Available online at www.sciencedirect.com
SCIENCE DIRECT
Carbohydrate Research 341 (2006) 1298–1311
Carbohydrate RESEARCH

Perspective

The Ramberg–Bäcklund reaction for the synthesis of C-glycosides, C-linked-disaccharides and related compounds

Richard J. K. Taylor,[a,*] Graeme D. McAllister[a] and Richard W. Franck[b,†]

[a]*Department of Chemistry, University of York, Heslington, York YO10 5DD, UK*
[b]*Department of Chemistry, Hunter College, 695 Park Avenue, New York City, NY 10021, USA*

Received 27 January 2006; received in revised form 6 March 2006; accepted 11 March 2006
Available online 2 May 2006

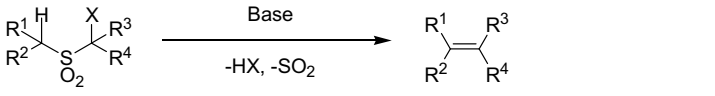
Abstract—The discovery of the Ramberg–Bäcklund procedure for preparing *exo*-glycals from S-glycoside dioxides, developed independently in (Old) York and New York, is reviewed. The methodology is successful with glucose, galactose, mannose, xylose, fucose, ribose, altrose, 2-deoxy-*arabino*-hexose (2-deoxy-glucose) and daunosamine derivatives, and has been used to prepare di-, tri- and tetra-substituted *exo*-glycals. More recent developments, such as one-pot variants, and protecting group-free procedures, are also covered. Synthetic applications of the *exo*-glycals, for example, to prepare β-glycosidase inhibitors, spirocyclic glucose derivatives, β-C-glycosides, *C*-glycosyl porphyrin glycoconjugates and *C*-glycosyl amino acids, are also discussed. Finally, applications of the Ramberg–Bäcklund process for the synthesis of known and novel C-glycosides, and in natural product synthesis, are reviewed.

Keywords: exo-Glycals; Synthesis; Glycosides; Disaccharides; Glycosyl amino acids; One-pot processes

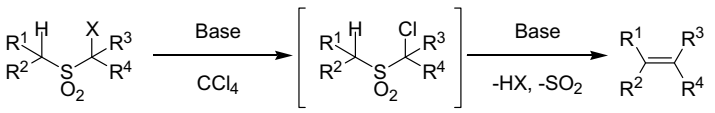
1. Introduction

The Ramberg–Bäcklund reaction, in which α-halogenated sulfones are converted into regio-defined alkenes on treatment with base (Eq. 1), has attracted considerable interest from both mechanistic and synthetic viewpoints, since its discovery in 1940.[1–3] The development of Meyers' modification (Eq. 2),[4] in which the sulfone undergoes an in situ halogenation-Ramberg–Bäcklund reaction, has further extended the synthetic utility of this process. This reaction, which has been widely employed to prepare natural and nonnatural targets, has been well reviewed.[2,3]

In the Taylor group in York, early contributions to this area concerned (i) the development of mild conditions for carrying out the Ramberg–Bäcklund reaction on α-iodosulfones, (ii) the isolation of episulfones from the Ramberg–Bäcklund reaction, (iii) the preparation of episulfones by the oxidation of episulfides, (iv) the generation and synthetic applications of episulfone α-



(1)

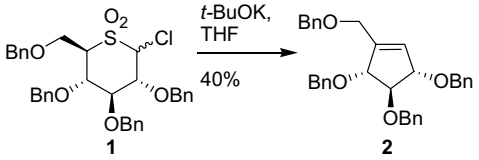


(2)

* Corresponding author. Fax: +44 1904 434523; e-mail addresses: rjkt1@york.ac.uk; rfranck@hunter.cuny.edu
† Fax: +1 212 772 5332.

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.03.013

anions and (v) the discovery of new variants of the process including the epoxy-Ramberg–Bäcklund reaction, and the tandem conjugate addition-Ramberg–Bäcklund reaction.[5] These procedures were utilised in a number of target syntheses including tetrahydrodicranenone B, *trans*-carbovir and unsaturated amino acids (e.g., conversion of methionine-derived sulfones into protected L-allyl glycine).[5] Having investigated the Ramberg–Bäcklund reactions of amino acid-derived sulfones, a study of sulfones derived from other 'chiral pool' substrates seemed appropriate. The initial idea was to utilise thiosugar-derived sulfones (e.g., **1**) in the Ramberg–Bäcklund reaction to prepare enantiopure cyclopentenes (e.g., **2**). It took some time to realise this aim, but it was eventually completed, one example being shown in Scheme 1.[6]



Scheme 1.

The major difficulty with this first foray into carbohydrate chemistry was that the preparation of the thiosugar precursors (e.g., **1**) was rather laborious. In the search for more readily available carbohydrate-derived sulfones, we decided to investigate the use of the readily available S-glycoside dioxides in the Ramberg–Bäcklund reaction. This topic, and its extensions into the preparation of C-glycosides, C-linked disaccharides, *C*-glycosyl amino acids, etc., is the subject of this review.

At about the same time, the Franck group in New York was focussed on the goal of the synthesis of **3b**, the C-glycoside analogue of daunomycin **3a** (Fig. 1), an antitumour anthracycline which was known to be deactivated by cleavage of the glycoside linkage. A promising approach, requiring tin chemistry to create the C-glycosidic linkage, had been described by Acton about a decade ago.[7,8] The New York efforts were centred on forging a C-linkage between a glycoside and an intact anthracycline. Proceeding after difficulties with phosphorus-based couplings, the Franck group also turned to the same concept being developed by the Taylor laboratory.[9]

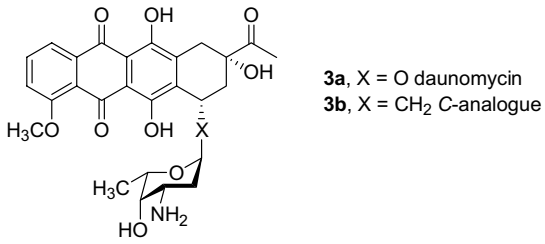
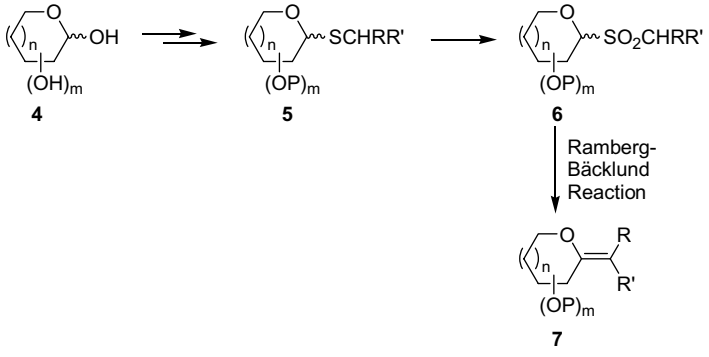


Figure 1. Daunomycin (**3a**) and its C-glycoside analogue (**3b**).

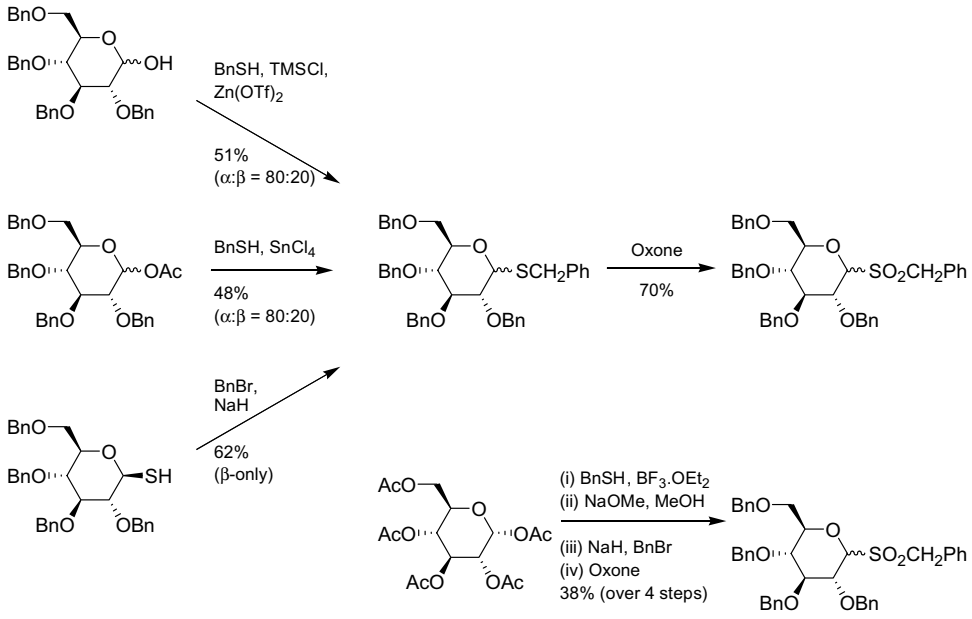
2. Initial studies—*exo*-glycal synthesis

The initial objective of both groups was to convert readily available furanose and pyranose systems **4** into the corresponding protected thioglycosides **5** and then sulfones **6**. The Meyers variant of the Ramberg–Bäcklund reaction using sulfones **6** would be expected to produce *exo*-glycals **7** (Scheme 2).

The parent 1-*exo*-methylene compounds (**7**, R = R′ = H) have been used as glycosidase inhibitors,[10–14] and are valuable synthetic intermediates.[15–22] A number of procedures have been published for the preparation of *exo*-methylene glycals,[15–25] but the method of choice would appear to be methylenation of the corresponding lactones using dicyclopentadienyl(dimethyl)titanium (or the Tebbe reagent).[17,21,22] Until recently, there has been no general method to prepare substituted *exo*-glycals **7** (R, R′ ≠ H), however.[26] The S-glycoside dioxides **6** required for this study were readily prepared from monosaccharides **4** using standard procedures as outlined in Scheme 3.[27–31]



Scheme 2. ($n = 0, 1$).

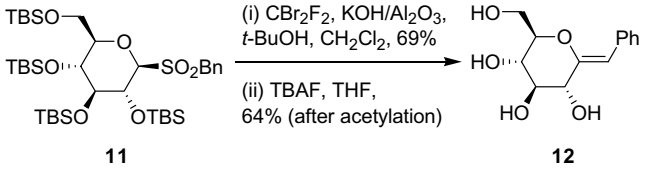


Scheme 3.

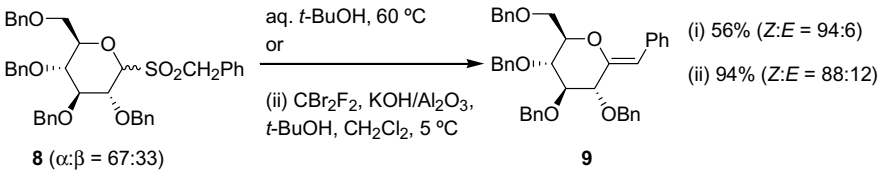
Initial studies to investigate the viability of the Ramberg–Bäcklund reaction to produce *exo*-glycals were carried out using the glucose-derived benzyl sulfone **8** (Scheme 4). Gratifyingly, the required *exo*-glycal **9** was formed in a reasonable yield, with the *Z*-product predominating, using Meyers' original conditions (CCl_4, KOH, 56%). However, when the modified conditions recently reported by Chan et al.[32] (CBr_2F_2, KOH/Al_2O_3) were employed, phenyl glycal **9** was produced in 94% yield.[33,34]

A range of *exo*-glycals were then prepared using this Ramberg–Bäcklund methodology (Fig. 2).[33,34] As can be seen, the glucose-derived methylene compound **10a** was prepared, as were the phenyl, methyl and ethyl substituted alkenes **9**, **10b**,**c** (all with the *Z*-alkene predominating). Although unoptimised, galactose, mannose, xylose, fucose and ribose derived alkenes **10d**–**h** were equally accessible. Tetra-substituted alkenes **10i**–**l** were also prepared by this methodology, although in these cases the required transformation was only observed using Meyers' conditions. Further work is needed to optimise these yields, but the availability of highly hindered glycals, particularly adamantene derivative **10l**, is noteworthy.

As mentioned, *exo*-glycals have proved to be valuable glycosidase inhibitors, but for the above methodology to be of use in this area it is important to be able to remove the hydroxyl protection without reducing or hydrolysing the enol ether moiety. Benzyl protection is not suitable for this purpose and the compatibility of other protecting groups with the Ramberg–Bäcklund conditions was explored. Sulfone **11**, protected by *t*-butyldimethylsilyl (TBDMS) groups, was therefore investigated and Ramberg–Bäcklund reaction proceeded smoothly: desilylation was accomplished using tetrabutylammonium fluoride (TBAF). This two-step sequence produced the unprotected enol ether **12** (which was acetylated for characterisation purposes) (Scheme 5).[34]



Scheme 5.



Scheme 4.

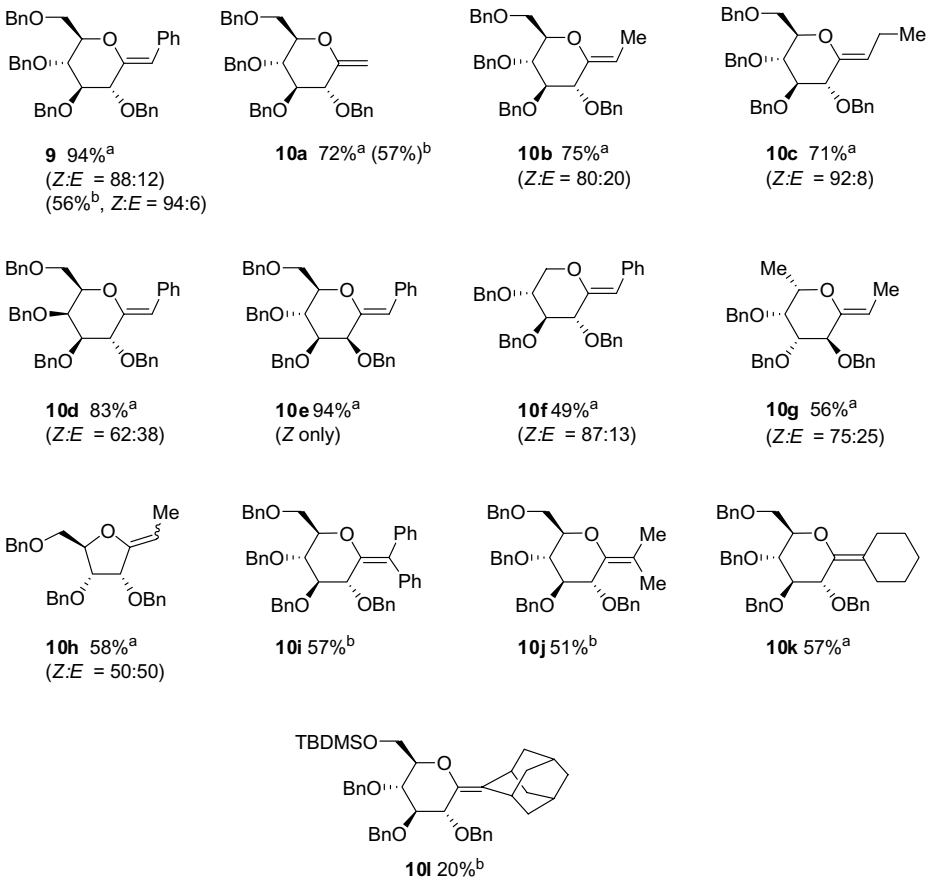


Figure 2. *exo*-Glycals prepared via Meyers' variant of the Ramberg–Bäcklund reaction (a = using CBr_2F_2;[32] b = using CCl_4[4]).

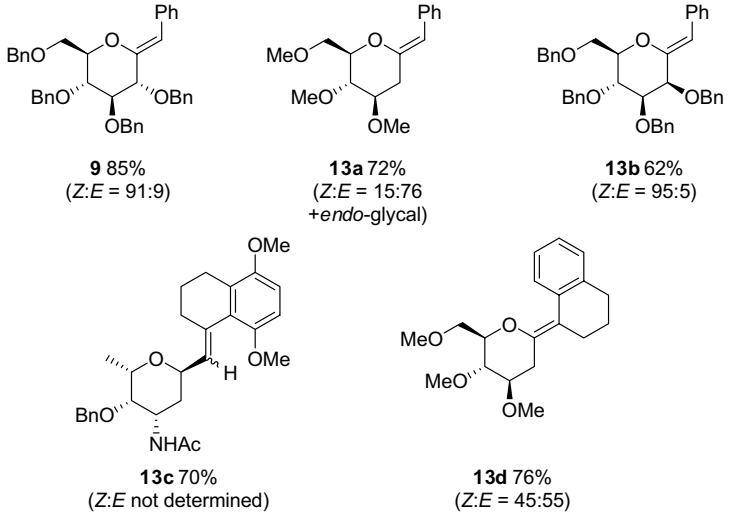
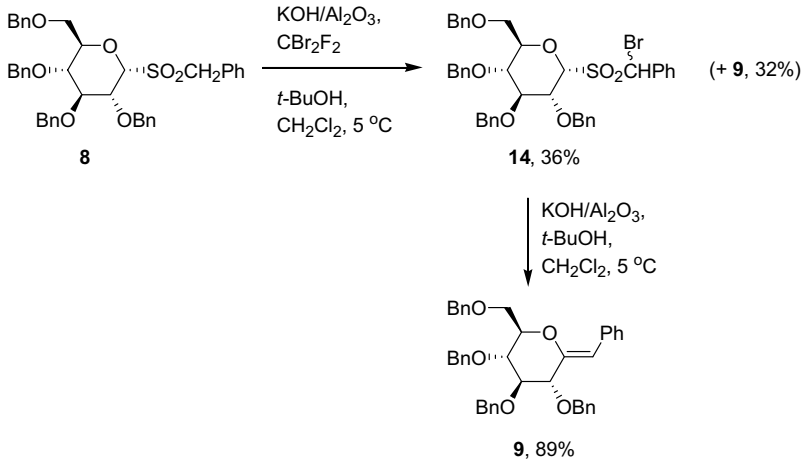


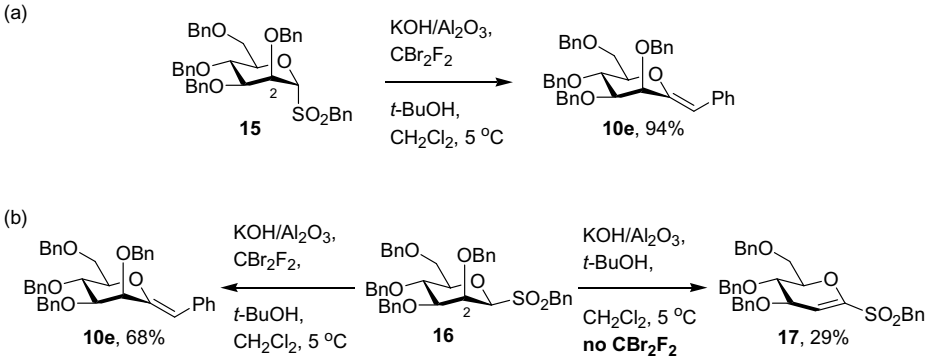
Figure 3. *exo*-Glycals prepared by Belica and Franck.[9] Yields refer to the Ramberg–Bäcklund reaction.

Similar results were published by Franck et al. at the same time (preparing **9**, **13a**–**d**, Fig. 3).[9,35] The daunomycin C-glycoside analogue **13c**, although not an *exo*-glycal, was obtained using the standard Chan conditions on the benzylic sulfone of a separately formed C-glycoside of daunosamine.

Investigations are underway to probe the mechanisms of these reactions: preliminary results from the York group are collected in Schemes 6 and 7. Thus, a brief treatment of sulfone **8** with a reduced amount of base and CBr_2F_2 produced the intermediate α-bromosulfone **14** in 36% yield, along with *exo*-glycal **9** (32%) and



Scheme 6.



Scheme 7.

unreacted starting material (Scheme 6). One diastereomer of bromide **14** was characterised by X-ray crystallography. Treatment of bromide **14** with base produced *exo*-glycal **9** in almost quantitative yield. Therefore, in the case of benzylic sulfones, at least, the reaction pathway seems to involve bromination at the benzylic position rather than at the anomeric site.

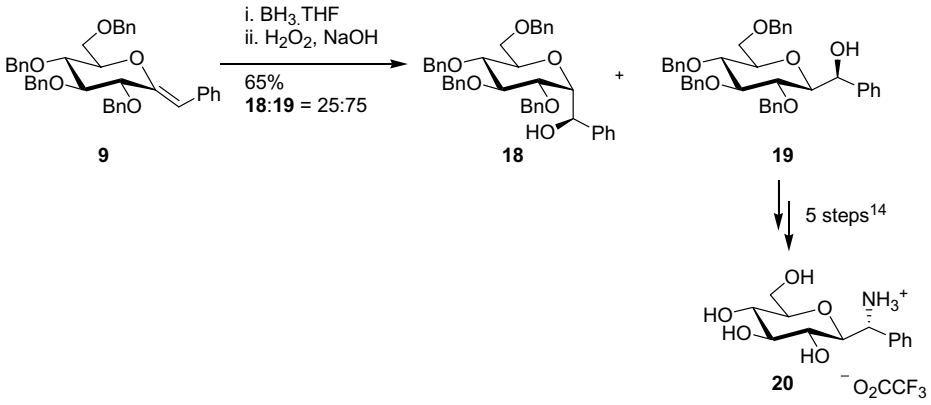
Further information was obtained using mannose derivatives (Scheme 7).[‡] The ready elimination of the axial C-2 substituent in mannose derivatives has bedevilled anomeric carbanion chemistry,[36] but such 1,2-glycal formation is not seen in the Ramberg–Bäcklund approach. Starting from the α-sulfone **15**, the *exo*-glycal **10e** was obtained in 94% yield (Scheme 7a). Even more surprisingly, a study of the β-mannose sulfone **16** revealed little, if any, elimination of the axial C-2 benzyloxy substituent (Scheme 7b). However, treatment of **16** with base (in the absence of CBr_2F_2) did produce 1,2-glycal **17**, as shown. These observations indicate that anomeric deprotonation must produce a conformation from which β-elimination is slow compared to the Ramberg–Bäcklund reaction (1,3-elimination). More detailed conformational discussions have been published.[34]

3. Synthetic applications of Ramberg–Bäcklund-derived *exo*-glycals

The York group also investigated synthetic applications of these novel *exo*-glycals.[37,38] As shown in Scheme 8, the *Z*-phenyl derivative **9** was utilised in a formal synthesis of C-glycoside **20**, reported to be a new β-glycosidase inhibitor by Schmidt and Dietrich.[14] Thus, hydroboration using borane–THF followed by oxidation gave a separable 25:75 mixture of α- and β-alcohols **18** and **19** in 65% overall yield. Schmidt and Dietrich converted alcohol **19** into enzyme inhibitor **20** in five high-yielding steps. The advantage of our new procedure is the brevity of the synthetic route: Schmidt and Dietrich required eight steps to prepare alcohol **19** from D-glucal.[14]

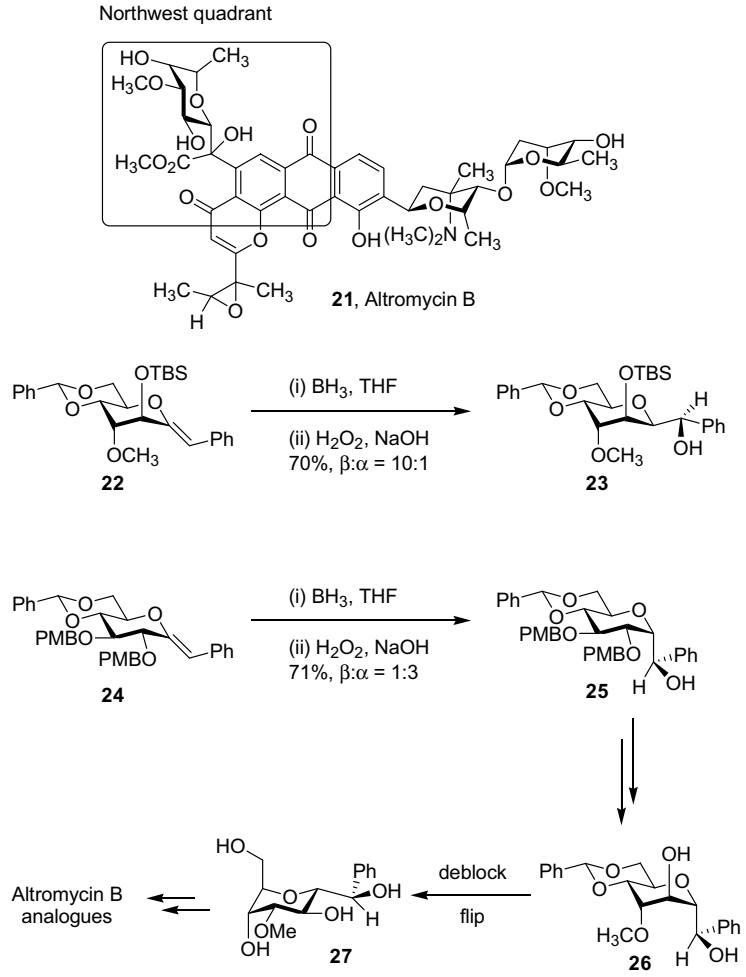
In studies to prepare the *C*-glycosidic northwest quadrant of altromycin B **21**,[39,40] the New York team also explored hydroborations of *exo*-glycals. When *exo*-glycal **22**, prepared via Ramberg–Bäcklund chemistry, was

[‡] McAllister, G. D.; Taylor, R. J. K. Unpublished results.



Scheme 8.

subjected to standard hydroboration conditions, the C-glycoside product **23** was formed with high β-selectivity. This outcome was not useful for the ultimate synthetic goal because it is the α-isomer in the $^4C_1$ conformation which is required, and which will hopefully then flip to the $^1C_4$ conformation of the C-glycoside of the northwest quadrant. When the same experiments were carried out with the glucose-derived glycal **24**, the desired α-C-glycoside **25** was the preferred (and desired) product which ultimately was converted into the altromycin model (Scheme 9).[41] It was not possible to rationalise the differences in hydroboration outcomes among glycals **9** and **24**, both with similar glucose conformations. Clearly, the protecting groups must have a powerful effect.



Scheme 9.

Belica and Franck also showed that the catalytic hydrogenation of *exo*-glycals **9**, **13a–d** (Fig. 3) was uneventful[9] and, in almost every example examined, the corresponding β-C-glycoside was the exclusive product (>95%). The two main problems with this simple and efficient method were that the common benzyl protecting group was subject to hydrogenolytic cleavage, which was not always desirable; and the α-C-glycoside configuration did not seem to be accessible by this method. The acid-catalysed silane, or 'ionic hydrogenation' method originally developed by Kursanov, and then applied to carbohydrates by Kishi and Sinaÿ,[42–44] was therefore studied (Scheme 10). Thus, Ramberg–Bäcklund product **29** was easily converted into its masked ketal form **30**. This species, via acetate **32**, was then subjected to anomeric carbonium ion formation coupled with hydride transfer in an *inter*-molecular manner from the axial face to afford β-C-glycoside **33**. To force the hydride transfer from the β-face to produce α-C-glycoside **36**, the hydride was delivered in an *intra*-molecular fashion, via a silane linked to the 4-hydroxy of galactose, that is, **34**. Needless to say, this is a nongeneral route for preparation of α-C-glycosides.

One observation of note is the use of $C_2Br_2F_4$ in the Ramberg–Bäcklund reaction of **28** to **29** in place of Chan's original CBr_2F_2. The higher boiling point ($C_2Br_2F_4$, bp 47 °C, cf. CBr_2F_2, bp 23 °C) allows many Ramberg–Bäcklund reactions that would otherwise be difficult at lower temperatures, and has been used by Franck in many later studies.

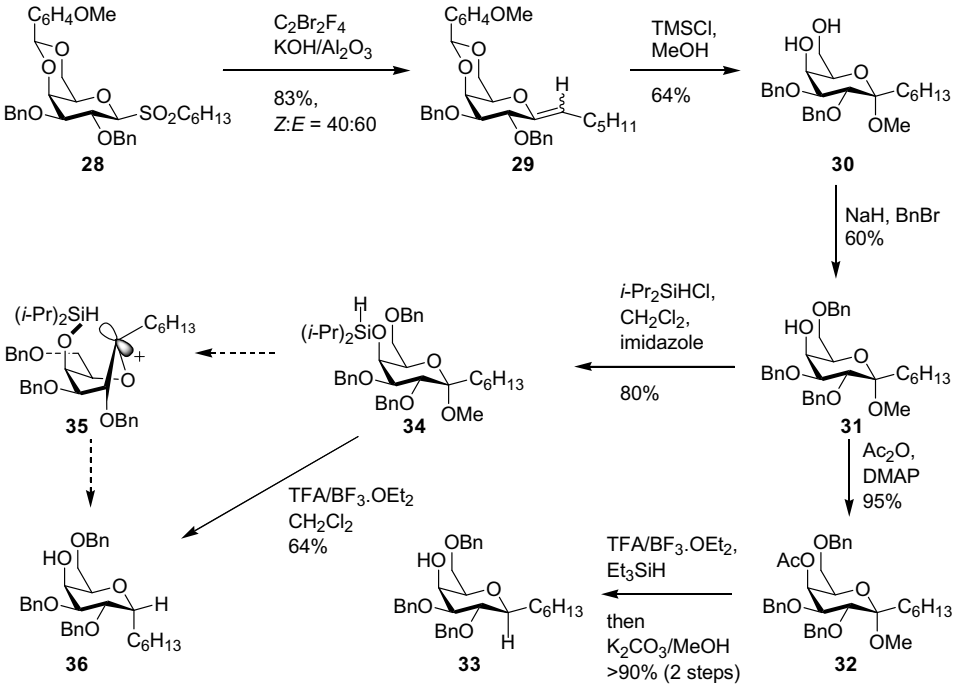
Ramberg–Bäcklund methodology was also used to prepare the spirocyclic sugars **41** and **42** (Scheme 11). These compounds, which are simplified analogues of natural products such as papulacandin D,[45] have recently been prepared by a photolytic route.[46] In the Ramberg–Bäcklund synthesis (Scheme 11), the benzylated thioglucose derivative **37**[27] was alkylated giving sulfide **38**, which was oxidised to sulfone **39**, both steps proceeding in good yield. The Ramberg–Bäcklund reaction proceeded smoothly on the unprotected alcohol **39** using Chan's CBr_2F_2 conditions[32] giving *exo*-glycal **40** in 73% yield. Cyclisation was effected by treatment of enol ether **40** with camphorsulfonic acid (CSA) in methanol to produce a separable mixture of spiroacetals **41** and **42** (30:70) in 75% yield.

Finally, *exo*-glycal **43** was used by Franck and co-workers in the synthesis of hydrolytically stable porphyrin glycoconjugates **44** and **45** (Scheme 12).[47]

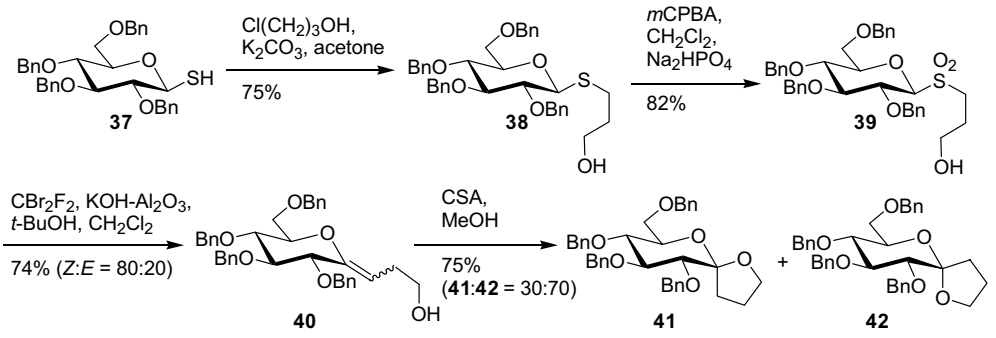
4. A simplified Ramberg–Bäcklund approach to C-glycosides

A stream-lined Ramberg–Bäcklund approach to C-glycosides was subsequently developed by the York group.[48] This involves the synthesis of glycosyl sulfones by Horner–Wadsworth–Emmons olefination of a glycosyl lactol **46** with phosphonate **47**, followed by subsequent Michael addition and Ramberg–Bäcklund reaction (Scheme 13).

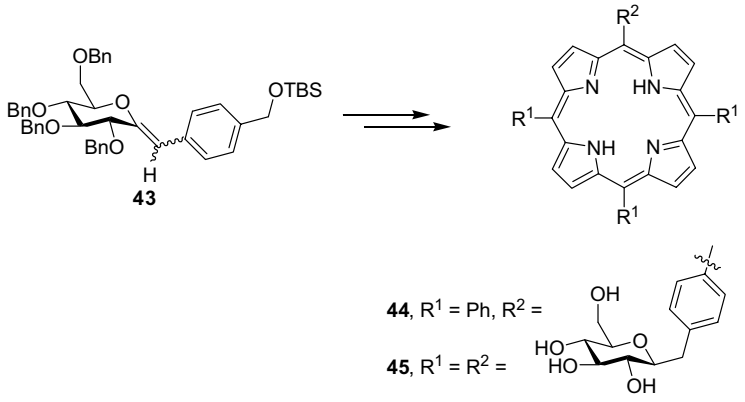
Proof-of-principle studies were carried out using phosphonate **47** and diisopropylidene mannofuranose **51** (Scheme 14). In this study, sulfone **52** was isolated in good yield as a single isomer after the HWE-conjugate



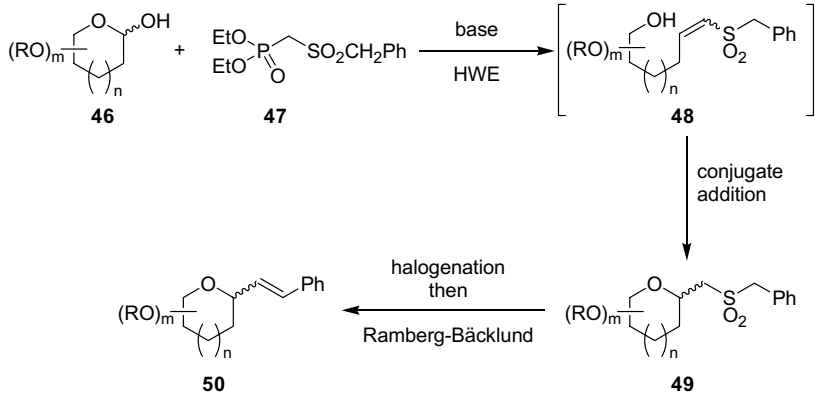
Scheme 10.



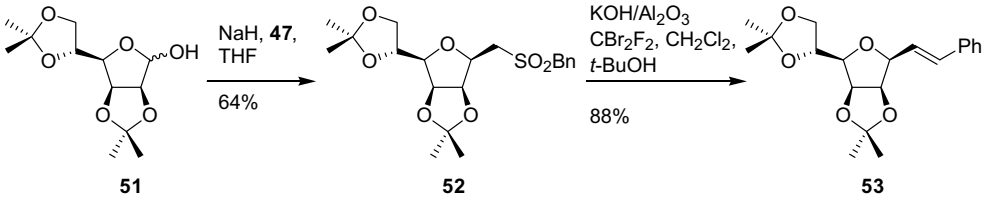
Scheme 11.



Scheme 12.



Scheme 13.



Scheme 14.

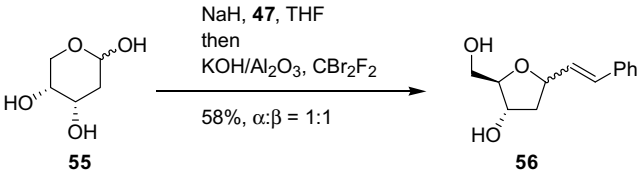
addition process. Reaction of **52** under Chan's one-pot halogenation/Ramberg–Bäcklund conditions gave C-glycoside **53** in excellent yield, as a single stereo- and geometric isomer [N.B. the use of Meyers' conditions (aq CCl_4, *t*-BuOH, KOH, 60 °C) only gave **53** in a 48% yield]. This study demonstrated that thioglycoside dioxides were not an essential requirement for the Ramberg–Bäcklund reaction on carbohydrate derivatives (see also Fig. 3, **13c**).

This sequence was used to prepare a range of protected furanose C-glycosides **54a–e** (Fig. 4).[48] In each case, Ramberg–Bäcklund reaction proceeded in good to excellent yield, with only the *E*-isomeric alkene product being observed.

The York group also showed that this sequence could be carried out in one-pot by adding KOH/Al_2O_3 and CBr_2F_2 to the reaction mixture after 18 h. C-Glycoside **53** was isolated in an excellent 78% yield (Scheme 15).[48] This approach is currently being optimised and extended.

5. A protecting group-free approach to C-glycosides using the Ramberg–Bäcklund reaction

The York group recently disclosed a protecting group-free approach to C-glycoside synthesis based on the above one-pot sequence.[49] 2-Deoxy-D-*erythro*-pentose (2-deoxy-ribose) **55** and phosphonate **47** gave C-glycoside **56** in good yield as a mixture of diastereomers under the one-pot procedure (Scheme 16).



Scheme 16.

This sequence is not limited to a single monosaccharide. D-Arabinose **57** and D-lyxose **59** were both converted into the corresponding C-glycosides by this method (acetylation was employed to aid purification, Scheme 17). These processes were not optimised, but serve to demonstrate the potential generality of the procedure.

6. The Ramberg–Bäcklund approach to C-linked disaccharides

The York group has also been able to access C-linked disaccharides using the Ramberg–Bäcklund reaction methodology (Scheme 18).[38] Alkylation of thiol **37** with iodide **61** (from the hydroboration/iodination of *exo*-glycal **10a**) gave the corresponding sulfide, which was immediately oxidised giving sulfone **62**. Ramberg–Bäcklund reaction using Meyers' conditions gave enol

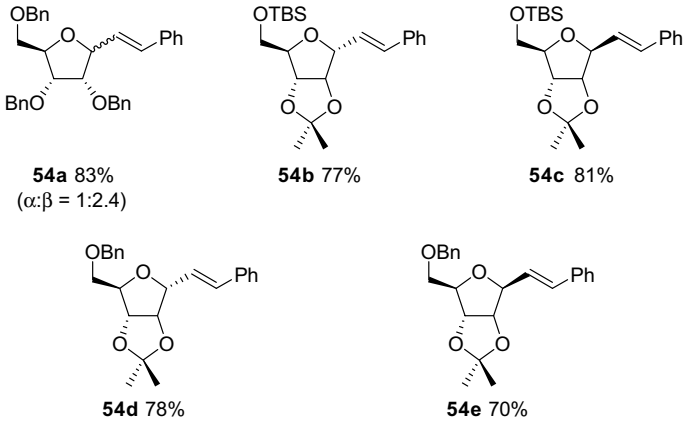
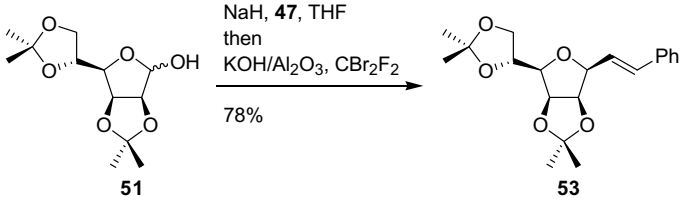
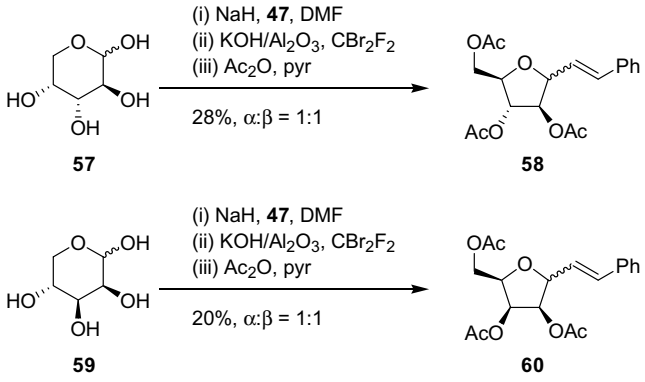


Figure 4. C-Glycosides prepared by the HWE/conjugate addition/Ramberg–Bäcklund sequence. Yields refer to Ramberg–Bäcklund step.



Scheme 15.



Scheme 17.

ether **63**, predominantly as the *Z*-isomer (*Z*:*E* = 91:9). Reduction with concomitant debenzylation, followed by acetylation for characterisation purposes, gave *C*-isotrehalose **64** in 69% over two steps.

Using this approach, *C*-homoisotrehalose **65** and methyl *C*-gentiobioside **66** were prepared (Fig. 5).

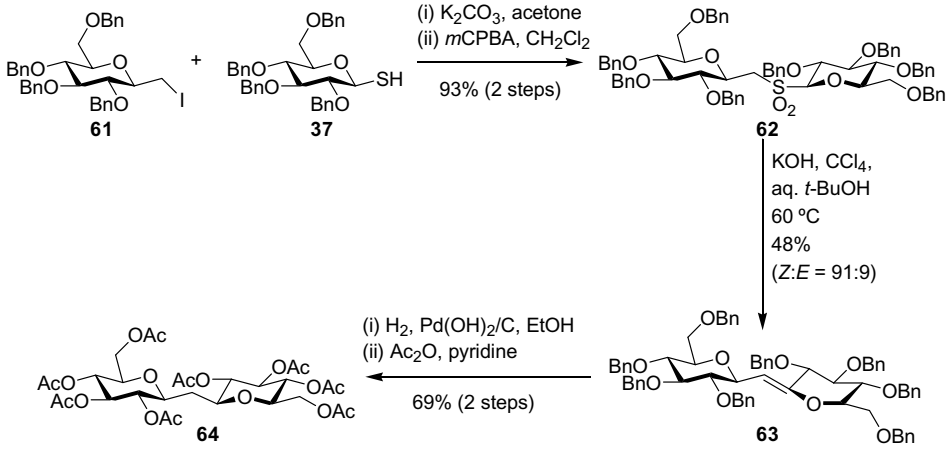
By using the novel glucose-derived phosphonate **67**, it proved possible to extend the HWE/conjugate addition/Ramberg–Bäcklund methodology to the synthesis of a novel C-linked disaccharide (Scheme 19).[48] Horner–Wadsworth–Emmons olefination/Michael addition with mannofuranose **51** proceeded smoothly giving sulfone **68** as a mixture of diastereomers. This mixture underwent Ramberg–Bäcklund reaction in good yield, giving alkene **69**. After reduction/deprotection and acetylation, novel C-disaccharide **70** was isolated in moderate yield.

7. The Ramberg–Bäcklund approach to C-linked glycosyl amino acids and glycerolipids

In addition to C-linked disaccharides, it proved possible to use the Ramberg–Bäcklund reaction in the synthesis of novel *C*-glycosyl amino acids **73** and **76**.[38,50] This was achieved in two separate approaches: (i) via glycosyl sulfone **71** (Scheme 20);[38] and (ii) by a hydroboration/Suzuki sequence from Ramberg–Bäcklund-derived *exo*-glycal **10a** (Scheme 21).[50]

An *exo*-glycal approach was subsequently used by Ohnishi and Ichikawa in the synthesis of the C-glycoside analogue of *N*-Fmoc-serine β-*N*-acetylglucosaminide **79** (Scheme 22).[51] Sulfone **77** underwent Ramberg–Bäcklund reaction using Chan's conditions to give *exo*-glycal **78** in 38% yield solely as the *Z*-isomer. Subsequent transformations gave the protected *C*-glycosyl amino acid **79**.

In recent years, Franck and co-workers have published a series of papers on the synthesis and biological activity of novel *C*-glycosyl glycerolipids **82**, **83** and **86**.[52,53] Schemes 23 and 24 outline their syntheses from glucosamine- and 2-deoxyglucose-derived sulfones **80** and **84**.



Scheme 18.

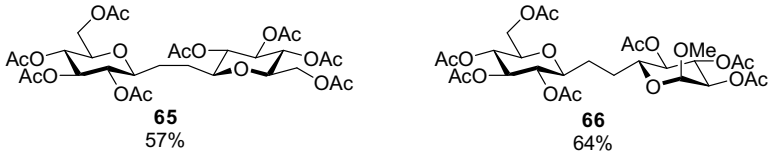
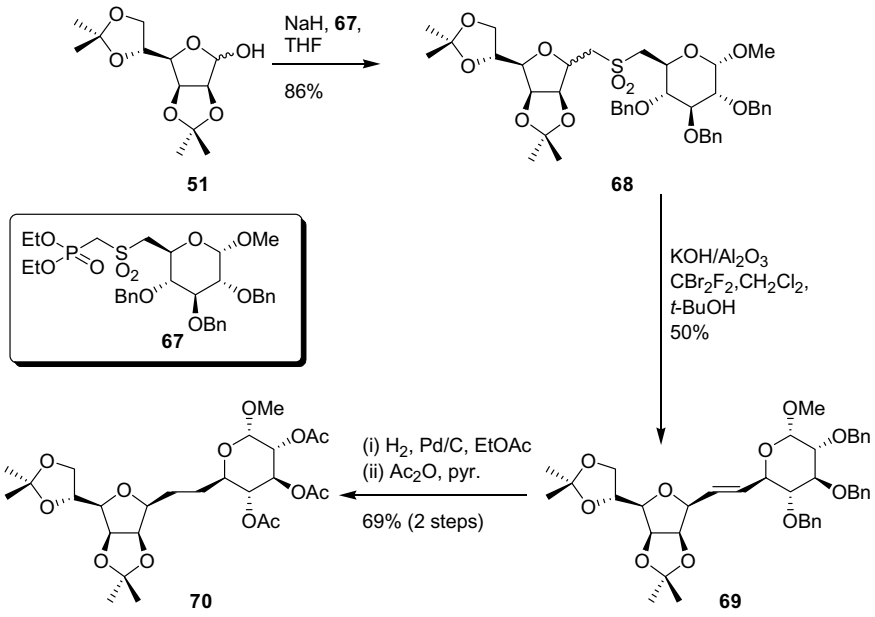
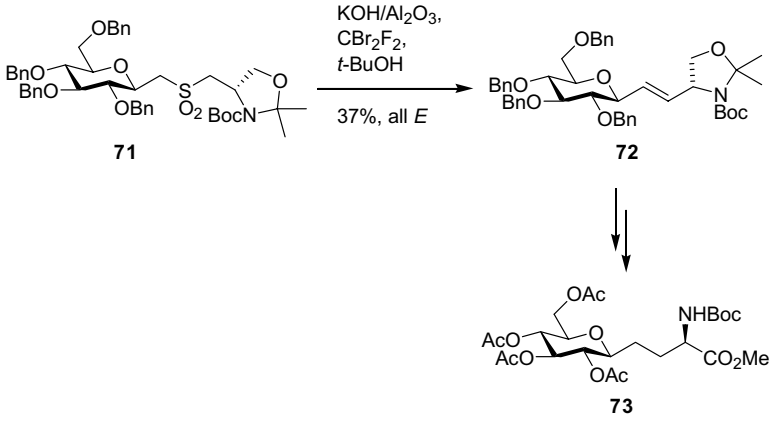


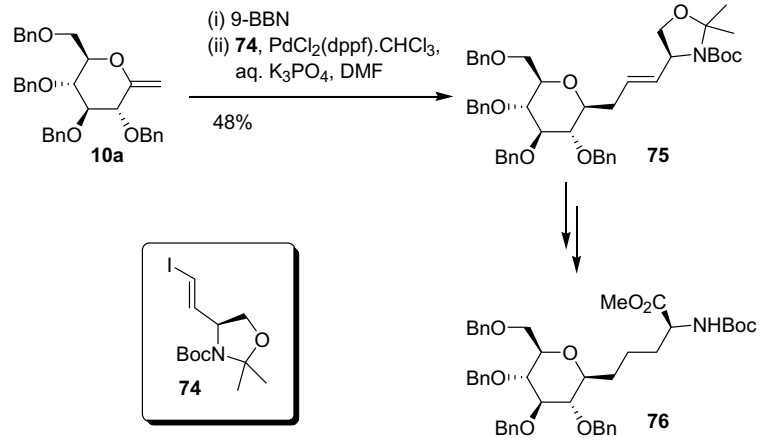
Figure 5. C-Glycosides **65** and **66**. Yields refer to the Ramberg–Bäcklund reaction.



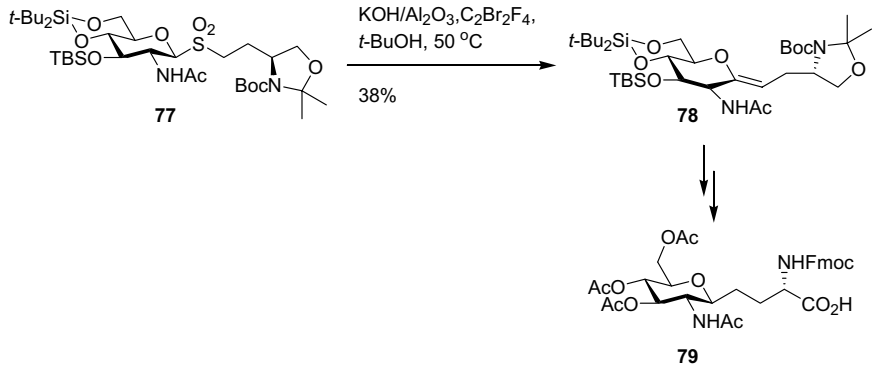
Scheme 19.



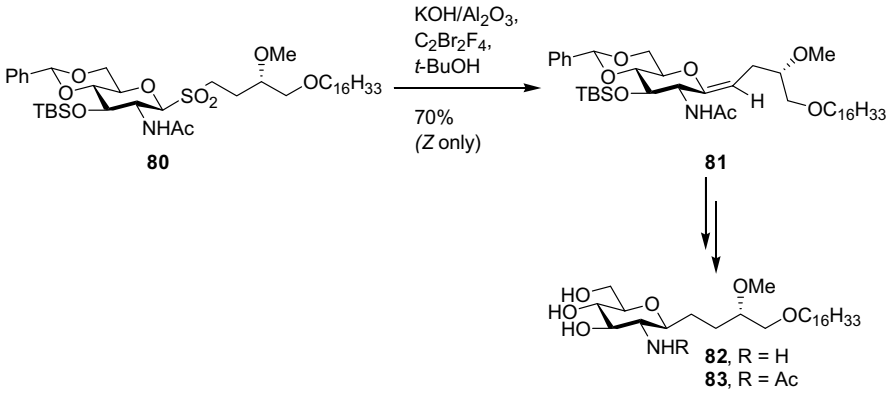
Scheme 20.



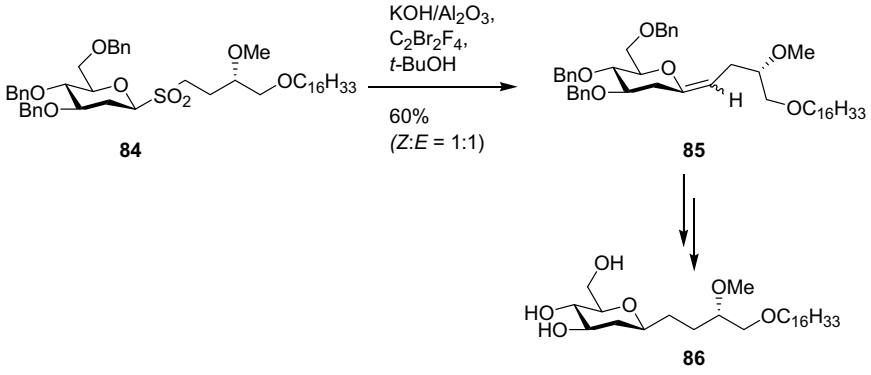
Scheme 21.



Scheme 22.



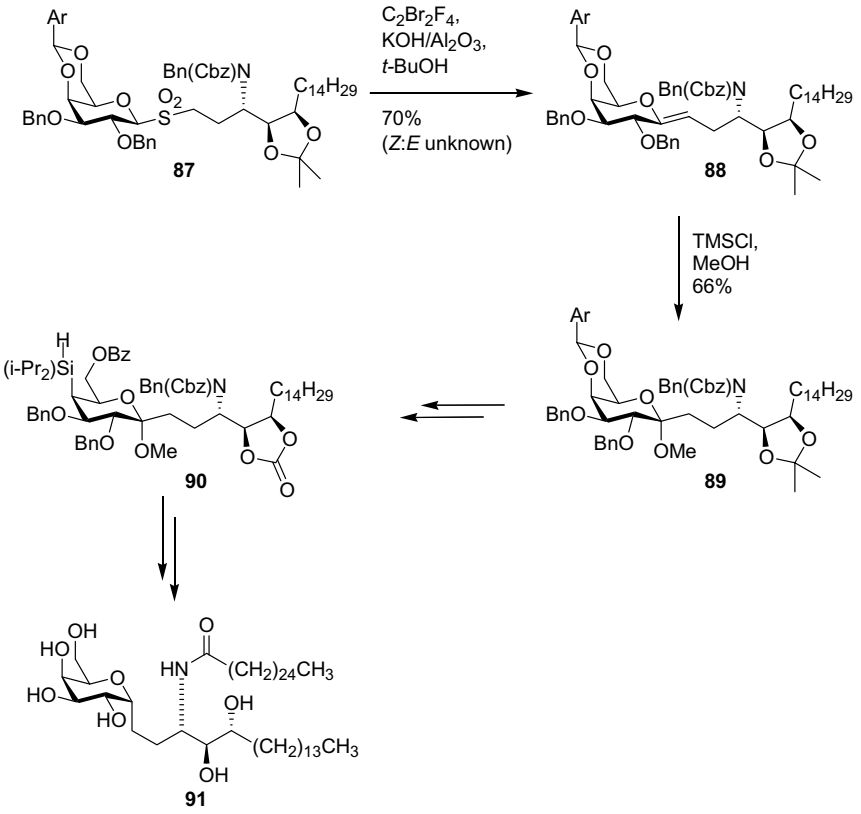
Scheme 23.



Scheme 24.

Of these three glycerolipids, **82** showed antiproliferative activity against SK-N-MC (neuronal), HS578T (breast) and DU145 (prostate) cells. IC_{50} values were comparable with those of the parent glycoside.

In 2004, Franck and co-workers published the synthesis and biological activity of the C-glycoside analogue of immunostimulant α-galactoceramide KRN7000.[54] Once again, this was achieved through Ramberg–Bäcklund reaction of sulfone **87**, giving *exo*-glycal **88** as an undetermined mixture of isomers (Scheme 25). A second key step in the sequence was the application of the *intra*-molecular hydride transfer method described in Scheme 10 to this more complex glycal system. In fact, the isopropylidene function of **89** and its derived 4-O-linked silane was not compatible with the acidic conditions required for activation of the anomeric centre; thus carbonate **90** was used as a more robust diol protecting group to permit the necessary reduction to take place.



Scheme 25. (Ar = *p*-methoxyphenyl).

Subsequent manipulations gave analogue **91**. This was shown to have remarkable activity in a range of assays, in particular a mouse malaria model, where **91** was shown to be approximately 1000 times more protective than the parent glycoside against the sporozoite stage of malaria.

8. Summary

The Ramberg–Bäcklund procedure for preparing *exo*-glycals from S-dioxides and related carbohydrate-derived sulfones, developed independently in York and New York, clearly has great synthetic potential. The methodology has been successfully applied to glucose, galactose, mannose, xylose, fucose, ribose, altrose and 2-deoxyglucose, and has been used to prepare di-, tri- and tetra-substituted *exo*-glycals. More recent developments, such as one-pot variants, and protecting group-free procedures, which are currently being optimised, should enhance the value of this new methodology. Synthetic applications of the product alkenes, for example, to prepare β-glycosidase inhibitors, spirocyclic glucose derivatives, β-C-glycosides, C-linked disaccharides, *C*-glycosyl amino acids, *C*-glycosyl glycerolipids, *C*-glycosyl porphyrin glycoconjugates, and natural products (approaches to altromycin B and the C-glycoside of daunomycin), illustrate the scope of the methodology. Research in this area is continuing, on both sides of the Atlantic, particularly concerning the application of the Ramberg–Bäcklund carbohydrate procedure to the preparation of bioactive targets.

Acknowledgements

The authors express their profound thanks to their collaborators on this Ramberg–Bäcklund adventure (which is never straightforward but always rewarding). These collaborators, whose names are listed in the references, gave generously in terms of their practical and intellectual skills—and their enthusiasm—and are ultimately responsible for the successes in this research area. The research efforts at York and Hunter were supported by the EPSRC and by the NIH, respectively.

References

1. Ramberg, L.; Bäcklund, B. *Ark. Kemi. Mineral. Geol.* **1940**, *27*, 1–50 (*Chem. Abstr.* **1940**, *34*, 4725).
2. Paquette, L. A. *Org. React.* **1977**, *25*, 1–71.
3. Taylor, R. J. K.; Casy, G. *Org. React.* **2003**, *62*, 357–475.
4. Meyers, C. Y.; Malte, A. M.; Matthews, W. S. *J. Am. Chem. Soc.* **1969**, *91*, 7510–7512.

5. Taylor, R. J. K. *Chem. Commun.* **1999**, 217–227.
6. McAllister, G. D.; Taylor, R. J. K. *Tetrahedron Lett.* **2001**, *42*, 1197–1200.
7. Acton, E. M.; Ryan, K. J.; Tracy, M.; Arora, S. K. *Tetrahedron Lett.* **1986**, *27*, 4245–4248.
8. Welch, S. C.; Levine, J. A.; Arimilli, M. N. *Synth. Commun.* **1993**, *23*, 131–134.
9. Belica, P. S.; Franck, R. W. *Tetrahedron Lett.* **1998**, *39*, 8225–8228.
10. Brockhaus, M.; Lehmann, J. *Carbohydr. Res.* **1977**, *53*, 21–31.
11. Lehmann, J.; Schwesinger, B. *Carbohydr. Res.* **1982**, *107*, 43–53, and references cited therein.
12. Brewer, C. F.; Hehre, E. J.; Lehmann, J.; Weiser, W. *Liebigs Ann.* **1984**, 1078–1087, and references cited therein.
13. Legler, G. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 319–384 (*exo*-glycals are covered on pp 348–357), and references cited therein.
14. Schmidt, R. R.; Dietrich, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1328–1329.
15. Wilcox, C. S.; Long, G. W.; Suh, H. *Tetrahedron Lett.* **1984**, *25*, 395–398.
16. RajanBabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458–5461.
17. Johnson, C. R.; Johns, B. A. *Synlett* **1997**, 1406–1408.
18. Lay, L.; Nicotra, F.; Panza, L.; Russo, G.; Caneva, E. *J. Org. Chem.* **1992**, *57*, 1304–1306.
19. Gervay, J.; Flaherty, T. M.; Holmes, D. *Tetrahedron* **1997**, *53*, 16355–16364.
20. Nicotra, F.; Panza, L.; Russo, G. *Tetrahedron Lett.* **1991**, *32*, 4035–4038.
21. Csuk, R.; Glänzer, B. I. *Tetrahedron* **1991**, *47*, 1655–1664, and references cited therein.
22. Ali, M. H.; Collins, P. M.; Overend, W. G. *Carbohydr. Res.* **1990**, *205*, 428–434.
23. Taillefumier, C.; Chapleur, Y. *Chem. Rev.* **2004**, *104*, 263–292.
24. Enderlin, G.; Taillefumier, C.; Didierjean, C.; Chapleur, Y. *Tetrahedron: Asymmetry* **2005**, *16*, 2459–2474.
25. Lin, C.-H.; Lin, H.-C.; Yang, W.-B. *Curr. Top. Med. Chem.* **2005**, *5*, 1431–1457.
26. Yang, W.-B.; Yang, Y.-Y.; Gu, Y.-F.; Wang, S.-H.; Chang, C.-C.; Lin, C.-H. *J. Org. Chem.* **2002**, *67*, 3773–3782.
27. Holick, S. A.; Anderson, L. *Carbohydr. Res.* **1974**, *34*, 208–213.
28. Durette, P. L.; Shen, T. Y. *Carbohydr. Res.* **1979**, *69*, 316–322.
29. Veeneman, G. H.; van Boom, J. H. *Tetrahedron Lett.* **1990**, *31*, 275–278.
30. Susaki, H. *Chem. Pharm. Bull.* **1994**, *42*, 1917–1918.
31. Li, P.; Sun, L.; Landry, D. W.; Zhao, K. *Carbohydr. Res.* **1995**, *275*, 179–184.
32. Chan, T.-L.; Fong, S.; Li, Y.; Man, T.-O.; Poon, C.-D. *Chem. Commun.* **1994**, 1771–1772, and references therein.
33. Griffin, F. K.; Murphy, P. V.; Paterson, D. E.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 8179–8182.
34. Griffin, F. K.; Paterson, D. E.; Murphy, P. V.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2002**, 1305–1322.
35. Belica, P. S.; Berthold, A.; Charles, N.; Chen, G.; Parhi, A.; Pasetto, P.; Pu, J.; Yang, G.; Franck, R. W. The Ramberg–Bäcklund Way to C-Glycosides. In *Modern Synthetic Methodologies Toward Glycomimetics*; Roy, R., Ed.; ACS-Symposium Series #896, 2005; pp 107–119.
36. Somsák, L. *Chem. Rev.* **2001**, *101*, 81–135.
37. Alcaraz, M.-L.; Griffin, F. K.; Paterson, D. E.; Taylor, R. J. K. *Tetrahedron Lett.* **1998**, *39*, 8183–8186.
38. Paterson, D. E.; Griffin, F. K.; Alcaraz, M.-L.; Taylor, R. J. K. *Eur. J. Org. Chem.* **2002**, 1323–1336.
39. Jackson, M.; Karwowski, J. P.; Theriault, R. J.; Hardy, D. J.; Swanson, S. J.; Barlow, G. J.; Tillis, P. M.; McAlpine, J. B. *J. Antibiot.* **1990**, *43*, 223–228.
40. Brill, G. M.; McAlpine, J. B.; Whittern, D. N.; Buko, A. M. *J. Antibiot.* **1990**, *43*, 229–237.
41. Pasetto, P.; Franck, R. W. *J. Org. Chem.* **2003**, *68*, 8042–8060.
42. Kursanov, D. N.; Parnes, Z. N.; Loim, N. M. *Synthesis* **1974**, 633–651.
43. Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976–4978.
44. Lancelin, J.-M.; Zollo, P. H. A.; Sinaÿ, P. *Tetrahedron Lett.* **1983**, *24*, 4833–4836.
45. Barrett, A. G. M.; Peña, M.; Willardsen, J. A. *Chem. Commun.* **1995**, 1145–1146, and 1147–1148 and references cited therein.
46. Martín, A.; Salazar, J. A.; Suárez, E. *J. Org. Chem.* **1996**, *61*, 3999–4006.
47. Pasetto, P.; Chen, X.; Drain, C. M.; Franck, R. W. *Chem. Commun.* **2001**, 81–82.
48. McAllister, G. D.; Paterson, D. E.; Taylor, R. J. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 1387–1391.
49. Jeanmart, S.; Taylor, R. J. K. *Tetrahedron Lett.* **2005**, *46*, 9043–9048.
50. Campbell, A. D.; Paterson, D. E.; Raynham, T. M.; Taylor, R. J. K. *Chem. Commun.* **1999**, 1599–1600.
51. Ohnishi, Y.; Ichikawa, Y. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 997–999.
52. Yang, G.; Franck, R. W.; Byun, H.-S.; Bittman, R.; Samadder, P.; Arthur, G. *Org. Lett.* **1999**, *1*, 2149–2151.
53. Yang, G.; Franck, R. W.; Bittman, R.; Samadder, P.; Arthur, G. *Org. Lett.* **2001**, *3*, 197–200.
54. Yang, G.; Schmieg, J.; Tsuji, M.; Franck, R. W. *Angew. Chem., Int. Ed.* **2004**, *43*, 3818–3822.