentin *Chem. Ber.* **111** 3311 (1978)
170. K-H Jung, R R Schmidt *Liebigs Ann. Chem.* 1426 (1979)
171. V A Timoshchuk *Zh. Obshch. Khim.* **57** 2375 (1987)
172. V A Timoshchuk *Carbohydr. Res.* **145** 131 (1985)
173. J Kiss *Adv. Carbohydr. Chem. Biochem.* **29** 229 (1974)
174. K D Philips, J Žemlička, J P Horwitz *Carbohydr. Res.* **30** 281 (1973)
175. J Kiss, P Taschner *J. Carbohydr. Nucl. Nucl.* **1** 279 (1974)
176. R Blattner, R J Ferrier, P C Tyler *J. Chem. Soc., Perkin Trans. 1* 1535 (1980)
177. J Kiss, W Arnold *Helv. Chim. Acta* **64** 1566 (1981)
178. J Kiss, P C Wyss *J. Carbohydr. Chem.* **4** 347 (1985)
179. A A Akhrem, V A Timoshchuk, I A Mikhailopulo *Carbohydr. Res.* **43** 195 (1975)
180. V A Timoshchuk, L N Kulinkovich, T I Olimpieva, E I Boreko, G V Vladyko *Khim.-Farm. Zh.* 49 (1988)
181. K Tajima *Tetrahedron Lett.* **27** 6095 (1986)
182. Jpn. P. 60 112 785 (85 112 785); *Chem. Abstr.* **104** 19 784w (1986)
183. T Chiba, P Sinaÿ *Carbohydr. Res.* **151** 379 (1986)
184. A Nudelman, J Herzig, H E Gottlieb, E Keinan, J Sterling *Carbohydr. Res.* **162** 145 (1987)
185. I Kitagawa, M Yoshikawa, Y Ikenishi, K S Im, I Yosioka *Tetrahedron Lett.* 549 (1976)
186. I Kitagawa, M Yoshikawa, K S Im, Y Ikenishi *Chem. Pharm. Bull.* **25** 657 (1977)
187. I Kitagawa, A Kadota, M Yoshikawa *Chem. Pharm. Bull.* **26** 3825 (1978)

188. D D Dhavale, E Tagliavini, C Trombini, A Umani-Ronchi *Tetrahedron Lett.* **29** 61 (1988)
189. A Holý *Collect. Czech. Chem. Commun.* **47** 2969 (1982)
190. C S Lee, K Maekawa *Agric. Biol. Chem.* **40** 785 (1976)
191. J J Baker, A M Mian, J R Tittensor *Tetrahedron* **30** 2939 (1974)
192. P Kováč, R Palovčik, V Kováčik, J Hirsch *Carbohydr. Res.* **44** 205 (1975)
193. M L Wolfrom, K Anno *J. Am. Chem. Soc.* **74** 5583 (1952)
194. H Weidmann, E Fauland, R Helbig, H K Zimmerman *Liebigs Ann. Chem.* **694** 183 (1966)
195. H Weidmann, H K Zimmerman *Liebigs Ann. Chem.* **684** 226 (1965)
196. G O Aspinall, O Igarashi, T N Krishnamurthy, W Mitura, M Funabashi *Can. J. Chem.* **54** 1708 (1976)
197. D Keglević *Adv. Carbohydr. Chem. Biochem.* **36** 57 (1979)
198. P Kováč, I Farkas, V Mihálov, R Palovčik, R Bognár *J. Carbohydr. Nucl. Nucl.* **3** 57 (1976)
199. P C Wyss, J Kiss, W Arnold *Helv. Chim. Acta* **58** 1847 (1975)
200. K Honma, K Nakazima, T Uematsu, A Hamada *Chem. Pharm. Bull.* **24** 394 (1976)
201. R R Schmidt, E Rücker *Tetrahedron Lett.* **21** 1421 (1980)
202. R R Schmidt, J Michel *Angew. Chem.* **92** 763 (1980)
203. R R Schmidt, M Stumpp, J Michel *Tetrahedron. Lett.* **23** 405 (1982)
204. R R Schmidt, P Hermentin *Angew. Chem.* **89** 58 (1977)
205. B Fischer, A Nudelman, M Ruse, J Herzig, H Gottlieb *J. Org. Chem.* **49** 4988 (1984)
206. G Snatzke, J Vlahov *Liebigs Ann. Chem.* 439 (1985)
207. V I Betaneli, M M Litvak, L V Bachinowsky, N Kochetkov *Carbohydr. Res.* **94** C1 (1981)
208. V I Betaneli, M M Litvak, M I Struchkova, L V Bakinovskii, N K Kochetkov *Bioorg. Khim.* **9** 87 (1983)
209. K Honma, A Hamada *Carbohydr. Res.* **73** 297 (1979)
210. J Oehlke *Pharmazie* **33** 644 (1978)
211. K Honma, A Hamada *Chem. Pharm. Bull.* **24** 818 (1976)
212. F B Anderson, D H Leaback *Chem. Ind.* 967 (1960)
213. H-W Fehlhaber, G Snatzke, I Vlahov *Liebigs Ann. Chem.* 637 (1987)
214. H Braun, M Wiessler *Angew. Chem., Int. Ed. Engl.* **19** 400 (1980)
215. K A Watanabe, A Matsuda, M J Halat, D H Hollenberg, J S Nisselbaum, J J Fox *J. Med. Chem.* **24** 893 (1981)
216. H Y Aboul-Enein *J. Carbohydr. Nucl. Nucl.* **4** 77 (1977)
217. L Dalgaard *Acta Chem. Scand., Ser. B* **37** 923 (1983)