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ELECTRO-ORGANIC REACTIONS. PART 33. REDUCTION OF SUGAR OXIMES

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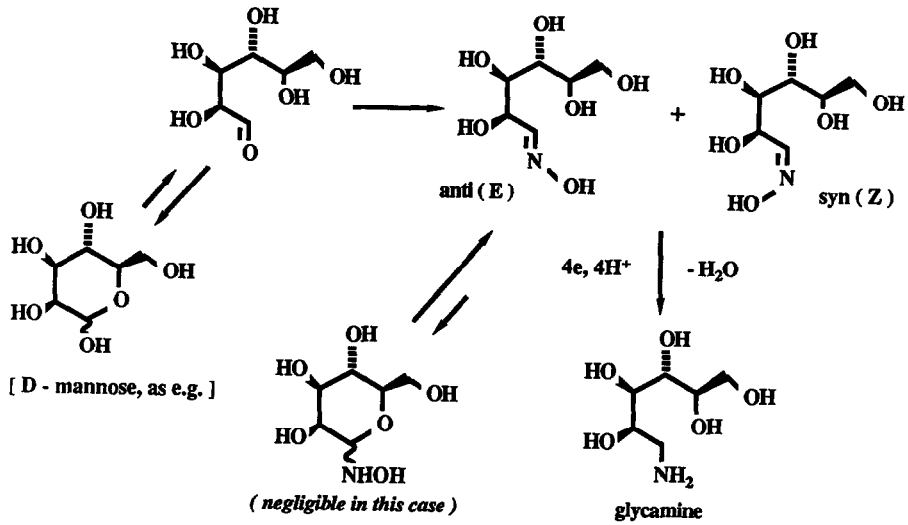
Abstract: Monosaccharide oximes reduce irreversibly at *ca.* -1.73V *vs* Ag/AgI in the presence of a proton donor; preparative scale constant current electro-reduction, in aqueous solution, gives efficient conversion into the corresponding glycamines which are isolated as Schiff base or acetate derivatives.

Lund[1] first reported the cathodic amination of relatively simple carbonyl compounds, *via in situ* formation of Schiff bases (imines). For saccharides, however, Schiff base formation must be consequent upon ring-opening of pyranoses or of furanoses. Furthermore, both the ring-opening and cathodic reduction reactions will be pH dependent. The route is likely to be important for the preparation of amino sugars (glycamines) and we report herein on reductive amination *via* oxime formation, part of a wider study[2] of C=N bond reduction in sugar derivatives. Sugar oximes have previously been converted into glycamines chemically[3] and by catalytic hydrogenation[4].

Electrochemical reduction of sugar oximes was found to be preparatively convenient; they are predominantly acyclic in solution, which appears to be important for cathodic reduction. The Scheme shows relevant reactions and equilibria; the study of preformed oximes is therefore useful in the context of developing methods whereby such intermediates are formed *in situ*.

Sugar oximes were prepared by conventional methods[4]. The oximes of L-arabinose, D-arabinose, D-ribose, D-mannose, and D-galactose were shown by ^{1}H and ^{13}C n.m.r. spectroscopy to be completely acyclic in D_2O solution; no signals due to the 1-C or 1-H of cyclic forms were observed. An earlier study[5] established that D-glucose oxime is also predominantly (70%) acyclic in aqueous solution. The acyclic oximes may be syn(Z) or anti(E) and the Z/E ratios have been measured by integration of the respective 1-H proton n.m.r. signals (Table) for the samples used in electrolyses.



SCHEME

Table. Sugar oximes: Conformation[a] and Cathodic Reduction[b]

Monosaccharide oxime	Z/E	Reduction yield (%)
L-Arabinose	2.00	61 (74)[d,e]
D-Arabinose	0.70	61[c]
D-Ribose	13.3	(73)[d,e]
D-Glucose	(0.24)[f]	9[c,e]
D-Mannose	0.08	62[c]
D-Galactose	0.38	51[c]

Footnote: (a) By ^{1}H n.m.r. spectroscopy (D_2O solution). (b) 0.5-1.0g in 50 cm^3 1M aqueous KCl in NaOAc/HOAc buffer (pH 5.6) - pH adjusted and maintained at 6-7 by regular addition of HCl, divided cell, Hg pool cathode, 0.83 Adm^{-2}, 5-6 $Fmol^{-1}$. (c) After electrolysis, catholyte made alkaline, salicaldehyde added, yellow salicylidene glycamine precipitates on cooling - recrystallised from methanol. (d) After electrolysis, solvent of catholyte removed and dry residue treated with Ac_2O-pyridine (room temperature, several days) - peracetylated product extracted into $CHCl_3$ after dilution with water. (e) Electrolyte, 0.1 M KCl/60% aqueous EtOH - pH maintained at 6-7 by regular addition of HCl. (f) Ref. 7; 70% in acyclic form.

Early polarographic experiments[6] indicated that the oxime function was reducible, but, for sugar oximes, no preparative scale experiments were performed. Cyclic voltammetric experiments [Hg bead cathode, DMF-Bu_4HSO_4 (0.1M), Ag/AgI reference, scan rate 400 mVs^{-1}], in the presence of quinol as proton donor, indicated that the sugar oximes referred to above gave well-defined reduction peaks at *ca.* -1.73V. The presence of the proton donor was essential; the reductions were irreversible in the scan rate range 150-500 mVs^{-1} and linear plots of i_p *vs.* $v^{1/2}$ indicated normal diffusion behaviour.

The oximes were reduced on a preparative scale in aqueous solution at constant current density and at a mercury pool cathode. The conditions were optimised for the reduction of arabinose oxime and involved buffering at pH 6-7 and a current density of 0.83 Adm^{-2}. The cathode potential was monitored during electrolysis and found to vary in the range -1.5 to -2.0V *vs.* Ag/AgCl. Isolation of the water-soluble glycamines was a problem and it proved to be necessary to isolate the products by *in situ* formation and precipitation, using salicylaldehyde, of Schiff bases. Peracetylation of the crude product was an alternative method for derivatisation and isolation. The results of such electrolyses for several monosaccharide oximes, on a 0.5-1.0g scale, are summarised in the Table. Of the two sets of conditions described, that involving aqueous ethanol solution and regular adjustment of pH is the more convenient. Hydrolysis of the Schiff base derivatives is facile; for the L-arabinose and D-galactose products the corresponding glycamine hydrochlorides were obtained, from the salicylidene derivatives, in 73% yield after treatment at 100°C for 15 minutes with 5% v/v aqueous HCl.

Yields of glycamine derivatives were generally >50%; it is not likely that formation and precipitation of the Schiff base is quantitative and it follows that the glycamine is probably formed in good yield. This contention is supported by the considerably higher yields recorded when peracetylation was used to derivatise the crude electrolysis product (Table, footnote). The only oxime which is significantly cyclised in aqueous solution, that of D-glucose, was least efficiently reduced. Glycamines formed from the oximes of D-xylose and D-ribose could not be precipitated as Schiff base derivatives but conversion of the crude electrolysis product into its acetyl derivative showed that for the ribose case reduction was efficient. In each case products were characterised by high resolution mass spectrometry, by ^1H n.m.r. spectroscopy, and in several cases by comparison with the products of catalytic hydrogenation. Although useful as a confirmation of structure, catalytic hydrogenation gave poor conversion (*ca.* 10%) for the oximes used in this study. Electrochemical reduction was much more efficient.

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