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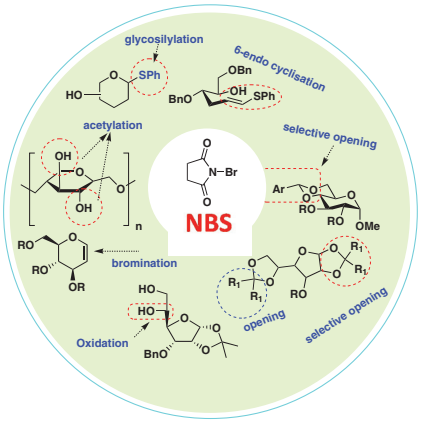
Application of *N*-Bromosuccinimide in Carbohydrate Chemistry

Smritilekha Bera[*a]
Dhananjoy Mondal[a]
Bhaskar Chatterjee[b]

[a] School of Chemical Sciences, Central University of Gujarat, Gandhinagar, Gujarat, India
lekha026@yahoo.com
[b] Department of Chemistry, Nabadwip Vidyasagar College, West Bengal, India



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Abstract This article describes the use of *N*-bromosuccinimide in different organic group transformations in carbohydrate chemistry. A comprehensive discussion on the synthesis of deoxysugars through selective *O*-benzylidene fragmentation, photobromination, halogenation, oxidation, and polymerisation of different carbohydrate moieties with the aid of *N*-bromosuccinimide (NBS) is presented. The use of NBS in the most significant glycosylation methods and in oligosaccharide synthesis is also discussed.

Keywords regioselectivity, glycosylation, cleavage, *N*-bromosuccinimide, oxidation

Introduction

The success of a synthesis relies not only on the characteristics of the substrate but also on the choice of the reagent employed in the reaction. Different organic reagents can react through different mechanisms and are vital to determining the profile of a reaction; that is, the composition and constitution of the reaction product. This is an essential element of chemistry and it is to be mentioned that the chemistry and reagents are complementary to each other. One such small well-known reagent is *N*-bromosuccinimide (NBS).

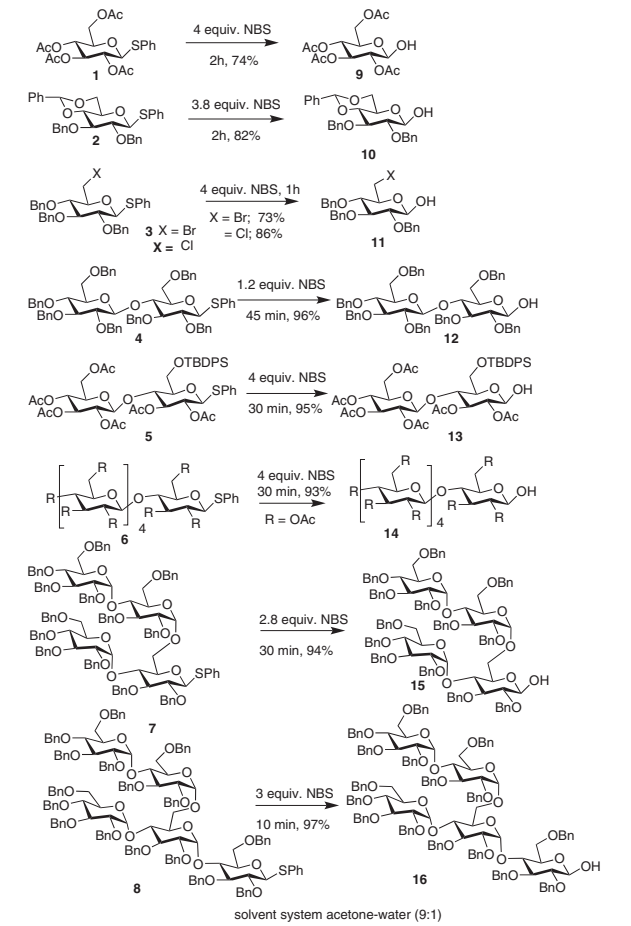
N-Bromosuccinimide is particularly advantageous as a bromine source for radical reactions and electrophilic addition reactions,[1–4] and as an oxidising agent in the presence of base without any bromine. Using NBS in aqueous dimethoxyethane, Corey and Ishiguro discovered that secondary alcohols can be oxidised selectively in the presence of primary alcohols.[5] Using a strong base, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), NBS also interacts with primary amides to generate a carbamate via the Hofmann rearrangement.[6] NBS electrophilically brominates the amine, followed by decarboxylation and the formation of an imine, which is further hydrolysed to produce an aldehyde and ammonia.[7,8] The bromination of allylic hydrogen, benzylic hydrogen and carbonyl α-hydrogen, namely the Wohl–Ziegler reaction was found to work with NBS.[9] Both the radical route (discussed above) and acid-catalysis are options for applying NBS to α-brominate carbonyl compounds.[10] Several bifunctional alkanes can be produced by substituting nucleophiles for water.[11]

A survey of the literature reveals that NBS has been used for the bromination of the side chain of aromatic compounds without radical initiator under microwave conditions,[12] and for regioselective monobromination of the aromatic substrate with the assistance of NBS in ionic liquid.[13] NBS also acts as a ligand in organometallic chemistry.[14] For silyl ethers[15] and THP ethers, NBS in water with cyclodextrin has been utilised as a deprotecting agent.[16] Moreover, many other reactions have been carried out using NBS, such as polymerisation and addition of organic amines to alkenes to generate nitrogen-containing organic compounds.[17,18]

NBS has been widely used with various aromatic and aliphatic compounds, and its application in carbohydrate chemistry is also significant.[19,20] This review article focuses on the role of NBS in protection, deprotection, and glycosylation reactions in the field of carbohydrate chemistry.

Removal of Functionalities

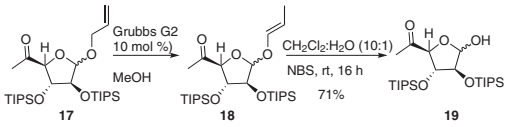
The production of complex oligosaccharides can be started with anomeric hydroxy sugars or glycosyl hemiacetal derivatives. These may be utilised directly in dehydrative glycosylation processes or converted into reactive glycosyl donors for the production of oligosaccharides or natural products. During their synthesis, orthogonal protection and deprotection of functionalities are necessary to obtain good yields.[21]



Scheme 1 Removal of thiophenyl group with NBS

Motawia et al. looked into the synthesis of complex oligosaccharides with orthogonal benzyl, allyl, and transient ester-blocking groups.[22] In a successful method, phenyl thioglycosides **1**–**8** were treated with NBS in aqueous acetone within a short period, and converted into *O*-glucosides **9**–**16**, respectively (Scheme 1). Under these reaction conditions, acetate, benzylidene acetal, *tert*-butyldiphenylsilyl, benzyl groups, and the *O*-glycosidic bond (e.g., di-, tetra-, and pentasaccharide thioglycosides) remain unaffected. Here, the electrophilic activation of sulfur primes the generation of an active sulfonium species, which then participates in the glycoside bond-forming reaction.[22]

It can be challenging to eliminate allyl functionality. In the work of Donohoe and colleagues, Grubbs second-generation catalyst (G2) was used to isomerise the allylic group of **17** to **18** before being removed by NBS to give **19** (Scheme 2). According to Donohoe, G2 herein functions by breaking down into the ruthenium hydride species, which does the dirty work.[23]



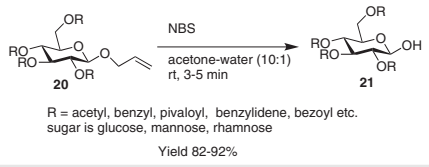
Scheme 2 Removal of allyl functionality

In the presence of NBS (1.1 equiv) in aqueous acetone, Panchadhayee and Misra hydrolyzed functionalised allyl glycosides **20** to their corresponding glycosyl hemiacetal derivatives **21**, forming hemiacetal derivative at room temperature in excellent yield, without using any acid activator, in three minutes (Scheme 3).[24] Under the reaction conditions, the protective hydroxy groups of the carbohydrate backbone, such as benzylidene, isopropylidene acetal, benzoyl, 4-methoxybenzyl, benzyl, *tert*-butyldiphenylsilyl, and acetyl, were unaffected, though the hemiacetal cleaves under Hanessian–Hullar's reaction conditions. Here, the allyl

Biographical Sketches

Dr. Smritilekha Bera earned her Ph.D. from the National Chemical Laboratory in Pune, India, under the supervision of Dr. Mukund K. Gurjar. After completing a three-year postdoctoral research associateship at the University of Manitoba in Canada and a two-year stay at the Rensselaer Polytechnic Institute in New York, she started working as a DST scientist in the School of Chemical Sciences, Central University of Gujarat, India. Her research focuses on synthesizing natural substances, heterocyclic building blocks, aminoglycosides, and synthetic glycosaminoglycans (hyaluronan, and chondroitin sulphate) for therapeutic use. She has been conducting independent research on the development and applications of organic nanoparticles and photoswitchable compounds. She has six book chapters, four patents, and more than fifty peer-reviewed articles published internationally.

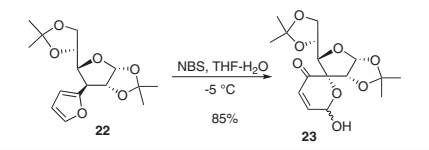
group and the bromonium ion (Br^+) produced by NBS combine to form an addition adduct, which, after allyl glycoside hydrolysis, produces the glycosyl hemiacetal derivatives.



Scheme 3 Allyl glycoside hydrolysis for glycosyl hemiacetal derivatives

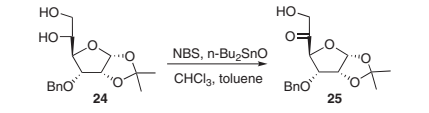
Oxidation

Sharma and co-workers[25] observed that the 3-C-furanyl-D-allose derivative **22** underwent an oxidative ring-opening reaction with NBS in aq. THF at –5 °C, forming lactols **23** (Scheme 4). Isopropylidene ketals remain unaffected in this instance.



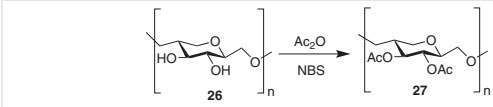
Scheme 4 Oxidative ring-opening of furan with NBS

Silva et al.[26] used a *n*-Bu_2SnO/NBS mixture in a combination of chloroform and toluene to regioselectively oxidise the 5-hydroxyl group of allofuranose derivative **24** to produce the 5-keto sugar **25** in a moderate yield (Scheme 5).



Scheme 5 Regioselective oxidation of isopropylidene-protected allofuranose

Sun et al. extended the scope of application of the above reaction to hemicellulose extracted from sugarcane bagasse, which was partially acetylated with acetic anhydride using NBS as a catalyst under mild, solvent-free conditions.[27] A series of reactions with temperature adjustments showed that the yields ranged from 66 to 84%, and that the degree of substitution (DS) was between 0.27 and 1.15. The degree of substitution increased with an increase of temperature between 18 and 80 °C, and with an increase in the reaction time from 0.5 to 5 h, demonstrating an important use of NBS as a catalyst (Scheme 6). The treatment of natural hemicellulose **26** with acetic anhydride is thus a convenient way to obtain ester derivatives of biopolymers such as **27**.

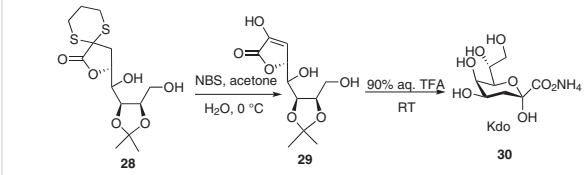


Scheme 6 Acylation of sugarcane bagasse hemicellulose

Under pseudo-first-order conditions and a temperature of 40 °C, the kinetics and mechanism of micellar catalysed NBS oxidation of dextrose (1:1) in an H_2SO_4 medium were studied.[28] According to the findings of the reactions investigated under a variety of experimental settings, NBS exhibits a first-order, fractional-order reliance on dextrose and a negative fractional-order dependence on sulfuric acid.

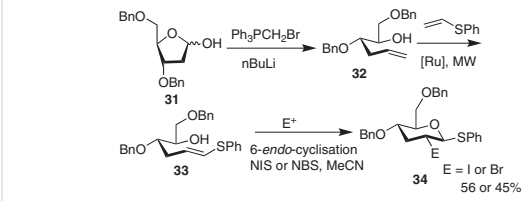
endo-Cyclisation

Ichiyanagi and colleagues[29] reported the chemical synthesis of 2-keto-3-deoxy-D-manno-octuosonic acid (Kdo) using NBS in aq. acetone for the deprotection of dithiane in compound **28** to yield the unsaturated lactone (**29**). The isopropylidene group was not cleaved, but was later removed with aq. TFA to give Kdo (**30**) (Scheme 7).



Scheme 7 Synthesis of Kdo with NBS

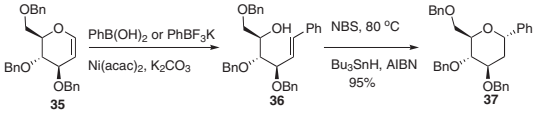
Boutureira and co-workers found that terminal alkene **32**, upon microwave-assisted cross-metathesis reaction with electron-rich phenyl vinyl sulfide (with Grubbs' second-generation catalyst), resulted in 3-deoxy sulfanyl alkenes **33** that underwent NIS- or NBS-mediated 6-*endo*-cyclisation to form the 2-iodo/bromo thioglycoside products **34**. The reaction was also extended to other interesting 2,3-dideoxy-D-ribosides compounds in reasonable yields (Scheme 8).[30]



Scheme 8 *endo*-Cyclisation with NBS

Ye and associates reported the synthesis of aryl-*C*-Δ^3-glycosides and 2-deoxy-α- or -β-*C*-glycosyl using a ring-opening-ring-closure methodology. Other than employing protic acid, Lewis acid, or PhSeCl, the ring-opened product

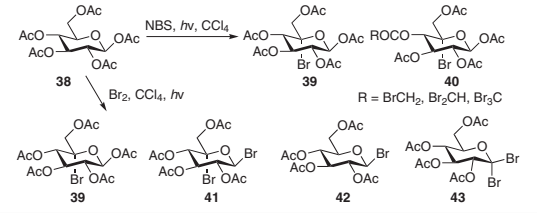
36 was transformed into aryl-C-glycosyl compound **37** *via* an NBS-mediated ring-closure process followed by reductive dehalogenation. Functional groups such as halides, bulky substituents, and various glycals (such as galactals, glucals, and xylals) with diverse electronic characteristics could be included without suffering any efficiency losses (Scheme 9).[31]



Scheme 9 Synthesis of an aromatic *C*-glycosyl derivative

Halogenation

Penta-*O*-acetyl-β-D-glucopyranose **38** is photobrominated with NBS in carbon tetrachloride, resulting in crystalline 5-bromo-derivative **39** in high yield through selective replacement of H-5 along with mono- and dibromoacetyl derivative **40**, as by-products. However, with bromine as a reagent, in addition to 5-bromo-derivative **39**, other by-products are also obtained as shown in Scheme 10. As the C-5 epimer of the penta-acetate yields identical products, it is hypothesised that the initial bromination occurs via a unique radical at the tertiary site.[32]

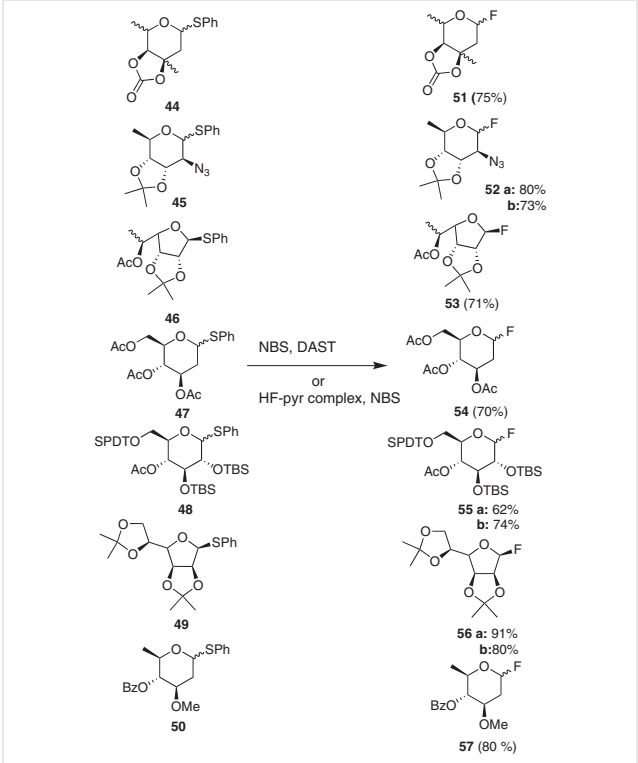


Scheme 10 Photobromination of penta-*O*-acetyl-β-D-glucopyranose

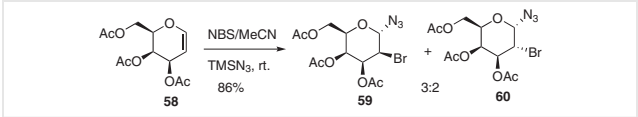
The direct conversion of thioglycosides **44**–**50** into glycosyl fluorides **51**–**57** utilising NBS and dimethylaminosulfur trifluoride (DAST) or HF-pyridine was described by Nicolaou and colleagues in 1984 in the presence of different functional groups including *O*-glycoside bonds (Scheme 11).[33]

The bromination of chitin was described by adding NBS and Ph_3P to a solution of chitin and LiBr in dimethylacetamide (DMA) solvent.[34]

A rapid, stereoselective, and high-yielding technique of haloazidation is the bromoazidation of glycal **58** with NIS/NBS and $TMSN_3$ as the source of bromide/iodide and azide. However, *trans*-bromo-azido derivative **59** formed from glycal with NBS and $TMSN_3$ within 5 minutes at room temperature (Scheme 12) in lower yields with the formation of chromatographically inseparable degraded products. Similar outcomes were obtained by substituting NBS with NIS, with 82% yield. Because the cyclic bromonium intermediate is less stable than the corresponding iodonium ion, it is more likely to be attacked by ring oxygen before being attacked by azide, as evidenced by the low *anti*-selectivity of NBS.[35]

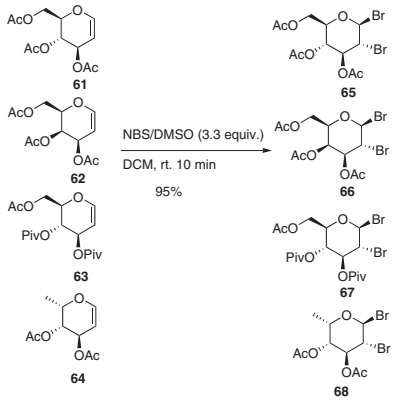


Scheme 11 Conversion of thioglycosides into glycosyl fluorides utilising NBS



Scheme 12 Azido-bromination of galactal triacetate

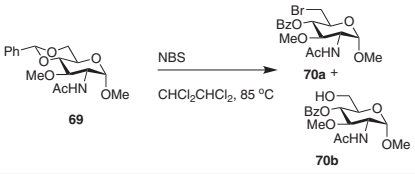
Lah et al.[36] employed the NBS/DMSO reagent to dibrominate tri-*O*-acetyl-D-glucal (**61**), resulting in the formation of 3,4,6-tri-*O*-acetyl-2-bromo-2-deoxy-α-glucopyranosyl-bromide (**65**) in 99% yield and 100% diastereoselectivity (also *cis*/*trans* selectivity). Similar outcomes were seen with other tri-*O*-acetyl, tri-*O*-pivaloyl-D-glucal, and deoxy sugar 3,4-di-*O*-acetyl-L-rhamnal (**62**–**64**), which produced the dibromo derivatives **66**–**68**, respectively, as the only products with 100% diastereoselectivity (Scheme 13).



Scheme 13 NBS/DMSO mediated dibromination of glucal derivatives

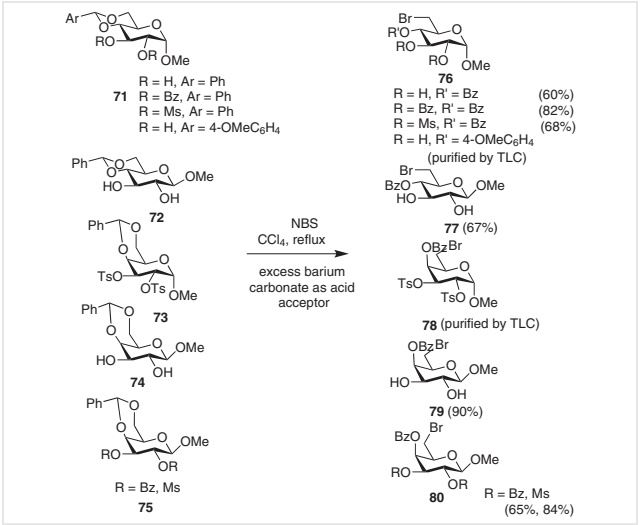
Fragmentation of *O*-Benzylidene Functionality in Carbohydrates

One of the most important applications of NBS in carbohydrates is the selective 4,6-*O*-benzylidene functionality opening of benzylidene acetals **69** to access deoxy sugars. The groups of Hanessian, Hullar, Roberts and Jeppesen studied the same reaction and mechanism with different substituted benzylidene acetals. In 1966, Hanessian was the first to describe the regioselective opening of 4,6-*O*-benzylidene acetals of *O*-benzylidene sugars in tetrachloroethane using NBS. When NBS was exposed to compound **69** in tetrachloroethane at 85 °C, the hydroxyl ion produced by the water of hydration competed with the bromide ion to attack the intermediate cyclic ion, resulting in about equal quantities of the 6-bromo product **70a** and the 6-OH product **70b** (Scheme 14).[37]



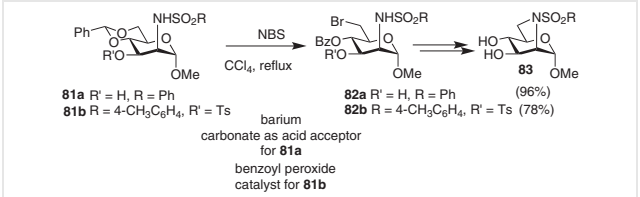
Scheme 14 Regioselective opening of 4,6-*O*-benzylidene acetals with NBS

In order to establish the scope and applications of the methyl 4,6-*O*-benzylidene hexopyranoside series, Hanessian and Plessas, worked on a series of *O*-benzylidene cleavage with NBS.[38] When methyl 4,6-*O*-benzylidene hexopyranosides **71** were heated at reflux with NBS in carbon tetrachloride or chlorinated hydrocarbon, the main products were methyl 4-*O*-benzoyl-6-bromo-6-deoxyhexopyranosides **76**. This method showed orthogonality with different protecting such as anhydro rings, which remained intact. The authors also established adaptability of the NBS-assisted reaction to benzylidene acetals of some disaccharides. For example, the expected product was produced by the NBS reaction of the 4,6:4′,6′-di-*O*-benzylidene derivative of α,α-trehalose dihydrate in a mixture of carbon tetrachloride and tetrachloroethane.[38] The authors also described the formation of the corresponding methyl 4-*O*-benzoyl-6-bromo-6-deoxyhexopyranosides, which are intermediates in the synthesis of biologically important polyfunctionally benzoylated carbohydrate aminodeoxy and deoxy sugar derivatives, by reacting methyl 4,6-*O*-benzylidene hexopyranosides with NBS (Scheme 15).[39]



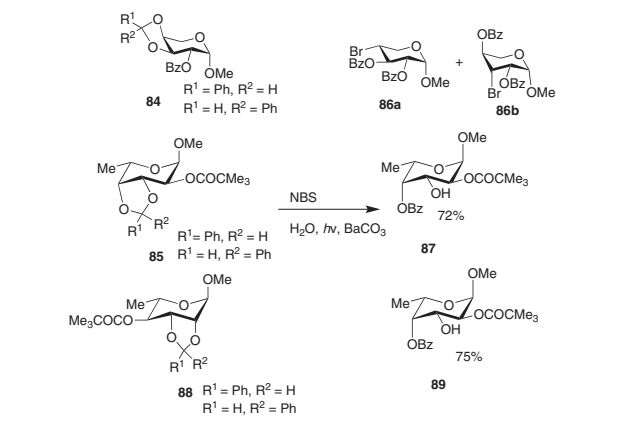
Scheme 15 NBS-mediated acetal opening of methyl 4,6-*O*-benzylidene hexopyranosides

A similar finding was made in 1966 by Failla, Hullar and Siskin,[40] who discovered that NBS interacts specifically with substituted benzylidene acetals to produce ω-bromo benzoates, wherein the bromine occupies the least substituted carbon. To produce substituted 3,7-oxazabicyclo[4.1.0]heptane (**83**), NBS reacted with D-glucopyranoside derivatives **81a** and **81b** to give 4-*O*-benzoyl-6-bromo-6-deoxy derivatives **82** in high yields. It is unlikely that the reaction of benzylidene acetals with NBS would result in 2,6-imino sugar derivatives as long as a suitable leaving group is not *trans*-vicinal to the nitrogen function (Scheme 16). The procedure was also used to synthesise substituted 2,5-oxazabicyclo[2.2.2] octanes and 2,6-imino polysaccharides.[41]



Scheme 16 Hullar method for benzylidene ring-cleavage with NBS

When the benzylidene acetals **84a–b** were opened with NBS in CCl_4 and barium carbonate in the presence of water and exposed to low-pressure mercury irradiation for 2.5 hours, only the 2,4-dibenzoate **86b** was isolated (62% yield), with no 2,3-dibenzoate (**86a**) detected.[42] A pyranoside with an axial benzoyloxy group along with an equatorial hydroxy group was produced when the benzylidene ring was opened under these conditions. It was predicted that similar reactions would be seen with analogous derivatives of L-fucose based on the regiospecific synthesis of **87** from **85a–b**, respectively. The L-rhamnose derivatives **88a–b** reacted under similar conditions to produce a single carbohydrate compound **89** in 75% yield (Scheme 17).

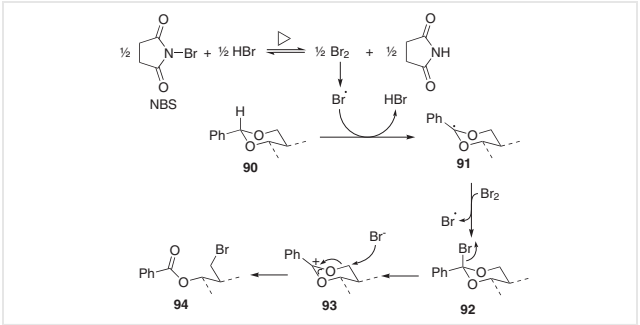


Scheme 17 Benzylidene acetal opening with NBS under low-pressure mercury irradiation

Mechanisms

To search for the probable mechanism of the NBS-mediated Hanessian–Hullar reaction, several groups investigated different types of reaction. Hanessian favoured the ionic mode of fragmentation whereas Hullar initially promoted it as a radical pathway. Gelas also support an ionic mechanism.[43] Following the work by Jeppesen,[44] Roberts later revealed the pure radical fragmentations of 4,6-*O*-benzylidene acetals with preferential cleavage of the primary C6–O6 bond in both the glucose and mannose derivatives.[45]

Control studies were carried out in 2004 by McNulty et al., and they concluded that an ionic process is most likely responsible for the fragmentation (Scheme 18).[46] The initial step was the removal of radical hydrogen from the arylidene acetal carbon by a bromine radical to generate acetal radical **91**, as NBS can form bromine (Br_2) in situ by interaction with HBr, which is present in a low concentration. Following this, propagation takes place during which the acetal radical undergoes Wohl–Ziegler bromination. The Benzylideneacetal (**90**) breaks down via an ionic pathway, leaving a stable cyclic carbocation (**91**), which is then opened by nucleophilic attack of the bromide ion at C6. The inversion of stereochemistry at C4 in compound **86b** is a clear illustration of the S_N2-pathway of the previous step. Usually, $BaCO_3$ functions as an acid scavenger.



Scheme 18 Radical mechanism for the benzylidene cleavage

Application in Carbohydrates

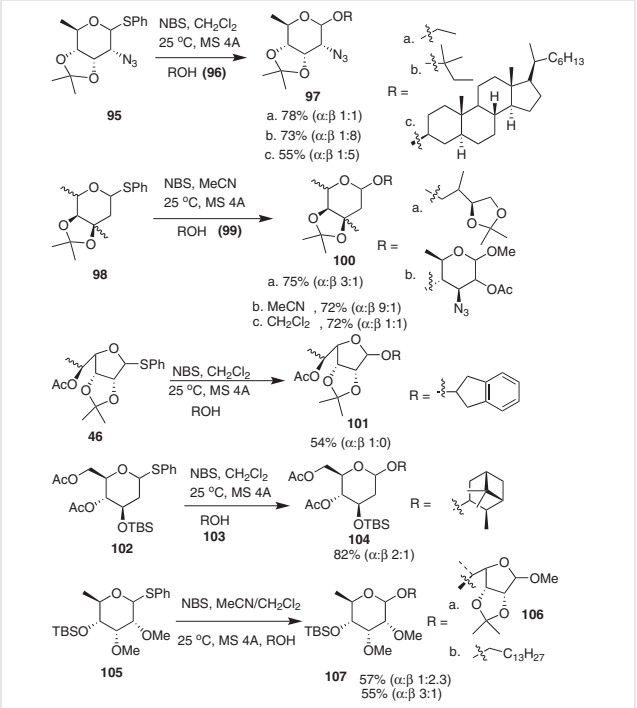
Fragmentation of *O*-Isopropylidene Functionality in Carbohydrates

The importance of the *O*-glycoside bond in nature and biomolecules is well known. The *O*-glycoside bond plays a key role in organic synthesis for the assembly of intricate frameworks containing carbohydrate residues. Thus, the methodology for the formation of the *O*-glycoside bond is of utmost interest. For glycosylation, glycosyl donors such as thioglycosides are often utilised in the presence of promoters such as methyl triflate, *N*-iodosuccinimide-triflic acid, and iodonium dicollidine perchlorate.[47a]

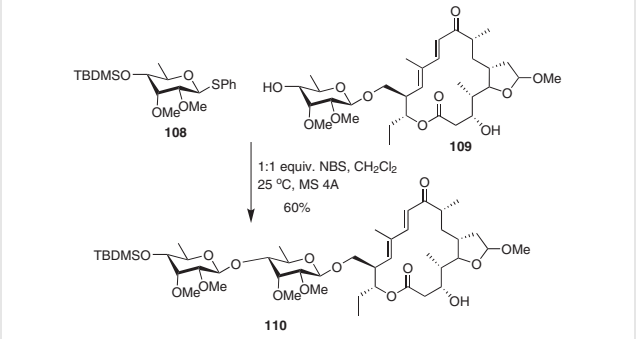
The group of Nicolaou developed a mild and general procedure of *O*-glycosidation from phenyl thioglycosides by reaction with NBS in CH_2Cl_2 under anhydrous conditions at 25 °C in the presence of different hydroxy compounds and 4Å molecular sieves, leading to *O*-glycosides (α- and β-anomers) in good to excellent yields within 15 minutes (Scheme 19).[47b]

For a demonstration of the applicability of the glycosidation reaction to complex and polyfunctional compounds, tylosin derivative **110** was constructed as shown in Scheme 20.

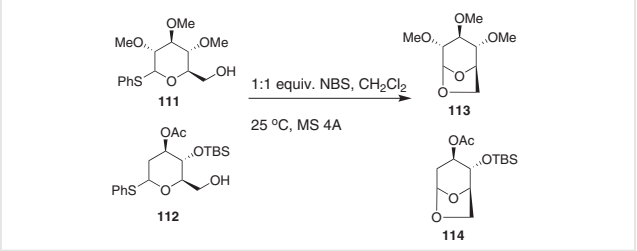
Additionally, as shown in Scheme 21, this reaction provides a straightforward route to internal acetals **113** and **114** in intramolecular situations, demonstrating the scope and applicability of this method.



Scheme 19 *O*-Glycosidation from phenyl thioglycosides upon reaction with NBS

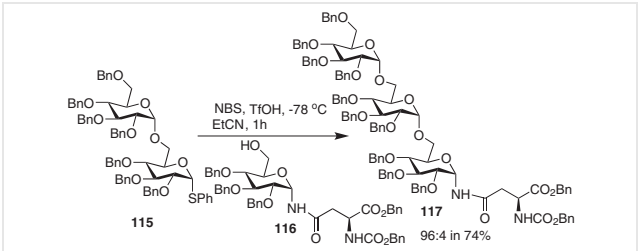


Scheme 20 Glycosidation reaction to give the complex and polyfunctional tylosin derivative



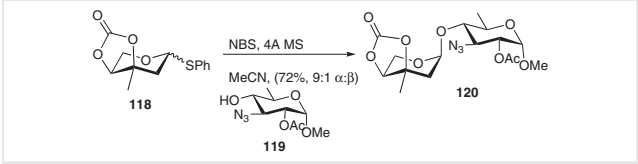
Scheme 21 Glycosidation for internal acetals with NBS

Sasaki and Tachibana[48] produced a stereocontrolled synthesis of the core trisaccharide **117** of nephritogenic glycopeptide, nephritogenoside, employing β-selective glycosylation without neighbouring-group participation. With the anticipated left and right segments **115** and **116**, coupling of these two fragments in a combination of NBS and trifluoromethanesulfonic acid (TfOH) in propionitrile at –78 °C gave trisaccharide **117** and its cc-anomer in 96:4 ratio and 74% combined yield (Scheme 22).



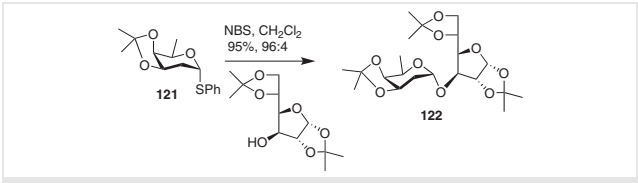
Scheme 22 NBS mediated β-selective glycosylation

A pioneering publication from Nicolaou's group on NBS application to activate phenyl thioglycosides serves as an early illustration.[47b] The results show that the method could be used to couple deoxythioglycoside **118** with a hindered sugar acceptor **119**, forming the required disaccharide **120** in 75% yield in a 9:1 (α/β) mixture (Scheme 23), although this work primarily focused on completely substituted sugars. Later, the Roush group used these conditions to construct the AB disaccharide unit of olivomycin A.[49]

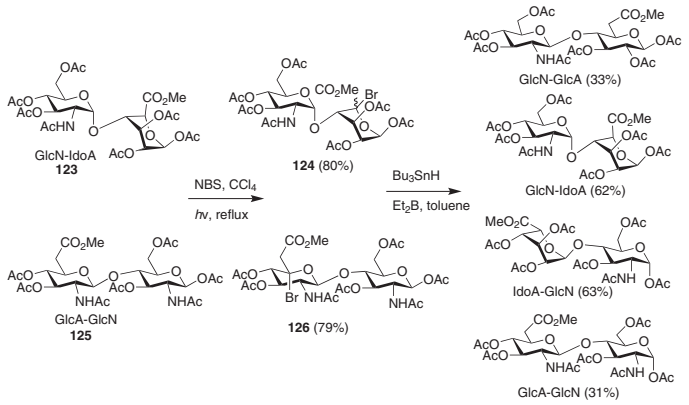


Scheme 23 NBS for oligosaccharide synthesis through activation of 2-deoxythioglycosides

Tatsuta and colleagues achieved selective glycosylation reactions even for conformationally constrained 2-deoxythioglycoside donors. To do this, they looked at what would happen if they protected the C-3 and C-4 alcohols in 2-deoxyfucose thioglycoside **121** by using an isopropylidene acetal. These sugars exhibited exceptionally selective reactions with straightforward glycosyl acceptors after being activated with NBS (Scheme 24).[50]



Scheme 24 Highly selective glycosylation reactions

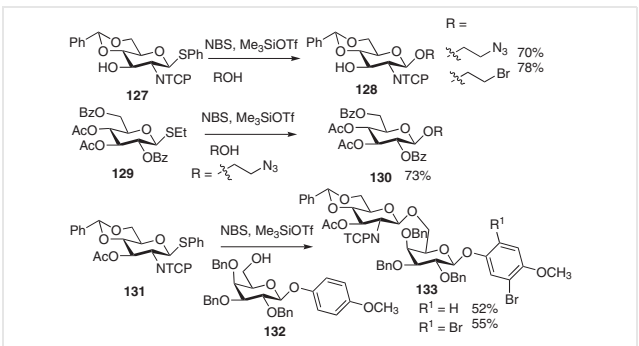


Scheme 25 Interconversion of IdoA to GlcA

Hsieh-Wilson et al.[51] synthesized disaccharide building blocks of natural heparan sulfate. With that aim, the monosaccharides interconversion of IdoA to GlcA in **123** proceeded in poor overall yield due to β-elimination or disaccharide decomposition in a notable amount. The epimerization of GlcA in **125** with NBS under UV light led to the production of the C-5 bromo compound **126** in 75% yield. This was followed by α-dehalogenation with Et_3B and Bu_3SnH at 20 °C to create the epimerized product IdoA-GlcN in 63% yield following Wong and colleagues method.[52] However, NBS-mediated bromination of **123** resulted in the formation of an epimeric combination of the C-5 bromo molecule **124**; subsequent α-dehalogenation with AIBN and Bu_3SnH at 110 °C produced disaccharide GlcN-GlcA in 33% yield (Scheme 25).

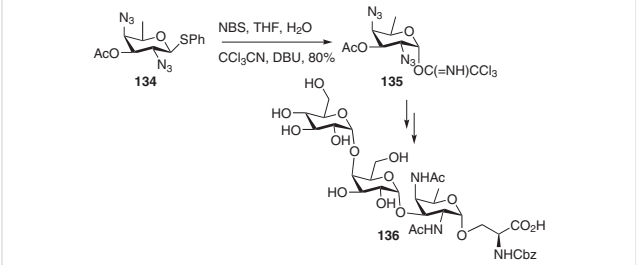
Synthesis of Hemiacetals

Qin et al. synthesised glycoconjugates in good yields by activating phenyl and ethyl thioglycosides with the NBS-Me_3SiOTf system to introduce a C2 spacer arm. Due to the neighbouring tetrachlorophthalimido group, the coupling of phenyl thioglycoside **127** with 2-bromo- or 2-azido-ethanol was possible without further protection of the free 3-hydroxy group (Scheme 26). In the case of the 4-methoxy group, bromination occurs on the aromatic ring in addition to glycosylation. The glycosides 2-bromoethyl and 2-azidoethyl are important intermediates in the synthesis of neoglyco conjugates. As a result, if the aromatic group is not sensitive to bromination, in either the glycosyl donor or acceptor, then NBS (cat.)/Me_3SiOTf reagent is a good thioglycoside promoter.[53]



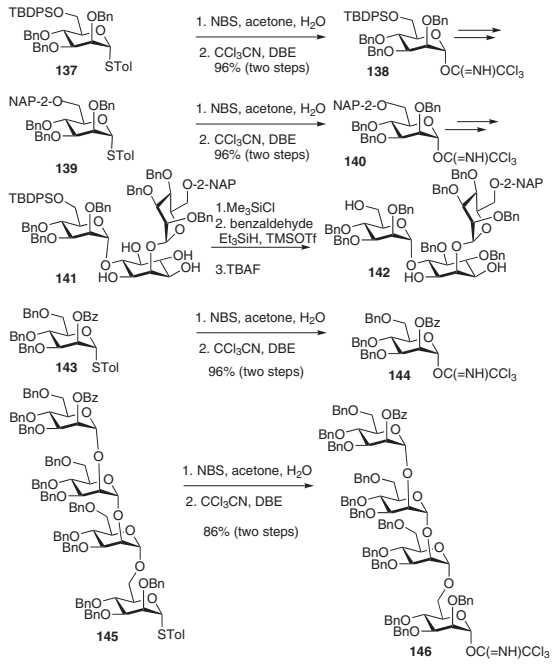
Scheme 26 Glycoconjugate synthesis by activating phenyl and ethyl thioglycosides with the NBS-Me_3SiOTf system

The synthesis of 2,4-diacetamido-2,4,6-trideoxy-D-galactose (DATDG) containing trisaccharide by Emmadi and Kulkarni[54] is given in Scheme 27. The stereoselective coupling of 2,4-diacetamido-2,4,6-trideoxy-α-D-hexose (DATDH) donor with the primary alcohol of an amino acid is a tough challenge. Following treatment with NBS, THF, and H_2O, the thioglycoside derivative **134** was converted into its corresponding hemiacetal, and the resulting hemiacetal was treated with trichloroacetonitrile and DBU to yield imidate donor **135**.



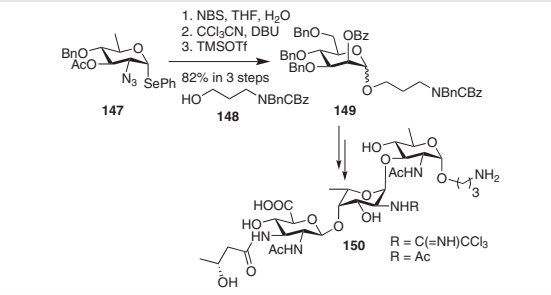
Scheme 27 NBS-mediated conversion of thioglycoside into hemiacetal

Patil et al. constructed **146** by following a linear glycosylation protocol converting the reducing end to the nonreducing end as a target to study tetraacylated phosphatidylinositol hexamannoside for antituberculosis activity. To that end, a single elongation unit **137** was used. Accordingly, first, the elongation unit was transformed from **137** to **138** utilizing NBS in aq. acetone followed by imidate formation in an overall 94% yield in two steps (Scheme 28).[55]



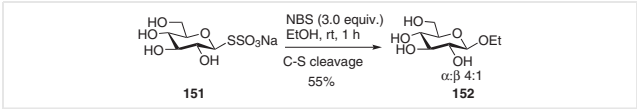
Scheme 28 Glycosylation using NBS

Seeberger, Yin and colleagues recently reported the complete synthesis of a highly functionalized trisaccharide repeating unit from *P. shigelloides* serotype 51. The D-quinovosamine building block was converted into its corresponding hemiacetal using NBS in aq. THF (Scheme 29). This was then treated with trichloroacetonitrile and DBU to yield the imidate, which was then coupled with linker acceptor **148** using TMSOTf promoter to yield **149** in 82% yields over three steps.[56]



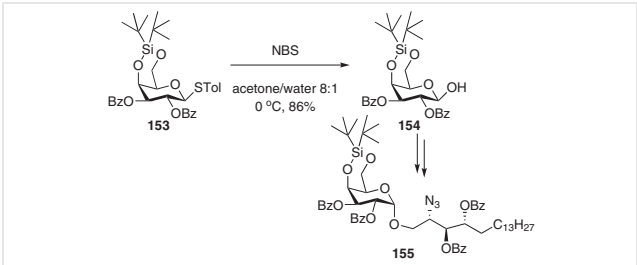
Scheme 29 Glycosilyation of selenyl glycoside with NBS

S-Glycosyl thiosulfate **151**, sometimes known as 'glycosyl Bunte salts', was employed for protection-free intramolecular glycosylation and alcoholysis by direct anomeric activation. NBS was discovered to be an efficient promoter for the solvolysis reactions with ethanol, yielding ethyl D-glucopyranoside **152** (Scheme 30).[57]



Scheme 30 NBS mediated solvolysis of glycosyl Bunte salts

Zong and co-workers in 2022, synthesized α-galactosylceramide **154** and its C-6 modified analogues from donor **153** (Scheme 31). The hydrolysis of thiolacetals was carried out with NBS.[58]



Scheme 31 Hydrolysis of thiolacetals using NBS

Conclusions

The regioselective and orthogonal modification of different functionalities in carbohydrates is crucial because of the wide application of such reactions in chemistry and biology. This review article has summarised the usage of N-bromosuccinimide in carbohydrate chemistry for various organic group transformations. NBS facilitates the production of deoxysugars *via* selective *O*-benzylidene fragmentation, photobromination, halogenation, oxidation, and polymerisation of various carbohydrate moieties.

Conflict of Interest

The authors declare no conflict of interest.

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