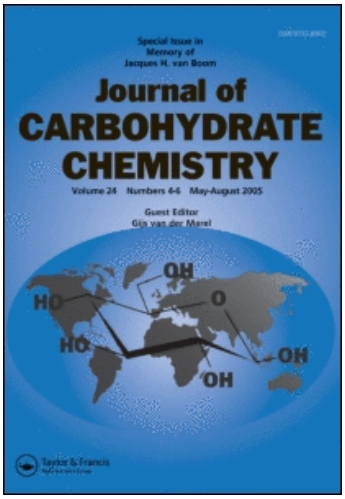

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Review Article: Anionic Conjugate Addition Reactions for the Preparation of Substituted Monosaccharides and Disaccharides

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REVIEW ARTICLE

ANIONIC CONJUGATE ADDITION REACTIONS FOR THE PREPARATION OF SUBSTITUTED MONOSACCHARIDES AND DISACCHARIDES

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1. INTRODUCTION

Conjugate addition reactions are widely used synthetic tools in general organic chemistry,[1] and starting in the early 1960s they were introduced into carbohydrate chemistry. Since then a considerable number of publications have described the utilisation of different types of conjugate addition reactions in the field of carbohydrate chemistry but to date this area has not been reviewed.

For brevity this review will be restricted to anionic conjugate additions with emphasis on recent literature reports; radical additions, conjugate reductions, cycloadditions (including dipolar cycloadditions) and reactions of or leading to carbasugars will not be included.

The different sections will deal with carbohydrate acceptors or donors in conjugate addition reactions and with carbohydrates involved in intramolecular reactions. As levoglucosenone is by far the most prominent carbohydrate molecule used in conjugate addition reactions,[2] some of its reactions will be discussed in a separate section.

2. CARBOHYDRATES AS ACCEPTORS

2.1. Reactions with C-nucleophiles

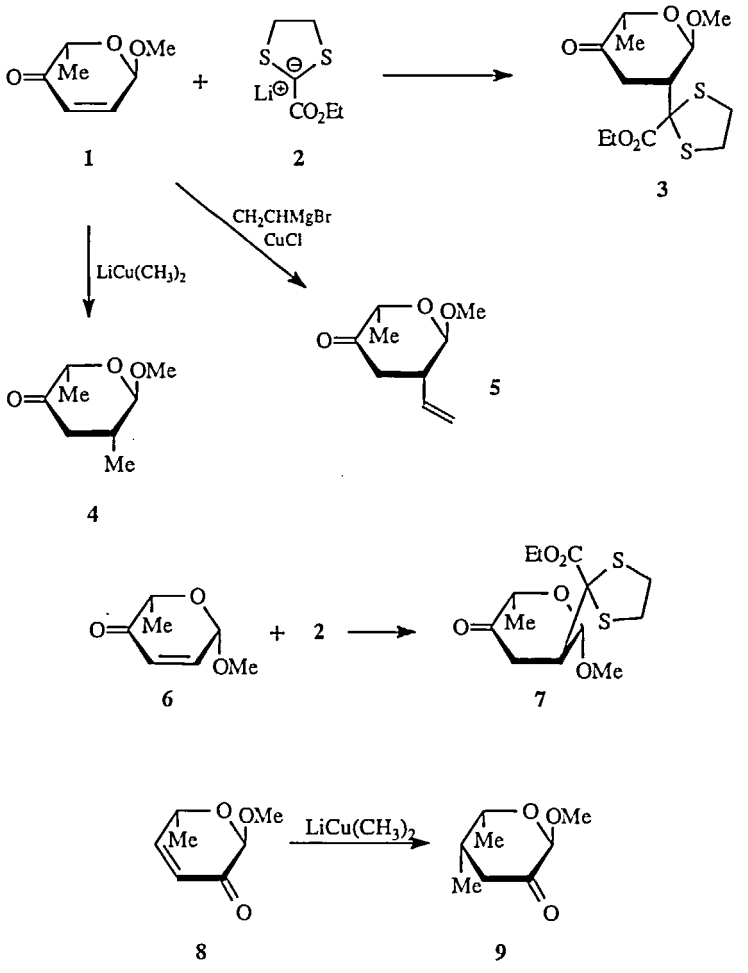
The reaction of carbohydrate acceptors with C-nucleophiles provides access to branched-chain sugars and C-glycosides. The most commonly used acceptor systems are unsaturated uloses or lactones and unsaturated nitro sugars. Early work[3] in the field of unsaturated uloses involved treatment of different enuloses, e.g., **1**, **6** or **8**, with lithiated compounds such as **2**, Me_2CuLi or vinyl magnesium bromide. The reactions lead to a variety of different branched-chain sugars, usually as one stereoisomer and in moderate to good yields (Scheme 1). The reaction of enulose **1** with different Michael donors gave **3**, **4**, and **5**, respectively. As in the reactions of the β-configurated compound **1**, the attack of the nucleophile on the α-configurated compound **6** occurs from the stericly less hindered side to give the *trans*-adduct **7**. Interestingly the reaction of **8** with Me_2CuLi led to the formation of **9** with the new C-4 methyl group *cis* to the neighbouring C-6 methyl group.

The reaction of **10** with either **2** or $CH_3C(SPh)_2Li$ gave an α/β-mixture of the C-glycosides **11** and **12** (Scheme 2). The same approach for the synthesis of C-glycosides was later used[4] to synthesise a variety of β-C-glycosides **14** from **13** using different silyl enol ethers as nucleophiles (Scheme 2). The initially formed titanium adducts rearranged to give the final products **14** in 40-90% yield.

A recent synthesis of branched-chain sugars starting from hex-2-enonolactone **15** using either alkyl cuprates or compounds of the general structure R'R"CHCOOR'" as nucleophiles, was described.[5] The yields were 55-98% and the formation of only one stereoisomer of **16** was observed (Scheme 3).

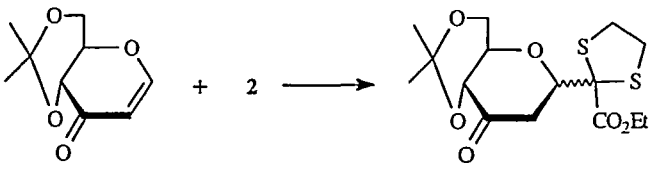
Branched furanoses en route to analogues of AZT were synthesised[6] using the addition of Me_2CuLi or $PhSCu(R'MgX)_n$ to the unsaturated lactone **17** with yields of **18** ranging from 67 to 87% (Scheme 3). Starting from the lactone **19** the addition of cyanide was found to be not very selective,[7] the unsaturated lactone itself racemized under the reaction conditions and the combined yields of the addition products **20** and **21** were about 40% (Scheme 3).

A study of the reaction of pentanedione or cyanide with nitro sugars **22**,[8] **26**,[9] or **29**[10] showed that the reaction proceeded stereoselectively to give different addition

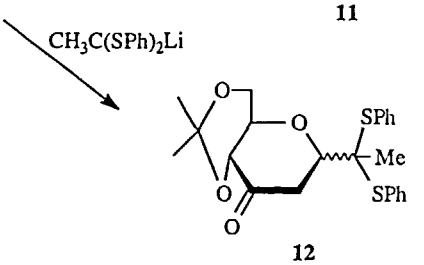


Scheme 1

products, depending on the reaction conditions (Scheme 4). The reaction of pentanedione with **22** for instance was strongly dependent on the solvent and led to the formation of **23** when performed in benzene, whereas in dioxane **24** was the observed product. The addition of cyanide to **22** in acetonitrile gave the axial addition product **25**. Treatment of **26** under the same conditions in dioxane gave a 4.5:1 mixture of **27** and **28**. The reaction of **29** with cyanide on the other hand led to **30** as single addition product (Scheme 5).

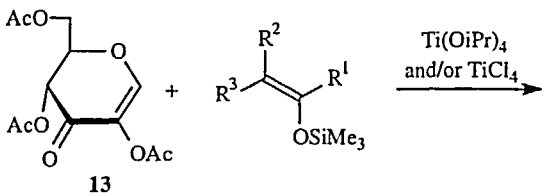


10 11

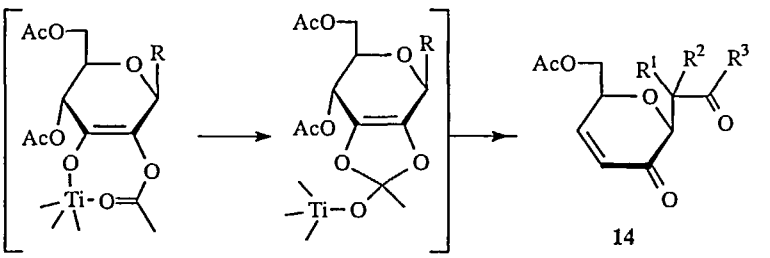


12

R^1	R^2	R^3
$-(CH_2)_4-$		H
$-(CH_2)_3-$		H
Ph	H	H
Me	H	H
H	Me	Me
O^tBu	H	H

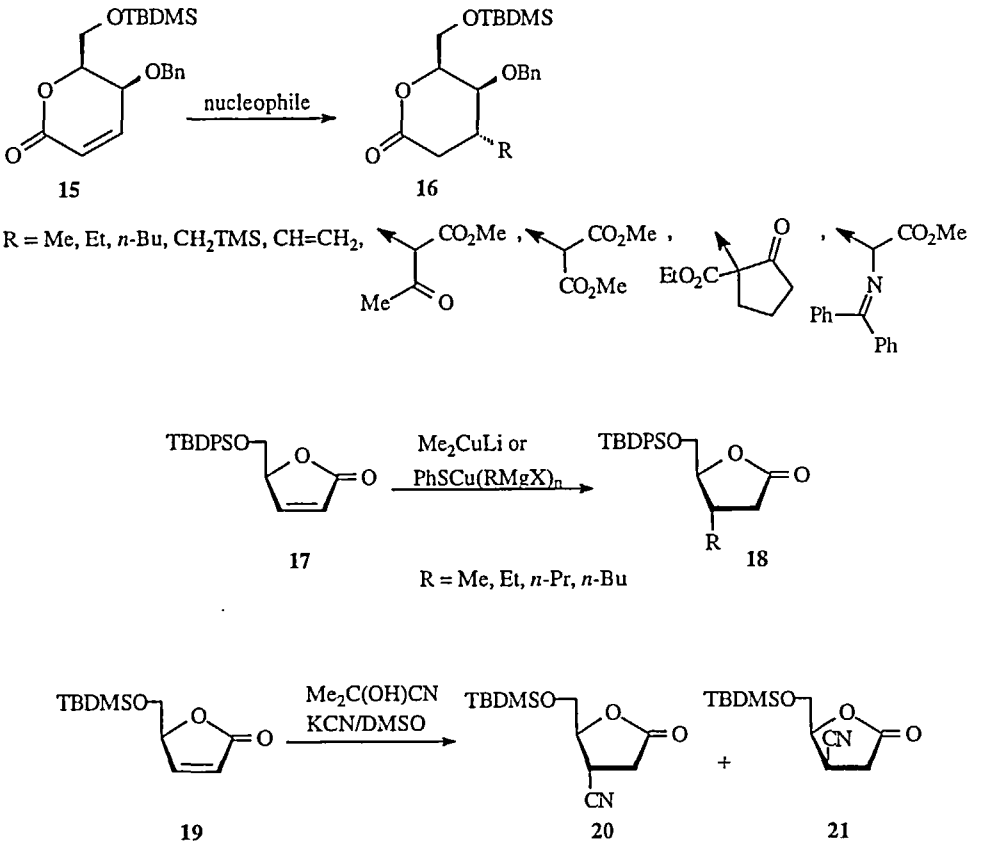


13



14

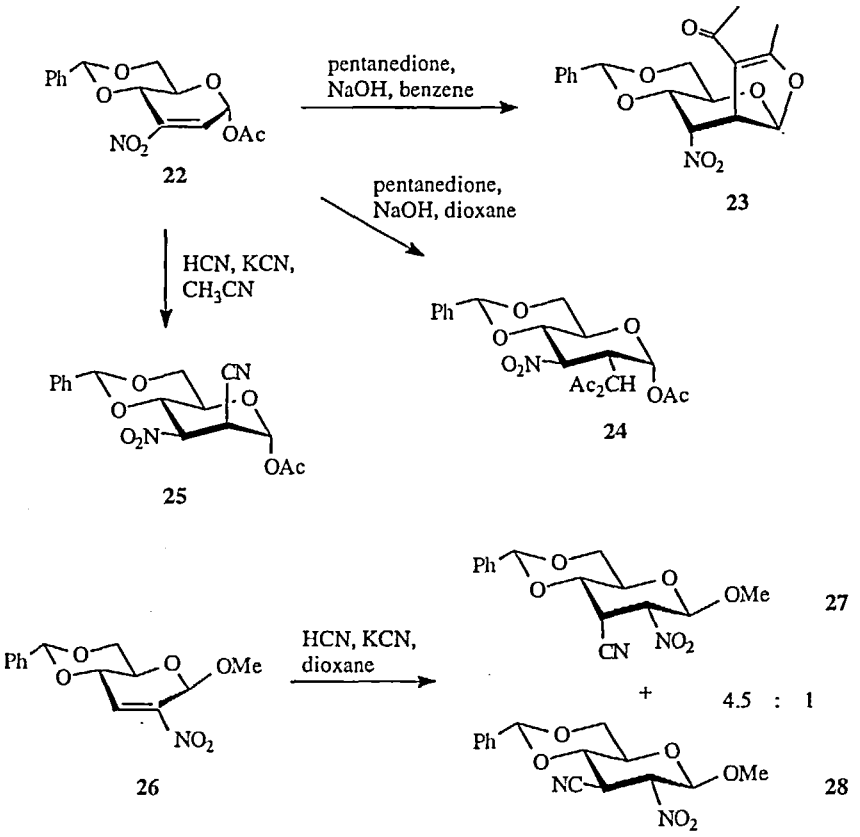
Scheme 2



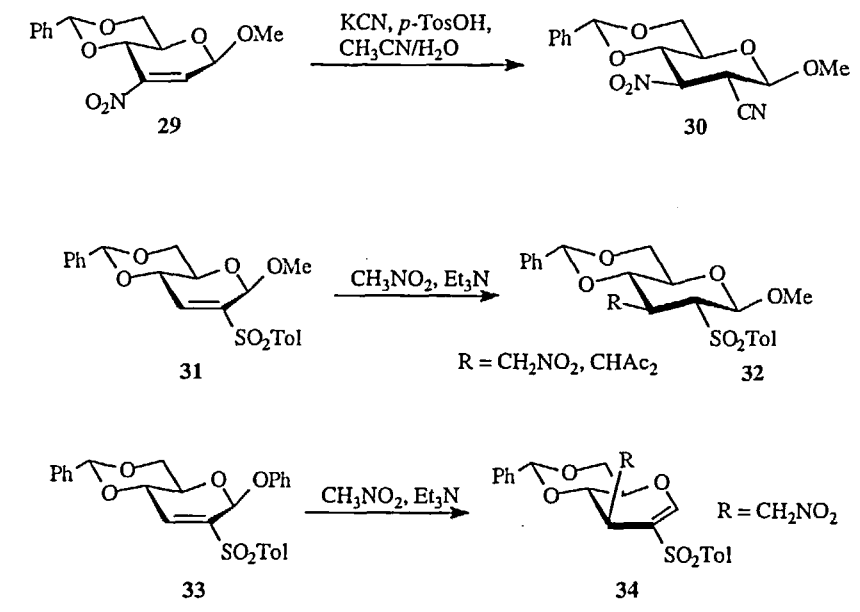
Scheme 3

Reactions similar to those of the unsaturated nitro sugars are found with the corresponding *p*-tolylsulfonyl derivatives as shown in Scheme 5. For instance, the addition of nitromethane or pentanedione to **31**[11] proceeded in a stereoselective fashion in yields of 78% and 92%, respectively. Treatment of the corresponding β-phenyl derivative **33** under the same conditions on the other hand led to an S_N2' reaction to give the 3-deoxy-1-enitol **34**.[11]

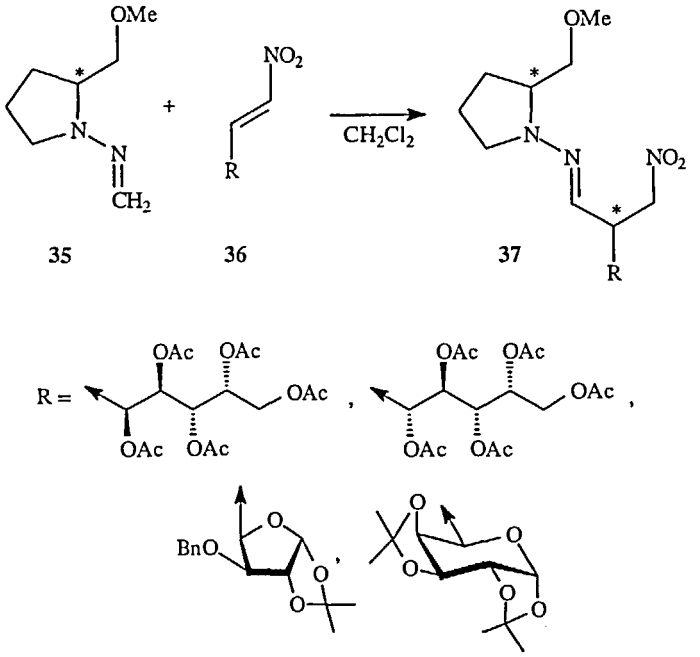
Diastereoselective synthesis of branched-chain sugars[12] was achieved using chiral hydrazones as cyanide equivalents for the addition to different nitro sugars (Scheme 6). The yields were generally higher than 70% and more than 96 de was observed in several cases.



Scheme 4



Scheme 5



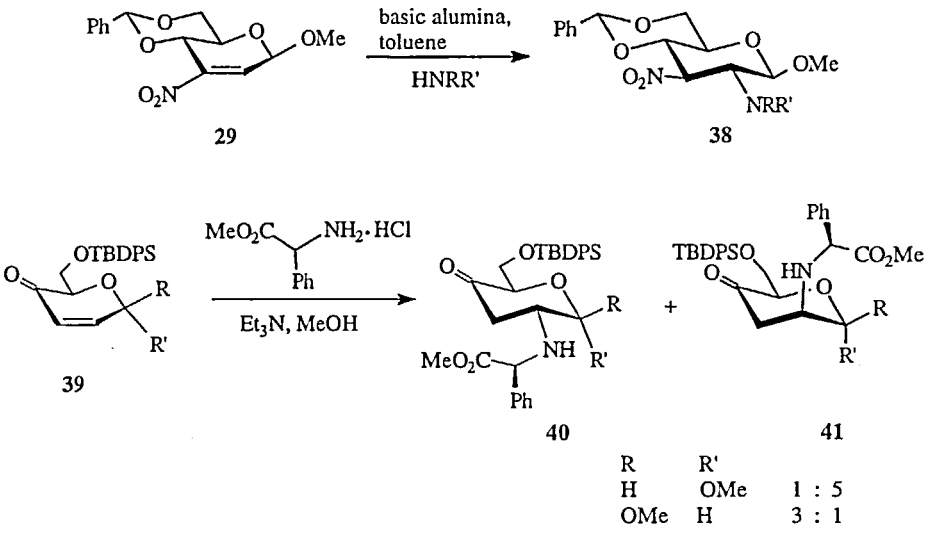
Scheme 6

2.2. Reactions with N-nucleophiles

The first report of a conjugate addition reaction in carbohydrate chemistry using N-nucleophiles[13] described the stereoselective addition of different amines to the unsaturated nitro sugar **29** giving compounds **38** in around 70% yield (Scheme 7). The examples included the addition of one amino acid (glycine), a reaction which was extended later[14] to other amino acids, and more recently[15] included using the enopyranuloses **39** as acceptors for the formation of mixtures of **40** and **41** (Scheme 7).

Amino sugars can be easily prepared by the reaction of suitable carbohydrate acceptors and an N-nucleophile. The most commonly used N-nucleophile is the azide anion. It has a high nucleophilicity, is a latent functionality for an amino group and is stable under many reaction conditions used in carbohydrate chemistry.

For different enopyranuloses the attack of the nucleophile can often be directed to either an axial or equatorial position. Switching from ammonia as nucleophile to

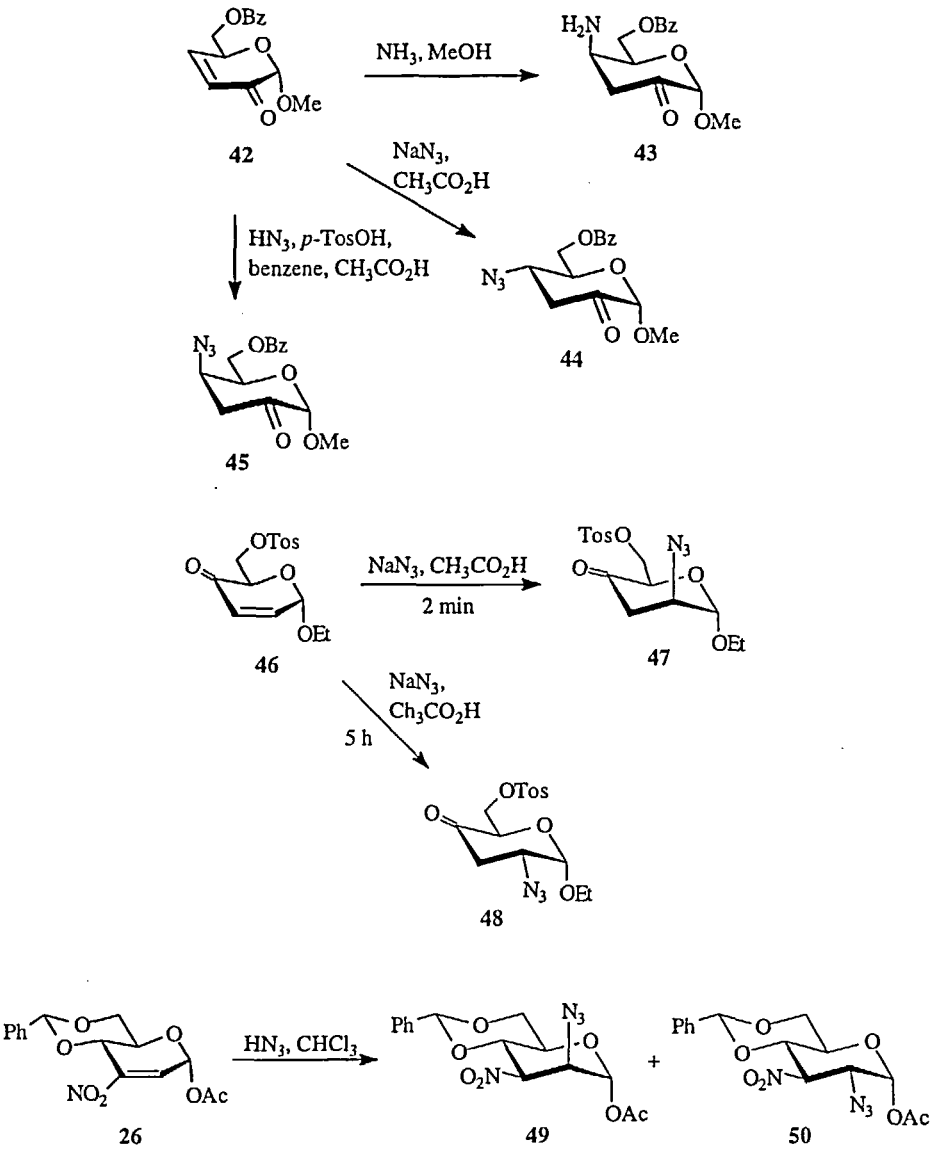


Scheme 7

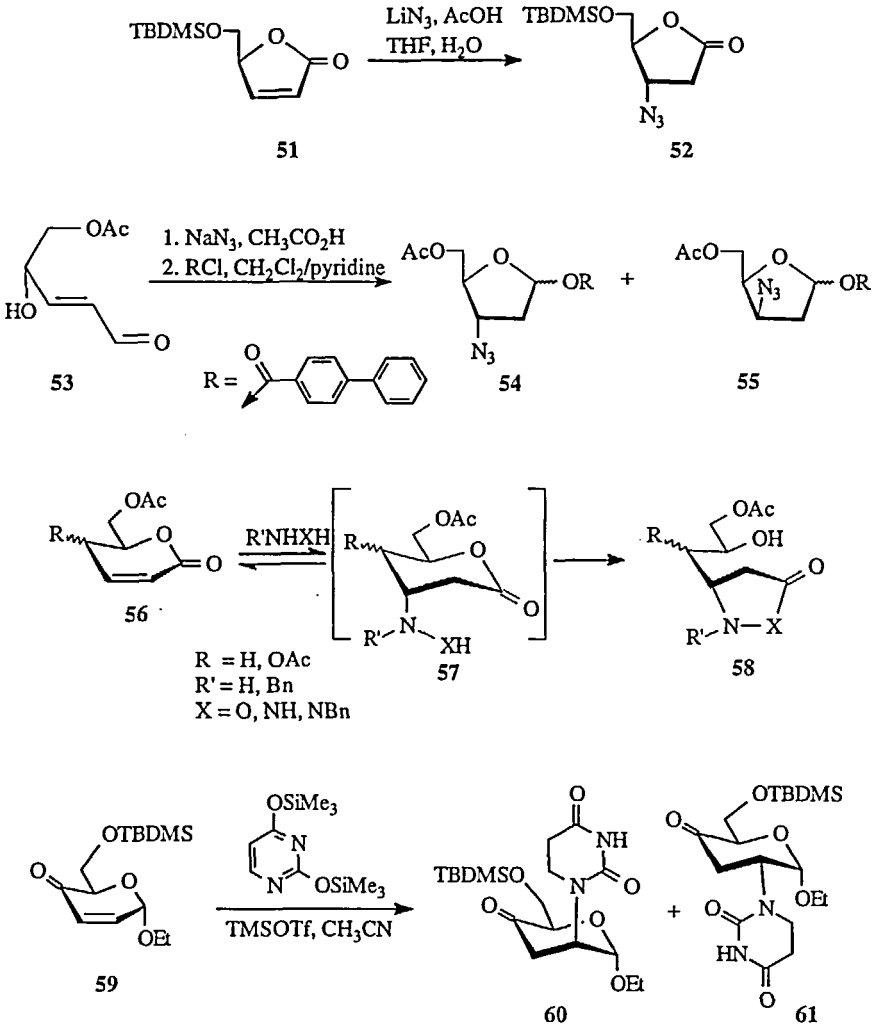
acidic azide in the reaction of **42** (Scheme 8) led to **44** with improved yields instead of **43**.[16] Changing from CH_3CO_2H/NaN_3 to HN_3/*p*-TosOH in CH_3CO_2H/benzene the direction of the nucleophilic attack was reversed again, leading to **45** as the single product.

When **46** was used as an acceptor, it was demonstrated[17] that the configuration of the product depended on whether the reaction was carried out under kinetic or thermodynamic control. Kinetic control favoured axial attack leading to **47**, whereas thermodynamic control gave **48** as a result of equatorial attack by the azide anion (Scheme 8), implying that the reaction is reversible.

A similar effect was found in the reaction of the α-anomer of the unsaturated nitro compound **22** (Scheme 8). The product of the reaction depended strongly on the reaction time,[18] short reaction times favouring axial attack and leading to **49** as the main product and longer reaction times leading to **50** as the favoured product. The yield for the combined products was 95%. However, under the same reaction conditions the corresponding β-configurated compound gave the equatorial addition product as the single product in 86% yield, regardless of reaction time. In some cases the resulting azido nitro sugars are rather labile and undergo an intramolecular S_N reaction to give triazole derivatives.[19]



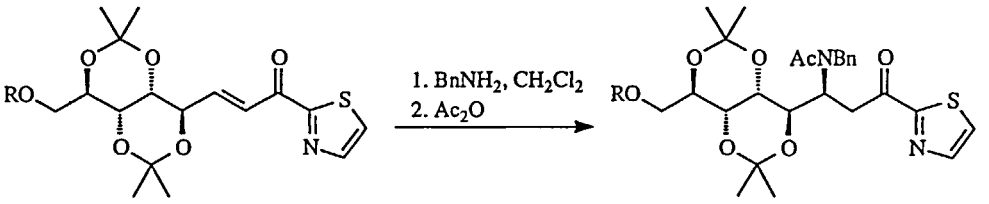
Scheme 8



Scheme 9

Addition reactions to unsaturated furanoid lactones[20] and open chain unsaturated sugar aldehydes[21] were used in different AZT syntheses. Whereas azide addition to the lactone **51** proceeded stereoselectively, it was not surprising that addition to the open chain aldehyde **53** gave a mixture of **54** and **55** (Scheme 9).

The synthesis of chiral diazolanones[22,23] and oxazolanones[24,23] starting from unsaturated sugar lactones such as **56** using hydrazines and hydroxylamines as donors



62 63

Scheme 10

has also been investigated. The initially formed addition products **57** reacted further to form the respective heterocyclic compounds **58**, generally in good yields (Scheme 9).

Other examples of conjugate addition of N-nucleophiles to unsaturated carbohydrates included the synthesis of isonucleosides[25] employing silylated bases as nucleophiles. The preparation of the isonucleosides proceeded in yields between 58% and 94%, and diastereomer ratios from 89:11 to 100:0 in favour of the axial product **60** (Scheme 9).

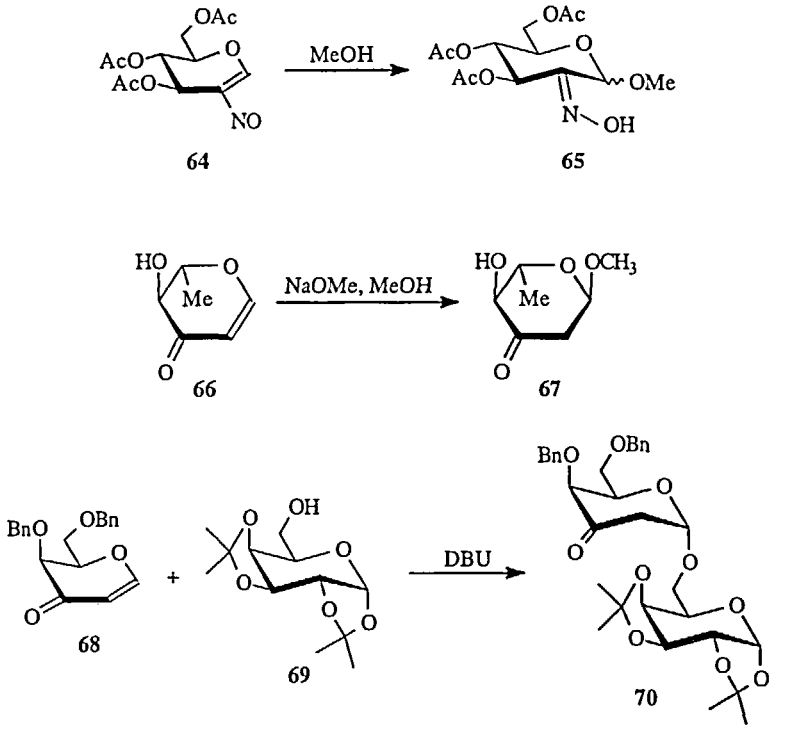
The synthesis of a sialic acid analogue[26] via the addition of benzylamine to the thiazoyl derivative **62** was reported (Scheme 10). The resulting product was a 2:1 mixture in favour of the isomer **63** with 85% overall yield.

2.3. Reactions with O-nucleophiles

Lemieux et al. published the first example of the addition of an O-nucleophile to an unsaturated carbohydrate.[27] The nitroso glycal **64** readily added methanol to give an α/β-mixture of the hydroxylimine **65** (Scheme 11).

It was demonstrated that hex-1-en-3-uloses react similarly with methanol,[3,28] i.e., the reaction of **66** with methanol under basic conditions led to the exclusive formation of the α-L-glycoside **67** in 80% yield (Scheme 11).[28]

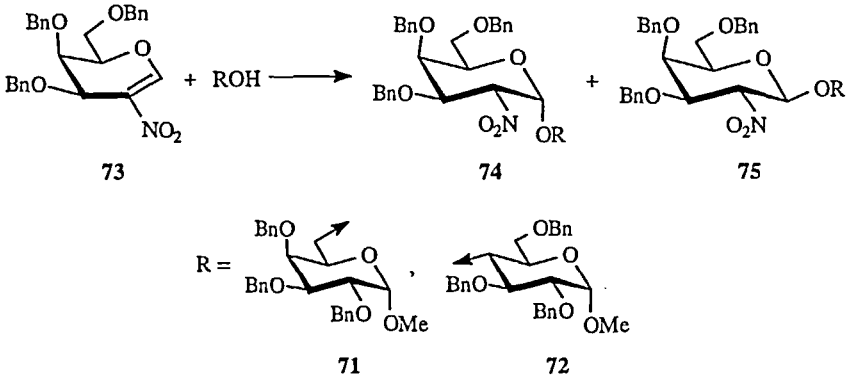
The addition of other alcohols to hex-1-en-3-uloses such as **68** was reported recently,[29] the additions proceeding with low to moderate yields but including the first synthesis of a disaccharide **70** by conjugate addition reaction and employing diisopropylidene galactose **69** as a nucleophile (Scheme 11).



Scheme 11

. The ability of nitroglycals to act as acceptors for conjugate addition reactions using carbohydrate alcohols as nucleophiles has recently been directed[30] for another disaccharide synthesis (Scheme 12). Methyl 2,3,4-tri-*O*-benzyl-α-D-galactopyranose **71** and methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranose **72** were used as O-nucleophiles under basic conditions with nitroglycal **73** as acceptor. The α/β-ratio of the products (**74** and **75**) ranged from 1:0 to 2:3 depending on the base used in the reaction with yields in the range of 79-89%. When $KN(SiMe_3)_2$ was used as base only the α-anomers were obtained. With **71** as the donor and KO*t*-Bu as the base the α/β-ratio was 2:3. With simpler primary alcohols the α/β-selectivity can be reversed from 8:1 to 1:8 by changing the base from NaOMe or KO*t*-Bu to Et_3N. Subsequent conversion of the nitro group to *N*-acetyl gave the corresponding GalNac-disaccharides.

The same approach was also very successful using serine and threonine as nucleophiles.[31] The addition of either Fmoc-L-Ser-*t*Bu or Boc-L-Ser-*t*Bu to **73**



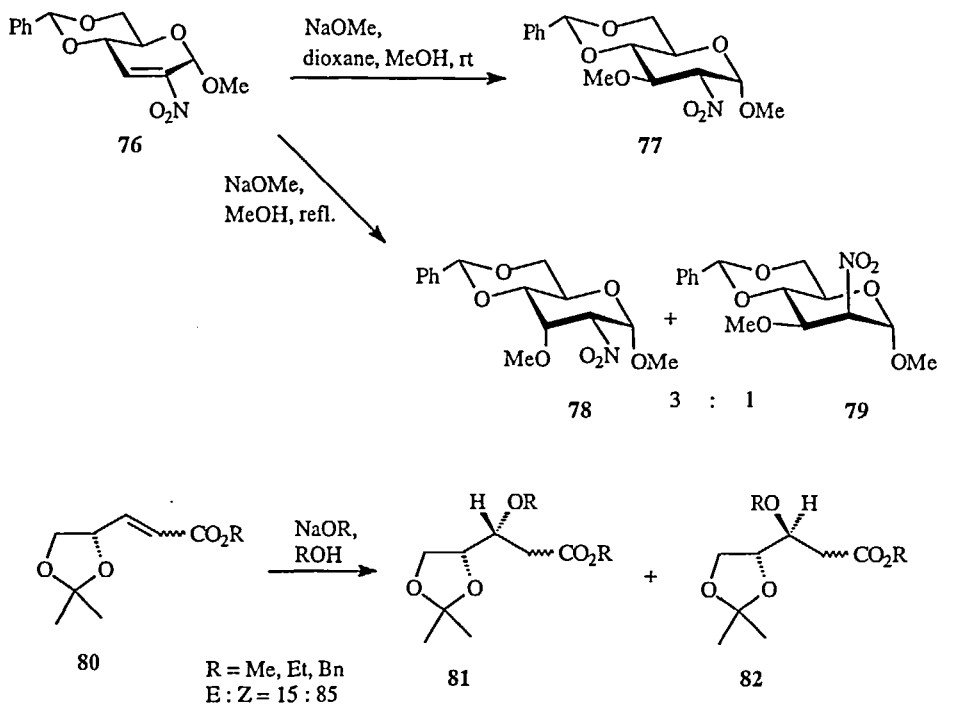
Scheme 12

proceeded in overall yields of more than 93% and an α/β-selectivity of about 6:1. With Boc-L-Thr-*t*Bu the addition gives the α-glycosides as single product in 80% yield. In both cases the nitro group was converted to *N*-acetyl to give the glycopeptide building blocks.

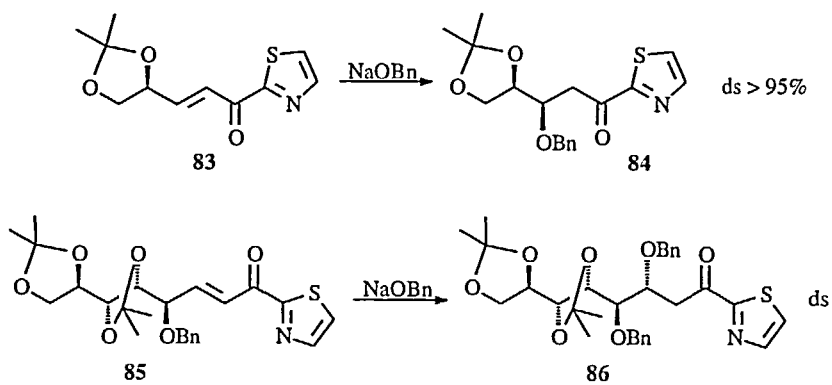
A detailed study of the addition of methanol to different unsaturated nitro sugars[32] showed that depending on the reaction conditions employed, different products with varying stereochemistry were formed (Scheme 13).[33] For the reaction of **76** the products obtained were either **77**, if the reaction was performed in dioxane at room temperature, or a mixture of **78** and **79**, when the reaction was carried out in refluxing methanol.

The stereoselective addition of different sodium alcoholates to the Wittig product of (*R*)-glyceraldehyde with methyl diethylphosphono acetate gave products with *threo/erythro*-ratios from 60:40 to 91:9 (Scheme 13).[34]

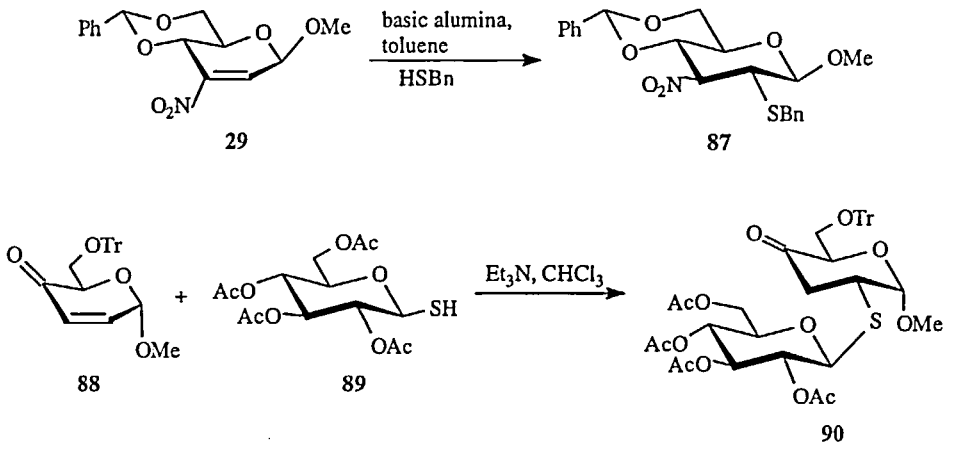
The stereoselective addition of benzyl alcohol to unsaturated 2-thiazoyl derivatives such as **83** or **85** was used in the synthesis of 3-deoxy-D-*glycero*-D-*galacto*-2-nonulosonic acid (Kdn) and 3-deoxy-D-*arabino*-2-heptulosonic acid (Dah)[35] following a sequence of several chain elongation/conjugate addition steps. Some examples of the method are given in Scheme 14. The reaction generally proceeded in good diastereoselectivity as shown for the formation of **84** and **86**.



Scheme 13



Scheme 14



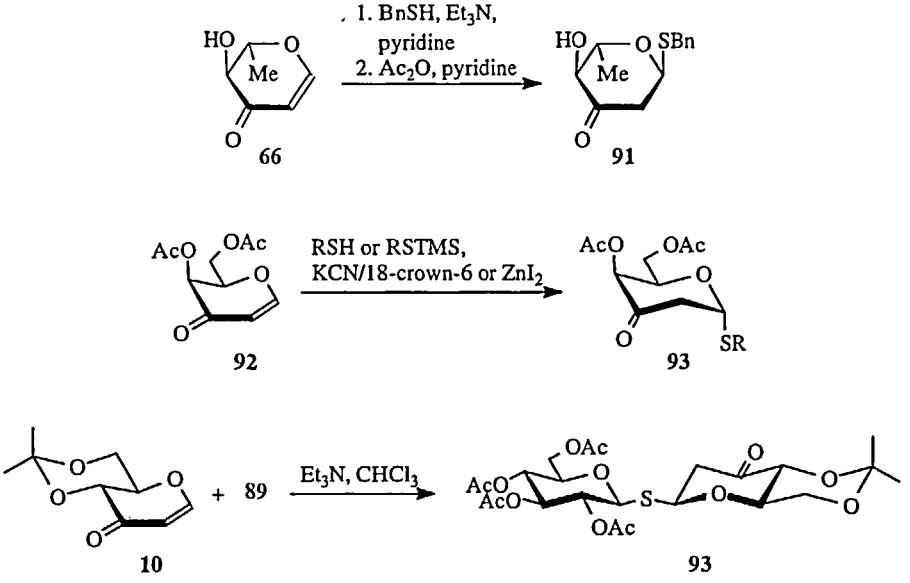
Scheme 15

2.4. Reactions with S-nucleophiles

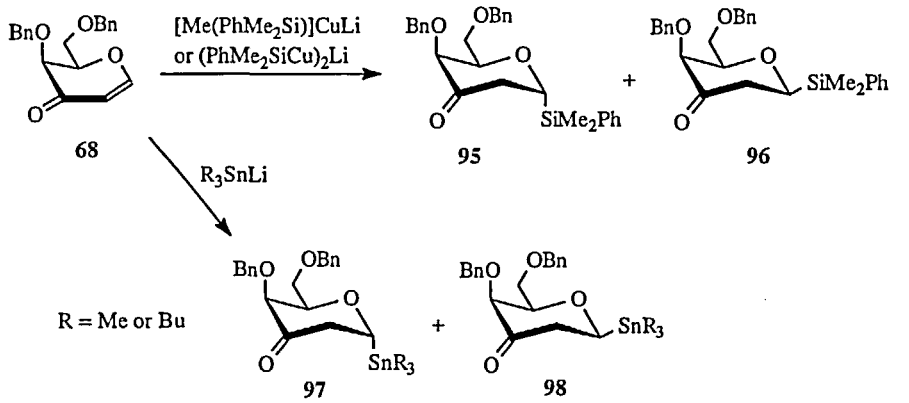
Thiols, as relatively soft and effective nucleophiles, generally add easily to conjugated systems. An early example of an addition of an S-nucleophile to a carbohydrate acceptor was the reaction of thiobenzyl alcohol with the nitro compound **29** leading to the single addition product **87** in 77% yield[13] (Scheme 15).

The addition of thioglucose **89** to hex-2-en-4-uloside **88** also led exclusively to equatorial attack and the thiodisaccharide **90** was obtained as single product in 90% yield.[36]

When hex-1-en-3-uloses were used as acceptors the resulting products were 2-deoxythioglycosides. The addition of thiobenzyl alcohol to **66** followed by acetylation gave the α-L-configurated thiobenzyl glycoside **91** in 85% yield (Scheme 16).[37] The addition of free or TMS-protected thiols to **92** with KCN/18-crown-6 or ZnI_2 as catalyst[29] gave the α-configurated 2-deoxythioglycosides **93** in 22-76% yield (Scheme 16). Reaction of **10** and thioglucose **89** with Et_3N as catalyst[36] led to the formation of the β-configurated trehalose-type disaccharide **94** in 45% yield (Scheme 16). The reduced yields in these cases were assigned to the sensitivity of the 2-deoxy-thioglycosides and competing retro-reactions.



Scheme 16



Scheme 17

2.5. Reactions with other nucleophiles

The reactions of conjugated systems with nucleophiles other than those mentioned above are very rare in carbohydrate chemistry. The preparation of silyl and tin glycosides using an approach via conjugate addition was described recently,[38] and the reaction of different glycals with $(PhMe_2SiCu)_2Li$ or $[Me(PhMe_2Si)]CuLi$ was explored. An example using the latter nucleophile is the reaction of **68** in which a mixture of the corresponding silyl glycosides **95** and **96** was obtained in 74-95% yield. The α/β ratio varied between 1:1 and >10:1, depending on the protecting groups and the nucleophile. Similarly, reaction of glycal **68** with either Me_3SnLi or Bu_3SnLi gave mixtures of the corresponding stannyl glycosides **97** and **98** in 79-95% with an α/β-ratio of >10:1 (Scheme 17).

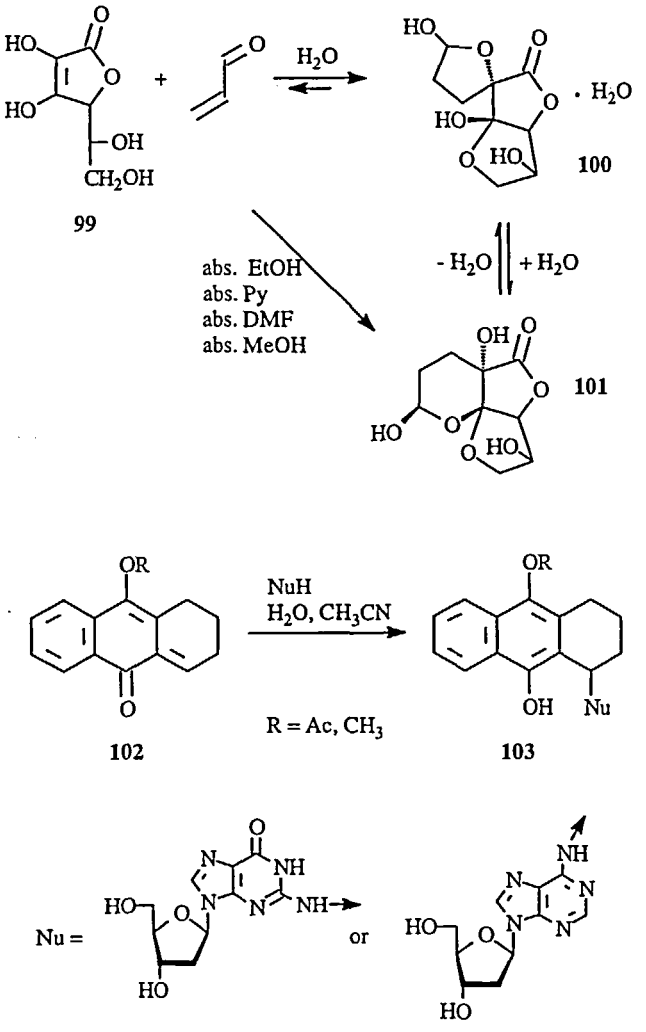
3. CARBOHYDRATES AS DONORS

Some examples where carbohydrates act as nucleophiles were already given in section 2.3 and 2.4, while others will be discussed in Section 5. Overall there are far fewer studies involving carbohydrates as donors compared to carbohydrates as acceptors. However, with conjugate addition reactions as alternative methods for the formation of O- and S-linked disaccharides (see above) or C-disaccharides (Section 5) this may change in the future.

3.1. Carbohydrates as C-nucleophiles

One of the very few examples in which carbohydrate structures act as C-nucleophiles is the reaction of ascorbic acid with acrolein.[39] After the initial formation of the carbon-carbon bond between the C-4 in acrolein and the C-2 of the ascorbic acid an intramolecular attack of the C-6 hydroxyl traps the stabilized carbocation. The formation of the hemiacetal is solvent dependant and the reaction could be directed to give either spiro compound **100** or tricyclic derivative **101** (Scheme 18).

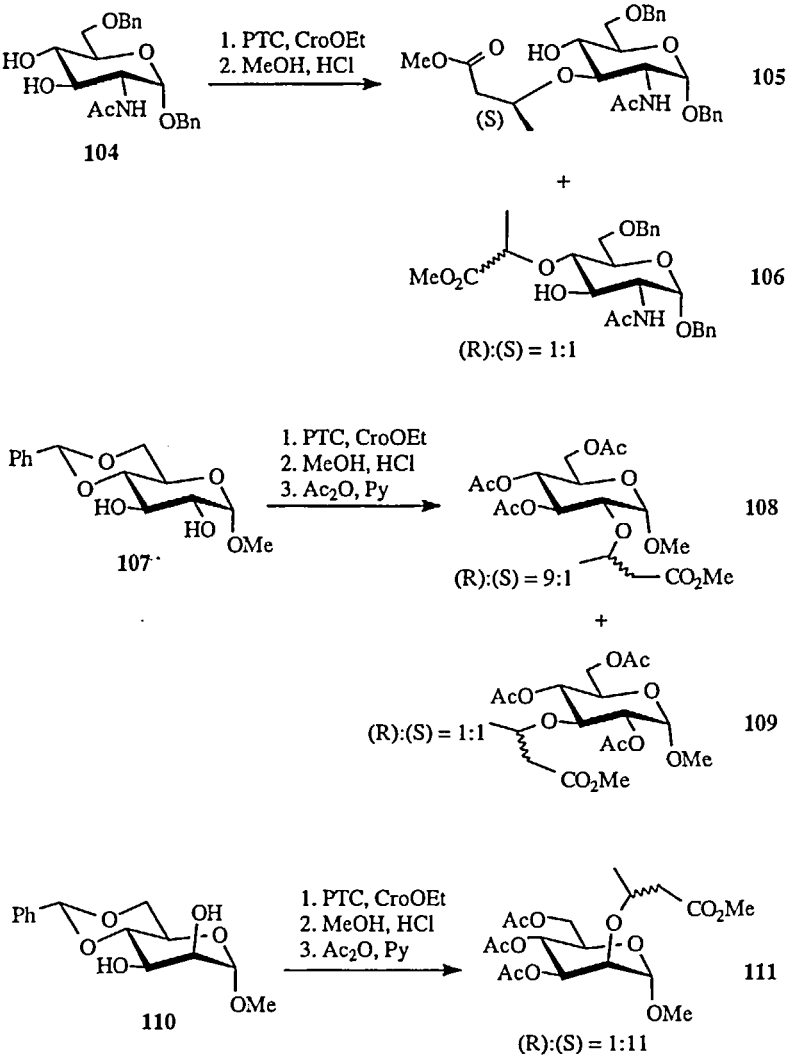
Some other examples for carbohydrates as C-nucleophiles in conjugate addition reactions are given in Section 5.



Scheme 18

3.2. Carbohydrates as N-nucleophiles

Nitrogen in carbohydrate structures has rarely been used as the nucleophile in intermolecular reactions with carbohydrates as donors to date. An exception is the reaction of the tetrahydroanthracenone derivative **102** with 2'-deoxyadenosine or 2'-deoxyguanosine[40] to give **103** as product of the addition (Scheme 18). The reaction proceeded with moderate yields and was not diastereoselective.



Scheme 19

3.3. Carbohydrates as O-nucleophiles

Some examples of reactions involving carbohydrates as O-nucleophiles were already discussed in section 2.3. Well known is the reaction of cellulose under basic conditions with acrylonitrile in the preparation of cyanoethyl cellulose.[41] The reactions of a variety of different carbohydrates with crotonic acid ethyl ester (CroOEt) under phase-transfer conditions are shown in Scheme 19.[42] Whereas the reaction of protected

carbohydrates with only one free hydroxyl group led to no steric induction with respect to the new stereocenter, the reaction of the diols **104**, **107** and **110** proceeded with good to excellent regioselectivity and high steric induction for the main products. The yields were 91% for the reaction of **104** (**105**:**106** = 5:1), 56% for the reaction of **107** (**108**:**109** = 4.5:1) and 95% for the reaction of **110** to give **111**.

3.4. Carbohydrates as S-nucleophiles

Examples for the reaction of carbohydrates as S-nucleophiles are given in Section 2.4. Some others will be discussed in Section 5.

4. INTRAMOLECULAR REACTIONS

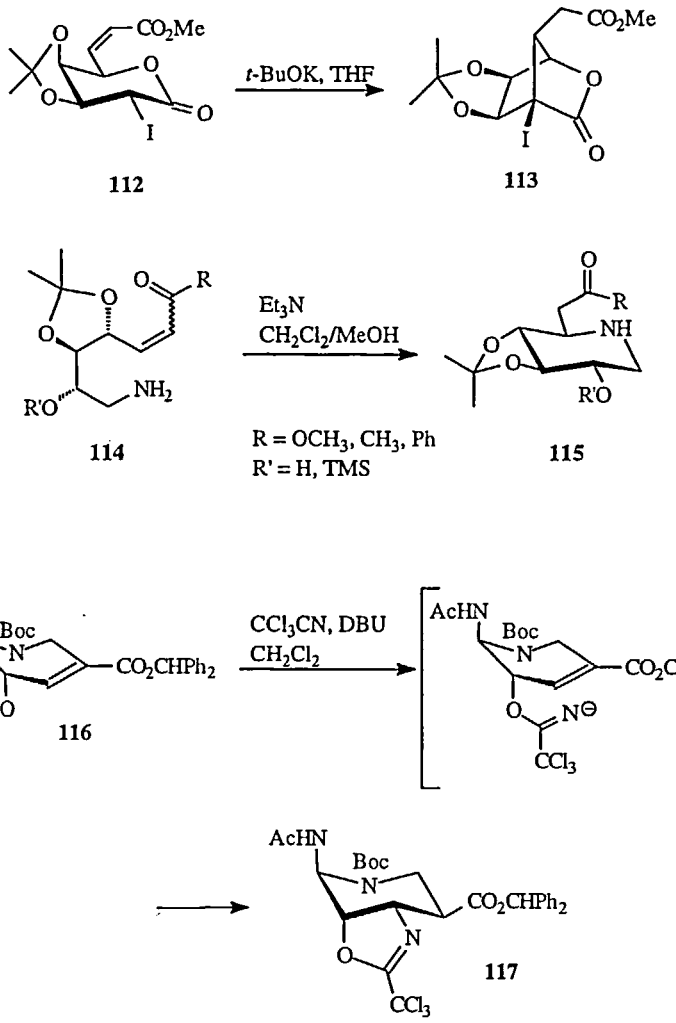
4.1. C-Nucleophiles

Despite the widespread use of the Robinson anellation and the Michael ring closure (MIRC) reaction in general organic chemistry, the intramolecular attack of a C-nuleophile is not very common in carbohydrate chemistry. One example is the formation of the bicyclic derivative **113** in 25% yield by intramolecular conjugate addition of **113** (Scheme 20).[43] Other examples are illustrated in the levoglucosenone section (Section 5).

4.2. N-Nucleophiles

Intramolecular addition of N-nucleophiles has been used in the synthesis of deoxynojirimycin (DNJ) and castanospermine derivatives. Starting from different donor-acceptors of general structure **114** (Scheme 20) stereoselective ring-closures proceeded in yields of 36-57%.[44]

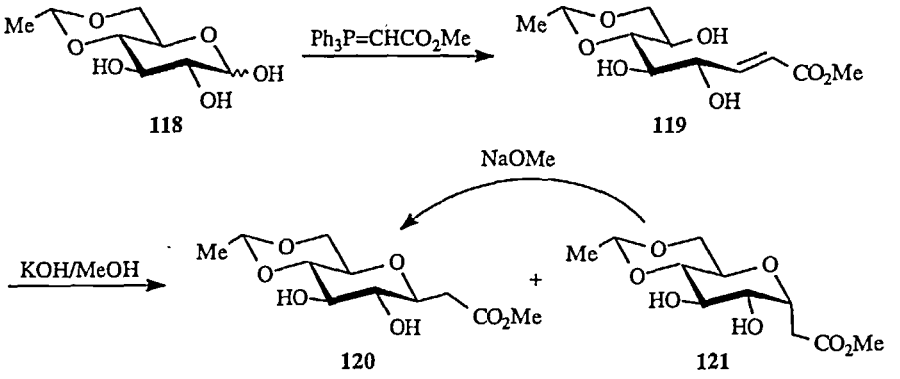
A further example was the stereoselective introduction of a second nitrogen to the azasugar **116**, achieved in 76% yield by use of a trichloroacetimidate as a temporary protecting group followed by intramolecular attack of the imidate nitrogen to give **117** (Scheme 20).[45]



Scheme 20

4.3. O-Nucleophiles

Intramolecular nucleophilic attack of oxygen is quite common in the formation of C-glycosides; e.g., the synthesis of C-glycosides using Wittig approaches[46] proceeded from **118** via the formation of **119** followed by an intramolecular attack of the free hydroxyl group to give **120**[47] (Scheme 21). The initial product was the α-



Scheme 21

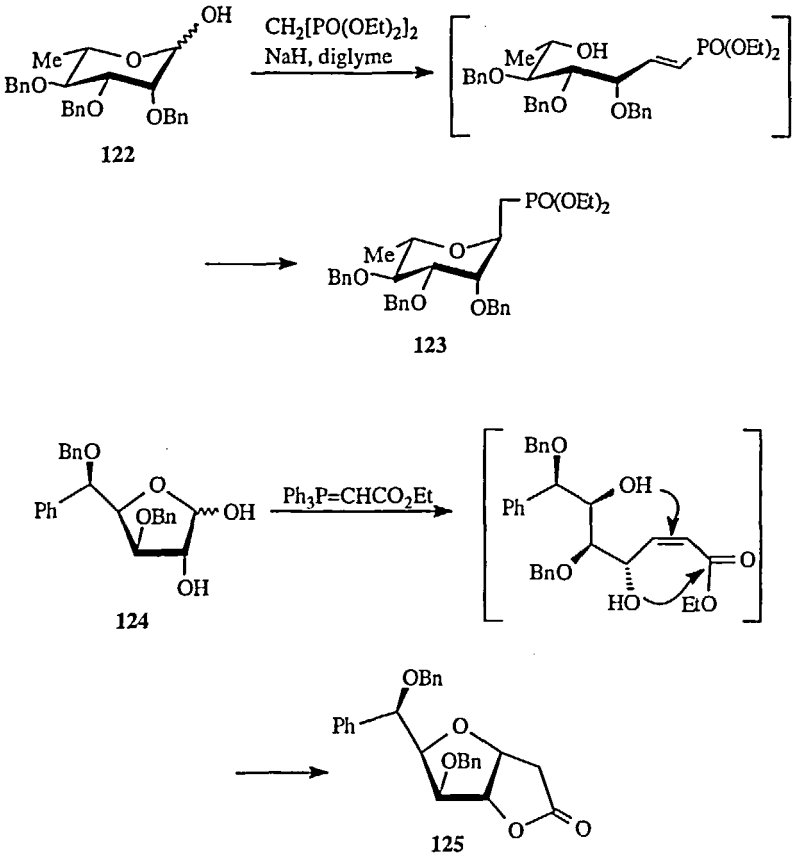
anomer **121** which under basic conditions was rapidly transformed to the thermodynamically more stable β-anomer **120**.[47,48]

An interesting variation of the latter reaction was the synthesis of **123** in which the electron-withdrawing group was a phosphonate (Scheme 22).[49] Thus, the initially obtained product derived from **122** under Wittig conditions reacted further in an intramolecular conjugate addition reaction to give the phosphonate **123**.

An analogous reaction resulted in the formation of the related furanoside C-glycosides. The chain elongation of **124** (Scheme 22) via a Wittig reaction led to **125** as result of an intramolecular reaction of the primary product of the Wittig olefination.[50]

Another approach described for furanoide C-glycoside formation is the use of sulfones for activation of the double bond.[51] An example is given in Scheme 23. The reaction of sulfone **126** with sodium methanolate gave derivative **127** in 60% yield over two steps.

The formation of anhydro sugars via intramolecular conjugate addition reactions was also possible. Starting from α,β-unsaturated lactones **128** or **130**, basic reaction conditions gave the corresponding anhydro sugars **129**[52] or **131**[5] respectively, in 50-68% yield (Scheme 23). An intramolecular ether-bridge between the two units of disaccharide **132** was also established via a conjugate addition reaction[53] leading to the derivative **133** in 59% yield.



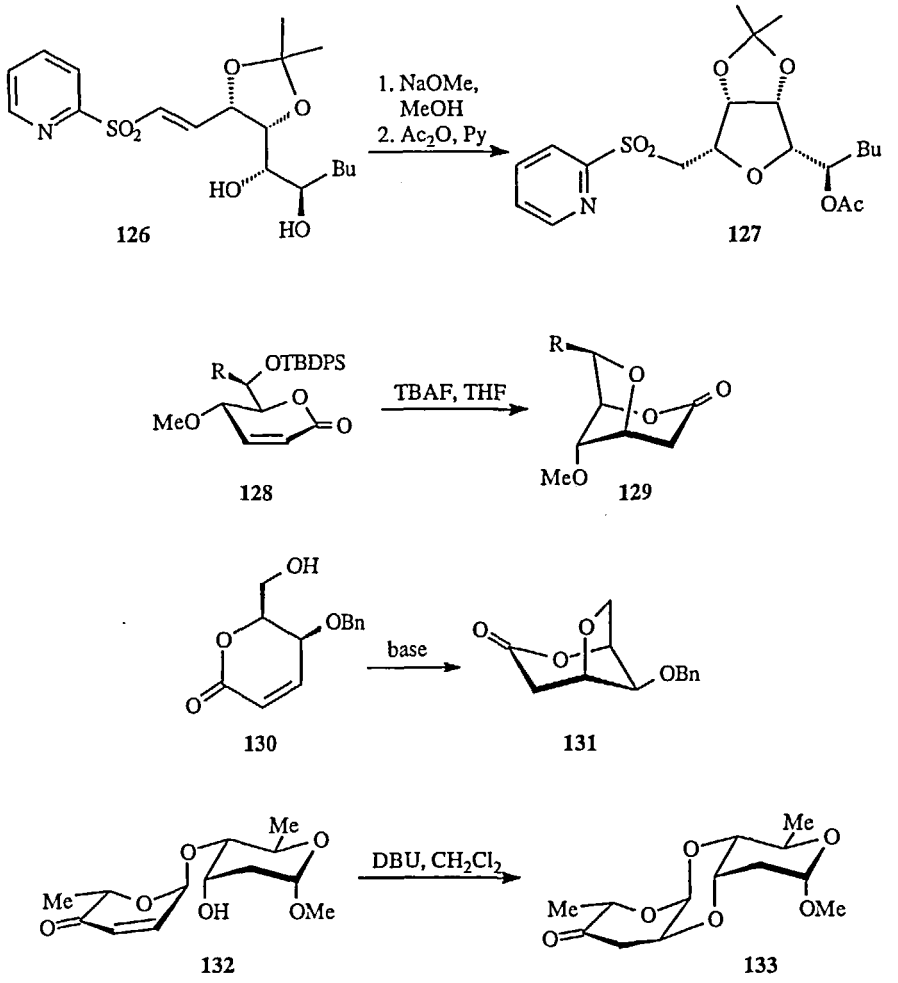
Scheme 22

5. REACTIONS OF LEVOGLUCOSENONE

5.1. Reactions with C-nucleophiles

The earliest reported reactions of C-nucleophiles with levoglucosenone (**134**) were the addition of methylmagnesium iodide[54] and lithium dimethylcuprate.[55] The yield was 64% in both cases and the products were the result of an axial attack of the nucleophile, no equatorial product being observed (Scheme 24).

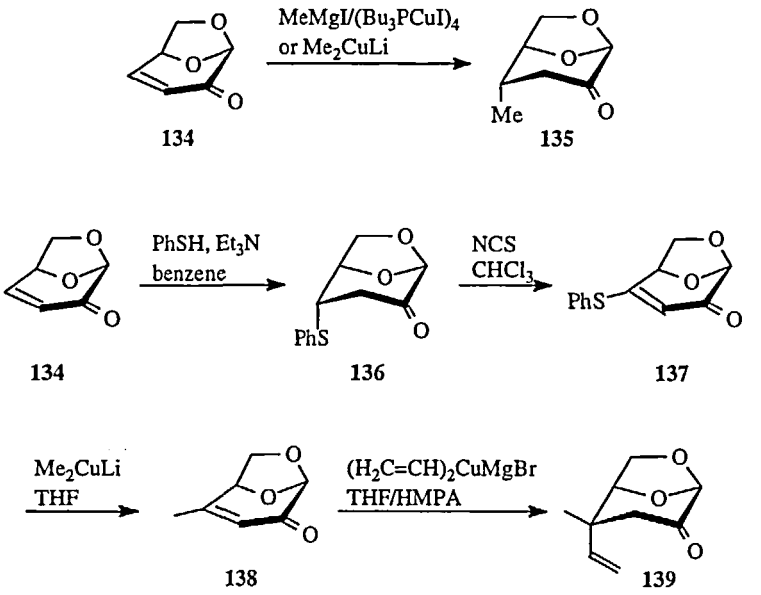
An interesting sequence of conjugate additions was realised in a synthesis of (+)-grandisol[56] from levoglucosenone (Scheme 24). The known[57] addition of



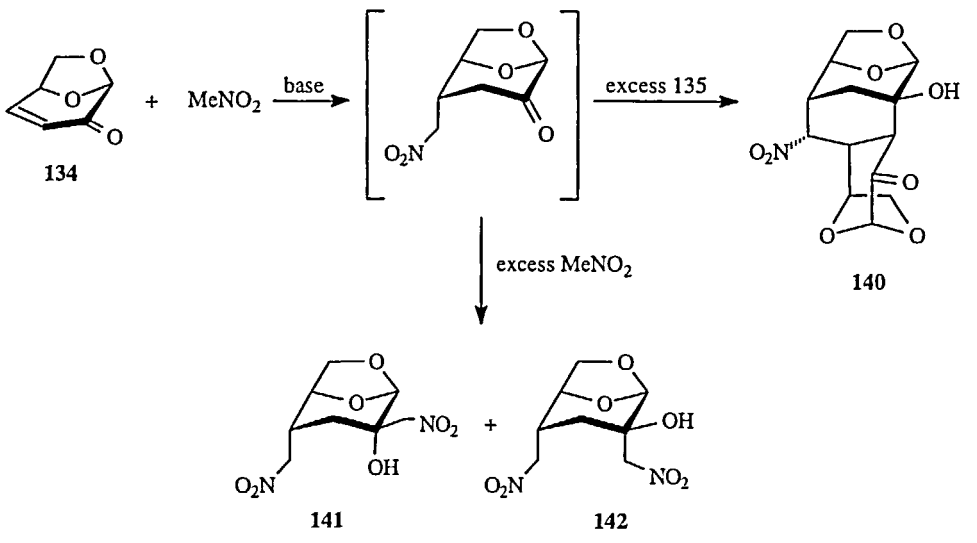
Scheme 23

thiophenol to **134** gave **136**, which was followed by reestablishment of the acceptor system. Subsequent reactions in turn with methyl- and then vinylcuprate in 62% and 61% yield, respectively, gave compound **139**.

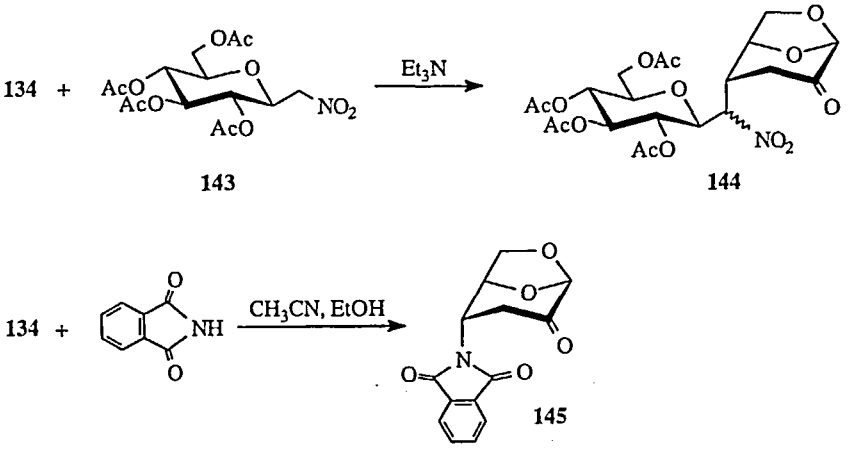
Another example of the addition of small C-nucleophiles with levoglucosenone was addition of nitromethane. Depending on the ratio of nitromethane and levoglucosenone, different products could be isolated (Scheme 25). Again only axial addition products were found. In a 1:1 mixture of **134** and nitromethane the initial



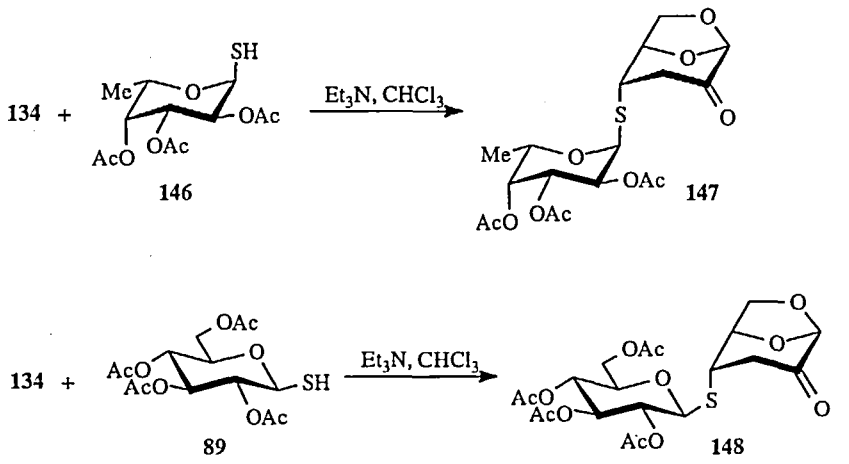
Scheme 24



Scheme 25



Scheme 26



Scheme 27

addition product could not be isolated. Instead a mixture of **141** and **140** was isolated in 61% and 18% yield, respectively.[58] An excess of nitromethane led to a mixture of **141** (89% yield) and **142** (9%) whereas an excess of **134** gave **140** as a single product in 95% yield.[59]

Reaction of nitromethyl-substituted sugar derivatives **143** with levoglucosenone (**134**) lead to C-disaccharide **144** (Scheme 26).[60,61] Again only the

product resulting from an axial approach of the nucleophile was observed. No ratios for the configuration of the stereocenters containing the nitro group were given as the nitro group was removed in the following steps.

The reaction of several nitroalkanes with **134** could also be promoted cathodically[62,63] leading to axial products exclusively with no or very low steric induction with respect to the chiral center containing the nitro group.

5.2. Reactions with N- and O-nucleophiles

When the addition of phthalimide to **134** was promoted cathodically[63] the reaction led to the formation of **145** in 95% yield (Scheme 26). However, the addition of O-nucleophiles to levoglucosenone is more common than the addition of N-nucleophiles. Examples include the addition of water under either basic or acidic conditions,[57] the addition of methanol[57] or benzyl alcohol.[64] In all cases the products contained the axially oriented nucleophile.

5.3. Reactions with S-nucleophiles

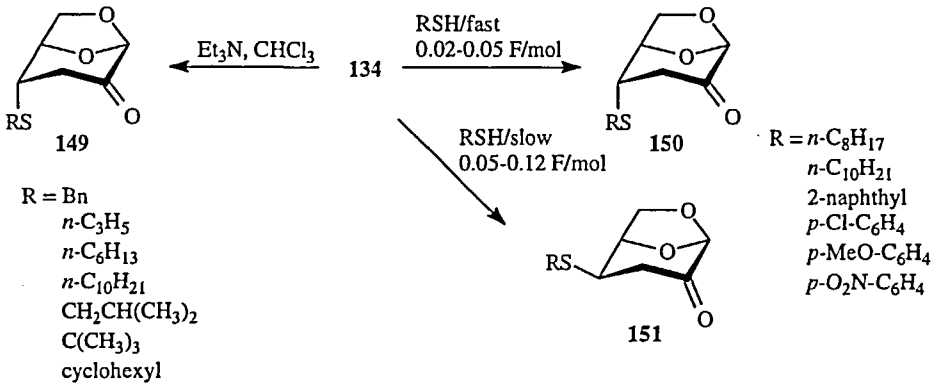
Thiols add easily to levoglucosenone under basic conditions. Again, the products were generally the result of an axial attack and formed in good yields (Scheme 28).[57,65]

In an extension of this reaction, thiodisaccharides were synthesised when either thiofucose **146**[66] or thioglucose **89**[36,67] was used as a nucleophile (Scheme 27). The reactions proceeded smoothly under base catalysis to yield the single isomers **147** and **148** in 91% and 85% yield, respectively.

In some cases the direction of the nucleophilic attack can be controlled. With an electrogenerated base under cathodic promotion of the reaction the addition of a variety of different thiols to levoglucoseneone (**134**) gave either **150** or **151** selectively in about 66% yield, depending on the reaction conditions (Scheme 28).[68]

6. SUMMARY AND CONCLUSIONS

Despite the large variety of different donor and acceptor molecules employed in anionic conjugate addition reactions of carbohydrates, some general trends seem to



Scheme 28

emerge. Although carbohydrate derived acceptors provide a highly steric environment, the addition of small nucleophiles like cyanide, azide or methanolate is often not very stereoselective. The addition to pyranoid derivatives generally allows better stereocontrol although examples for stereoselective reactions of furanoses and open chain sugars were reported.

Using carbohydrates as acceptors the addition of carbanions to enuloses or unsaturated nitro sugars proceeded with good to excellent regio- and stereoselectivity to yield branched sugar derivatives and C-glycosides. The reaction is most commonly used with pyranoses but examples for the furanoses and open chain forms can also be found. The addition of cyanide on the other hand usually led to mixtures of stereoisomers. An exception was the reaction of 3-*C*-nitro-hex-2-enopyranosides with cyanide where single addition products were formed.

The addition of amines to enuloses or unsaturated nitro sugars and even open chain forms proceeded generally in a stereoselective fashion. The stereoselectivity was reported to be lower in some cases where protected amino acids were used as donors. The addition of azide often led to mixtures, but careful control of the reaction conditions allowed the isolation of single reaction products in some cases.

The reaction of primary or secondary alcohols as O-nucleophiles with different enuloses or unsaturated nitro sugars proceeded stereoselectively in many cases. Addition of sodium benzylate to open chain unsaturated sugars could also be achieved

with high diastereoselectivity. The use of nitro glycals as acceptors allowed the preparation of O-glycosides and disaccharides in a stereoselective fashion in excellent yields.

The addition of S-nucleophiles generally proceeded with excellent stereoselectivity. The use of thiosugars as nucleophiles led to the formation of thiodisaccharides in high yield and with excellent stereocontrol.

If carbohydrate diols were used as donors the regio- and stereoselective formation of chiral ethers was observed. These could be isolated in very good yields.

The intramolecular addition of an O-nucleophile was the key step in the course of a synthesis of C-glycosides following a Wittig protocol. With perhaps the exception of a deoxynojirimycin synthesis, which can be envisioned as a more general approach to this class of compounds, the other examples of intramolecular reactions are singular examples that are limited to special cases.

Excellent stereocontrol is generally achieved with levoglucosenone as acceptor where the attack of the nucleophile exclusively occurs from the side opposite to the anhydro bridge. The only exception is the cathodically promoted addition of thiols where the addition can occur from either side of the molecule, depending on the exact reaction conditions.

Judging by the literature published so far, the most promising applications of anionic conjugate addition reactions of carbohydrates seem to be in the synthesis of branched-chain deoxy sugars, the synthesis of higher monosaccharides using a chain elongation/conjugate addition protocol, and the use of nitro glycals as an alternative method for the preparation of glycosides of 2-acetamido-2-deoxyhexoses.

7. ACKNOWLEDGEMENT

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