CHIROPTICAL PROPERTIES OF 2-METHYL-1,4-LACTONES; REVISED ABSOLUTE CONFIGURATION OF 2-DEOXY-2-C-METHYL-*erythro*-D-PENTONO-1,4-LACTONES

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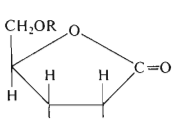
Received July 24th, 1973

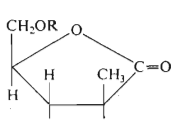
The effect of branching at position 2 on the chiroptical properties and ring deformation of five-membered lactones has been examined.

In connection with syntheses of nucleosides containing an anomalous sugar moiety, the absolute configuration at the $C_{(2)}$ carbon atom in isomeric 2-deoxy-2-C-methyl-*erythro*-D-pentonolactones *I* and *II* was examined[1]. Because of the steric similarity of the hydroxylic function[2,3] and the methyl group, an analogous effect of these two groups was assumed on the chirality of lactones. We have therefore examined the changes in ORD and CD values due to substitution of the α-hydrogen atom in 1,4-lactones by the methyl group and wish to present the results in this paper. The above optical properties have been measured on compounds of the D-series, namely, four pairs of 1,4-lactones of ribonic acid (*III*), arabonic acid (*IV*), lyxonic acid (*V*), and xylonic acid (*VI*) as well as the corresponding 2-C-methyl derivatives[4] *VII*, *VIII*, *IX*, and *X*, then allonolactone[5] (*XI*), the two 2-deoxy-1,4-lactones, namely, 2-deoxy-*erythro*-D-pentono-1,4-lactone[6] (*XII*) and 2-deoxy-*arabino*-D-hexono-1,4-lactone[7] (*XIII*), 2,3-dideoxy-2-C-methyl-*glycero*-D-pentono-1,4-lactone (*XIV*), and the unsaturated 2,3-dideoxy-2-C-methyl-*glycero*-D-pent-2-enono-1,4-lactone (*XV*). The group of these free lactones was extended by two 2,3-O-isopropylidene derivatives (*XVI* and *XVII*, *cf.*[4]) of the lactones *III* and *VII*.

Lactones *V* and *VI* were prepared from D-lyxose and D-xylose by the hypoiodite oxidation[8]. Concerning the hitherto unreported compounds, the crystalline 2-C-methyl-D-arabonolactone *VIII* was prepared analogously to the sirupous optical counterpart[9,10] of the L-series; the lesser discrepancy in optical rotation values might be ascribed to the different forms. Lactone *IX* was prepared by *cis*-hydroxylation of the unsaturated lactone *XVIII* which is formed as a by-product in the synthesis of lactones *I* and *II* (ref.[1]), and deblocking of the oxidation product *XIX*. The accompanying *ribo* derivative *XX* was separated by chromatography. The configuration of compound *XX* was established by conversion into the known derivatives.



I; R = H
XXIII; R = *p*-toluyl



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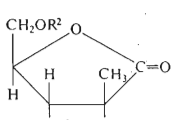
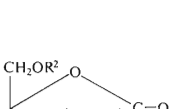
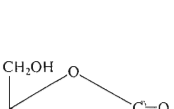


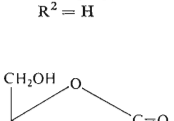
VII; R^1, R^2 = H
XX; R^1 = H, R^2 = *p*-toluyl
XVII; $2R^1$ = isopropyliden
R^2 = H



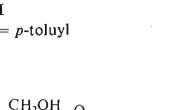
IX; $R^1 = R^2$ = H
XIX; R^1 = H, R^2 = *p*-toluyl



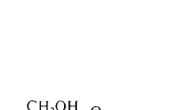
VIII



X



XII

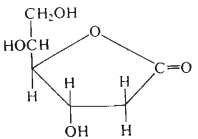


XI

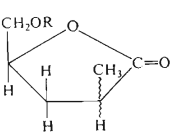
When the attempted epoxidation of the unsaturated lactone *XVIII* failed, 2-C-methyl--D-xylonolactone (*X*) was obtained by the alkaline hydrolysis of 2-bromo-2-deoxy--2-C-methyl-3,5-di-O-*p*-toluyl-*erythro*-D-pentono-1,4-lactone[1,11] (*XXI*) along with the above mentioned *ribo* isomer *VII* and *arabino* isomer *VIII*. In the hydrolysis, an epoxide ring is obviously formed which is again reopened in the course of the isolation process under the formation of the two *trans*-lactones *VIII* and *X* while the formation of the *cis*-lactone *VII* is probably due to the direct hydrolysis of the bromo derivative *XXI*. The similarity of the lactone *X* with the *ribo* isomer *VII* in optical properties (Table I), melting points, and the elemental analysis led to difficulties during the isolation and identification process. As demonstrated by the periodate oxidation, the lactone *X* represents a *xylo* isomer. Lactone *XIV* was pre-

pared by removal of the protecting group from the derivative *XXII*, an additional by-product in the synthesis of lactones *I* and *II* (ref.[1]).

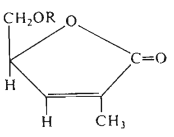
The synthesis of lactones *I* and *II* was started from the protected lactones *XXIII* and *XXIV* which were obtained by hydrogenolysis of the bromo lactone *XXI* (ref.[1,11]) along with the above mentioned compounds *XVIII* and *XXII*. The protected lactones *XXIII* and *XXIV* are difficult to separate; the $[\alpha]$ value was therefore calculated by extrapolation from values of mixtures of the two components, the ratio of which was determined by means of NMR spectra. The attempted deblocking of lactones *XXIII* and *XXIV* by alkaline alcoholysis led in both cases to sirupous products which were erroneously ascribed[1,11] the structure of lactones *I* and *II*. The low $[\Phi]_{227}$ values of these sirups are, however, due to accidental contaminants. By chromatography on silica gel, an identical substance has been now isolated in both cases, melting at 102°C and analyzing $C_6H_8O_3$. The assumption that an unsaturated lactone *XV* is involved is incompatible with the mass and NMR spectrum which indicate the presence of two methyl groups. On the basis of this spectral evidence, the substance was finally identified as 3,5-dimethyl-5-hydroxy-2(5*H*)-furanone[12–14] (*XXV*). The alcoholysis of lactones *XXIII* and *XXIV* was thus accompanied by removal of the group from position 3 and by a rearrangement. To verify this hypothesis, the protected unsaturated lactone *XVIII* was subjected to alcoholysis under analogous conditions. The furanone *XXV* was again obtained as the product. The optical inactivity of this substance might be ascribed to racemisation during the opening



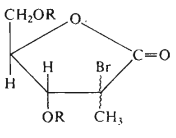
XIII



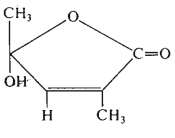
XIV; R = H
XXII; R = *p*-toluyl



XV; R = H
XVIII; R = *p*-toluyl
XXVI; R = acetyl



XXI; R = *p*-toluyl



XXV

of the lactone ring and removal of the hydroxylic function from position 5. This reaction course is not surprising in view of involvement of a β-position in respect to the double bond conjugated with the carboxylic group.

The unsaturated lactone *XV* was prepared by hydrolysis of the protected lactone *XVIII* in aqueous acetic acid under catalysis of hydrochloric by heating under pressure. Also in this case a partial reaarangement took place under the formation of the furanone *XXV* which was separated by chromatography on a weakly basic anion exchange resin freshly preconverted into the OH^- cycle. In addition to the rearrangement, the hydrolysis was under vigorous conditions accompanied by a partial acetylation of the free hydroxylic function at position 5 under the formation of compound *XXVI*.

Analogously to compound *XV*, the free lactones *I* and *II* were obtained by acid hydrolysis of a mixture of the protected lactones *XXIII* and *XXIV* (the ratio of isomers in this mixture was determined previously). The reaction products comprised the furanone *XXV*, the unsaturated lactone *XV*, its 5-acetyl derivative *XXVI*, and the free lactones *I* and *II*. The furanone *XXV* was removed by chromatography on a weakly basic anion exchange resin; the two unsaturated compounds *XV* and *XXVI* were removed by ozonolysis. According to NMR, the final product contained the two lactones *I* and *II* in the ratio 1 : 1, markedly different from that of the starting compounds. Since the attempted separation of the isomers *I* and *II* failed, numerous fractions were prepared by chromatography. The ratio of isomers in these fractions was determined by means of NMR and the $[\alpha]$, CD, and ORD data were measured. The values of the individual lactone *II* were calculated by extrapolation. A successful route to the individual lactone *I* (the 2-(*R*)-isomer) was finally found to consist in ozonolysis of the protecting toluyl groups in the lactone *XXIII*.

For the chiroptical constants of the said lactones along with some coupling constants derived from NMR spectra see Table I. As observed by Okuda[2], the sign of the first extremum of the ORD curve in sugar 1,4-lactones depends exclusively on the absolute configuration at the $C_{(2)}$ carbon atom. In the D-series, the first extremum value of lactones with the hydroxylic function in the (*R*)-configuration is negative while a positive value corresponds to the (*S*)-configuration. A completely analogous dependence has been found by Beecham[3,16] for the sign of CD curves. It may be seen from Table I that branching at position 2 of the four parent 1,4-pentonolactones *III* – *VI* due to an additional methyl group leads in all cases to a decrease of the first extremum absolute value of the ORD curve as well as of the CD value but not to such an extent to cause the change of the sign. Furthermore, the branched lactones differ from the unsubstituted lactones in the dissymetry factor ($\Delta\varepsilon/\varepsilon$). With most sugar lactones, this value is about 0·042 and 0·056 (ref.[3]). In these lines are also the values of the allonolactone *XI* and the xylolactone *VI*, while that of the lyxonolactone *V* is somewhat lower. On the other hand, the dissymetry factor of 2-C-methyl lactones is roughly one order lower. It may be thus assumed that the as-

symetry of the molecule is in all cases affected by substitution with a methyl group in an analogous manner. According to the interpretation of Beecham[17], the hydroxyl at position 2 tends to occupy the pseudoequatorial orientation. Consequently, the

TABLE I
Spectral Properties of Sugar 1,4-Lactones

Lactone	Configuration	$\Delta\varepsilon$	λ_{max}	$[\Delta\varepsilon/\varepsilon]$	$[\Phi]$	λ_{Φ}	$J_{3,4}$	$J_{4,5'}$	$J_{4,5''}$
III	*ribo*	$-4{\cdot}23^a$	220^a	$0{\cdot}054^a$	$-5\,200^b$	—	$0{\cdot}6^c$	3·5	3·5
VII	*ribo*	−0·54	222	0·0065	-200 ± 28^d	232	7·1	2·4	5·0
IV	*arabo*	$+5{\cdot}05^a$	219^a	$0{\cdot}057^a$	$+9\,850^b$	230	$7{\cdot}5^e$	$2{\cdot}5^e$ 1·1	$3{\cdot}9^e$ 3·5
VIII	*arabo*	+2·30	223	0·0022	+4 000	237	$7{\cdot}9^e$	$2{\cdot}5^e$ 2·0	$4{\cdot}8^e$ 4·5
V	*lyxo*	+3·63	218	0·035	+7 080	235	2·8	—	—
X	*lyxo*	+0·96	224	0·0076	+3 890	238	4·0	5·0	5·0
VI	*xylo*	−4·3	218	0·055	−3 670	237	$7{\cdot}1^e$	$3{\cdot}1^e$ 2·8	$3{\cdot}1^e$ 3·4
X	*xylo*	−0·71	223	0·0067	$<-600^d$	232	3·4 $3{\cdot}5^e$	5·5	5·5
XI		−3·78	220	0·048	—	—	—	—	—
XII		−0·71	208	—	−1 260	225	—	—	—
XIII		+0·75	212	—	—	—	—	—	—
I		−1·97	212	—	−3 240	228	$1{\cdot}1^f$	$3{\cdot}0^f$	$4{\cdot}6^f$
II[g]		$+0{\cdot}8 \pm 0{\cdot}3$	—	—	$+2\,800^d$	230	$4{\cdot}8^f$	$1{\cdot}5^f$	—
XIV		+0·08	218	0·0013	$<+900^d$	225	—	—	—
XV		−7·6 +0·1	211 245	—	—	—	1·8	3·9	5·4
XVI	*ribo*	−2·68	224	—	−4 100	240	$0{\cdot}5^c$	2·2	2·2
XVII	*ribo*	−2·35	224	—	−3 850	240	0·7	3·0	3·0

[a] Value of Beecham[3]. [b] Rough ORD curves were reported by Okuda[2]. [c] Abraham reports $J_{3,4} = 0{\cdot}5$ in hexadeuterioacetone[15]. [d] The first maximum is superimposed on the ascending part of a band lying out of the apparatus range. With the lactone *VII*, the bands were numerically separated on a computer by the least-square method; the data of lactones *II*, *X*, and *XIV* represent a rough estimation. [e] In pentadeuteriopyridine. [f] The 3,5-O-di-*p*-toluyl derivatives *XXIII* and *XIV*. [g] Extrapolation.

ring is deformed and the $C_{(3)}$ carbon atom projects bellow the plane of the lactone ring formed by the C—CO—O—C atoms when the 2-hydroxylic function is in the (*R*)-configuration (*i.e.*, with the *ribo* and *xylo* derivatives) or above this plane in the case of the (*S*)-configuration of the 2-hydroxylic function (*i.e.*, with the *arabino* and *lyxo* derivatives), see Fig. 1*a* and 1*b*. A negative or a positive sign, respectively, of the ORD and CD curves then corresponds to these two conformations of the lactone ring. The introduction of a methyl group into the position 2 results in a competition between the methyl and hydroxyl groups for the pseudoequatorial orientation and thus in a dynamic equilibration of the ratio of the two conformers leading to a decrease of the absolute ORD and CD values.

The change in the lactone ring conformation may also be judged from the change in apparent coupling constants of protons at $C_{(3)}$ and $C_{(4)}$ ($J_{3,4}$) in NMR spectra. The situation at $C_{(3)}$ and $C_{(4)}$ due to deviation of $C_{(3)}$ bellow or above the lactone ring plane is apparent from the Newman projection (Fig. 2). Arrows show the change of torsion angle between $H_{(3)}$ and $H_{(4)}$ protons due to a decrease (caused by branching at position 2) of the deviation from the lactone ring plane. Since the coupling constant decreases with angles from 0° to 90° and increases with angles from 90° to 180° (*cf.*[18]), the introduction of a methyl group into position 2 should result in an increase of the $J_{3,4}$ value in the *ribo*, *lyxo*, and *xylo* series while a decrease should be observed in the *arabino* series (higher contribution of conformers with the torsion angle less differing from 90°). It may be seen from Table I that the expected change occurred in the first two cases only, while an opposite change took place with the *arabino* and *xylo* derivative. This discrepancy might be explained as follows. The values obtained by measurements represent an average for a mixture of conformers which are in a dynamic equilibrium. This equilibrium depends on the solvent as it is apparent from different $J_{4,5'}$ and $J_{4,5''}$ values of lactones *IV* and *VIII* in two different solvents. Since the chiroptical data and NMR spectra were measured under different conditions, any speculations on their relations are only of an approximative character.

It is also of interest to compare the data of the isopropylidene derivatives *XIV* and *XVII* with those of the parent lactones *III* and *VII*. The accordance of the Cotton effect as well as coupling constants $J_{3,4}$ of compounds *III* and *XIV* has been mentioned earlier[15]. On the other hand, the corresponding branched compounds *VII* and *XVII* strongly differ from each other both in chiroptical data and in the coupling constants $J_{3,4}$. With respect to these two values, the isopropylidene derivative *XVII* does not considerably differ from the unbranched counterpart *XVI* (and thus from the parent ribonolactone *III*) while the pair of the free lactones *III* and *VII* exhibited the highest differences in this respect. Moreover, the ORD curve of the branched isopropylidene derivative *XVII* lacks the ascending part of the band lying at shorter wavelengths out of the range of the apparatus (characteristic also of the lactone *VII*); see Table I, note *d*. It may be thus assumed that the branching due to introduction of a methyl

group into position 2 has a considerably weaker influence on the equilibrium of the isopropylidene conformers than on that of the corresponding free lactones.

As it may be seen from the above comparison of the four pairs of five-membered sugar lactones, the influence of the methyl group and the hydroxylic function at position 2 on the sign of CD and ORD curves is of the same order of magnitude. Consequently, the branched 2-deoxy lactone *I* (ORD and CD negative) is ascribed the (2-*R*)-configuration and the lactone *II* (ORD and CD positive) the (2-*S*)-configuration. Since these free lactones *I* and *II* correspond to the protected lactones *XXIII* and *XXIV*, the absolute configuration at $C_{(2)}$ of the latter compounds is opposite to that proposed by us earlier[1,11]. We did not succeed in determining the $J_{3,4}$ value with the free lactones *I* and *II*, but in the case of the protected compounds *XXIII* and *XXIV*, this value is in qualitative accordance with the earlier considerations.

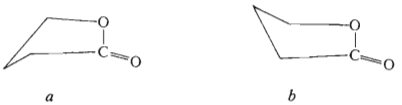


FIG. 1

Conformation of 1,4-Lactones of the D-Series

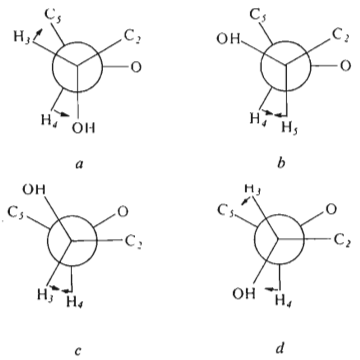


FIG. 2

The Change of the Torsion Angle Due to a Decrease of the Deviation of $C_{(3)}$ from the Plane of the Ring

$C_{(3)}$ below the plane of the ring: *ribo* configuration (*III* and *VII*) (*a*), *xylo* configuration (*VI* and *X*) (*b*), $C_{(3)}$ above the plane of the ring: *lyxo* configuration (*V* and *IX*) (*c*), *arabino* configuration (*IV* and *VIII*) (*d*).

The configurations were confirmed by chemical means. Thus, the mixture of lactones *XXIII* and *XXIV* (the (*R*)-isomer predominated) was reduced with lithium aluminium hydride and the resulting isomeric 2-deoxy-2-C-methyl-*erythro*-D-pentitols (not isolated) were treated successively with sodium periodate and then bromine to afford a mixture of β-hydroxyisobutyric acids. Their phenylcarbamates exhibited a positive rotation which corresponds according to Sprecher and Sprison[19] to the expected (*S*)-configuration.

In addition to the above lactones, we have examined some other compounds obtained as by-products or in connection with another problems. The CD values of the two 2-deoxy lactones *XII* and *XIII* are somewhat high despite the unsubstituted position 2. The lowest CD value was observed in the case of the dideoxy lactone *XIV* (homogeneous on NMR) while the unsaturated lactone *XV* (containing two hydrogen atom less) exhibits two bands of opposite signs. In the latter case, a chromophore of a different character is involved.

EXPERIMENTAL

Unless stated otherwise, thin-layer chromatography was performed on silica gel with gypsum as binder and ethyl acetate as solvent, and column chromatography was carried out on silica gel previously partially deactivated by the addition of 20% water. Melting points were taken on a heated microscope stage (Kofler block). Optical rotational dispersion was measured on a JASCO ORD (UV) 5 apparatus, circular dichroism on a Rousel-Jouan Dichrograf II CD-185 apparatus, and mass spectra on a AEI MS 902 apparatus. NMR spectra were taken in hexadeuteriodimethyl sulfoxide (hexamethyldisiloxane as internal standard) on a Varian HA 100 apparatus.

2-C-Methyl-D-arabinose

Methyl 2-C-methyl-D-arabinopyranoside was prepared analogously to the corresponding enantiomer[9,10]. The pyranoside (1·68 g; 10 mmol) was dissolved in water (50 ml) and the solution refluxed in the presence of Dowex 50 (H^+) ion exchange resin (5 ml). The reaction course was checked by thin-layer chromatography. When the spot of the starting material disappeared (after 5 h), the solution was filtered and the resin washed with additional water. The filtrate and washings were combined, evaporated under diminished pressure, and the crude residue chromatographed on a column of silica gel (200 g). Elution with ethyl acetate (1 000 ml) afforded 1·45 g (94%) of a sirup, homogeneous on thin-layer chromatography. Optical rotation: $[\alpha]_D^{20} -5{\cdot}9°$ (*c* 4·4, water); reported[10] (L-enantiomer): $[\alpha]_D^{23} -2°$ (*c* 0·8, water). Benzylphenylhydrazone: m.p. 131—132°C (methanol); $[\alpha]_D^{20} -32{\cdot}6°$ (*c* 0·23, chloroform). For $C_{19}H_{24}N_2O_4$ (344·4) calculated: 66·26% C, 7·02% H, 8·13% N; found: 66·18% C, 7·06% H, 8·26% N.

2-C-Methyl-D-arabono-1,4-lactone (*VIII*)

2-C-Methyl-D-arabinose (0·33 g; 2 mmol) was oxidized with iodine in alkali[8]. The resulting demineralised solution was evaporated under diminished pressure and the residue heated at 70°C/0·1 Torr for 6 h. The aqueous solution of the product was passed through a column of Zerolite G (OH^-). Chromatography on 50 g of silica gel (ethyl acetate as solvent) afforded 0·26 g (66%) of the lactone *VIII* in the form of a monohydrate, m.p. 63—65°C (moist ethyl acetate). IR spectrum: 1 775 cm^{-1} (lactone), 1 637 cm^{-1} (water). Optical rotation: $[\alpha]_D^{20} +82{\cdot}5°$ (*c* 0·9, water); reported[10] in the L-series: $[\alpha]_D^{20} -106°$. For $C_6H_{10}O_5 \cdot H_2O$ (180·2) calculated: 40·00% C,

6·71% H; found: 40·18% C, 6·82% H. Prior to NMR measurements, the sample was heated at 70°C/0·1 Torr for 5 h.

2-C-Methyl-5-O-*p*-toluyl-D-lyxono (and D-ribono)-1,4-lactone *XIX* and *XX*, resp.

To a solution of the unsaturated lactone[1] *XVIII* (5 g; 20 mmol) in acetone (50 ml) there was added dropwise under stirring at 0°C a solution of potassium permanganate (2·4 g; 15 mmol; 110%) in acetone (200 ml) at the same rate as the color disappeared. The mixture was maintained neutral by occasional additions of acetic acid (total 1 ml) and kept at room temperature overnight. The precipitate of manganese dioxide was collected with suction and washed with acetone. The filtrate and washings were combined, evaporated, the residue dissolved in chloroform (20 ml), the solution washed with water (20 ml), dried, and evaporated. The residue (5 g) was chromatographed on five $17 \times 40 \times 0{\cdot}2$ cm layers of loose silica gel (contg. 20% water) in chloroform. Two bands were visible under UV light. The faster band afforded total 2·7 g (47%) of the *ribo* derivative *XX*, m.p. 103—104°C (di-n-propyl ether). For $C_{14}H_{16}O_6$ (280·3) calculated: 59·99% C, 5·75% H; found: 60·32% C, 5·82% H. The slower band afforded total 0·9 g (16%) of the *lyxo* derivative *XIX*, m.p. 136—137°C (diisopropyl ether). For $C_{14}H_{16}O_6$ (280·3) calculated: 59·99% C, 5·75% H; found: 60·00% C, 5·62% H.

2-C-Methyl-2,3,5-tri-O-*p*-toluyl-D-ribono-1,4-lactone

A mixture of the *ribo* derivative *XX* (0·14 g; 0·5 mmol), pyridine (1 ml), and *p*-toluyl chloride (0·15 ml) was kept at 100°C for 5 h and then processed as usual to afford 0·2 g (77%) of the title lactone, m.p. 138·5°C (diisopropyl ether), $[\alpha]_D^{20} + 122°$ (*c* 0·5, chloroform). For $C_{30}H_{28}O_8$ (516·5) calculated: 69·75% C, 5·46% H; found: 69·47% C, 5·39% H. An in every respect identical sample (mixed melting point determination, optical rotation) was prepared by an analogous procedure from the free lactone *VII*.

2,3-O-Isopropylidene-2-C-methyl-5-O-*p*-toluyl-D-ribono-1,4-lactone

A mixture of the *ribo* derivative *XX* (0·14 g; 0·5 mmol), acetone (5 ml), triethyl orthoformate (0·2 ml), and a drop of methanolic hydrogen chloride was kept at 20°C for 12 h, neutralised with an aqueous suspension of silver carbonate, filtered, and the filtrate evaporated under diminished pressure. Yield, 0·1 g (62%) of the isopropylidene derivative, m.p. 94—96°C (cyclohexane). For $C_{17}H_{20}O_6$ (320·3) calculated: 63·74% C, 6·29% H; found: 64·04% C, 6·42% H. An identical sample, m.p. 93—95°C (cyclohexane), undepressed on admixture with the above specimen, was obtained (yield 0·29 g; 82%) from 2,3-O-isopropylidene-2-C-methyl-D-ribonolactone[4] (*XVII*; 0·2 g; 1 mmol), pyridine (5 ml), and *p*-toluyl chloride (0·3 ml) (6 h at 100°C).

2-C-Methyl-2,3,5-tri-O-*p*-toluyl-D-lyxono-1,4-lactone

Toluylation (analogous to that of the *ribo* derivative *XX*) of the *lyxo* derivative *XIX* afforded 80% of the title lactone, m.p. 163—165°C (di-n-propyl ether), $[\alpha]_D^{20} - 5{\cdot}9°$ (*c* 0·47, chloroform). For $C_{30}H_{28}O_8$ (516·5) calculated: 69·75% C, 5·46% H; found: 69·83% C, 5·46% H.

2-C-Methyl-D-lyxono-1,4-lactone *(IX)*

To a solution of the lactone *XIX* (0·7 g; 2·5 mmol) in methanol (10 ml) there was added methanolic barium methoxide until the alkaline reaction was permanent. The mixture was kept at 20°C

overnight, neutralised with dry ice, and evaporated to dryness. A suspension of the residue in water (10 ml) was shaken with Dowex 50 (H^+) ion exchange resin (2 ml) for 2 h and filtered. The filtrate was evaporated to dryness and the residue was heated for 5 h at 70°C/0·1 Torr. The resulting crude lactone was purified over Zerolite G and by chromatography on silica gel analogously to the *arabino* derivative *VIII*. The eluate was evaporated, the residue dissolved in water, the aqueous solution filtered with Norite, and the filtrate freeze-dried to afford 0·19 g (44%) of the hemihydrate of the lactone *IX*, m.p. 102—104°C. IR spectrum: 1 778 cm^{-1} (lactone), 1 630 cm^{-1} (water). Periodic acid uptake[20]: 1·12 mol (after 1 h). For $C_6H_{10}O_5 \cdot \frac{1}{2}H_2O$ (171·2) calculated: 42·10% C, 6·48% H; found: 42·20% C, 6·44% H. Prior to NMR measurements, the sample was heated at 70°C/0·1 Torr for 5 h.

2-C-Methyl-D-xylono-1,4-lactone (*X*)

To a solution of 2-bromo-2-deoxy-2-C-methyl-3,5-di-O-*p*-toluyl-D-*erythro*-pentono-1,4-lactone[1] (2·3 g; 5 mmol) in methanol (50 ml) there was added dropwise 2M methanolic barium methoxide until the alkaline reaction was permanent. The mixture was kept at 20°C overnight and neutralised with dry ice. The methanol was removed by distillation, the residue triturated with water, and the mixture washed with chloroform to remove methyl toluate. The aqueous suspension was passed through a column of Dowex 50 (H^+) ion exchange resin (10 ml), and the effluent treated under stirring with moist silver carbonate (1 g). The silver salts were filtered off, the filtrate stirred with Dowex 50 (H^+) ion exchange resin (5 ml), and the mixture filtered again. The aqueous solution was evaporated to dryness under diminished pressure and the residue heated at 70°C/0·1 Torr for 5 h. The crude product (1·2 g) was dissolved in water, the aqueous solution passed through 10 ml of Zerolite G (OH^-), the effluent evaporated under diminished pressure, and the residue chromatographed on silica gel (200 g). Elution with chloroform (200 ml) afforded 0·2 g (28%) of 2,3-anhydro-2-C-methyl-D-pentonolactone, b.p. 110°C/0·5 Torr (bath temperature), $[\alpha]_D^{20}$ +43·3° (*c* 1·1, water). For $C_6H_8O_4$ (144·1) calculated: 50·00% C, 5·60% H; found: 50·05% C, 5·75% H. In the thin-layer chromatography (R_F 0·7), the epoxide test with potassium iodide and methyl red was positive. Elution with 3 : 1 chloroform–ethyl acetate (1 000 ml) afforded 0·5 g of a substance (probably the 2-O-methyl derivative), b.p. 125—130°C/0·01 Torr (bath temperature) which was epoxide-negative and was not investigated further. Elution with ethyl acetate alone (1 000 ml) afforded 0·5 g (62%) of a mixture of lactones *VII*, *VIII*, and *X*. This mixture was rechromatographed on 100 g of silica gel in ethyl acetate, 50 ml fractions being taken. There was obtained 0·1 g (12%) of the *xylo*-lactone *X* (from fractions 4 to 6), a mixture of lactones *VII* and *X* (fractions 7 to 10), and 0·15 g (19%) of the lactone *VIII* (fractions 12 to 14). The lactone *X* melted at 161°C (ethyl acetate); mixed melting point depression with the lactone *VII*, 135—150°C. Optical rotation of *X*: $[\alpha]_D^{20}$ +93·1° (*c* 0·8, water). IR spectrum of *X*: 1 775 cm^{-1} (lactone). Periodic acid uptake after 1 h: 0·4 mol per 1 mol of *X* (*cf.*[20]). For $C_6H_{10}O_5$ (162·1) calculated: 44·44% C, 6·22% H; found: 44·45% C, 6·16% H.

(2-*R*,*S*)-2-Deoxy-2-C-methyl-3,5-di-O-*p*-toluyl-*erythro*-D-pentono-1,4-lactones (*XXIII* and *XXIV*, resp.)

The mixture of lactones *XXIII* and *XXIV* obtained by the reported[1] hydrogenation of the bromolactone *XXI* was separated by chromatography on silica gel and crystallisation into three fractions; the proportion of isomers was determined by NMR spectra. Fraction 1, 30·8% of the *S*-isomer and 69·2% of the *R*-isomer; $[\alpha]_D^{20}$ +2·9° (*c* 1·78, chloroform). Fraction 2, 93·3% of the *S*- and 6·7% of the *R*-isomer; $[\alpha]_D^{20}$ +42·3° (*c* 1·24, chloroform). Fraction 3, 100% of the *R*-isomer; $[\alpha]_D^{20}$ —15·4° (*c* 1·55, chloroform).

R-Isomer XXIII. $[\alpha]_D^{20}$ $-16{\cdot}2 \pm 0{\cdot}3°$ (chloroform; by extrapolation). NMR spectrum: 1·35 (d, 3 H, $J_{2,Me} = 7{\cdot}3$, CH_3); 3·13 (n, H, $J_{2,3} = 6{\cdot}7$, $H_{(2)}$); 5·68 (dd, H, $J_{3,4} = 1{\cdot}1$, $H_{(3)}$); 4·85 (m, H, $J_{4,5'} = 4{\cdot}6$, $J_{4,5''} = 3{\cdot}0$, $H_{(4)}$); 5·07 (m, H, $H_{(5)}$); 5·20 (m, H, $H_{(5)}$).

S-Isomer XXIV. $[\alpha]_D^{20}$ $+47{\cdot}4 \pm 0{\cdot}3°$ (by extrapolation). NMR spectrum: 1·48 (d, 3 H, $J_{2,Me} = 7{\cdot}4$, CH_3); 2·97 (m, H, $J_{2,3} = 6{\cdot}2$, $H_{(2)}$); 5·37 (dd, H, $J_{3,4} = 4{\cdot}8$, $H_{(3)}$); 4·78 (m, H, $J_{4,5} = 1{\cdot}5$, $H_{(4)}$).

3,5-Dimethyl-5-hydroxy-2(5 *H*)-furanone (*XXV*)

To a solution of the unsaturated lactone[1] *XVIII* (1·23 g; 5 mmol) in methanol (10 ml) there was added dropwise with stirring 2M methanolic barium methylate until the alkaline reaction was permanent. The mixture was kept at room temperature overnight and neutralised with dry ice. The methanol was evaporated and the residue shaken for 2 h with 10 ml of water and 2 ml of Dowex 50 (H^+) ion exchange resin. The resin was filtered off and washed with water. The filtrate and washings were combined, evaporated to dryness, and the residue heated at 70°C/0·05 Torr for 6 h. The crude residue was brought to crystallisation by the addition of one drop of methanol and freezing at −70°C. Sublimation at 100°C/0·01 Torr afforded 0·5 g (78%) of compound *XXV*, m.p. 102°C (*cf.*[12−14]). Mass spectrum: 128 (M), 113 (M−CH_3), 100 (M—CO), 85 (M−CH_3−CO), 69 (M−2 CH_3−CO). NMR spectrum: 1·66 (s, 3 H, CH_3—C<), 1·85 (d, 3 H, $J_{3,Me} = 1{\cdot}5$, CH_3—C=C); 6·85 (q, H, C=CH); ~3·95 (very broad s, H, OH). For $C_6H_8O_3$ (128·1) calculated: 56·25% C, 6·29% H; found: 56·19% C, 6·33% H.

2,3-Dideoxy-2-C-methyl-*glycero*-D-pent-2-enono-1,4-lactone (*XV*)

To a solution of the protected lactone[1] *XVIII* (1·23 g; 5 mmol) in 50% aqueous acetic acid (20 ml) there was added 0·5 ml of conc. hydrochloric acid and the mixture heated in a sealed glass tube at 120°C for 6 h. The content was then cooled down, filtered to remove *p*-toluic acid, and the filtrate evaporated to dryness (thin-layer chromatography and detection under UV light, showed an absorbing spot, R_F 0·5, corresponding to the furanone *XXV*; two additional spots, R_F 0·8 and 0·48, were detected with concentrated sulfuric acid which does not react with the furanone *XXV*). The residue was dissolved in water and the aqueous solution passed through a column of Zerolite G (20 ml) freshly brought into the OH^- cycle. The effluent was evaporated and the residue (0·5 g; the absence of the furanone *XXV* was indicated by thin-layer chromatography) chromatographed on silica gel (100 g) in ethyl acetate, 50 ml fractions being taken. Fractions 4−6 contained 0·15 g (18%) of the acetate of the unsaturated lactone *XXVI*, a sirup, b.p. 90−100°C/0·01 Torr (bath temperature); NMR spectrum: 1·94 (t, 3 H, $J_{3,Me} = 1{\cdot}8$, $J_{4,Me} = 1{\cdot}8$, CH_3—C=C); 2·06 (s, 3 H, —OAc); 4·25 (m, 2 H, $J_{4,5'} = 5{\cdot}5$, $J_{4,5''} = 3{\cdot}9$, $J_{gem} = 12{\cdot}1$, CH_2); 5·08 (m, H, $H_{(4)}$); 6·99 (t, H, C=CH). For $C_8H_{10}O_4$ (170·2) calculated: 56·46% C, 5·95% H; found: 57·07% C, 6·42% H. Fractions 8−12 contained 0·32 g (50%) of the unsaturated lactone *XV*, a sirup, b.p. 90−110°C/0·01 Torr (bath temperature), $[\alpha]_D^{20}$ −84·4° (*c* 1·6, water), NMR spectrum: 1·95 (t, 3 H, $J_{3,Me} = 1{\cdot}7$, $J_{4,Me} = 2{\cdot}1$, CH_3—C=C); 3·05 (m, H, OH); 3·84 (m, 2 H, $J_{4,5'} = 5{\cdot}4$, $J_{4,5''} = 3{\cdot}9$, $J_{gem} = 12{\cdot}4$, CH_2); 5·01 (m, $H_{(4)}$); 7·07 (m, H, $J_{3,4} = 1{\cdot}8$, C=CH). For $C_6H_8O_3$ (128·1) calculated: 56·25% C, 6·29% H; found: 56·19% C, 6·31% H. Elution of the Zerolite column with 10% aqueous formic acid (50 ml) and evaporation of the effluent to dryness afforded 0·1 g (15%) of the crude furanone *XXV*.

Alkaline Hydrolysis of Lactones *XXIII* and *XXIV*

The mixture (7 : 3; 0·38 g; 1 mmol) of lactones *XXIII* and *XXIV* was hydrolysed with methanolic barium methoxide analogously to the unsaturated lactone *XV*, demineralised with Dowex 50 (H^+) ion exchange resin, and the aqueous filtrate evaporated under diminished pressure. The residual sirup was heated at 70°C/0·1 Torr for 6 h. A sample of the crude product was subjected to thin-layer chromatography; an absorbing spot of the furanone *XXV* was detected under UV light. Two additional spots were detected with conc. sulfuric acid. One of them (R_F 0·25) reacted fastly with neutral aqueous potassium permanganate and corresponded to the unsaturated lactone *XV*; the other one (R_F 0·4) reacted slowly with this reagent. The crude product (0·13 g) was passed through a column (10 ml) of Zerolite G (OH^- cycle) and the effluent evaporated. The residue (40 mg) exhibited the two last mentioned spots on thin-layer chromatography and was not processed further.

(2-*RS*)-2-Deoxy-2-C-methyl-*erythro*-D-pentono-1,4-lactones (*I* and *II*, resp.)

A mixture of lactones *XXIII* and *XXIV* (93 : 7; 1·9 g; 5 mmol) was dissolved in 50% aqueous acetic acid (20 ml) and conc. hydrochloric acid (0·5 ml) and the resulting solution was heated in a sealed glass tube at 120°C for 6 h. *p*-Toluic acid was removed by filtration and the filtrate evaporated under diminished pressure. The residue was coevaporated with two 10 ml portions of water to remove traces of acids. As shown by thin-layer chromatography, compounds *XV*, *XXV*, and *XXVI* (R_F values 0·8, 0·5, and 0·48, resp.) were present. The most intensive spot corresponded to that (R_F 0·4) of an unidentified substance from the alkaline hydrolysis. Another spot (R_F 0·75) was in the neighbourhood of the acetyl derivative *XXVI*. An aqueous solution of the crude residue was passed through 20 ml of Zerolite G (OH^-) and the effluent concentrated under diminished pressure to the volume of about 10 ml. Ozone was then passed through the concentrate at 0°C and the reaction course checked by thin-layer chromatography. As soon as the mixture was free of components reacting rapidly with neutral aqueous potassium permanganate (compounds *XV* and *XXVI*), the ozonisation was interrupted. The reaction mixture was then heated on a steam bath for 1 h, cooled down, passed through 10 ml of Zerolite G (OH^-), and the effluent evaporated under diminished pressure. The residue (0·5 g) was chromatographed on silica gel (100 g) in ethyl acetate. Fractions 4 to 6 (50 ml each) afforded 30 mg of a sirup (R_F 0·75) which was not examined furthermore; a mixture of acetates of the principal product was probably involved. Fractions 9 to 14 afforded 0·34 g (46%) of a mixture of lactones *I* and *II* in the ratio 1 : 1 as indicated by NMR spectrum (intensities of signals of the corresponding methyl group signals). Mass spectrum: 147 (M + 1), 146 (M), 118 (M−CO), 115 (M−CH_2OH), 98 (M−CH_2OH−OH ?), 71 (M−CH_2OH−CO_2), 58 (glyoxal ?). For $C_6H_{10}O_4$ (146·1) calculated: 49·31% C, 6·90% H; found: 47·88% C, 6·88% H. For the purpose of ORD and CD measurements, the mixtures of free isomeric lactones were chromatographed on 200 parts (by weight) of silica gel and separated into two fractions (in another experiment, into three fractions). The ratio of *R*- and *S*-isomers in these fractions was determined by NMR spectra. The head fractions contained a greater proportion of the *S*-isomer.

Ozone was bubbled through a solution of the *R*-lactone *XXIII* (m.p. 124°C; 0·75 g; 2 mmol) in 50% aqueous acetic acid (20 ml) at 20°C. The ozonisation was checked by thin-layer chromatography (detection under UV light). As soon as the aromatic-ring-containing components disappeared, the ozonisation was interrupted, the reaction mixture diluted with water (20 ml), heated gradually over 1 h to 100°C, and the refluxed for 1 h. The volatile portions were distilled off under diminished pressure, the residue dissolved in water, and passed through a column of Zerolite G in the OH^- cycle (10 ml). The effluent was evaporated under diminished pressure and the

residue (0·18 g) chromatographed on silica gel (20 g) in ethyl acetate. Fractions 7 to 11 (10 ml each) contained 96 mg (36%) of the lactone *I* homogeneous on NMR.

Lactone I (*R*-isomer). Optical rotation: $[\alpha]_D^{20}$ +10·06° (*c* 0·54, water). NMR spectrum: 1·15 (d, 3 H, $J_{2'Me}$ = 7·0, CH_3); 2·7 (m, H, $J_{2,3'}$ = 7·1, $H_{(2)}$); 3·68 (m, 2 H, CH_2); 4·25–4·4 (complex m, 2 H, $H_{(3)}$ + $H_{(4)}$).

Lactone II (*S*-isomer). Optical rotation: $[\alpha]_D^{20}$ +43·4° (by extrapolation). NMR spectrum (a mixture of the two isomers was measured and the signals of *R*-isomers were omitted): 1·01 (d, 3 H, $J_{2,Me}$ = 7·0, CH_3); 2·49 (m, H, $J_{2,3}$ = 2·6, $H_{(2)}$); 3·51 (m, 2 H, CH_2).

β-Hydroxyisobutyric Acid N-Phenylcarbamate

A mixture of lactones *XXIII* and *XXIV* ($[\alpha]_D^{20}$ +3·5° *i.e.* *R*/*S* equal to 7 : 3; 0·56 g; 1·5 mmol) was dissolved in ether (70 ml) and added dropwise with stirring into 0·5M ethereal lithium aluminium hydride (10 ml). The whole was refluxed for 5 h and decomposed with water. The ethereal layer was discarded and the aqueous layer subjected to centrifugation to remove the precipitate. The clear supernatant was treated with Dowex 50 (H^+) ion exchange resin (10 ml) and filtered. The filtrate was evaporated under diminished pressure and the residual mixture of 2-deoxy-2-C-methyl-*erythro*-D-pentitols oxidized with sodium periodate and bromine according to a reported method[19]. The resulting mixture of hydroxyisobutyric acids was dissolved in ether (2 ml) and mixed with phenyl isocyanate (0·5 ml). After 1 h, the ethereal solution was added with stirring into saturated aqueous sodium hydrogen carbonate, the precipitate filtered off, and the filtrate acidified to pH 1. The acid portions were extracted with chloroform, the extract dried, evaporated, and the residue chromatographed on a 17 × 40 × 0·2 cm layer of loose silica gel in a 48 : 8 : 4 mixture of benzene, methanol, and acid acetic to afford (detection under UV light) an absorbing zone, R_F 0·57. Elution with ethyl acetate and evaporation of the eluate afforded a residue exhibiting a positive dispersion curve ascending to shorter wavelengths[19].

2,3-Dideoxy-2-C-methyl-*glycero*-D-pentono-1,4-lactone (*XIV*)

To a solution of the lactone[1] *XXII* (0·25 g; 1 mmol) in methanol (10 ml) there was added dropwise saturated methanolic barium methoxide until the alkaline reaction was permanent. After additional 15 h at 20°C, the hydrolysate was neutralised with dry ice and the methanol distilled off under diminished pressure. The residue was diluted with water (10 ml), shaken with Dowex 50 (H^+) ion exchange resin (5 ml) for 2 h, the resin filtered off, and washed with water. The filtrate and washings were combined, evaporated under diminished pressure, and the residue heated at 70°C/0·1 Torr for 6 h. The crude product was dissolved in water and the aqueous solution passed through 10 ml of Zerolite G (OH^-). The effluent was evaporated and the residue (0·12 g) chromatographed on silica gel (20 g) in ethyl acetate to afford 80 mg (65%) of the lactone *XIV* as a sirup. For $C_6H_{10}O_4$ (134·1) calculated: 55·37% C, 7·75% H; found: 54·84% C, 7·81% H.

2-Deoxy-*erythro*-D-pentono-1,4-lactone (*XII*)

The deoxyribonolactone *XII* was prepared by oxidation of deoxyribose with bromine according to a reported procedure[6] and the crude lactone was purified as above. Prior to the CD measurements, ozone was bubbled for 1 h at 0°C through the aqueous solution of the specimen. IR spectrum: 1772 cm^{-1} (lactone). Optical rotation: $[\alpha]_D^{20}$ +18·5° (*c* 0·31, water); reported[6] in the L-series: $[\alpha]_D^{20}$ −13·8°.

2-Deoxy-3,5-di-O-*p*-toluyl-*erythro*-D-pentono-1,4-lactone

A mixture of the deoxyribonolactone *XII* (0·13 g; 1 mmol), pyridine (5 ml), and *p*-toluyl chloride (0·32 g; 2 mmol) was processed as usual to afford 0·25 g (70%) of the protected lactone, m.p. 112—113°C (sublim.), $[\alpha]^{20} -1°$ (*c* 0·52, chloroform). For $C_{21}H_{20}O_6$ (368·4) calculated: 68·47% C, 5·47% H; found: 68·34% C, 5·33% H.

Thanks are due for physical measurements to Dr I. Frič and Mrs H. Pilařová (ORD, CD), Dr M. Synáčková (NMR), Dr L. Dolejš and Dr A. Trka (mass spectra), Dr J. Krupička and Mrs V. Blabolilová (polarography), and for elemental analyses to Dr J. Horáček and Mrs V. Rusová, all of this Institute.

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Translated by J. Pliml.