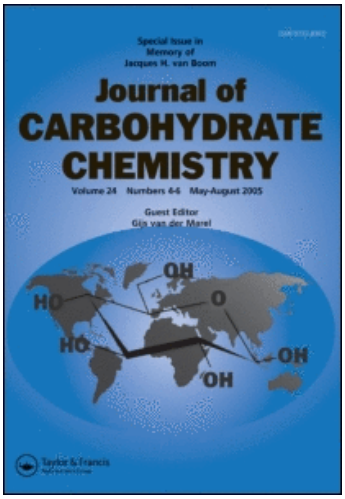

Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Tronchet, Jean M. J. , Zosimo-Landolfo, Guido , Galland-Barrera, Griselda and Barbalat-Rey, Françoise(1991) 'Communication: Blocked Disaccharide Analogs Bearing an Oxyimino Interglycosidic Bridge', Journal of Carbohydrate Chemistry, 10: 4, 723 — 728

To link to this Article: DOI: 10.1080/07328309108543945

URL: http://dx.doi.org/10.1080/07328309108543945

J. CARBOHYDRATE CHEMISTRY, 10(4), 723-728 (1991)

COMMUNICATION

BLOCKED DISACCHARIDE ANALOGS BEARING AN OXYIMINO INTERGLYCOSIDIC BRIDGE[1]

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Received December 11, 1990 - Final Form January 7, 1991

Oligosaccharide units in which a ONH group replaces the usual oxy bridge have been encountered in nature, for ex. in the antitumor antibiotic calicheamicin γ^{I},[2] and the biological importance of this peculiar interglycosidic junction has been emphasized.[3] The N-O bond is very different from the bonds habitually found in carbohydrate chemistry, owing, in particular, to its weakness and the presence of lone-pairs on its two hetero atoms. These characteristics considerably affect the conformational properties of molecules like calicheamicin. As we have developed,[4] in the CHARMm force field,[5] parameters pertaining to this bond, we needed models of disaccharides of this type to fit computed results in with experimental data. These O-N-disaccharide derivatives were easily obtained from the *O*-aminosugar derivative **1**.[6]

Reacted with one of the carbonyl sugar derivatives **2**,[7] **3**,[8] or **4**,[9] **1** gave the corresponding oximes **5**, **6**, or **7** respectively. From their time-averaged PMR spectra (TABLES I and II), it was obvious that these oximes in solution existed as a mixture of *E* and *Z* isomers and in the case of the aldoximes **6** and **7**, the configurational assignment was easily made on the basis of the chemical shift of the N=CH methine proton, more deshielded in the *E* than in the *Z* isomer.[10] Cyanoborohydride reduction in acidic conditions of **5**, **6**, and **7** led respectively to the title compounds **8**, **9**, and **10**, whose study by variable temperature

PMR and molecular mechanics will be reported later. The *N*-acetyl derivative **11** and the triazene derivative **12** were easily prepared from **10**.

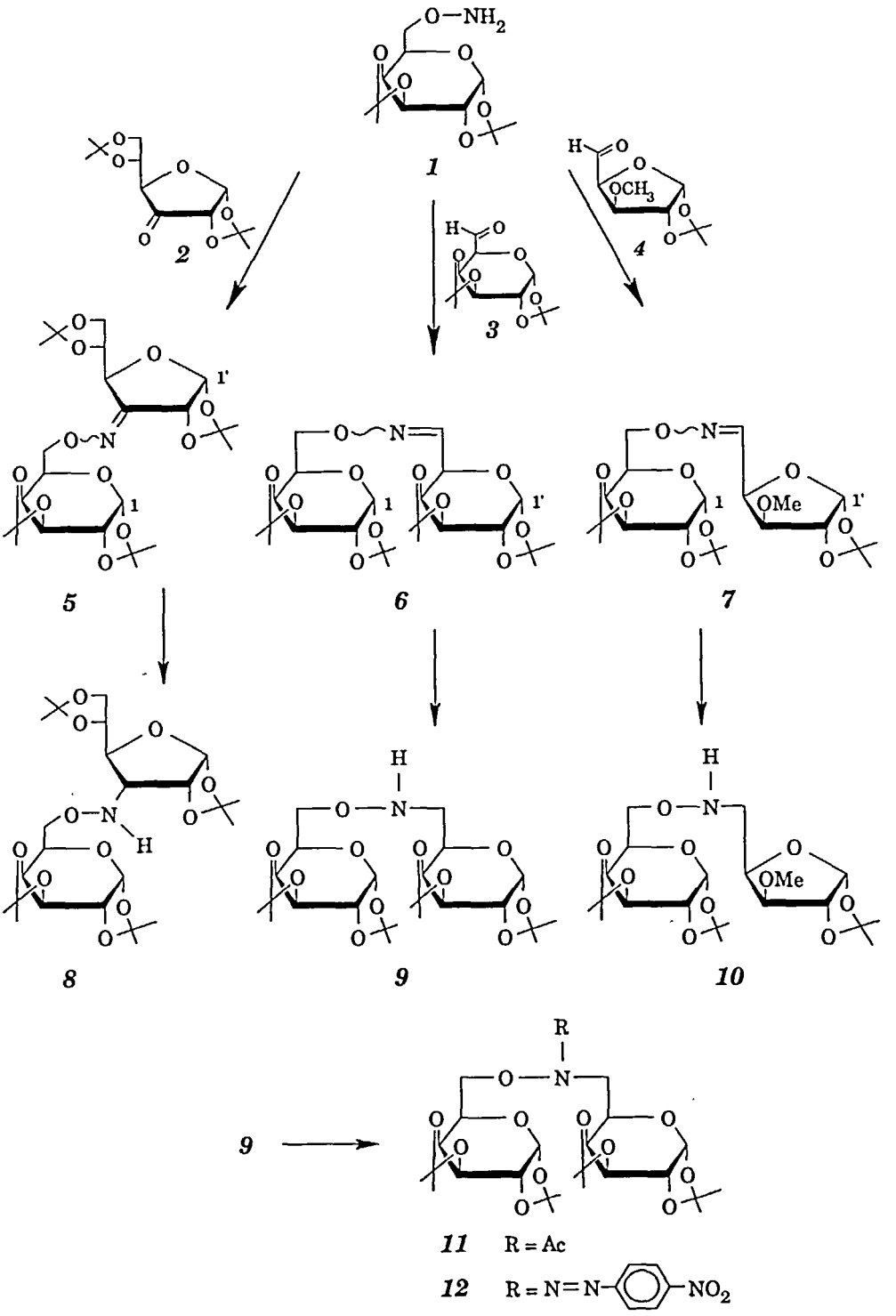

TABLE I. Chemical shifts of compounds 5-12 (PMR, 200 MHz, $CDCl_3$, δ values)

Compd	H-C_1	H-C_2	H-C_3	H-C_4	H-C_5	H-C_6	H-C'$_1$	H-C'$_2$	H-C'$_3$	H-C'$_4$	H-C'$_5$	H-C'$_6$	Others
5[a]	5.51	4.33	4.60	——	4.12 - 4.45	——	5.97	5.20		4.84	4.41	3.89 4.00	
E-6[b]	5.54	4.33	4.62	——	4.15 - 4.30	——	5.57	4.33	4.62	~4.20	4.41	7.49	
Z-6	5.50	~4.30	4.70	——	4.10 - 4.30	——	5.58	~4.30	~4.72	~4.30	~4.93	6.78	
E-7[c]	5.55	4.32	4.68	——	4.15 - 4.30	——	5.95	4.65	3.76	4.70	7.50		3.40 (CH_3O)
Z-7	5.55	4.32	4.68	——	4.15 - 4.30	——	5.95	4.61	4.17	5.15	6.89		3.40 (CH_3O)
8	5.57	4.33	4.61	4.20	4.09	3.89	5.85	4.74	3.57	3.78	4.40	4.05 4.10	6.11 (NH)
9	5.52	4.30	4.59	— 4.08-4.25—		3.88	5.54	4.30	4.61	— 4.08-4.25—		3.15	5.96 NH)
10	5.55	4.35	4.60	4.20	4.18	3.86	5.89	4.59	3.70	4.43	3.20 3.27		5.78 (NH) 3.40 (CH_3O)
11	5.52	4.32	4.61	——	3.95 - 4.30	——	5.57	4.30	4.64	— 3.95-4.30—		3.66 3.84	2.23 (CH_3CO)
12	5.55	~4.40	4.66	——	4.08 - 4.48	——	5.60	~4.40	4.69	—— 4.08 - 4.48——			8.20 and 7.65 (AA'BB' system, Ar)

[a] Major isomer. [b] *E*/*Z* = 1.25. [c] *E*/*Z* = 0.3.

TABLE II. Coupling Constants of Compounds 5-12 (J in Hz)

Compd	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{5',6'}$	Others
5[a]	5.0	2.4	8.0	4.4			7.4	$J_{2',4'}$ 1.0, $J_{6'a,6'b}$ 7.6 $J_{4',5'}$ 2.8, $J_{4,5}$ 2.2
E-6	5.0	2.5	6.0	5.0	2.5	6.0	7.0	$J_{4',5'}$ 2.0
Z-6	4.4	2.2	6.0	4.4	2.2	6.0	4.0	$J_{4',5'}$ 2.0
E-7	5.0	2.5	8.0	4.0	0	3.5		$J_{4',5'}$ 7.0
Z-7	5.0	2.5	8.0	4.0	0	3.5		$J_{4',5'}$ 3.5
8	5.0	2.5	8.0	4.0	5.0	10.0	7.0 7.0	$J_{3,NH}$ 11.0, $J_{6a,6b}$ 8.0 $J_{4',5'}$ 4.0, $J_{4,5}$ 1.5
9	5.0	2.5	8.0	5.0	2.5	8.0	?	
10	5.0	2.2	8.0	4.0	0	3.2		$J_{5a,5b}$ 13.0, $J_{4',5'a}$ 7.0, $J_{4',5'b}$ 5.0
11	5.0	2.2	8.0	5.0	2.2	8.0	8.5	$J_{6'a,6'b}$ 15.0
12	5.0	2.2	8.0	5.0	2.2	8.0	?	

[a] Major isomer.

TABLE III. Some Data relative to Disaccharide Analogs 5-12.

Compd	Yield	M.p.	Elementary Analysis					
			Calcd			Found		
			C	H	N	C	H	N
5	63	syrup	55.91	7.23	2.72	55.79	7.45	2.69
6	61	154-156	55.91	7.23	2.72	55.78	7.15	2.70
7	60	124-128	54.89	7.24	3.05	54.70	7.45	2.96
8[a]	60	syrup	55.70	7.60	2.71	55.71	7.76	2.62
9[b]	59	syrup	55.70	7.60	2.71	55.84	7.68	
10[c]	70	syrup	54.65	7.64	3.03	54.39	7.48	3.30
11[d]	84	123-125	55.80	7.38	2.50	56.12	7.61	2.45
12[e]	40	syrup	54.05	6.35	8.40	54.30	6.39	8.22

[a] $[\alpha]_D^{20}$ -1.6° (c 0.2); [b] $[\alpha]_D^{22}$ -108° (c 1.7); [c] $[\alpha]_D^{21}$ -54.5° (c 1.1); [d] $[\alpha]_D^{22}$ -47° (c 1.7); [e] $[\alpha]_D^{28}$ -81° (c 0.7)

EXPERIMENTAL

General Procedures. See ref. 11. For the chromatographic separations, silica gel and 2:1 AcOEt/hexane were used. PMR data are collected in TABLES I and II, other data in TABLE III. Optical rotations were measured on $CHCl_3$ solutions.

Preparation of oximes. A solution of **1** (2.75 g, 10 mmol) and of one of the carbonyl sugars derivatives **2-4** (10.5 mmol) in ether (50 mL) was kept at room temp. for 12 h. A mixture of *E* and *Z* oximes (**5-7**) was obtained by column chromatography.

Reduction of oximes. To a solution of one of the oximes **5-7** (1 mmol) and $NaBH_3CN$ (5.5 mmol) in MeOH (100 mL), 1M HCl was added dropwise to maintain the pH at 2-3. After completion of the reaction, the mixture was neutralized (aqueous saturated $NaHCO_3$) extracted with Et_2O (3x50 mL), and the organic phase concentrated, then submitted to column chromatography to give the *N*-*O*-diglycosylhydroxylamine derivatives **8-10**.

6-*O*-(*N*-Acetyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-ylamino)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (11). A solution of **9** (1 g,

2 mmol) in dry pyridine (30 mL) and Ac_2O (15 mL) was kept 14 h at room temp., then extracted as usual. Column chromatography gave **11**.

6-*O*-(6-deoxy-1,2:3,4-di-*O*-isopropylidene-*N*-*p*-nitrophenylazo-α-D-galacto-pyranos-6-ylamino)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (12). A solution of **9** (1 g, 1.93 mmol) and *p*-nitrobenzenediazonium tetrafluoroborate (500 mg, 2.2 mmol) in EtOH (100 mL) was kept at room temp. for 0.5 h, then aqueous saturated $NaHCO_3$ (100 mL) was added and the mixture extracted with Et_2O (3x50 mL). **12** was purified by thick layer chromatography.

ACKNOWLEDGMENT

This work was supported by the Swiss National Science Foundation (Grant 20-26460-89).

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