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3-*O*-Acyl triggered tandem Lewis acid catalyzed intramolecular cyclization of diacetone glucose derivatives to 5-*O*-acyl-3,6-anhydro-D-glucose

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ABSTRACT

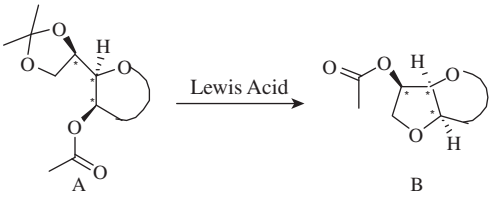
BF_3 mediated one-pot conversion of 3-*O*-acyl-D-glucose-1,2:5,6-diacetonide derivatives to 5-*O*-acyl-3,6-anhydro-D-glucose is described through a tandem selective intramolecular cyclization sequence.

Carbohydrate chirons are versatile compounds with proven end uses in organic synthesis.[1] Discovery of new reactions and elegant preparation of chiral templates from abundantly available carbohydrates continue to attract the attention of synthetic organic chemists.

We report here a novel reaction (Scheme 1) that involves transformation of chiral acyloxy tetrahydrofuranodioxalane **A** to acyloxy tetrahydrofuran derivative **B** with retention of sterochemistry at all the stereo centers. The reaction is triggered by activation of the neighboring acyloxy group by a Lewis acid. The protocol developed here is unique and new to carbohydrate chemistry.

The protocol has been adequately demonstrated on a wide array of carbohydrate derivatives **1a–d**, **2e–h**, **3i,j** to give their corresponding 3,6-anhydro-D-glucose derivatives **4a–h**. Such bicyclic carbohydrate templates have been earlier evaluated for antiviral activity as modified nucleosides[2] and the bicylic chiral template itself has been the key starting material for the synthesis of natural products viz., furanodictine A and furanodictine B, possessing neuronal differentiation activity.[3] The rigid structural frame of 3,6-anhydro-D-glucose earlier has been used for designing new chiral resolving agents.[4]

As a starting point for this study, a wide range of carbohydrate derivatives with variation of acyl substituents, such as formyl-**1a,2e,3i,j**, acetyl-**1b,2f**, benzoyl-**2d,h** and xanthyl-**1c,2g** on C-3-hydroxy; and alkyl and phenyl substituents on 1,3-dioxalane ring



Scheme 1. General synthesis of acyl anhydro-D-glucose.

have been prepared from the corresponding hydroxy derivatives **1–3** by the literature described methods and were fully characterized by spectral methods.[5] 3-*O*-Formyl-α-D-glucofuranose derivatives **1a, 2e, 3i,** and **j** were obtained by reaction of the respective 3-hydroxy derivatives **1, 2, and 3** with triphosgene/DMF/NaH under modified Vilsmeyer conditions; 3-*O*-methylthiothiocarbonyl derivatives **1c** and **2g** by reaction of **1 and 2**, respectively, by reaction with carbondisulfide/methyl iodide/NaH in THF.

With the desired 3-*O*-acyl glucofuranose derivatives in hand, a series of experiments were carried out to check the suitability of the substrate and catalysts for the transformation (Scheme 1). Initially, substrates **1a–d** bearing 2,2-dimethyl-1,3-dioxalane on the C-5,6-carbon were reacted with $BF_3{\cdot}Et_2O$ in CH_2Cl_2 at room temperature for 3 h to observe the formation of the corresponding 3,6-anhydro-D-glucose derivatives **4a–d**, respectively, in 54.5–88.0% yields (Scheme 2) (Table 1). The 3-*O*-formyl derivative **1a** was found to be superior among the acyl substituents tried for the purpose in terms of yield.

It was then decided to study whether the bulk of substituents on the neighboring 1,3-dioxalane ring has any decisive role in the progress of the reaction. It was expected that the

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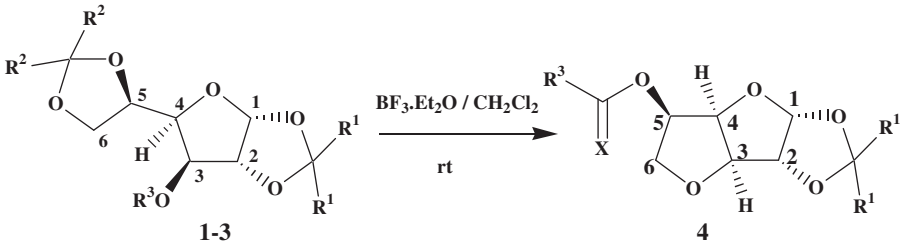


1) $R^1 = R^2 = :C(CH_3)_2$, $R^3 = H$
2) $R^1 = R^2 = :C(CH_2)_5$, $R^3 = H$
3) $R^1 = :C(CH_2)_5$, $R^2 = :C(CH_3)_2$, $R^3 = H$
5) $R^2, R^3 = H$

1a) $R^1 = R^2 = CH_3$, $R^3 = HCO$
1b) $R^1 = R^2 = CH_3$, $R^3 = COCH_3$
1c) $R^1 = R^2 = CH_3$, $R^3 = CSSCH_3$
1d) $R^1 = R^2 = CH_3$, $R^3 = COPh$
2e) $R^1 = R^2 = (CH_2)_5$, $R^3 = HCO$
2f) $R^1 = R^2 = (CH_2)_5$, $R^3 = COCH_3$
2g) $R^1 = R^2 = (CH_2)_5$, $R^3 = CSSCH_3$
2h) $R^1 = R^2 = (CH_2)_5$, $R^3 = COPh$
3i) $R^1 = CH_3$, $R^2 = (CH_2)_5$, $R^3 = HCO$
3j) $R^1 = (CH_2)_5$, $R^2 = CH_3$, $R^3 = HCO$

4a) $R^1 = CH_3$, $R^3 = H$, X=O
4b) $R^1 = CH_3$, $R^3 = CH_3$, X=O
4c) $R^1 = CH_3$, $R^3 = SCH_3$, X=S
4d) $R^1 = CH_3$, $R^3 = Ph$, X=O
4e) $R^1 = (CH_2)_5$, $R^3 = H$, X=O
4f) $R^1 = (CH_2)_5$, $R^3 = CH_3$, X=O
4g) $R^1 = (CH_2)_5$, $R^3 = SCH_3$, X=S
4h) $R^1 = (CH_2)_5$, $R^3 = Ph$, X=O

Scheme 2. Preparation of 5-*O*-acyl-3,6-anhydro-D-glucose derivatives.

Table 1
$BF_3{\cdot}Et_2O$ catalyzed reaction of **1**–**3** to **4**

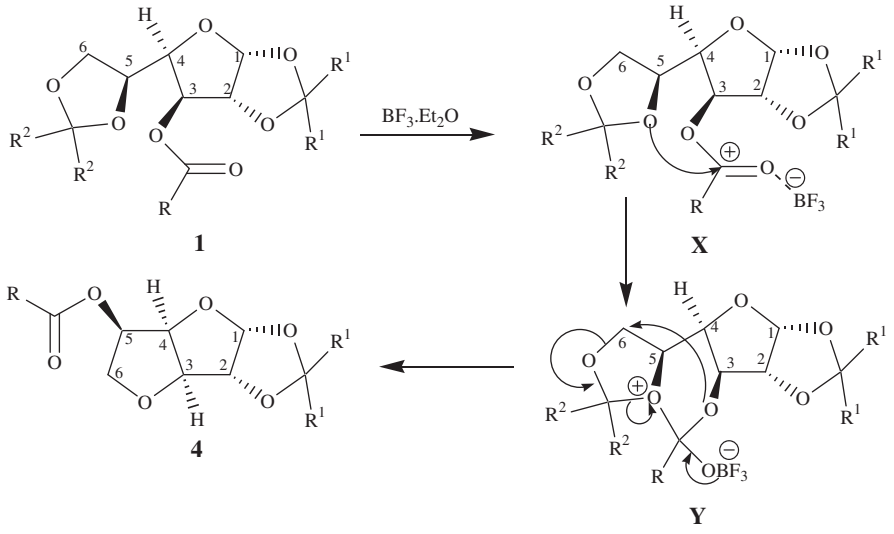
Substrate **1**		Product **2**		Yield (%)
3-*O*-Formyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose	**1a**	3,6-Anhydro-5-*O*-formyl-1,2-*O*-isopropylidene-α-D-glucofuranose	**4a**	88.0
3-*O*-Acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose	**1b**	5-*O*-Acetyl-3,6-anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose	**4b**	75
1,2:5,6-Di-*O*-isopropylidene-3-*O*-methylthio thiocarbonyl-α-D-glucofuranose	**1c**	3,6-Anhydro-(5-*O*-methylthio thiocarbonyl)-1,2-*O*-isopropylidene-α-D-glucofuranose	**4c**	67
3-*O*-Benzoyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose	**1d**	3,6-Anhydro-5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucofuranose	**4d**	54.5
1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-formyl-α-D-glucofuranose	**2e**	3,6-Anhydro-1,2-*O*-cyclohexylidene-5-*O*-formyl-α-D-glucofuranose	**4e**	78.4
3-*O*-Acetyl-1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose	**2f**	3,6-Anhydro-5-*O*-acetyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose	**4f**	65.1
1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-methylthio thiocarbonyl-α-D-glucofuranose	**2g**	3,6-Anhydro-5-*O*-methylthio thiocarbonyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose	**4g**	63.6
3-*O*-Benzoyl-1,2:5,6-di-*O*-cyclohexylidene-α-D-glucofuranose	**2h**	3,6-Anhydro-5-*O*-benzoyl-1,2-*O*-cyclohexylidene-α-D-glucofuranose	**4h**	52.3
3-*O*-Formyl-5,6-cyclohexylidene-1,2-*O*-isopropylidene-α-D-glucofuranose	**3i**	3,6-Anhydro-5-*O*-formyl-1,2-*O*-isopropylidene-α-D-glucofuranose	**4a**	89.9
1,2-Cyclohexylidene-3-*O*-formyl-5,6-isopropylidene-α-D-glucofuranose	**3j**	3,6-Anhydro-1,2-*O*-cyclohexylidene-5-*O*-formyl-α-D-glucofuranose	**4e**	85.6

Table 2
Study of various catalysts for the transformation of **1a** to **4a**

Entry	Catalyst (100 mol %)	Time (h)	**4a**	Product yield (%)	
				1,2-*O*-Isopropylidene α-D-glucofuranose (**5**)	1,2:5,6-Di-*O*-isopropylidene-α-D-glucofuranose(**1**)
i	$TiCl_4$	8	0	71	25
ii	$SnCl_4$	5	0	78	17
iii	*p*-TSA-pyridine	3	0	87	10
iv	$AlCl_3$	1	0	77	13
v	$Ce(NH_4)_2(NO_3)_6$	3	0	76	15
vi	$Bi(NO_3)_3{\cdot}5H_2O$	3	0	74	10
vii	CF_3COOH	1	0	79	17
viii	$BF_3{\cdot}Et_2O$	3	89.9	0	0

intramolecular cyclization requires planarity to proceed smoothly and the bulky groups would deter the reaction. Accordingly, substrates **2e–h** bearing bulky cyclohexylidene on the 1,3-dioxalane ring were reacted with $BF_3{\cdot}Et_2O$ in CH_2Cl_2 under similar reaction conditions to obtain the corresponding 3,6-anhydro-D-glucose derivatives **4e–h** in 52.3–78.4% yield (Table 1), respectively. Among these derivatives, once again the 3-*O*-formyl derivative **2e** was found to be superior and the presence of bulky substituents on the 1,3-dioxalane have no effect. Finally, the other two possible 3-*O*-formyl derivatives **3i** and **3j** were reacted under similar conditions to obtain the corresponding **4a** and **4e**, respectively, in 89.9% and 85.6% yields (Table 1).

In order to find a suitable catalyst that could improve the yield and substrate selectivity; several catalysts were tried for the reaction of **1a** (Table 2). Most of the catalysts resulted in deprotection of the neighboring 1,3-dioxalane ring and or the 3-*O*-acyl group resulting in the formation of 1,2-*O*-isopropylidene-α-D-glucofuranose and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose almost



Scheme 3. Plausible mechanisam.

quantitatively. Among the catalysts tried for the purpose, BF3 etherate was found to be the most suitable for the transformation of **1**–**3** to **4** in terms of yield and simplicty. The bulk on the dioxalane ring did not play any decisive role on the progress of the reaction.

From the mechanism point of view, the cascade reaction is triggered by Lewis acid activation of 3-*O*-acyl substituent of 1 to form the acyl cation intermediate X. Stabilization of the acyl cation by the electron rich neighboring oxygen atom of the dioxolane leads to 3 → 5 acyl migration and intramolecular cyclization via the transition state Y to give 3,6-anhydro-D-glucose derivative **4** (Scheme 3).

In conclusion, a new reaction is described wherein the 3-*O*-formyl, acetyl, xanthyl, and benzoyl ester derivatives of isopropylidene and cyclohexylidene-D-glucofuranose derivatives, undergo tandem intramolecular cyclization reaction, on activation by Lewis acid with concomitant migration of the acyl group to give the corresponding 3,6-anhydro-D-glucose derivatives. A new method to synthesize 3,6-anhydro-D-glucose has been achieved.

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Supplementary data

Supplementary data (experimental data) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.07.034.

References and notes

1. (a) De Clercq, E. *J. Med. Chem.* **1995**, *38*, 2491–2517; (b) De Clercq, E.; Van Aerschot, A.; Herdewijn, P.; Baba, M.; Pauwels, R.; Balzarini, J. *Nucleosides Nucleotides* **1989**, *8*, 659–671; (c) Leroy, G.; Wade, Jr. *J. Chem. Educ.* **1985**, *62*, A190; (d) Taylor, E. W.; Van Roey, P.; Schinazi, R. F.; Chu, C. K. *Antiviral Chem. Chemother.* **1990**, *1*, 163–173.
2. (a) Mitsuya, H.; Yarchoan, R.; Broder, S. *Science* **1990**, *249*, 1533–1544; (b) Okabe, M.; Sun, R. C. *Tetrahedron Lett.* **1998**, *30*, 2203–2206; (c) Yang, C. O.; Kurz, W.; Engui, E. M.; McRoberts, M. J.; Verheyden, J. P. H.; Kurz, L. J.; Walker, K. A. M. *Tetrahedron Lett.* **1992**, *33*, 41–44; (d) Hrebabecky, H.; Dockal, J.; Holy, A. *Collect. Czech. Chem. Commun.* **1994**, *59*, 1408–1419; (e) Nurolaini, K.; Htar, T. T.; De Clercq, E.; Jan, B.; Claire, S. *Bioorg. Med. Chem.* **2004**, *12*, 3247–3257.
3. (a) Kikuchi, H.; Saioto, Y.; Komiya, J.; Takaya, Y.; Honma, S.; Nakahata, N.; Ito, A.; Oshima, Y. *J. Org. Chem.* **2001**, *66*, 6982–6987; (b) Mereyala, H. B.; Baseeruddin, M.; Koduru, S. R. *Tetrahedron: Asymmetry* **2004**, *15*, 3457–3460; (c) Hidemi, Y.; Yuji, S.; Kunihiko, T. *Tetrahedron Lett.* **2004**, *45*, 1599–1601.
4. (a) Mereyala, H. B.; Pallavi, P. *Tetrahedron: Asymmetry* **2003**, *14*, 2683–2685; (b) Mereyala, H. B.; Fatima, L.; Pallavi, P. *Tetrahedron: Asymmetry* **2004**, *15*, 585–587; (c) Mereyala, H. B.; Koduru, S. R.; Cheemalapati, V. N. *Tetrahedron: Asymmetry* **2006**, *17*, 259–267.
5. (a) Iacono, S.; Rasmussen, J. R. *Org. Synth., Coll.* **1990**, *7*, 139–141; (b) Barrett, A. G. M.; Braddock, D. C.; James, R. A.; Koike, N.; Procopiou, N. A. P. *J. Org. Chem.* **1998**, *63*, 6273–6280.