Synthesis of methyl 4-methyl amino-6-deoxy-3-C-methyl 2,3-di-O-methyl- α -D-altropyranoside

ATTA-UR-RAHMAN*, NAMGI HONG AND JUJI YOSHIMURA
Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Technology, Nagatsuta, Midori-ku Yokohama, 227 Japan.

(Received 2nd January, 1983)

Introduction

The organism producing anticancer antibiotic named sibiromycin, possessing activity against a number of transplantable tumors of animals has been isolated from the culture filterate of Actinomycetes streptosporanigum sibricum. This contains a novel branched chain amino sugar. Recently, Dyong and his coworkers [1] have reported the synthesis of methyl 2-0-acetyl-4,6-dideoxy-3-C-methyl-4-tosylamino- α -D-altropyranoside, as a key intermediate for the synthesis of sibirosamine, through (2,3-) sigmatropic rearrangement of the corresponding 3-C-hex-2-enopyranoside followed by the vicinal cis-oxyamination of C=C bond [2].

Our object was to synthesize methyl 4-methyl amino-4, 6-di-deoxy-3-C-methyl-2,3-di-methyl-α -D-altropyranoside (17), an intermediate which can lead to methyl sibirosaminide (20), a sugar moiety present in sibiromycin [3].

Results and Discussion

Synthesis of methyl 2,3-di-O-methyl-α -D-sibirosaminide. We had few points under our mind, before we planned to synthesize methyl-α -D-sibirosaminide (20), first point that molecule should have axial hydroxyl group at 2-position, the second point to develop 3-C methyl branching group and the third point, introduction of N-methyl amino group at 4-position as in the derivative. Furthermore, the protection of the two hydroxyl groups at 2 and 3 position was carreid out by methylation, but lastly failed in de-O-methylation reaction with boron tribromide or boron trichloride, in order to acquire de-O-methylated product (18) which could lead to final product (20).

Two possible routes have been tried to synthesize methyl 4-azido-4,6-dideoxy-3-C-methyl-2,3-di-O-methyl-α -D-altropyranoside (24). In the first route, methyl 6-deoxy-3-C-methyl-2, 3-di-O-methyl-α -D-arabino-hexopyranoside-4-ulose (12) was reduced with sodium borohydride in aqueous methanol to give a mixture of two isomers which were separated on t.l.c., finally on examining the n.m.r. parameters, we concluded the ratios 1:3.68 of altro (11) and ido isomer (21). From this conclusion we can deduce that the carbonyl function of (12) was reduced much from the equatorial side to give the desired product (21) while the axial attack gives the altro derivatives (11). The 4-hydroxyl derivatives (21) was mesylated with methyl sulfonyl chloride under normal procedure gave methyl 4,6-di-deoxy-4-mesyl-2,3-di-O-methl-α-D-idopyranoside (22), the n.m.r. parameters are given in the table-1. It was directly treated with sodium

*Unesco Fellow 1979-1980

Present Address: Institute of Chemistry, University of Sind, Jamshoro, Pakistan.

azide in dimethylformamide under usual procedure, but could not be isolated in a pure form of (24). In another trial methyl 4-chloro-4, 6-di-deoxy-2, 3-di-O-methyl-α-idopyranoside (23) obtained by the treatment of (11) in pyridine with sulfuryl chloride was directly undergone azidation, using sodium azide and HMPA solution, but our trial remain unsuccessful. Otherwise, if we succeeded in these reaction then we could easily reduce the azide group into 4-amino derivative (14), therefore we, modified our scheme and planned to prepare compound (14) by the conversion of 4-ulose into oxime (13) which was transformed into the desired derivative (17) by the successive course of reactions.

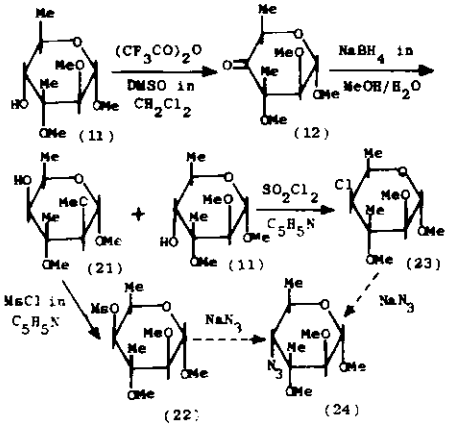

Fig.No.1

The treatment of methyl4,6-O-benzylidene-2,3-anhydro-α-D-allopyranoside (4) with sodium methoxide in methanol, gave methyl 4,6-O-benzylidene-2-O-methyl-α-D-altropyranoside (5) has already been confirmed by J. Yoshimura et al [4]. Oxidation of methyl 4,6-O-benzylidene-2-O-methyl- α-D-altropyranoside, by the procedure of Yoshimura [4] gave 3-ulose derivative (6) in 85% yield. Then it was converted into 3-methyl branching product (7) using the Grignard's reagents in 76% yield. The coupling constants of the ring protons $J_{1,2}$=0 and $J_{4,5}$=9.0 indicates clearly that the pyranose ring of (6) exists in C-1 chair conformation. Therefore, it is reasonable to believe that the nucleophile will preferentially attack to the carbonyl group from the equitorial direction, unless any special factor affects the selectivity. The configuration of 3-C methyl group was determined in the previous literature.

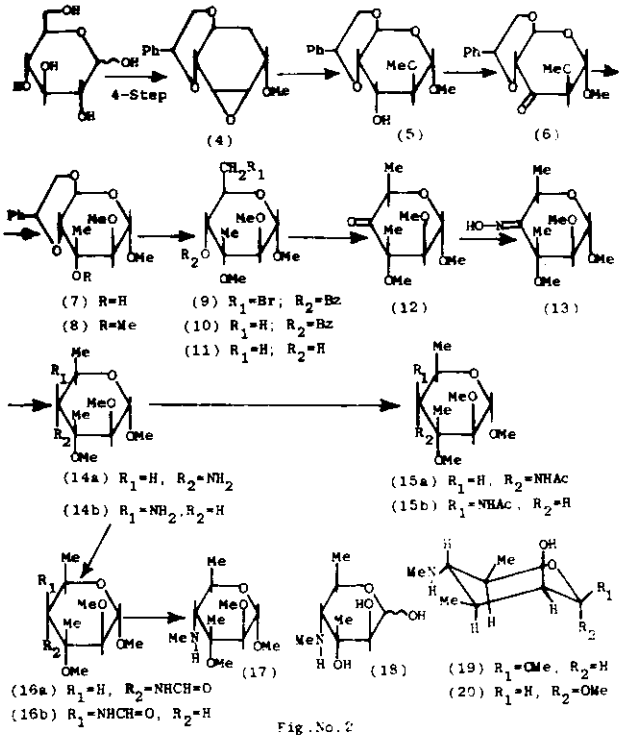

Fig.No.2

The compound (7) was then methylated with sodium hydride and methyl iodide in dimethyl sulfoxide to give methyl 4,6-O-benzylidene-3-C-methyl-2,3-di-O-methyl-α-D-altropyranoside (8) in a firly good yield. This produt was then treated with N-bromosuccinimide in carbon tetrachloride using method of Hanessain-Huller [5] to afford methyl 4-O-benzoyl-6-bromo-6-deoxy-3-C-methyl-2, 3-di-O-methyl-α-D-altropyranoside (9) in 75% yield. The n.m.r. parameters of (9) are given in the Table-1.

The 6-bromo product (9) was reduced with tributyl stannene in benzene in presence of catalytic amount of α α azo -bis-isobutyronitrile to give the corresponding 6-deoxy derivative (10) in 70% yield whose structure was ascertained by n.m.r. data, especially by the appearance of new signals due to C-6 methyl group (δ 1.21, doublet) and by H-5 (δ 4.30, octet).

The removal of benzoyl group at C-4 position of (10) by refluxing with sodium methoxide in methanol gave the desired compound (11) in 90% yield. The infrared spectrum shows no carbonyl group absorption, the absorption at 3500-3550 cm^{-1} which indicate the presence of Sec-hydroxyl group in the given molecule, the n.m.r. spectrum show the presence of 4-hydroxyl group (d, J=12 Hz, OH) in the product, the remaining parameters given in the table-1. The (11) was oxidized with a mixture of dimethyl sulfoxide and triflourocetic anhydride in methylene chloride giving the corresponding 4-ulose derivative (12) in quantitative yield. This compound is supposed to be important in our project because N-methyl amino derivative (17) is the key itermediate, otherwise we have to choose the alternate way for acquiring this functional group at 4-position (in Fig. No.). The ulose derivative (12) was treated with hydroxyamine hydrochloride buffered with sodium acetate in methanol to give methyl 4,6-di-deoxy-4-(hydroxyimino)-3-C-methyl-2,3-di-O-methyl-α-D-arabinohexopyranoside (13) in 91% yield. A signal for the oxime formation appearing at δ 8.7 region (s, =N-OH) in the n.m.r. spectrum given in the table-1. The catalytic reduction of oxime (13) by platinium oxide in glacial acetic acid gave amine derivative as a mixture of altro (14a) and ido derivative (14b) in 60% yield. The presence of NH_2 group can easily be detected by the infrared spectrum NH_2 3250 and 3450 cm^{-1}. The ratio of the two isomers was confirmed to be 2.6:1 by n.m.r. spectra of its N-acetyl derivative (15a) and 15b). The structures of (14a) and (14b) were determined by the coupling constant between H_4 and H_5 (14a, 5.8 Hz) and 14b, 2.0 Hz), indicating a slight deviated C-1 conformation of the altro isomer 14a.

The N-formylation was done by Sheehan's method [6] that is, a mixture of (14a) and (14b) in 1N sodium hydroxide at low temperature was treated with p-nitrophenyl formate in tetrahydrofuran carefully. The mixture was passed through a column of amberlite IR-50 and finally the desired product (16a and 16b) was got in 76% yield, which was reduced with lithium aluminium hydride in benzene-ether to give N-methyl amine derivative in 85% yield. Separation of the product gave the D-altro isomer (17) as a syrup and the structure was ascertained by the n.m.r. spectrum given in the table-1.

The comparative study of the product (17) with methyl sibirosamine [3] shows a slight difference in the chemical shift of N-methylamino group and similiarly for the groups. The de-O-methylation of (17) into D-sibirosamine could not be achieved [7] by the boron trichloride or boron tribromide under the usual procedure. Therefore, in order to make methyl sibirosamine it is necessary to chose some other protecting group, and also need some study for choosing other selective reagent to remove the imposed groups.

Experimental

All melting points were determined with Yanaco micromelting points apparatus. The solution were evaporated under reudced pressure at a bath temperature not exceeding 45-55°C. Optical rotations were measured in 0.5 dm tube

TABLE-1 Chemical shifts(δ/ppm) and coupling constants (Hz) of ring Protons

Compounds	H_1	H_2	H_4	H_5	H_6	$H_{6'}$	OCH_3	CH_3	-OH	other
9	4.79(s)	3.52(d)	5.24(d)	4.50(oct)	3.4(m)	3.60(m)	3.32(s)	1.26(s)		
			$J_{4,5}$=9.5	$J_{5,6}$=$J_{5,6'}$=6.0			3.44(s)			
							3.47(s)			
10	4.72(s)	3.36(s)	5.17(d)	4.30(oct)	1.21(d)		3.37(s)	1.28(s)		
			$J_{4,5}$=9.5	$J_{5,6}$=7.0			3.45(s)			
							3.99(s)			
11	4.60(s)	3.48(s)	3.16(d)	3.82(oct)	1.30(d)		3.25(s)	1.32(s)	2.16(d)	
							3.37(s)		J=12	
							3.41(s)			
12	4.68(d)	3.61(d)		4.18(q)	1.34(d)		3.33(s)	1.44(s)		
	$J_{1,2}$=4.0			$J_{5,6}$=7.5			3.43(s)			
							3.52(s)			
13	4.57(d)	3.35(d)		4.87(q)	1.49(d)		3.38(s)	1.51(s)		8.7(s)=N-OH
	$J_{1,2}$=2			$J_{5,6}$=7.5			3.46(s)			
15a and 15b Ratio to be 2.6:1 [altro(δ 3.94, $J_{4,5}$=5.8 H, H-5)]: [ido (δ 4.38, $J_{4,5}$=2.0 Hz, H-5]										
17	4.59(s)	3.35(s)	2.35(d)	3.80(oct)	1.26(d)		3.42(s)	1.30(s)		2.50(s)-N-ME
($CDCl_3$)			$J_{4,5}$=10	$J_{5,6}$=6			3.36(s)			H
							3.22(s)			
20	4.65(d)	3.45(d)	2.98(d)	3.94(dq)			3.38(s)	1.37(s)		2.8(s) $N-CH_3$
	$J_{1,2}$=1.7	$J_{2,1}$=1.7		$J_{5,4}$=10				3-CH_3		
								1.41(d)		
								5-CH_3		
								$J_{CH_3,5}$=6.2		
21	4.70(s)	3.12(s)	3.08(d)	4.28(q)			3.22(s)	1.23(d)	2.76(d)	
							3.40(s)	$J_{5,6}$=7.5	(-OH)	
							3.42(s)	1.38(s)		
22	4.58(d)	3.42(d)	4.49(d)	4.30(dd)			3.27(s)	1.26(d)		3.07(s) -OMs
	$J_{1,2}$=3.0		J=3	$J_{4,5}$=3.			3.36(s)	J=7.5		
				$J_{5,6}$=7.5			3.42(s)	1.34(s)		

a Carl Zeiss LEP-AI polarimeter, using chloroform as a solvent unless otherwise stated. Ir spectra were recorded with a Hitachi Model EPI-GS grating spectrometer. n.m.r. spectra were taken with JMS PBS 100 spectrometer in deuterio chloroform containing tetramethylsilane as an internal reference. Chemical shifts and coupling constant were recorded in δ and Hz units and IR frequencies in cm^{-1}.

Methyl 4,6-O-benzylidene-2-O-methyl-α-D-altropyranoside(5).

To 400 ml(12.5 mole) of dry methanol, was gradually added 9.2 g(4). The mixture was boiled under reflux on a water bath for 20-24 hours. The mixture was cooled to room temperature and then concentrated under vaccum, the residue was thoroughly extracted with chloroform, and washed with water. The combined extracts and washing were evaporated to dryness. A thick syrup was obtained which crystallized on adding ether. The crystals were wahsed with light petroleum ether and had mp 90-94°C. The yield 20.1 g (87%). Recrystallization from ethanol gave a homogenous substance, mp 98-99°C.

Methyl 4,6-O-benzylidene-2-O-methyl-α-D-altropyranosid-3-ulose(6)

To a solution of 5.27 g (0.067 mole) of dimethyl sulfoxide and 10 ml of methylene dichloride cooled below-65°C with dry ice-acetone bath, was added dropwise 6.8 g (0.05 mole) of trifuluroacetic anhydride in 10 ml of methylene dichloride with stirring for 15-20 minutes and after that 5 g (0.016 mole) of (5) in methylene dichloride. The mixture was worked up as reported in the literature [4]. After evaporation of the solvent gave 85% yield of (6).

Methyl 4,6-O-benzylidene-3-C-methyl-2-O-methyl-α-D-altropyranoside (7).

To a suspension of magnesium turning (0.72 g, 0.29 mole) in 15 ml of dry ether was added with stirring at room temperature of 25°C. The temperature of the flask was controlled by keeping in ice bath. After 10-15 minutes of stirring 2.95 g (0.01 mole) of dry 3-ulose derivative (6) was added alongwith 15 ml of dry benzene. The stirring was continued for 6-8 hours when t.l.c. showed the disappearance of the starting material. Then it was worked out in the usual way. The required material (7) collected by the evaporation of the solvent in 76% yield.

Methyl 4,6-O-benzylidene-3-C-methyl-2,3-di-O-methyl-α D-altropyranoside (8).

To a solution of dry dimethylsulfoxide 8.5 g (0.027 mole) of (7) was added and stirred for a while then 2 g (0.083 mole) of sodium hydride was mixed, and the mixture was stirred at room temperature for 25-30 minutes. Then, 23.6 g (0.16 mole) of methyl iodide was added dropwise, and stirred for three hours. The reaction mixture was worked out in the usual way to give 2,3-di-O-methyl derivative (8).

Methyl 4-O-benzoyl-6-bromo-6-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-altropyranoside (9).

To a solution of 8.8 g (0.027 mole) of (8) in 150 ml of dry carbon tetrachloride, 6.1 g (0.03 mole) of N-bromo-succinimide and 13 g (0.06 mole) of barium carbonate were refluxed on an oil bath with constant stirring. The colour of the content in the flask changed and the reaction was complete with in six hours of refluxing. Then, the reaction mixture was worked out as usual to

give (9) in 75% yield. Mp 136-138°C $[\alpha]D^{18}$ + 56°(c 1.0, MeOH); NMR:δ4.79 (s,H-1), 3.52(d,H-2), 5.24(d,H-2), 5.24(d, $J_{4,5}$=9.5, H-4), 4.50 (oct, J_{4} $_{6}$'=H-6'), 8.19-8.0 and 7.7-7.3 (m,Ph), 3.32,3.44 and 3.47 (3 x (OMe), 1.26(s, CMe).

Methyl 4-O-benzoyl-6-deoxy-3-C-methyl -2,-3-di-O-methyl-α-D-altropyranoside (10).

To a solution of 10.3 g (0.025 mole) of (9) in 150 ml of dry benzene was added 15 g (0.051 mole of tributyl stannane and catalytic amount of α,α-azo-bis-isobutryronitrile (ABIN). The mixture was refluxed on a water bath for about 18-20 hours. After complete conversion it was concentrated and the tin complex was removed by silica gel column chromatography using n-hexane as eluent. After that the product was evaporated to give (10) in 70% yield, mp. 103-104°C; $[x]_{D}18$+58°C(c 1.0, MeOH); NMR: 4.72 (s,H-1), 3.36 (s,H-2), 5.17(d,$J_{4,5}$=9.5, H-4), 4.30 (oct, H-5),1.21(d,$J_{5,6}$=7,H-6), 9.20-8.05 and 7.7-7.38(m,Ph), 3.37, 3.45 and 3.49(3 x OMe), 1.28(s, CMe).

Methyl 6-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-altropyranoside (11).

To 150 ml of dry methanol was added 0.6g (0,26 mole) of sodium with stirring and then 5 g (0.015 mole) of (10) dissolved in 100 ml of methanol and the mixture was refluxed for 12 hours on a water bath, the t.l.c test shows the disappearance of the starting material. The mixture was cooled to room temperature and concentrated to dryness under vaccum, the residue was extracted several times with methylene dichloride, and the extracts were washed with 2% acetic acid, water, and dried. The solvent was evaporated to give (11) in 90% yield, as a syrup, $[\alpha]_{D}18$+38°(c 1.0, MeOH); NMR: 4.60(s,H-1), 3.48(s, H-2), 3.16(d, $J_{4,5}$=10, H-4), 3.82(oct, H-5), 1.30(d,$J_{5,6}$=6, H-6, 2.16(d, J=12, OH), 3.25, 3.37 and 3.41(3 x OMe), 1.32(s, CMe).

Methyl 6-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-altropyranoside-4-ulose (12).

To a solution of 2.63 g (0.033 mole) of dry dimethyl sulfoxide and 5 ml of methylene dichloride was added dropwise 3.4 g (0.025 mole) of triflouroacetic anhydride alongwith 10 ml of methylene dichloride under cooling below -65°C with a dry ice-acetone bath and the mixture was stirred for 20 minutes. Then 2.50 g (0.11 mole) of 4-hydroxy derivative (11) and 5 ml of methylene dichloride was dropped into the mixture and stirred for 30 minutes. After that triethylamine was dropped to neutralize the reaction mixture keeping the temperature below -65°C, then it was worked up under the usual procedure to give (12) as a syrup in 80% yield. $[\alpha]D^{18}$ + 190° (c 1.7, MeOH); IR:Y_{co} 1740 cm^{-1}, NMR:δ4.68(d, $J_{1,2}$ =4, H-1), 3.61(d, H-2), 3.18(q, $J_{5,6}$=7.5, H-5), 1.34(d, H-6), 3.33, 3.43 and 3.52 (3 x OMe), 1.44 (s, CMe). Found: C, 55.07; H, 8.28% Calcd. for $C_{10}H_{18}O_{5}$: C, 55.02; H,8.53%.

Methyl 6-deoxy-methyl-2,3-di-O-methyl -α-D-arabinopyranoside-4-ulose oxime (13).

To a solution of 2.1 g (0.01 mole) of (12) in 15 ml of 50% aqueous methanol, was added 2,3 g of hydroxylamine hydrochloride. The mixture was stirred

for 15-20 minutes at room temperature, then it was buffered by the addition of 1.5 g of crystalline sodium acetate. The mixture was boiled for few minutes and kept at room temperature for 24 hours. Finally, the crystals were filtered off, and recrystallized with hot ethanol, mp 65-67 °C; [α] D^{18}+124° (c 1.5, MeOH); NMR: 4.57 (d, J_{12}=2, H-1), 3.35 (d, H-2), 4.87 (q, $J_{5,6}$=7.5 H-5), 1.49 (d, H-6), 3.38, 3.38 and 3.46 (3 xOMe), 8.7 (s, N-OH), 1.51 (s, CMe).

Found: C, 51.56; H, 8.10% calcd, for $C_{10}H_{19}O_5N$: C, 51.63; H, 8.18%.

Methyl 4-amino-6-deoxy-3-C-methyl-2, 3-di-O-methyl-α-D-altropyranoside(14).

The 900 mg of (13) was hydrogenated by using 300 mg of platinium oxide and 4 ml of acetic acid. The mixture stirred for 20 hours under hydrogen gas atmosphere. The undissolved material was filtered off and the filterate was concentrated to give a mixture of altro and arabino derivative in 60% yield.

In order to determined the ratio of the two isomers a small fraction (120 mg) of the mixture was acetylated using 2 g of acetic anhydride and 2 ml of methanol. The ratio of the two isomers was determined from n.m.r. spectrum of acetylated products (15) to be 2.6 : 1 altro (3.94, J_{45}=5.8 m, H-5): ido (4.38, $J_{4,5}$ = 2.0, H-5).

Found C, 54.85; H, 9.53% Calcd For $C_{10}H_{21}O_4N$: C, 54.91; H, 9.62%.

Methyl 4-formylamino-6-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-altropyranoside(16).

To a solution of 0.6 g (2.73 m mole) of (14) in 10 ml of dry tetrahydrofuran was added dropwise 0.65 g (4.0 m mole) of p-nitrophenyl formate alongwith 10 ml of tetrahydrofuran, and the mixture was stirred in ice bath and for six hours at room temperature. Then, the reaction mixture was extracted with ether to remove p-nitrophenol and concentrated and the remaining solution was passed through a flash column of Waco-gel C-300 (benzene-acetone 3:1 v/v). The eluent was concentrated in vaccum gave the mixture of N-formate 51.0 mg in 76% yield.

Found: C, 53.53; H, 8.49% Calcd for $C_{11}H_{21}O_5N$: C, 53.57; H, 8.53%.

Methyl 4-methylamino-4,6-di-deoxy-3-C-methyl-2,3-di-O-mehtyl-α-D-altropyranoside(17).

The reduction of (16) 0.5 g was carried out in benzene ether with 0.2 g of lithium aluminium hydride. The reaction was heated on an oil bath for 16 hours then hydrolyzed by addition of limited amount of water. The suspended lithium complex was filtered off, and then the filterate dried over $MgSO_4$. The residue obtained after removing the solvent was distilled in vaccum. Finally, this mixture was separated on a silica gel column using chloroform as eluent gave (17) as a syrup, [α]D_{15}+67° (c 0.9, MeOH), NMR: 4.59 (s, H-1), 3.35 (s, H-2), 2.45 (d, $J_{4,5}$=10, H-4), 3.80 (oct, $J_{4,5}$=10, $J_{5,6}$=6, H-5), 1.26 (d, H-6), 3.42, 3.36 and 3.22 (3 x OMe), 2.50 (s, NMe), 1.30 (s, CMe). Found: C, 56.71; H, 9.92% Calcd for $C_{11}H_{23}O_4N$: C, 56.77; H, 9.90%.

Reduction of Methyl 6-deoxy-3-methyl-2,3-di-O-methyl-D-hexopyranoside-4-ulose(12)into a mixture of(11)and(21).

To a solution of 2.1 g (0.01 mole) of (12) in 15 ml of 50% aqueous methanol, was added 1.5 g of sodium borohydride in portions. The mixture was magnetically stirred for 6-7 hours at room temperature. The mixture was checked on t.l.c plate indicating the conversion into a mixture of (11) and 21) in quantitative amount. The mixture was then filterd off, and then diluted with small amount of water. Finally, it was concentrated to a syrup, again diluted with small amount of methanol and removed the solvent under vaccum, the process of dilution repeated 3-4 times so that all borated complex may be removed. The mixture separated on a silica gel column eluted with benzene-acetone mixture. The component separated first have the similar physical data of the product (11), while the rest have $[\alpha]_D^{20}$ + 42°(c 1.0 MeOH); NMR: 4.70 (s, H-1), 3.12(s, H-2), 3.08 (d, H-4), 4.28 (q, H-5), 2.76), 2.76 (d, OH), 3.22, 3.40 and 3.42 (3 x OMe), 1.23 (d, CMe).

4-Chloro-4,6-di-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-idopyranoside (23).

When methyl 6-deoxy-3-C-methyl-2, 3-di-O-methyl-α-D-altropyranoside 2.1 g (0.01 mole) was diluted in 10 ml of dry pyridine, after then 2.5 ml of thionyl chloride was added dropwise with constant stirring at zero degree. After six hours it was checked on a t.l.c plate showed the conversion of starting material. Then reaction mixture diluted in ice-water, extracted with dichloroethane. The combined extracts were washed successively with water, finally dried over sodium sulphate. The solvent was evaporated to dryness, gave 80% yield of the gulo-hexopyranoside derivative. The n.m.r parameter is in confirmity with the group present in the given derivative.

Reaction of compound (23) with sodium azide in HMPA.

The 4-chloro derivative (24) (1 g) was heated in dry hexamethylphosphoric-triamide (10 ml) with sodium azide (1 g) at 130° for 24 hours. The colled mixture was then poured into water and precipitated solid filtered off, and washed well with water, dried over sodium sulphate, and evaporated to a syrup which was tried for crystallization to give the azide derivative. The infrared spectrum indicated very weak absorption of azide group, and a sharp peak of chloro group. On a t.l.c plate indicated that some azidation had occured during the course of reaction.

Methyl 6-deoxy-3-C-methyl-2,3-di-O-methyl-4-methylsulfonyl-α-D-idopyranoside (22).

To the solution of methyl 6-deoxy-3-C-methyl-2,3-di-O-methyl-α-D-idopyranoside(21)(2 g) in 5 ml of pyridine was added methanesulfonylchloride (2.5 ml) dropwise added with constant stirring at 0°. The mobility of the reaction indicated on t.l.c plate after 12 hours, then mixture diluted in ice-cold water and extracts with ether(12 ml x 3). The combined ether extracted were washed successively with water, saturated sodium carbonate and again with water. After being dried over sodium sulphate the ether was evaporated to dryness. The mesylated derivative (22) obtained in 80% yield. The infrared spectrum is in confirmity with the structure, the n.m.r. parameters are 4.58(d, $J_{1,2}$=3.0,H-1),3.42(d,H-2),4.49(d,J=3, H-4),4.30(dd,$J_{4,5}$=3,$J_{5,6}$=7.5,H-5), 3.27,3.36 and 3.42(3xOMe),1.26(d, J=7.5),1.34(s,CH_3), and 3.07(s,OMe).

Attempted reaction of (22)with sodium azide in HMPA.

The 4-mesylgulopyranosidederivative (22) (0.5 g) was heated in dry HMPA (10 ml) with (1 g) sodium azide at 130° to 150° for 24 hours. The reraction product was treated under similar method to obtain azide derivative as mentioned in the previous experiment. The results of the two experiments are similar. The low yield is probably due to the stereo-electronic group present in the compound.

References

1. I.Dyong and G. Schulte, *Tetrahedron Lett.*, *603*, *1980*
2. K.B.Sharpless, A.O.Chong and K.Oshima, *J.Org.Chem.*, ***41***, *177(1976)*.
3. G.F.Cause, T.P.Prebrachenskai, B.P.Invanitskaya and M.A. Susekarikovo, *Antbiotiki*, ***14***, *963(1969)*.
4. P.M.Collins, D.Gardiner, S.Kumar, and W.G.Overend, *J.Chem.Soc., Perkin Trans*, ***1***, *2596 (1972)*; K.Sato and J.Yoshimura, *Bull.Chim.Soc, Jpn.*, ***51***, *2116(1978)*.
5. S.Hanessain, *Carbohydr.Res.*, ***1***, *86(1966)*; D.L.Failla, T.L.Hullar and S.B. Siskin, *Cehm.Commun.*, *716(1966)*
6. J.C.Sheehan and D.D.H.Yang, *J.Am.Chem.Soc.*, ***80***, *1154(1958)*; F.Beninton, R.P.Morin and L.C. Clark, *Jr.*, *J.Org.Chem.*, ***23***, *19(1958)*.
7. K.Hess amd F.Newmann, *Ber.*, ***68***, *1371(1935)*; L.Hough, J.KN. Jones and W.H. Wadmann, *J.Chem.Soc.*, ***64***, *1128(1942)*; T.G.Bonner, and E.J.Bourne and McNalley, *J.Chem.Soc.*, ***1***, *2929(1960)*.