2-*C*-Formyl Glycals: Emerging Chiral Synthons in Organic Synthesis

Namakkal G. Ramesh,*[a] and Kalpattu K. Balasubramanian[b]

Keywords: Carbohydrates / Chiral pool / Chirality / C-nucleosides / Synthesis methods

Naturally occurring carbohydrates and their derivatives have been useful during the last few decades as "chiral pool" constituents in the enantioselective synthesis of biologically active natural and non-natural products. The ready availability of a wide range of carbohydrates in nature and their multichiral architecture, coupled with their well defined stereochemistry, make them attractive starting materials in organic synthesis. The synthesis of key intermediates by incorporation of suitable functional groups onto carbohydrates, which can then be further exploited, has always been a challenging task. In this context, 2-*C*-formyl glycals, a new class of carbohydrates incorporating an α,β-unsaturated carbonyl system, have recently emerged as potential synthons for numerous organic transformations. Four different syntheses of 2-*C*-formyl glycals have been reported so far. However, the importance of 2-*C*-formyl glycals has become well established after our development of a more general, one-step synthesis, employing the well known Vilsmeier–Haack reaction. Synthetic transformations of these 2-*C*-formyl glycals have resulted in a variety of new compounds of significant synthetic and biological interest. 2-*C*-Formyl glycals have been shown to be ideal substrates for chemo-, regio- and stereoselective glycosidation, nucleophilic addition/substitution and cycloaddition reactions. The reported syntheses and applications of these important "chiral intermediates" are presented.

1. Introduction

The total synthesis of biologically active natural compounds continues to dominate the field of synthetic organic chemistry.[1] Moreover, the crucial finding that only a particular enantiomer is bio-active in most chiral racemic drugs demands their synthesis in enantiomerically pure forms. Even though several methods for performing enantioselective syntheses are to hand, the use of a readily available chiral starting material with a well defined absolute stereochemistry has several advantages over other approaches. During the last few decades, naturally occurring carbohydrates, which are inexpensive, readily available and endowed with a wealth of stereochemical and functional attributes, have served extensively as "chiral pool" resources in

[a] Department of Chemistry, Indian Institute of Technology − Delhi, Hauz Khas, New Delhi 110 016, India
Fax: (internat.) +91-(0)11-26862037
E-mail: ramesh@chemistry.iitd.ac.in
[b] Shasun Chemicals and Drugs Ltd., R & D Centre, 60, Velachery Road, Chennai 600 042, India
Fax: (internat.) +91-(0)44-22452462
E-mail: kkb@shasun.com

N. G. Ramesh (born 1965) received his B.Sc. (1985), M.Sc. (1987) and M.Phil. (1988) degrees from St. Joseph's College (Autonomous), affiliated to the Bharathidasan University, Tiruchi, Tamil Nadu, India. In 1988 he joined the group of Prof. K. K. Balasubramanian at the Indian Institute of Technology, Madras, India for his Ph.D. program and obtained his doctorate degree in 1993 on his thesis entitled "Chemistry of Unsaturated Hexopyranoses". He spent a couple of years as a postdoctoral fellow with Prof. Alfred Hassner at Bar-Ilan University, Israel (1994−1995) and with Prof. Binne Zwanenburg at the University of Nijmegen, The Netherlands (1996−1997). He was also selected as a JSPS postdoctoral fellow and spent two years with Prof. Yasuyuki Kita at Osaka University, Japan (1998−2000). On his return from Japan, he joined the Indian Institute of Technology, New Delhi, India as an assistant professor in May 2000. His areas of research include synthetic organic chemistry, carbohydrate chemistry and asymmetric synthesis.

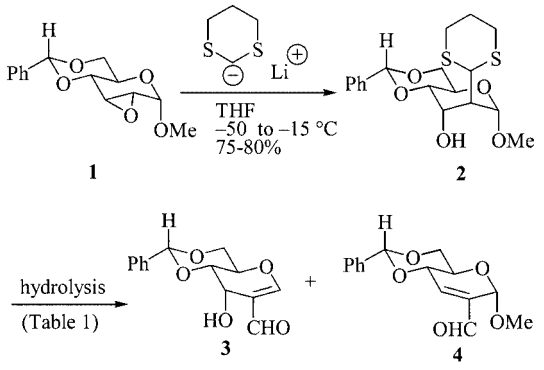
K. K. Balasubramanian was born on 5th September 1939 in Mylapore, Chennai, India. He did his Chemistry Honours at Loyola College, Chennai (1957−1960) and his M.Sc. in Organic Chemistry in the Department of Organic Chemistry, University of Madras, Chennai (1960−1961). He did his Ph.D. with Prof. B. S. Thyagarajan in the Department of Organic Chemistry, University of Madras, Chennai (1961−1965) in the area of molecular rearrangements, mainly on the Claisen rearrangement of 1,4-diyl-but-2-yne aryl ethers. He worked as a postdoctoral fellow with Prof. C. L. Stevens at the University of Michigan, Detroit in the area of keto sugars. He then joined the Department of Organic Chemistry, University of Madras as a scientific pool officer and then in 1971 moved to the Indian Institute of Technology − Chennai, Madras as a lecturer, from where he retired as a full professor in September 2000. Currently, he is an Executive Director at R & D Centre, Shasun Chemicals and Drugs Ltd., Chennai, India. He is a Fellow of the Indian Academy of Sciences and the Indian National Science Academy. He has supervised 30 research scholars for the Ph.D. degree and published 136 papers. He was an Alexander van Humboldt Foundation Fellow, a guest scientist at the National Institute of Standards and Technology (1993−1994) and also a visiting professor at the University of Nancy (March−August 1984). His areas of research interests are synthetic carbohydrate chemistry and pericyclic reactions.

MICROREVIEWS: This feature introduces the readers to the author's research through a concise overview of the selected topic. Reference to important work from others in the field is included.

the total synthesis of a wide range of molecules.[2] However, the scope of carbohydrates as chiral building blocks relies on the development of convenient key intermediates capable of meeting these requirements. It is well recognized that the versatility of sugar nuclei as stereochemical templates is enhanced by the incorporation of an α,β-unsaturated carbonyl system, a pioneering example in this regard being Fraser−Reid's synthesis and exploitation of alkyl hex-2-enopyranose-4-uloses.[3] Syntheses and applications of other carbohydrate-based enones, including those in furanoid series, are also known.[4] In this context, 2-*C*-formyl glycals, a new class of sugars bearing α,β-unsaturated carbonyl systems, have recently emerged as versatile intermediates in the area of carbohydrates in particular and synthetic organic chemistry in general. The presence of an α,β-unsaturated carbonyl moiety has extended the versatility of 2-*C*-formyl glycals as potential synthons, as is evident from the number of publications that have been appearing in the literature in recent years. The synthetic potential of 2-*C*-formyl glycals was established by us after the development of a convenient route to their synthesis through the well known Vilsmeier−Haack reaction.[5] These 2-*C*-formyl glycals provide a ready route to 2-*C*-substituted glycals, an important class of branched chain deoxy sugars and unsaturated nucleosides.[6] In addition, they have been used for the synthesis of homologated conjugated enals, annulated glycopyranosides, C-glycosides, heterocyclic compounds and in the total synthesis of polyene antibiotic "restrictic-in". In view of the increasing importance of 2-*C*-formyl glycals as "chiral synthons" in both carbohydrate and synthetic organic chemistry, a brief review on this topic is considered timely and of great interest to organic chemists. This microreview highlights the various methods available for the synthesis of 2-*C*-formyl glycals and their synthetic applications reported by our group and by others.

2. Syntheses of 2-*C*-Formyl Glycals

2.1 Synthesis by a Dithiane-Based Methodology: Although racemic compounds with a structural resemblance to 2-*C*-formyl glycals, synthesised by means of a hetero-Diels−Alder reaction of malanodialdehyde, were reported by Tietze et al. in 1982,[7] the first workers to synthesize 2-*C*-formyl glycals and to study their behaviour towards Diels−Alder reactions were Lukacs et al.[8,9] Their synthetic sequence for 2-*C*-formyl allal **3** involves opening of the epoxide ring of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**1**, readily available from D-glucose) with dithiane anion, followed by oxidative removal of the dithiane unit of **2** by use of ceric ammonium nitrate, resulting in the free aldehyde with concomitant elimination of the aglycon moiety (Scheme 1, Table 1; Entry 2). The overall yield of the product is high. Use of other hydrolytic conditions on **2** resulted in mixtures of α,β-unsaturated aldehydes **3** and **4** (Table 1). This procedure, however, is circuitous and limited specifically to the synthesis of 2-*C*-formyl allal **3**.

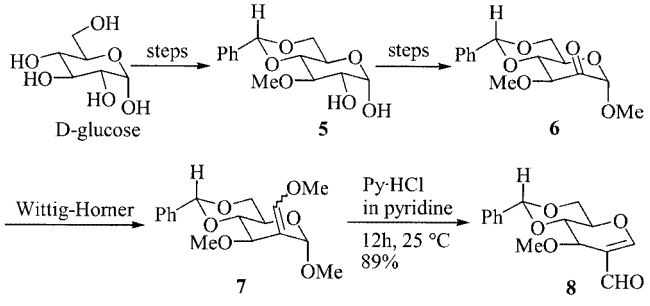


Scheme 1. Dithiane-based approach to the synthesis of 2-*C*-formyl allal

Table 1. Hydrolysis of dithiane derivative **2**

Entry	Reaction conditions	Yield (%) **3**	**4**
1	MeI/$CaCO_3$	57	16
2	CAN	92	0
3	HgO/$HgCl_2$; MeCN/H_2O	11	66

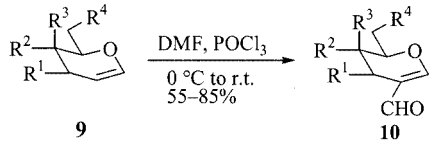
2.2 Synthesis by the Hydrolysis of Sugar Enol Ethers: This elegant methodology, also developed by Lukacs and co-workers, involves an overall transformation of hemiacetal **5** into a conjugated enal **8**.[9,10] Thus, α-alkoxy vinyl ether **7** (i.e., an unsaturated glucoside, prepared from the corresponding ulose **6**), when subjected to mildly acidic hydrolysis, afforded the corresponding 2-*C*-formyl glucal **8** in 89% yield (Scheme 2). The synthesis of a variety of sugar-based conjugated enals by this procedure is also demonstrated. The reaction condition is mild and the yields are generally high.



Scheme 2. Synthesis of 2-*C*-formyl glucal by hydrolysis of sugar enol ethers

2.3 Synthesis by Vilsmeier−Haack Reaction: The Vilsmeier−Haack reaction (discovered as early as 1927) is recognized as one of the best methods for the direct formylation of electron-rich aromatic nuclei, enolizable ketones, enol ethers and other active hydrogen compounds.[11] This reaction continues to receive wide attention in organic chemistry because of its simplicity and convenience. Piancatelli and co-workers extended this reaction to the for-

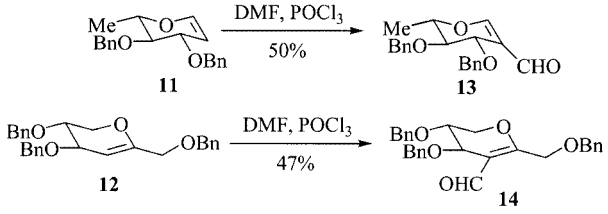
mylation of 5,6-dihydro-4*H*-pyran (a cyclic enol ether).[12] We investigated this reaction and extended its scope to glycals (carbohydrate-derived cyclic enol ethers), successfully synthesising 2-*C*-formyl glycals, in one step, in good yields (Scheme 3).[5]



Scheme 3. Synthesis of 2-*C*-formyl glycals by the Vilsmeier–Haack reaction

Tri-*O*-methyl-D-glucal (**9a**) (readily available from D-glucose) afforded the corresponding 2-*C*-formyl glucal **10a** in 60% yield on treatment with DMF and $POCl_3$ (Table 2; Entry 1). The reaction is also successful with a few other glycals (**9b**–**9e**). The yields are found to be higher in the *galactal* series than in the *glucal* series (Table 2; Entries 3–5;). The ready availability of the glycal substrates, mild reaction conditions and generally good yields, coupled with the compatibility of acid-sensitive groups such as trityl ethers, make our methodology an attractive one for the synthesis of 2-*C*-formyl glycals in comparison with the methods reported earlier.[8–10] The reaction was, however, not successful with acetyl- and isopropylidene-protected glycals **9f** and **9g** (Table 2; Entries 6 and 7).

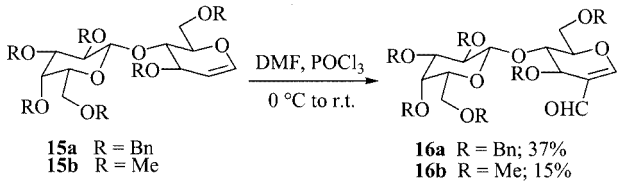
Subsequent to our report, a Friedel–Crafts-type acylation of glycals was reported by Priebe et al.[13] Very recently, Lellouche and co-workers observed that the use of a $(CF_3SO_2)_2O{\cdot}DMF$ combination instead of the classical Vilsmeier–Haack complex ($POCl_3{\cdot}DMF$) on glucal **9b** resulted in a moderate increase in the yield of the product **10b**.[14] Peseke and co-workers have successfully extended



Scheme 4. Vilsmeier–Haack formylation of L-rhamnal and D-fructal

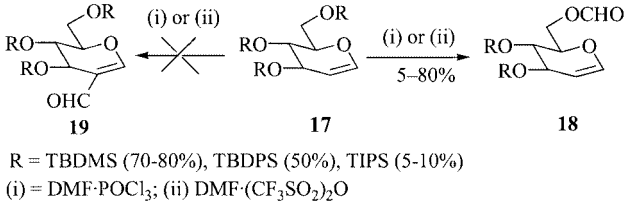
our methodology to formylate di-*O*-benzyl-L-rhamnal (**11**) and tri-*O*-benzyl-D-fructal (**12**, Scheme 4).[15]

Feit and co-workers[16] have also recently extended this reaction to disaccharide glycals, in the form of hexa-*O*-benzyl lactal **15a** and hexa-*O*-methyl lactal (**15b**). The desired formyl glycals **16a** and **16b** were obtained in moderate yields (Scheme 5).



Scheme 5. Vilsmeier–Haack reactions of disaccharide glycals

Contrasting behaviour of the Vilsmeier–Haack reagent towards silyl-protected glucal was reported by Lellouche and co-workers.[14,17] When tri-*O*-silyl ethers of D-glucal **17** were treated with Vilsmeier–Haack reagent, selective silyl deprotection of the C-6 primary hydroxy group and its subsequent *O*-formylation occurred, to give compound **18** (Scheme 6). Neither *C*-formylation, to afford 2-*C*-formyl glucal **19**, nor di- or tri-*O*-formylated glucal was obtained even in the presence of an excess of the reagent. Such an effect of the substituent on the course of the reaction is noteworthy.



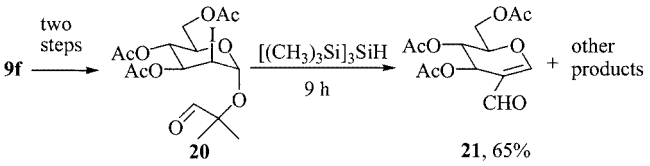
Scheme 6. Selective deprotection and *O*-formylation of silylated glucal by use of the Vilsmeier–Haack reagent

2.4 Synthesis by Formyl Group Transfer: Jung et al., in their attempts to synthesize 2-*C*-formyl glycopyranosides by intramolecular radical-initiated formyl group transfer, isolated 3,4,6-tri-*O*-acetyl-2-*C*-formyl-D-glucal (**21**) as a side product.[18] The free radical-promoted cyclization of iodosugar **20** with either tris(trimethylsilyl)silane or tributylstannane afforded mixtures of four products, one of which was 2-*C*-formyl glucal **21**, in varying proportions depending on

Table 2. Vilsmeier–Haack reactions of glycals

Entry[a]	Glycal	R^1	R^2	R^4	R^3	Product	Time (h)	Yield (%)
1	**9a**	OMe	OMe	OMe	H	**10a**	4	60
2	**9b**	OBn	OBn	OBn	H	**10b**	8	55
3	**9c**	OMe	H	OMe	OMe	**10c**	8	80
4	**9d**	OBn	H	OBn	OBn	**10d**	8–9	85
5	**9e**	OMe	H	OTr	OMe	**10e**	8–9	72
6	**9f**	OAc	OAc	OAc	H	–	–	–
7	**9g**	OMe	isopropylidene		H	–	–	–

[a] Me = methyl; Bn = benzyl; Tr = trityl (triphenylmethyl); Ac = acetyl.



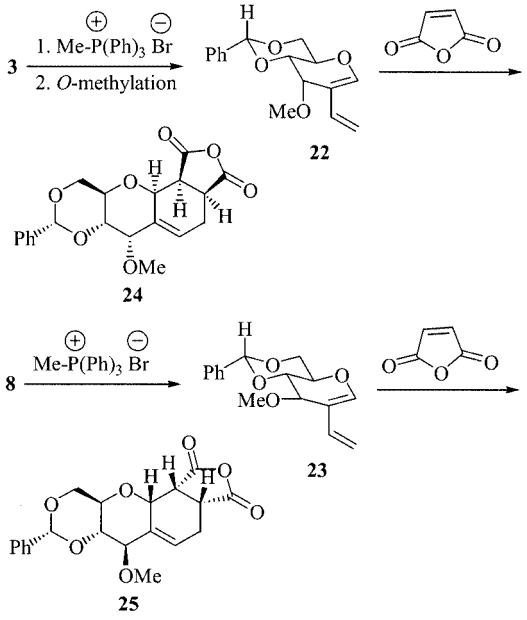
Scheme 7. 2-*C*-Formyl glucal through a formyl group transfer

the reaction conditions. However, 2-*C*-formyl glucal **21** could be obtained as the major product (but not exclusively) in 65% yield by performing the reaction for a longer time with tris(trimethylsilyl)silane (Scheme 7). This methodology, although compatible with acid-sensitive acetyl groups, is circuitous and involves ozonolysis and radical reactions.

Among the various available methods for the synthesis of 2-*C*-formyl glycals, our one-step Vilsmeier−Haack formylation of glycals has been found to be simple, convenient and general, and also to use less expensive chemicals. Several research groups have utilised our methodology to synthesize and study the applications of 2-*C*-formyl glycals.

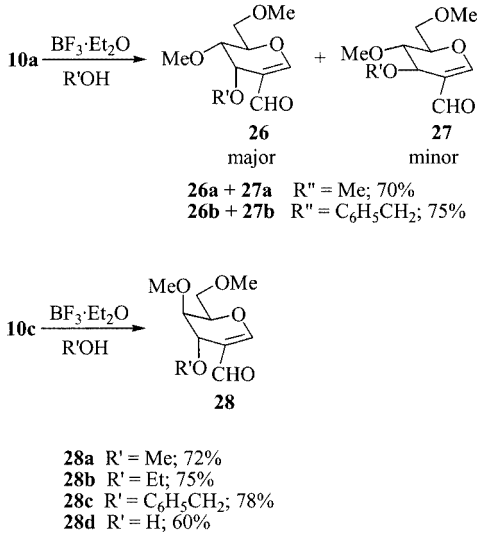
3. Synthetic Applications of 2-*C*-Formyl Glycals

3.1 Synthesis and Diels−Alder Reactions of Carbohydrate Dienes Derived from 2-*C*-Formyl Glycals: A stereocontrolled route, starting from 2-*C*-formyl glycals, to annulated C-glycopyranosides, a new class of C-glycosides, was developed by Lukacs et al.[19] Wittig olefination of 2-*C*-formyl glycals **3** (followed by *O*-methylation) and **8** afforded the C-3 epimeric dienes **22** and **23**, which underwent π-facial selective Diels−Alder reactions with maleic anhydride to give the respective adducts **24** and **25** exclusively (Scheme 8). The authors observed that the methoxy group at C-3 in the dienes **22** and **23** exerts an *anti*-directing effect on the approach of the dienophile. No such facial selectivity is observed in the absence of any stereodirecting group at C-3. Linear acetylenic dienophiles also react readily with the dienes **22** and **23**, preferentially, but not exclusively, *anti* to the C-3 methoxy group. An explanation for such behaviour has been proposed on the basis of the interaction between the dienophile and the C-3 methoxy group in the transition state. From the experimental evidence, it has been concluded by the authors that such *anti*-facial selectivity is purely due to steric reasons. Apart from stereochemical considerations, this paper provides an easy route to a new class of annulated and benzannulated glycopyranosides,[20] compounds with potential biological significance.



Scheme 8. Synthesis and Diels−Alder reaction of carbohydrate dienes derived from 2-*C*-formyl glycals

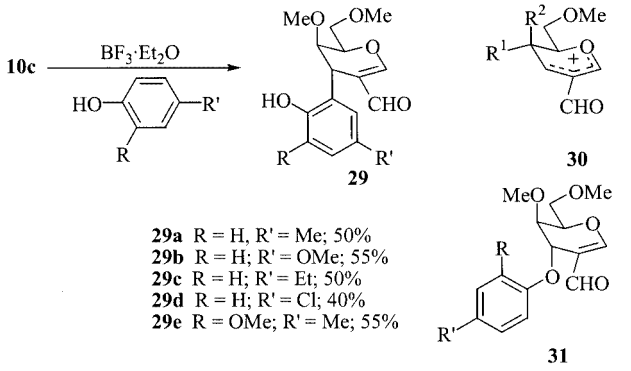
3.2 One-Step Synthesis of 2-*C*-Formyl Allal and Gulal: An interesting observation was that, although 2-*C*-formyl glycals **10** bearing an α,β-unsaturated system were ideally suitable for Michael reaction, they did not undergo either acid- or base-catalysed Michael addition reactions with alcohols or phenols under standard conditions. However, a more rewarding finding by our group was that they were readily converted into the epimeric 2-*C*-formyl allal **26** and 2-*C*-formyl gulal **28** in one step by treatment of the 2-*C*-formyl glycals **10a** and **10c** with $BF_3{\cdot}Et_2O$ in the presence of an alcohol or water (Scheme 9).[21] The reaction proceeds with unexpected inversion of configuration at C-3 of the sugar. With water as the nucleophile, the reaction involves an overall "inversion with deprotection". It should be noted that allose and gulose are rare and expensive sugars, and that synthesis of compounds **26** or **28** from the parent sugars would otherwise be expensive and circuitous.



Scheme 9. One-step synthesis of 2-*C*-formyl allal and 2-*C*-formyl gulal

Interestingly, with phenols as nucleophiles, glycal **10c** afforded the corresponding *C*-arylated products **29** under the above conditions, and not *O*-arylated products **31** (Scheme 10).[22]

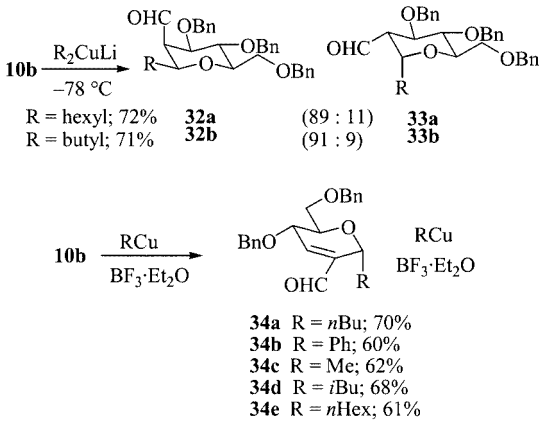
From the experimental findings, it was suggested that the reaction proceeds through the Lewis acid-catalysed formation of an allylic cation **30**, followed by preferential attack



Scheme 10. Synthesis of 3-*C*-arylhexoses by C-3 arylation of 2-*C*-formyl glycals

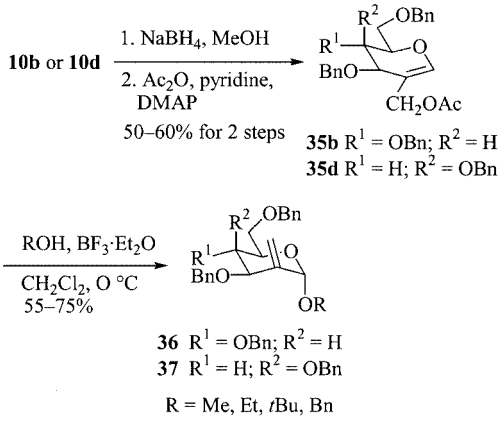
of the alcohols/phenols at C-3 from the axial side. Moreover, the isolation of a small amount of *O*-arylated product **31** (R = H, R′ = Cl) from the reaction between *p*-chlorophenol and glycal **10c** is an indication that the initial attack of the phenol on cation **30** takes place through the oxygen, with a subsequent Lewis acid-catalysed formal [1,3] rearrangement to afford the *C*-arylated product **29**.[23]

3.3 C-Glycosylation of Organocopper Reagents with 2-*C*-Formyl Glucal: Cossy et al., however, were successful in performing a Michael-type addition (1,4-addition) reaction on 2-*C*-formyl glycal **10b** with organocopper reagents.[24] Interestingly, the outcome of the reaction was found to depend on the nature of the copper reagents. Thus, addition of lithium dialkylcuprates to 2-*C*-formyl glucal **10b** resulted in a facile 1,4-addition reaction to afford the corresponding 2-*C*-formyl-C-glycosides **32** and **33**, the β anomer **32** being the predominant one (Scheme 11). In contrast, treatment of **10b** with alkylcopper reagent in the presence of $BF_3{\cdot}Et_2O$ resulted in a carbon-Ferrier-type rearrangement to furnish the 2-*C*-formyl-2,3-unsaturated-C-glycosides **34** with α anomers as the only isolable product. This reaction was found to be general for a variety of alkylcopper reagents (Scheme 11).[24]



Scheme 11. C-glycosylation of organocopper reagents with 2-*C*-formyl glucal

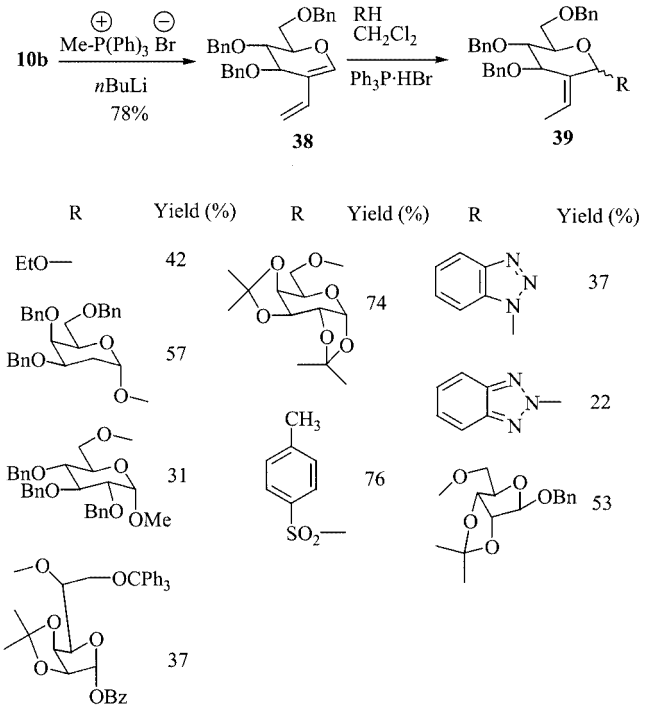
3.4 Synthesis of 2-*C*-Methylene Glycosides: 2-*C*-Substituted carbohydrates are an important class of branched chain deoxy sugars and constituents of unsaturated nucleosides.[6] The 2-*C*-methylene group in particular is a key structural feature of molecules involved in mechanism-based inactivation of the enzyme ribonucleotide diphosphate reductase.[25] From the synthetic point of view, 2-*C*-methylene glycosides have been used as precursors for *C*-disaccharides.[26] A facile synthesis of 2-*C*-methylene glycosides from 2-*C*-formyl glycals was first developed by our group;[27,28] our synthetic sequence is depicted in Scheme 12. Reduction of the aldehyde groups (viewed also as vinylogous esters) of 2-*C*-formyl glycals **10b** and **10d** with sodium borohydride, followed by acylation, afforded acetoxymethylglycals **35b** and **35d**, which can be regarded as examples of a new "Ferrier system".[29] Subsequent treatment with an alcohol in the presence of $BF_3{\cdot}Et_2O$ afforded the corresponding 2-*C*-methylene glycosides **36** and **37** in good yields, the α anomers being the major product in all cases (Scheme 12).[27]



Scheme 12. $BF_3{\cdot}Et_2O$-catalysed synthesis of 2-C-methylene glycosides

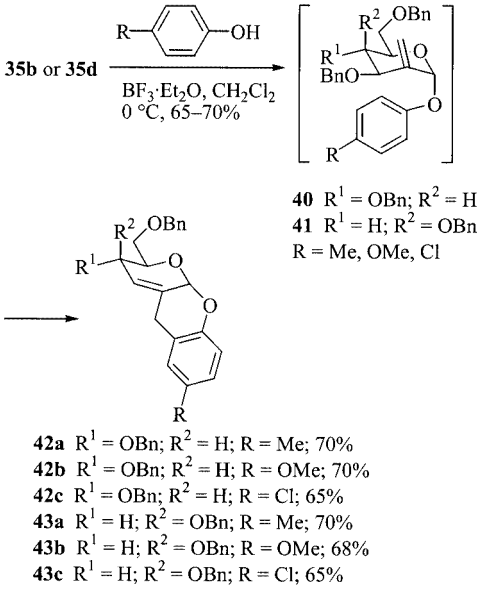
Vankar and co-workers, in their efforts to improve and possibly reverse the anomeric selectivity, recently carried out a detailed investigation of the effects of different acid catalysts on the above reaction.[30] All the catalysts tried, such as Nafion-H, Montmorillonite K-10 and $LiClO_4$, bring about the above transformation of 2-*C*-acetoxymethyl glycals with alcohols in good yields. Similarly to our results, only α anomers were isolated in all their examples.

Feit and co-workers[16] have recently reported the synthesis of 2-*C*-(β-methyl)methylene glycosides from the 2-ethenyl-D-glucal **38**, in turn obtained in 78% yield by Wittig−type methylenation of 2-*C*-formyl glycals **10b** with methyl triphenylphosphonium bromide in the presence of *n*-butyllithium as a base. Glycal **38**, on treatment with alcohols (including free OH groups of sugars) in the presence of catalytic amounts of triphenylphosphonium bromide, underwent electrophilic addition to afford the 2-*C*-(β-methyl)methylene glycosides **39**. A variety of other nucleophiles (nitrogen and sulfur) have also been used in this reaction (Scheme 13).[16] The authors have also synthesized a variety of other *C*-2-vinyl glycals and *C*-2-butadienyl glycals. The *exo*-(β-methyl)methylene group of **39** provides scope for further elaboration.



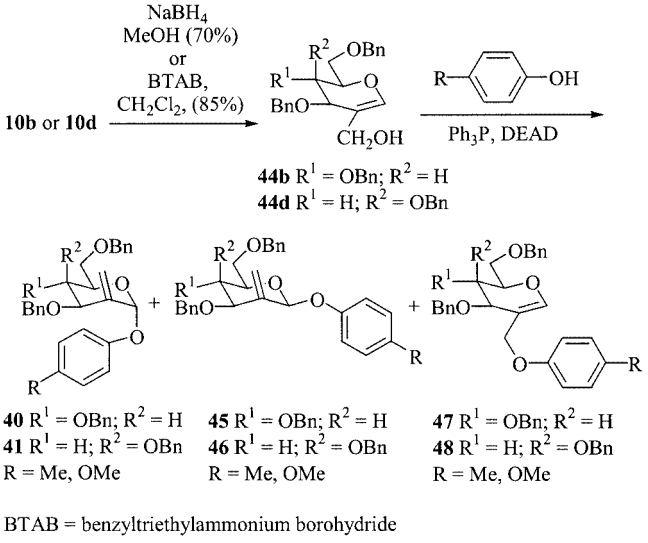
Scheme 13. Synthesis of 2-*C*-(β-methyl)methylene glycosides from 2-*C*-formyl glycals

3.5 Unexpected Synthesis of Chiral Pyranobenzopyrans: With phenols as nucleophiles in the reaction described above (Scheme 12), in the presence of $BF_3{\cdot}Et_2O$ as catalyst, the corresponding 2-*C*-methylene-*O*-aryl glycosides **40** and **41** could not be isolated. Surprisingly, the 2-*C*-methylene-*O*-aryl glycosides formed during the reaction underwent a tandem cyclization to afford chiral pyrano[2,3-*b*][1]benzopyrans **42** and **43** in high yields (Scheme 14).[31] These pyranobenzopyrans can be viewed as annulated pyranosides, and examples of such compounds, especially in chiral form, are rare.[32] This reaction provides a novel and direct route to such ring systems.



Scheme 14. Synthesis of chiral pyrano[2,3-*b*][1]benzopyrans

3.6 Synthesis of 2-*C*-Methylene-*O*-aryl Glycosides: In contrast to the outcome of $BF_3{\cdot}Et_2O$ catalysis in the reactions between phenols and 2-*C*-acetoxymethyl glycals (Scheme 14), 2-*C*-methylene-*O*-aryl glycosides **40**, **41**, **45** and **46** could indeed be synthesized by use of the Mitsunobu reaction.[33] Treatment of alcohols **44b** and **44d** with phenols in the presence of Ph_3P and diethyl azodicarboxylate (DEAD) afforded the corresponding 2-*C*-methylene-*O*-aryl glycosides as mixtures of α and β anomers in varying proportions (Table 3). The reaction was found to be diastereoselective in the *galactal* series, affording only the α anomer, with the β anomer not being obtained at all (Scheme 15).[34]

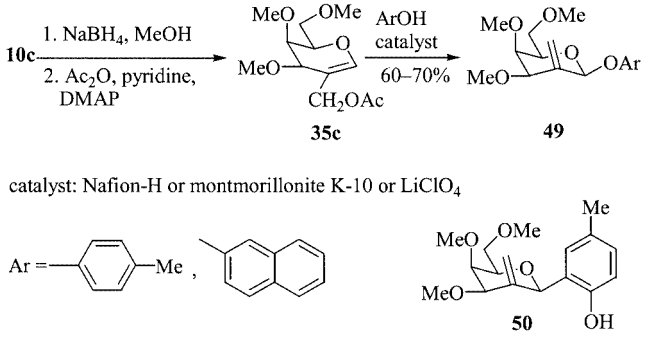


Scheme 15. Synthesis of 2-*C*-methylene-*O*-aryl glycosides by a Mitsunobu approach

Table 3. Synthesis of 2-*C*-methylene-*O*-aryl glycosides by a Mitsunobu approach

Entry	Alcohol	Product	R	Ratio	Total yield (%)
1	**44b**	**40a** + **45a** + **47a**	Me	40:40:20	85
2	**44b**	**40b** + **45b** + **47b**	OMe	38:38:24	82
3	**44d**	**41a** + **46a** + **48a**	Me	85:0:15	82
4	**44d**	**41b** + **46b** + **48b**	OMe	80:0:20	75

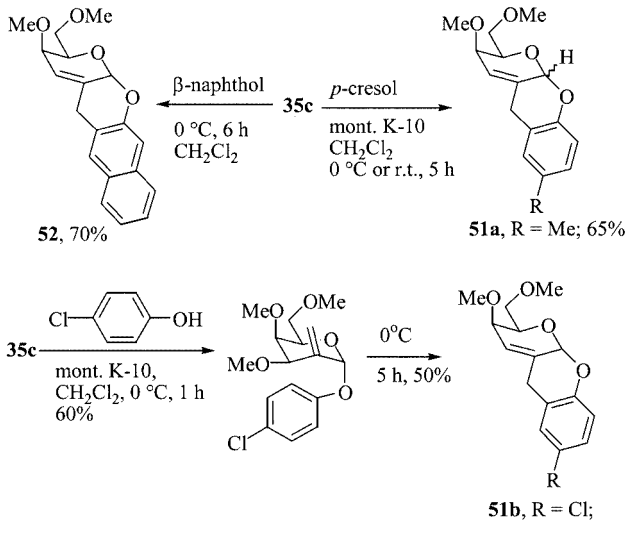
A stereoselective synthesis of 2-*C*-methylene-β-*O*-aryl glycosides from 2-*C*-acetoxymethyl galactal **35c** was reported by Vankar's group.[30] Nafion-H and $LiClO_4$ were found to catalyse the Ferrier-type rearrangement of **35c** with *p*-cresol and β-naphthol to afford the corresponding β-*O*-aryl glycosides **49** stereoselectively and in good yields (Scheme 16). The parent phenol did not undergo a clean reaction under these conditions. This reaction, however, has not been extended to the *glucal* series. An interesting, though not surprising, observation was that with Montmorillonite K-10 as a catalyst, treatment of β-naphthol with **35c**



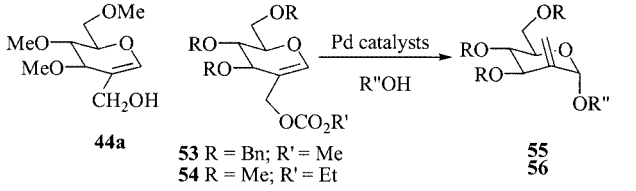
Scheme 16. Stereoselective synthesis of 2-*C*-methylene-β-*O*-aryl glycosides reported by Vankar's group[30]

afforded the corresponding β-*O*-aryl glycoside, whereas *p*-cresol under the same conditions yielded not the *O*-aryl glycoside, but the *C*-aryl glycoside **50** in 62% yield.

Because of the difference in the courses of the reactions between glycal **35** and phenols catalysed by $BF_3{\cdot}Et_2O$ (Scheme 14)[31] and by Montmorillonite K-10 (Scheme 16),[30] a reinvestigation of Vankar's work on the Montmorillonite K-10-catalysed reaction between glycal **35c** and *p*-cresol and β-naphthol was carried out by us.[35] The outcome of our reinvestigation contrasted with the reported results of Vankar's group. In our hands, treatment of the glycal **35c** with *p*-cresol in the presence of Montmorillonite K-10 as a catalyst, yielded (in 5 h) the chiral pyranobenzopyran **51a** (R = Me) and not the *C*-aryl glycoside **50** as reported by Vankar.[30] Similarly, treatment of the glycal **35c** with β-naphthol yielded the corresponding chiral naphthopyran **52**, again in contrast to the claims of Vankar and co-workers, who obtained the *O*-aryl glycoside. On treatment of *p*-chlorophenol with the glycal **35c**, however, the exomethylene glycoside **49** (Ar = *p*-C_6H_4-Cl) was isolated initially, while use of a longer reaction time provided the chiral benzopyranopyran **51b** (R = Cl) (Scheme 17).



Scheme 17. Reinvestigation of the Montmorillonite K-10-catalysed reaction between glycal **35c** and phenols



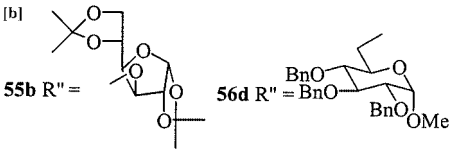
Scheme 18. Palladium-catalysed stereoselective synthesis of 2-*C*-methylene-α-O-glycosides

Table 4. Palladium-catalysed stereoselective synthesis of 2-*C*-methylene-α-O-glycosides

Compound	R	R"	Pd catalyst	Yield (%)	Ref.
55a	Bn	*p*-CH_3-C_6H_4-	$[Pd_2(dba)_3]$/dppb	49	[36]
55b	Bn	[b]	$[Pd_2(dba)_3]$/dppb	54	[36]
56a	Me	Bn	$[Pd(PPh_3)_4]$	65	[30]
56b	Me	*p*-CH_3-C_6H_4-	$[Pd(PPh_3)_4]$	[a]	[30]
56c	Me	β-naphthyl	$[Pd(PPh_3)_4]$	[a]	[30]
56d	Me	[b]	$[Pd(PPh_3)_4]$	[a]	[30]

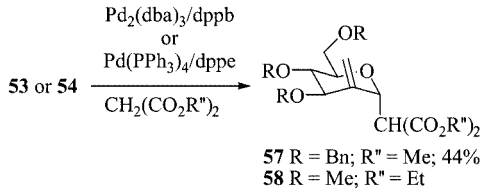
[a] Yield not reported.

[b]



A reversal in the anomeric selectivity of 2-*C*-methylene-*O*-glycosides and *O*-aryl glycosides was noticed when palladium catalysts were used. The allylic carbonates **53** and **54** (prepared from **44b** and **44a**, respectively) underwent smooth reactions with substituted phenols in the presence of $[Pd_2(dba)_3]$/dppb or $[Pd(PPh_3)_4]$ to afford the corresponding 2-*C*-methylene-α-*O*-aryl glycosides **55** and **56** exclusively (Scheme 18, Table 4).[30,36] Other aliphatic alcohols also underwent this reaction to give the corresponding α-*O*-alkyl glycosides (Table 4). The anomeric selectivity has been attributed to the formation of the π-allyl palladium complex from the β-face, followed by attack of the nucleophile from the α-face. The regiospecific *O*-alkylation (not *C*-alkylation) is in good agreement with the fact that alkylation occurs under electronic control in the case of π-allyl system bearing an oxygen at one terminal. This reaction has been investigated only in the *glucal* series and has not been extended to the *galactal* series. Indeed, it would be worthwhile to extend this reaction to the *galactal* series to examine the effect of axial substituent at C-4, which may have a steric influence on the formation of π-allyl palladium complex from the β-face.

3.7 Synthesis of 2-*C*-Methylene-C-glycosides: Two similar palladium-catalysed approaches for the synthesis of 2-*C*-methylene-C-glycosides have been reported. Treatment of allyl carbonates **53** or **54** with dialkyl malonate in the presence of a suitable palladium catalyst $[Pd_2(dba)_3$/dppb or $[Pd(PPh3)_4]$/dppe afforded the 2-*C*-methylene-α-C-glycosides **57** and **58** in moderate yields (Scheme 19).[30,36]

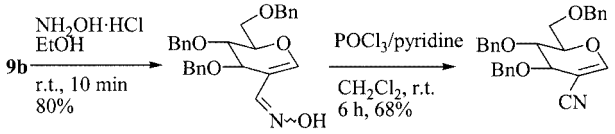


57 R = Bn; R" = Me; 44%
58 R = Me; R" = Et

Scheme 19. Palladium-catalysed synthesis of 2-*C*-methylene-C-glycosides

Wolf et al. have reported a similar approach for the synthesis of 2′-*C*-methylene nucleosides by the condensation of a silylated base with a π-allyl palladium complex derived from 2-*C*-acetoxymethyl-furanoid glycal.[37]

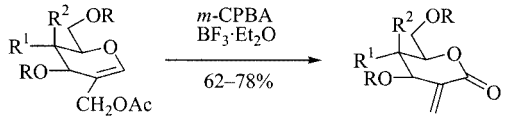
3.8 A Simple Synthesis of 2-*C*-Cyano Glucal from 2-*C*-Formyl Glucal: We have accomplished a simple synthesis of the 2-*C*-cyano glucal **60** in two steps from the 2-*C*-formyl glucal **9b**.[35] Glucal **9b**, upon treatment with hydroxylamine hydrochloride in ethanol at room temperature, afforded the corresponding oxime **59**, which was smoothly dehydrated to the 2-*C*-cyano glucal **60** by use of $POCl_3$ and pyridine (Scheme 20). This provides an easy and alternate route to the synthesis of 2-*C*-cyano glucal.[38] The presence of a cyano group in such systems provides scope for further exploration of its chemical[39] and biological[40] properties.



59 **60**

Scheme 20. Synthesis of 2-*C*-cyano glucal

3.9 Synthesis of α-Methylene-δ-valerolactones: A simple approach to the α-methylene-δ-valerolactones **61** was developed by Vankar's group.[30] Oxidation of the 2-*C*-acetoxymethyl glycals **35a**−**d** with *m*CPBA in the presence of $BF_3{\cdot}Et_2O$ at −65 °C afforded the lactones **61a**−**d** in good yields (Scheme 21).

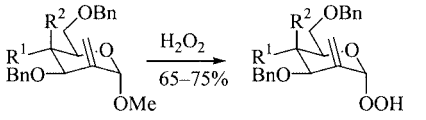


35a R = Me; R^1 = OMe; R^2 = H
35b R = Bn; R^1 = H; R^2 = OBn
35c R = Me; R^1 = H; R^2 = OMe
35d R = Bn; R^1 = H; R^2 = OBn

61a R = Me; R^1 = OMe; R^2 = H; 65%
61b R = Bn; R^1 = H; R^2 = OBn; 62%
61c R = Me; R^1 = H; R^2 = OMe; 76%
61d R = Bn; R^1 = H; R^2 = OBn; 78%

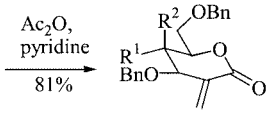
Scheme 21. Synthesis of α-methylene-δ-valerolactones from 2-*C*-acetoxymethyl glycals

Earlier, Chmielewski and co-workers had synthesized the optically active α-methylene-δ-valerolactones **61b** and **61d** in two steps from the 2-*C*-methylene-α-methyl glycosides **36a** and **37a**. Anomeric oxidation of **36a** and **37a** with hydrogen peroxide afforded sugar hydroperoxides **62** and **63**, respectively. On treatment with an acetic anhydride/pyridine



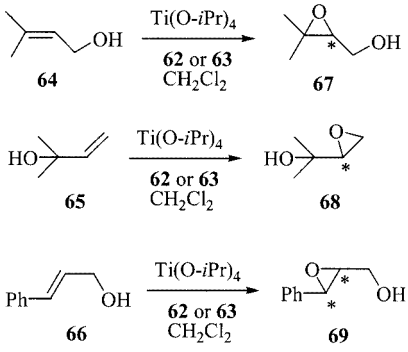
36a R^1 = OBn; R^2 = H
37a R^1 = H; R^2 = OBn

62 R^1 = OBn; R^2 = H
63 R^1 = H; R^2 = OBn



61b R^1 = OBn; R^2 = H
61d R^1 = H; R^2 = OBn

Scheme 22. Synthesis of α-methylene-δ-valerolactones from 2-*C*-methylene glycosides



Scheme 23. Asymmetric epoxidation of allylic alcohols with anomeric hydroperoxides derived from 2-*C*-formyl glycals

mixture, these afforded the lactones **61b** and **61d** in 81% yield (Scheme 22).[41]

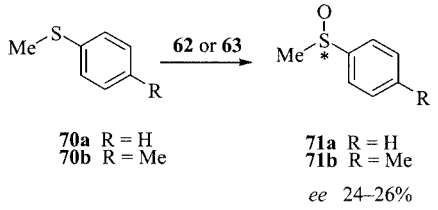
Lactones **61**, thanks to the presence of an α,β-unsaturated moiety, are potential synthons and have been used as precursors in the synthesis of *C*-disaccharides.[42] A few reports on the synthesis of lactones **61** are known,[43] and the two methodologies presented provide alternate ways of preparing these important intermediates.

3.10 Applications of the Hydroperoxides 62 and 63 (Prepared from 2-*C*-Formyl Glycals) as Chiral Oxidants: Chmielewski's group have also utilised sugar hydroperoxides **62** and **63** (prepared from the corresponding 2-*C*-formyl glycals) as chiral oxidants for the enantioselective epoxidation of the allylic alcohols **64**, **65** and **66**.[41] The *enantiomeric excesses* of the epoxides range from 4−44% (Scheme 23). It has been observed that the optical induction by hydroperoxide **63** is higher than that of **62**. Moreover, it has been reported that the *ee* obtained in the oxidation of alcohol **64** by the hydroperoxide **63** (Table 5; Entry 4) is the best outcome obtained so far when a chiral hydroperoxide was used as the epoxidation reagent. Also noteworthy is the epoxidation of tertiary alcohols such as **65**, as earlier attempts to prepare the corresponding epoxy alcohol by Sharpless epoxidation had failed.[44]

Asymmetric oxidation of the methyl aryl sulfides **70** by the hydroperoxides **62** and **63** also gave the corresponding sulfoxides **71** in ≈25% *ee* (Scheme 24).[41]

Table 5. Asymmetric epoxidation of allylic alcohols with sugar hydroperoxides

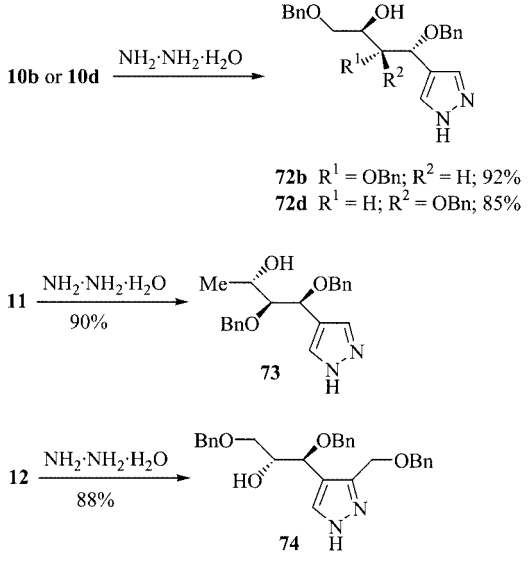
Entry	Allyl alcohol	Oxidant	Epoxy alcohol	*ee* (%)	Absolute configuration
1	**64**	**62**	**67**	28	(+)-(*R*)
2	**65**	**62**	**68**	04	(−)-(*S*)
3	**66**	**62**	**69**	10	(2*R*,3*S*)
4	**64**	**63**	**67**	44	(+)-(*R*)
5	**65**	**63**	**68**	11	(−)-(*S*)
6	**66**	**63**	**69**	18	(2*R*,3*S*) 25



Scheme 24. Asymmetric sulfoxidation of prochiral sulfides by use of sugar hydroperoxides derived from 2-*C*-formyl glycals

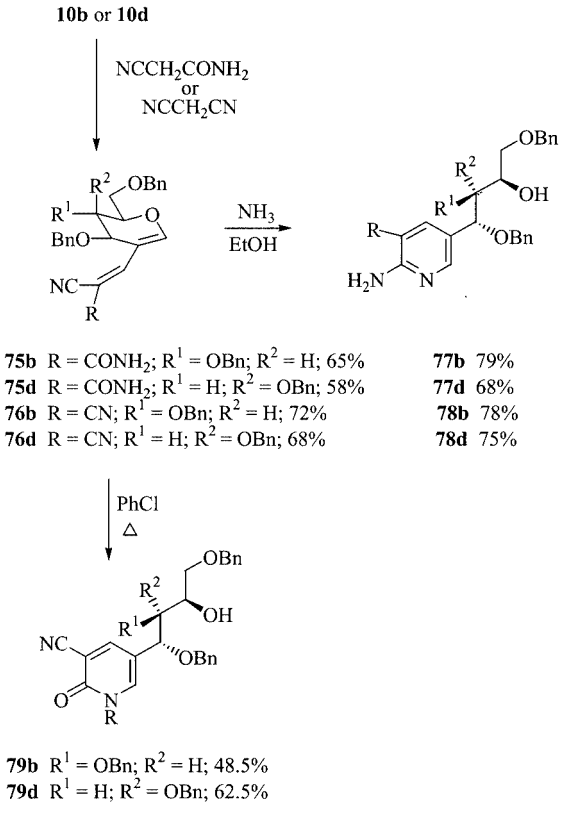
3.11 Synthesis of Acyclo-C-nucleosides from 2-*C*-Formyl Glycals: C-nucleoside analogues with an open-chain sugar moiety have been shown to possess significant biological activities,[45] due to which there has been a great interest in the synthesis of acyclo-C-nucleosides.

Peseke and co-workers have utilised the push-pull effect of 2-*C*-formyl glycals and reported simple one-pot syntheses of a variety of acyclo-C-nucleosides.[46] Treatment of 2-*C*-formyl glycals **10b**, **10d**, **11** and **12** with hydrazine hydrate in refluxing ethanol afforded the *C*-(1*H*-pyrazol-4-yl)alditols **72b**, **72d**, **73** and **74**, respectively, in good yields (Scheme 25).[15]



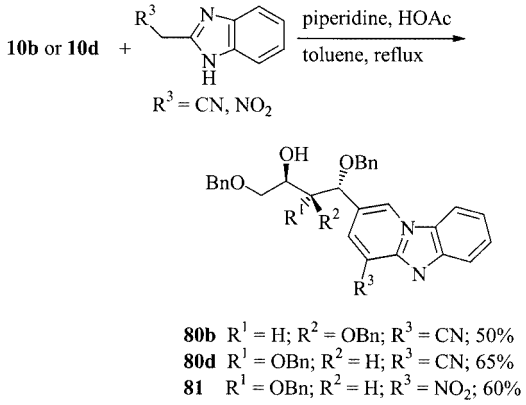
Scheme 25. Synthesis of acyclo C-nucleosides from 2-*C*-formyl glycals

Pyridine acyclo-C-nucleosides have also been synthesized in two steps from 2-*C*-formyl glycals. Treatment of 2-*C*-formyl glycals **10b** and **10d** with cyanoacetamide or malononitrile, with pyridinium acetate as the catalyst, yielded the branched chain sugars **75** and **76**, which on exposure to ammonia in ethanol afforded the nicotinamide and nicotinonitrile derivatives **77** and **78**, respectively (Scheme 26).[15,47] Prolonged treatment of the 2-*C*-formyl glycals **10b** and **10d** with cyanoacetamide in the presence of pyridinium acetate furnished the pyridone derivatives **79b** (R = H) and **79d** (R = H, Scheme 26). Similar treatment of the 2-*C*-formyl glycals **11** and **12** produced the corresponding pyridine acyclo-C-nucleosides.[15]



Scheme 26. Synthesis of pyridine acyclo-C-nucleosides from 2-*C*-formyl glycals

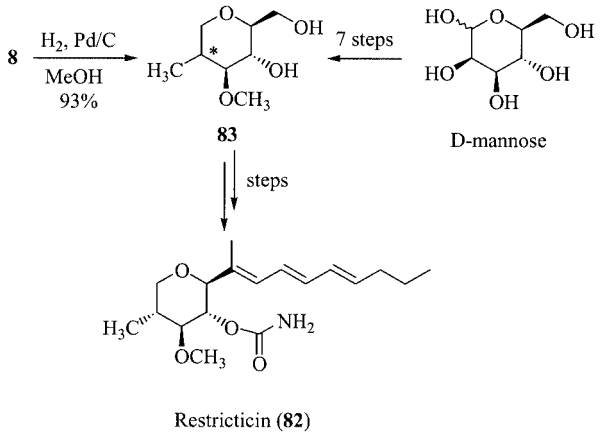
Interestingly, the above reaction with 2-cyano-*N*-(4-methoxyphenyl)acetamide afforded the acyclo C-nucleosides **79** (R = C_6H_4−OMe-*p*) in good yields in a single step.[48] The reactions were also successful with acetoacetamide, affording the corresponding pyridone C-nucleosides. The push-pull functionality of 2-*C*-formyl glycals **10b** and **10d** also



Scheme 27. Synthesis of polycyclic acyclo C-nucleosides from 2-*C*-formyl glycals

allowed reactions with C,N-dinucleophiles, furnishing polycyclic analogues of acyclo C-nucleosides. Thus, when **10b** and **10d** were treated with 2-benzimidazolylacetonitrile or 2-nitromethylbenzimidazole, the corresponding acyclo C-nucleosides **80** and **81** were obtained in moderate to good yields, each in a single step (Scheme 27).[48] In a similar way, glycal **10d** reacted with 2-aminobenzimidazole and 3-amino-1,2,4-triazole to yield the respective substituted pyrimidine C-nucleosides in moderate yields.[49]

3.12 Total Synthesis of Polyene Antibiotic "Restricticin": Restricticin (**82**),[50] isolated from fungi of the genus *Penicillium*, represents a novel type of polyene antibiotics. Jendrzejewski and co-workers reported the first total synthesis of restricticin.[51] In one of their approaches they utilised the 2-*C*-formyl glucal **8** to synthesize the key intermediate **83**. Compound **8** afforded **83** in 93% yield upon hydrogenation over Pd/C in MeOH. An alternate approach to **83**, starting from D-mannose, has also been reported. It is noteworthy that the diastereomeric ratio of **83** was higher in the former route (1.4:8.6) than in the latter one (2.4:7.6). A total synthesis of restricticin from **83** has been accomplished by a sequence of steps (Scheme 28).



Scheme 28. Total synthesis of restricticin by the use of 2-*C*-formyl glucal

4. Conclusions

In recent years, 2-*C*-formyl glycals have gained importance as valuable precursors for various synthetic applications. We have developed, through the use of a well known "name reaction", a simple and convenient methodology for the synthesis of 2-*C*-formyl glycals and demonstrated their synthetic utility. Few other methods are also available for the synthesis of 2-*C*-formyl glycals. It is noteworthy that many research groups have utilised 2-*C*-formyl glycals for various synthetic transformations, such as synthesis of annulated glycopyranosides, C-glycosides, optically active sugar peroxides, heterocycles, α-methylene-δ-valerolactones etc. The ready access to these diversely functionalized carbohydrate intermediates is likely to spur further interest in their applications in synthetic organic chemistry.

Acknowledgments

We thank Dr. K. Vijayakumaran, Chennai, India for his valuable suggestions and comments.

[1] K. C. Nicolaou, D. Vourloumis, N. Winssinger, P. S. Baran, *Angew. Chem. Int. Ed.* **2000**, *39*, 44.
[2] K. C. Nicolaou, H. J. Mitchell, *Angew. Chem. Int. Ed.* **2001**, *40*, 1576; S. J. Danishefsky, J. R. Allen, *Angew. Chem. Int. Ed.* **2000**, *39*, 836; S. Hanessain, *Total Synthesis of Natural Products: The "Chiron" Approach*, Organic Chemistry series, **1983**, *3*, Pergamon, Oxford; B. Fraser-Reid, R. C. Anderson, *Fortschr. Chem. Org. Naturst.* **1980**, *39*, 1.
[3] B. Fraser-Reid, A. Mclean, E. W. Usherwood, *J. Am. Chem. Soc.* **1969**, *91*, 5392; B. Fraser-Reid, *Acc. Chem. Res.* **1985**, *18*, 347; Z. Benko, B. Fraser-Reid, S. P. Mariano, A. L. J. Beckwith, *J. Org. Chem.* **1988**, *53*, 2066; B. Fraser-Reid, R. Underwood, M. Osterhout, J. A. Grossman, D. Liotta, *J. Org. Chem.* **1986**, *51*, 2152; J. L. Primeau, R. C. Anderson, B. Fraser-Reid, *J. Am. Chem. Soc.* **1983**, *105*, 5874; B. V. Rao, J. B. Chan, N. Moskowitz, B. Fraser-Reid, *Bull. Soc. Chim. Fr.* **1993**, *130*, 428; M. A. Rahman, D. R. Kelly, R. M. Srivastava, B. Fraser-Reid, *Carbohydr. Res.* **1985**, *136*, 91.
[4] For some recent examples of synthesis and applications of sugar-based enones: M. Hayashi, H. Kawabata, S. Shimono, A. Kakehi, *Tetrahedron Lett.* **2000**, *41*, 2591; A. Dondoni, A. Marra, A. Boscarato, *Chem. Eur. J.* **1999**, *5*, 3562; A. Kirschning, U. Hary, C. Plumeier, M. Ries, L. Rose, *J. Chem. Soc., Perkin Trans. 1* **1999**, 519; O. Achmatowicz, B. Szechner, J. K. Maurin, *Tetrahedron* **1997**, *53*, 6035; For a very recent example on the application of open-chain carbohydrate enals: R. Pathak, A. K. Shaw, A. P. Bhaduri, *Tetrahedron* **2002**, *58*, 3535; For examples on furanoid units: K. Mo Sun, B. Fraser-Reid, *Synthesis* **1982**, 29; K. Mo Sun, R. M. Guiliano, B. Fraser-Reid, *J. Org. Chem.* **1985**, *50*, 4774; A. Sundin, T. Frejt, G. Magnusson, *Tetrahedron Lett.* **1985**, *26*, 5605; K. L. Bhat, S. Y. Chen, M. M. Jouillie, *Heterocycles*, **1985**, *23*, 691.
[5] N. G. Ramesh, K. K. Balasubramanian, *Tetrahedron Lett.* **1991**, *32*, 3875.
[6] H. Satoh, Y. Yoshimura, M. Watanabe, N. Ashida, K. Ijichi, *Nucleosides Nucleotides* **1998**, *17*, 65; H. Sugimura, K. Osumi, T. Koyama, *Chem. Lett.* **1991**, 1379; J. Herscovici, J. M. Ergon, K. Antonakis, *Carbohydr. Res.,* **1985**, *142*, 324; K. Bischofberger, A. J. Brink, O. G. de Villiers, R. H. Hall, A. J. Jordaan, *J. Chem. Soc., Perkin Trans. 1* **1977**, 1472; A. Rosenthal, M. Sprinzl, *Can. J. Chem.* **1970**, *48*, 3253; V. Samano, M. J. Robins, *Synthesis* **1991**, *283*, M. H. Ali, P. M. Collins, W. G. Overend, *Carbohydr. Res.,* **1990**, *205*, 428.

[7] L-F. Tietze, K-H. Glusenkamp, K. Harms, G. Remberg, *Tetrahedron Lett.* **1982**, *23* 1147.
[8] J. C. Lopez, E. Lameignere, G. Lukacs, *J. Chem. Soc., Chem. Commun.* **1988**, 514.
[9] J. C. Lopez, E. Lameignere, C. Burnouf, M. de los A. Laborde, A. A. Ghini, A. Olesker, G. Lukacs, *Tetrahedron* **1993**, *35*, 7710.
[10] C. Burnouf, J. C. Lopez, M. de los A. Laborde, A. Olesker, G. Lukacs, *Tetrahedron Lett.* **1988**, *29*, 5533.
[11] For reviews on Vilsmeier−Haack reaction: G. Jones, S. Stanforth, *Org. React.* **2000**, *56*, 355; C. M. Marson, *Tetrahedron* **1992**, *48*, 3659; W. G. Jackson, A. M. Sargeson, P. A. Tucker, A. D. Watson, *J. Am. Chem. Soc.* **1981**, *103*, 533; S. Seshadri, *J. Sci. Ind. Res.* **1973**, *32*, 128.
[12] G. Piancatelli, G. D'Ottavi, A. Scettri, *Annali di Chimica* **1972**, *62*, 394.
[13] W. Priebe, G. Grynkiewicz, N. Neamati, *Tetrahedron Lett.* **1992**, *33*, 7681.
[14] J-P. Lellouche, S. Koeller, *J. Org. Chem.* **2001**, *66*, 693.
[15] I. Rudloff, K. Peseke, H. Reinke, *J. Prakt. Chem.* **1998**, *340*, 334.
[16] B-A. Feit, I. K. Kelson, A. Gerull, S. Abramson, R. R. Schmidt, *J. Carbohydrate Chem.* **2000**, *19*, 661.
[17] S. Koeller, J-P. Lellouche, *Tetrahedron Lett.* **1999**, *40*, 7043.
[18] M. E. Jung, S. W. T. Choe, *Tetrahedron Lett.* **1993**, *34*, 6247; S. W. T. Choe, M. E. Jung, *Carbohydr. Res.* **2000**, *329*, 731.
[19] C. Burnouf, J. C. Lopez, F. G. Calvo-Flores, M. de los A. Laborde, A. Olesker, G. Lukacs, *J. Chem. Commun. Chem. Soc.* **1990**, 823.
[20] For some recent examples on the synthesis of annulated pyranosides: D. Sinou, K. Bedjeguelal, *J. Carbohydr. Chem.* **2001**, *20*, 335; J. Marco-Contelles, J. Ruiz-Caro, *Carbohydr. Res.,* **2001**, *335*, 71 and references cited therein; C. Taillefumier, Y. Chapleur, *Can. J. Chem.* **2000**, *78*, 708; B. Fraser-Reid, X. T. Chen, D. Haag, K. J. Henry, A. T. McPhail, *Chirality* **2000**, *12*, 488.
[21] C. Booma, K. K. Balasubramanian, *J. Chem. Soc., Perkin Trans. 1* **1993**, 393.
[22] C. Booma, K. K. Balasubramanian, *Tetrahedron Lett.* **1992**, *33*, 3049.
[23] For a related Lewis acid-catalysed formal [1,3] rearrangement reported from our group: N. G. Ramesh, K. K. Balasubramanian, *Tetrahedron Lett.* **1992**, *33*, 3061.
[24] J. Cossy, H. Rakotoarisoa, *Synlett* **2000**, 734.
[25] A. Matsuda, K. Takenuki, M. Tanaka, T. Saski, T. Ueda, *J. Med. Chem.* **1991**, *34*, 812; C. H. Baker, J. Banzon, J. M. Bollinger, J. Stubbe, V. Samano, M. J. Robins, B. Lippert, E. Jarvi, R. Resvick, *Chemtracts-Organic Chemistry* **1991**, *4*, 426.
[26] E. D. Rekai, G. Rubinstenn, J-M. Mallet, P. Sinäy, *Synlett* **1998**, 831.
[27] C. Booma, K. K. Balasubramanian, *J. Chem. Soc., Chem. Commun.* **1993**, 1394.
[28] For the synthesis of *C*-2-methylene glycosides by other approaches: L. Alcaraz, A. Cridland, E. Kinchin, *Org. Lett.* **2001**, *3*, 4051; G. Wong, B. Fraser-Reid, *Can. J. Chem.* **1994**, *72*, 69.
[29] R. J. Ferrier, N. Prasad, *J. Chem. Soc., C* **1969**, 570; For articles about classical Ferrier rearrangements from our group: B. Shanmugasundaram, A. K. Bose, K. K. Balasubramanian, *Tetrahedron Lett.* **2002**, *43*, 6795. B. S. Babu, K. K. Balasubramanian, *Tetrahedron Lett.* **2000**, *41*, 1271; B. S. Babu, K. K. Balasubramanian, *Tetrahedron Lett.* **1999**, *40*, 5777; B. S. Babu, K. K. Balasubramanian, *Synth. Commun.* **1999**, *29*, 4299; S. Sowmya, K. K. Balasubramanian, *Synth. Commun.* **1994**, *24*, 2097; For some very recent examples of classical Ferrier rearrangements from other groups: J. S. Yadav, B. V. S. Reddy, K. B. Reddy, M. Satyanarayana, *Tetrahedron Lett.* **2002**, *43*, 7009, R. Swamy, Y. Venkateswarulu, *Synthesis* **2002**, 598; J. S. Yadav, B. V. S. Reddy, *Synthesis* **2002**, 511; A. A-H. Abdel-Rahman, G. A. Winterfeld, M. Takhi, R. R. Schmidt, *Eur. J. Org. Chem.* **2002**, *4*, 713.
[30] A. Gupta, Y. D. Vankar, *Tetrahedron* **2000**, *56*, 8525.
[31] C. Booma, K. K. Balasubramanian, *Tetrahedron Lett.* **1993**, *34*, 6757.
[32] For a report on the synthesis of pyrano[3,2-*c*]benzopyrans: H. Miyazaki, K. Honda, M. Asami, S. Inoue, *J. Org. Chem.* **1999**, *64*, 9507.
[33] O. Mitsunobu, *Synthesis* **1981**, 1; D. L. Hughes, *Org. React.,* **1992**, *42*, 335; D. L. Hughes, *Org. Prep. Proced. Int.* **1996**, *28*, 127.
[34] N. G. Ramesh, K. K. Balasubramanian, *Tetrahedron* **1995**, *51*, 255.
[35] S. Bhagavathy, Ph.D. Thesis, Indian Institute of Technology − Madras, Chennai, India, **2003**; S. Bhagavathy, K. K. Balasubramanian, unpublished results.
[36] S. Bouoit, C. Goux, D. Sinou, *Carbohydr. Lett.* **1997**, *2*, 267.
[37] J. Wolf, C. Monneret, R. Pontikis, J. C. Florent, *Eur. J. Org. Chem.* **1998**, 2417.
[38] R. H. Hall, A. Jordaan, *J. Chem. Soc., Perkin Trans. 1* **1973**, 1059.
[39] R. H. Hall, K. Bischofberger, A. J. Brink, O. G. De Villiers, A. Jordaan, *J. Chem. Soc., Perkin Trans. 1* **1979**, 781.
[40] E. C. K. Lai, S. A. Morris, I. P. Street, S. G. Withers, *Bioorg. Med. Chem.* **1996**, *4*, 1929.
[41] H-J. Hammen, E. Hoft, D. Mostowicz, A. Mishnev, Z. Urbanczyk-Lipkowska, M. Chmielewski, *Tetrahedron* **1997**, *53*, 185.
[42] B. Giese, M. Hoch, C. Lamerth, R. R. Schmidt, *Tetrahedron Lett.* **1988**, *29*, 1375.
[43] J. Kast, M. Hoch, R. R. Schmidt, *Liebigs Ann. Chem.* **1991**, 481; C. V. Ramana, M. Nagarajan, *Synlett* **1997**, 763.
[44] M. G. Finn, K. B. Sharpless in "*Asymmetric Synthesis*", (Ed.: J. D. Morrison), Academic Press, New York, *5*, **1985**, 247.
[45] H. J. Schaeffer, L. Beauchamp, P. de Miranda, G. B. Elion, D. J. Bauer, P. Collins, *Nature* (London) **1978**, *272*, 583; C. K. Chu, S. J. Cutler, *J. Heterocyclic Chem.* **1986**, *23*, 289; R. J. Remy, J. A. Secrist, *Nucleosides & Nucleotides* **1985**, *4*, 411.
[46] K. Peseke, H. Feist, J. Quincoces, *Targets in Heterocyclic Systems* **2001**, *5*, 299.
[47] I. Rudloff, M. Michalik, A. Montero, K. Peseke, *Synthesis* **2001**, 1686.
[48] A. Montero, H. Feist, M. Michalik, J. Quincoces, K. Peseke, *Synthesis* **2002**, 664.
[49] A. Montero, H. Feist, M. Michalik, J. Quincoces, K. Peseke, *J. Carbohydr. Chem.* **2002**, *21*, 305.
[50] S. Matsukuma, T. ohtsuka, H. Kotaki, H. Shirai, T. Sano, K. Watanabe, N. Nakayama, Y. Itezono, M. Fujiu, N. Shimma, K. Yokose, T. Okuda, *J. Antibiot.* **1992**, *45*, 151; R. E. Schwartz, C. Drufresne, J. E. Flor, A. J. Kempf, K. E. Wilson, T. Lam, J. Onishi, J. Milligan, R. A. Fromtling, G. K. Abruzzo, R. Jenkins, K. Glazomitsky, G. Bills, L. Zitano, S. M. D. Val, M. N. Omstead, *J. Antibiot.* **1991**, *44*, 463; O. D. Hensens, C. F. Wichmann, J. M. Liesch, F. L. Van Middlesworth, K. E. Wilson, R. E. Schwartz, *Tetrahedron* **1991**, *47*, 3915.
[51] S. Jendrzejewski, P. Ermann, *Tetrahedron Lett.* **1993**, *34*, 615.

Received June 25, 2003
Early View Article
Published Online October 16, 2003

