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Catalytic ceric ammonium nitrate mediated synthesis of 2-deoxy-1-thioglycosides

Somak Paul and Narayanaswamy Jayaraman*

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

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Abstract—Synthesis of 2-deoxy-1-thioglycosides from glycals, mediated by catalytic amounts of ceric ammonium nitrate is reported. Apart from the 2-deoxy-1-thioglycosides, formation of the 2,3-unsaturated enose, corresponding to the Ferrier product, is also observed, especially for the glucal substrates. A radical oxocarbenium ion and a thiolate intermediates are most likely to mediate the reaction. Upon synthesis of 2-deoxy-1-thioglycosides, few representative glycosylation reactions with both aglycosyl and glycosyl acceptors were performed and α-anomeric 2-deoxy glycosides were obtained exclusively.

Keywords: Carbohydrates; Deoxysugars; Enoses; Thioglycosides

1. Introduction

1,2-Unsaturated glycopyranosides, namely, glycals, are versatile synthetic intermediates for the elaboration to a number of functionalized glycosyl derivatives.[1] A major utility of glycals is their conversion to 2-deoxy glycosyl derivatives, mediated primarily by the lanthanum salt, namely, Ce^{IV}. The azidonitration reaction, reported by Lemiuex and Ratcliffe,[2] is an excellent example to illustrate the facile reactivity of glycals in the presence of metal salts. The azidonitration reaction mediated by ceric ammonium nitrate (CAN) provides a general method to prepare 2-azido-2-deoxy glycosides.[3] The mechanism of CAN-mediated azidonitration is presumed to proceed through either by the attack of the vinyl ether double bond by the azide radical or the transfer of azide via a ceric–azide complex. We were interested to extend this reaction with other radicals or nucleophiles, so as to derive the corresponding 2-azido-2-deoxy glycopyranoses or pyranosides. A reaction of interest in this respect was to incorporate alkylthio moiety at the anomeric center of a 2-azido-2-deoxy glycoside. In these efforts to derive a thioglycoside of 2-azido-2-deoxy-sugar derivative, a clean and facile formation of 2-deoxy-1-thioglycoside was encountered upon subjecting the glycal to CAN-mediated reaction in the presence of NaN_3 and a thiol source. Details of the synthesis of 2-deoxy-1-thioglycosides with this new method are reported herein. Being excellent activated glycosyl donors, few representative glycosylation reactions were performed with the newly formed 2-deoxy-1-thioglycosides.

2. Results and discussion

Early attempts were focused primarily on the conversion of the glycals to the corresponding 2-azido-2-deoxy-1-thioglycosides. Thus, 3,4,6-tri-*O*-acetyl galactal (**1**) was reacted with NaN_3 and EtSH in the presence of CAN in MeCN, in a procedure similar to an azidonitration reaction. This reaction led neatly to the formation of an anomeric mixture of ethyl 2-deoxy-3,4,6-tri-*O*-acetyl-1-thio-D-*lyxo*-hexopyranoside (**5**, **6**) (Scheme 1), without incorporation of the azide moiety. Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-1-thio-D-*threo*-hex-2-enopyranoside (**12**, **13**), corresponding to the Ferrier reaction product,[4] was also isolated.

* Corresponding author. Tel.: +91-80-2293-2406/2403; fax: +91-80-2360-0529; e-mail: jayaraman@orgchem.iisc.ernet.in

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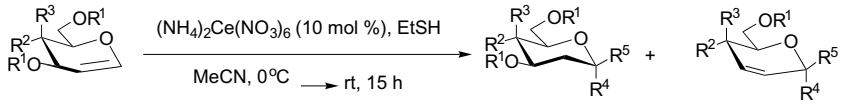


1: R^1 = Ac, R^2 = H, R^3 = OAc

2: R^1 = Ac, R^2 = OAc, R^3 = H

3: R^1 = Bn, R^2 = H, R^3 = OBn

4: R^1 = Bn, R^2 = OBn, R^3 = H

5: R^1 = Ac, R^2 = H, R^3 = OAc, R^4 = SEt, R^5 = H

6: R^1 = Ac, R^2 = H, R^3 = OAc, R^4 = H, R^5 = SEt

7: R^1 = Ac, R^2 = OAc, R^3 = H, R^4 = H, R^5 = SEt

8: R^1 = Bn, R^2 = H, R^3 = OBn, R^4 = SEt, R^5 = H

9: R^1 = Bn, R^2 = H, R^3 = OBn, R^4 = H, R^5 = SEt

10: R^1 = Bn, R^2 = OBn, R^3 = H, R^4 = SEt, R^5 = H

11: R^1 = Bn, R^2 = OBn, R^3 = H, R^4 = H, R^5 = SEt

12: R^1 = Ac, R^2 = H, R^3 = OAc, R^4 = SEt, R^5 = H

13: R^1 = Ac, R^2 = H, R^3 = OAc, R^4 = H, R^5 = SEt

14: R^1 = Ac, R^2 = OAc, R^3 = H, R^4 = SEt, R^5 = H

15: R^1 = Ac, R^2 = OAc, R^3 = H, R^4 = H, R^5 = SEt

16: R^1 = Bn, R^2 = OBn, R^3 = H, R^4 = SEt, R^5 = H

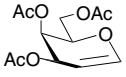
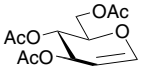
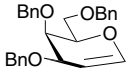
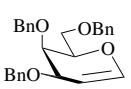
17: R^1 = Bn, R^2 = OBn, R^3 = H, R^4 = H, R^5 = SEt

Scheme 1. CAN-mediated synthesis of thioglycosides **5**–**11** and 1-thio-2,3-unsaturated enoses **12**–**17**.

An examination of the literature shows that a method to prepare such 2-deoxy-1-thioglycosides was to treat the glycal with a specially treated sulfonic acid resin, in the presence of a soluble halide ion.[5] A reagent system comprising of (diacetoxyiodo)benzene, NaN_3 and diphenylselenide was also known previously to prepare an analogous 2-azido-2-deoxy-1-seleno-glycosides.[6]

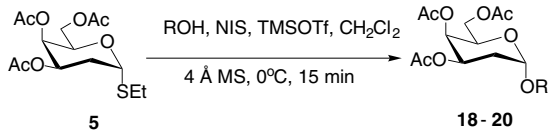
Reaction of glycals with CAN and EtSH in MeCN afforded the 2-deoxy-1-thioglycosides as a mixture of α- and β-anomers. The results of the reaction with *O*-acetylated and *O*-benzylated galactals and glucals are presented in Scheme 1 and Table 1. Apart from the thioglycoside, the Ferrier product is also formed under the reaction conditions and the Ferrier product resulted significantly with glucals than galactals. In all the cases, a catalytic amount of CAN is found to be sufficient to mediate the reaction and experiments performed without CAN did not lead to any conversion. Also, excess CAN afforded the products similar to that of the reaction mediated by catalytic amounts. In an attempt to minimize the Ferrier product, the reaction was conducted in varied conditions such as low temperatures

Table 1. Yield, α:β ratio of 2-deoxythioglycosides (**5**–**11**) and 2,3-unsaturated-1-thio enoses (**12**–**17**)

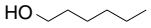
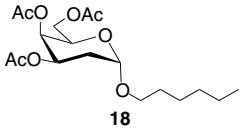
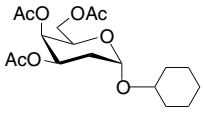
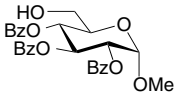
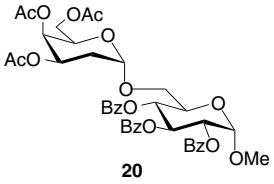
Substrate identity	Substrate	Products			
			Yield (α:β) (%)		Yield (α:β) (%)
1		**5**, **6**	70 (14:11)[a]	**12**,**13**	9 (95:5)[b]
2		**7**	35 (β only)[a]	**14**, **15**	55 (31:19)[b]
3		**8**, **9**	85 (3:2)[a]	—	—
4		**10**, **11**	68 (1.2:1)[b]	**16**, **17**	15 (4:1)[b]

[a] Isolated yields.
[b] Estimated from the ^{1}H NMR spectrum.

Table 2. NIS/TMSOTf-mediated glycosylation of 2-deoxy-1-thioglycoside with acceptor alcohols



5 **18 - 20**

Entry	Glycosyl donor	Acceptor alcohol	Product	Yield (%)
1	**5**		 **18**	90
2	**5**		 **19**	83
3	**5**		 **20**	75

(−20 and −35 °C) and solvent such as CH_2Cl_2, however, none of these conditions altered the ratio of the product formed significantly.

The catalytic amount of CAN required to mediate the above reaction points to the possibility that the reaction involves a radical mechanism. An electron transfer from the glycal to form the radical oxocarbenium ion would be more preferable in the formation of 1-thioglycosides and the Ferrier products.

The formation of 1-thioglycosides **5**–**11** and the 2,3-unsaturated enose products **12**–**17** largely depends on the *gluco*-or *galacto*-configurations of the glycal. It is likely that 3-*O*-acetyl group in the *gluco*-configuration is able to release the acetyl radical more freely than that in the *galacto*-configuration. Also, the formation of the radical oxocarbenium ion and the thiolate anion should be relatively faster, since the addition of NaN_3 did not affect the course of the reaction, indicating the absence of the formation of ceric-azide intermediate, as suggested for the reactions involving CAN–NaN_3 in the typical azidonitration reactions.[2]

Upon synthesis of 2-deoxy-1-thioglycosides, few thioglycosides-mediated glycosylation reactions were performed. The results of NIS-TMSOTf-promoted glycosylation with aglycosyl as well as a glycosyl acceptors are presented in Table 2. The glycosylation proceeded smoothly to afford the α-anomer of the glycosides exclusively and in good yields.

A detailed ^{1}H NMR characterizations of **5**–**11** and **18**–**20** (Tables 3–5) were conducted to confirm the configurations of all newly formed compounds. The coupling constant $J_{2a,3} \sim 12.0$ Hz in the 2-deoxy derivatives indicates a diaxial orientation of H-2_a and H-3 protons. Lack of the coupling between H-4 and H-5 for compounds **5**, **6**, **8**, **9**, and **18**–**20** as well as a $J_{4,5}$ of ~7.5–9.5 Hz for the compounds **10** and **11** confirm *lyxo*- and *arabino*-configurations, respectively. The pattern of the H-1 resonance (Figs. 1 and 3) with a coupling constant of $J_{1,2a} \sim 5.7$ Hz (for compounds **5**, **8**, **10**) and of $J_{1,2a} \sim 3$ Hz (for compounds **18**–**20**) indicates the α-configuration at the anomeric center. In comparison, all β-isomers exhibited H-1 resonance as double doublets (Fig. 2) with $J_{1,2a} \sim 11.7$ Hz and $J_{1,2e} \sim 2$–3 Hz. Absence of a coupling between H-1 and H-2_e for compounds **5**, **8**, **10**, and **18**–**20** and a coupling between H-4 and H-5 for compounds **5**, **6**, **8**, **9**, and **18**–**20** is associated with an *anti*-periplanar orientation of the ring oxygen to one of the protons involved in vicinal coupling.[7,8] Assignments of the resonances of ^{1}H NMR and ^{13}C NMR (Fig. 4) for all compounds were confirmed further with the aid of ^{1}H–^{1}H COSY, ^{1}H–^{1}H TOCSY and ^{1}H–^{13}C HMQC experiments.

A number of methods are known to prepare 2-deoxyglycosides, few of which are: (i) radical-mediated dehalogenation,[9,10] desulfurization,[11] and deselenelation[12] of halo-, thio- or phenylseleno-group at the C-2 of the glycoside, respectively; (ii) deiodination at the C-2 of a pyranose by $Na_2S_2O_4$;[13] (iii) treatment of the glycals with acceptor alcohol in the presence (a) triphenylphosphine hydrobromide,[14] (b) CAN,[15] (c) $CeCl_3 \cdot 7H_2O$–NaI[16] and (d) specially treated sulfonic acid resin-soluble halide ion reagent.[5]

Table 3. ^{1}H NMR chemical shift and multiplicities in $CDCl_3$ of compounds **5**–**11** and **18**–**20**

	5[a]	**6**[a]	**7**[b]	**8**[b]	**9**[b]	**10**[a]	**11**[a]	**18**[a]	**19**[a]	**20**[a]
H-1	5.54 (d)	4.68 (dd)	4.58 (app. dd)	5.43 (d)	4.43 (dd)	5.45 (d)	4.52 (dd)	4.93 (d)	5.09 (d)	4.97 (d)
H-2_a	2.44 (ddd)		1.77 (ddd)	2.59–2.35[d]	2.13 (ddd)	2.05 (ddd)	1.78 (ddd)	2.01–1.97[c] (band)	2.06–1.91[c] (band)	2.03–1.91[c] (band)
		2.07–2.00[c] (band) (H-$2_{a,e}$)								
H-2_e	1.88 (dd)		2.30 (app. dd)	1.89 (dd)	1.98 (app. dd)	2.26 (dd)	2.36 (ddd)	1.86 (dd)	1.81–1.66[c] (band)	1.82–1.76[c] (band)
H-3	5.20 (ddd)	5.02 (ddd)		3.57–3.54 (m)	3.55–3.41 (broad)	3.87 (ddd)	3.70–3.65 (m)	5.22 (ddd)	5.24 (ddd)	
			4.97–4.92 (m) (H-3,H-4)							5.24–5.16 (m) (H-3,H-4)
H-4	5.33 (app. s)	5.29 (app. d)		3.81–3.75 (broad)	3.77 (app. s)	3.61 (app. t)	3.50 (app. t)	5.25 (app. s)	5.26 (app. s)	
H-5	4.55 (app. t)	3.85 (app. t)	3.58–3.54 (m)	4.18 (app. t)		4.14 (ddd)	3.70–3.65 (m)	4.08 (app. t)	4.17 (app. t)	4.07 (app. t)
					3.55–3.41 (broad) (H-5, H-6a,b)					
H-6_a		4.17 (dd)	4.20 (dd)			3.81 (dd)			4.02 (d)	
	4.11 (app. d)			3.81–3.75 (broad)			3.46–3.42 (m)	4.02 (app. d)		3.90 (app. t)
	(H-6a,b)			(H-6a,b)			(H-6a,b)	(H-6a,b)		(H-6a,b)
H-6b		4.11 (dd)	4.03 (dd)			3.76 (dd)			4.01 (d)	
SCH_2	2.68–2.52 (m)	2.79–2.67(m)	2.72–2.59 (m)	2.59–2.35 (m)	2.72–2.51(m)	2.78–2.48 (m)	2.78–2.48 (m)	—	—	—
CH_3	1.30	1.29	1.23	1.16	1.18	1.29	1.23	—	—	—
$COCH_3$	2.14 (s), 2.04 (s), 1.98 (s)	2.14, 2.07–2.00 (band)	2.00 (s), 1.97 (s), 1.96 (s)	—	—	—	—	2.01–1.97 (band), 1.91 (s)	2.06–1.91 (band)	2.03–1.91 (band), 1.82–1.76 (band)
$PhCH_2$	—	—	—	4.84 (d), 4.49–4.30 (m)	4.85 (d), 4.60–4.49 (m), 4.37–4.30 (m)	4.89 (d), 4.69–4.59 (m), 4.55 (d)	4.88 (d), 4.64–4.56 (m), 4.49–4.46 (m)	—	—	—
Ph-H	—	—	—	7.26–7.13 (m)	7.24–7.14 (m)	7.34–7.16 (m)	7.34–7.16 (m)	—	—	8.01–7.88 (m), 7.45–7.19 (m)
Others signal	—	—	—	—	—	—	—	3.56 (m), 3.32 (m), 1.66–1.25 (m), 0.83 (t)	3.48 (m), 1.81–1.66 (m), 1.28–1.14 (m)	6.08 (t), 5.56 (t), 5.24–5.16 (band), 4.17 (m), 3.79 (dd), 3.55 (dd), 3.41 (s)

[a] ^{1}H NMR recorded in 400 MHz NMR instrument.
[b] ^{1}H NMR recorded in 300 MHz NMR instrument.
[c] Signal overlapped with $COCH_3$ signal.
[d] Signal overlapped with SCH_2 signal.

Table 4. The ^1H–^1H coupling constants (Hz) for compounds **5**–**11** and **18**–**20**

Compound	$J_{1,2a}$	$J_{1,2e}$	$J_{2a,2e}$	$J_{2a,3}$	$J_{2e,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
5[a]	5.8	~0	12.9	12.7	4.9	3.1	~0	6.4	6.4	[c]
6[a]	10.8	3.0	[d]	11.0	5.9	2.7	~0	6.6	6.6	11.3
7[b]	11.7	[d]	11.8	11.7	3.3	[d]	[d]	5.1	2.5	12.3
8[b]	5.4	~0	12.9	[d]	4.2	[d]	[d]	6.3	6.3	[d]
9[b]	11.4	3.0	11.7	11.7	[d]	[d]	~0	[d]	[d]	[d]
10[a]	5.7	~0	13.2	11.7	3.0	7.7	7.7	4.2	1.8	10.6
11[a]	11.7	1.6	11.8	11.8	5.0	9.6	9.6	[d]	[d]	[d]
18[a]	3.0	~0	12.3	12.3	4.7	3.0	~0	6.4	6.4	[c]
19[a]	3.1	~0	[d]	12.2	4.8	3.0	~0	6.6	6.6	[d]
20[a,e]	2.5	~0	[d]	[d]	[d]	[d]	[d]	6.5	6.5	[c]

[a] ^1H NMR recorded in 400 MHz instrument.
[b] ^1H NMR recorded in 300 MHz instrument.
[c] Respective protons are both chemically and magnetically equivalent.
[d] Not determined.
[e] Coupling constant of the 2-deoxy sugar of disaccharide is presented.

Table 5. ^{13}C NMR chemical shift assignment of compound **5**–**11** and **18**–**20**

Compound	C-1	C-2	C-3	C-4	C-5	C-6	S-CH_2	Others signals
5[a]	79.93	30.27	66.72	66.72	66.80	62.38	24.77	170.44–169.87, 20.80–20.69, 14.74
6[a]	80.29	31.63	69.33	65.40	74.48	62.03	25.09	170.42–169.97, 20.77–20.66, 15.01
7[b]	79.85	29.66	71.77	68.94	75.89	66.66	25.07	170.75–169.74, 20.87–20.69, 14.95
8[b]	80.12	31.30	73.32	73.21	70.38	69.37	24.64	138.74–127.99, 75.40-69.90, 14.75
9[b]	80.14	32.50	74.06	73.45	70.04	69.29	24.53	138.85–127.21, 78.32–71.74, 14.97
10[a]	80.10	35.78	78.01	77.97	71.75	69.48	24.79	138.47–127.45, 77.21–71.43, 14.84
11[a]	80.66	36.95	79.27	78.41	71.76	68.79	24.83	138.39–127.50, 76.99–70.83, 15.01
18[a]	97.37	29.67	66.54	66.30	66.74	62.56	—	170.55–170.11, 67.89, 31.57, 29.67, 29.38, 25.87, 22.56, 20.87–20.73, 14.10
19[a]	95.47	30.71	66.60	66.39	66.83	62.56	—	170.47–170.35, 75.39, 33.29, 31.53, 29.65, 25.23, 23.92, 20.85–20.71
20[a]	97.48	29.80	66.09	65.90	66.74	62.62	—	170.45–165.21, 133.40–128.25, 96.96, 72.05, 70.40, 69.44, 68.21, 66.69, 55.59, 20.69–20.54

[a] ^{13}C NMR recorded in 100 MHz instrument.
[b] ^{13}C NMR recorded in 75 MHz instrument.

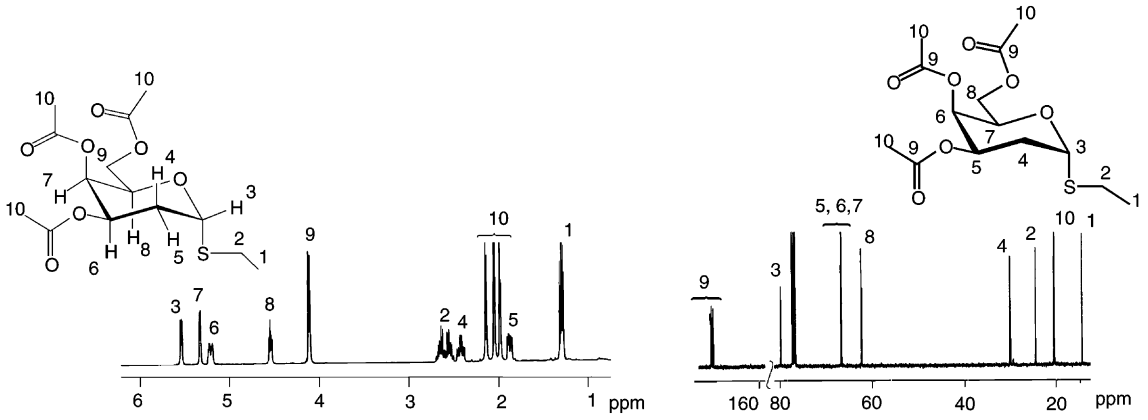


Figure 1. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **5** in $CDCl_3$.

A desire for the development of methods for preparing 2-deoxyglycosides is based on the importance of such units present in many biologically important natural products, such as, olivomycin, chromomycin, campactin, calicheamycin, and many other antitumor antibiotics.[17] The method described herein should be useful, since an activated glycosyl donor, namely, 2-deoxy-1-thioglycoside, is derived. Such activated glycosyl donor should find utility in the glycosylation of a variety of glycosyl acceptors.

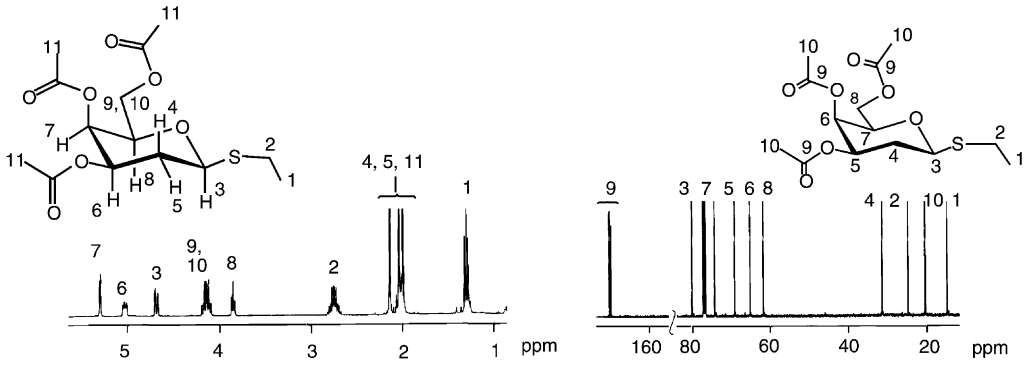


Figure 2. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra of **6** in $CDCl_3$.

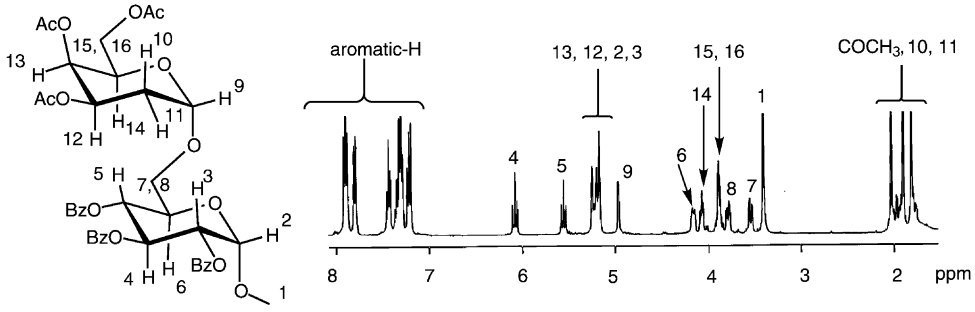


Figure 3. ^{1}H NMR (400 MHz) spectrum of **20** in $CDCl_3$.

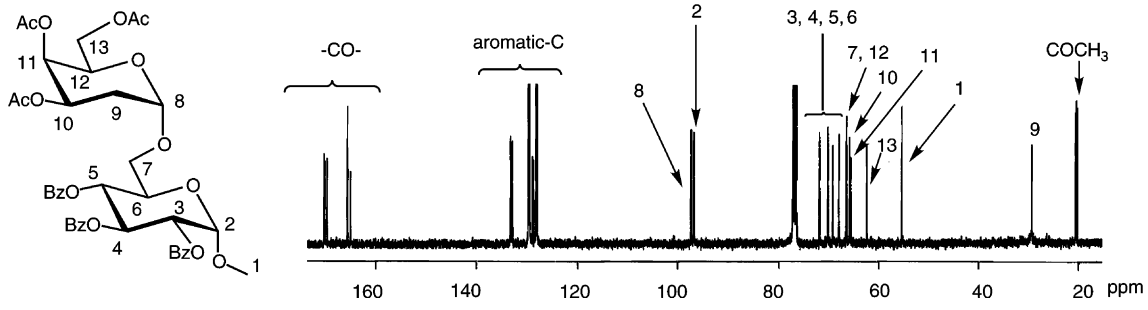


Figure 4. ^{13}C NMR (100 MHz) spectrum of **20** in $CDCl_3$.

3. Experimental

3.1. General methods

Chemicals were purchased from commercial sources and were used without further purification. CAN (AR grade) was dried at 60–70 °C for 48 h at high vacuum before being used. Solvents were dried and distilled according to the literature procedures. Analytical TLC was performed on commercial Merck plates coated with silica gel GF_{254} (0.25 mm). Silica gel (100–200 mesh) was used for column chromatography. Optical rotations were recorded on a Jasco Model DIP-370 polarimeter at the sodium D line at 25 °C. High-resolution mass spectra were obtained from Q-TOF instrument by electrospray ionization (ESI) technique. ^{1}H and ^{13}C NMR spectral analyses were performed on a spectrometer operating at 300/400 and 75/100 MHz, respectively, with residual solvent signal acting as the internal standard. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; m, multiplet; band, several overlapping signals and br., broad.

3.2. General procedure for the synthesis of 2-deoxy-1-thioglycosides

A mixture of tri-*O*-acetyl/tri-*O*-benzyl glycal (1 mmol), CAN (10 mol%) in MeCN was stirred at 0 °C for 15 min. A solution of EtSH (5 mmol) in MeCN was added dropwise to the reaction mixture and stirring

was continued for 15 h at room temperature, the reaction mixture extracted with ether, dried, concentrated in vacuo. The resulting crude product was subjected to column chromatography to afford 2-deoxy-1-thioglycosides.

3.3. Ethyl 2-deoxy-3,4,6-tri-*O*-acetyl-1-thio-α-D-lyxo-hexopyranoside (5)

39%; R_f = 0.45 (35% EtOAc/pet.ether); $[\alpha]_D$ +263 (*c* 1.2, $CHCl_3$). HR-MS: *m/z* calcd for $C_{14}H_{22}O_7SNa$ = 357.0984. Found: 357.0970.

3.4. Ethyl 2-deoxy-3,4,6-tri-*O*-acetyl-1-thio-β-D-lyxo-hexopyranoside (6)

31%; R_f = 0.38 (35% EtOAc/pet.ether); $[\alpha]_D$ +29 (*c* 1.00, $CHCl_3$). HR-MS: *m/z* calcd for $C_{14}H_{22}O_7SNa$ = 357.0984. Found: 357.0981.

3.5. Ethyl 2-deoxy-3,4,6-tri-*O*-acetyl-1-thio-β-D-arabino-hexopyranoside (7)

35%; R_f = 0.41 (35% EtOAc/pet.ether); $[\alpha]_D$ −45 (*c* 1.2, $CHCl_3$). HR-MS: *m/z* calcd for $C_{14}H_{22}O_7SNa$ = 357.0984. Found: 357.1000.

3.6. Ethyl 2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-α-D-lyxo-hexopyranoside (8)

51%; R_f = 0.44 (15% EtOAc/pet.ether); $[\alpha]_D$ +133 (*c* 0.98, $CHCl_3$). HR-MS: *m/z* calcd for $C_{29}H_{34}O_4SNa$ = 501.2076. Found: 501.2095.

3.7. Ethyl 2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-β-D-lyxo-hexopyranoside (9)

34%; R_f = 0.37 (15% EtOAc/pet.ether); $[\alpha]_D$ −29 (*c* 0.94, $CHCl_3$). HR-MS: *m/z* calcd for $C_{29}H_{34}O_4SK$ = 517.1815. Found: 517.1841.

3.8. Ethyl 2-deoxy-3,4,6-tri-*O*-benzyl-1-thio-D-arabino-hexopyranoside (10, 11)

68%; R_f = 0.33 (15% EtOAc/pet.ether). HR-MS: *m/z* calcd for $C_{29}H_{34}O_4SK$ = 517.1815. Found: 517.1837.

3.9. Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-1-thio-D-threo-hex-2-enopyranoside

9%; R_f = 0.31 (15% EtOAc/pet.ether). α-anomer (**12**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ : 6.11 (dd, 1 H, *J* = 2.8, 10.2 Hz, H-3), 6.02 (d, 1H, *J* = 10 Hz, H-2), 5.66 (app. s, 1H, H-1), 5.08 (dd, 1H, *J* = 2.4, 4.8 Hz, H-4), 4.55 (app. t, 1H, *J* = 4.9 Hz, H-5), 4.27–4.22 (m, 2H, H-6a, H-6b), 2.79–2.60 (m, 2H, SCH_2), 2.09 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 1.33 (t, 3H, *J* = 7.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ : 170.57, 170.29, 131.99 (C-2), 123.67 (C-3), 79.68 (C-1), 66.61(C-4), 63.43 (C-5), 62.65 (C-6), 25.59 (SCH_2), 20.79, 20.71, 15.21. β-anomer (**13**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ : 5.87–5.77 (m, 2H, H-3, H-2), 5.29 (app. s, 1H, H-1), 5.07–5.04 (m, 1H, H-4), 4.20–4.24 (m, 2H, H-6a, H-6b), 3.98–3.90 (m, 1H, H-5), 2.53–2.65 (m, 2H, SCH_2), 2.09 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 1.32 (t, 3H, *J* = 7.5 Hz, CH_3). HR-MS: *m/z* calcd for $C_{12}H_{18}O_5SNa$ = 297.0773. Found: 297.0763.

3.10. Ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-1-thio-D-erythro-hex-2-enopyranoside[18]

55%; R_f = 0.32 (15% EtOAc/pet.ether). α-anomer (**14**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.94 (dd, 1 H, *J* = 2.1, 10.5 Hz, H-3), 5.78 (d, 1H, *J* = 10.5 Hz, H-2), 5.58 (br. s, 1H, H-1), 5.37 (dd, 1H, *J* = 1.5, 9.3 Hz, H-4), 4.35–4.15 (m, 3H, H-5, H-6a, H-6b), 2.79–2.59 (m, 2H, SCH_2), 2.09 (br. s, 6H, $COCH_3$), 1.26 (t, 3H, *J* = 7.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 170.69, 170. 21, 129.04 (C-2), 126.71 (C-3), 80.02 (C-1), 66.67 (C-4), 65.03 (C-5), 62.91 (C-6), 25.99 (SCH_2), 20.92, 20.69, 15.22. β-anomer (**15**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 5.94–5.85 (m, 2H, H-3, H-2), 5.40 (app. s, 1H, H-1), 5.29 (app. d, 1H, *J* = 8.1 Hz, H-4), 4.25–4.22 (m, 2H, H-6a, H-6b), 3.88–3.82 (m, 1H, H-5), 2.75–2.57 (m, 2H, SCH_2), 2.09 (br. s, 6H, $COCH_3$), 1.29 (t, 3H, *J* = 7.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 170.74, 170.15, 130.44 (C-2), 127.01 (C-3), 78.80 (C-1), 74.75 (C-4), 64.70 (C-5), 63.26 (C-6), 23.24 (SCH_2), 20.92, 20.76, 15.04. HR-MS: *m/z* calcd for $C_{12}H_{18}O_5SNa$ = 297.0773. Found: 297.0777.

3.11. Ethyl 4,6-di-*O*-benzyl-2,3-dideoxy-1-thio-D-erythro-hex-2-enopyranoside

15%; R_f = 0.47 (15% EtOAc/pet.ether). α-anomer (**16**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.33–7.23 (m, 10H, aromatic-H), 5.95 (d, 1H, *J* = 10.2 Hz, H-2), 5.85 (dd, 1H, *J* = 1.8, 10.1 Hz, H-3), 5.57 (br s, 1H, H-1), 4.66–4.45 (m, 4H, $PhCH_2$), 4.25 (dd, 1H, *J* = 1.7, 9.2 Hz, H-4), 3.79–3.74 (m, 2H, H-5, H-6a), 3.69 (dd, 1H, *J* = 1.8, 10.6 Hz, H-6b), 2.77–2.62 (m, 2H, SCH_2), 1.28 (t, 3H, *J* = 7.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 138.18, 138.10, 128.39 (C-2), 128.34, 127.89, 127.88, 127.85, 127.77 (C-3), 80.29 (C-1), 73.32 (C-4), 71.09, 70.23, 68.99 (C-5), 68.87(C-6), 25.98 (SCH_2), 15.32. β-anomer (**17**): ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.31–7.24 (m, 10H, aromatic-H), 6.01 (dd, 1H, *J* = 1.9, 10.2, H-3), 5.81 (dd, 1H, *J* = 1.8, 10.2 Hz, H-2), 5.37 (d, 1H, *J* = 1.8 Hz, H-1), 4.58–4.41 (m, 4H, $PhCH_2$), 4.18–4.15 (m, 3H, H-4, H-6a, H-6b), 4.07–4.09 (m, 1H, H-5), 2.73–2.58 (m, 2H, SCH_2), 1.26 (t, 3H, *J* = 7.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 138.39, 137.91,

129.11 (C-2), 128.57, 128.44, 127.94, 127.73, 127.63 (C-3), 127.55, 79.10 (C-1), 77.89, 73.39 (C-4), 71.30, 70.02 (C-5), 69.77 (C-6), 23.65 (SCH_2), 15.23. HR-MS: *m/z* calcd for $C_{22}H_{26}O_3SNa$ = 393.1500. Found: 393.1508.

3.12. General procedure for the synthesis of 2-deoxy glycosides

To a stirred solution of 2-deoxy-1-thioglycoside (1 mmol), alcohol (1.2 mmol), NIS (1.2 mmol) and molecular sieves (4 Å) (0.4 g) in CH_2Cl_2 (6 mL) at 0 °C, TMSOTf (10 mol% in CH_2Cl_2) was added. After 15 min stirring at 0 °C, the reaction mixture was extracted with CH_2Cl_2, washed with aq $Na_2S_2O_3$ (5%) solution, brine, and concentrated in vacuo. The desired 2-deoxy glycoside was purified by column chromatography.

3.13. Hexyl 2-deoxy-3,4,6-tri-*O*-acetyl-α-D-lyxo-hexopyranoside (18)

90%; R_f = 0.59 (35% EtOAc/pet.ether); $[\alpha]_D$ +93 (*c* 1.5, $CHCl_3$). HR-MS: *m/z* calcd for $C_{18}H_{30}O_8Na$ = 397.1838. Found: 397.1835.

3.14. Cyclohexyl 2-deoxy-3,4,6-tri-*O*-acetyl-α-D-lyxo-hexopyranoside (19)

83%; R_f = 0.51 (35% EtOAc/pet.ether); $[\alpha]_D$ +108 (*c* 1.00, $CHCl_3$). HR-MS: *m/z* calcd for $C_{18}H_{28}O_8Na$ = 395.1682. Found: 395.1667.

3.15. Methyl 2,3,4-tri-*O*-benzoyl-6-*O*-(2-deoxy-3,4,6-tri-*O*-acetyl-α-D-lyxo-hexopyranosyl)-α-D-glucopyranoside (20)

75%; R_f = 0.69 (60% EtOAc/pet.ether); $[\alpha]_D$ +83 (*c* 1.07, $CHCl_3$). HR-MS: *m/z* calcd for $C_{40}H_{42}O_{16}Na$ = 801.2371. Found: 801.2401.

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