Reactions of saccharides catalyzed by molybdate ions. XXII.* Oxidative degradation of D-galactose phenylhydrazones

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Received 4 March 1977

D-Galactose phenylhydrazone was degraded with hydrogen peroxide in the presence of molybdate ions to D-lyxose in 50% yield. The oxidative degradation of D-galactose 2,5-dichlorophenylhydrazone and D-galactose 2,4-dinitrophenylhydrazone gave D-lyxose and D-galactose in the ratio 4:1 and 1:9, respectively. 2,6-Anhydro-1-deoxy-1-nitro-D-galactitol was prepared from D-lyxose.

Фенилгидразон D-галактозы разрушается перекисью водорода в присутствии молибдатных ионов с 50%-ным превращением в D-ликсозу. В случае окислительной деградации 2,5-дихлорфенилгидразона D-галактозы образуется D-ликсоза и D-галактоза в отношении 4:1, в случае же 2,4-динитрофенилгидразона D-галактозы в отношении 1:9. Из D-ликсозы был приготовлен 2,6-ангидро-1-дезокси-1-нитро-D-галактитол.

Treatment of 1-deoxy-1-nitroalditols in alkaline medium with hydrogen peroxide in the presence of molybdate ions leads to the formation of corresponding aldoses [1]. This reaction is, particularly with nitroalditols prepared from L-ribose [2] and D-glucose [3], accompanied by a parallel elimination reaction leading back to the starting aldoses. *Schulz* and *Somogyi* [4] treating L-rhamnose phenylhydrazone with oxygen in acetone or 2,3,4,5,6-penta-*O*-acetyl-D-galactose phenylhydrazone in benzene, obtained the corresponding 1-hydroperoxo derivatives which decomposed in alcohol solution of sodium methanolate to the corresponding pentoses. Similarity between D-galactose phenylhydrazone and 1-deoxy-1-nitro-D-galactitol (in salt form) regarding the C=N linkage was the main reason why we have examined the behaviour of D-galactose phenylhydrazone under the conditions of oxidative decomposition of nitroalditols.

*For Part XXI see *Chem. Zvesti* **32**, 372 (1978).

Oxidative decomposition of sodium salts of 1-deoxy-1-nitro-D-galactitol or 1-deoxy-1-nitro-L-mannitol afforded the corresponding aldohexoses. The starting aldopentoses were formed in low amounts only (<5%). Under the same conditions of the reaction, but in the absence of hydrogen peroxide, the nitrohexitols were continuously decomposed by a retrogressive reaction to the starting aldopentoses (about 30% of nitroalditol converted to the starting aldose after 5 h reaction time). Contrary to the acyclic structures, 2,6-anhydro-1-deoxy-1-nitro-D-galactitol or 2,6-anhydro-1-deoxy-1-nitro-L-mannitol were relatively resistant under the conditions of oxidative decomposition (at equimolar ratio with sodium hydroxide) and, accordingly, their conversion to the starting aldopentoses was very low. Under the conditions of oxidative decomposition of nitroalditols as well as under higher alkalinity or in the absence of alkali, D-galactose phenylhydrazone gave always D-lyxose and D-galactose. At equimolar ratio of D-galactose phenylhydrazone and sodium hydroxide the ratio of D-lyxose to D-galactose was 4:1. The portion of D-galactose increased with the decrease in alkalinity (Table 1). In the absence of

Table 1

Effect of alkalinity (mmoles of NaOH) on oxidative degradation of D-galactose phenylhydrazone (10 mmoles) with hydrogen peroxide under catalysis with molybdate ions

NaOH mmoles	D-Lyxose	:	D-Galactose
0	1		1
1	1		1
2.5	3		2
5	7		3
10	4		1
20	4		1

molybdate ions the oxidative degradation to D-lyxose did not proceed. In the case of oxidative decomposition of disubstituted derivatives of D-galactose phenylhydrazone, the final ratio of aldoses formed was considerably affected by substituents (Table 2).

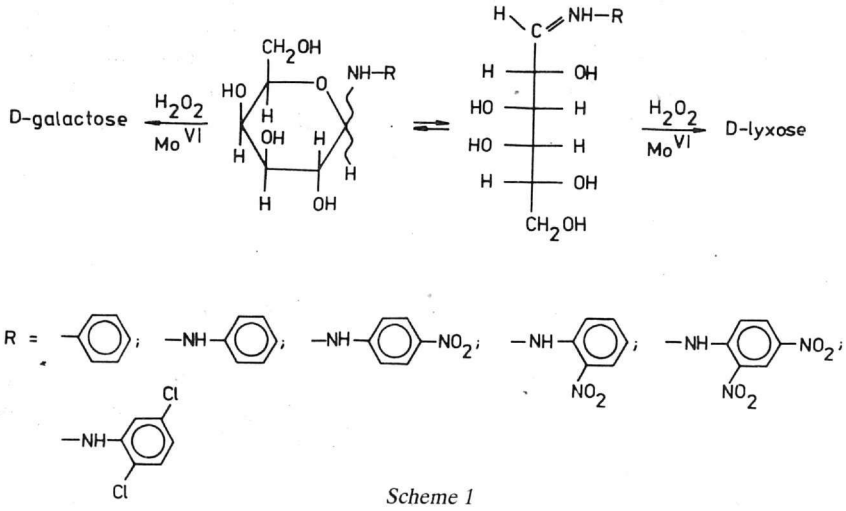
Phenylhydrazones of aldoses are generally stable in alkaline medium. They are known to occur both in cyclic and acyclic structures [5]. In solutions they form various equilibria depending on the nature of solvents as well as on the nature of saccharide and aromatic moiety. Oxidation of phenylhydrazones with peroxoacids involves an electrophilic attack on the nitrogen atom [6]. The oxidation of aldose phenylhydrazones with hydrogen peroxide under catalysis with molybdate ions probably begins with an electrophilic attack at the aldimine nitrogen atom (acyclic structure) and at the nitrogen atom involved in the glycosidic bond (cyclic

Table 2

Oxidative degradation of the derivatives of D-galactose phenylhydrazone and *N*-phenyl-D-galactosylamine

Starting D-galactose hydrazone	D-Lyxose	:	D-Galactose
Phenyl-	1		1
2-Nitrophenyl-	1		1
4-Nitrophenyl-	1		1
2,4-Dinitrophenyl-	1		9
2,5-Dichlorophenyl-	4		1
N-Phenyl-D-galactosylamine	1		9

structure) (Scheme 1). The assumption that this oxidation takes place at the mentioned nitrogen atom is supported by the fact that *N*-phenyl-D-galactosylamine also is degraded to D-lyxose (*ca*. 10%) under the conditions of oxidative decomposition of nitroalditols (regardless the presence or absence of alkali in the medium). The oxidation product of *N*-substituted aldimine is probably transformed to *N*-substituted amide of D-galactonic acid which is further oxidized and degraded to aldose shorter by one carbon (Weerman degradation). The oxidation product of a cyclic structure is hydrolyzed giving the starting aldose. The equilibrium ratio of the cyclic and acyclic structure of phenylhydrazone thus determines the final ratio of aldoses formed.



Scheme 1

Oxidative degradation of D-galactose phenylhydrazone was employed for the preparation of D-lyxose. This procedure gave D-lyxose in 50% yield, however, its isolation from the reaction mixture was rather laborious.

Experimental

Substituted D-galactose phenylhydrazones (2-nitro-, 4-nitro-, 2,4-dinitro-, and 2,5-dichloro-) were prepared by the reaction of D-galactose with equimolar amount of the corresponding phenylhydrazine derivative in ethanol (boiled under reflux for 2 h, for 8 h in the case of 2,4-dinitro derivative). Purity of crystalline D-galactose phenylhydrazones was examined by thin-layer chromatography on Silufol (Lachema, Brno) in chloroform—methanol 6 : 1. D-Galactose phenylhydrazone was prepared as follows: A solution of D-galactose (200 g) in water (250 ml) was mixed with methanol (250 ml) and phenylhydrazine (130 ml) and left to stand at 40—50°C for 1 h. After addition of water (500 ml), the mixture was crystallized for 24 h to give chromatographically homogeneous D-galactose phenylhydrazone (240—265 g; 80—85%).

Effect of alkalinity on oxidative degradation of D-galactose phenylhydrazone

A suspension of 10 mmoles of D-galactose phenylhydrazone in 10 ml of water was successively mixed with 1 ml of 12% aqueous solution of $Na_2MoO_4 \cdot 2H_2O$, 0—20 mmoles of NaOH (in 2 M solution) and then adjusted to a volume of 25 ml with water. After addition of 4 ml of 15% hydrogen peroxide in two portions within 1 h the mixture was left to stand at room temperature for 5 h and filtered. The filtrate was subjected to chromatography on Whatman No. 1 paper in *n*-butanol—ethanol—water (5 : 1 : 4), and after detection of sugars with the hydrogen phthalate-aniline reagent, the ratio of D-lyxose and D-galactose was determined by direct scanning of the chromatogram with an ERI-10 densitomer (Zeiss, Jena) (Table 1).

Oxidative degradation of the derivatives of D-galactose phenylhydrazone and N-phenyl-D-galactosylamine

A suspension of 5 mmoles of D-galactose phenylhydrazone or any of its derivatives (2-nitro-, 4-nitro-, 2,4-dinitro-, 2,5-dichloro-) or *N*-phenyl-D-galactosylamine in 20 ml of water was successively mixed with 1 ml of 6% solution of $Na_2MoO_4 \cdot 2H_2O$, 2 ml of 15% hydrogen peroxide, and 10 ml of methanol. After 6 h the reaction mixture was filtered and chromatographed to determine the ratio of D-lyxose and D-galactose as described above (Table 2).

Preparation of D-*lyxose*

D-Galactose phenylhydrazone (270 g) was suspended in water (2000 ml) followed by addition of 12% aqueous solution of sodium molybdate (100 ml) and, in portions, during 2 h, 15% aqueous solution of hydrogen peroxide (400 ml) at a rate to keep the temperature of the reaction mixture below 35°C. After being left for 24 h, the mixture was filtered, the filtrate extracted with ethyl acetate and the aqueous phase concentrated to half-volume, purified with charcoal and deionized on ion exchangers (catex in H^+ form, anex in acetate form). The deionized solution was evaporated to sirup (*ca*. 160 g) which was crystallized from methanol (300 ml) to separate D-galactose. The mother liquor was evaporated to sirup representing crude D-lyxose (*ca*. 80 g), $[\alpha]_D^{23}$ −12.5° (*c* 2, water) contaminated by about 5% of D-galactose. Crystalline, chromatographically homogeneous D-lyxose was obtained by purification *via* *N*-phenyl-D-lyxosylamine [7].

*Preparation of 2,6-anhydro-1-deoxy-1-nitro-*D-*galactitol*

The crude product of D-lyxose obtained as just described gave on nitromethane synthesis 1-deoxy-1-nitro-D-galactitol [8]. 1-Deoxy-1-nitro-D-galactitol (20 g) was dissolved in water (100 ml) and heated at 90—95°C for 30 h. The mixture was then evaporated under reduced pressure and the residue was crystallized from ethanol to give 2,6-anhydro-1-deoxy-1-nitro-D-galactitol (8 g). The mother liquor was concentrated and chromatographed on a column (3 × 90 cm) of Dowex 1, X-8, 100—200 mesh, in acetate form, eluted with water (elution order of compounds: D-lyxose, 1-deoxy-1-nitro-D-galactitol, 2,6-anhydro-1-deoxy-1-nitro-D-galactitol) to give additional portion of 2,6-anhydro-1-deoxy-1-nitro-D-galactitol (6.5 g). Thus the overall yield was 80%. Recrystallization from methanol afforded 2,6-anhydro-1-deoxy-1-nitro-D-galactitol, m.p. 142—143°C, $[\alpha]_D^{23}$ −55.9 ± 0.2° (*c* 2, water).

For $C_6H_{11}O_6N$ calculated: 37.31% C, 5.74% H, 7.25% N; found: 37.57% C, 5.73% H, 7.13% N.

After chromatography on Whatman No. 1 paper in *n*-butanol—ethanol—water (5 : 1 : 4), following mobilities relative to that of D-lyxose (1.00) were found: for 1-deoxy-1-nitro-D-galactitol 1.49, for 2,6-anhydro-1-deoxy-1-nitro-D-galactitol 2.10.

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Translated by P. Biely