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STRUCTURE AND SOME REACTIONS OF CORIOSE

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Abstract—Coriose was obtained in a higher yield from the root of *Coriaria japonica*. The structure, D-*altro*-3-heptulose (I) was determined by the sodium borohydride reduction which yielded volemitol (II) and D-*glycero*-D-*altro*-hepitol (IV). Other reactions in agreement with this structure (I) were also carried out: The oxidative degradation of coriose in cold alkali produced a pentanolactone syrup which was reduced to ribose, while the degradation at elevated temperature gave a hexanolactone syrup which yielded ribose on treatment with ferric acetate–hydrogen peroxide. The rearrangement of coriose in alkali at room temperature to 2-heptuloses was investigated. Lead tetraacetate oxidation of coriose produced D-glyceraldehyde and D-glyceric acid

THE isolation of coriose from the fruit, leaf and stem of *Coriaria japonica* A. Gray together with other carbohydrates, including sedoheptulose, methyl α-D-galactoside and volemitol, has been reported.[1] Coriose has now been isolated in higher yield from a concentrated extract of the root of this plant. This sugar, m.p. 169–171°, $[\alpha]_D^{13}$ +21·7° (equilibrium, water), analyzed as $(CH_2O)_n$, and strongly reduces Fehling solution and Tollens' reagent. The result of an attempted hypoiodite oxidation shows that this sugar is a ketose. The reaction with phenylhydrazine in aqueous acetic acid carried out in an analogous way to the formation of glucosazone resulted in formation of a tarry product. These properties are identical with those of the sugar which was isolated from the stem of the same plant by Kariyone *et al.* who named it coriose and regarded it as a hexulose.[2] The structure of coriose has now been shown to be D-*altro*-3-heptulose (I) based on the results of following reactions.

Coriose differs from the common monosaccharides in colour reactions either in the test tube or on filter paper, although the R_f values with several developing solvent mixtures on paper-partition chromatography (PPC) are in the range of a monosaccharide. It was recovered from treatment with hot dilute hydrochloric acid. A crystalline benzoate was produced, m.p. 100–102°, the analysis of which and the ratio of the aliphatic and aromatic protons in the NMR spectrum is in agreement with a heptose-pentabenzoate, $C_{42}H_{34}O_{12}$.

Upon the reduction with sodium borohydride, coriose yielded a mixture of polyalcohols from which a constituent, m.p. 153–154°, was first crystallized and identified as volemitol (II)[3]. During oxidative degradation of coriose in 1N KOH at 0–2°, slow consumption of oxygen was observed. After removing the alkali with cation-exchange resin, the solution was extracted with ether. The ether extract showed a spot corresponding to glycolic acid on PPC and TLC. The mother liquor, after concentration and heating, showed on PPC a spot which could be regarded as that of a pentanolactone. This lactone was reduced with sodium amalgam

to a product which was identified as ribose on PPC using three kinds of developing solvent mixtures, and also by GLC of trimethylsilyl ether. This result indicates that the oxidative cleavage of coriose occurs between C-2 and C-3. Since analogous oxidation of sedoheptulose (III),[4] perseulose[5] and D-*glycero*-D-*manno*-octulose[6] has been known to cause the cleavage between C-1 and C-2, the result of the oxidative cleavage of coriose in addition to the production of volemitol on the sodium borohydride reduction indicates that coriose is a 3-heptulose as shown by the structure I. The mother liquor of volemitol, obtained on the sodium borohydride reduction, then should contain D-*glycero*-D-*altro*-heptitol (IV). This has been proved by the isolation of IV from the mother liquor and identification with synthetic D-*glycero*-D-*altro*-heptitol.[7] These results establish the structure of coriose as D-*altro*-3-heptulose (I).

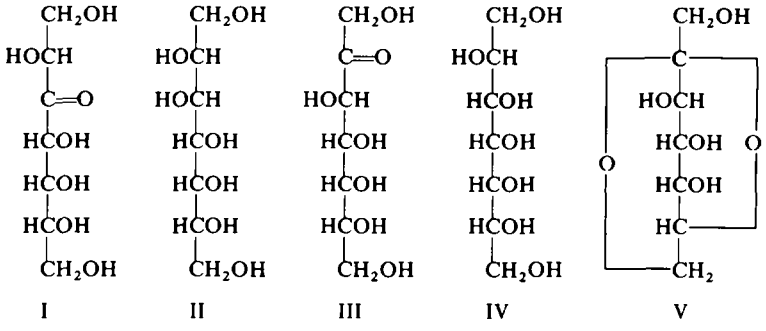
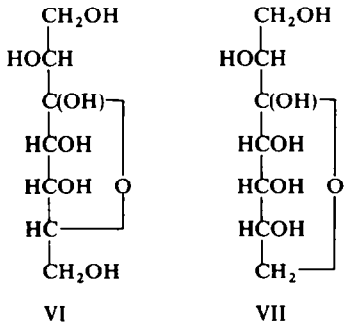


CHART 1

Further reactions of coriose are all in agreement with this structure. The oxidative cleavage of coriose in alkali at 30–31°, in which one mole equivalent of oxygen was consumed quickly, yielded a syrupy product whose R_f value on PPC corresponds to that of hexanolactone. This lactone yielded upon oxidation with ferric acetate–hydrogen peroxide,[8] ribose which was identified with an authentic specimen on PPC and GLC. Such different results depending on temperature are considered to be due to Lobry de Bruyn-Alberda van Ekenstein transformation[9] which occurs at higher temperature, and this was proved by the following experiment.

A solution of coriose in limewater was kept at room temperature for two weeks and during this time the rearrangement was examined by PPC and shown to be slow. Coriose gives a dark brown colour with orcinol–trichloroacetic acid and 2-heptuloses show blue spots.[10] The solution was treated with cation-exchange resin and the concentrated solution was then treated with acid to produce sedoheptulosan (V).[11] Faster rearrangement of coriose was observed in 1N KOH at 30–31°. On the other hand, the treatment of coriose in 1N KOH at 0° for 24 hr resulted in recovery of coriose although the mother liquor of the recovered coriose exhibited the spot corresponding to sedoheptulose on PPC to show that the rearrangement had taken place to a small extent. These results suggest that the oxidative degradation of the equilibrium mixture of coriose and 2-heptuloses, which was formed by the rearrangement of the former, preferentially occurred for 2-heptuloses. Analogous rearrangement of coriose was also observed in hot pyridine.



VI VII

CHART 2

Upon the oxidation with two moles of lead tetraacetate followed by hydrolysis, coriose yielded D-glyceraldehyde and D-glyceric acid to show that the selective cleavage[12] occurred at first between C-3 and C-4. This oxidative cleavage should take place in furanose VI or pyranose VII, preferably in VI in accordance with the proposal by Perlin and Brice for the oxidation of ordinary monosaccharides.[12]

The presence of this unique monosaccharide in the plant as a natural product was already confirmed by PPC and GLC of the juices pressed from the fruit and stem,[1] and isolation from the rhizome where a higher accumulation of this sugar occurs. The rearrangement of sedoheptulose to D-*altro*-3-heptulose and the identification of the latter with one of the minor products from the extract of *Primula officinalis* JACQ. has been reported by Begbie and Richtmyer without details of the properties.[13] This sugar from *Primula* could be presumed to occur in the plant rather than to be an artefact formed by rearrangement of other heptoses during the isolation. Although no other 3-ketose has hitherto been detected in nature, wider distribution of coriose in plants may be expected.

EXPERIMENTAL

Unless otherwise specified, identification of crystalline products was made by mixed m.p. and comparison of IR spectra, and IR spectra were measured in KBr disks. NMR spectra were recorded with TMS as internal standard in $CDCl_3$ using a Varian A-60 spectrometer. Specific rotations were recorded with a Rex Photoelectric Polarimeter. GLC was run on Shimazu GC-1C with hydrogen flame ionization detector, employing a stainless steel column, 225 cm × 3 mm, packed with 1·5% SE-30 on Chromosorb W; column temp 190°; carrier gas: N_2 56 ml/min; detector temp 210°. PPC was run on Toyo Roshi No. 50 filter paper by the ascending method using solvent A, n-BuOH–pyridine–water (6:4:3), solvent B, n-BuOH–EtOH–water (40:11:19), solvent C, EtOAc–AcOH–HCOOH–water (18:3:1:4), solvent D, EtOAc–pyridine–water–AcOH (5:5:3:1), solvent E, 1-pentanol-5M aq HCOOH (1:1)[14] and solvent F, phenol saturated with water, etc. Detection was made by orcinol–trichloroacetic acid–n–BuOH saturated with water (1:30:200) for heptuloses, Tollens' reagent or $AgNO_3$ in conjunction with NaOH in EtOH[15] for reducing sugars, alkaline hydroxylamine (made by mixing equal volumes of 1N methanolic $NH_2OH \cdot HCl$ and 1·1N methanolic KOH)–$FeCl_3$[16] for lactones and esters, and sodium metaperiodate–benzidine (first sprayed with saturated $NaIO_4$ aq, and then with a mixture, 0·1M-benzidine in EtOH and 0·8–HCl (1:1))[17] for polyhydroxy substances in general, etc. Concentrations of aqueous solutions were carried out *in vacuo* at temps not exceeding 45°. Ion-exchange resins used were Amberlite IR-120, IR-45 and IRA-410 (Rohm and Haas Co.). Silicic acid acc. to Stahl (E. Merck) was coated on the TLC plates (0·25 mm).

Isolation of coriose from the root of Coriaria japonica

The root of *Coriaria japonica* A. GRAY, cut into small pieces and dried (11·5 kg), were extracted with

boiling MeOH and the extract concentrated to 4 l. After standing, the crystalline ppt accompanied by viscous material was filtered off and refluxed with MeOH (400 ml). The insoluble crude crystals (73 g) were recrystallized from EtOH–water to yield coriose, m.p. 169–171°.

Pentabenzoylcoriose

BzCl (1 ml) was slowly added to an ice-chilled soln of coriose (260 mg) in pyridine (9 ml). After standing at room temp for 30 min, the mixture was poured into ice-water (50 ml). After extracting with $CHCl_3$, the $CHCl_3$ soln was washed with dil HCl, $NaHCO_3$aq, and with water, and then dried over $MgSO_4$ and K_2CO_3. The solvent was evaporated to give a pale yellow oily residue which crystallized on addition of MeOH. The crystalline mass was washed with MeOH and filtered off (423 mg). A further crop of crystals was obtained from the mother liquor (105 mg). Recrystallization from MeOH afforded colourless fine needles, m p 100–102°; ν (Nujol) 3420, 1708, 1600, 1583 cm^{-1}; NMR ($CDCl_3$) 4·0–5·5 (aliph-H_8), 1·8–3·0 (arom-H_{25}), 5·87 τ (s, OH_1). (Found: C, 69·32; H, 4·90. $C_{42}H_{34}O_{12}$ requires: C, 69·04; H, 4·66%).

Attempted reaction of coriose with dil-HCl

(a) A soln of I (100 mg) in 0·5N HCl (1 ml) was heated on a boiling water-bath for 1 hr. A small amount of brown ppt was filtered off, and the pale brown filtrate was passed through a column of IR-45 (2 ml) and concentrated. The syrupy residue was dissolved in boiling MeOH, and the soln was evaporated to give a residue which on standing deposited a crystalline colourless mass, m.p. 160–163°, which was identified with I.

(b) The recovered I from the treatment (a) was dissolved in 2N HCl (1 ml), and heated on a boiling water-bath for 1 hr. A dark brown ppt was filtered off and the filtrate was passed through an IR-45 column, and concentrated. The residue was dissolved in hot MeOH, and a small amount of brown insoluble material was filtered off. The filtrate showed on PPC (solvent D), I as the main reducing spot (R_f 0·59), and a faster small spot (R_f 0·83), but no other reducing spot. Distillation of the solvent gave crystals, m.p. 157–162°, which were identified with I.

Reduction of coriose with $NaBH_4$

A soln of $NaBH_4$ (0·13 g) in water (10 ml) was added to a stirred soln of I (1·0 g) in water (20 ml) over a period of 10 min at 0–2°, and the mixture was kept at this temp for 2 days. The colour reaction on the filter paper with orcinol–trichloroacetic acid during the reaction showed that the rearrangement to 2-heptulose was negligible. After making slightly acidic with dil AcOH, the reaction mixture was passed through columns of IR-120 and IRA-410. The syrup obtained from the effluent on solvent distillation was dissolved in hot EtOH and the soln was concentrated to 10 ml. A crystalline mass was deposited, filtered off and recrystallized twice from EtOH, and then from MeOH–EtOH to afford colourless crystals, m.p. 153–154°, $[\alpha]_D^{12}$ +2° (c = 1·02, water). A single spot was shown on PPC (solvent D, $NaIO_4$–benzidine) at R_f 0·43. (Found: C, 39·82; H, 7·87. Calc. for $C_7H_{16}O_7$: C, 39·62; H, 7·60%). This product was identified as volemitol. The mother liquor of the crude volemitol was concentrated to a syrupy residue to which EtOH was added to afford a crystalline ppt which was removed. The mother liquor gave a small amount of coriose which was filtered off and the mother liquor was concentrated to yield crystals, m.p. 125–128°, which were identified as D-*glycero*-D-*altro*-heptitol. (Found: C, 39·46; H, 7·49. Calc. for $C_7H_{16}O_7$: C, 39·62; H, 7·60%).

Oxidative degradation of coriose in alkali

(a) *At* 0–2°. To an ice-chilled soln of I (100 mg) in water (0·8 ml) was added a cold soln of 2N KOH (0·8 ml), and the mixture was shaken in an O_2 atm at 0–2° for 2 days. The soln was then passed through a column of IR-120, concentrated and extracted with ether. The ether soln was distilled to give a residue which showed on PPC (solvent E, methyl red in borate buffer) a spot at R_f 0·48 which was identified as glycolic acid. The identity was further shown by TLC (n-butyl formate–90% formic acid–water, 7:2:1).[18] The mother liquor of the ether extraction was concentrated to a syrup and heated at 80° *in vacuo*. The resultant syrup which showed on PPC (solvent B, alkaline hydroxylamine–$FeCl_3$) a spot at R_f 0·40 was reduced with NaHg in the presence of sodium hydrogen oxalate[19] to yield a syrupy product which was identified as ribose by PPC with three kinds of solvent mixtures, A, B and C, and also by GLC of trimethylsilyl ether.[20]

(b) *At* 30–31°. To a soln of I (300 mg) in water (2·25 ml) was added 2N KOH (2·25 ml) and the mixture was shaken in an O_2 atm at room temp (30–31°). One mole equiv of O_2 was consumed in 2 hr, and then

the absorption stopped. After shaking for an additional 3 hr, the soln was passed through a column of IR-120, and the effluent was distilled. The residual syrup was heated at 80° for 2 hr, the resultant lactone syrup was dissolved in water (7 ml), and the soln was heated with $CaCO_3$ (450 mg) on a boiling water-bath for 2 hr, and then filtered. To the syrupy residue after evaporation of the filtrate was added MeOH (10 ml), and ppt was filtered off (249 mg). To this Ca-salt was added a soln of $Ba(OAc)_2$ (19 mg) and $Fe_2(SO_4)_3$ (13 mg) in water (2 ml), and the mixture was heated to boiling with stirring for 10 min. After filtration through Celite, the filtrate was cooled to 40°, and then 30% H_2O_2 (0·12 ml) was added. The same amount of H_2O_2 was added 15 min later. The mixture was filtered and passed through columns of IR-120 and IR-45, and concentrated to a syrup. PPC with solvents A, B and C (*o*-aminobiphenyl hydrogenoxalate[21]) showed almost a single spot which was identified as ribose. A further identification was done by GLC of trimethylsilyl ether.

Rearrangement of coriose in alkali

(a) *In limewater.* A soln of coriose (192 mg) in water (15 ml) was mixed with limewater (5 ml), and the mixture was stored for 2 weeks at room temp. The soln was passed through IR-120, and then concentrated to a syrup which showed on PPC sedoheptulose as the main spot besides the spot of coriose. This syrup was heated with 2·7% H_2SO_4, and treated with IRA-410. The neutral effluent was evaporated and the residue was dissolved in boiling MeOH. On evaporation and seeding, a crystalline product was obtained and identified as sedoheptulosan.

(b) *In* 1N KOH *at* 30–31°. A soln of I (6 mg) in 1N KOH (0·1 ml) was kept at 30–31°. Half of the soln was passed through a column of IR-120 1·5 hr later, and concentrated to a syrup which showed on PPC (solvent F, orcinol–trichloroacetic acid) sedoheptulose as the main spot, another fast moving blue spot, and a faint spot of I. The other half of the soln was left standing for an additional 2 hr at 30–31°. The resultant soln showed spots of the two products and an almost negligible spot of I. GLC of trimethylsilyl ether, however, showed peaks corresponding to coriose and sedoheptulose.

(c) *In* 1N KOH *at* 0–2°. Coriose (6 mg) was dissolved in 1N KOH (0·1 ml) at 0°, and the soln was kept at 0–2° for 24 hr. After passing through a column of IR-120, the effluent was distilled. On addition of MeOH the residue was crystallized to give I. The mother liquor of I showed on PPC (solvent F) spots of I and II with orcinol–trichloroacetic acid, but showed almost a single spot of I as a reducing substance. GLC of trimethylsilyl ether also showed recovery of I.

(d) *In pyridine.* A soln of I (5 mg) in warm pyridine was refluxed for 4·5 hr, and distilled. The brown residue showed on PPC (solvent A and F, orcinol–trichloroacetic acid) sedoheptulose as the main spot.

Lead tetraacetate oxidation of coriose

Coriose (500 mg) was dissolved in water (3 ml) and the soln was diluted with AcOH (150 ml). $Pb(OAc)_4$ (corresponding to 2·11 g dry wt) was added to the stirred soln. After the oxidant dissolved, the lead was precipitated by adding oxalic acid (0·52 g) in AcOH. Stirring was continued for a further 20 min, and the suspension was filtered off. The filtrate was concentrated to a syrup and extracted with EtOAc. Distillation of the EtOAc soln afforded a syrupy product which was hydrolyzed in 0·05N H_2SO_4 for 8 hr at 50°. The ppt was filtered off and to the stirred filtrate was added IRA-410 (regenerated with 1N $NaHCO_3$). The resin was filtered and washed with water. The combined filtrate and washing showed a spot moving on PPC(n-BuOH–pyridine–water, 10:4:3, and solvent A) at the same rate as D-glyceraldehyde prepared from D-fructose.[12] After concentrating to a syrup (230 mg), the methone derivative was prepared in the phosphate buffer. m.p. 198–200°, $[\alpha]_D^{20}$ +212° (c = 2·0, EtOH). This dimethone was identified as D-glyceraldehyde dimethone.

The resin was shaken with 1N H_2SO_4 (30 ml) for 90 min, filtered and washed with water. The filtrate combined with the washing was neutralized with $Ba(OH)_2$ and the ppt was filtered through Celite. The filtrate was treated with IR-120 and concentrated. Water was added and the distillation resumed, and the procedure was repeated four times. The residual syrup was dried *in vacuo* (70 mg). It showed the characteristic blue colour with naphthoresorcinol–H_2SO_4,[22] and showed a single spot corresponding to glyceric acid on PPC (solvent E, methyl red in borate buffer) and TLC (n-butyl formate–90% formic acid–water, 7:2:1, v/v). $[\alpha]_D^{20}$ −1·8 (*c* = 3·0 water); *v* (liquid film) 3700–2200, 1735, 1220, 1115, 1060, 1000 cm^{-1}. This syrup was dissolved in water, neutralized with $Ca(OH)_2$, and concentrated. EtOH was added and Ca-salt was filtered; $[\alpha]_D^{20}$ +9·9° (*c* = 2·52, H_2O).

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