An Alternative Synthesis of Nojirimycin and Idonojirimycin

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Starting from easily accessible 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose, a five-step synthesis of nojirimycin (5-amino-5-deoxy-D-glucopyranose) and idonojirimycin (5-amino-5-deoxy-L-idopyranose) is described. For characterization and structure assignment, ^{1}H and ^{13}C NMR, EI and CI mass spectra of the prepared precursors were also studied. Nojirimycin and idonojirimycin were isolated and characterized *via* corresponding bisulfite addition products.

Nojirimycin (5-amino-5-deoxy-D-glucopyranose, *I*) [1, 2], an antibiotic produced by several strains of *Streptomyces* and *Bacillus* [3, 4] has attracted attention of chemists and biologists for many years. The potential chemotherapeutic importance has prompted considerable synthetic interest in this naturally occurring specific glycohydrolase inhibitor [5—9]. Most of classical chemical total syntheses utilize suitable *O*-protected D-glucose derivatives as a starting material [2, 10—22].

We now report on a synthetic route using the known 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose (*III*) [23—26] as a starting compound, applying the reaction sequence as follows. In the first step, an addition of ammonia to *III* (according to an analogy from the literature [27]) affords 5-acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-glucofuranose (*IV*) and 5-acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-β-L-idofuranose (*V*). Subsequent separation of these C-5 epimers is facile because compound *IV* is oily while *V* is solid and can be easily crystallized from the reaction mixture (x_r = *ca.* 1 1.5). The second step represents a protection of hydroxyl group at C-3 of D-*gluco* epimer *IV* as an *O*-tetrahydropyranyl ether to produce *VI*. In this stage, protection of C-3-OH as an acetyl would be also suitable but the use of acetic anhydride and pyridine resulted in the formation of a mixture of two compounds (w_r = 1.5 1). Although, based on NMR and mass (EI and CI (pyridine)) spectral data, the required 3-*O*-acetylated product represents just more abundant component, this reaction step would be ineffective regarding the overall yield of the final product. The second component was not characterized. In the third step, the nitromethylene group is oxidized to an aldehyde under mild neutral reaction conditions using potassium permanganate giving 5-acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-α-D-*gluco*-hexodialdo-1,4-furanose (*VII*). In the fourth step, reduction of C-6-aldehyde group in compound *VII* with sodium borohydride gave 5-acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-α-D-glucofuranose (*VIII*). Owing to the formation of a new asymmetric centre at C-2 atom of tetrahydropyranyl ring, compounds *VI*—*VIII* represented a mixture of two isomers (clearly detectable by ^{1}H and ^{13}C NMR spectra) but regarding the total deprotection in the final reaction step, their separation was unnecessary. Because of instability of nojirimycin under acidic and neutral conditions [2], deprotection of *VIII* to free base should prove difficulties. Therefore, in the last step, triethyloxonium fluoroborate and sulfur dioxide were used for cleavage of protective groups in *VIII* and simultaneous formation of 5-ammonio-5-deoxy-D-glucitol-1-sulfonate, a more stable and readily isolable and characterizable crystalline bisulfite adduct of nojirimycin (*XVI*) [2, 28]. Analogously, C-5 epimeric idonojirimycin (5-amino-5-deoxy-L-idopyranose, *II*) was obtained in the form of 5-ammonio-5-deoxy-L-iditol-1-sulfonate (*XVII*) from 5-acetamido-L-*ido* isomer *V* applying the same reaction sequence and reaction conditions.

To facilitate ^{1}H and ^{13}C NMR spectral data interpretation for unambiguous structure assignment of key compounds *VIII* and *XIII*, these were additionally converted by mild deprotection of 3-*O*-tetrahydropyranyl ether and subsequent acetylation to corresponding 3,6-*O*-diacetates *X* and *XV*, respectively.

Based on the fact that the first, second, and fourth steps are high yielding (91 %, 97 %, and 92 %, respectively), the third and fifth steps afford about 78 % and 68 % of products and considering a mixture (x_r = *ca.* 1 1.5) of C-5 epimers in the first step, the overall *ca.*

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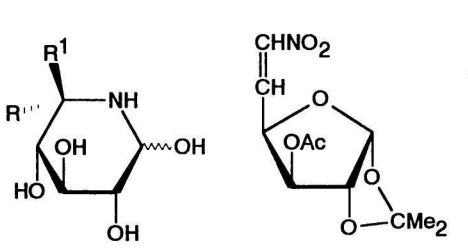

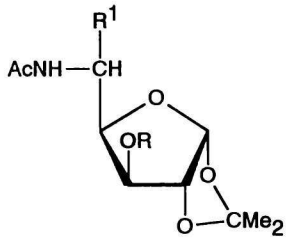
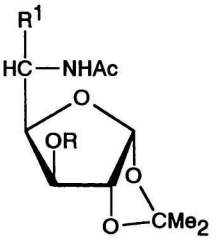
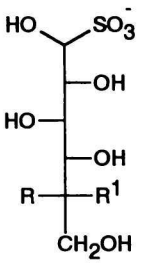

I R = H, $R^1 = CH_2OH$
II R = CH_2OH, R^1 = H

THP = 2-tetrahydropyranyl

III

IV R = H, $R^1 = CH_2NO_2$
VI R = THP, $R^1 = CH_2NO_2$
VII R = THP, R^1 = CHO
VIII R = THP, $R^1 = CH_2OH$
IX R = H, $R^1 = CH_2OH$
X R = Ac, $R^1 = CH_2OAc$

V R = H, $R^1 = CH_2NO_2$
XI R = THP, $R^1 = CH_2NO_2$
XII R = THP, R^1 = CHO
XIII R = THP, $R^1 = CH_2OH$
XIV R = H, $R^1 = CH_2OH$
XV R = Ac, $R^1 = CH_2OAc$

XVI R = H, $R^1 = NH_3^+$
XVII R = NH_3^+, R^1 = H

Scheme 1

Table 1. Characterization of the Prepared Compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.
			C	H	N	S	%	°C
IV	$C_{11}H_{18}N_2O_7$	290.28	45.52	6.25	9.65		37	*a*
			45.24	6.29	9.72			
V	$C_{11}H_{18}N_2O_7$	290.28	45.52	6.25	9.65	–	54	177—178
			45.31	6.30	9.53			
VI[b]	$C_{16}H_{26}N_2O_8$	374.39	51.33	7.00	7.48	–	97	
			51.50	7.17	7.40			
VII[b]	$C_{16}H_{25}NO_7$	343.38	55.97	7.34	4.08		78	
			56.73	7.42	4.03			
VIII[b]	$C_{16}H_{27}NO_7$	345.40	55.64	7.88	4.10	–	92	*a*
			55.51	7.94	4.09			179—180[c]
IX	$C_{11}H_{19}NO_6$	261.28	50.57	7.33	5.36	–	99	*a*
			50.72	7.41	5.32			
X	$C_{15}H_{23}NO_8$	345.35	52.17	6.71	4.06		88	139—140
			52.22	6.74	4.02			
XI[b]	$C_{16}H_{26}N_2O_8$	374.39	51.33	7.00	7.48	–	98	
			51.45	7.07	7.51			
XII[b]	$C_{16}H_{25}NO_7$	343.38	55.97	7.34	4.08		77	
			56.06	7.31	4.11			
XIII[b]	$C_{16}H_{27}NO_7$	345.40	55.64	7.88	4.06		93	*a*
			55.70	7.91	4.02			141—142[c]
XIV	$C_{11}H_{19}NO_6$	261.28	50.57	7.33	5.36		98	*a*
			50.65	7.30	5.40			
XV	$C_{15}H_{23}NO_8$	345.35	52.17	6.71	4.06	–	91	89—90
			52.21	6.70	4.09			
XVI	$C_6H_{15}NO_8S$	261.25	27.59	5.79	5.36	12.27	68	138—140[d]
			27.70	5.86	5.40	12.19		
XVII	$C_6H_{15}NO_8S$	261.25	27.59	5.79	5.36	12.27	67	140—143
			27.49	5.83	5.32	12.21		

a) Oily product; *b*) a mixture of 3-*O*-(2-tetrahydropyranyl) isomers; *c*) for crystalline isomer; *d*) Ref. [2] and Ref. [28] give for *XVI* m.p. = 145—147 °C and m.p. = 135—137 °C, respectively.

43 % yield represents 17 % of nojirimycin (*I*) and 26 % of epimeric idonojirimycin (*II*) starting from *III*. Calculated on starting D-glucose, it represents overall 8 % of *I* and 12 % of *II* (because compound *III* can be obtained from D-glucose in *ca.* 47 % overall yield).

Some characteristics of the prepared compounds are summarized in Table 1. The NMR spectral data are shown in Tables 2 and 3. Mass spectral data of

Table 2. ^{1}H NMR Data of the Prepared Compounds

Compound	Chemical shifts, δ										
	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	$C(CH_3)_2$		$NCOCH_3$	NH
IV[a]	5.92 d	4.55 d	4.12 d	4.20 dd	4.76 ddd	4.87 dd	4.72 dd	1.49 s	1.35 s	2.00 s	
V[a]	5.95 d	4.57 d	4.20 d	4.34 dd	4.79 ddd	4.77 dd	4.71 dd	1.50 s	1.35 s	2.00 s	
VI	5.92 d	4.50 d	4.33 d	4.48 dd	4.41—5.08 m			1.51 s	1.32 s	1.99 s	6.80 d
VI[b]	5.92 d	4.78 d	4.20 d	4.40 dd	4.41—5.08 m			1.50 s	1.31 s	2.00 s	6.46 d
VIII	5.93 d	4.50 d	4.36 d	4.47 dd	3.63—4.07 m			1.50 s	1.33 s	1.98 s	6.87 d
VIII[b]	5.92 d	4.79 d	4.13 d	4.25 dd	3.63—4.07 m			1.52 s	1.33 s	2.00 s	6.60 d
X	5.91 d	4.47 d	5.32 d	4.23 dd	4.58 m	4.31 dd	4.27 dd	1.51 s	1.32 s	1.93 s	5.59 d
XI	5.93 d	4.49 d	4.35 d	4.50 dd	4.46—5.22 m			1.48 s	1.31 s	1.98 s	6.88 d
XI[b]	5.93 d	4.80 d	4.21 d	4.41 dd	4.46—5.22 m			1.48 s	1.31 s	2.00 s	6.40 d
XIII	5.94 d	4.51 d	4.33 d	4.38 dd	3.65—3.96 m			1.49 s	1.31 s	2.01 s	6.72 d
XIII[b]	5.94 d	4.82 d	4.15 d	4.35 dd	3.65—3.96 m			1.50 s	1.32 s	2.02 s	6.63 d
XV	5.92 d	4.51 d	5.21 d	4.35 dd	4.52 dt	4.10 d	4.10 d	1.51 s	1.32 s	2.01 s	6.49 d

	Coupling constants/Hz							
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{5,NH}$
IV[a]	3.6	0	2.6	8.8	5.7	6.2	14.7	
V[a]	3.7	0	2.9	8.4	4.3	7.3	14.3	
VI	3.7	0	3.2	5.9				6.9
VI[b]	3.7	0	3.1	5.8			–	8.1
VIII	3.8	0	3.2	6.8	–			6.3
VIII[b]	3.7	0	2.9	6.8	–			8.4
X	3.7	0	3.0	8.9	5.0	4.1	11.6	9.8
XI	3.7	0	3.3	6.0		–	–	9.3
XI[b]	3.7	0	3.3	5.9	–			8.6
XIII	3.8	0	3.0	7.3				8.2
XIII[b]	3.8	0	3.1	7.2				7.3
XV	3.8	0	3.1	6.3	5.8	5.8	0	8.4

a) Measured in CD_3OD; *b*) corresponding 3-*O*-(2-tetrahydropyranyl) isomer.

Table 3. ^{13}C NMR Data of the Prepared Compounds

Compound	Chemical shifts, δ										
	C-1	C-2	C-3	C-4	C-5	C-6	C=O	$\underline{C}Me_2$	$C(\underline{C}H_3)_2$	$NCO\underline{C}H_3$	Others
III	104.6	83.1	76.0	76.6	134.2	141.2	169.3	112.7	26.7, 26.1		20.5[a]
IV[b]	107.5	87.4	78.0	81.9	49.5	76.1	175.0	114.1	28.2, 27.5	23.7	
V[b]	107.2	88.1	77.7	81.3	50.5	76.2	174.6	114.1	28.2, 27.6	23.7	–
VI	105.3	82.8	77.5	79.9	46.8	75.7	170.3	112.1	26.9, 26.2	23.0	100.5[c]
VI[d]	104.9	83.1	77.3	81.9	47.2	75.9	170.5	118.8	26.7, 26.1	23.1	101.8[c]
VIII	104.8	82.5	78.3	79.1	52.1	64.8	170.8	111.8	27.1, 26.7	23.5	98.6[c]
VIII[d]	104.6	83.7	79.1	82.5	49.3	64.0	170.2	111.6	26.6, 26.1	23.3	102.4[c]
X	105.0	83.2	77.8	74.6	45.9	64.5	170.7, 169.9, 169.3	112.2	26.7, 26.2	23.3	20.9[a], 20.8[a]
XI	105.0	82.9	77.4	79.7	46.3	75.3	169.9	112.1	26.6, 26.0	22.9	100.5[c]
XI[d]	104.6	83.7	77.3	81.8	47.0	75.5	170.1	111.9	26.5, 26.0	22.9	101.8[c]
XIII	104.6	82.8	78.1	78.6	51.2	64.4	170.9	111.8	26.6, 26.1	23.4	97.7[c]
XIII[d]	102.3	84.1	78.6	77.9	52.1	64.2	171.2	111.7	26.6, 26.1	23.4	102.3[c]
XV	103.9	83.2	76.7	76.0	46.4	63.5	170.2, 169.5, 169.4	111.7	26.2, 25.7	22.8	20.4[a], 20.3[a]

a) CH_3 in acetyl; *b*) measured in CD_3OD; *c*) C-2 in tetrahydropyranyl; *d*) corresponding 3-*O*-(2-tetrahydropyranyl) isomer.

selected compounds are given in Experimental.

EXPERIMENTAL

Starting 3-*O*-acetyl-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-*xylo*-hex-5-enofuranose (*III*) was prepared from D-glucose (4 steps) according to the known procedure [23, 26]. The other used chemicals were commercially available products (Merck, Aldrich, Fluka).

Melting points were determined with a Boetius PHMK 05 microscope. ^{1}H and ^{13}C NMR spectra

(in $CDCl_3$, internal standard Me_4Si) were measured with Bruker AM-300 spectrometer operating at 300.13 MHz and 75.46 MHz working frequencies, respectively. The EI and CI (pyridine) mass spectra (70 eV) were recorded on a Finnigan MAT SSQ 710 instrument, applying the direct sample-introduction technique. Specific optical rotations were obtained with a Perkin—Elmer 241 polarimeter (10 cm cell). Microanalyses were performed on a Fisons EA 1108 analyzer. All reactions were monitored by TLC on silica gel plates (Merck) using following eluents: ethyl acetate—hexane (φ_r = 10 1 (A) or φ_r = 2 1 (B)), chloroform—methanol (φ_r = 4 1(C)), and ethyl acetate (D). Visualization was effected with iodine vapour or sulfuric acid. Column chromatography was performed as flash chromatography on silica gel 60 (Merck, "230—400 mesh") with the same eluents.

5-Acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-α-D-glucofuranose (*IV*) and 5-Acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-β-L-idofuranose (*V*)

Starting compound *III* (9.7 g; 35.5 mmol) was dissolved in methanol (200 cm^3) saturated with ammonia at 0 °C and the solution was left to stand at 5 °C for 24 h. The solvent was evaporated under diminished pressure giving a crude mixture of *IV* and *V* (yellowish foam). Using ethyl acetate—hexane (φ_r = 5 1) as a solvent, compound *V* crystallizes in the form of white needles (3.4 g). The residual mixture was separated on a column of silica gel using eluent A to give faster moving oily *IV* (3.8 g, 37 %) and a further portion of crystalline *V* (2.2 g, totally 54 %). Total yield of *IV* and *V*: 91 %.

For *IV*: R_f = 0.48 (A). [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = + 11°

For *V*: R_f = 0.32 (A). [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = −29°

5-Acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-3-*O*-(2-tetrahydropyranyl)-α-D-glucofuranose (*VI*) and 5-Acetamido-5,6-dideoxy-1,2-*O*-isopropylidene-6-nitro-3-*O*-(2-tetrahydropyranyl)-β-L-idofuranose (*XI*)

A mixture of *IV* (3.2 g; 11.0 mmol), 3,4-dihydro-2*H*-pyran (1.86 g; 22.0 mmol), and pyridinium *p*-toluenesulfonate (0.55 g; 2.2 mmol) in dry dichloromethane (50 cm^3) was stirred at 25 °C for 48 h. Then ether (50 cm^3) was added and the mixture was washed with brine (50 cm^3). Organic layer was dried over Na_2SO_4, filtered and solvents were evaporated under diminished pressure. The crude product was purified with charcoal in ether to give *VI* (yellowish oil) in almost quantitative yield. Compound *XI* (yellowish oil) was prepared by the same method starting from *V*

For *VI*: R_f = 0.50 (B). [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = + 14° EI mass spectrum, *m/z* (I_r/%): 359 (3), 291 (6), 243 (7), 196 (9), 168 (7), 100 (36), 85 (100), 67 (12), 57 (13), 43 (33).

For *XI*: R_f = 0.49 (A). [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = −23°

5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-α-D-*gluco*-hexodialdo-1,4-furanose (*VII*) and 5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-α-D-glucofuranose (*VIII*)

To a solution of *VI* (3.5 g; 9.3 mmol) in 0.1 M-KOH (225 cm^3) aqueous magnesium sulfate (60 cm^3, 2 M solution) and sufficient amount of water (350 cm^3) were added. A solution of potassium permanganate (0.98 g; 6.2 mmol) in water (100 cm^3) was then added dropwise to the stirred mixture at 0—5 °C. The colour of permanganate disappeared rapidly upon the addition and manganese dioxide was produced. When the addition was completed, the reaction product was extracted thoroughly with ethyl acetate. Organic layer was dried over Na_2SO_4, filtered and solvent was evaporated under reduced pressure affording aldehyde *VII* (colourless oil, 2.5 g, 78 %). R_f = 0.30 (D). EI mass spectrum, *m/z* (I_r/%): 344 (7, $[M + 1]^+$), 314 (12), 260 (20), 242 (11), 212 (13), 154 (10), 114 (15), 100 (40), 85 (100), 57 (15), 43 (52). CI (pyridine) mass spectrum, *m/z*: 423 $[M + 80]^+$

Aldehyde *VII* (2.5 g; 7.3 mmol) was dissolved in ethanol (100 cm^3) and sodium borohydride (530 mg; 14.0 mmol) was added under stirring at 25 °C. After 4 h, acetic acid was added with care to neutrality and solvents were evaporated under reduced pressure. The residue was extracted with ether, extract decolourized with charcoal, and solvent evaporated to give *VIII* (2.1 g, 92 %) as a mixture of two isomers having R_f = 0.69 (C) and R_f = 0.53 (C). Crystallization of this mixture using ethyl acetate and hexane as a solvent afforded pure crystalline faster moving isomer (1.1 g) and oily slower moving isomer which was not further purified.

For *VIII* (crystalline isomer): [α](D, 20 °C, ρ = 10 g dm^{-3}, CH_3OH) = −25° EI mass spectrum, *m/z* (I_r/%): 346 (3, $[M + 1]^+$), 314 (12), 262 (23), 156 (10), 100 (36), 85 (100), 60 (21), 43 (32). CI (pyridine) mass spectrum, *m/z*: 425 $[M + 80]^+$

Identical mass spectral data were registered for oily isomer.

5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-β-L-ido-hexodialdo-1,4-furanose (*XII*) and 5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-3-*O*-(2-tetrahydropyranyl)-β-L-idofuranose (*XIII*)

Starting from *XI*, these compounds were prepared using essentially the same method as described for compounds *VII* and *VIII*. Compound *XIII* represented

a mixture of two isomers: crystals, $R_f = 0.53$ (C) and oil, $R_f = 0.36$ (C).

For *XIII* (crystalline isomer): [α](D, 20 °C, $\rho = 10$ g dm^{-3}, CH_3OH) = −44° EI and CI (pyridine) mass spectral data were identical with those given for *VIII*. Oily isomer exhibited the same mass spectral data.

5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (*IX*), 5-Acetamido-5-deoxy-3,6-di-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose (*X*), 5-Acetamido-5-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose (*XIV*), and 5-Acetamido-5-deoxy-3,6-di-*O*-acetyl-1,2-*O*-isopropylidene-β-L-idofuranose (*XV*)

A mixture of *VIII* (0.8 g; 2.3 mmol) and pyridinium *p*-toluenesulfonate (58.3 mg; 0.23 mmol) in ethanol (95 %, 25 cm^3) was stirred at 55 °C for 4 h. After standing overnight at 25 °C, the solvents were removed under diminished pressure to give crude *IX* ($R_f = 0.49$ (C)) in almost quantitative yield. This was without isolation and purification acetylated with acetic anhydride (2 cm^3) in pyridine (5 cm^3) at 25 °C for 24 h. The solvents were evaporated under reduced pressure and the residue was crystallized from ethyl acetate to give white crystals of *X* (0.7 g, 88 %). Starting from *XIII*, compounds *XIV* ($R_f = 0.39$ (C)) and *XV* were prepared analogously as *IX* and *X* with an exception that *XV* was crystallized from ether.

For *X*: $R_f = 0.79$ (C). [α](D, 20 °C $\rho = 10$ g dm^{-3}, CH_3OH) = + 20° EI mass spectrum, *m/z* (I_r/%): 346 (18, $[M + 1]^+$), 330 (21), 272 (30), 201 (39), 154 (31), 143 (46), 112 (28), 84 (44), 60 (18), 43 (100). CI (pyridine) mass spectrum, *m/z*: 425 $[M + 80]^+$

For *XV*: $R_f = 0.68$ (C). [α](D, 20 °C, $\rho = 10$ g dm^{-3}, CH_3OH) = −14° EI and CI (pyridine) mass spectral data were identical with those registered for *X*.

5-Ammonio-5-deoxy-D-glucitol-1-sulfonate (*XVI*) and 5-Ammonio-5-deoxy-L-iditol-1-sulfonate (*XVII*)

To a solution of *VIII* (0.69 g; 2.0 mmol) in dry dichloromethane (10 cm^3) triethyloxonium fluoroborate (2 cm^3 of 1 M solution in CH_2Cl_2; 2.0 mmol) was added dropwise over a period of 5 min at 5 °C and the resulting mixture was stirred at 25 °C for 8 h under anhydrous conditions. The solution was concentrated under diminished pressure and the residue was dissolved in water (5 cm^3). The resulting solution was saturated with sulfur dioxide under ice-cooling and left at room temperature in well closed flask for 5 days with occasional heating at 35—40 °C. After cooling and addition of methanol (5 cm^3) saturated at 0 °C with sulfur dioxide, the separated crystals were filtered off and recrystallized from a mixture of water and methanol to give pure *XVI* (355 mg, 68 %) exhibiting the same analytical data as described [2, 28]. Starting from *XIII*, compound *XVII* was obtained by essentially the same procedure as described above.

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REFERENCES

1. Ishida, N., Kumagai, K., Tsuruoka, T., and Yumoto, H. J. *J. Antibiot., Ser. A 20*, 66 (1967).
2. Inouye, S., Tsuruoka, T., Ito, T., and Niida, T. *Tetrahedron 24*, 2125 (1968).
3. Murao, S. and Miyata, S., *Agric. Biol. Chem. 44*, 219 (1980).
4. Schmidt, D. D. Frommer, W., Müller, L., and Truscheit, E., *Naturwissenschaften 66*, 584 (1979).
5. Truscheit, E., Frommer, W. Junge, B., Müller, L., Schmidt, D. D. and Wingender, W., *Angew. Chem. 93*, 738 (1981).
6. Tyms, A. S., Berrie, E. M., Ryder, T. A., Nash, R. J. Hegarty, M. P Taylor, D. L., Mobberly, M. A., Davis, J. M., Bell, E. A., Jeffries, D. J., Taylor-Robinson, D., and Fellows, L. E., *Lancet 1987*, 1025.
7. Evans, S. V., Fellows, L. E., Shing, T. K. M., and Fleet, G. W. J., *Phytochemistry 24*, 1953 (1985).
8. Liu, P S., *J. Org. Chem. 52*, 4714 (1987).
9. Fleet, G. W. J., Karpas, A., Dwek, R. A., Fellows, L. E., Tyms, A. S., Petursson, S., Namgoong, S. K., Ramsden, N. G., Smith, P W., Son, J. C., Wilson, F., Witty, D. R., Jacob, G. S., and Rademacher, T. W., *FEBS Lett. 237*, 128 (1988).
10. Paulsen, H., Sangster, I., and Heyns, K., *Chem. Ber. 100*, 802 (1967).
11. Paulsen, H. and Todt, K., *Adv. Carbohydr. Chem. 23*, 115 (1968).
12. Saeki, H. and Ohki, E., *Chem. Pharm. Bull. 16*, 2477 (1968).
13. Klemer, A., Hofmeister, U., and Lemmes, R., *Carbohydr. Res. 68*, 391 (1979).
14. Bernotas, R. C. and Ganem, B., *Tetrahedron Lett. 25*, 165 (1984).
15. Bernotas, R. C. and Ganem, B., *Tetrahedron Lett. 26*, 1123 (1985).
16. Setoi, H., Takeno, H., and Hashimoto, M., *Chem. Pharm. Bull. 34*, 2642 (1986).
17. Broxterman, H. J. G. van der Marel, G. A., Neefjes, J. J., Ploegh, H. L., and van Boom, J. H., *Rec. Trav. Chim. Pays-Bas 106*, 571 (1987).
18. Tsuda, Y., Okuno, Y., and Kanemitsu, K., *Heterocycles 27*, 63 (1988).
19. Schmidt, R. R., Michel, J., and Rucker, E., *Liebigs Ann. Chem. 1989*, 423.
20. Chida, N., Furuno, Y., and Ogawa, S., *J. Chem. Soc., Chem. Commun. 1989*, 1230.
21. Beaupere, D., Stasik, B., Uzan, R., and Demailly, G., *Carbohydr. Res. 191*, 163 (1989).

22. Anzeveno, P. B. and Creemer, L. J., *Tetrahedron Lett. 31*, 2085 (1990).
23. Whistler, R. L. and Pyler, R. E., *Carbohydr. Res. 12*, 201 (1970).
24. Takayanagi, H., Seo, K., Yamashita, M., Yoshida, H., Ogata, T., and Inokawa, S., *Carbohydr. Res. 63*, 105 (1978).
25. Yamamoto, H., Murata, H., Inokawa, S., Yamashita, M., Armour, M.-A., and Nakashima, T. T., *Carbohydr. Res. 133*, 45 (1984).
26 Hanaya, T. Yamamoto, H., and Yamamoto, H., *Bull. Chem. Soc. Jpn. 65*, 1154 (1992).
27. Paulsen, H., *Ann. 665*, 166 (1963).
28. Vasella, A. and Voeffray, R., *Helv. Chim. Acta 65*, 1134 (1982).

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