259. L-Erythruronic Acid Derivatives as Building Blocks for Nucleoside Analogs. Synthesis of 4′-*C*-Aryl-D-ribonucleosides

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Summary

2,3-*O*-Cyclohexylidene-L-erythruronic acid (**6**) available in 83% yield from D-ribonolactone (**7**), was treated with phenylmagnesium bromide to give the D-ribo and L-lyxo derivatives **10** and **11** in high yields (*Scheme 1* and *2*). The diastereoselectivity depended on the temperature and mode of operation *(Table 1)*. The absolute configuration of **10** and **11** was determined by correlation with (*R*)- and (*S*)-phenylethanediol (**17** and **16**) respectively, excluding intramolecular hydride shifts during formation of **10** and **11**. Reaction of **6** with methoxymethoxyphenyllithium gave the lactones **18** and **19**. The L-*lyxo* isomer **19** was transformed in high yields into the D-*ribo* lactone **18**. Compound **10** was transformed into the adenosine analoge **24** by reduction with Diisobutylaluminium hydride, hydrolysis, acetylation and nucleoside synthesis according to *Vorbrüggen (Scheme 3)*. Its structure was deduced from its UV., NMR. and CD. data and from those of the isopropylidene derivative **25**. Similarly, **18** was transformed into the adenosine analog **29** and into the isopropylidene derivative **30**.

1. Introduction. – Several nucleoside antibiotics with unusual side chains at C(4′) are known, such as Sinefungin (**1**) [1], the octosyl acid A (**2**) [2], the Polyoxins such as Polyoxin J (**3**) [3a] and others [3b]. Nucleosides of this type have been prepared either from ribosides upon modification of the hydroxymethyl group [4] or by glycosidation of appropriate, modified sugar derivatives [5]. Total synthesis has lead to some unusual, but racemic analogs, disubstituted at C(4′) [6].

We were attracted by a scheme which is based upon a retrosynthetic dissection of *ribo*-nucleosides with a modified side chain R into three building blocks I–III, as in **4**. The central building block II should possess two electrophilic sites, allowing a sequential attachment of a side chain R and a base B. It corresponds to a chiral, non-racemic equivalent of *meso*-tartaric dialdehyde. While leading to analogs which

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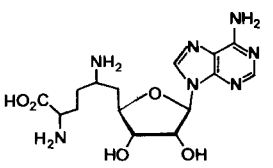

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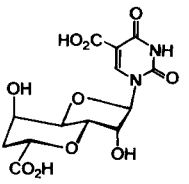

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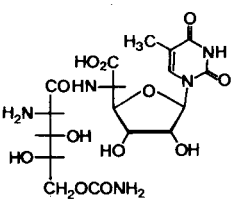

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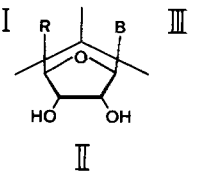

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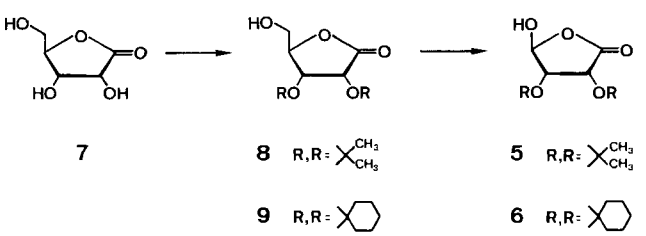
may be difficult to obtain otherwise such as 4′-*C*-aryl-nucleosides, this approach has to control the diastereoselectivity of the addition to the electrophilic centre both at C(1) and at C(4). In the following, we describe the application of this approach to the synthesis of the adenosine analogs **24** and **29** *(Scheme 3)*.

2. Synthesis of 4-*C*-Aryl-D- *ribo* and -L-*lyxo*tetroses. – Protected building blocks, corresponding to the fragment II in **4** are the 2,3-*O*-isopropylidene- and 2,3-*O*-cyclohexylidene-L-erythruronic acids (**5** and **6**). The former has been prepared from L-rhamnose in an overall yield of about 43% (3 steps) [7]. We have prepared both **5** and **6** in a new, advantageous way by acetalation of D-ribonolactone (**7**) to give **8** or **9**, followed by periodate cleavage of the corresponding sodium salts and acidification[4]) *(Scheme 1)*. The acetals **5** and **6** are obtained in overall yields of 72 and 83%.

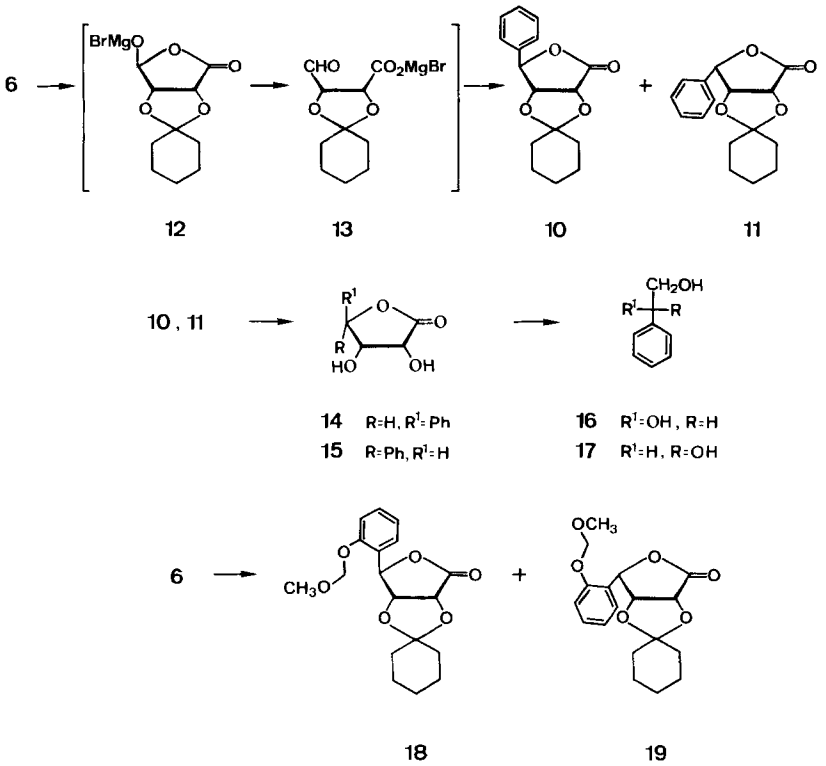
Addition of **6** to an excess of phenylmagnesium bromide at 10° gave two isomeric, crystalline lactones **10** and **11** (*cf.* [9]) in a combined yield of 81% *(Scheme 2)*. They were easily separated by chromatography. The relative configuration of **10** and **11** was deduced from their ^{13}C-NMR. spectra, where the C(3) and C(4) signals

Scheme 1



4) See [8] for a preliminary communication. The readily crystallizing **6** has since become available from *Fluka*, Buchs.

Scheme 2



appeared at lower field (81.84 and 84.10 ppm) in the case of the major isomer **10** and at higher field (78.81 and 80.34 ppm) in the case of the minor isomer **11**, in accordance with a 3,4-*trans*(*ribo*)- and 3,4-*cis*(*lyxo*)-configuration [10]. The less revealing ^{1}H-NMR. spectra displayed coupling constants $J(3,4)=0$ Hz for **10** and $J(3,4)=2$ Hz for **11**. The absolute configuration of the products, however, could not *a priori* be unequivocally related to the one of the starting material **6**, since two reaction paths had to be considered. In the more probable one [9], an aldehydo carboxylate (**13**) is formed and attacked by phenylmagnesium bromide to give, after workup, the D-*ribo*- and L-*lyxo*-lactones **10** and **11** *(Scheme 2)*. However, phenylmagnesium bromide could also add to the lactone carbonyl group of the pseudoacid salt **12**. Ring opening, followed by an intramolecular *Cannizzaro* reaction (*cf.* [11]) then leads to the enantiomeric L-*ribo* and D-*lyxo*-hydroxycarboxylates.

Determination of the absolute configuration at C(4) of **10** and **11** by correlation with (+)-(*S*)-phenylethanediol **16** excluded the second mechanism. Hydrolysis of **10** and **11** with aqueous formic acid gave the dihydroxylactones **14** and **15**, respectively. Periodate cleavage of the *ribo*-diol **14**, followed by treatment with sodium borohydride gave the (−)-(*R*)-phenylethanediol **17** in about 73% from **10**, while the *lyxo*-diol **15** gave the (+)-(*S*)-phenylethanediol **16**, proving the D-*ribo* and L-*lyxo*-configuration for **10** and **11**, respectively.

Table 1. *Diastereoselectivity in the reaction of* **6**

A) With phenylmagnesium bromide

Temperature	Mode of addition	Yield	% **10** (D-*ribo*)	% **11** (L-*lyxo*)
10°	normal[a])	81%	58	42
10°	inverse[b])	76%	43	57
−40°	normal	79%	39	61
−40°	inverse	80%	25	75

B) With methoxymethoxyphenyllithium

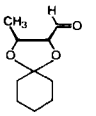
Temperature	Mode of addition	Yield	% **18** (D-*ribo*)	% **19** (L-*lyxo*)
0°	normal	65%	46	54
0°	inverse	66%	39	61
−40°	normal	71%	26	74
−40°	inverse	76%	20	80

[a]) Addition of **6** to the organometallic reagent.
[b]) Addition of the organometallic reagent to **6**.

Attempts to improve the diastereoselectivity of the *Grignard* reaction (see *Table 1*) showed that lowering the temperature and inverse addition (adding phenylmagnesium bromide to **6**) favored the formation of the L-*lyxo* isomer. The ratios of the isomers **10** and **11** varied between 58:42 (10°, normal addition) and 25:75 (−40°, inverse addition)[5]). A parallel behaviour was observed in the addition of methoxymethoxyphenyllithium [14] to **6**, leading to the D-*ribo*- and L-*lyxo*-lactones **18** and **19** (*Scheme 2* and *Table 1*). The D-*ribo*-lactone **18**, was, however, easily obtained in a yield of 89% from the L-*lyxo* isomer **19** by treating **19** with piperidine to give the corresponding hydroxyamide, and then treating this amide with methanesulfonyl chloride and triethylamine [15].

3. Nucleoside synthesis. – The reduction of the aldonolactones **10** and **18** with diisobutylaluminiumhydride [16] gave the aldoses **21** and **26**, respectively *(Scheme 3)*, in a high yield. In order to obtain 1,2-*trans*-configurated nucleosides, the cyclohexylidene acetal **21** was hydrolyzed and acetylated to give a mixture of the anomeric triacetates **22** (69%) and **23** (20%). This mixture was treated with 1.1 equiv.

[5]) The chelation model for 1,2-induction in the *Grignard* reaction of 2-alkoxy-aldehydes [12] predicts formation of the L-*lyxo*-lactones. The reaction of the aldehyde **20** with ethylmagnesium bromide (−78°, inverse addition) gave the *lyxo*- and *ribo*-isomers in a ratio of 6:4 [13]. It is not easy to evaluate the role of the carboxyl group. The organometallic reagents may form chelates of different reactivity involving the formyl group and RO–C(3) or the formyl and the carboxylate group. The latter group could also direct the approach of the reagent.



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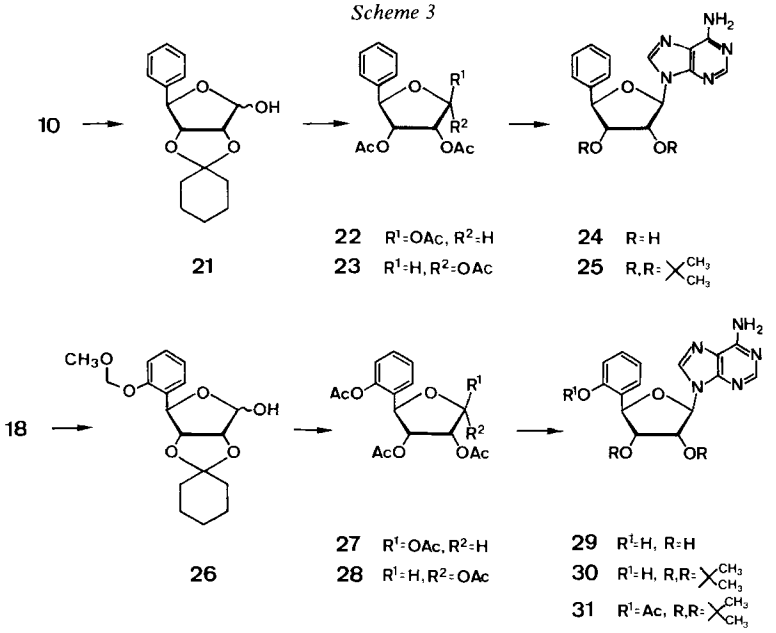
Scheme 3



of N^6-Benzoyl-$N^{6,9}$-bis(trimethylsilyl)adenine [17] [18] in the presence of $SnCl_4$, according to *Niedballa & Vorbrüggen* [19] and the product deprotected with methanolic ammonia to give the crystalline adenosine analog **24** (66%). No isomers were detected. The UV. spectrum, with a maximum at 260 nm (MeOH, $\varepsilon = 14\,600$) indicated glycosidation at N(9) [20]. The CD. spectrum was very similar to the one of adenosine *(cf. Table 2)* in accordance with a β-D-configuration [21]. The ^{1}H-NMR. spectra of **24** were not conclusive with regard to the anomeric configuration, but the ^{1}H-NMR. spectrum of the isopropylidene derivative **25** satisfied *Imbach*'s criteria for a β-D-configuration, showing a chemical-shift difference for the isopropylidene methyl groups ($\Delta\delta$ CH_3) of 0.28 ppm and a coupling constant $J(3',4') = 5$ Hz [22] [23]. Finally, the ^{1}H-NMR. spectra of **24** indicated a predominant **N**-conformation[6]) ($J(1',2') = 4.2$ Hz; $J(3',4') = 6$ Hz) [25] and a slightly higher degree of puckering ($J(2',3') = 6$ Hz) then observed for adenosine [26].

In order to prepare the hydroxyphenyl nucleoside **29** *(Scheme 3)* the hemiacetal **26** was treated with diluted hydrochloric acid. The crude product was acetylated and then acetolyzed[7]), yielding the anomeric tetraacetates **27** (72%) and **28** (18%). This mixture was treated first with N^6-benzoyladenine [17] in the presence of hexamethyldisilazane and trimethylsilyl triflate [27] and then with ammonia in methanol affording the microcrystalline adenosine analog **29** (68%).

The UV. spectra of **29** ($\lambda_{max}^{MeOH} = 260$ nm, $\varepsilon = 14\,400$) indicated glycosidation at N^9. The anomeric configuration was deduced from the ^{1}H-NMR. spectrum of the

[6]) For the meaning of the **N**- and **S**-conformation in the chemistry of carbohydrates see [24].

[7]) Preliminary experiments showed that under similar conditions as used in the hydrolysis of **21** large amounts of a by-product were formed (anhydroderivative?).

Table 2. *CD. spectra of the compound* **24**, **29**, **30** *and* **31**

Compound	Solvent	CD. Envelopes							
		λ [nm]	$[\theta]$ [°cm² d mol⁻¹]	λ [nm]	$[\theta]$ [°cm² d mol⁻¹]	λ [nm]	$[\theta]$ [°cm² d mol⁻¹]	λ [nm]	$[\theta]$ [°cm² d mol⁻¹]
Adenosine [21]	EtOH			268	−3860				
24	MeOH			265	−1770				
29	MeOH	288	1330	272	−4000	250	2960	223	−8150
	NaOH 0.1N	305	3850	272	−1000	250	2200		
30	MeOH	292	560	272	−4300	250	1500	223	−14000
31	MeOH			260	−3500				

isopropylidene derivative **30** ($\delta\Delta_{CH_3}$=0.27 ppm; $J(3',4')$=3.2 Hz) [22] [23]. The conformational equilibrium of the furanose ring of **29** is shifted towards the S-conformation[6]) ($J(1',2')$=6 Hz; $J(3',4')$=4 Hz) [26]. The CD. spectra of the hydroxyphenyl compounds **29** and **30** differ only by the molecular ellipticities of their maxima *(Table 2)*. They are distinctly different from the one of the corresponding phenylderivative **24**. Although this difference could be due to a *syn*-conformation of the base, the CD. spectra being similar in the region 240–300 nm to the ones measured, *e.g.*, for 8-(*α*-hydroxyisopropyl)adenosine, for which a *syn*-conformation was postulated [28], the chemical shift values for H–C(2) and H–C(8) which are expected to be different in *syn*- and *anti*-conformers, resp. [29] are about the same for **24** and **29**. *Follmann* has shown that a variety of CD. curves with both negative and positive *Cotton* effects in the long- and short-wavelength regions are observed for adenosine derivatives possessing a modified substituent at C(4′) for which he assumed an *anti*-conformation [29] [30]. The difference of the CD. spectra of **24** and **29** and **30** on the other hand could be due to any of the factors discussed by *Follmann viz.* direct or indirect interactions of the C(4′) substituent with the chromophoric base, inducing conformational and/or electronic changes of the latter.

Financial support by the *Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung* and by *Sandoz AG*, Basel is gratefully acknowledged. We thank also *W. Bernhard, N. Bild, M. Cosandey, J.-P. Fasel, A. Lorenzi, A. Meier* and *F. Nidegger* for the CD., NMR. and mass spectra and for the microanalyses.

Experimental Part

General remarks. – S. [31]. ^{1}H-NMR. spectra were measured on a *Varian EM-390* (90 MHz) or on a *Varian XL-200* (200 MHz) spectrometer in $CDCl_3$ (unless otherwise indicated) and ^{13}C-NMR. spectra on a *Varian XL-100-12 FT* at 25.2 MHz in $CDCl_3$ (unless otherwise indicated). Specific rotations ($[\alpha]_D$) were measured on a *Perkin-Elmer* Polarometer *241* at 25° using 1-dm cell at 365, 436, 546, 578 and 589 nm in $CHCl_3$ (unless otherwise indicated). The specific rotations at 589 nm was determined using a regression curve, unless an ORD. effect was noted in which case the value obtained at 589 nm was considered. UV. spectra were measured on a *Perkin-Elmer 555* spectrometer at room temperature. CD. spectra were measured on a *Jasco, J-5000 C* Spectrophotometer in MeOH at room temperature. For the chromatography the following solvent mixtures were used: A = ethyl acetate/hexane 1:1; B = ethyl acetate/hexane 1:2; C = ethyl acetate/CH_2Cl_2/hexane 1:1:2; D = *i*PrOH/EtOH 1:1; E = ethyl acetate/EtOH/H_2O 15:2:1.

Preparation of 2,3-O-cyclohexylidene-D-ribonolactone (**9**). A solution of 2 g (13 mmol) D-ribonolactone in 40 ml cyclohexanone, 100 mg $FeCl_3$ (anhydrous, *Merck*) and 3 g of activated *Sikkon (Fluka)* were stirred for 2.5 h at 50°. The cooled mixture was stirred with 400 mg $Na_2CO_3 \cdot 10\,H_2O$ and 1 g of charcoal (10 min), filtered through *Celite* and evaporated *in vacuo*. The residue was evaporated 3 times with H_2O and 3 times with benzene. Crystallization from CH_2Cl_2 and hexane gave 2.64 g (89%) of the title compound. An analytical sample was prepared by sublimation at 120°/0.02 bar. M.p. 128–129° ([32]: 128–130°), Rf (A) 0.25, $[\alpha]_D = -54.6°$ ($c = 0.986$) ([32]: $[\alpha]_D^{22} = -54°$ ($c = 1.53$)). – IR.: 3635*m*, 3490*w* br., 2950*s*, 2870*m*, 1790*s* br., 1465*w*, 1453*m*, 1433*w*, 1370*m*, 1358*m*, 1340*w*, 1292*w*, 1274*w*, 1248*w*, 1186*m*, 1166*s*, 1147*m*, 1120*s*, 1089*s*, 1063*m*, 1033*w*, 1010*m*, 971*m*, 942*m*, 928*m*, 912*m*, 882*w*, 850*w*, 831*w*. – ^{1}H-NMR.: 1.2–1.8 (*m*, 10 H); 3.16 (*t*, $J = 5.5$, 1 H, HO–C(5), exchange with D_2O); 3.76 ($d \times d \times d$, $J = 12.2$, 5.5 and 1.8, 1 H, H–C(5′)); 3.92 ($d \times d \times d$, $J = 12.2$, 5.5 and 2.4, 1 H, H–C(5)); 4.63 ($d \times d$, $J = 2.4$ and 1.8, 1 H, H–C(4)); 4.75 (*d*, $J = 5.5$, 1 H); 4.85 (*d*, $J = 5.5$, 1 H). – ^{13}C-NMR.: 23.71 (*t*), 23.81 (*t*), 24.76 (*t*), 34.87 (*t*), 36.33 (*t*), 61.72 (*t*), 75.28 (*d*), 77.78 (*d*), 83.13 (*d*), 113.71 (*s*), 175.31 (*s*). – MS.: 229 (1, $M^+ + 1$), 228 (11, M^+), 200 (2), 199 (16), 186 (11), 185 (100), 172 (4), 169 (4), 98 (3), 97 (3), 85 (6), 83 (4), 81 (4), 69 (4), 55 (16), 43 (2), 42 (3), 41 (4).

$C_{11}H_{16}O_5$ (228.24) Calc. C 57.89 H 7.07% Found C 58.01 H 7.19%

Preparation of 2,3-O-isopropylidene-L-erythruronolactone (**5**). A solution of 1 g (5.3 mmol) of **8** [33] and 212 mg (1 mol-equiv.) of NaOH in 50 ml H_2O at 40° was treated with a solution of 1.17 g (1 mol-equiv.) of $NaIO_4$ in 5 ml H_2O at 0°. After 15 min at 4°, 500 mg $BaCl_2 \cdot 10\,H_2O$ in 3 ml H_2O were added and the precipitate filtered off through *Celite*. The filtrate was acidified to pH = 3 with 2N HCl at 0°. Normal workup with ethyl acetate gave a solide (790 mg, 85%), m.p. 95–97°, which after crystallization from ethyl acetate and hexane gave 730 mg (78%) of **5**, m.p. 103–104°, $[\alpha]_D = -54.6°$ ($c = 1.25$). – IR.: 3585*m*, 3520*w* br., 3440*w* br., 3020*w*, 2990*m*, 1790*s* br., 1700*w*, 1452*w*, 1425*m*, 1387*m*, 1380*m*, 1310*w*, 1220*m* br., 1152*s*, 1090*s*, 1030*w*, 977*m*, 960*m*, 925*m*, 910*m*, 851*m*. – ^{1}H-NMR. ((D_6)-acetone): 1.36 (*s*, 3 H, CH_3); 1.40 (*s*, 3 H, CH_3); 3.3 (*m*, 1 H, exchanges with D_2O, HO); 4.63 (br. *d*, $J = 5.5$, 1 H); 4.96 (*d*, $J = 5.5$, 1 H); 5.76 (br. *s*, 1 H, H–C(4)). – ^{13}C-NMR.: 25.72 (*qa*), 26.60 (*qa*), 74.91 (*d*), 79.84 (*d*), 99.45 (*d*), 114.54 (*s*). – MS.: 159 (12), 145 (5), 100 (7), 85 (19), 71 (9), 60 (9), 59 (100), 55 (7), 43 (13), 42 (9), 41 (17), 39 (7).

Preparation of 2,3-O-cyclohexylidene-L-erythruronolactone (**6**). A solution of 20.95 g (91.7 mmol) of **9** and 3.672 g (1 mol-equiv.) of NaOH in 150 ml H_2O at 40° was treated with a solution of 19.63 g (1 mol-equiv.) of $NaIO_4$ in 120 ml H_2O at 0°. After 10 min at 4°, 11.21 g $BaCl_2 \cdot 10\,H_2O$ in 50 ml H_2O were added and the ppt. filtered off through *Celite*. The filtrate was acidified to pH = 3 with 2N HCl at 0°. Normal workup with ethyl acetate gave a solide (20.75 g, 105%) which after crystallization from ether and hexane gave 18.28 g (93%) of **6**. Sublimation at 100°/0.02 bar gave an analytical sample. M.p. 107–108°, Rf (A) 0.15, $[\alpha]_D = -39.8°$ ($c = 1.655$). – IR.: 3595*w*, 3520*w* br., 2950*m*, 2870*m*, 1795*s* br., 1755*m S*, 1465*w*, 1453*m*, 1433*m*, 1370*m*, 1348*w*, 1337*w*, 1315*w*, 1295*w*, 1275*w*, 1165*s*, 1110*s*, 1068*m*, 1033*w*, 977*m*, 963*m S*, 927*s*, 912*m*, 850*w*, 830*w*. – ^{1}H-NMR.: 1.2–1.8 (*m*, 10 H); 4.63 (br. *d*, $J = 5.5$, 1 H); 4.91 (*d*, $J = 5.5$, 1 H); 4.8–5.5 (*m*, 1 H, exchanges with D_2O, HO–C(4)); 5.81 (br. *s*, 1 H, H–C(4)). – ^{13}C-NMR.: 23.62 (*t*), 23.79 (*t*), 24.64 (*t*), 35.15 (*t*), 36.20 (*t*), 74.75 (*d*), 79.42 (*d*), 99.79 (*d*), 115.33 (*s*). – MS.: 215 (5, $M^+ + 1$), 214 (25, M^+), 185 (28), 172 (10), 171 (100), 143 (6), 140 (6), 100 (33), 99 (15), 98 (10), 81 (20), 69 (9), 55 (55), 43 (8), 42 (12), 41 (13), 39 (6).

$C_{10}H_{14}O_5$ (214.23) Calc. C 56.07 H 6.59% Found C 56.15 H 6.70%

Preparation of 2,3-O-cyclohexylidene-4-C-phenyl-D-ribo- and L-lyxo-tetronolactones (**10** *and* **11**). A) *Normal addition at 10°.* A solution of 1 g (4.66 mmol) of **6** in 5 ml THF was added in dropwise at 10° to a solution of PhMgBr prepared from 0.34 g (13.9 mmol) of Mg and 2.196 g (13.9 mmol) of freshly distilled bromobenzene and the mixture stirred for further 2 h at 10°. The mixture was then poured into an ice-cold mixture of 1M aq. $KHSO_4$ and ice and extracted with CH_2Cl_2. Normal processing gave 1.3 g (102%) of crude product. Chromatography on 120 g silica gel (ethyl acetate/CH_2Cl_2/hexane 1:1:2) gave 613 mg (47%) of **10** and 442 mg (34%) of **11**.

Data of **10**. M.p. 76–76.5°, Rf (C) 0.52, $[\alpha]_D = -34.8°$ ($c = 1.15$). – IR.: 3040*w*, 2950*s*, 2870*m*, 1790*s*, 1605*w*, 1500*w*, 1465*w*, 1455*s*, 1435*w*, 1370*m*, 1350*m*, 1340*m*, 1310*w*, 1290*m*, 1276*m*, 1250*m*, 1180*s*, 1165*s*, 1150*m*, 1115*s* br., 1060*s*, 1035*m*, 1005*m*, 999*m*, 950*m*, 940*m*, 930*m*, 910*m*, 860*w*, 850*m*, 830*w*. – ^{1}H-NMR.: 1.20–1.90 (*m*, 10 H); 4.70 (*d*, $J = 4$, 1 H); 4.83 (*d*, $J = 4$, 1 H); 5.61 (*s*, 1 H, H–C(4)); 7.10–7.60

(*m*, 5 H). – ^{13}C-NMR. ((D$_6$)acetone): 24.34 (*t*), 24.53 (*t*), 25.36 (*t*), 35.54 (*t*), 37.16 (*t*), 74.83 (*d*), 81.84 (*d*), 84.10 (*d*), 114.58 (*s*), 126.38 (*d*), 129.43 (*d*), 129.62 (*d*), 137.71 (*s*), 174.27 (*s*). – MS.: 275 (1, $M^+ + 1$), 274 (21, M^+), 273 (100, $M^+ - 1$), 246 (3), 245 (21), 232 (10), 231 (10), 230 (85), 202 (6), 173 (4), 159 (14), 130 (17), 54 (23).

$C_{16}H_{18}O_4$ (274.32) Calc. C 70.06 H 6.61% Found C 70.10 H 6.72%

Data of **11**. M.p. 212–212.5°, Rf (C) 0.28, $[\alpha]_D = +6.5°$ ($c = 1.16$). – IR.: 3070*w*, 3030*w* br., 2950*s*, 2870*m*, 1790*s*, 1500*w*, 1455*m*, 1435*w*, 1370*m*, 1355*w*, 1340*m*, 1320*m*, 1290*m*, 1270*m*, 1180*s*, 1165*s*, 1125*s*, 1080*m*, 1070*m*, 1035*m*, 1020*m*, 1005*m*, 980*m*, 935*s*, 910*m*, 855*w*, 845*w*, 825*w*, 700*m*. – ^{1}H-NMR.: 1.21–1.77 (*m*, 10 H); 4.92 (*d*, $J = 2$, 1 H); 4.95 (*s*, 1 H); 5.50 (*d*, $J = 2$, 1 H, H–C(4)); 7.20–7.50 (*m*, 5 H). – ^{13}C-NMR. ((D$_6$)acetone): 24.34 (*t*), 2443 (*t*), 25.33 (*t*), 35.99 (*t*), 37.21 (*t*), 77.29 (*d*), 78.81 (*d*), 80.34 (*d*), 114.37 (*s*), 127.62 (*d*), 128.72 (*d*), 128.95 (*d*), 135.35 (*s*), 174.82 (*s*). – MS.: 275 (1, $M^+ + 1$), 274 (9, M^+), 273 (53, $M^+ - 1$), 245 (20), 232 (8), 231 (55), 159 (24), 139 (19), 131 (23), 130 (43), 105 (94), 104 (16), 103 (15), 98 (15), 97 (12), 96 (19), 77 (12), 76 (31), 68 (12), 54 (100), 40 (19).

$C_{16}H_{18}O_4$ (274.32) Calc. C 70.06 H 6.61% Found C 70.07 H 6.65%

B) *Normal addition at −40°*. A solution of 1 g (4.66 mmol) of **6** in 5 ml THF was added dropwise at −40° to a suspension of PhMgBr prepared as above. After stirring the mixture for further 6 h at −40°, it was warmed to r.t. and poured into 1M aq. $KHSO_4$ and ice. Workup as indicated above gave 1.43 g (112%) of crude product. Chromatography gave 403 mg (31%) of **10** and 624 mg (48%) of **11**.

C) *Inverse addition at 10°*. A suspension of PhMgBr prepared as above was added dropwise at 10° to a solution of 1 g (4.66 mmol) of **6** in 5 ml THF. After stirring the mixture for further 2 h at 10°, it was poured into an ice-cold mixture of 1M aq. $KHSO_4$. Workup as indicated above gave 1.46 g (115%) of crude product. Chromatography as indicated above gave 429 mg (33%) of **10** and 559 mg (43%) of **11**.

D) *Inverse addition at −40°*. A suspension of PhMgBr prepared as above was added dropwise at −40° to a solution of 1 g (4.66 mmol) of **6** in 5 ml THF. After stirring the mixture for 6 h at −40°, it was warmed to r.t. and poured into 1M aq. $KHSO_4$ and ice. Workup as indicated above gave 1.53 g (120%) of crude product. Chromatography as indicated above gave 260 mg (20%) of **10** and 780 mg (60%) of **11**.

*Preparation of 4-C-phenyl-*D*-ribo-tetronolactone* (**14**). A mixture of 0.1 g of **10** and 3 ml of 80% aq. formic acid were stirred for 10 min at 60°. The residue, obtained after evaporation of the volatile components *in vacuo* at r.t. was dried in h.v., crystallized from 2-propanol and toluene and sublimed at 100°/0.05 bar to give 68 mg (96%) of **14**, m.p. 142–143°, $[\alpha]_D = +32.4°$ ($c = 0.75$, MeOH). – IR. (KBr): 3535*s*, 3450*s* br., 3370*s* br., 3325 *S*, 3062*w*, 3040*w*, 2990*w*, 2970*w*, 2940*m*, 2900*w*, 1765*s* br., 1607*w*, 1496*m*, 1480*w*, 1451*m*, 1420*w*, 1400*m*, 1360*m*, 1330*m*, 1310*m*, 1290*m*, 1265*m*, 1258*m*, 1230*m*, 1210*m*, 1190*s*, 1175*s*, 1130*s*, 1080*s*, 1020*s*, 1005*m*, 980*m*, 950*m*, 870*m*, 860*m*, 840*w*, 785*m*, 768*m*, 740*s*, 732*s*, 700*s*. – ^{1}H-NMR. ((D$_6$)acetone): 2.67–3.13 (*m*, 2 H, exchanges with D_2O, HO); 4.20–4.53 (*m*, 2 H, H–C(2) and H–C(3)); 5.42 (br. *s*, 1 H, H–C(4)); 7.27–7.50 (*m*, 5 H). – ^{13}C-NMR. ((D$_6$)-acetone): 68.68 (*d*), 75.01 (*d*), 85.35 (*d*), 125.87 (*d*), 128.93 (*d*), 129.18 (*d*), 137.88 (*s*), 175.43 (*s*). – MS.: 195 (1,2, M^+), 194 (5, M^+), 177 (2), 176 (6), 166 (10), 150 (2), 149 (2), 148 (3), 147 (3), 133 (3), 132 (12), 131 (30), 130 (6), 121 (3), 120 (14), 119 (3), 107 (8), 106 (100), 105 (9), 104 (13), 103 (19), 102 (35), 91 (13), 90 (73), 79 (30), 78 (13), 77 (28), 65 (14), 60 (50), 50 (19), 38 (11).

$C_{10}H_{10}O_4$ (194.19) Calc. C 61.85 H 5.19% Found C 61.91 H 5.22%

*Preparation of 4-C-phenyl-*L*-lyxo-tetronolactone* (**15**). From 0.1 g (0.36 mmol) of **11** in a similar way as **14**. After crystallization from toluene, sublimation at 120°/0.01 bar gave 60 mg (93%) of **15**, m.p. 230° (dec.), $[\alpha]_D = +28.8°$ ($c = 0.38$, MeOH). – IR. (KBr): 3450*s* br., 3335*s* br., 3090*w*, 3043*w*, 3020*w*, 2990*w*, 2935*w*, 2928*w*, 1767*s* br., 1718 *S*, 1500*w*, 1460*m*, 1435*m*, 1400*m*, 1370*w*, 1337*m*, 1310*m*, 1290*s*, 1221*m*, 1195*s*, 1153*s*, 1118*m*, 1081*m*, 1033*w*, 990*s*, 970 *S*, 925*s*, 855*m*, 830*m*, 795*m*, 781*m*, 750*s*, 700*s*. – ^{1}H-NMR. ((D$_6$)acetone): 2.67–2.90 (*m*, 2 H, exchanges with D_2O, HO); 4.54–4.85 (*m*, 2 H, H–C(2) and H–C(3)); 5.43 (*d*, $J = 4$, 1 H, H–C(4)); 7.20–7.50 (*m*, 5 H). – ^{13}C-NMR. ((D$_6$)acetone): 72.30 (*d*), 72.80 (*d*), 81.27 (*d*), 127.69 (*d*), 128.60 (*d*), 135.93 (*s*), 176.03 (*s*). – MS.: 195 (1.2, M^+), 194 (15, M^+), 176 (12), 166 (12), 150 (13), 148 (2), 132 (12), 131 (24), 130 (4), 121 (5), 120 (29), 119 (13),

108 (11), 107 (98), 105 (11), 104 (14), 102 (20), 101 (25), 92 (26), 90 (100), 78 (31), 77 (15), 76 (26), 64 (20), 59 (53), 50 (16), 43 (11), 27 (11).

$C_{10}H_{10}O_4$ (194.19) Calc. C 61.85 H 5.19% Found C 61.78 H 5.20%

*Preparation of (−)-(*R*)-1-phenylethane-1,2-diol* (**17**) *from* **14**. A solution of 87 mg (0.44 mmol) of **14** in 5 ml hot H_2O was cooled under stirring to 0°. After adding a solution of 105.4 mg (1.1 mol-equiv.) of $NaIO_4$ in 1 ml H_2O over a period of 5 min, the mixture was stirred for 20 min at 0° and then saturated with NaCl. Normal workup with ethyl acetate gave 94 mg (100%) of a clear oil. The solution of this oil in 2 ml abs. EtOH was added over 10 min to an ice-cold solution of 101 mg (2.7 mmol) of $NaBH_4$ in 5 ml EtOH. The mixture was stirred at r.t. overnight, taken to dryness *in vacuo* and the residue dissolved at 0° with 4 ml 1M aq. $KHSO_4$. Normal workup with ether/satd. NaCl-solution gave 46.3 mg (82%) of a colorless oil, that was purified on prep. TLC. (ether) and then crystallized from ether and hexane to give 43 mg (76%) of **17**, m.p. 66–67°, Rf (D) 0.62, $[\alpha]_D = -56.5°$ ($c = 1.01$, Et_2O). – IR.: 3615*m*, 3430*m* br., 3070*m*, 3015*m*, 2935*m*, 2885*m*, 1952*w* br., 1880*w* br., 1813*w* br., 1607*w*, 1495*m*, 1455*m*, 1390*m* br., 1350*w*, 1330*w*, 1285*w*, 1179*w*, 1089*m*, 1063*s*, 1045*s*, 1030*s*, 917*w*, 891*m*, 831*w*, 701*s*.

*Preparation of (+)-(*S*)-1-phenylethane-1,2-diol* (**16**). A) From 4-*C*-phenyl-L-*lyxo*-tetronolactone (**15**) as described for the preparation of its antipode **17** from **14** (yield: 87 mg of **15** gave 46 mg of **16** (77%)); Rf-values and IR. spectra indistinguishable from those of **17**. M.p. 66–67°, $[\alpha]_D = +56.2°$ ($c = 1.39$, Et_2O).

B) *From (+)-*L*-mandelic acid.* After reducing 1.52 g (10 mmol) (+)-L-mandelic acid with 759 mg $LiAlH_4$ according to [34], the crude material (1.1 g, 83%) was purified by distillation at 140°/0.01 bar and crystallization from ether and hexane: 1.0 g (73%) of **16**, m.p. 65.5–66.5°, $[\alpha]_D = +55.5°$ ($c = 3.04$, Et_2O). – IR.: same as of a sample obtained from **14**. – ^{1}H-NMR.: 3.3–3.9 (*m*, 4 H, 2 H exchanges with D_2O); 4.6–4.8 (*m*, 1 H); 7.26 (br. *s*, 5 H).

*Preparation of 2,3-*O*-cyclohexylidene-4-*C*-phenyl-*D*-ribo-tetrose* (**21**). To a solution of 0.2 g (0.73 mmol) of **10** in 20 ml abs. toluene at −78° were added dropwise and under N_2 0.92 ml of a 20% solution of DIBAH in toluene *(Schering)*. After stirring the mixture for 10 min at −78°, 0.1 ml MeOH was added, the mixture warmed to r.t. and poured into 50 ml 1M aq. $KHSO_4$. Normal workup with CH_2Cl_2 and chromatography on 15 g silica gel (ethyl acetate/hexane 1:2) gave 0.201 g (99%) of **21**, Rf (B) 0.40, $[\alpha]_D = +36.1°$ (5 min) → +38.1° (3 h; $c = 1.45$). – IR.: 3680*w* br., 3615*m*, 3510*w*, 3100*w*, 3080*w*, 3040*w*, 3020*m*, 2995*s*, 2875*m*, 1607*w*, 1500*w*, 1468*w*, 1455*m*, 1436*w*, 1375*m*, 1360*w*, 1337*w*, 1290*m*, 1276*m*, 1254*m*, 1225*m* br., 1170*m*, 1151*m*, 1100*s*, 1080*s S*, 1060*s*, 1040*s*, *S*, 1008*w*, 980*m*, 946*m*, 932*m S*, 917*m*, 853*m*, 838*w*, 700*m*. – ^{1}H-NMR.: 1.23–2.00 (*m*, 10 H); 3.25 (br. *s*, 0.4 H, exchanges with D_2O, HO); 4.10 (*d*, $J = 3$, 0.6 H, exchanges with D_2O, HO); 4.56–4.93 (*m*, 2 H); 5.16 (*d*×*d*, $J = 6.3$ and 3, 1 H); 5.43 (*d*×*d*, $J = 9$ and 3, 0.6 H, H−C(1)); 5.59 (*s*, 0.4 H, H−C(1)); 7.10–7.53 (*m*, 5 H). – ^{13}C-NMR.: 23.55 (*t*), 23.69 (*t*), 23.98 (*t*), 24.96 (*t*), 34.52 (*t*), 34.65 (*t*), 36.07 (*t*), 36.63 (*t*), 78.97 (*d*), 81.75 (*d*), 85.68 (*d*), 85.89 (*d*), 88.88 (*d*), 96.19 (*d*), 103.36 (*d*), 113.62 (*s*), 115.49 (*s*), 125.38 (*d*), 126.08 (*d*), 127.39 (*d*), 127.53 (*d*), 128.18 (*d*), 128.41 (*d*), 138.63 (*s*), 140.42 (*s*). – MS.: 277 (12, $M^+ + 1$), 276 (88, M^+), 247 (16), 233 (96), 205 (12), 161 (24), 133 (30), 132 (56), 131 (32), 123 (10), 122 (76), 106 (32), 105 (100), 104 (16), 103 (14), 99 (100), 98 (64), 83 (14), 81 (24), 77 (40), 70 (16), 69 (24), 56 (11), 55 (56), 51 (10), 43 (10), 42 (16), 41 (10).

$C_{16}H_{20}O_4$ (276.35) Calc. C 69.54 H 7.30% Found C 69.45 H 7.34%

*Preparation of 1,2,3-tri-*O*-acetyl-4-*C*-phenyl-α- and β-*D*-ribo-tetroses* (**23** *and* **22**). A solution of 210 mg (0.76 mmol) of **21** in 20 ml 60% aq. acetic acid was heated at 60° for 2 h, cooled to r.t. and taken to dryness in h.v. The residue was kept with 5 ml acetic anhydride and 5 ml pyridine at 10° for 45 min and again taken to dryness in h.v. Chromatography of the residue on 15 g silica gel (ethyl acetate/hexane 1:3) gave 168 mg (69%) of **22** and 57 mg (20%) of **23**.

Data of **22**. Oil, Rf(A) 0.43, $[\alpha]_D = +1.7$ ($c = 5.71$). – IR.: 3020*w* br., 2970*w*, 2920*w*, 1750*s* br., 1660*w*, 1492*w*, 1450*w*, 1430*w*, 1370*s*, 1305*w*, 1100*m*, 1072*m*, 1059*s*, 1028*m*, 1000*s*, 975*m*, 958*m*, 906*m*, 892*m*, 693*w*. – ^{1}H-NMR.: 2.05 (*s*, 3 H); 2.15 (*s*, 6 H); 5.10–5.40 (*m*, 3 H, H−C(2), H−C(3) and H−C(4)); 6.33 (*s*, 1 H, H−C(1)); 7.35 (br. *s*, 5 H). – ^{13}C-NMR.: 20.48 (*qa*), 21.02 (*qa*), 74.15 (*d*), 75.74 (*d*), 82.39 (*d*), 97.97 (*d*), 125.77 (*d*), 128.33 (*d*), 128.47 (*d*), 137.89 (*s*), 168.87 (*s*), 169.19 (*s*), 169.35 (*s*). – MS.: 322 (1, M^+), 264 (4), 263 (23), 203 (14), 202 (100), 191 (8), 173 (5), 161 (32), 160 (84), 150 (5),

149 (35), 145 (23), 144 (7), 133 (11), 132 (20), 131 (33), 122 (5), 115 (10), 107 (55), 106 (5), 105 (56), 104 (5), 103 (34), 102 (5), 91 (7), 77 (8), 43 (86).

$C_{16}H_{18}O_7$ (322.32) Calc. C 59.62 H 5.63% Found C 59.70 H 5.64%

Data of **23**. Oil, Rf (A) 0.36, $[\alpha]_D = +57.6°$ ($c = 1.26$). – IR.: 3020*w* br., 2960*w*, 2940*m*, 2840*w*, 1750*s* br., 1600*w*, 1492*w*, 1450*m*, 1370*s*, 1310*w*, 1130*m*, 1093*s*, 1080*m*, 1067*s*, 1046*s*, 1012*s*, 945*m*, 910*m*, 900*m*, 840*w*, 696*w*. – ^{1}H-NMR.: 2.04 (*s*, 3 H); 2.14 (*s*, 6 H); 5.10–5.50 (*m*, 3 H, H–C(2), H–C(3) and H–C(4)); 6.61 (*d*, $J = 4.5$, 1 H, H–C(1)); 7.34 (br. *s*, 5 H). – ^{13}C-NMR.: 20.25 (*qa*), 20.64 (*qa*), 21.00 (*qa*), 69.39 (*d*), 74.87 (*d*), 84.12 (*d*), 93.86 (*d*), 125.51 (*d*), 128.33 (*d*), 128.50 (*d*), 137.24 (*s*), 169.05 (*s*), 169.37 (*s*), 169.75 (*s*). – MS.: 323 (1, $M^+ + 1$), 322 (1, M^+), 264 (6), 263 (24), 262 (7), 207 (5), 203 (17), 202 (61), 192 (5), 191 (9), 162 (5), 161 (31), 160 (50), 157 (7), 150 (5), 149 (39), 145 (39), 133 (14), 132 (31), 131 (43), 122 (23), 119 (5), 115 (7), 113 (5), 108 (9), 107 (57), 106 (9), 105 (87), 104 (6), 103 (44), 102 (5), 91 (9), 79 (5), 77 (17), 73 (7), 43 (100), 18 (5).

$C_{16}H_{18}O_7$ (322.32) Calc. C 59.62 H 5.63% Found C 59.49 H 5.55%

*Preparation of 9-(4-*C*-phenyl-β-*D*-*ribo*-tetrofuranosyl)adenine* (**24**). A solution of 500 mg (1.5 mmol) of a 1:3 mixture of **23** and **22** in 30 ml 1,2-dichloroethane was stirred with 0.45 ml of $SnCl_4$ and 1 g of 4-Å molecular sieve for 30 min under N_2 and then treated with 650 mg (1.65 mmol) of N^6-benzoyl-$N^{6,9}$-bis(trimethylsilyl)adenine [17] [18]. After stirring the mixture for 1 h at r.t. it was filtered, diluted with 20 ml CH_2Cl_2 and processed in a normal way. Chromatography of the crude product on 70 g silica gel (CH_2Cl_2/EtOH 15:1) gave 639 mg (80%) of an oil, which was dissolved in 20 ml of MeOH saturated with ammonia. After 15 h at r.t., the mixture was taken to dryness *in vacuo* and the residue crystallized twice in MeOH to give 325 mg (82%) of **24**, m.p. 176–177° (dec.), Rf (E) 0.41, $[\alpha]_D = +28.2$ ($c = 1.367$, MeOH). – UV. (MeOH): 260 (14600). – UV. (HCl 0.1 N): 258 (15100). – UV. (NaOH 0.1 N): 260 (15300). – CD. (MeOH); $[\theta]_{265} = -1770$. – IR. (KBr): 3700–2500*s*, 1650*s* br., 1608*s*, 1582*m*, 1482*m*, 1459*m*, 1427*m*, 1380*m*, 1340*m*, 1304*m*, 1252*m*, 1215*m*, 1183*m*, 1128*s*, 1072*s*, 1060*s*, 965*m*, 925*w*, 900*w*, 870*w*, 830*m*, 803*m*, 770*m*, 750*m*, 728*m*, 705*m*. – ^{1}H-NMR. ($(CD_3)_2SO$): 4.43 (*d*×*d*×*d*, $J = 6.75$, 6 and 5.75, 1 H, H–C(3′)); 4.76 (*d*×*d*×*d*, $J = 6$, 5.25 and 4.2, 1 H, H–C(2′)); 4.88 (*d*, $J = 6$, 1 H, H–C(4′)); 5.42 (*d*, $J = 6.75$, 1 H, exchanges with D_2O, HO); 5.63 (*d*, $J = 5.25$, 1 H, exchanges with D_2O, HO); 6.05 (*d*, $J = 4.2$, 1 H, H–C(1′)); 7.2–7.6 (*m*, 7 H, 2 H exchanges with D_2O); 8.23 (*s*, 1 H, H–C(2)); 8.43 (*s*, 1 H, H–C(8)). – ^{13}C-NMR. ($(CD_3)SO$): 72.67 (*d*), 75.57 (*d*), 84.19 (*d*), 88.21 (*d*), 118.97 (*s*), 126.06 (*d*), 127.49 (*d*), 127.97 (*d*), 139.40 (*s*), 139.93 (*d*), 149.07 (*s*), 152.50 (*d*), 155.84 (*s*). – MS.: 314 (5, $M^+ + 1$), 313 (6, M^+), 278 (5), 254 (5), 225 (5), 224 (9), 207 (11), 194 (18), 190 (6), 178 (40), 165 (7), 164 (78), 148 (7), 137 (6), 136 (100), 135 (88), 131 (5), 121 (5), 120 (12), 119 (8), 109 (5), 108 (22), 107 (6), 105 (9), 104 (5), 103 (15), 92 (6), 91 (44), 82 (5), 81 (6), 79 (7), 78 (6), 77 (11), 67 (5), 66 (6), 65 (7), 55 (6), 54 (6), 45 (6), 43 (9), 28 (7), 18 (11).

$C_{15}H_{15}N_5O_3$ (313.32) Calc. C 57.50 H 4.82 N 22.35% Found C 57.33 H 4.89 N 22.26%

*Preparation of 2,3-*O*-isopropylidene-9-(4-*C*-phenyl-β-*D*-*ribo*-tetrofuranosyl)adenine* (**25**). A solution of 10 mg (0.03 mmol) of **24** and 0.5 mg *p*-toluenesulfonic acid [35] in 1 ml acetone and 0.5 ml dimethoxypropane was stirred for 1 h, at 50°, taken to dryness *in vacuo*, the residue was purified on prep. TLC. (ethyl acetate/EtOH/H_2O 15:2:1) to gave 9.6 mg (85%) of **25**. – ^{1}H-NMR. ($(CD_3)_2SO$): 1.35 (*s*, 3 H); 1.63 (*s*, 3 H); 5.06 (*d*, $J = 5$, 1 H, H–C(4′)); 5.08 (*d*×*d*, $J = 5$ and 5, 1 H, H–C(3′)); 5.54 (*d*×*d*, $J = 5$ and 2.9, 1 H, H–C(2′)); 6.26 (*d*, $J = 2.9$, 1 H, H–C(1′)); 7.2–7.4 (*m*, 7 H); 8.17 (*s*, 1 H, H–C(2)); 8.35 (*s*, 1 H, H–C(8)).

*Preparation of 2,3-*O*-cyclohexylidene-4-*C*-(2-methoxymethoxyphenyl)-*D*-ribo- and* L*-lyxo-tetronolactones* (**18** *and* **19**). A) *Normal addition at 0°*. A solution of 2.1 ml butyllithium in hexane (3.6 mmol) was added at r.t. under N_2 to 0.502 ml TMEDA (= *N, N, N′, N′*-tetramethylethylenediamine). The mixture was cooled to 0° and treated dropwise with 500 mg (3.6 mmol) methoxymethoxybenzene [36]. The suspension was stirred for 2 h at 0°, warmed to 10°, treated dropwise with a solution of 250 mg (1.16 mmol) of **6** in 5 ml ether, stirred for further 3 h at 10° and then poured into a mixture of 1 M aq. $KHSO_4$ and ice. Normal workup with CH_2Cl_2 and chromatography on 40 g silica gel ethyl acetate/hexane 1:3) gave 117 mg (30%) of **18** and 136 mg (35%) of **19**.

Data for **18**. Oil, Rf (A) 0.46, $[\alpha]_D = -10.8°$ ($c = 1.069$). – IR.: 3010*w*, 2950*s*, 2915*m*, 2870*m*, 2840*w*, 1787*s*, 1607*m*, 1595*w*, 1496*m*, 1460*m*, 1452*m*, 1410*w*, 1373*m*, 1350*w*, 1340*m*, 1315*w*, 1291*m*, 1164*s*, 1125*s*, 1115*s*, 1088*m*, 1056*m*, 1038*m*, 990*s*, 958*m*, 940*m*, 938*m*, 912*w*, 900*w*, 865*w*, 850*w*, 830*w*. –

^{1}H-NMR.: 1.4–1.8 (*m*, 10 H); 3.46 (*s*, 3 H); 4.66 (*d*, *J* = 6, 1 H); 4.73 (*d*, *J* = 6, 1 H); 5.10 (*d*, *J* = 6.5, 1 H); 5.23 (*d*, *J* = 6.5, 1 H); 5.36 (*s*, 1 H, H–C(4)); 6.8–7.4 (*m*, 4 H). – ^{13}C-NMR.: 23.70 (*t*), 23.84 (*t*), 24.84 (*t*), 35.01 (*t*), 36.26 (*t*), 56.45 (*qa*), 75.69 (*d*), 80.40 (*d*), 84.57 (*d*), 94.00 (*t*), 113.89 (*d*), 114.45 (*s*), 121.72 (*d*), 124.81 (*s*), 128.76 (*d*), 130.65 (*d*), 154.05 (*s*), 174.34 (*s*). – MS.: 334 (2, M^+), 236 (3), 189 (10), 175 (3), 160 (3), 147 (9), 146 (4), 143 (4), 135 (3), 132 (5), 131 (32), 119 (13), 118 (10), 97 (3), 91 (5), 81 (3), 69 (3), 55 (11), 45 (100), 44 (4), 42 (3), 41 (8), 39 (3).

$C_{18}H_{22}O_6$ (334.38) Calc. C 64.65 H 6.63% Found C 64.75 H 6.60%

Data for **19**. M.p. 85.5–86.5°; Rf (A) 0.39, $[\alpha]_D = +69.9°$ ($c = 1.148$). – IR.: 3030*w*, 3005*w*, 2940*s*, 2905*m*, 2860*m*, 2823*w*, 1788*s*, 1606*m*, 1593*w*, 1492*m*, 1460*m*, 1450*m*, 1430*w*, 1405*w*, 1370*m*, 1340*m*, 1320*m*, 1310*m*, 1287*m*, 1267*m*, 1179*s*, 1160*s*, 1122*s*, 1082*m*, 1050*m*, 1000*s*, 980*m*, 937*m*, 910*m*, 850*w*, 840*w*. – ^{1}H-NMR.: 1.4–1.8 (*m*, 10 H); 3.43 (*s*, 3 H); 4.82 (*d*, *J* = 6, 1 H, H–C(2)); 5.00 (*d* × *d*, *J* = 6 and 4, 1 H, H–C(3)); 5.16 (*s*, 2 H); 5.73 (*d*, *J* = 4, 1 H, H–C(4)); 6.8–7.4 (*m*, 4 H). – ^{13}C-NMR.: 23.58 (*t*), 24.65 (*t*), 35.58 (*t*), 36.32 (*t*), 56.10 (*qa*), 75.90 (*d*), 76.53 (*d*), 76.64 (*d*), 94.19 (*t*), 112.99 (*d*), 114.43 (*s*), 121.42 (*d*), 122.71 (*s*), 126.98 (*d*), 129.10 (*d*), 153.03 (*s*), 174.02 (*s*). – MS.: 334 (4, M^+), 302 (4), 219 (8), 192 (3), 189 (12), 185 (6), 176 (4), 175 (8), 160 (3), 147 (12), 146 (5), 143 (7), 141 (3), 140 (8), 135 (4), 132 (4), 131 (30), 121 (6), 119 (7), 118 (5), 113 (4), 111 (4), 107 (3), 99 (8), 98 (3), 97 (9), 91 (4), 83 (4), 81 (7), 79 (3), 77 (4), 69 (4), 65 (3), 55 (21), 46 (4), 45 (100), 42 (4), 41 (13), 39 (5).

$C_{18}H_{22}O_6$ (334.38) Calc. C 64.65 H 6.63% Found C 64.77 H 6.68%

B) *Normal addition at −40°*. A solution of 250 mg (1.16 mmol) of **6** in 5 ml ether was added dropwise at −40° to a suspension of the aryllithium prepared as indicated above. After stirring the mixture for further 3 h at −40°, it was warmed to r.t. and poured into 1M aq. $KHSO_4$ and ice. Normal workup with CH_2Cl_2 and chromatography gave 70 mg (18%) of **18** and 206 mg (53%) of **19**.

C) *Inverse addition at 0°*. The solution of the aryllithium, prepared as indicated above, was added dropwise to a solution of 250 mg (1.16 mmol) of **6** in 5 ml ether at 0°. The mixture was stirred for 3 h at 0°, workup as indicated above gave, after chromatography 101 mg (26%) of **18** and 156 mg (40%) of **19**.

D) *Inverse addition at −40°*. The solution of the aryllithium, prepared as indicated under *A*, was added dropwise to a solution of 250 mg (1.16 mmol) of **6** in 5 ml ether at −40°. The mixture was stirred for 3 h at −40°, warmed to r.t. and worked up as indicated under A to give, after chromatography, 58 mg (15%) of **18** and 238 mg (61%) of **19**.

Preparation of **18** *from* **19**. A solution of 300 mg (0.9 mmol) of **19** in 3 ml piperidine and 10 ml abs. THF was warmed for 3 h at 60° and taken to dryness *in vacuo*. The residue was dissolved in 15 ml CH_2Cl_2 and 0.5 ml triethylamine, cooled to 0° and treated dropwise with a solution of 0.9 ml methanesulfonyl chloride in 5 ml CH_2Cl_2. The resulting suspension was stirred for 15 min at 0°, poured into a mixture of 1M aq. $KHSO_4$ and ice (final pH = 3) and worked up in a normal way with CH_2Cl_2. Chromatography of the residue on 30 g silica gel (AcOEt/hexane 1:2) gave 264 mg (89%) of **18**.

*Preparation of 2,3-O-cyclohexylidene-4-C-(2-(methoxymethoxy)phenyl)-*D*-ribo-tetrose* (**26**). After reducing 1.45 g (4.3 mmol) of **18** with 7 ml of a DIBAH solution (20% in toluene) as described for the preparation of **21**, chromatography of the crude product on 140 g silica gel (ethyl acetate/hexane 1:2) gave 1.410 g (95%) of **26** as a clear oil, $[\alpha]_D = +2.1°$ ($c = 1.23$), no mutarotation. – IR.: 3610*w*, 3500*w* br., 3010*m*, 2950*s*, 2870*m*, 1605*m*, 1590*w*, 1490*m*, 1432*m*, 1410*w*, 1370*m*, 1335*w*, 1285*m*, 1158*s*, 1118*s*, 1085*s*, 1053*s*, 1000*s*, 945*m*, 940*m*, 910*m*, 850*m*. – ^{1}H-NMR.: 1.3–1.9 (*m*, 10 H); 3.5 (*s*, 3 H); 3.6–3.8 (*m*, 1 H, exchanges with D_2O); 4.35–4.8 (*m*, 2 H); 5.2 (*s*, 2 H, OCH_2O); 5.25–5.50 (*m*, 2 H); 6.75–7.50 (*m*, 4 H).

*Preparation of 1,2,3-tri-O-acetyl-4-C-(2-acetoxyphenyl)-α- and β-*D*-ribo-tetroses* (**28** *and* **27**). A solution of 1.4 g (4.16 mmol) of **26** in 100 ml 0.2M aq. HCl was kept for 7 h at 50°, cooled to 10°, neutralized with *Amberlite IR-45* (OH^-) and filtered. The filtrate was freeze-dryed, and a solution of the residue in 20 ml pyridine and 20 ml acetic anhydride kept for 7 h at 10°. The solvents were evaporated in h.v. and a solution of the residue in 15 ml acetic acid, 15 ml acetic anhydride and a trace of conc. H_2SO_4-solution was left at r.t. for 1 h after which time the mixture was evaporated under h.v., chromatography of the residue on 150 g silica gel (ethyl acetate/hexane 1:2) gave 1.13 g (72%) of **27** and 0.291 g (18%) of **28**.

Data of **27**. M.p. 105–106°, Rf (A) 0.40, $[\alpha]_D = -7.7°$ ($c = 1.38$). – IR.: 3030*w* br., 1755*s* br., 1490*w*, 1455*w*, 1425*w*, 1375*m*, 1180*m*, 1110*m*, 1090*m*, 1060*m*, 1040*m*, 1005*m*, 960*m*, 895*w*. – ^{1}H-NMR.: 2.03 (*s*, 3 H); 2.13 (*s*, 3 H); 2.16 (*s*, 3 H); 2.30 (*s*, 3 H); 5.40 (br. *s*, 3 H, H–C(2), H–C(3) and H–C(4));

6.30 (*s*, 1 H, H–C(1)); 6.95–7.5 (*m*, 4 H). – ^{13}C-NMR.: 20.31 (*qa*), 20.46 (*qa*), 20.90 (*qa*), 21.00 (*qa*), 74.14 (*d*), 75.22 (*d*), 77.34 (*d*), 98.00 (*d*), 122.56 (*d*), 126.30 (*d*), 126.92 (*d*), 129.25 (*d*), 129.79 (*s*), 148.07 (*s*), 168.82 (*s*), 169.07 (*s*). – MS.: 278 (6), 219 (3), 218 (7), 177 (9), 176 (45), 165 (5), 159 (5), 149 (3), 148 (10), 147 (41), 136 (4), 134 (24), 131 (12), 130 (5), 123 (11), 121 (4), 119 (5), 118 (5), 107 (5), 103 (4), 91 (3), 43 (100).

$C_{18}H_{20}O_9$ (380.36) Calc. C 56.84 H 5.30% Found C 56.76 H 5.25%

Data of **28**. Oil, Rf (A) 0.34, $[\alpha]_D = +55.0°$ ($c = 1.289$). – IR.: 3020*w* br., 1750*s* br., 1487*w*, 1452*w*, 1430*w*, 1370*m*, 1177*m*, 1112*m*, 1095*m*, 1045*m*, 1010*m*, 940*m*, 905*w*. – ^{1}H-NMR.: 2.03 (*s*, 3 H); 2.13 (*s*, 6 H); 2.28 (*s*, 3 H); 5.30–5.45 (*m*, 3 H, H–C(2), H–C(13) and H–C(4)); 6.6 (br. *d*, $J = 3.5$, H–C(1)); 7.0–7.5 (*m*, 4 H). – ^{13}C-NMR.: 20.18 (*qa*), 20.47 (*qa*), 20.78 (*qa*), 20.96 (*qa*), 69.28 (*d*), 73.71 (*d*), 79.93 (*d*), 93.69 (*d*), 122.61 (*d*), 126.14 (*d*), 126.54 (*d*), 129.31 (*s* + *d*), 147.61 (*s*), 168.44 (*s*), 168.90 (*s*), 169.33 (*s*), 169.49 (*s*). – MS.: 321 (3), 278 (7), 219 (6), 218 (9), 189 (3), 177 (11), 176 (51), 165 (7), 159 (7), 149 (4), 148 (11), 147 (41), 136 (4), 135 (6), 134 (25), 131 (13), 130 (7), 123 (15), 121 (4), 119 (5), 118 (5), 107 (5), 103 (6), 91 (3), 45 (7), 43 (100).

$C_{18}H_{20}O_9$ (380.36) Calc. C 56.84 H 5.30% Found C 56.66 H 5.17%

*Preparation of 9-[4-C-(2-hydroxyphenyl)-β-*D*-ribo-tetrofuranosyl]adenine* (**29**). To a solution of 380 mg (1 mmol) of a 3:1 mixture of **27** and **28** in 10 ml CH_3CN was added 239 mg (1 mmol) of N^6-benzoyladenine, 444 mg (2 mmol) of trimethylsilyl triflоromethanesulfonate and 116 mg of (0.8 mmol) hexamethyldisilazane. The mixture was heated under N_2 for 1 h to 60°, diluted with 20 ml CH_2Cl_2 and processed in a normal way (satd. aq. $NaHCO_3$-soln., CH_2Cl_2, satd. NaCl-soln.) to give a residue, which was dissolved in 20 ml of MeOH saturated with ammonia and kept for 48 h at r.t. Evaporation of the solvent and filtering of the residue through 100 g of *Sephadex G-10* (MeOH) gave 223 mg (68%) of **29**, m.p. 135° (dec.), Rf (E) 0.36, $[\alpha]_D = -8.0°$ ($c = 0.985$, MeOH). – UV. (MeOH): 260 (14400). – UV. (HCl 0.1N): 258 (15700). – UV. (NaOH 0.1N): 246 (13900), 261 (15600), 315 (4100). – CD. (MeOH): $[\theta]_{223} = -8150$, $[\theta]_{250} = +2960$, $[\theta]_{272} = -4000$, $[\theta]_{288} = +1330$. – IR. (KBr): 3700–2500*s*, 1650*s*, 1607*s*, 1578*s*, 1501*m*, 1480*s*, 1455*s*, 1421*m*, 1374*m*, 1337*s*, 1302*s*, 1292*s*, 1246*s*, 1220*m*, 1180*m*, 1130*s*, 1082*m*, 1065*m*, 1041*s*, 993*m*, 970*m*, 895*m*, 863*m*, 850*m*, 832*m*, 796*m*, 757*s*, 742*m*, 721*m*. – ^{1}H-NMR. ($(CD_3)_2SO$): 4.31 (*d* × *d*, $J = 5$ and 4, 1 H, H–C(3′)); 4.80 (*d* × *d*, $J = 6$ and 5, 1 H, H–C(2′)); 5.15 (*d*, $J = 4$, 1 H, H–C(4′)); 5.99 (*d*, $J = 6$, 1 H, H–C(1′)); 6.7–6.9 (*m*, 2 H); 7.05–7.2 (*m*, 1 H); 7.25–7.45 (*m*, 3 H); 8.19 (*s*, 1 H, H–C(2)); 8.42 (*s*, 1 H, H–C(8)). – ^{13}C-NMR. ($(CD_3)_2SO$): 72.23 (*d*), 74.25 (*d*), 81.19 (*d*), 87.05 (*d*), 115.16 (*d*), 118.89 (*s*), 119.18 (*d*), 125.48 (*s*), 127.54 (*d*), 128.66 (*d*), 139.99 (*d*), 149.68 (*s*), 152.69 (*d*), 154.65 (*s*), 156.01 (*s*). – MS.: 147 (6), 136 (22), 135 (100), 134 (13), 131 (6), 108 (29), 107 (21), 106 (9), 91 (7), 81 (10), 79 (13), 78 (17), 77 (11), 66 (5), 54 (9), 53 (7), 51 (6), 44 (9), 43 (6), 38 (7).

$C_{15}H_{15}N_5O_4$ (329.32) Calc. C 54.70 H 4.59 N 21.26% Found C 54.41 H 4.69 N 20.98%

*Preparation of 2,3-*O*-isopropylidene-9-[4-C-(2-hydroxyphenyl)-β-*D*-ribo-tetrofuranosyl]adenine* (**30**). This compound was prepared from **29** as described for the preparation of **25** from **24** (yield: 10 mg (83%) of **30** from 10 mg (0.3 mmol) of **29**). – ^{1}H-NMR. ($(CD_3)_2SO$): 1.33 (*s*, 3 H); 1.60 (*s*, 3 H); 5.07 (*d* × *d*, $J = 6$ and 3.2, 1 H, H–C(3′)); 5.3 (*d*, $J = 3.2$, 1 H, H–C(4′)); 5.55 (*d* × *d*, $J = 6$ and 3.8, 1 H, H–C(2′)); 6.18 (*d*, $J = 3.8$, 1 H, H–C(1′)); 6.7–7.3 (*m*, 6 H); 8.15 (*s*, 1 H, H–C(2)); 8.40 (*s*, 1 H, H–C(8)).

REFERENCES

[1] *R.J. Suhadolnik,* 'Nucleosides as Biological Probes', Wiley-Interscience, New York 1979, p. 19.
[2] *K. Soo Kim & W.A. Szarek,* Can. J. Chem. *59*, 878 (1981).
[3] a) *R.J. Suhaldolnik,* 'Nucleosides as Biological Probes', Wiley-Interscience, New York 1979, p. 30. b) *T. Ito, A. Takatsuki, K. Kawamura, K. Sato & G. Tamura,* Agric. Biol. Chem. *44*, 695 (1980).
[4] *W. Meyer & H. Follmann,* Chem. Ber. *113*, 2530 (1980).
[5] *H. Ohrui, H. Kuzuhara & S. Emoto,* Tetrahedron Lett. *1971*, 4267.
[6] *T. Sato, M. Watanabe & R. Noyori,* Heterocycles *14*, 761 (1980).
[7] *J.N. Baxter & A.S. Perlin,* Can. J. Chem. *38*, 2217 (1960).

[8] *A. Vasella*, 'Modern Synthetic Methods', Vol. 2, R. Scheffold, Ed. 1980, p. 173.
[9] *H. des Abbayes, C. Neveu & F. Salmon-Legagneur*, Bull. Soc. Chim. France *1973*, 2686.
[10] *D. Horton & Z. Walaszek*, Carbohydr. Res. *105*, 111 (1982).
[11] *R. Cernik, G.-A. Craze, O.S. Mills & I. Watt*, J. Chem. Soc., Perkin Trans. II *1982*, 361.
[12] *W. Clark Still & J.H. McDonald*, Tetrahedron Lett. *1980*, 1031; *M.L. Wolfrom & S. Hanessian*, J. Org. Chem. *27*, 1800 (1962).
[13] *R. Bernadi, C. Fuganti & P. Grasselli*, Tetrahedron Lett. *1981*, 4021.
[14] *H. Christensen*, Synth. Commun. *5*, 65 (1975).
[15] *H. Iwasaki & B. Witkop*, J. Am. Chem. Soc. *86*, 4698 (1964).
[16] *E. Winterfeld*, Synthesis *1975*, 617.
[17] *P. Kohn, R.H. Samaritano & L.M. Leiner*, Synth. Proc. Nucl. Acid Chem. *1*, 120 (1968).
[18] *I. Iwai, T. Nishimura & B. Shimizu*, Synth. Proc. Nucl. Acid Chem. *1*, 136 (1968).
[19] *U. Niedballa & H. Vorbrüggen*, Angew. Chem. *82*, 449 (1970); Angew. Chem. Int. Ed. *9*, 461 (1970).
[20] *N.J. Leonard & J.A. Deyrup*, J. Am. Chem. Soc. *84*, 2148 (1962).
[21] *J.S. Ingwall*, J. Am. Chem. Soc. *94*, 5487 (1972).
[22] *B. Rayner, C. Tapiero & J.-L. Imbach*, Carbohydr. Res. *47*, 195 (1976).
[23] *M. Mac Coss, M.J. Robins, B. Rayner & J.-L. Imbach*, Carbohydr. Res. *59*, 575 (1977).
[24] *C. Altona & M. Sundaralingam*, J. Am. Chem. Soc. *94*, 8205 (1972); *C. Altona & M. Sundaralingam*, J. Am. Chem. Soc. *95*, 2333 (1973).
[25] *D.B. Davies & S.S. Danyluk*, Biochemistry *13*, 4417 (1974).
[26] *G. Ah-Kow, F. Terrier, M.-J. Pouet & M.-P. Simonnin*, J. Org. Chem. *45*, 4399 (1980).
[27] *H. Vorbrüggen & B. Bennua*, Chem. Ber. *114*, 1279 (1981).
[28] *D.W. Miles, M. Farmer & H. Eyring*, Proc. Natl. Acad. Sci. USA *77*, 3398 (1980).
[29] *H. Follmann & G. Gremels*, Eur. J. Biochem. *47*, 187 (1974).
[30] *H. Follmann, I. Kuntz & W. Zacharias*, Eur. J. Biochem. *58*, 31 (1975).
[31] *A. Vasella & R. Voeffray*, Helv. Chim. Acta *65*, 1953 (1982).
[32] *A.M. Sepulchre, A. Gateau & S.D. Gero*, Carbohydr. Res. *24*, 311 (1972).
[33] *R. Bisaz*, ETH-thesis No. 5500, 1975.
[34] *E.L. Eliel & D.W. Delmonte*, J. Org. Chem. *21*, 597 (1956).
[35] *J.A. Rabi & J.J. Fox*, J. Org. Chem. *37*, 3898 (1972).
[36] *J.P. Yardley & H. Fletcher*, Synthesis *1976*, 244.