SYNTHESIS OF EIGHT STEREOISOMERIC 5-(ADENIN-9-YL)-2,3,4-TRIHYDROXYPENTANOIC ACIDS*

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Condensation of 5-O-*p*-toluenesulfonyl-2,3-O-isopropylidene-D-ribonolactone (*XIIIb*) with sodium salt of adenine afforded compound *XIV* which on alkaline, followed by acid, hydrolysis gave the (2*R*,3*R*,4*R*)-isomer *V*. The (2*S*,3*S*,4*S*)-isomer *VIII* was prepared analogously from the L-ribonolactone derivative *XVb via* the adenine derivative *XVI*.

Compound *XVIIc* was transformed by reaction with adenine into 6-(adenin-9-yl)-6-deoxy-D-glucose (*XIX*); similarly, 6-(adenin-9-yl)-6-deoxy-D-mannose (*XXI*) was prepared from the protected D-mannofuranoside *XX*. Oxidation of compounds *XIX* and *XXI* in alkaline medium afforded the (2*S*,3*R*,4*R*)-isomer *VI*, 1,2:3,4-Di-O-isopropylidene-D-galactopyranose (*XXIIa*) was transformed into 6-(adenin-9yl)-6-deoxy-D-galactose (*XXIIIb*) which was oxidatively cleaved to give the (2*S*,3*S*,4*R*)-isomer *VII*. Methyl 5,6-di-O-methanesulfonyl-2,3-O-isopropylidene-D-mannofuranoside (*XXVIb*) was transformed into the reactive L-gulofuranoside derivative *XXVIIe* which on condensation with adenine and oxidative cleavage gave the (2*S*,3*R*,4*S*)-isomer *IX*. The (2*R*,3*S*,4*R*)-isomer *XI* was prepared analogously from the D-gulofuranose derivative *XXXIb*. Starting from L-mannose, the (2*R*,3*S*,3*S*)-derivative *X* was prepared *via* the 6-(adenin-9-yl)-6-deoxy-L-mannofuranoside derivative *XXXc*. Methyl 5-O-*p*-toluenesulfonyl-2,3-O-isopropylidene-L-lyxofuranoside *XXXVb* was transformed into 5-(adenin-9-yl)-5-deoxy-2,3-O-isopropylidene-L-lyxofuranose (*XXXVII*) which was oxidized to the lactone *XXXVIII*; this compound on successive alkaline and acid hydrolysis afforded the (2*R*,3*R*,4*S*)-isomer *XII*.

The discovery that naturally occurring D-eritadenine (4-(adenin-9-yl)-(2*R*,3*R*)-dihydroxybutanoic acid *I*; see ref.[1]) exhibits a hypocholesterolaemic activity gave an impetus to detailed investigation of synthetic approaches to this and related compounds[2]. Two isomeric 5-(adenin-9-yl)-2,3,4-trihydroxypentanoic acids, incorrectly named[3] "homoeritadenines", have already been prepared, however, in spite of the original data[4,5], activity of these compounds cannot match that of the compound *I* (ref.[2]). Within the framework of our investigation of aliphatic nucleoside analogues, we described recently an extraordinarily high activity of stereoisomeric eritadenines (*I*–*IV*) which inactivate S-adenosyl-L-homocysteine hydrolase[6], an enzyme important for regulation of biological methylations. Like other inhibitors of this enzyme, D-erita-

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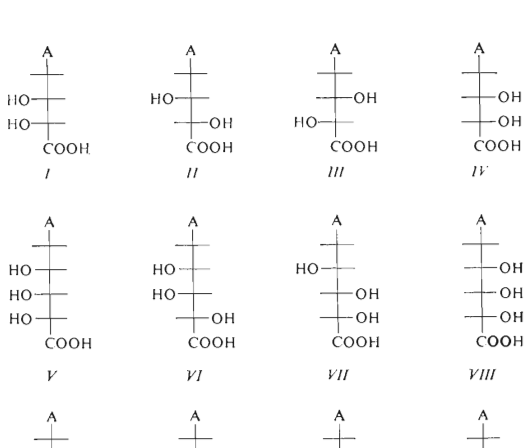
denine (*I*) and its enantiomer *II* exhibit also a significant antiviral effect[7]. Therefore, an investigation of structure-activity relationship in the series of hydroxy-substituted 9-(ω-carboxyalkyl)adenines, analogous to the compounds *I*–*IV*, could be interesting. This communication describes the synthesis of 5-(adenin-9-yl)-2,3,4-trihydroxypentanoic acids.



A = (adenin-9-yl) residue.

SCHEME 1

Because of the presence of three asymmetric carbon atoms in these compounds, eight stereoisomers *V*–*XII* are possible (Scheme 1) six of which have not been prepared as yet. As mentioned above, eritadenines are extraordinarily potent enzyme inhibitors (for *I*: $IC_{50} \sim 10^{-9}$ mol l^{-1}); it was therefore necessary to prepare stereochemically very pure compounds, free of even traces of compounds *I*–*IV*, and at the same time to find sufficiently sensitive methods, separating the stereoisomers *V*–*XII* from each other and particularly from the compounds *I*–*IV*.

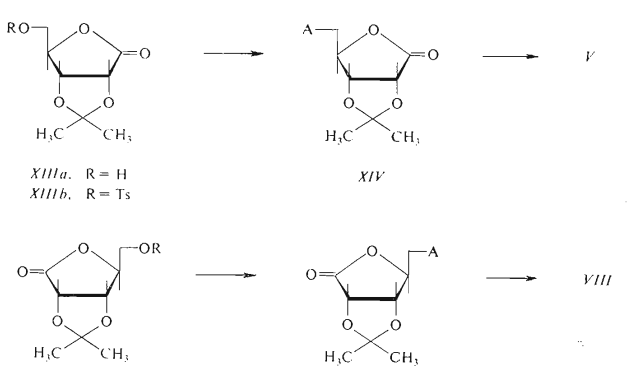
Like eritadenines[7], the compounds *V*–*XII* can in principle be prepared by the following three methods: *a*) by hydrolysis of 5-(adenin-9-yl)-5-deoxyaldopentonolactones[3]: this route is limited by the availability of the starting 2,3-protected lactones, on the other hand, the products cannot be contaminated with the compounds *I*–*IV*; *b*) by Nef oxidation of 6-(adenin-9-yl)-6-deoxyaldohexoses with oxygen in an alkaline medium[3] (although more generally applicable, this reaction is always accompanied by more profound degradations to the compounds *I*–*IV*); *c*) by oxidation of 2,3,4-protected 1-(adenin-9-yl)-1-deoxyaldopentitols (this method is limited by accessibility of the starting compounds: the free alditols can be easily prepared[8] but their specific protection is difficult). All these reaction types have been used in synthesis of the compounds *V*–*XII*.

The apparently facile conversion of the well accessible 5-(adenin-9-yl)-5-deoxyaldopentoses[3,8–10] into the compounds *V*–*XII* by oxidation of aldoses to aldonic acids was unsuccessful: hypoiodites, hypobromites or hypochlorites react with the adenine ring even in a buffered medium; attempted selective oxidation of the aldehyde (hemiacetal) function with such reagents as permanganate, bromate, ceric salts, or osmium or ruthenium tetroxide resulted in degradation of the molecule. For generation of ruthenium tetroxide it is not possible to employ periodate since the molecule contains vicinal hydroxy groups; attempts to replace periodate with analogous oxidation reagents (such as bromate, permanganate, bismuthate or ceric salts) were unsuccessful.

The (2*R*,3*R*,4*R*)-isomer* *V* was obtained using the described[3] reaction of 5-O-*p*-toluenesulfonyl-2,3-O-isopropylidene-D-ribonolactone (*XIIIb*) with sodium salt of adenine. Alkaline saponification, followed by acid hydrolysis, afforded compound *V* (Scheme 2). In the same manner we synthesized the (2*S*,3*S*,4*S*)-enantiomer *VIII*: the starting 2,3-O-isopropylidene-L-ribonolactone (*XVa*), prepared from D-ribose[7], was transformed into the 5-O-*p*-toluenesulfonyl derivative *XVb* which on reaction with adenine gave compound *XVI*. Removal of the protecting group led to the desired compound *VIII* (Scheme 2).

The described[3] preparation of compound *VI* started from 1,2-O-isopropylidene-3,5-O-benzylidene-6-O-*p*-toluenesulfonyl-D-glucopyranose[9]. In our present work we used the easily accessible 3,5-di-O-benzoyl derivative *XVIIc* which on reaction with adenine afforded the well characterizable adenine derivative *XVIII*. Methanolysis of *XVIII*, followed by acid hydrolysis, gave 6-(adenin-9-yl)-6-deoxy-D-glucose (*XIX*). Oxidation of this compound in alkaline medium afforded the (2*S*,3*R*,4*R*)-isomer *VI* as the principal product which, however, was accompanied by D-eritadenine (*I*). The pure compound *VI* was obtained by efficient chromatography on Dowex 1 and cellulose.

* The compounds *V*–*XII* can be named according to the aldonic acids nomenclature: *V* is thus 5-(adenin-9-yl)-5-deoxy-L-ribonic acid. We prefer, however, the substituted pentanoic acid notation.



XIIIa, R = H
XIIIb, R = Ts

XIV

V

XVa, R = H
XVb, R = Ts

XVI

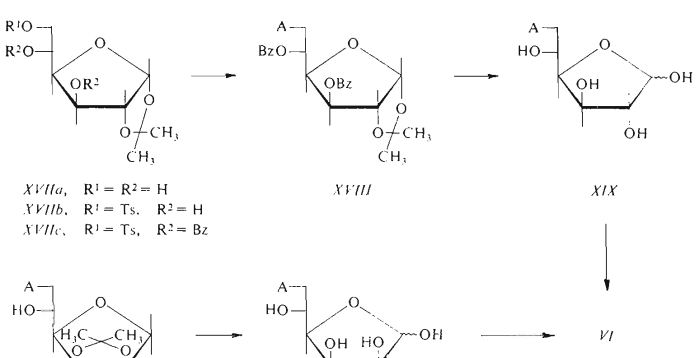
VIII

A = adenin-9-yl, Ts = *p*-toluenesulfonyl residue.

SCHEME 2

Since during the preparation from 6-(adenin-9-yl)-6-deoxyaldohexoses the asymmetry of the $C_{(2)}$ carbon atom disappears, it is possible to prepare the same product from two epimeric derivatives: in this case the compound *VI* was obtained also from methyl 6-(adenin-9-yl)-6-deoxy-2,3-O-isopropylidene-α-D-mannofuranoside (*XX*), described in one of our previous communications[10]. Compound *XXI*, prepared by acid hydrolysis of *XX*, was oxidized in an alkaline medium to compound *VI* which was contaminated with *I* (analogously to the first method) (Scheme 3).

1,2:3,4-Di-O-isopropylidene-α-D-galactopyranose[11] (*XXIIa*) was transformed into the *p*-toluenesulfonyl derivative *XXIIb* which on reaction with adenine afforded smoothly 6-(adenin-9-yl) derivative *XXIIIa*. Its acid hydrolysis gave 6-(adenin-9-yl)-6-deoxy-D-galactose (*XXIIIb*) which was subsequently oxidized in an alkaline medium to the (2*S*,3*S*,4*R*)-isomer *VII*. The same product was obtained also by an independent synthesis starting from 1-(adenin-9-yl)-1-deoxy-2,3-O-isopropylidene-5-O-trityl-D-arabitol (*XXIVa*), accessible by a multiple-step synthesis from 3,4-O-isopropylidene-D-mannitol[8]. This compound (*XXIVa*) was benzoylated, the 5-O-trityl group selectively removed and the arising derivative *XXV* was oxidized with periodate in the presence of ruthenium dioxide. Removal of the protecting groups by methanolysis and acid hydrolysis afforded compound *VII*, identical with the product obtained from D-galactose (Scheme 4).



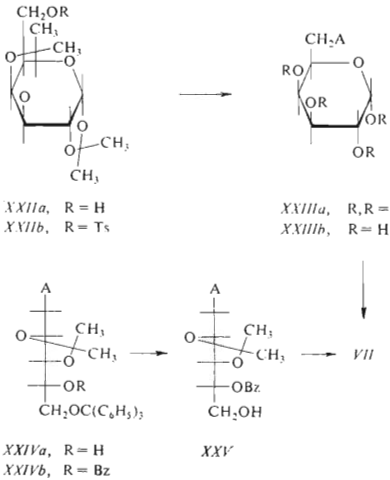
A = adenin-9-yl, Bz = benzoyl, Ts = *p*-toluenesulfonyl residue.

SCHEME 3

Synthesis of the (2*S*, 3*R*,4*S*)-isomer *IX* started from an L-gulose derivative: the recently described[12] conversion of methyl 5,6-di-O-methanesulfonyl-2,3-O-isopropylidene--α-D-mannofuranoside (*XXVIb*) by epimerization at $C_{(5)}$ was in the present work modified by using the more nucleophilic sodium benzoate instead of the originally employed acetate. As expected, this reaction gave an approximately equimolecular mixture of 6-mono- and 5,6-dibenzoate (*XXVIIb* and *XXVIIa*, respectively) which both were methanolyzed to methyl 2,3-O-isopropylidene-α-L-gulofuranoside (*XXVIIc*). Tosylation of this compound, followed by benzoylation of the intermediate *XXVIId*, afforded the fully protected 6-O-*p*-toluenesulfonyl derivative *XXVIIe*, suitable for condensation with adenine (in this reaction it is advisable to protect all the hydroxy groups of the *p*-toluenesulfonyl derivative, as proved for the D-*xylo*[8,10], D-*manno*[10] as well as D-*gluco* series). Condensation with sodium salt of adenine, followed by methanolysis, gave the derivative *XXVIII* which on acid hydrolysis and subsequent alkaline oxidation afforded the acompound *IX*, containing minor amounts of the *threo*-derivative *III* (Scheme 5).

The two isomers *X* and *XI* were synthesized starting from L-mannose: this sugar was prepared from L-arabinose by the described procedure[13], however, its isolation was modified by direct transformation into 2,3:5,6-di-O-isopropylidene-L-mannofuranose[14] (*XXIXa*).

The substituted methyl α-L-mannofuranoside *XXIXb*, prepared by glycosidation[15], on partial acid hydrolysis afforded the 2,3-O-monoisopropylidene derivative *XXIXc* which afforded the fully protected 6-O-*p*-toluenesulfonyl derivative *XXXb* by the



XXIIa, R = H
XXIIb, R = Ts

XXIIIa, R,R = $(CH_3)_2C$
XXIIIb, R = H

XXIVa, R = H
XXIVb, R = Bz

XXV

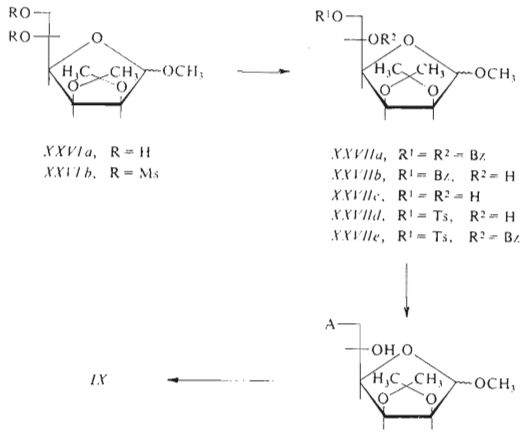
A = adenin-9-yl, Bz = benzoyl, Ts = *p*-toluenesulfonyl residue.

Scheme 4

above-mentioned techniques. The usual reaction sequence (condensation with adenine to *XXXc*, deblocking and oxidation of the obtained 6-(adenin-9-yl)-6-deoxy-L-mannose) gave the (2*R*,3*S*,4*S*)-isomer *X*, accompanied by minor amounts of compound *IV* (Scheme 6).

The compound *XXIXc* was transformed first into the 5,6-dimethanesulfonyl derivative *XXIXd* the reaction of which with sodium benzoate followed by methanolysis resulted in methyl 2,3-O-isopropylidene-α-D-gulofuranoside (*XXXIa*). The 6-O--*p*-toluenesulfonyl-5-O-benzoyl derivative *XXXIb*, prepared from *XXXIa*, reacted with sodium salt of adenine and the product was methanolyzed to the compound *XXXII*. Its acid hydrolysis and alkaline oxidation afforded the (2*R*,3*S*,4*R*)-isomer *XI*, containing small amount of the *threo*-isomer *II* (Scheme 6).

The last isomer of 5-(adenin-9-yl)-2,3,4-trihydroxypentanoic acid was synthesized starting from the blocked derivative of L-lyxose. The compound *XXXb* was prepared recently from methyl 2,3-O-isopropylidene-D-ribofuranoside[16] *via* the methyl

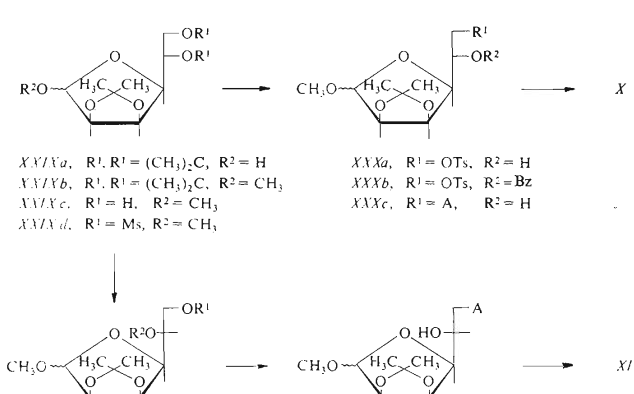


A = adenin-9-yl, Bz = benzoyl, Ms = methanesulfonyl, Ts = *p*-toluenesulfonyl residue.

SCHEME 5

uronate *XXXIII*. In the present work we used a modified preparation of *XXXIII* by oxidation with periodate in the presence of ruthenium, suitable for larger-scale preparations[7]. According to the literature[16], the compound *XXXIII* undergoes an alkali-induced epimerization at $C_{(4)}$ to give the compound *XXXIV* which can be isolated by chromatography. We found that the epimers can be well separated also in the stage of the blocked L-lyxofuranoside *XXXVa* or even the 5-O-*p*-toluenesulfonyl derivative *XXXVb*. Condensation of the *p*-toluenesulfonate *XXXVb* with sodium salt of adenine afforded *XXXVI* which was transformed by acid hydrolysis into 5-(adenin-9-yl)-5-deoxy-L-lyxose (*XXXVII*). Reaction with acetone gave selectively the 2,3-O-isopropylidene derivative *XXXVIII* whose hemiacetal function was oxidized with periodate in the presence of ruthenium. Saponification and hydrolytic removal of the protecting group led to the (2*R*,3*R*,4*S*)-isomer *XII* (Scheme 7).

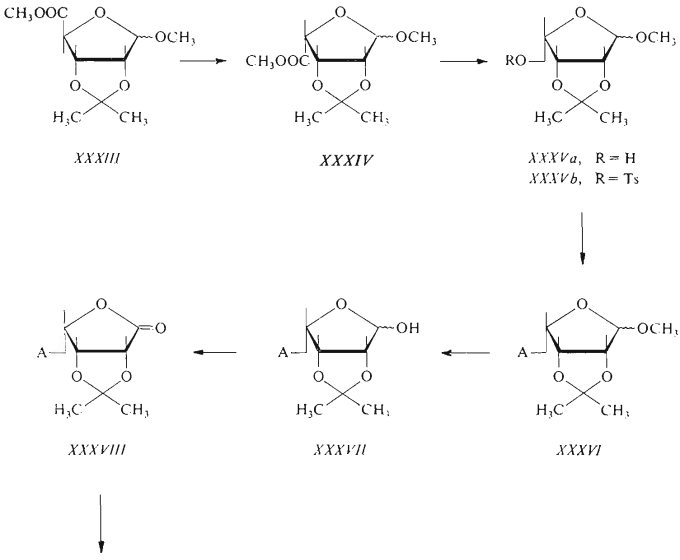
All the prepared derivatives *V*–*XII* were purified first by chromatography on a strongly basic anion exchange resin; this procedure not only separated neutral contaminants but partially also the compounds *I*–*IV*, present in all oxidation products of substituted aldohexoses (method *b*). These very undesirable contaminants



A = adenin-9-yl, Bz = benzoyl, Ms = methanesulfonyl, Ts = *p*-toluenesulfonyl residue.

SCHEME 6

were completely removed by chromatography on cellulose in an ammonia-containing system. Properties of the thus-obtained isomeric compounds *V*–*XII* are given in Table I. In weakly alkaline systems, all these compounds exhibit the same electrophoretic mobilities, identical with those of the eritadenines *I*–*IV*. Chromatographic separation of the two groups of compounds is also not satisfactory; although the acids *V*–*XII* can be separated from the eritadenines *I*–*IV* in an ammonia-containing system, the efficiency of this separation depends strongly on the degree of saturation with ammonia (and thus on temperature) and is therefore limited. For analytical purposes, HPLC appeared to be the method of choice: the chromatography was performed in an acid buffer, containing 11-aminoundecanoic acid[17]. Under conditions of isocratic elution, not only the stereoisomeric compounds *V*–*XII* are separated from each other (*i.e.* compounds of *ribo*, *arabo*, *lyxo* and *xylo* configura-



SCHEME 7

tion) but they are separated also from the *erythro* and *threo* isomers of compounds *I–IV*. Therefore, we used this technique for checking the purity of the obtained derivatives.

Even in acid media, the compounds *V–XII* behave as carboxylic acids rather than lactones. This is obviously due to formation of zwitterions involving the adenine amino group, as indicated also by the limited solubility of these compounds in water. Therefore, for further investigation they were mostly transformed into their water-soluble lithium salts.

6-(Adenin-9-yl)-6-deoxyaldohexoses, used in this work several times as intermediates, can also serve as starting compounds in synthesis of 1-(adenin-9-yl)-1-deoxyaldohexitols[8].

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Unless stated otherwise, the solutions were taken down at 40°C/2 kPa and compounds were dried at 13 Pa over phosphorus pentoxide. Paper chromatography was carried out on a paper Whatman No 1 in the system S1 2-propanol–concentrated ammonia–water (7 : 1 : 2), paper electrophoresis on Whatman No 3 MM in buffer E1 0·05M triethylammonium hydrogen carbonate, pH 7·5 (20 V/cm, 1 h). Chromatography on silica gel was performed on Silufol UV_{254} plates (Kavalier, Czechoslovakia) in the systems S2 chloroform, S3 chloroform–ethanol (95 : 5), S4 chloroform–ethanol (9 : 1), S5 chloroform–ethanol (4 : 1), S6 benzene–ether (7 : 3), S7 benzene–ethyl acetate (8 : 1), S8 benzene–ethyl acetate (7 : 3), S9 ethyl acetate, S10 ethyl acetate–light petroleum (1 : 1), S11

TABLE I

Properties of 5-(Adenin-9-yl)-2,3,4-trihydroxypentanoic acids

Compound	Configuration			$[\alpha]_D^{20}$ [a]	R_F (S1) E_{Up} [b]	τ, min [c]	λ_{max} (ε_{max}) [d]
	C2	C3	C4				
V	*R*	*R*	*R*	+ 7·7°	0·25 0·46	8·9	262 (14 400)
VI	*S*	*R*	*R*	+23·5°	0·29 0·42	9·3	262 (14 500)
VII	*S*	*S*	*R*	+25·1°	0·27 0·46	11·7	262 (14 400)
VIII	*S*	*S*	*S*	− 7·1°	0·25 0·46	8·9	262 (14 700)
IX	*S*	*R*	*S*	−22·8°	0·22 0·44	13·4	262 (14 500)
X	*R*	*S*	*S*	−25·2°	0·29 0·42	9·3	262 (14 800)
XI	*R*	*S*	*R*	+23·2°	0·22 0·44	13·4	262 (14 100)
XII	*R*	*R*	*S*	−26·2°	0·27 0·46	11·4	262 (14 300)
I	*R*	*R*	—	—	0·36 0·46	10·4	—
II	*S*	*R*	—	—	0·41 0·44	13·0	—

[a] (c = 0·5, 1M-HCl); [b] electrophoretic mobility in E1 referred to Up; [c] elution time (HPLC); [d] at pH 2.

tetrachloromethane–chloroform (3 : 1). Preparative chromatography on silica gel was run on 40 × 16 × 0·3 cm loose layers of silica gel, containing a fluorescent indicator (Service Laboratories of the Institute) or on a dry-packed column (200 g) of silica gel according to Pitra (30 to 40 μ). Preparative chromatography on cellulose was performed on a column (80 × 4 cm) of microcrystalline cellulose (Macherey and Nagel) in the system S1 (20 ml/h, fraction 1 h). High performance liquid chromatography (HPLC) was carried out on a column of Separon SI C18 (250 × 4 mm); elution (2 ml/min) with 0·1M ammonium dihydrogen phosphate, pH 3·95, 0·002M in 11-aminoundecanoic acid; detection at 260 nm. The solutions were deionized on a column of Dowex 50X8 (H^+ form; 200 ml) by elution with water until the UV absorption and conductivity of the eluate dropped; adenine-containing compounds were eluted with 2·5% ammonia. Chromatography on Dowex 1X2 (acetate) was carried out using a 100—150 ml column; after application of the material, the column was washed with water till UV absorption of the eluate dropped and then with acetic or formic acid (linear gradient). The fractions were analyzed by chromatography (S1) and HPLC. The UV spectra were taken in aqueous solutions on a Specord UV-VIS spectrophotometer (Carl Zeiss, Jena), ^{1}H NMR spectra on a Varian 100 instrument in deuteriochloroform or hexadeuteriodimethyl sulfoxide (internal standard hexamethyldisiloxane); chemical shifts given in ppm, coupling constants in Hz.

5-(Adenin-9-yl)-5-deoxy-2,3-O-isopropylidene-D-ribonolactone (*XIV*) (ref.[3])

A solution of *p*-toluenesulfonyl chloride (28·5 g; 0·15 mol) in pyridine (100 ml) was added dropwise at 0°C in the course of 30 min to a stirred solution of compound *XIIIa* (ref.[7]) (18·8 g; 0·1 mol) in pyridine (100 ml). After stirring in ice for 4 h and standing at 0°C for 48 h, the mixture was poured on ice (500 g) and extracted with chloroform (4 × 200 ml). The extract was washed with water (2 × 100 ml), dried over magnesium sulfate and taken down *in vacuo*. The residue was codistilled with toluene (4 × 100 ml) to remove pyridine, dissolved in benzene and filtered through a column of neutral alumina (100 g). The product was eluted with benzene (1 litre), the eluate taken down and the residue dried *in vacuo*, leaving 11·1 g (42·5%) of *XIIIb* as a yellowish oil, R_F 0·60 (S2). This product (42·5 mmol) in dimethylformamide (20 ml) was added to a suspension of sodium salt of adenine (prepared *in situ* by stirring a mixture of 50 mmol of adenine, 50 mmol of sodium hydride and 100 ml of dimethylformamide at 60°C for 1 h). The mixture was stirred at 100°C for 18 h under exclusion of moisture and taken down at 50°C/13 Pa. The residue was codistilled with toluene under the same conditions (2 × 100 ml), taken up in boiling chloroform (700 ml total) and the extract was filtered through Celite. After evaporation of the filtrate *in vacuo*, the residue was chromatographed on a column of silica gel (elution with S3) and the combined fractions were crystallized from ethanol, yielding 3·8 g (29·3%) of compound *XIV*, m.p. 197°C, $[\alpha]_D^{20}$ +31·6° (*c* 0·5, 1M-HCl), R_F = 0·51 (S1), 0·48 (S5), E_{Up} = 0·43 (E1). For $C_{13}H_{15}N_5O_4$ (305·3) calculated: 51·14% C, 4·95% H, 22·94% N; found: 51·33% C, 5·77% H, 22·71% N.

5-(Adenin-9-yl)-5-deoxy-2,3-O-isopropylidene-L-ribonolactone (*XVI*)

The compound *XVa* (see ref.[7]; 3·8 g; 20 mmol) was transformed into the *p*-toluenesulfonyl derivative *XVb* as described for the compound *XIIIb*; yield 3·9 g (74·7%); R_F 0·60 (S2). A solution of the product (14·9 mmol) in dimethylformamide (15 ml) was added to a suspension of sodium salt of adenine (20 mmol) in dimethylformamide (30 ml), the reaction and work-up being carried out as described for the compound *XIV*. Yield 1·30 g (28·3%) of *XVI*, m.p. 192—193°C (ethanol–ether), $[\alpha]_D^{20}$ −30·5° (*c* 0·5, 1M-HCl), R_F 0·51 (S1,) 0·48 (S5). For $C_{13}H_{15}N_5O_4$ (305·3) calculated: 51·14% C, 4·95% H, 22·94% N; found: 51·42% C, 4·89% H, 22·73% N.

6-(Adenin-9-yl)-6-deoxy-3,5-di-O-benzoyl-1,2-O-isopropylidene-α-D-glucofuranose (*XVIII*)

p-Toluenesulfonyl chloride (19 g; 0·1 mmol) was added at 0°C to a solution of 1,2-O-isopropylidene-α-D-glucofuranose[14] (*XVIIa*; 21·5 g; 92·5 mmol) in pyridine (80 ml). After stirring at 0°C for 2 h and standing in a refrigerator overnight the mixture was decomposed with water (5 ml) and after 1 h taken down. The residue was taken up in chloroform (200 ml), the solution washed with water (3 × 50 ml), dried over magnesium sulfate and evaporated *in vacuo*, leaving 32·2 g (98%) of chromatographically pure (R_F 0·20 in S9) compound *XVIIb*. Benzoyl chloride (23·3ml; 0·2 mol) was added dropwise at 0°C to a stirred solution of the obtained *XVIIb* in pyridine (150 ml). The mixture was set aside at 0°C for 2 days, decomposed with ethanol (5 ml), after 1 h poured on ice (1 kg) and extracted with chloroform (3 × 200 ml). The extract was washed with water (3 × 100 ml), dried over magnesium sulfate and taken down. The residue was taken up in tetrachloromethane and chromatographed on a column of silica gel. After washing with tetrachlorochloromethane (1 litre) the product was eluted with the system S11 (R_F 0·50 in S11). The residue was dried, affording 35·5 g (70% based on *XVIIb*) of compound *XVIIc* as an amorphous foam.

A solution of this product (63 mmol) in dimethylformamide (40 ml) was added to a suspension of sodium salt of adenine (60 mmol) in dimethylformamide (200 ml). After stirring at 100°C for 18 h, the mixture was taken down at 50°C/13 Pa. The residue was extracted with hot chloroform (1 litre), the extract filtered through Celite, taken down and the residue was chromatographed on a column of silica gel in chloroform. Crystallization of the product-containing fraction from ethanol–light petroleum afforded 11·1 g (33·9% based on adenine) of compound *XVIII*, m.p. 120–121°C. R_F 0·34 (S3). For $C_{28}H_{27}N_5O_7$ (545·5) calculated: 61·64% C, 4·99% H, 12·84% N; found: 62·14% C, 5·01% H, 13·16% N. ^{1}H NMR spectrum ($CDCl_3$): 1·27 + 1·47 (2 s, 2 × 3 H) $(CH_3)_2C$; 4·37 (dd, 1 H, $J_{4',3'} = 3·0$, $J_{4',5'} = 9·0$) $H_{4'}$; 4·55 (dd, 1 H, $J_{6'',5'} = 5·0$, $J_{6'',6'} = 16·0$)$H_{6''}$; 4·63 (d, 1 H, $J_{2',1'} = 3·8$, $J_{2',3'} = 1·0$) $H_{2'}$; 4·91 (dd, 1 H, $J_{6',5'} = 3·0$, $J_{6',6''} = 16·0$) $H_{6'}$; 5·41 (d, 1 H, $J_{3',2'} = 1·0$, $J_{3',4'} = 3·0$) $H_{3'}$; 5·65 (m, 1 H) $H_{5'}$; 6·0 (d, 1 H, $J_{1',2'} = 3·8$) $H_{1'}$; 6·10 (br, 2 H) NH_2; 7·20–8·0 (m, 10 H) arom.; 7·86 (s, 1 H) H_2; 7·99 (s, 1 H) H_8.

6-(Adenin-9-yl)-6-deoxy-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (*XXIIIa*)

Concentrated sulfuric acid (3·6 ml), followed by D-galactose (90 g; 0·5 mol), was added to a stirred suspension of freshly fused zinc chloride (108 g) in acetone (1 100 ml). After stirring for 4 h, a suspension of sodium carbonate (180 g) in water (320 ml) was added, the mixture was stirred for 1 h and filtered. The salts were washed with acetone (500 ml), the filtrate was taken down *in vacuo* and the residue was extracted with ether (3 × 200 ml). The extract was dried over magnesium sulfate, taken down and the residue was distilled *in vacuo* to give 57·4 g (44%) of compound *XXIIa*, b.p. 120–121°C/13 Pa; R_F 0·25 (S2).

p-Toluenesulfonyl chloride (20 g; 0·105 mol) was added in portions to a stirred solution of the compound *XXIIa* (26 g; 0·1 mol) in pyridine (100 ml) at 0°C. The mixture was stirred in ice for 1 h, set aside at room temperature overnight and decomposed with water (5 ml). After standing for 1 h, the mixture was diluted with ethyl acetate (1 litre), washed with water (3 × 200 ml) and taken down. The residue (*XXIIb*; R_F 0·52 in S2) was codistilled with toluene (4 × 100 ml) and dissolved in dimethylformamide (100 ml). This solution was added to a suspension of sodium salt of adenine (0·1 mol) in dimethylformamide (300 ml) and the mixture was heated to 100°C for 15 h. The product was isolated in the same manner as described for the compound *XVIII*. Crystallization from ethyl acetate (addition of light petroleum) afforded 11·0 g (29·2% based

on *XXIIa*) of compound *XXIIIa*, m.p. 191–192°C, $[\alpha]_D^{20}$ +1·0° (*c* 0·5, dimethylformamide). R_F 0·59 (S4). For $C_{17}H_{23}N_5O_5$ (377·4) calculated: 54·10% C, 6·14% H, 18·56% N; found: 54·51% C, 6·37% H, 18·41% N. UV-spectrum (pH 2): λ_{max} 262 nm (14 700); (pH 12): λ_{max} 263nm (15 000).

6-(Adenin-9-yl)-6-deoxy-D-galactose (*XXIIIb*)

A solution of compound *XXIIIa* (3·8 g; 10 mmol) in 0·25M sulfuric acid was warmed to 37°C for 24 h (the reaction was complete according to S5). After dilution with water (100 ml) the mixture was neutralized with barium hydroxide to pH 7·0, warmed to 70°C and filtered through Celite which was then washed with boiling water (300 ml). The filtrate was taken down *in vacuo* and the residue crystallized from ethanol (with addition of ether), affording 2·75 g (93%) of compound *XXIIIb* which did not melt below 250°C; $[\alpha]_D^{20}$ +74·5° (*c* 0·5, 0·1M-HCl). R_F 0·39 (S1). For monohydrate $C_{11}H_{17}N_5O_6$ (315·3) calculated: 41·90% C, 5·44% H, 22·22% N; found: 41·60% C, 5·28% H, 21·87% N. UV-spectrum (pH 2): λ_{max} 262 nm (14 800); (pH 12): λ_{max} 264 nm (15 000).

Methyl 2,3:5,6-Di-O-isopropylidene-α-D-mannofuranoside (ref.[16])

A mixture of D-mannose (104·5 g; 0·58 mol), acetone (1 500 ml), anhydrous cupric sulfate (150 g) and concentrated sulfuric acid (5 ml) was stirred overnight in a stoppered flask, the solid was filtered off and washed with acetone (200 ml). The filtrate was stirred with sodium hydrogen carbonate (100 g) till neutral, made alkaline with triethylamine, filtered and taken down *in vacuo*. The residue was dissolved in hot acetone (200 ml) and light petroleum was added under stirring until the solution became turbid and crystals separated. After standing in a refrigerator overnight, 141 g (93·5%) of 2,3:5,6-di-O-isopropylidene-α-D-mannofuranose were obtained. A solution of this product in dimethylformamide (500 ml) was treated with sodium hydride in portions (total 12 g; 0·5 mol) under cooling with ice. After 30 min at 0°C, methyl iodide (47 ml; 0·75 mol) was added dropwise during 30 min, the temperature being kept below +20°C. The mixture was stirred without cooling overnight, taken down at 50°C/13 Pa and the residue was taken up in ethyl acetate (500 ml). The solution was washed with water (3 × 100 ml), dried over magnesium sulfate and taken down. Distillation of the residue afforded 108·5 g (79%) of the product, b.p. 137–139°C/13 Pa; R_F 0·62 (S6). For $C_{13}H_{22}O_6$ (274·3) calculated: 56·92% C, 8·08% H; found: 57·15% C, 8·29% H.

Methyl 5,6-Di-O-benzoyl-2,3-O-isopropylidene-α-L-gulofuranoside (*XXVIIa*) and Methyl 6-O-Benzoyl-2,3-O-isopropylidene-α-L-gulofuranoside (*XXVIIb*)

A solution of methyl 2,3:5,6-di-O-isopropylidene-α-D-mannofuranoside (108 g; 0·394 mol) in 0·1M-HCl in 50% aqueous ethanol (1 litre) was set aside at room temperature overnight[15], neutralized with Amberlite IR 45 and filtered. The resin was washed with ethanol and the filtrate was taken down (R_F 0·15 in S10, quantitative reaction). The residue was dried by codistillation with pyridine (3 × 100 ml), dissolved in pyridine (250 ml) and cooled with ice. Methanesulfonyl chloride (73 ml; 0·94 mol) was added dropwise to the stirred solution during 30 min. After stirring overnight, the mixture was diluted with ethyl acetate (1 litre), washed with water (5 × 200 ml), dried over magnesium sulfate and taken down. Crystallization of the residue from ethyl acetate–light petroleum gave 79 g (51%) of compound *XXVIb*, m.p. 144–145°C, in accord with the literature[15].

A stirred mixture of the compound *XXVIb* (78 g; 0·2 mol), sodium benzoate (115 g; 0·8 mol) and dimethylformamide (500 ml) was refluxed (bath temperature 150°C) for 7 h, diluted with ethyl acetate (1 litre) and filtered. The solid was washed with ethyl acetate (500 ml) and the filtrate was taken to dryness *in vacuo*. The residue was dissolved in ethyl acetate (500 ml), the solution was washed with water (3 × 100 ml), dried over magnesium sulfate and taken down. The residue was chromatographed on a column of silica gel (250 g) in benzene and the product, R_F 0·46 (S7), was crystallized from a mixture of ethyl acetate and light petroleum. Yield 20·0 g (22·5%) of compound *XXVIIa*, m.p. 104–105°C, $[\alpha]_D^{20}$ +86·7° (*c* 0·5, chloroform). For $C_{24}H_{26}O_8$ (442·5) calculated: 65·15% C, 5·92% H; found: 64·66% C, 5·72% H. Elution with benzene–ethyl acetate (95 : 5) afforded compound *XXVIIb*, R_F 0·10 (S7), which was crystallized from ethyl acetate–light petroleum; yield 16 g (23·5%), m.p. 76–78°C, $[\alpha]_D^{20}$ +56·1° (*c* 0·5, chloroform). For $C_{17}H_{22}O_7$ (338·4) calculated: 60·34% C, 6·55% H; found: 59·85% C, 6·37% H.

Methyl 2,3-O-Isopropylidene-α-L-gulofuranoside (*XXVIIc*)

A solution of an equimolar mixture (30 g) of compounds *XXVIIa* and *XXVIIb* in 0·1M sodium methoxide (250 ml) was set aside overnight, neutralized with Dowex 50X8 (H^+ form) and filtered. The Dowex was washed with methanol (100 ml) and the filtrate was taken down. The residue was chromatographed on a column of silica gel (150 g) in chloroform to remove methyl benzoate. The product was eluted with chloroform–ethyl acetate (3 : 1). The eluate was taken down and crystallized to give 15·2 g (83%) of compound *XXVIIc*, m.p. 78°C, R_F 0·50 (S9); $[\alpha]_D^{20}$ +82·5° (*c* 0·5, methanol); reported[12] m.p. 76·5–77°C, $[\alpha]_D^{20}$ +82·3° (methanol). For $C_{10}H_{18}O_6$ (234·2) calculated: 51·27% C, 7·74% H; found: 51·42% C, 7·43% H.

The compound *XXVIIc* was prepared also from pure separate samples (0·5 g) of the compounds *XXVIIa* and *XXVIIb*; the obtained products had identical $[\alpha]_D$ and m.p. values.

Methyl 6-(Adenin-9-yl)-6-deoxy-2,3-O-isopropylidene-α-L-gulofuranoside (*XXVIII*)

p-Toluene sulfonyl chloride (11·4 g; 60 mmol) was added at 0°C to a solution of compound *XXVIIc* (11·7 g; 50 mmol) in pyridine (50 ml). The mixture was stirred at 0°C for 1 h, set aside at room temperature overnight, decomposed with water (10 ml), after 1 h taken down and partitioned between ethyl acetate (400 ml) and water (100 ml). The organic layer was washed with water (2 × 100 ml), dried over magnesium sulfate and taken down. The residue was co-distilled with toluene (3 × 100 ml), dissolved in acetonitrile (200 ml) and the solution was added to benzoyl cyanide (9·1 g; 61·8 mmol), followed by triethylamine (1 ml). After 3 h the mixture was taken down *in vacuo* and the residue chromatographed on a column of silica gel (150 g) in chloroform, affording 22·5 g (91%) of chromatographically pure *XXVIIe* (R_F 0·34 in S2). A solution of this product (45 mmol) in dimethylformamide (40 ml) was added to a suspension of sodium salt of adenine (50 mmol) in dimethylformamide (100 ml). After stirring at 100°C for 18 h the mixture was taken down *in vacuo*, the residue was mixed with 0·1M sodium methoxide (250 ml) and set aside overnight. The mixture was neutralized with Dowex 50X8 (H^+ form), made alkaline with triethylamine, filtered and the Dowex was washed with methanol (200 ml). The filtrate was evaporated *in vacuo*, the residue extracted with boiling chloroform (1 litre), the extract filtered through Celite and taken down. Crystallization from methanol afforded 7·0 g (40% based on *XXVIIc*) of compound *XXVIII*, m.p. 204–205°C; $[\alpha]_D^{20}$ +41·5° (*c* 0·5, methanol); R_F 0·55 (S5). UV spectrum (pH 2): λ_{max} 261 nm (14 700). For $C_{15}H_{21}N_5O_5$ (351·4) calculated: 51·27% C, 6·02% H, 19·94% N; found: 51·55% C, 6·18% H, 19·80% N.

2,3:5,6-Di-O-isopropylidene-L-mannofuranose[13] (*XXIXa*)

To a stirred mixture of L-arabinose (150 g; 1 mol) and nitromethane (500 ml) 1M sodium methoxide solution (1 350 ml) was added during 10 min. After stirring overnight under exclusion of moisture, the product was collected on filter, washed with methanol and light petroleum and dried *in vacuo*. A solution of this product in ice-cold water (900 ml) was added dropwise during 30 min to a stirred mixture of water (250 ml) and concentrated sulfuric acid (200 ml) in a 5 l beaker. Water (2·5 l) was added and the mixture was neutralized to pH 6—7 with sodium carbonate. After cooling to 30°C, a solution of phenylhydrazine (100 ml) in acetic acid (250 ml) was added and the mixture was stirred in ice for 2 h. The product was collected on filter, washed with water, ethanol and ether and dried *in vacuo*. A mixture of the product, benzoic acid (25 g), benzaldehyde (250 ml), water (2 l) and ethanol (400 ml) was refluxed for 3 h, cooled and decanted. The aqueous layer was washed with chloroform (3 × 200 ml), decolorized with charcoal and taken down *in vacuo*. The residue was mixed with ethanol, filtered, the solid washed with ethanol and the filtrate taken down *in vacuo*. After drying at 70°C/13 Pa, the residue was mixed with acetone (500 ml), anhydrous cupric sulfate (50 g), ethyl orthoformate (30 ml) and concentrated sulfuric acid (3 ml) and stirred for 24 h. The insoluble portion was removed by filtration, washed with acetone (200 ml) and the filtrate was stirred with barium carbonate (50 g) till the mixture was neutral. The suspension was filtered and the solid washed with acetone (200 ml). The filtrate was taken down and the residue chromatographed on a column of silica gel (200 g) in chloroform. The thus-obtained product was crystallized from ether—light petroleum; yield 55 g (21% based on L-arabinose) of compound *XXIXa*, m.p. 120—121°C. Thin-layer chromatography of the product revealed a spot identical with that of the D-enantiomer (R_F 0·60 in S2).

Methyl 5-O-Benzoyl-2,3-O-isopropylidene-6-O-*p*-toluenesulfonyl-α-L-mannofuranoside (*XXXb*)

Methyl iodide (100 ml) was added to a stirred mixture of compound *XXIXa* (54·0 g; 0·207 mol), dimethylformamide (250 ml) and silver oxide (100 g). The mixture was stirred overnight (calcium chloridetube) and filtered through Celite. Dimethylformamide was removed *in vacuo*, the residue was taken up in chloroform and the solution was again filtered through Celite. Evaporation of the filtrate and distillation of the residue *in vacuo* afforded 47·6 g (84%) of compound *XXIXb*, b.p. 137 to 138°C/13 Pa; R_F 0·62 (S6). A mixture of this product (174 mmol), 50% aqueous ethanol (400 ml) and concentrated hydrochloric acid (4 ml) was set aside overnight (R_F 0·15, S6), neutralized with Amberlite IR 45, filtered and the Amberlite washed with methanol. The filtrate was taken down *in vacuo*, the residue codistilled with pyridine (3 × 100 ml), taken up in pyridine (200 ml) and the solution (containing compound *XXIXc*) was divided into two equal parts.

One part (100 ml; 87 mmol of *XXIXc*) was treated with *p*-toluenesulfonyl chloride (17 g; 89 mmol) under cooling with ice, stirred in ice for 1 h and set aside overnight. The mixture was decomposed with water (5 ml) and after 1 h diluted with ethyl acetate (500 ml). After washing with water (4 × 100 ml), the organic layer was taken down *in vacuo* and the residue codistilled with toluene (3 × 100 ml). Chromatography on silica gel (150 ml) in chloroform afforded 22·3 g (64%) of *XXXa*, R_F 0·56 (S3) (*XXIXc*: R_F 0·25), as a glass.

The thus-obtained compound *XXXa* (55·5 mmol) was dissolved in pyridine (60 ml) and benzoyl chloride (8 ml; 69 mmol) was added dropwise at 0°C under stirring. After stirring for 2 h at 0°C the mixture was set aside overnight and decomposed with water (10 ml). After 1 h ethyl acetate (500 ml) was added, the solution was washed with water (3 × 100 ml) and taken down. Codistillation of the residue with toluene (3 × 100 ml) and crystallization from ethyl acetate and light petroleum afforded 21·3 g (76%) of compound *XXXb*, m.p. 133—134°C, $[\alpha]_D^{20}$ −47·0°

(*c* 0·5, chloroform). For $C_{26}H_{28}SO_9$ (516·5) calculated: 60·45% C, 5·46% H, 6·21% S; found: 60·74% C, 5·47% H, 6·47% S. ^{1}H NMR spectrum ($CDCl_3$): 1·16 + 1·32 (2s, 2 × 3 H) $(CH_3)_2C$; 2·24 (s, 3 H) CH_3-phenyl); 3·24 (s, 3 H) OCH_3; 4·26 (dd, 1 H, $J_{4,3} = 3·5$, $J_{4,5} = 8·0$) H_4; 4·48 (d, 1 H, $J_{2,3} = 6·0$) H_2; 4·33 (m, 2 H) 2 H_6; 4·78 (dd, 1 H, $J_{3,2} = 6·0$, $J_{3,4} = 3·5$) H_3; 4·83 (s, 1 H, $J_{1,2} = 0·5$) H_1; 5·34 (dt, 1 H, $J_{5,4} = 8·0$, $J_{5,6} = J_{5,6'} = 3·0$) H_5; 7·0—8·0 (m, 9 H) aromatic protons.

Methyl 6-(Adenin-9-yl)-6-deoxy-2,3-O-isopropylidene-α-L-mannofuranoside (*XXXc*)

The compound *XXXb* (20·6 g; 40 mmol) was added to a suspension of sodium salt of adenine (50 mmol) in dimethylformamide, the mixture was stirred at 100°C for 15 h and taken down *in vacuo*. The residue was codistilled with toluene, dissolved in 0·1M sodium methoxide (200 ml), the solution was set aside overnight and neutralized with Dowex 50X8 (H^+ form). The ion exchange resin was filtered off, washed with methanol (100 ml) and the filtrate was taken down *in vacuo*. The residue was extracted with boiling chloroform (500 ml), the extract filtered through Celite and taken down. The product was crystallized from methanol, yielding 7·6 g (54%) of chromatographically homogeneous compound *XXXc*, m.p. 191°C; $[\alpha]_D^{20}$ −56·0° (*c* 0·5, dimethylformamide); R_F 0·42 (S4). For $C_{15}H_{21}N_5O_5$ (351·4) calculated: 51·27% C, 6·02% H, 19·94% N; found: 50·91% C, 5·71% H, 19·99% N.

Methyl 2,3-O-Isopropylidene-5,6-di-O-methanesulfonyl-α-L-mannofuranoside (*XXIXd*)

Methanesulfonyl chloride (17 ml; 0·22 mol) was added dropwise during 20 min to an ice-cooled and stirred solution of compound *XXIXc* (87 mmol) in pyridine (100 ml). After stirring for 1 h in ice and standing overnight, the mixture was treated with water (10 ml) and after 1 h diluted with ethyl acetate (500 ml). The mixture was washed with water (4 × 100 ml), taken down, the residue codistilled with toluene (3 × 100 ml) and dissolved in hot ethyl acetate. Light petroleum was gradually added to this solution at such a rate as to allow crystals to separate. After standing in refrigerator overnight, the product was collected on filter, washed with light petroleum and dried *in vacuo*. Yield 30·1 g (86%) of compound *XXIXd*, m.p. 142—143°C; $[\alpha]_D^{20}$ −33·6° (*c* 0·5; chloroform). For $C_{12}H_{22}S_2O_{10}$ (390·4) calculated: 36·91% C, 5·68% H, 16·42% S; found: 36·54% C, 5·55% H, 16·29% S.

Methyl 2,3-O-Isopropylidene-α-D-gulofuranoside (*XXXIa*)

Compound *XXIXd* (29·3 g; 75 mmol) was added at 100°C to a suspension of sodium benzoate (0·3 mol) in dimethylformamide (500 ml). The mixture was stirred at 150°C for 12 h (calcium chloride tube), diluted with ethyl acetate (1 litre), washed with water (3 × 200 ml) and taken down. The residue was taken up in chloroform (300 ml), and the solution was filtered through Celite. The solvent was evaporated and the dry residue was allowed to stand with 0·1M sodium methoxide (200 ml) overnight. The mixture was neutralized with Dowex 50X8 (H^+ form), filtered, the Dowex was washed with methanol and the filtrate was taken down. Chromatography of the residue on silica gel (150 g) in chloroform and then in chloroform–ethyl acetate (3 : 1) afforded the compound *XXXIa* which upon crystallization from ethyl acetate–light petroleum melted at 77—78°C. Yield 10·5 g (60%); $[\alpha]_D^{20}$ −79·5° (*c* 0·5; methanol). Its chromatographic behaviour was identical with that of *XXVIIc* (R_F 0·40 in S19). For $C_{10}H_{18}O_6$ (234·2) calculated: 51·27% C, 7·74% H; found: 51·53% C, 7·91% H.

Methyl 5-O-Benzoyl-2,3-O-isopropylidene-6-O-*p*-toluenesulfonyl-α-D-gulofuranoside (*XXXIb*)

p-Toluenesulfonyl chloride (6·3 g; 33 mmol) was added at 0°C to a solution of compound *XXXIa* (6·6 g; 28 mmol) in pyridine (30 ml). The mixture was stirred at 0°C for 1 h and at room temperature overnight. After decomposition with water (5 ml) the mixture was diluted with ethyl acetate (500 ml), washed with water (4 × 50 ml) and taken down. The residue was codistilled with toluene (3 × 50 ml) and dried *in vacuo*. The obtained chromatographically pure (R_F 0·80 in S9; for *XXXIa* R_F 0·35) product (11 g) was dissolved in acetonitrile (150 ml) and treated with benzoyl cyanide (4·6 g; 35 mmol) and triethylamine (1 ml). After 1 h the mixture was taken down and the residue was chromatographed on silica gel (150 g) in chloroform. Crystallization from ethyl acetate–light petroleum gave 8·9 g (61%) of compound *XXXIb*, m.p. 100—101°C; $[\alpha]_D^{20}$ −27·5° (*c* 0·5; chloroform); R_F 0·60 (S2). For $C_{26}H_{28}SO_9$ (516·5) calculated: 60·45% C, 5·46% H, 6·21% S; found: 60·81% C, 5·80% H, 6·59% S.

Methyl 6-(Adenin-9-yl)-6-deoxy-2,3-O-isopropylidene-α-D-gulofuranoside (*XXXII*)

Compound *XXXIb* (8·2 g; 16 mmol) was added to a suspension of sodium salt of adenine (20 mmol) in dimethylformamide (80 ml) and the mixture was heated to 100°C for 15 h. Further work-up procedure was the same as described for the compound *XXXc*. Crystallization from methanol afforded 4·3 g (76·5%) of compound *XXXII*, m.p. 205°C; $[\alpha]_D^{20}$ −40.0° (*c* 0·5; methanol); R_F 0·55 (S5). For $C_{15}H_{21}N_5O_5$ (351·4) calculated: 51·27% C, 6·02% H, 19·94% N; found: 51·10% C, 6·00% H, 19·75% N.

Methyl 2,3-O-Isopropylidene-D-riburonate (*XXXIII*)

A solution of sodium periodate (129 g; 0·60 mol) in water (540 ml) was mixed with acetone (1 litre) and then with a solution of methyl 2,3-O-isopropylidene-D-ribofuranoside (61·2 g; 0·30 mol, prepared according to ref.[7]) in 250 ml acetone. A solution of ruthenium oxychloride (3 ml; 60 mg RuO_2) was added. The mixture was stirred without cooling till the reaction was complete (5 h; S8), decomposed with methanol (5 ml) and filtered. The salts were washed with acetone (200 ml), the filtrate concentrated *in vacuo* to about 500 ml and the remaining material extracted with dichloromethane (5 × 100 ml). The extract was dried over magnesium sulfate and taken down *in vacuo*. The residue was dissolved in ether (300 ml), cooled with ice and treated with an excess of ethereal solution of diazomethane, the end of reaction being determined by thin-layer chromatography (R_F 0·60 in S8). Evaporation of solvent and distillation *in vacuo* gave 62·0 g (89%) of the product, b.p. 116—118°C/40 Pa. For $C_{10}H_{16}O_6$ (232·2) calculated: 51·72% C, 6·95% H; found: 52·02% C, 7·09% H.

Methyl 2,3-O-Isopropylidene-5-O-*p*-toluenesulfonyl-β-L-lyxofuranoside (*XXXVb*) (ref.[17])

A solution of compound *XXXIII* (51 g; 0·22 mol) in 0·2M sodium methoxide (1 litre) was set aside at room temperature for 3·5 h and neutralized with dry Dowex 50X8 (H^+ form). The Dowex was filtered off and washed with methanol. Evaporation of the solvent and distillation afforded 37 g (73%) of a mixture of *XXXIII* and *XXXIV* (for *XXXIII* R_F 0·45, for *XXXIV* R_F 0·30; S8). This product was dissolved in ether (150 ml) and added dropwise to a suspension of lithium aluminium hydride (5 g) in ether (200 ml) so as to keep gentle boiling. After refluxing for 1·5 h, the mixture was decomposed with ethyl acetate (20 ml), water (20 ml) and 4M sodium hydroxide (20 ml) and filtered. The inorganic material was washed with ether, the filtrate was dried over magnesium sulfate and taken down. The residue was chromatographed on silica gel (200 g) in ethyl acetate, affording 25 g (76%) of compound *XXXVa* (R_F 0·58 in S9; the epimeric D-*ribo*

derivative R_F 0·70). A solution of this product (0·122 mol) in pyridine (100 ml) was added dropwise to an ice-cooled and stirred solution of *p*-toluenesulfonyl chloride (39 g; 0·20 mol) in pyridine (150 ml). After standing for 48 h at 0°C the mixture was decomposed with water (10 ml) and taken down *in vacuo*. The residue was dissolved in ethyl acetate (300 ml), washed with water (3 × 100 ml) and evaporated. The residue was codistilled with toluene (3 × 100 ml) and crystallized from ethyl acetate–light petroleum to give 29·7 g (69% based on *XXXVa*) of compound *XXXVb*, m.p. 77°C (reported[17] m.p. 76·5—78°C).

Preparation of 5-(Adenin-9-yl)-2,3,4-trihydroxypentanoic Acids *V*—*XI*

A) A solution of the lactone *XIV* or *XVI* (5 mmol) in 0·25M sulfuric acid (25 ml) was set aside at room temperature overnight. The mixture was adjusted to pH 10—10·5 with barium hydroxide, after standing for 1 h neutralized to pH 7·0 with dilute sulfuric acid and filtered through Celite which was then washed with hot water (100 ml). The filtrate was taken down *in vacuo* and the residue was dissolved in water (10 ml). The solution was adjusted to pH 8·5—9·0, applied on a column of Dowex 1X2 (acetate) and eluted (3 ml/min) first with water to drop of UV absorption and then with 0—1M acetic acid (linear gradient; 2 l each). The fractions were followed by HPLC and thin-layer chromatography in S1. Fractions, containing the pure product, were combined and taken down *in vacuo*. The residue was three times codistilled with water, suspended in the same solvent and the mixture was adjusted to pH 7·0 with lithium hydroxide. The solution was taken down, the residue codistilled with ethanol (2 × 20 ml), dissolved in methanol and precipitated with ether. Lithium salt of the product was filtered, washed with ether and dried *in vacuo*. In this way, derivative *V* was prepared from compound *XIV* in 76% yield and compound *VIII* from lactone *XVI* in 78% yield. The content, determined spectrophotometrically at 262 nm (ε 14 500) >95%.

B) A solution of 30 mmol of substituted 6-(adenin-9-yl)-6-deoxyaldohexofuranose (*XX*, *XXVIII*, *XXXc* or *XXXII*) in 0·25M sulfuric acid (200 ml) was heated to 70°C till the reaction was complete (usually 3—4 h; monitored by thin-layer chromatography in S5). The mixture was neutralized with sodium hydroxide, made up to 1 litre with water, mixed with sodium hydroxide (3·2 g; 80 mmol) and stirred under oxygen (0·1—0·2 MPa overpressure) overnight. After acidification with Dowex 50X8 (H^+ form), the suspension was applied on a column of the same ion exchange resin (100 ml). The column was washed with water till the UV absorption disappeared and then UV-absorbing material was eluted with 2·5% ammonia. This eluate was taken down and the residue was dissolved in water (20 ml). The solution was adjusted to pH 8·5—9·0 with ammonia and purified by chromatography on Dowex 1X2 according to the method *A*. The fraction of the almost pure product was chromatographed on a column of cellulose in S1. Fractions which were homogeneous according to HPLC were combined, taken down and applied on a column of Dowex 50X8 (Li^+ form; 50 ml). Elution with water gave a UV-absorbing eluate which was taken down and the lithium salt was isolated according to method *A*. Using this method, lithium salts of the following compounds were isolated: *VI* (47%, from *XX*, 43%, from *XIX*), *VII* (64%, from *XXIIIa*), *IX* (57%, from *XXVIII*), *X* (46%, from *XXXc*) and *XI* (61%, from *XXXII*). Compound *VII* was prepared in the same manner from the free pyranose *XXIIIb* (omitting the acid hydrolysis) in 69% yield. Properties of the thus-prepared compounds are given in Table I.

5-(Adenin-9-yl)-(2*R*,3*R*,4*S*)-trihydroxypentanoic Acid (*XII*)

A solution of compound *XXXVb* (50·5 g; 0·15 mol) in dimethylformamide (100 ml) was added dropwise during 30 min at 120°C to a stirred mixture of adenine (20·5 g; 0·15 mol), potassium

carbonate (21 g) and dimethylformamide (175 ml). After stirring at 120°C for 16 h (calcium chloride tube) the mixture was filtered, the material on filter washed with dimethylformamide (50 ml) and the filtrate taken down *in vacuo*. The residue was extracted with hot chloroform (1 litre), the extract filtered through Celite and taken down. The residue was crystallized from ethanol, affording 13·8 g (29% based on *XXXVb*) of compound *XXXVI*, contaminated with some adenine. A mixture of this product (43 mmol) and 0·25M-H_2SO_4 (200 ml) was set aside at room temperature overnight, neutralized with barium hydroxide, filtered through Celite which was then washed with hot water (500 ml) and the filtrate was taken down *in vacuo*. The residue was dried *in vacuo* and stirred with a mixture of dimethylformamide (200 ml), acetone (160 ml), ethyl orthoformate (80 ml) and 6M-HCl in dimethylformamide (added to acid reaction) until the mixture was homogeneous. After standing overnight, the mixture was made alkaline with triethylamine, filtered and taken down at 50°C/13 Pa. The residue was dissolved in acetone (420 ml) and mixed with a solution of sodium periodate (9 g; 42 mmol) in water (180 ml) and a solution of ruthenium oxychloride (20 mg RuO_2). The mixture was stirred at room temperature overnight, filtered and the salts were washed with acetone (100 ml). The acetone was removed from the filtrate *in vacuo* and the aqueous phase was applied on a column of Dowex 50X8 (H^+ form; 200 ml). The column was washed with water until the eluate showed no UV absorption and the product was eluted with 2·5% ammonia. The ammonia eluate was taken down and the residue was heated with 0·25M-H_2SO_4 (100 ml) to 70°C for 3 h. The mixture was made alkaline (pH 10) with barium hydroxide, after 1 h neutralized with sulfuric acid, filtered and the filtrate was worked up according to the method *B*. Purification on Dowex 1X2 and cellulose afforded 2 g (17% based on *XXXVI*) of the lithium salt *XII*, pure according to HPLC; content (spectrophotometrically): 90%.

5-(Adenin-9-yl)-(2*S*,3*S*,4*R*)-trihydroxypentanoic Acid (*VII*) from Compound *XXIVa*

Triethylamine (0·5 ml) was added to a solution of the compound *XXIVa* (see ref.[8]; 8·9 g; 16 mmol) and benzoyl cyanide (2·5 g; 19 mmol) in chloroform (100 ml) and the mixture was set aside overnight. After evaporation, the residue (*XXIVb*, R_F 0·22 in S2; *XXIVa*, R_F 0·13 in S2) was allowed to stand for 4 h with acetone (180 ml), methanol (20 ml) and conc. sulfuric acid (2 ml). Thin-layer chromatography in S4 showed quantitative reaction (*XXIVb*, R_F 0·43; *XXV*, R_F 0·33). After addition of barium carbonate (30 g) the mixture was stirred till neutral, filtered through Celite and taken down *in vacuo*. The residue was dissolved in chloroform (20 ml) and added with stirring to ether (200 ml). Light petroleum (200 ml) was added, the product was collected on filter, washed with light petroleum and dried *in vacuo*, affording 5·0 g (75% based on *XXIVa*) of chromatographically pure compound *XXV*.

This product (12 mmol) was mixed successively with a solution of sodium periodate (5·4 g; 25 mmol) in 70% aqueous acetone (150 ml) and a solution of ruthenium oxychloride (containing 10 mg RuO_2). The mixture was stirred overnight, treated with ethanol (5 ml) and after 30 min filtered. The salts were washed with acetone (100 ml) and the filtrate was taken down. The residue was taken up in chloroform (200 ml), the solution was washed with water (2 × 50 ml), dried over magnesium sulfate and taken down. The residue was refluxed with 0·2 sodium methoxide (100 ml), after 90 min neutralized with Dowex 50X8 (H^+ form), made alkaline with triethylamine and filtered. The solid was washed with methanol (100 ml) and the filtrate was taken down. The residue was triturated with ether, filtered, washed with ether, dried *in vacuo* and refluxed with 80% formic acid (100 ml) for 1 h. The mixture was taken down, the residue codistilled with water (4 × 50 ml) and dissolved in water (24 ml). The solution was made alkaline with ammonia

(pH 8·5—9) and further treated according to the general method *B*, affording 0·75 g (21·5%) of lithium salt of compound *VII* which was homogeneous on HPLC and identical with the material obtained from the compound *XXIIIb*. The content (spectrophotometrically) >95%.

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