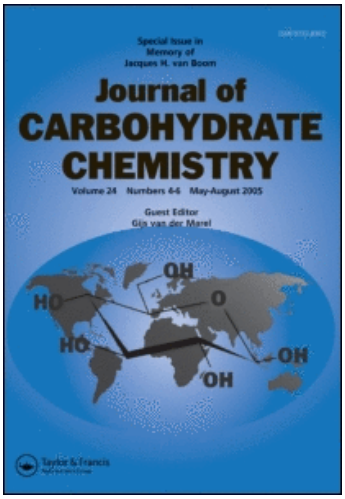

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Zirconium(IV) Chloride Catalyzed Synthesis of 2,3-Unsaturated C, N, O, S, and Heteroaromatic Glycosylation in the Ferrier Rearrangement

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Zirconium(IV) Chloride Catalyzed Synthesis of 2,3-Unsaturated C, N, O, S, and Heteroaromatic Glycosylation in the Ferrier Rearrangement[#]

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ABSTRACT

The reaction of tri-*O*-acetyl-D-glucal with nucleophiles to afford the corresponding 2,3-unsaturated glycopyranosides in excellent yields by zirconium(IV) chloride in acetonitrile at ambient temperature has been demonstrated.

Key Words: Ferrier rearrangement; 2,3-Unsaturated glycopyranosides; Nucleophiles; Heteroaromatics; Protected amino acids; Zirconium(IV) chloride.

INTRODUCTION

Unsaturated carbohydrates are a versatile class of compounds in synthetic organic chemistry in which alkyl, aryl 2,3-unsaturated glycosides are important building blocks in many bioactive molecules.[1] C-glycosyl, N-glycosyl reactions are important chiral intermediates for the synthesis of biologically active natural products[2] such as antivirals,[3,4] antitumor agents,[3,4] C-glycosyl antibiotics,[5] palytoxin,[6] spongistatin,[7] halichondrin,[8] glycopeptides,[9,10] glycoprotein modified carbohydrates,[11] and nucleosides.[12]

Products of C-glycosidation are important intermediates due to their propensity for further functionalization. For instance, allyl glycosides are amenable to hydroxylation, epoxidation, amino hydroxylation, and hydrogenation, while glycosyl cyanides are useful chiral intermediates[13] due to the readily transformed cyanide group. Alternatively, glycosyl azides are important precursors for the synthesis of glycosyl amine.

RESULTS AND DISCUSSION

The well-known Ferrier rearrangement,[14] involving Lewis acid catalyzed allylic rearrangement, is widely used to obtain 2,3-unsaturated glycosides and thus gives access to the aforementioned structures. A variety of reagents are used to effect this transformation, which include strong acids such as BF_3OEt_2,[15,16] $SnCl_4$,[17,18] and TMSOTf.[19] Other reagents such as acidic montmorillonite K-10,[20] DDQ,[21] $InCl_3$,[22,23] and $BiCl_3$[24] triflates such as $Sc(OTf)_3$,[25,26] and $Yb(OTf)_3$[27,28] are also known to bring about the Ferrier rearrangement under different conditions. However, many of these procedures suffer from disadvantages such as strong oxidizing conditions, high acidity, longer reaction times, unsatisfactory yields, low stereoselectivity, and use of a large amount of reagent or catalyst. For instance, various amounts of BF_3 OEt_2[9,10] are often needed to effect the transformation, while metal triflates can be highly expensive. No single catalyst is able to perform to carryout C, N, O, S, and heteroaromatic glycosylation reaction in the Ferrier rearrangement.

Previously, $ZrCl_4$ has been used as an efficient catalyst in acetalization, dithioacetalization,[29,30] and 1,3-oxathiolanes of carbonyl compounds. Also it has been used in transthioacetalizations of acetals,[31] and in the synthesis of chloromethyl esters.[32] In view of the current thrust on catalytic processes, there is merit in developing a truly catalytic method to prepare 2,3-unsaturated C-glycosyl, glycosyl azide from silylated nucleophiles such as allyltrimethyl silane, trimethylsilyl cynide, and allyltrimethyl azide using

inexpensive and nonpolluting reagents. Herein, we wish to report zirconium(IV) chloride catalyzed glycosylation with silylated nucleophiles, heteroaromatics, and protected amino acids. The reaction proceeds efficiently at ambient temperature and the products are obtained in excellent yields (Sch. 1). Furthermore, other functionalities such as Bz, Bn, NHBOC, NHCBz, Ac, OMe, allyl, CN, and N_3 are compatible under the reaction conditions. The reaction conditions are very mild and no by-products are observed. We first examined the reaction of tri-*O*-acetyl-D-glucal with allyltrimethyl silane in the presence of zirconium(IV) chloride in acetonitrile at ambient temperatures affording the corresponding 2,3-unsaturated glycopyranoside in 95% yield (Tab. 1 entry a). This success encouraged us to extend the generality of the reaction. The glycosidation of tri-*O*-acetyl glucal with trimethylsilyl cyanide, allyltrimethyl azide, and protected amino acids proceeded smoothly (Tab. 1). These compounds are potential precursors for the synthesis of glycopeptide building blocks.

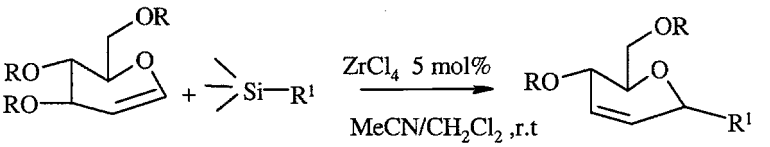
In conclusion, the present procedure has the advantages of mild reaction conditions, high stereoselectivity, reduced reaction time, inexpensive catalyst, high yields of products, and simple experimental work-up procedure for the preparation of 2,3-unsaturated glycosylated products. Zirconium(IV) chloride catalyzed Ferrier glycosylation has been developed to produce structurally diverse C, N, O, S, and heteroaromatic glycosylation reaction in the Ferrier rearrangement and will be an important addition to the existing methodologies.

EXPERIMENTAL

General procedure: A solution of glucal (1 mmol) and nucleophiles (1.1 mmol) in MeCN (10 mL) was treated with zirconium(IV) chloride (5 %mol) and stirred for an appropriate time (Tab. 1) at rt. After completion of the reaction, the solvent was removed from the reaction mixture under reduced pressure, water was added and the reaction contents were extracted into EtOAc. The organic layer was dried over anhyd. Na_2SO_4 and concentrated to give the crude product, which was purified by silica gel chromatography eluting with ethyl acetate : hexane (2 : 8) to give pure 2,3-unsaturated glycopyranosides in high yields (Tab. 1).

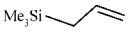
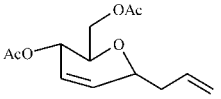
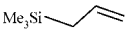
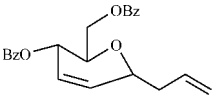
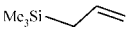
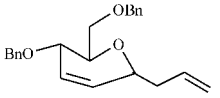
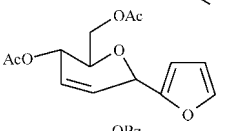
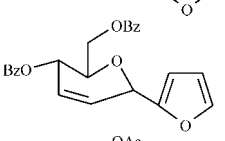
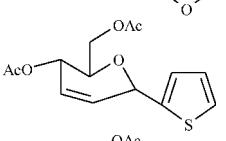
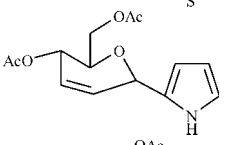
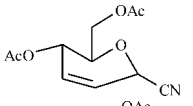
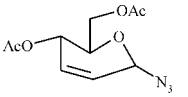
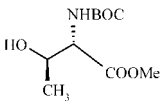
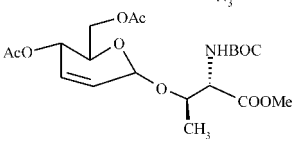
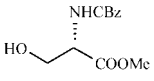
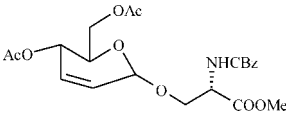
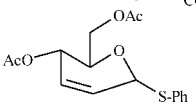
C-Allyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (a): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.08 (s, 6H, Ac), 2.35–2.45 (m, 2H, H_a-1^1, H_b-1^1), 3.95 (dt, 1H, $J_{5,6} = 6.5$ and $J_{5,4} = 3.7$ Hz), 4.10–4.20 (m, 2H, H_a-6, H_b-6), 4.25–4.30 (m, 1H, H_a-4), 5.05–5.20 (m, 3H, H_a-3, H_a-2, H_a-2^1), 5.75–5.95 (m, 3H, H_a-1, H_a-3^1, H_b-3^1). FAB-MS: 255 ($M^+ + 1$).

C-Allyl 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside (c): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.21–2.3 (m, 1H, H_a-1^1), 2.4–2.5 (m, 1H, H_b-1^1), 3.61 (dd,



Scheme 1.

Table 1.

Entry	Acceptor	2,3-Unsaturated Glycoside	Time (min)	Yield (%)[a]	Anomeric ratio (a/b)[b]	Ref.
a)			60	96	10 : 1	
b)			60	95	9 : 1	[22,23]
c)			60	96	11 : 1	
d)			60	64	8 : 2	[22,23]
e)			60	66	8 : 2	[22,23]
f)			30	56	8 : 3	[22,23]
g)			30	55	9 : 3	[22,23]
h)	Me_3Si-CN		30	75	10 : 1	[24]
i)	Me_3Si-N_3		30	70	8 : 3	[24]
j)			45	81	7 : 4	
k)			45	85	9 : 2	
l)	Ph-SH		60	87	10 : 1	[1]

[a]Isolated yield as pure anomeric mixtures after purification.
[b]The anomeric ratio was determined on the basis of the integration ratios of the anomeric hydrogens in the ^{1}H NMR spectra at 200 MHz.

2H, $J_{6,6} = 4$ Hz, $J_{5,6} = 4$ Hz, H_a-6, H_b-6), 3.73 (d, 1H, $J_{5,6} = 5$ Hz, H_a-5), 3.96 (d, 1H, $J_{4,3} = 5$ Hz, H_a-4), 4.28 (br d, 1H, $J_{3,4} = 5$ Hz, H-3), 4.4–4.5 (dd, 2H, $J_{1,1} = 6$ Hz, $J_{1,1} = 6$ Hz, OCH_2), 4.53–4.6 (dd, 2H, $J_{1,1} = 6$ Hz, $J_{1,1} = 6$ Hz, OCH_2), 5.0 (d, 1H, $J_{2,3} = 4$ Hz, H_a-3^1), 5.1 (d, 1H, $J_{2,3} = 5$ Hz, H_b-3^1), 5.76–5.82 (m, 2H, H_a-2, H_a-1), 5.83 (d, 1H $J_{1,2} = 6$ Hz, H_a-1), 7.2–7.3 (m, 10H, Ar) FAB-MS: 351($M^+ + 1$).

2-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)furan (d): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.98 (s, 3H, Ac), 2.1 (s, 3H, Ac), 4.03 (dt, 1H, $J_{5,6} = 1.8$, $J_{5,4} = 6$ Hz, H_a-3), 4.15 (m, 1H, H_a-5), 4.30 (m, 2H, OCH_2, H_a-6, H_b-6), 4.81 (t, 1H, $J_{2,1} = 6$ Hz, $J_{2,3} = H_a$-2), 5.07 (dd, 1H, $J_{4,5} = 6$ Hz, $J_{4,3} = 8$ Hz, H_a-4), 6.13 (d, 1H, $J = 3.5$ Hz, H_a, Aryl), 6.34 (dd, 1H, $J_{2,1} = 2.5$, $J_{2,3} = 3.5$ Hz, Hb, Aryl), 6.51 (d, 1H, $J_{1,2} = 4$ Hz, H_a-1), 7.37 (d,1H, $J = 2.5$ Hz, H_c, Aryl) FAB-MS: 281 ($M^+ + 1$).

N-(tert-butoxycarbonyl)-*O*-(4,6-di-*O*-acetyl 2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl)-L-threonine methyl ester (j): $[\alpha]_D^{25} + 42.39^0$ ($c = 1$, $CHCl_3$): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.31 (d, $J = 6.3$ Hz, 3H CH_3), 1.42 (s, 9H, $C(CH_3)_3$), 2.08 (s, 6H,OAc), 3.78 (s, 3H, COOMe), 4.08–3.80 (m, 5H, H_a-5, H_a-6, H_b-6, α-CH, β-CH), 4.95 (brs, 1H, H_a-1), 5.15 (d, $J_{NH\alpha} = 9.8$ Hz,1H, NH), 5.26 (dd $J_{3,4} = 1.1$ Hz, $J_{4,5} = 9.8$ Hz, 1H, H_a-4), 5.65 (brs, 1H, H-2), 5.84 (brs, 1H, H-3) FAB-MS: 446 ($M^+ + 1$).

N-(benzyloxycarbonyl)-*O*-(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside)-L-serine methyl ester (k): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.08 (s, 6H, OCOCH3), 3.75 (s, 3H, COOMe), 3.9–4.03 (m, 2H, H_a-6, H_b-6), 4.10–4.22 (m, 3H, α-CH, β-CH_2), 4.42–4.55 (m, 1H H-5), 5.09 (s, 2H, OCH_2-Ph), 5.20 (d, 1H, $J = 10$ Hz, H-4), 5.72–5.88 (m, 3H, H-1, H-2, H-3), 7.28–3.80 (m, 5H, Ar) FAB-MS: 466 ($M^+ + 1$).

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REFERENCES

1. Williams, N.R.; Wander, J.D. *The Carbohydrate Chemistry and Biochemistry*; Academic Press: New York, 1980, 761.
2. Postema, M.H.D. *C-Glycoside Synthesis*; CRS Press: Boca Raton, 1995.
3. Schmidt, R.R.; Effenberger, G. Umsetzung von *O*-(glucopyranosyl) imidaten mit elektronenreichen heterocyclen.-synthese von C-Glucosiden. Liebigs Ann. Chem. **1987**, 825–831.
4. Dianez, M.J.; Galan, J.; Gomez-Sanchez, A.; Lopez-Castra, A.; Rico, M. Studies on sugar nitro-olefins. Part 7 Synthesis of 3-(Alditol-1-yl)-1, 2, 3, 5, 6, 7 hexahydro- and -1, 5, 6, 7-tetrahydro-indol-4-ones. X-Ray molecular structure of (3S)-3- (1, 2, 3, 4, 5, - pental-*O*-acetyl-D-galacto-pentitol-1-yl)-1, 2, 3, 5, 6, 7, -hexahydroindol-4-one. J. Chem. Soc., Perkin Trans. 1. **1987**, 581–588.
5. Macdonald, S.J.F.; Huizinga, W.B.; Mckenzie, T.C. Retention of configuration in the coupling of aluminated heterocycles with glycopyranosyl fluorides. J. Org. Chem. **1988**, *53*, 3371–3373.

6. Lewis, M.D.; Cha, J.K.; Kishi, Y. Highly stereoselective approaches to α- and β-C-glycopyranosides. J. Am. Chem Soc. **1982**, *104*, 4976–4978.
7. Paterson, L.; Keown, L.E. Studies in marine macrolide synthesis: stereocontrolled synthesis of the F-ring subunit of spongistation 1 (altohytinA). Terahedron Lett. **1997**, *38*, 5727–5730.
8. Horitha, K.; Sakkurai, Y.; Nagasawa, M.; Hachiya, S.; Yonemistu, O. Synthetic studies of halichondrin B, an antitumor polyether macrolide isolsation from a marine sponge. Synthesis of C27-C36 subunit *via* completely stereoselective C-glycosylation to the F-ring. Synlett **1994**, 43–45.
9. Winterfeld, G.A. Conjugate addition of phenols to a 2-nitroglactal-synthesis of -*O*-(2-acetamido-2-deoygalactosyl) tyrosine. University of Konstanz Germany, 2000; PhD. Dissertation.
10. Durgan, B.J.; Jackson, R.F.W. Synthesis of C-linked glycosyl amino acid derivatives using organozinc reagents. Synlett **1996**, 859–861.
11. Schmidt, R.R.; Angerbauer, R. Simple de-novo synthesis of reactive pseudoglycals (hex-2-enopyranosides)-stereospecific α-glycoside copling. Angew Chem. Int. Ed. Engl. **1977**, *16*, 783–784.
12. Schmidt, R.R.; Angerbauer, R. A convenient preparation of 2, 3-unsturated N-galactosyl derivatives. Carbohydr. Res. **1979**, *72*, 272–275.
13. Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon: Oxford, 1983.
14. Ferrier, R.J.; Prasad, N.J. Unsaturated carbohydrates. Part IX. Sythesis of 2,3 dideoxy-α-D-erythro-hex-2-enopyranosides from tri-*O*-acetyl-D-glucal. J. Chem. Soc. **1969**, 570–575.
15. Descotes, G.; Martin, J.C. Surl' isomerisation du 1,5-anhydro-3,4,6 tri-*O*-benzyl-1,2-didesoxy-D-arabino-hex-1-enitol on presence d acides de Lewis. Carbohydr. Res. **1977**, *56*, 168–172.
16. Klaffke, W.; Pudlo, P.; Springer, D.; Thiem, J. Artificial deoxy glycosides of anthracyclines. Liebigs Ann. Chem. **1991**, 509–512.
17. Grynkiewicz, G.; Priebe, W.; Zamojski, A. Synthesis of alkyl 4,6 di-*O*-acetyl-2, 3-dideoxy α-D-threo-hex-2-enopyranosides from 3,4,6, tri-*O*-acetyl 1,5-anhydro-2-deoxy-D-lyxo-hex-1-enitol(3,4,6-tri-*O*-acetyl-D-galactal). Carbohydr. Res. **1979**, *68*, 33–41.
18. Bhate, P.; Horton, D.; Priebe, W. Allylic rearrangement of 6-deoxyglycals having practical utlity. Carbohydr. Res. **1985**, *144*, 331–337.
19. Drwe, R.D.; Fraser-Reid, B. α-C-Glycopyranosides from Lewis acid catalyzed condensation of acetylated glycals and enol silanes. J. Chem. Soc., Chem. Commun. **1981**, 1180–1181.
20. Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M. Practical glycosidation method of glycals using montmorillonite K-10 as an environmentally acceptable and inexpensive industrial catalyst. Synlett **1995**, 306–308.
21. Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M.; Konoshita, M. Glycosidation of glycals by 2,3-dichloro-5,6 dicyano-p-benzoquinone (DDQ) as a catalytic promoter. J. Chem. Soc., Chem. Commun. **1993**, 704–706.
22. Babu, B.S.; Balasubramanian, K.K. Indium trichloride catalyzed glycosidation. An expeditious synthesis of 2,3-unsaturated glycopyranosides. Tetrahedron Lett. **2000**, *41*, 1271–1274.

23. Yadav, J.S.; Reddy, B.V.S.; Raman, J.V.; Niranjan, N.; Kumar, K.S.; Kunwar, A.C. $InCl_3$-catalyzed stereoselective synthesis of C-glycosyl heteroaromatics. Terahedron Lett. **2002**, *43*, 2095–2098.
24. Swamy, N.R.; Venkateswarlu, Y. An efficient method for synthesis of 2,3-unsaturated glycopyranosides catalyzed by Bismuth trichloride in Ferrier rearrangement. Synthesis **2002**, 598–600.
25. Yadav, J.S.; Reddy, B.V.S.; Chand, P.K. $Sc(OTf)_3$-catalyzed C-glycosidation of glycals: a facile synthesis of allyl glycosides, glycosyl cyanides and glycosyl azides. Tetrahedron Lett. **2001**, *42*, 4057–4059.
26. Yadav, J.S.; Reddy, B.V.S.; Murthy, C.V.S.R.; Kumar, G.M. Sacandium triflate catalyzed Ferrier rearrangement: An efficient synthesis of 2,3-unsaturated glycopyranosides. Synlett **2000**, 1450–1451.
27. Takhi, M.; Abdel-Rahman, A.A.H.; Schmidt, R.R. Highly stereoselective synthesis of pseudoglycals *via* $Yb(OTf)_3$ catalyzed Ferrier glycosylation. Synlett **2001**, 427–429.
28. Takhi, M.; Abdel-Rahman, A.A.H.; Schmidt, R.R. $Yb(OTf)_3$ catalyzed C-glycosiltion: Highly stereoselective synthesis C-pseudoglycals. Tetrahedron Lett. **2001**, *42*, 4053–4053.
29. Firouzabadi, H.; Iranpoor, N.; Karimi, B. Zirconium terachloride($ZnCl_4$) catalyzed highly chemoselective and efficient transthioacetalization of acetals. Synlett **1999**, 319–320.
30. Patney, H.K.; Margan, S. Zirconium(IV) chloride-silica catalyzed thioacetalization of carbonyl compounds. Tetrahedron Lett. **1996**, *37*, 4621–4622.
31. Firouzabadi, H.; Iranpoor, N.; Karimi, B. Zirconium tetrachloride ($ZnCl_4$) catalyzed highly chemoselective and efficient acetalization of carbonyl compounds. Synlett **1999**, 321–323.
32. Mudry, K.B.; Rajaraman, S.; Soundararajan, N. A practical synthesis of chloromethyl esters from acid chlorides and trioxane or paraformaldehyde promoted by Zirconium tetrachloride. Tetrahedron Lett. **2002**, *43*, 6317–6318.

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