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Note

Synthesis of new anhydro and branched-chain cyclitols [1,2]

Zoltán G. Tóth, István F. Pelyvás *, Csaba Szegedi, Péter Benke, Erika Magyar, Tünde Miklovicz, Gyula Batta, Ferenc Sztaricskai *

Research Group of Antibiotics of the Hungarian Academy of Sciences, P.O. Box 70, Debrecen H-4010, Hungary

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Abstract

Starting from D-glucose and D-(−)-quinic acid (**5**) (1*S*,5*R*,6*S*)-5-azido-6-benzyloxycyclohex-2-en-1-ol (**3**), and the structurally related α,β-unsaturated alcohols **7** and **8**, respectively, were prepared. They have been transformed, by treatment with 3-chloroperoxybenzoic acid, into (1*R*,2*S*,3*R*,5*S*,6*R*)-3-azido-2-benzyloxy-5,6-epoxycyclohexane-1-ol (**4**) and the two diastereoisomeric 4,5-isopropylidenedioxycyclohexane-1-ols **9** and **10**. Thermal Claisen rearrangement of the allylic alkcohols **3**, **7** and **8** resulted in the functionalized branched-chain cyclohexenyl acetamides **12**, **13** and **14**, respectively. The prepared new cyclitols are useful starting materials for further derivatization to obtain novel enzyme-inhibitors, including phosphorylated cyclitols with "second-messenger" properties. © 1997 Elsevier Science Ltd.

Keywords: Cyclitols; Enzyme inhibitors

Since the discovery of the role of D-*myo*-inositol 1,4,5-triphosphate ($Ins P_3$) as an intracellular second messenger for calcium mobilization [1], as well as certain anhydro and aminocyclitol derivatives (such as cyclophellitol [2] and conduramines [3], respectively) possessing glycosidase enzyme inhibitory activity [4], interest in the chemical synthesis of cyclitol derivatives [5] has greatly increased. In continuation of our research aimed at the preparation of chiral cyclitols from carbohydrates [6] and related substances, we now report on the synthesis of novel azido, anhydro and branched-chain cyclitols for enzyme-inhibitory investigations and further chemical derivatization, including phosphorylation.

The carbohydrate-based synthesis of anhydrocyclitols started from (2*S*,3*R*,5*R*)-3-azido-2-benzyloxy-5-hydroxycyclohexanone (**1**), prepared [7] in this laboratory from D-glucose in eleven steps with a ca. 6% overall yield. β-Elimination of the C-5 hydroxyl group of **1** was effected by treatment with methanesulfonyl chloride in pyridine to give the unstable enone **2** as shown by the appearance of two olefinic protons at δ 7.0 and 6.02 ppm in the ^1H NMR spectrum. For the stereoselective reduction of the keto function in **2**, the Luche procedure [8] employ-

* Corresponding authors.

[1] A part of this work was presented at the *5th International Conference on Chemical Synthesis of Antibiotics and Related Microbial Products*, Debrecen (Hungary), 1–6 September, 1996, Abstr. OL-8.

[2] Dedicated to Professor Dr. Hans Paulsen on the occasion of his 75th birthday.

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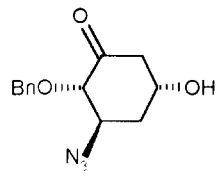

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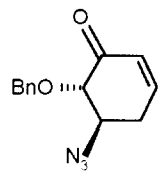

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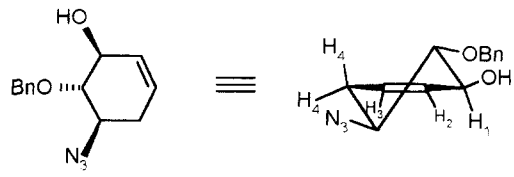

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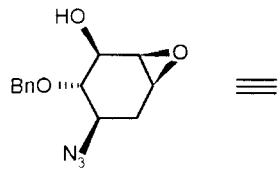

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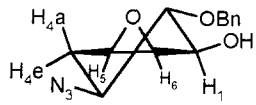

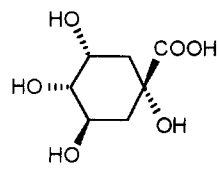

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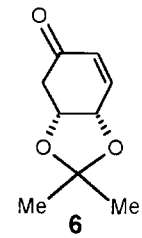

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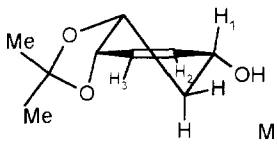

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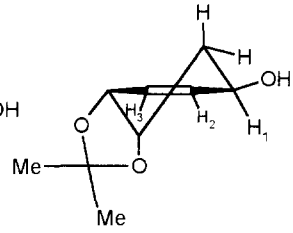
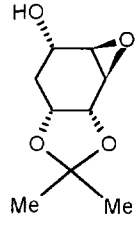


(1*R*)-**8**



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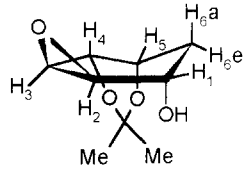
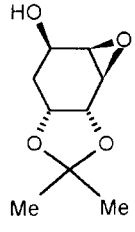


(1*S*,2*R*,3*R*,4*S*,5*R*)



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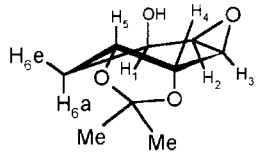
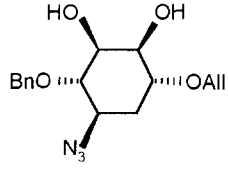


(1*R*,2*R*,3*R*,4*S*,5*R*)



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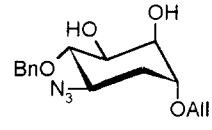
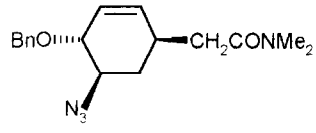
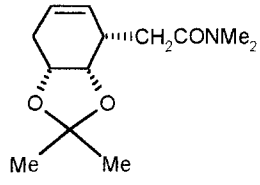


(1*S*,2*S*,3*S*,4*R*,6*R*)



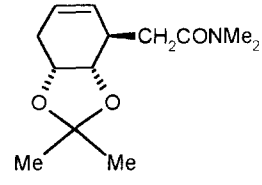
(1*R*,4*R*,5*R*)

12



(1*S*,5*R*,6*S*)

13



(1*R*,5*R*,6*S*)

14

ing sodium borohydride and cerium(III) chloride in methanol was found the best, affording a ca. 9:1 mixture of the (1*S*,5*R*,6*S*)-allyl alcohol **3** and the corresponding C-1 diastereoisomer (the latter of which could not be isolated in pure form). The values of the ^{1}H NMR coupling constants observed for **3** ($J_{1,6}$ 7, $J_{5,6} = J_{4a,5}$ = 10.5, and $J_{4e,5}$ 6 Hz) revealed that the C-1 hydroxyl group is *trans-pseudoequatorially* oriented to the C-6 benzyloxy function in the favoured $^6H_5$ half-chair conformer.

For obtaining the desired anhydrocyclitols the olefinic bond of the allyl alcohol **3** was epoxidized with 3-chloroperoxybenzoic acid to furnish a separable 8:1 mixture of two compounds. The major epox-

ide **4**, isolated in 62% yield, had an (1*R*,2*S*,3*R*,5*S*,6*R*) absolute configuration as proved by NOE difference experiments. Thus, irradiation of the ^{1}H NMR spectrum of **4** with the frequencies of H-4a and H-4e caused a 1.5% and 5% NOE enhancement, respectively, of the H-5 signal (δ 3.18). This observation, as well as that irradiation with the H-1 frequency, resulted in a 6% NOE enhancement of the signal of H-6 at $\delta = 3.25$ clearly proved that the protons H-5 and H-6 are closer to H-4e and H-1, and thus the epoxy function, the C-1 hydroxyl group, and the H-4a proton are located on the same side of the cyclohexane ring.

A noncarbohydrate-based route to anhydrocyclitols structurally related to **4** involved conversion of D-(−)-quinic acid (**5**) into (4*S*,5*R*)-4,5-*O*-isopropylidenedioxycyclohex-5-en-4-one (**6**) by means of modifications of known procedures [9,10]. Then the Luche reduction of **6**, as described for **3**, afforded a 2:1 separable mixture of the two α,β-unsaturated alcohols (1*S*)-**7** and (1*R*)-**8**. Based on the values of the ^{1}H NMR coupling constants measured for the major product **7** ($J_{1,6a} = J_{5,6a} = 9$, $J_{1,6e}$ 4.5, $J_{5,6e}$ 4.5, $J_{3,4}$ 2, and $J_{4,5}$ 5.5 Hz) the C-1 hydroxyl group is *pseudoequatorial* and *cis*-oriented to the dioxolane ring ($^5H_6$ conformation). In the minor isomer **8** the hydroxyl group at C-1 is also *pseudoequatorial* ($J_{1,6a}$ 10 and $J_{1,6e}$ 4.5 Hz), but *trans* to the acetal function in the favoured $^6H_5$ conformer ($J_{5,6a}$ 2.5 and $J_{5,6e}$ 2 Hz).

According to ^{13}C NMR data, epoxidation of the allyl alcohols **7** and **8** with 3-chloroperoxybenzoic acid in dichloromethane produced the anhydrocyclitols **9** and **10** as the major products, with 92 and 86% diastereomeric excess, respectively. The conformation of **9** and **10** and the steric arrangement of the anhydro ring was studied by means of ^{1}H NMR, COSY, and NOE experiments. Thus, the small values (2.0–4.5 Hz) of the coupling constants observed for **9**, as well as irradiation with the frequency of H-1 (causing a 5% NOE enhancement of the H-6a signal) and with that of H-2 (resulting in a small NOE effect in the signal of H-1), indicated that the anhydro ring and the OH-1 substituent are in *trans* relation in **9**. On the other hand, the ^{1}H NMR data of **10** ($J_{1,2} = J_{1,6a} = J_{1,6e} = 3$, $J_{5,6a}$ 11, $J_{5,6e}$ 1.5, and $J_{3,4} = J_{4,5} =$ 5.2 Hz) suggested a *cis* steric arrangement of the epoxide and OH-1 functions.

Opening of the oxirane ring of compounds **4**, **9**, and **10** with nucleophiles permits the synthesis of functionalized (azido and amino) cyclitol derivatives that are suitable for phosphorylation to obtain various analogues of InsP_3 with potential 'second messenger' properties. For such purposes **4** was treated with allyl alcohol in the presence of boron trifluoride etherate to afford, in 80% yield, (1*S*,2*S*,3*S*,4*R*,6*R*)-6-allyloxy-4-azido-3-benzyloxycyclohexane-1,2-diol (**11**). A *diaxial*-opening of the oxirane ring was concluded from the values ($J_{1,2}$ 3.0, $J_{2,3} = J_{3,4} = 9.0$, $J_{4,5a}$ 11.5, $J_{4,5e}$ 4, $J_{5a,6}$ 3, and $J_{5e,6}$ 4 Hz) of the ^{1}H NMR coupling constants, demonstrating that compound **11** exists in a $^3C_6$ chair conformation. This high-yielding oxirane ring cleavage with allyl alcohol is of practical importance for distinguishing between the C-3 and C-6 hydroxyl functions upon deprotection (and subsequent phosphorylation) of a 1,2-acetal derivative of the azidocyclitol **11**.

Synthetic analogues of the natural branched-chain cyclitols and anhydrocyclitols may be of interest for biological investigation including structure–activity relationship studies. For the synthesis of related compounds, unsaturated cyclitols **3**, **7**, and **8** were subjected to a thermal Claisen rearrangement [11] with *N*,*N*-dimethylacetamide dimethyl acetal. The functionalized cyclohexenyl acetamides **12**, **13** and **14**, respectively, were isolated in over 70% yield. The NMR data clearly showed that the amide-acetal rearrangement expectedly proceeded with a complete chirality transfer from carbon C-1 of the enol to the β-position. As an example, the values of the $J_{1,6}$ coupling constants ($J_{1,6}$ 10 and $J_{1,6'}$ 2.5 Hz) indicate the (1*R*,4*R*,5*R*) absolute configuration of **12**, and thus the *cis* arrangement of the C-1 and C-5 substituents.

Further chemical derivatization and biological investigation of the prepared new anhydro and branched-chain cyclitol derivatives are in progress

1. Experimental

General.—Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 283 B instrument. ^{1}H (200 MHz) and ^{13}C NMR spectra (50.3 MHz) were recorded with a Bruker 200 SY spectrometer (internal TMS). See Tables 1 and 2. Mass spectra were recorded with AEI-MS 902 and VG-7035 instruments. TLC and column chromatography were performed on Kieselgel 60 F_{254} (E. Merck) and Silica Gel 60 (E. Merck), using (A) 6:4 hexane–ethyl acetate, (B) 96:4 toluene–methanol, (C) 9:1

Table 1
^{13}C NMR data for compounds **3**, **4** and **7–14** [a]

Compound	Solvent	Chemical shifts (δ) in ppm									
		C-1	C-2	C-3	C-4	C-5	C-6	$PhCH_2$-	$C(CH_3)_2$	$C(CH_3)_2$	Others
3	Acetone-d_6	85.52	131.56 [b]	124.61 [b]	31.99	61.53	73.55	75.02	–	–	–
4	Acetone-d_6	82.20	72.81	60.80	30.19	51.73	58.32	75.44	–	–	–
7	Acetone-d_6	65.16	137.73 [b]	123.92 [b]	73.02	71.17	35.77	–	28.30 25.96	109.89	–
8	Acetone-d_6	62.51	135.30 [b]	126.73 [b]	73.36	71.90	35.13	–	27.76 26.24	108.64	–
9	Acetone-d_6	64.60	54.56	52.49	72.51	71.22	25.92	–	28.19 25.39	109.36	–
10	Acetone-d_6	63.21	56.55	55.05	74.19	70.54	26.94	–	27.53 25.24	109.41	–
11	$CDCl_3$	74.76	81.99	71.79	60.12	29.73	70.27	75.04	–	–	-$OCH_2CH=CH_2$; 117.09 -$OCH_2CH=CH_2$; 134.31 -$OCH_2CH=CH_2$; 138.04
12	$CDCl_3$	44.91	132.73 [b]	122.04 [b]	78.21	57.83	38.70	72.13	–	–	-CH_2CO 35.85 -$N(CH_3)_2$ 35.39; 37.20
13	Acetone-d_6	35.08	132.22	126.13	34.96	74.90	77.23	–	26.60 24.81	107.90	-CH_2CO 28.94 -$N(CH_3)_2$ 35.36; 37.32
14	Acetone-d_6	37.89	132.39 [b]	125.65 [b]	36.53	73.93	79.15	–	28.48 25.88	108.69	-CH_2CO 29.99 -$N(CH_3)_2$ 35.64; 37.88

[a] Obtained at 50.3 MHz.
[b] Signals are interchangeable.

Table 2
^{1}H NMR data for compounds **2–4** and **7–14** [a]

Compound	Solvent	Chemical shifts (δ) in ppm									
		H-1	H-2	H-3	H-4	H-5	H-6	PhCH_2-	C(CH_3)$_2$	OH	Others
2	Acetone-d_6	–	6.02	7.00	2.44 (a) 2.88 (e)	4.50	4.49	4.72 5.08	–	–	–
3	Acetone-d_6	4.33	5.59	5.59	2.02 (a) 2.42 (e)	3.73	3.45	4.95	–	4.50	–
4	Acetone-d_6	4.05	3.38	3.57	1.68 (a) 2.43 (e)	3.18	3.25	4.85	–	4.57	–
7	Acetone-d_6	4.07	5.71	5.95	4.41	4.28	1.62 (a) 2.06 (e)	–	1.28 1.37	3.80	–
8	Acetone-d_6	4.27	5.54	5.84	4.42	4.43	1.62 (a) 2.32 (e)	–	1.26 1.26	3.46	–
9	Acetone-d_6	3.92	3.26	2.89	4.22	4.21	1.67 (a) 1.90 (e)	–	1.19 1.34	3.24	–
10	Acetone-d_6	4.27	3.00	3.23	4.17	4.19	1.55 (a) 1.91 (e)	–	1.22 1.29	4.10	–
11	$CDCl_3$	3.94–4.05	3.81	3.52	3.94–4.05	1.81 (a) 2.06 (e)	3.94–4.05	4.80	–	2.82 2.82	-OCH_2CH=CH$_2$ 3.67 -OCH$_2$CH=CH$_2$ 5.86 -OCH$_2$CH=CH_2 5.17; 5.25
12	$CDCl_3$	3.08	5.74	5.81	4.81	4.53	2.03 (a) 2.19 (e)	4.20 4.38	–	–	-N(CH_3)$_2$ 2.94; 2.99 -CH_2CO 2.34
13	Acetone-d_6	2.56	5.54	5.72	1.98 (a) 2.25 (e)	4.48	4.48	–	1.22 1.25	–	-N(CH_3)$_2$ 2.89; 3.04 -CH_2CO 2.48
14	Acetone-d_6	2.49–2.60	5.68	5.68	2.10 (a) 2.38 (e)	4.30	3.89	–	1.28 1.38	–	-N(CH_3)$_2$ 2.83; 3.04 -CH_2CO 2.65

[a] Obtained at 200 MHz.

toluene–MeOH, (D) 7:3 hexane–ethyl acetate, (E) 98:2 CH_2Cl_2–MeOH, (F) 1:1 hexane–ethyl acetate, and (G) 95:5 ether–MeOH as the developing system/eluent. Evaporations were carried out under diminished pressure at 35–40 °C.

(5R,6S)-5-Azido-6-benzyloxycyclohex-2-enone (**2**).—To a stirred, cold (0 °C) solution of **1** (1.02 g, 3.9 mmol) in dry pyridine (20 mL) was added dropwise methanesulfonyl chloride (0.37 mL, 4.7 mmol), and then the reaction mixture was allowed to warm up to room temperature. After 4 h it was diluted with CH_2Cl_2 (40 mL) and washed with satd aq $NaHCO_3$ (2 × 20 mL) and water (2 × 20 mL), dried (Na_2SO_4) and concentrated. Co-evaporation with dry toluene (2 × 15 mL) resulted in unstable syrupy **2**, which was used without further purification, R_f 0.5 (A): IR ν_{max} (KBr) 2106 (N_3), 1694 (C=O) cm^{-1}.

(1S,5R,6S)-5-Azido-6-benzyloxycyclohex-2-en-1-ol (**3**).—To a solution of crude **2** (0.12 g, 0.46 mmol) in dry methanol (3 mL) was added $CeCl_3 \cdot 6H_2O$ (0.16 g, 0.46 mmol), the mixture was cooled to 0 °C and then $NaBH_4$ (17.4 mg, 0.46 mmol) was added in three portions with vigorous stirring. After 3 h the reaction mixture was evaporated, the residue was diluted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers was concentrated. The residue was dissolved in water (20 mL) and extracted with CH_2Cl_2 (2 × 10 mL), the organic layer was dried ($MgSO_4$) and concentrated, and the residue was subjected to column chromatography (B → C) to obtain 80 mg (70%) of **3** as a pale yellow syrup: $[\alpha]_D$ +106.2° (*c* 1.16 $CHCl_3$), IR: ν_{max} (KBr) 2106 (N_3), 3418 (OH) cm^{-1}. MS: *m/z* 245 $[M]^+$, 244 $[M-H]^+$, 216 $[M-H-N_2]^+$. Anal. Calcd for $C_{13}H_{15}N_3O_2$ (245.28): C, 63.66; H, 6.16; N, 17.13. Found: C, 63.92; H: 6.29; N, 17.25.

(1R,2S,3R,5S,6R)-3-Azido-2-benzyloxy-5,6-epoxycyclohexan-1-ol (**4**).—A mixture of **3** (0.45 g, 1.84 mmol), 85% 3-chloroperoxybenzoic acid (0.56 g, 2.8 mmol) and CH_2Cl_2 (8.0 mL) was stirred at room temperature for 22 h, when TLC (*D*) showed that the conversion of **3** to **4** was complete. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and then washed with 5% aq $Na_2S_2O_3$ (2 × 5 mL), 1% aq NaOH (2 × 5 mL), and water (2 × 7 mL), dried ($MgSO_4$), concentrated, and purified by means of column chromatography (10:0 → 3:7 hexane–ethyl acetate) to obtain pure **4** (297 mg, 62%): mp 119–120 °C; $[\alpha]_D$ +76.9° (*c* 0.9 in $CHCl_3$), R_f 0.17 (*D*). Anal. Calcd for $C_{13}H_{15}N_3O_3$ (261.28): C, 59,76; H, 5.78; N, 16.08. Found: C, 59.55; H, 6.00; N, 15.98. The (1*S*)-diastereoisomer of **4** was also isolated as a byproduct: 39.8 mg (8%): $[\alpha]_D$ +50.9° (*c* 0.91 in $CHCl_3$), R_f 0.31 (*D*).

(1S,4S,5R)- and (1R,4S,5R)-4,5-O-isopropylidenedioxycyclohex-2-en-1-ol (**7** and **8**).—Reduction of **6** [9,10] (0.2 g, 1.19 mmol) with sodium borohydride (45 mg, 1.19 mmol) in methanol (5 mL) in the presence of $CeCl_3 \cdot 6H_2O$ (0.422 g, 1.19 mmol) was carried out as described above for the preparation of **3**. The reduction was complete in ca. 30 min, and workup that included chromatographic purification (100:0 → 98:2 CH_2Cl_2–MeOH) gave as the first product to elute (1*S*)-**7** (118 mg, 58%): $[\alpha]_D$ −68.7° (*c* 1.16 in $CHCl_3$), R_f 0.42 (E). Anal. Calcd for $C_9H_{14}O_3$ (170.2): C, 63.51; H, 8.29. Found: C, 63.63; H, 8.22. Eluted second was (1*R*)-**8** (59 mg, 29%): $[\alpha]_D$ +40.2° (*c* 2.56 in $CHCl_3$), R_f 0.21 (E). Anal. Calcd for $C_9H_{14}O_3$ (170.2): C, 63.51; H, 8.29. Found: C, 63.77; H, 8.34.

(1S,2R,3R,4S,5R)-2,3-Epoxy-4,5-isopropylidenedioxycyclohexane-1-ol (**9**).—Epoxidation of **7** (0.2 g, 1.16 mmol) with 85% 3-chloroperoxybenzoic acid (0.47 g, 2.3 mmol) in CH_2Cl_2 (6.0 ml) for 48 h was carried out as described for the preparation of **4**, to give syrupy **9** (187 mg, 87%): $[\alpha]_D$ −58.1° (*c* 1.15 in $CHCl_3$), R_f 0.5 (*A*). Anal. Calcd for $C_9H_{14}O_4$ (186.20): C, 58.05; H, 7.57. Found: C, 58.21; H, 7.62.

(1R,2R,3R,4S,5R)-2,3-Epoxy-4,5-isopropylidenedioxycyclohexane-1-ol (**10**).—Conversion of **8** (0.2 g, 1.16 mmol) into the epoxy compound **10** was performed as described for **4** and **9** to give 153 mg (72%) of crystalline **10**: mp 98–99 °C, $[\alpha]_D$ +9.5° (c 1.09 in $CHCl_3$), R_f 0.29 (*E*). Anal. Calcd for $C_9H_{14}O_4$ (186.20): C, 58.05; H, 7.57. Found: C, 57.86; H, 7.73.

(1S, 2S, 3S, 4R, 6R) - 6 - Allyloxy - 4 - azido - 3 - benzyloxycyclohexane - 1, 2 - diol (**11**).—To a stirred solution of **4** (76 mg, 0.29 mmol) in CH_2Cl_2 (10 mL), allyl alcohol (128 μL, 1.88 mmol) and $BF_3 \cdot Et_2O$ (75 μL, 0.61 mmol) were added. After stirring at room temperature for 3.5 h, the mixture was neutralized with Et_3N, diluted with CH_2Cl_2 (10 mL), washed with water (3 × 5 mL), dried (Na_2SO_4) and concentrated. Column chromatography of the residue (with eluent F) gave syrupy **11** (74 mg, 80%): $[\alpha]_D$ +27.9° (*c* 0.8 in $CHCl_3$), R_f 0.43 (*A*). Anal. Calcd for $C_{16}H_{21}N_3O_4$ (319.02): C, 60.18; H, 6.58; N, 13.17. Found: C, 60.33; H, 6.71; N, 13.35.

N,N-*Dimethyl [(1R,4R,5R)-5-azido-4-benzyloxycyclohex - 2 - enyl]acetamide* (**12**).—A mixture of **3** (0.505 g, 2.06 mmol) and *N,N*-dimethylacetamide dimethyl acetal (8.7 mL, 59.9 mmol) was slowly

heated from 25 °C to 140 °C (bath temperature) in the distillation flask of a micro-distillation apparatus fitted with a short Vigreux column. The distillate collected at 80–110 °C was recycled into the distillation flask, and the mixture was kept at 140 °C for 30 min. It was then cooled and co-evaporated with toluene (3 × 10 mL), and the residue was dissolved in CH_2Cl_2 (20 mL). The solution was washed with water (2 × 5 mL), dried ($MgSO_4$), and concentrated. Flash column chromatography of the residue (*G*) resulted in syrupy **12**: 479 mg (74%): $[\alpha]_D$ −117° (*c* 1.0 in $CHCl_3$), R_f 0.28 (*G*). Anal. Calcd for $C_{17}H_{22}N_4O_2$ (314.39): C, 64.89; H, 7.00; N, 17.81. Found: C, 65.11; H, 7.13; N, 18.01.

N,N-*Dimethyl [(1*S,*5*R,*6*S*)-*5,6*-O-*isopropylidene-dioxycyclohex-2-enyl]acetamide* (**13**).—The Claisen rearrangement of **7** (0.406 g, 2.38 mmol) with *N,N*-dimethylacetamide dimethyl acetal (6.0 mL, 40.5 mmol) was carried out as described above for the preparation of **12** to furnish pure **13** (429 mg, 75.3%): mp. 65–68 °C, $[\alpha]_D$ −16° (*c* 0.9 in $CHCl_3$), R_f 0.5 (G). IR: ν_{max} (KBr) 1646 (amide) cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO_3$ (239.31): C, 65.25; H, 8.85; N, 5.85. Found: C, 64.97; H, 9.05; N, 5.71.

N,N-*Dimethyl [(1*R,*5*R,*6*S*)-*5,6*-O-*isopropylidene-dioxycyclohex-2-enyl]acetamide* (**14**).—The Claisen rearrangement of **8,** performed in an analogous manner as described for the conversion of **7**, gave 447 mg (78%) of syrupy **14**: $[\alpha]_D$ −85° (*c* 1.16 in $CHCl_3$), R_f 0.46 (G). Anal. Calcd for $C_{13}H_{21}NO_3$ (239.31): C, 65.25; H, 8.85; N, 5.85. Found: C, 65.51; H, 8.92; N, 6.08.

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References

[1] M.J. Berridge, *Annu. Rev. Biochem.*, 56 (1987) 159–169.
[2] S. Atsumi, K. Umezawa, H. Iinuma, H. Naganawa, H. Nakamura, Y. Iitaka, and T. Takeuchi, *J. Antibiot.*, 43 (1990) 49–53.
[3] G. Legler and R. Bollhagen, *Carbohydr. Res.*, 233 (1992) 113–123.
[4] G. Legler, *Adv. Carbohydr. Chem. Biochem.*, 48 (1990) 319–384.
[5] D.C. Billington, *The Inositol Phosphates: Chemical Synthesis and Biological Significance*, VCH Verlagsgesellschaft mbH, Weinheim, 1993.
[6] P. László, I.F. Pelyvás, F. Sztaricskai, L. Szilágyi, and Á. Somogyi, *Carbohydr. Res.*, 175 (1988) 227–239.
[7] I.F. Pelyvás, M. Mádi-Puskás, Z. G. Tóth, Zs. Varga, M. Hornyák, Gy. Batta, and F. Sztaricskai, *J. Antibiot.*, 48 (1995) 683–695.
[8] N. Chida, M. Ohtsuka, K. Nakazawa, and S. Ogawa, *J. Org. Chem.*, 56 (1991) 2976–2983.
[9] B.M. Trost and A.G. Romero, *J. Org. Chem.*, 51 (1986) 2332–2342.
[10] J.E. Audia, L. Boisvert, A.D. Patten A. Villalobos, and S.J. Danishefsky, *J. Org. Chem.*, 54 (1989) 3738–3740.
[11] I.F. Pelyvás, T. Lindhorst, and J. Thiem, *Liebigs Ann. Chem.*, (1990) 761–769.