CONTRACTION OF THE PYRANOSIDE RING IN METHYL 3-ACETAMIDO-3,6-DIDEOXY-2-O-METHANESULFONYL-α-L-GLUCO- AND -α-L-GALACTOPYRANOSIDE

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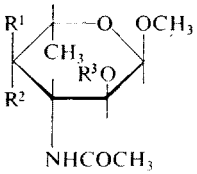
During the reaction of methyl 3-acetamido-3,6-dideoxy-2-O-methanesulfonyl-α-L-glucopyranoside (*I*) with sodium methoxide in methanol, or sodium ethoxide in ethanol, contraction of the pyranoside ring takes place and a mixture of diastereoisomeric methyl 2,5-dideoxy-2-C-(alkoxyacetamidomethyl)-α-L-arabinofuranosides *II* and *III*, or *VIII* and *IX* is formed. Methyl 3-acetamido-3,6-dideoxy-2-O-methanesulfonyl-α-L-galactopyranoside (*XII*) when reacted with sodium ethoxide in ethanol affords the same products as its *gluco* isomer *I*, *i.e.* derivatives *VIII* and *IX*. In the reaction of 4-O-methyl derivative of compound *I* with sodium methoxide in methanol a contraction of the pyranoside ring does not take place. For the rearrangement of pyranoside derivatives *I* and *XII* to furanoside derivatives *II* and *III*, or *VIII* and *IX* a mechanism is proposed supposing the formation of the acyclic intermediate (*C*) with an aldehyde group on carbon atom 4 and a double bond between carbon atoms 2 and 3 of the original pyranoside skeleton; this intermediate is probably cyclized to furanoside cation (B_1) which is a precursor of compounds *II* and *III*, or *VIII* and *IX*. The structure of the compounds with a furanoside skeleton was derived from the PMR spectra.

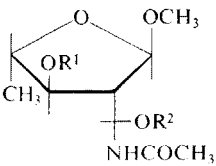
In a preceding communication[1] we described how in the reaction of methyl 3-acetamido-3,6-dideoxy-2-O-methanesulfonyl-α-L-glucopyranoside[2] (*I*) with sodium methoxide in methanol a contraction of the pyranoside ring took place and two diastereoisomeric methyl 2,5-dideoxy-2-C-(methoxyacetamidomethyl)-α-L-arabinofuranosides *II* and *III* were formed. Their acetylation with acetic anhydride in pyridine gave corresponding 3-O-acetyl derivatives *IV* or *V*, while on methylation with methyl iodide in N,N-dimethylformamide in the presence of barium oxide corresponding 3-O-methyl derivatives *VI* or *VII*, respectively, were obtained. The structures of compounds *II* and *III* were determined from their PMR spectra. The presence of a methine group which is not bound with a nitrogen or oxygen function followed from the chemical shift of the corresponding proton (Table I); the presence of an OH or NH group was proved by isotopic exchange experiments, and topological continuity of vicinal proton interactions by decoupling experiments. In the determination of the configuration of compounds *II* and *III* we supposed on the basis of stereochemical principles[3] and the analogy with described rearrangements[4-6] that the contraction of the pyranoside ring of substance *I* was caused by an antiparallel arrangement of the $C_{(3)}$—$C_{(4)}$ bond and the $C_{(2)}$-O-sulfonyloxy group in the $^1C_4$ conformation. Such an arrangement also followed from the PMR spectrum of compound *I* and it should enable an

intramolecular substitution of the methanesulfonyloxy group, accompanied by a contraction of the six-membered ring to a five-membered one without changing the relative configuration of the substituents on the carbon atoms 1, 4 and 5 in the original pyranoside skeleton. Should the rearrangement take place without a change in conformation of compound *I* in the transition state, then $C'_{(2)}$-diastereoisomers with an α-L-*ribo* configuration should be formed (Scheme 1, path *A*, A_1, A_2). In the alternative case, *i.e.* with a change in the conformation of substance *I* in the transition state, $C'_{(2)}$-diastereoisomers with the α-L-*arabino* configuration could be formed (Scheme 1, path *B*, B_1, B_2). Hence, we limited the problem of the determination of the configuration of compounds *II* and *III* to the determination of the configuration on carbon atom 2; it was determined from the magnitude of the coupling of protons H_1 and H_2. As follows from the PMR spectra of various pentofuranosides the values of $J_{1,2}$ from 0 to 3 Hz are typical of the *trans*-configuration of H_1 and H_2, while for the *cis* configuration $J_{1,2} = 4 - 5$ Hz (ref.[7-10]). In the PMR spectra of compounds *II* and *III*, as well as in the spectra of their derivatives *IV*—*VII*, we found $J_{1,2} = 1{\cdot}3 - 2{\cdot}5$ Hz, which indicated a *trans*-configuration of H_1 and H_2 and hence also α-L-*arabino* configuration of compounds *II* and *III*.

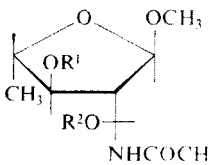
The formation of compounds *II* and *III* with the α-L-*arabino* configuration is not quite evident, because according to the Franck–Condon principle the formation of substances with the α-L-*ribo* configuration should be more probable (Scheme 1,



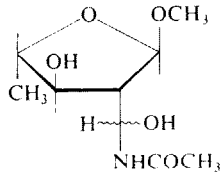
I, $R^1 = OH$, $R^2 = H$, $R^3 = CH_3SO_2-$
XII, $R^1 = H$, $R^2 = OH$, $R^3 = CH_3SO_2-$
XIII, $R^1 = CH_3O-$, $R^2 = H$, $R^3 = CH_3SO_2-$
XIV, $R^1 = CH_3O-$, $R^2 = H$, $R^3 = H$



II, $R^1 = H$, $R^2 = CH_3$
IV, $R^1 = CH_3CO-$, $R^2 = CH_3$
VI, $R^1 = CH_3$, $R^2 = CH_3$
VIII, $R^1 = H$, $R^2 = C_2H_5$
X, $R^1 = CH_3CO-$, $R^2 = C_2H_5$



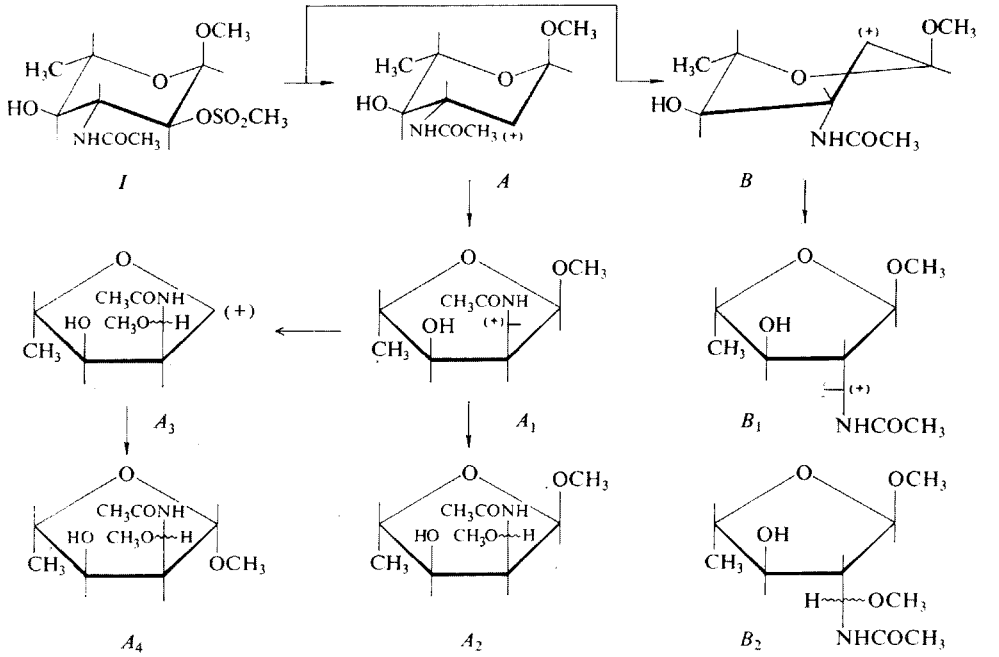
III, $R^1 = H$, $R^2 = CH_3$
V, $R^1 = CH_3CO-$, $R^2 = CH_3$
VII, $R^1 = CH_3$, $R^2 = CH_3$
IX, $R^1 = H$, $R^2 = C_2H_5$
XI, $R^1 = CH_3CO-$, $R^2 = C_2H_5$



XV

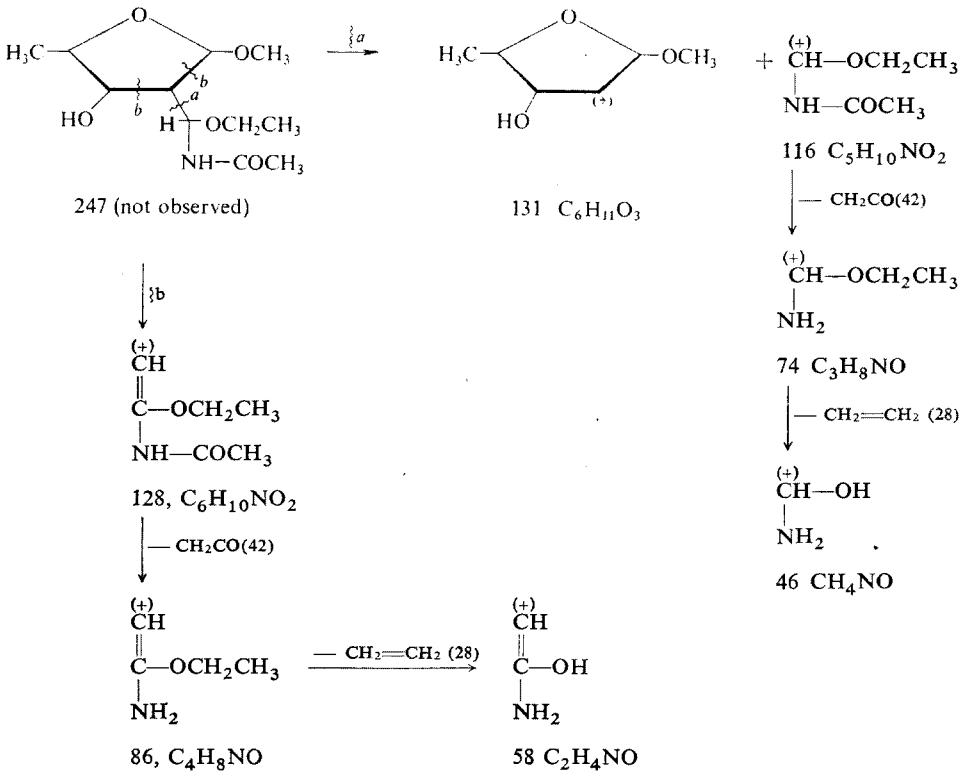
path A, A_1, A_2). Therefore, in this study, we endeavoured to elucidate other aspects of the mentioned rearrangement. One of the possibilities for the preference of the *ribo* configuration was (in spite of the low value of $J_{1,2}$ measured for substances *II* – *VII*) that these substances have β-L-*ribo* configuration. The methoxy group on anomeric carbon atom could participate in the reaction by saturating the electron deficit on the carbon atom $C'_{(2)}$ of the carbonium cation with the α-L-*ribo* configuration, while the electron deficit occurring on the anomeric centre would be liquidated by the approach of the methoxylate anion from the reaction medium (Scheme 1, path A, A_1, A_3, A_4). If this interpretation is correct, then the reaction of compound *I* with alcoholate other than sodium methoxide should afford analogues of compound *II* or *III*, resp., the aglycone of which would be identical with the alcoholate used, while the methoxyl group would be located in the side chain on the carbon atom $C'_{(2)}$.

Therefore we acted on compound *I* with sodium ethoxide in ethanol. We found that compound *I* reacted with sodium ethoxide more easily than with sodium methoxide, and that two substances were again formed, *VIII* and *IX*. After chromatographic separation on a column of alumina we obtained both substances in pure state; their acetylation with acetic anhydride in pyridine gave crystalline O-acetyl derivatives *X*,



SCHEME 1

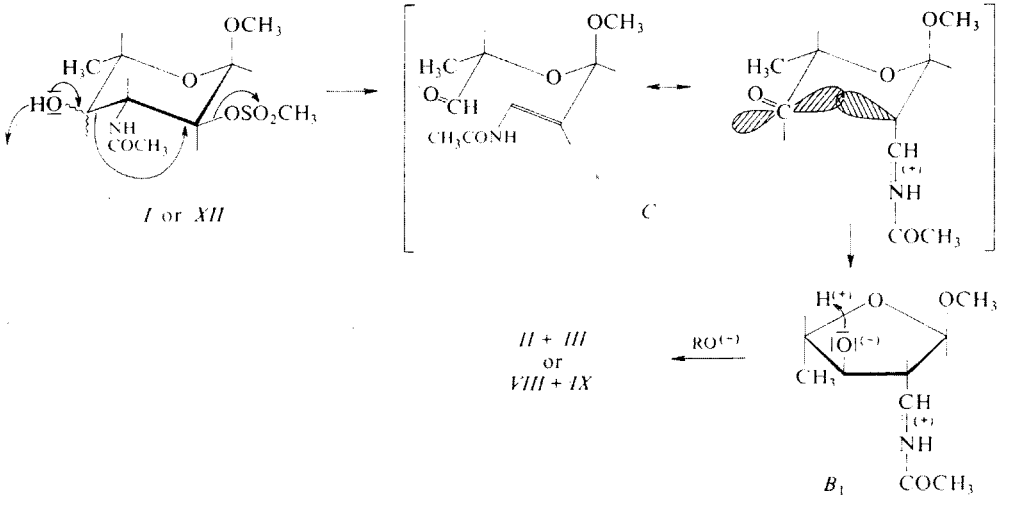
or *XI*, respectively. From the analysis of the PMR spectra of compounds *VIII* and *IX* (Table I) it follows that both substances have the same topological continuity of vicinal interactions and the same distribution of chemical shifts as substances *II* and *III*. The same is true for the correlation of acetate *X* with acetate *IV*. The mass spectra of compounds *VIII* and *IX* differed in the intensities of some ions only and were similar to the spectra of compounds *II* and *III*. In the case of the pair of compounds *VIII* and *IX* an intensive ion of *m/e* 116 and the composition $C_5H_{10}NO_2$ was found. The structure of this ion, $CH_3CO—NH=CH—OC_2H_5$, was confirmed by direct analysis of the daughter ions (Scheme 2). In contrast to this an abundant ion *m/e* 102 corresponding to $CH_3CO—NH=CH—OCH_3$ was found in the mass spectrum of compounds *II* and *III*. From this it follows that compound *VIII* or *IX*, respectively, is methyl 2,5-dideoxy-2-C-(ethoxyacetamidomethyl)-α-L-pentofuranoside. The result of acid hydrolysis of compound *VIII* confirmed this conclusion (see below). Hence, during the rearrangement of compound *I* to compounds *VIII* and *IX* it is the alkoxyl group from the reaction medium which enters into the asymmetric centre



SCHEME 2

in the side chain; this further confirms the original supposition of the invariance of the centre on the anomeric carbon atom.

Further we acted with sodium ethoxide in ethanol on methyl 3-acetamido-3,6--dideoxy-2-O-methanesulfonyl-α-L-galactopyranoside[12] (*XII*), *i.e.* on a substance differing from substance *I* only in the configuration on the carbon atom 4. According to the PMR spectrum the $^1C_4$ conformation is again typical of the molecule of compound *XII*, *i.e.* compound *XII* affords the same starting conditions for the contraction of its ring as we considered important[1] in the case of compound *I*. We found that in this reaction compounds *VIII* and *IX* are again formed in a ratio approximately equal to that formed from compound *I*. The identity of compounds *VIII* and *IX* with the products of the reaction of compound *I* with sodium ethoxide in ethanol was corroborated by comparison of physical constants, IR, mass and PMR spectra, and the conversion to corresponding O-acetyl derivatives *X* or *XI*, respectively. In contrast to this on reaction of methyl 3-acetamido-3,6-dideoxy-2-O-methanesulfonyl--4-O-methyl-α-L-glucopyranoside (*XIII*) (prepared from *I* by methylation) with sodium methoxide in methanol methyl 3-acetamido-3,6-dideoxy-4-O-methyl-α-L-glucopyranoside (*XIV*) was obtained. We proved the structure of compound *XIV* by its mesylation, which gave compound *XIII*. Hence, it is evident that an indispensable condition for the contraction of the pyranoside ring of compound *I* is the presence of a free hydroxy group in the position 4; during the rearrangement of compound *I* or *XII* to substances with a furanoside skeleton a disappearance and a reconstruction of the asymmetric centre on the carbon atom 4 of the original pyranoside skeleton probably takes place.



SCHEME 3

TABLE I
Characteristic Parameters of PMR Spectra

Compound[a]	H_1	H_2	H_3	H_4	H_5	$H_{2'}$	NH	CH_3CO	OCH_3	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{2,2'}$	$J_{2'NH}$
II[b,c,d]	4·70	2·04	3·28	3·71	1·15	4·93	8·03	1·89	3·17	2·2	5·7		6·2	8·2	9·6
									3·22	(2·2)		(7·3)	(6·2)	(8·2)	(9·5)
III[b,c,e]	4·63	2·15	3·46	3·75	1·18	5·05	8·03	1·91	3·21	2·5	6·3	7·5		6·3	9·5
									3·24	(2·5)	(6·0)	(7·4)	(6·2)	(6·5)	(9·5)
IV[f]	4·94	2·30	4·42	4·18	1·31	5·01	6·47	2·07[g]	3·36[g]	1·3	2·9	5·3	6·2	9·2	9·1
										(1·3)	(2·9)	(5·1)	(6·3)	(9·1)	(9·5)
IV[b,c]	4·86	2·26	4·56	3·91	1·20	4·91	8·21	2·02	3·20	1·2	3·8	6·1	6·1	8·9	9·6
								1·87	3·26	(1·3)	(3·8)		(6·4)	(8·9)	(10)
V[f]	4·87	2·26	4·79	4·21	1·31	5·34	7·08	2·01	3·35[g]	1·3	3·4	6·1	6·4	3·4	9·6
								2·10		(1·3)	(3·4)	(6·3)	(6·3)	(3·4)	(10)
VI[f]	4·86	2·25	3·18	4·04	1·36	5·12	5·77	2·07	3·35	2·0	4·8	6·6	6·3	8·3	9·8
									3·37[g]	(2·1)	(4·8)	(6·3)	(6·3)	(8·6)	
VII[f]	4·82	2·39	3·30	4·05	1·34	5·18	5·93	2·05	3·36	1·7	3·8	6·2	6·3	6·1	9·9
									3·38[g]	(1·7)	(4·0)	(6·3)	(6·3)	(6·1)	(10)
VIII[f,h]	4·88	2·22	3·53	3·95	1·32	5·20	6·26	2·05	3·38	2·2	5·4			8·4	9·5
										(2·5)		(6·1)	(6·1)	(8·6)	(9·5)
IX[f,i]	4·66	2·18	3·65	3·97	1·32	5·34	6·05	2·04	3·36	3·8	7·2			8·5	9·7
										(3·8)		(7)	(6·0)	(8·5)	(10)
IX[b,c,j]	4·61	2·13	3·36	3·73	1·19	5·10	8·06	1·90	3·35	2·4	6·2			6·2	9·7
										(2·4)		(7·9)	(6·0)	(6·6)	(10)
XI[f,k]	4·86	2·25	4·83	4·22	1·33	5·41	7·04	2·01	3·37	1·5	3·5	6		3·5	9·6
								2·11		(1·5)	(3·5)		(6·4)	(3·5)	(10)
XV[c,l,m]	4·79	2·26	3·43	3·79	1·21	5·23	6·84	1·91	3·31	2·7	8·5		6·3	8·5	8·2
										(2·5)		(6·3)	(6·2)	(8·2)	

The facts observed seem to agree with the mechanism which supposes the formation of an intermediate with an aldehyde group on the carbon atom 4 during the reaction of compound *I* or *XII* with alcoholates (Scheme 3, compound *C*). Cyclisation of the intermediate *C* should give the carbonium ion B_1 which after the approach of the alkoxylate anion from the reaction medium affords compounds *II* and *III*, or *VIII* and *IX*, respectively. Of course, such an explanation permits a variability in the configuration on carbon atom 3 of the furanoside ring of compounds *II*, *III*, *VIII* and *IX*. Under the supposition of the invariance of configuration on the anomeric centre and on carbon atom 5 in the original pyranoside ring (though here this supposition need not necessarily be valid) and in view of the magnitude of the coupling constant $J_{1,2}$ the substances with a furanoside skeleton should have α-L-*arabino* or α-L-*lyxo* configuration, *i.e.* either both or one of them α-L-*arabino* and the second α-L-*lyxo* configuration and *vice versa*. As it is evident from the comparison of the PMR spectra of the pairs *II* and *III* (hexadeuteriodimethyl sulfoxide), *IV* and *V* ($CDCl_3$), *VI* and *VII* ($CDCl_3$), and *VIII* and *IX* ($CDCl_3$) (Table I) a certain variability exists in the PMR parameters. This variability may be caused simultaneously or separately by the differences in conformation of the furanoside ring and by the differences in the configuration of the asymmetric centres, and in the case of the coupling constants also by the errors of the first order analysis. In our case the chemical shifts are the most characteristic for comparison, because in all spectra considered they have a quasi-first order distribution and, hence, are least hampered by errors of first-order analysis. From their comparison in the case of the above mentioned pairs it follows that the chemical shifts of protons H_4 and H_5 ($\Delta \leqq 0{\cdot}04$ p.p.m.) are practically invariant, while the protons H_1, H_2, H_3, H_2' show a more significant variability. This fact indicates that the configuration on the carbon atom 4 is in all furanosides the same, which further implies the identity of the configuration on the carbon atom 3 as well; this means that both products of the rearrangement have the same configuration, either α-L-*arabino* or α-L-*lyxo*. From the comparison of the PMR spectra of compounds *II* and *IV* (hexadeuteriodimethyl sulfoxide) and compounds *IX* and *XI* ($CDCl_3$) practically the same acetylation shifts follow ($\Delta^{(j)}\delta H_i = \delta H_i(C_j\text{-OH}) - \delta H_i(C_j\text{-OCOCH}_3)$ for protons H_4 and H_5. The values $\Delta^{(3)}\delta H_4(II) = -0{\cdot}20$ p.p.m.,

[a] Measured on a Varian HA-100 instrument; all data from first-order analysis, chemical shifts in δ-scale, internal standard tetramethylsilane if not otherwise stated; splittings indicated as J_{ij}, the first values taken from multiplets of H_i, the second ones, in parentheses, from multiplets of H_j. [b] In hexadeuteriodimethyl sulfoxide containing a small ammount of deuteriochloroform. [c] Internal standard hexamethyldisiloxane (HMDS), δ(HMDS) = 0·06 p.p.m.. [d] OH : 5·01 p.p.m. (J = 5·3 Hz). [e] OH : 5·00 p.p.m. (J = 5·5 Hz). [f] In deuteriochloroform. [g] Relative intensity 6 H. [h] C_2H_5 : : 1·19 p.p.m. (*t*, J = 7 Hz), 3·50 p.p.m. (m). [i] C_2H_5 : 1·20 p.p.m. (t, J = 7 Hz), 3·35 p.p.m. (m). [j] OC_2H_5 : 1·12 p.p.m. (t, J = 7 Hz), 3·45 p.p.m. (m); 3-OH : 4·96 p.p.m. (J = 5·4 Hz), [k] OC_2H_5 : 1·17 p.p.m. (t, J = 7 Hz), 3·58 p.p.m. (m). [l] In trideuterioacetonitrile [m] 2'-OH : : 4·14 p.p.m. (J = 4·7 Hz).

$\Delta^{(3)}\delta H_5(II) = -0{\cdot}05$ p.p.m., and the values $\Delta^{(3)}\delta H_4(IX) = -0{\cdot}25$ p.p.m. and $\Delta^{(3)}\delta H_5(IX) = -0{\cdot}01$ p.p.m. are consistent with the known vicinal β- and γ-effects in such cases of topological arrangement of substituents on the fragment $C_i(H, CH_3)$-$C_j(OR)$ (R = H, CH_3CO) when the OR group and H_i have a quasi *cis*-orientation[13-15]. From this point of view H_4 and the OH group on the carbon atom 3 in compounds *II*, *III* and *VIII* and *IX* should have *cis*-configuration and the substances themselves an α-L-*arabino* configuration. The observed variability of the chemical shifts of H_1, H_2 and H_3, as well as of their vicinal couplings is evidently a consequence of different configuration on the carbon atom 2' and the possible changes in conformation of the furanoside ring induced by it. Some suppositions concerning the configuration on the furanoside ring may be also made on the basis of the variation of the coupling constants $J_{1,2}$, $J_{2,3}$ and $J_{3,4}$, following from the comparison of the PMR spectra of compounds *II*, *III*, *VIII* and *IX*, and the derivatives corresponding to them. The PMR spectra of anomeric pairs of a series of per-O-acetyl- or per-O-benzoyl-pentofuranoses[10] have shown that the vicinal couplings of the *cis*-protons are of the order of 4–7 Hz and of the *trans*-protons about 0–7·5 Hz. These ranges correspond well to the known dependence of the vicinal coupling $^3J_{i,j}$ on the dihedral angle $\varphi(H_iH_j)$. In Fig. 1 extreme conformations of the five-membered ring (C_i, C_j, C_k, C_l, C_m) with a pseudorotation angle $\varphi(C_k, C_m) = 0 \pm 60°$ are represented for both C_i-epimers. In the case when the five-membered ring is not *ortho*-annelated with some

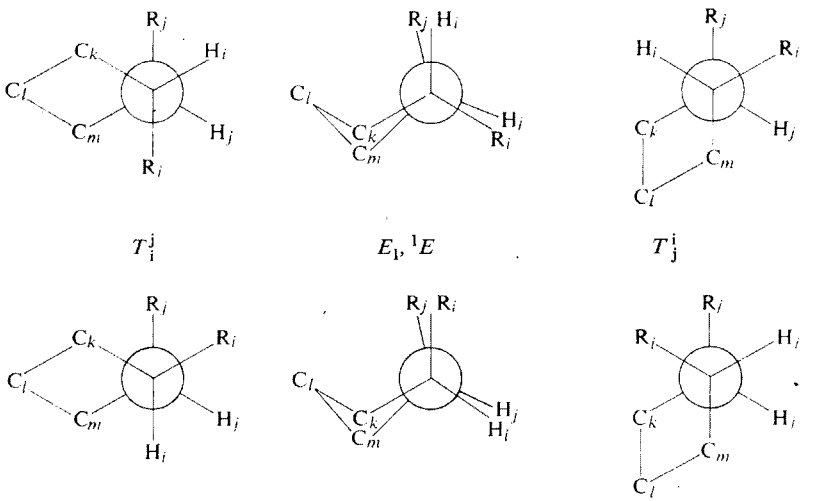


FIG. 1

Schematic Illustration of Extreme Conformations in a Five-Membered Ring $C_iC_jC_kC_lC_m$ for the Case of *cis*- and *trans*-Configuration of Vicinal H_i and H_j Protons (see discussion of interaction constants)

further rigid cyclic system this angle is normally smaller, roughly by $\varnothing(C_k, C_m) = 0 \pm 30°$. The ranges of the dihedral angles $\varnothing(H_i, H_j\text{-}trans) \approx 120 \pm 30°$ and $\varnothing(H_i, H_j\text{-}cis) \approx 0 \pm 30°$ and the ranges of ${}^3J_{i,j}(trans) \approx {}^3J(90°) \ldots {}^3J(150°)$ and ${}^3J_{i,j}(cis) \approx {}^3J(30°) \ldots {}^3J(0°)$ correspond to this. In view of the fact that ${}^3J(90°) \approx \approx 0 \pm 0{\cdot}5$ Hz and that the occurence of ${}^3J(0°)$ is less probable in consequence of the disadvantage of the eclipsed conformation on the C_i-C_j fragment, the variation range of ${}^3J(trans)$ should be substantially higher than for ${}^3J(cis)$. In the case of furanosides both ranges, ${}^3J(trans)$ and ${}^3J(cis)$ are appreciably superimposed and a direct assignment usually may be carried out only in the case of ${}^3J(trans)$, and only then when the observed values of the vicinal interaction are of the order of ${}^3J_{i,j} \ll 4$ Hz (ref.[10]), as for example in the case of the already discussed coupling constant $J_{1,2}$. In the case of other coupling constants $J_{2,3}$ and $J_{3,4}$ of the compounds listed in Table I substantially higher ranges have been observed, *i.e.* $J_{2,3} = 2{\cdot}9 - 8{\cdot}5$ Hz and $J_{3,4} = 5{\cdot}3$ to $7{\cdot}9$ Hz. Neverthesess, the extreme values again indicate rather a *trans*-configuration in both cases. For example, the decrease of the $J_{2,3}$ and $J_{3,4}$ values and simultaneously of the $J_{1,2}$ value, caused by acetylation or methylation of the OH group in the position 3, is typical. This variation cannot be interpreted unambiguously on the basis of electronegativity only, and it rather indicates the variation of conformational factors, *i.e.* of the corresponding dihedral angles. As it follows from the Dreiding

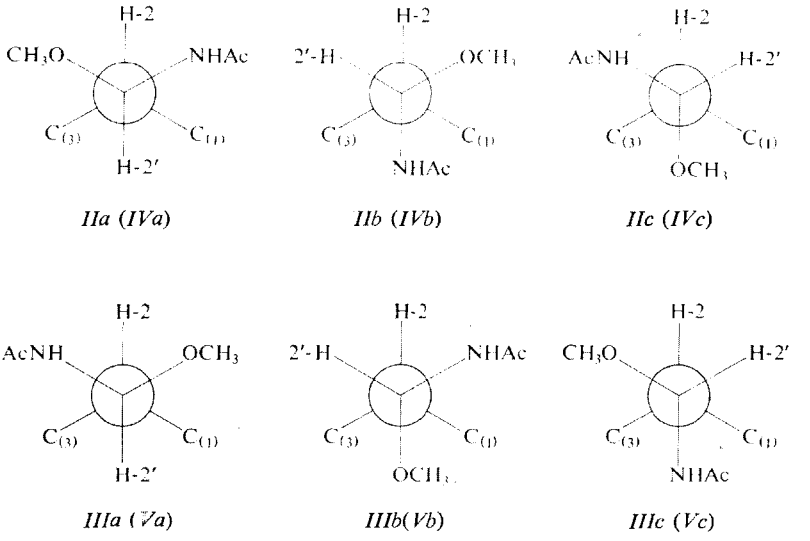


FIG. 2

Newman's Projections of Staggered Rotamers of the Fragment $C_{(2)} - C_{(2')}$ of Compounds *II* and *III* (see discussion of the configuration of center $C_{(2')}$)

models the variation of the angle $\measuredangle(C_k, C_m)$ is gradually spread over the cycle, which has (for example in the case of *all-trans* configuration of H_i, H_j) a unidirectional increase or decrease of $\measuredangle(H_i, H_j)$ as a consequence. This should be especially typical in the case of an isolated five-membered ring, for two consecutive fragments C_i-C_j, and for any conformations *E* or *T*. The observed synchronous variation of $J_{1,2}$ (*trans*) and $J_{2,3}$ into the region $^3J < 4$ Hz also indicates, in this sense, the probability of $J_{2,3}$(*trans*). Analogous variations have been observed, for example, in some 5(R)-5--C-alkyl-5-C-phenyl-D-xylofuranosides[16] with the *trans*-configuration of H_1, H_2 and H_3. In principle, this consideration is also valid for the comparison of the observed variations of $J_{3,4}$ with the variations of $J_{2,3}$ and $J_{1,2}$. However, in the case of $J_{3,4}$ the implication of a *trans*-configuration need not be valid. The optimum for the interpretation of the coupling constants is again an α-L-*arabino* configuration.

For the determination of the configuration on the asymmetric centre in the side chain we took as base[1] the comparison of the coupling constants $J_{2,2'}$ of substances *II* – *VII*. In view of the possibility of the rotational isomerization around the $C_{(2)}$-$C_{(2')}$ bond $J_{2,2'}$ may be generally interpreted[11] as the average value $\langle J_{2,2'} \rangle = \sum n_i J_i$ in terms n_i and J_i(H, H) of staggered conformers *a*, *b* and *c*, as represented in Fig. 2. In this approximation the increase or the decrease of $J_{2,2'}$, induced chemically, corresponds simply to the increase or the decrease of the preference of the H, H-*trans* conformer. In the case of compound *II* the acetylation of the 3-OH group induced a small increase of $J_{2,2'}$(*II*) = 8·2 Hz (hexadeuteriodimethyl sulfoxide) to $J_{2,2'}$ (*IV*) = 8·9 Hz (hexadeuteriodimethyl sulfoxide), or 9·1 Hz($CDCl_3$), while in the case of compound *III* it induced a significant decrease of $J_{2,2'}$ (*III*) = 6·4 Hz (hexadeuteriodimethyl sulfoxide) to $J_{2,2'}$ (*IV*) = 3·4 Hz ($CDCl_3$). An analogous variation of the splitting of $J_{2,2'}$ was observed for the methylation of the 3-OH group; in this case, however, the changes of $J_{2,2'}$ are very small and comparable roughly with the errors of measurement (±0·2 Hz). The changes observed can be interpreted under the supposition that in the case of O-acetyl derivatives *IV* and *V* the dipole-dipole interactions of the 3-O-acetyl and the 2'-acetamido group play an important role; under this supposition the conformer should be always preferred in which the mentioned interaction is minimum. This is the case for the gauche-rotamer *IIIb* or *Vb*, and in the case of the *trans*-rotamer for *IIa* or *IVa*, resp., *i.e.* in the case when compounds *II* or *IV* have configuration *S* on the asymmetric centre in the side chain, and the compounds *III* or *V* *R* configuration.* Analogously (Table I), compound *VIII* should have configuration *S* and compound *IX* configuration *R*.

The supposition of the α-L-*arabino* configuration for substances with a furanoside skeleton is in good agreement with the proposed mechanism (Scheme 3). The intermediate *C* with the aldehyde group on the carbon atom 4 should assume such a con-

* In paper[1] the formulas are interchanged by error; the configuration on the carbon atom 2' in the formulae (2), (4) and (6) should be *R*, and in the formulae (3), (5) and (7) it should be *S*.

formation in which the C=O group would be *syn*-periplanar with the $C_{(5)}$-H bond, *i.e.* a conformation with minimum steric and dipole-dipole interactions[17]. For a recyclization to the furanoside cation B_1 this intermediate should react in its quasi-chair conformation, preserving as far as possible the orbital symmetry. From the scheme it is evident that such a transition state leads to furanoside derivatives with α-L-*arabino* configuration.

In connection with the structure elucidation of compounds *II*, *III*, *VIII* and *IX* we carried out a few hydrolytic experiments aiming at the transformation of the side chain. Under the effect of dilute acetic acid at room temperature we obtained from compound *IX* compound *XV* in an approximately 20% yield; the latter compound showed in its IR spectrum the presence of an acetamido group. In its PMR spectrum the same topological continuity of the coupling constants and an analogous distribution of vicinal chemical shifts has been demonstrated as in compounds *VIII* and *IX*. On the carbon atom 2' the presence of an OH group has been demonstrated, forming a doublet at 4·14 p.p.m. with $J' = 4{\cdot}7$; the proton on carbon 2' forms a triplet of doublets at 5·23 p.p.m. with $J_{2',OH} = 4{\cdot}4$ Hz and $J_{2,2'} = J_{2',NH} = 4{\cdot}7$ Hz. Hence, we assigned substance *XV* the structure of methyl 2,5-dideoxy-2-C-(hydroxyacetamido methyl)-α-L-arabinofuranoside. The attempts at its hydrolysis to a furanoside derivative with a free aldehyde group on carbon atom 2' led to a mixture of substances.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured on an apparatus of the firm Opton at 20°C and 0·5—1·0 g per 100 ml concentration. The infrared spectra were taken with a Perkin Elmer 325 apparatus. The mass spectra were measured with an LBK 9000 and a Varian NAT 311 instrument. Samples for analysis were dried at 20°C and 0·1 Torr. The solvents were evaporated on a rotatory evaporator under reduced pressure (water pump) at a temperature not exceeding 50°C. The light petroleum used for crystallization had m.p. 45—60°C. Preparative chromatographies were carried out on alumina (Reanal), deactivated with 3% of water and on silica gel (Lachema, Brno), 70—200 μ. The "conventional working up" means extraction of the chloroform solution containing the reaction product with cold 5% sulfuric acid, water, 1% sodium hydrogen carbonate and water, drying over magnesium sulphate and evaporation.

Methyl 2,5-Dideoxy-2-C-[(*S*)-methoxyacetamidomethyl]-α-L-arabinofuranoside (*II*) and its (*R*)-diastereoisomer (*III*)

A solution of compound *I* (1·0 g; 3·37 mmol) in 42 ml of a 0·21M sodium methoxide solution in methanol was refluxed for 8 hours. The reaction mixture was cooled, neutralized with 1M hydrochloric acid and evaporated. The residue was extracted with acetone, the extract evaporated and the residual syrup chromatographed on a column of alumina (50 g). Elution was carried out with chloroform and single chromatographic fractions were evaporated and analysed on loose thin layers of alumina (dimensions 9 × 23 cm, system chloroform–ethanol 100 : 5, detection with iodine vapours). Substance *III* (46 mg) was eluted first from the column; containing a sub-

stance as impurity having a slightly higher R_F value. Then, gradually, compound *III* (230 mg; 29.4%; chromatographically pure) was eluted followed by compound *II* (270 mg; 34·4%); elution of the column with a mixture of chlorofrom–ethanol 100 : 1 gave 75 mg (7·5%) of compound *I*. Compound *II* was crystallized from acetone–light petroleum, m.p. 141—143°C, $[\alpha]_D$ −56 ± 2° (chloroform). For $C_{10}H_{19}NO_5$ (233·2) calculated: 51·49% C, 8·21% H, 6·00% N, 26·61% CH_3O; found: 51·48% C, 8·20% H, 5·99% N, 26·55% CH_3O. Compound *III* was crystallized from a mixture of ether and light petroleum, m.p. 114—116°C, $[\alpha]_D$ −63·5 ± 1° (chloroform). For $C_{10}H_{19}NO_5$ (233·2) calculated: 51·49% C, 8·21% H, 6·00% N, 26·61% CH_3O; found: 51·43% C, 8·46% H, 5·93% N, 26·69% CH_3O. Compounds *II* and *III* are labile even in a weakly acid medium; for example they decompose in commercial chloroform or on a silica gel column.

Methyl 3-O-Acetyl-2,5-dideoxy-2-C[(*S*)-methoxyacetamidomethyl]-α-L-arabinofuranoside (*IV*)

Acetic anhydride (0·3 ml) was added to a solution of 91 mg of compound *II* in 3 ml of pyridine and the mixture was allowed to stand at room temperature for 48 hours. It was decomposed with water, diluted with chloroform and worked up in the conventional manner. Yield 97 mg of compound *IV* which was crystallized for analysis from an ethyl acetate–light petroleum mixture, m.p. 109—111°C. For $C_{12}H_{21}NO_6$ (275·3) calculated: 52·35% C, 7·69% H, 5·09% N; found: 52·05% C, 7·43% H, 5·11% N.

Methyl 3-O-Acetyl-2,5-dideoxy-2-C-[(*R*)-methoxyacetamidomethyl]-α-L-arabinofuranoside (*V*)

Using the same procedure as above (for compound *IV*) 103 mg (93%) of compound *V* crystallized from light petroleum were obtained from 94 mg of compound *III*. The m.p. of the product was 76·5—78·5°C. For $C_{12}H_{21}NO_6$ (275·3) calculated: 52·35% C, 7·69% H, 5·09% N; found: 51·94% C, 7·93% H, 4·83% N.

Methyl 2,5-Dideoxy-2-C-[(*S*)-methoxyacetamidomethyl]-3-O-methyl-α-L-arabinofuranoside (*VI*)

Barium oxide (1·2 g) and methyl iodide (1·2 ml) were added to a solution of 124 mg of compound *II* in 3·5 ml of N,N-dimethylformamide and the mixture was stirred at room temperature for 3·5 hours, then 1·5 hours at 45°C. After cooling it was filtered, the solid material on the filter was washed with acetone and the combined filtrates were evaporated. The residue was dissolved in chloroform and the chloroform solution washed with 1% sodium sulfite and water, dried over magnesium sulfate and evaporated. The residue was purified on a column of 15 g of alumina using benzene–ethanol 100 : 1 as eluent. Yield 121 mg (92%) of compound *VI* which was crystallized from light petroleum for analysis, m.p. 104—105°C. For $C_{11}H_{21}NO_5$ (247·3) calculated: 53·42% C, 8·56% H, 5·66% N, 37·65% CH_3O; found: 53·20% C, 8·77 H, 5·65% N, 37·90% CH_3O.

Methyl 2,5-Dedeoxy-2-C-[(*R*)-methoxyacetamidomethyl]-3-O-methyl-α-L-arabinofuranoside (*VII*)

Using the same procedure as for the preparation of compound *VI* 117 mg (77%) of compound *VII* were obtained from 145 mg of compound *III*. The product was crystallized from ether–light petroleum, m.p. 115—117°C. For $C_{11}H_{21}NO_5$ (247·3) calculated: 53·42% C, 8·56% H, 5·66% N, 37·65% CH_3O; found: 53·20% C, 8·77% H, 5·65% N, 37·90% CH_3O.

Methyl 2,5-Dideoxy-2-C-[(*S*)-ethoxyacetamidomethyl]-α-L-arabinofuranoside (*VIII*) and its (*R*)-Diastereoisomer (*IX*)

a) A solution of 1·00 g (3·37 mmol) of compound *I* in 42 ml of 0·21M sodium ethoxide solution in ethanol was refluxed for 2 hours. The mixture was cooled, neutralized with gaseous carbon dioxide and filtered. The filtrate was evaporated and the residual syrup extracted with acetone. The acetone extract was filtered and evaporated. The syrupy residue (750 mg) was chromatographed on a column of alumina (130 g) with chloroform. Thirty mg of a compound melting at 107—150°C were eluted first, the R_F value of which on a thin layer of alumina was slightly higher than the R_F value of compound *IX* (system chloroform–ethanol 10 : 1, detection with iodine vapours); after double crystallization from a mixture of ethyl acetate–light petroleum its m.p. was 120—145°C and the substance was not further analysed. In subsequent chromatographic fractions 72 mg of compound *IX* were obtained, which contained the above substance as impurity, then 206 mg (24·8%) of chromatographically pure compound *IX* and 270 mg (32·4%) of compound *VIII*. Compound *VIII* was crystallized from a mixture of ethyl acetate–light petroleum, m.p. 112—113°C (the substance melts and resolidifies within the 104—106°C temperature range); $[\alpha]_D$ −42 ± 2° (chloroform). For $C_{13}H_{21}NO_5$ (247·3) calculated: 53·43% C, 8·56% H, 5·67% N; found: 53·38% C, 8·69% H, 6·05% N. Compound *IX* was crystallized from a mixture of ether and light petroleum, m.p. 92—94°C, $[\alpha]_D$ −62 ± 1° (chloroform). For $C_{11}H_{21}NO_5$ (247·3) calculated: 53·43% C, 8·56% H, 5·67% N; found: 53·70% C, 8·59% H, 5·59% N.

b) A solution of 750 mg (2·52 mmol) of compound *XII* (ref.[12]) in 31 ml of a 0·21M sodium ethoxide solution was refluxed for 2 hours and then worked up as above. After chromatographic separation on a column of alumina (100 g) the following fractions were eluted: 45 mg of a compound of m.p. 90—155°C (after six-fold crystallization from ethyl acetate–light petroleum the m.p. was 127—150°C), 68 mg of compound *IX* containing a substance of the same R_F value as the substance of m.p. 127—150°C as impurity, then 170 mg (27%) of chromatographically pure compound *IX*, and 205 mg (33%) of compound *VIII*. Both substances were crystallized in the same manner as described above, and they were identical in all respects with the products of the reaction of *I* with sodium ethoxide.

Methyl 3-O-Acetyl-2,5-dideoxy-2-C-[(*S*)-ethoxyacetamidomethyl]-α-L-arabinofuranoside (*X*)

0·2 ml of acetic anhydride were added to a solution of compound *VIII* (60 mg) in 3 ml of pyridine and the mixture was allowed to stand at room temperature overnight. After decomposition with water it was diluted with chloroform and worked up in the conventional manner. Yield 60 mg of compound *X*, m.p. 106—108°C, which did not change after crystallization from ether–light petreoleum, $[\alpha]_D$ −63° (chloroform). For $C_{13}H_{23}NO_6$ (289·3) calculated: 53·97% C, 8·01% H, 4·84% N; found: 53·95% C, 8·05% H, 5·05% N.

Methyl 3-O-Acetyl-2,5-dideoxy-2-C-[(*R*)-ethoxyacetamidomethyl]-α-*L*-arabinofuranoside (*XI*)

Using the same procedure as for the preparation of compound *X* 82 mg of compound *XI* were synthetized from 76 mg of compound *IX*; m.p. 126—129°C. After crystallization from ether–light petroleum the m.p. rose to 128—130°C, $[\alpha]_D$ −61° (chloroform). For $C_{13}H_{23}NO_6$ (289·3) calculated: 53·97% C, 8·01% H, 4·84% N; found: 54·27% C, 8·28% H, 4·56% N.

Methyl 3-Acetamido-3,6-dideoxy-2-O-methanesulfonyl-4-O-methyl-α-L-glucopyranoside (*XIII*)

a) A mixture of 1·00 g (3·37 mmol) of compound *I*, 15 ml of N,N-dimethylformamide, 5 g of barium oxide, and 5 ml of methyl iodide was heated under stirring in a flask at 40°C for 4 hours.

The flask was wrapped in an aluminum foil. An additional 2 ml of methyl iodide were then added. After 28 hours methyl iodide was evaporated and the mixture filtered, the residue on the filter was washed with chloroform. The combined filtrates were diluted with 50 ml of chloroform and washed with water, 1% sodium sulfite and water; the aqueous washings were re-extracted with chloroform. The combined chloroform extracts were dried over magnesium sulfate and evaporated. The residue was crystallized from a mixture of etyl acetate and light petroleum, yielding 882 mg (84%) of compound *XIII*, m.p. 182–183°C. For analysis compound *XIII* was recrystallized from the same mixture of solvents, m.p. 184–185°C, $[\alpha]_D$ −104·5° (chloroform). For $C_{11}H_{21}NO_7S$ (311·4) calculated: 42·42% C, 6·80% H, 4·50% N, 10·30% S; found: 42·43% C, 6·88% H, 4·77% N, 10·49% S.

b) Methanesulfonyl chloride (0·1 ml) was added to a solution of 70 mg of compound *XIV* in 2 ml of pyridine at −70°C. The mixture was allowed to stand at −15°C for 16 hours and then decomposed with water; after addition of 2 ml of a 5% sodium hydrogen carbonate solution the mixture was evaporated, lastly with toluene. The residue was chromatographed on a column of 10 g of silica gel (Lachema, 70–200 μ) using a mixture of chloroform and ethanol 100 : 2 as eluent. Substance *XIII* (88 mg; 94%) was eluted, m.p. 180–182°C, which after crystallization from ethyl acetate–light petroleum had the same constants as the substances obtained under *a*); their IR spectra in chloroform were also identical.

Reaction of Methyl 3-Acetamido-3,6-dideoxy-2-O-methanesulfonyl-4-O-methyl-α-L-glucopyranoside (*XIII*) with Sodium Methoxide

A solution of 440 mg (1·41 mmol) of compound *XIII* in 18 ml of 0·2M sodium methoxide in methanol was refluxed and the reaction course followed by thin-layer chromatography on silica gel G (using the system chloroform–ethanol 10 : 1 and the detection by spraying with a 5% solution of cerium(IV) sulfate in 10% sulfuric acid and heating). After 88 hours refluxing when the starting compound was no longer present in the mixture it was cooled, neutralized by introducing gaseous carbon dioxide and evaporated. The residue was chromatographed on a column of silica gel (25 g) using chloroform–ethanol 100 : 1 up to 100 : 3 for elution. In earlier fractions first 7 mg and then 40 mg of chromatographically pure, syrupy fractions were eluted (the substances decomposed on standing), and later 226 mg (68·5%) of compound *XIV* were obtained from the eluted fractions. After crystallization from ethyl acetate the compound melted at 247–250°C (sublimation), $[\alpha]_D$ −174° (ethanol). For $C_{10}H_{19}NO_5$ (233·3) calculated: 51·49% C, 8·20% H, 6·00% N; found: 51·38% C, 8·36% H, 5·95% N.

Hydrolysis of Compound *VIII*

A solution of 127 mg of compound *VIII* in 6 ml of 50% acetic acid was allowed to stand at room temperature for 18 hours. According to thin-layer chromatography on silica gel G (chloroform–ethanol 5 : 1) the reaction mixture contained a small amount of the unreacted compound *VIII* and also a substance of R_F approximately 0·35. The mixture was evaporated and the residue chromatographed on 10 g of silica gel. Benzene–ethanol 100 : 3 eluted 15 mg of compound *VIII*, benzene–ethanol 100 : 5 eluted 29 mg of a syrupy compound of R_F approx. 0·35, and 40 mg of compound *XV* having the same R_F value. Its crystallization from ethyl acetate–light petroleum gave 29 mg of compound *XV*, m.p. 120–121°C, IR spectrum (KBr): 1675, 1660, 1540 cm^{-1} (amide), 3100 – 3500 cm^{-1} (OH). For $C_9H_{17}NO_5$ (219·2) calculated: 6·62% N; found: 6·39% N.

The analyses were carried out in the department of organic analysis (head Dr L. Helešic) of the Central Laboratories, Institute of Chemical Technology, Prague, the mass spectra were

maesured in the department of mass spectroscopy (head Dr V. Kubelka) of the above Central Laboratories and also by Dr Z. Sedmera, Microbiological Institute, Czechoslovak Academy of Sciences, Prague. The IR spectra were measured in the department of spectral analysis of the above mentioned Central Laboratories. We thank the members of the departments mentioned for their help. Further we thank Dr J. Čapková and Miss E. Kvapilová for the performance of some experiments and Professor O. Červinka for stimulating discussions.

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