REDUCTION OF GLYCOSYLNITROMETHANES TO GLYCOSYLMETHYLAMINES WITH FERROUS SALTS

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Reduction of β-D-galactopyranosylnitromethane, β-D-glucopyranosylnitromethane and 1-deoxy-1-nitro-D-*glycero*-L-*manno*-heptitol with ferrous hydroxide afforded β-D-galactopyranosylmethylamine (*I*), β-D-glucopyranosylmethylamine (*II*) and 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol (*III*), respectively. Thanks to the high conversion of the nitro derivatives and the simple isolation, this method is very suitable for preparation of glycosylmethylamines. The structure of products in their underivatized form was proved by mass spectrometry.

Glycosylmethylamines, *i.e.* 2,6- or 2,5-anhydro-1-amino-1-deoxyalditols, represent an important group of saccharides which, *e.g.* can be used in the preparation of 1-deoxy-2-ketoses[1-4]. β-D-Galactopyranosylmethylamine was employed in the preparation of β-D-galactopyranosyl-(4-nitrophenyl)triazene, inhibitor of *E. coli* β-galactoxidase[5]. α-D-Mannopyranosylmethylamine exhibits an insulin-like activity[6]. Most of the synthetic approaches consist in catalytic hydrogenation of glycosylnitromethanes, over Raney nickel[7,8] or Adams catalyst[1,7]. β-D-Galactopyranosylmethylamine was prepared by reaction of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide with cyanide ions, followed by reduction of the intermediate with lithium aluminium hydride[2]. Aromatic amines are frequently prepared by reduction of nitroaromatic compounds with ferrous hydroxide[9], highly selective for this type of reduction. In the present communication we utilized this reaction for synthesis of glycosylmethylamines from the starting glycosylnitromethanes.

Treatment of an aqueous solution of β-D-galactopyranosylnitromethane with ferrous sulfate and ammonia at about 100°C (15 min) afforded β-D-galactopyranosylmethylamine (*I*) in 96% yield. β-D-Glucopyranosylnitromethane was transformed in the same way into β-D-gluctopyranosylmethylamine (*II*) in 95% yield. Both glycosylmethylamines were converted also into their crystalline hydrochlorides. The procedure, applied to 1-deoxy-1-nitro-D-*glycero*-L-*manno*-heptitol, led to 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol (*III*) with simultaneous formation of D-galactose. The aminoalditol *III* was isolated as its hydrochloride in 26% yield.

In spite of great number of hydroxy groups in the compounds *I*–*III*, we obtained their reproducible mass spectra working at electron energy 12 eV. The mass spectra

of both glycosylmethylamines *I* and *II* qualitatively agreed (Fig. 1). They exhibited $[M + H]^+$ and less intensive $M^{+\cdot}$ ions which on elimination of H_2O and NH_3 gave rise to doublets, *m/z* 176 ($C_7H_{12}O_5$: $C_7H_{14}NO_4$ 2 : 1) and the ions at *m/z* 175 ($C_7H_{13}NO_4$). The spectra contained ions typical for fragmentation of pyranoid saccharide structures[10]; peaks due to ions of the fragmentation series E ($C_6H_{12}NO_4$) at *m/z* 162 ($C_6H_{12}NO_4$: $C_6H_{10}O_5$ 3 : 1), D at *m/z* 133 ($C_5H_9O_4$), K at *m/z* 74 ($C_3H_6O_2$), and F at *m/z* 73 ($C_3H_5O_2$). In addition to these characteristic ions the spectra displayed intensive peaks due to the following ions arising from precursors of higher mass by loss of H_2O, NH_3 or CH_3NH_2, or radicals $^{\cdot}CH_2OH$ or $^{\cdot}CH_2NH_2$: *m/z* 146 ($C_6H_{10}O_4$), 145 ($C_6H_9O_4$), 128 ($C_6H_8O_3$), 103 ($C_4H_9NO_2$), 102 ($C_4H_8NO_2$), 97 ($C_5H_5O_2$), and 30 (CH_4N).

In contrast with the spectra of glycosylmethylamines, the 12 eV mass spectrum of compound *III* (Fig. 1) displayed surprisingly abundant $[M + H]^+$ ions of *m/z* 212. The ions *m/z* 180, 150, 120, 90, 60 and 30 arise by cleavage of bonds

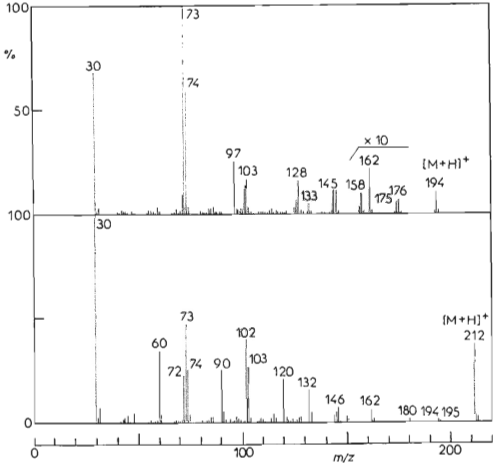
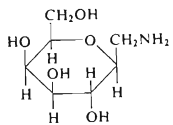


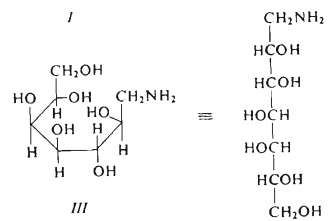
FIG. 1

Mass spectra (12 eV) of β-D-galactopyranosylmethylamine (*I*) and 1-amino-1-deoxy-D-*glycero*--L-*manno*-heptitol (*III*)

between the carbon atoms of 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol, proving its acyclic structure.



I



III

The ferrous hydroxide reduction of nitrosaccharides represents thus an alternative method of preparation of the corresponding saccharide amines. As seen from the described examples, it is advantageous particularly for reduction of such nitrosaccharides which in alkaline medium cannot directly lose a nitroalkane molecule. Glycosylnitromethanes, which fulfil this condition, can be thus easily converted into glycosylmethylamines.

EXPERIMENTAL

Specific rotations were measured on a Perkin–Elmer 141 polarimeter and melting points were determined on a Kofler hot-stage. Elemental analyses were carried out on a Perkin–Elmer 240 automatic analyzer. Composition of the reaction mixtures and purity of the saccharides were followed by paper chromatography in 1-butanol–ethanol–water 5 : 1 : 4; spots were detected by anilinium hydrogen phthalate and sodium periodate. Mass spectra were measured on a JMS-D 100 (JEOL) instrument (electron energy 12 eV, emission 300 μA, sample evaporation at 200 to 250°C, ionization chamber temperature 220°C). High resolution experiments were performed on an MS 902 S (AEI) instrument (70 eV; 100 μA, ionization chamber temperature 150°C). Resolving power of the instrument was $R_{10\%} = 20\,000$.

β-D-Galactopyranosylmethylamine (*I*)

A solution of β-D-galactopyranosylnitromethane[11] (3 g) in hot water (30 ml) was added to a stirred boiling solution of ferrous sulfate heptahydrate (26·4 g) in water (60 ml). Concentrated aqueous ammonia was then added portionwise (à 3—5 ml) under stirring until the mixture had an strong alkaline reaction. After boiling for 10 min (the alkaline reaction was kept by addition

of further ammonia), the precipitate was filtered and washed with dilute ammonia. The filtrate was cooled, mixed with Dowex 1X8 (OH^-; 100 g) and the suspension was concentrated on a rotatory evaporator under diminished pressure to half of the original volume. The ion-exchange resin was filtered off and washed with water (3 × 100 ml). Concentration of the filtrate afforded pure amine *I* (2·5 g; 96%) which after two crystallizations from methanol melted at 191—192 °C; $[\alpha]_D^{21}$ +29 ± 0·5° (*c* 2, water); reported[2] m.p. 191—192°C, $[\alpha]_D^{20}$ +30·0° (*c* 1·61, water). Mass spectrum of the underivatized compound is shown in Fig. 1.

Dissolution of the amine *I* (0·5 g) in 0·2M-HCl (13 ml), evaporation and crystallization of the residue from methanol afforded the hydrochloride (0·5 g; 84%), m.p. 210—211°C, $[\alpha]_D^{21}$ +30·5 ± ± 0·5° (*c* 2, water). Reported[2] m.p. 211°C and $[\alpha]_D^{20}$ +31·3° (*c* 0·53, water).

β-D-Glucopyranosylmethylamine (*II*)

The title compound was prepared from β-D-glucopyranosylnitromethane[11] (2 g) as described for preparation of compound *I*; yield 1·65 g (95%) of the crude amine. After two crystallizations from methanol the product melted at 142—143°C; $[\alpha]_D^{20}$ +2·7 ± 0·3° (*c* 4, water). For $C_7H_{15}NO_5$ calculated: 43·52% C, 7·83% H, 7·25% N; found: 43·35% C, 8·03% H, 7·22% N. Mass spectrum of the underivatized compound agreed qualitatively with that of compound *I* (Fig. 1).

The hydrochloride monohydrate was prepared as described for compound *I*; m.p. 81—83°C, $[\alpha]_D^{20}$ −2·9 ± 0·3° (*c* 2, water). For $C_7H_{18}ClNO_6$ calculated: 14·31% Cl; found: 14·30% Cl.

1-Amino-1-deoxy-D-*glycero*-L-*manno*-heptitol (*III*)

1-Deoxy-1-nitro-D-*glycero*-L-*manno*-heptitol[12] (1·5 g) was reduced as described for β-D-galactopyranosylnitromethane. The obtained syrupy material (1·1 g) which showed an alkaline reaction and contained D-galactose was dissolved in water (10 ml), the solution was treated with Dowex 50WX8 (H^+; 5 g) and the mixture was stirred for 0·5 h. The ion-exchange resin was removed by filtration and washed with water (3 × 10 ml). Evaporation of the filtrate afforded D-galactose (0·6 g). The ion-exchange resin was suspended in 1·5M-NH_4OH (25 ml), filtered and washed with 1·5M-NH_4OH (2 × 5 ml). The filtrate was taken down *in vacuo* and the operation was repeated three times after dissolution of the residue in water. Finally, the evaporation residue was dissolved in water (5 ml) and the solution was adjusted to pH 5 with 0·2M-HCl (8·8 ml). Evaporation of water and crystallization of the residue from methanol afforded 1-amino-1-deoxy-D-*glycero*-L-*manno*-heptitol hydrochloride (0·4 g; 26%), m.p. 172—174°C, $[\alpha]_D^{20}$ −4·5 ± 0·3° (*c* 2, water). Reported[13] m.p. 150—152°C, $[\alpha]_D^{20}$ −3·5° (*c* 1·1, water). A solution of the hydrochloride (0·1 g) in water (2 ml) was mixed with Dowex 1X8 (OH^-; 2 g) and set aside for 0·5 h. The resin was filtered off, washed with water (3 × 5 ml), the filtrate was taken down and the residue was subjected to mass spectral measurement (Fig. 1).

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