A New Efficient Access to Glycono-1,4-lactones by Oxidation of Unprotected Itols by Catalytic Hydrogen Transfer with $RhH(PPh_3)_4$-Benzalacetone System

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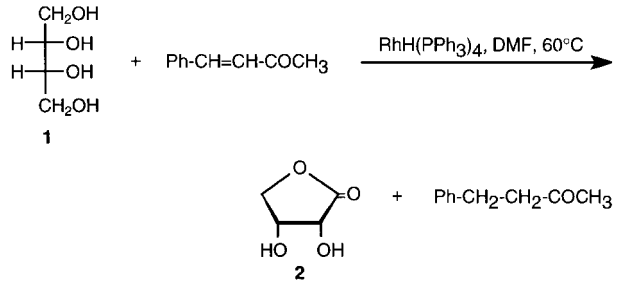
Abstract: Treatment of unprotected pentitols and hexitols with $RhH(PPh_3)_4$-benzalacetone system leads exclusively to glycono-1,4-lactones in 60-96% yield.

The literature records a number of methods for the conversion of diols to lactones in yields varying from good to poor. These include: silver carbonate on Celite,[1] stoichiometric $RuCl_2(PPh_3)_3$ in benzene,[2] $CuSO_4$-$KMnO_4$,[3] tetrapropylammonium perruthenate-4-methylmorpholine *N*-oxide,[4] and catalytic hydrogen transfer (C.H.T) [benzalacetophenone-$RuH_2(PPh_3)_4$] at 140°C.[5] To our knowledge, the latter is the only method which has been described to oxidize protected pentitols to afford the corresponding pentonolactones[6] and no method was applicable for the oxidation of unprotected itols to glyconolactones.

In a previous paper we described the oxidation of protected or unprotected lactols to glycono-1,4-lactones, in mild conditions, by C.H.T with benzalacetone as hydrogen acceptor and $RhH(PPh_3)_4$(hydridotetrakis triphenylphosphine rhodium I) as catalyst.[7]

We report here the use of this system for the oxidation of unprotected itols to prepare glycono-1,4-lactones.

As a matter of fact, we observed that treatment of *meso* erythritol **1** with $RhH(PPh_3)_4$ (0.2 eq) and benzalacetone (4 eq) in DMF for 3 hours at 60°C led to the racemic mixture of D,L-erythrono-1,4-lactone **2** in 95% isolated yield (Scheme 1). This method was also applied to other unprotected itols (tetritols, pentitols and hexitols) and efficiently yielded the glycono-1,4-lactones as shown in the Table.



Scheme 1

Pentitols and hexitols which have a plane of symmetry, for example *meso* erythritol **1**, D-xylitol **8**, D-galactitol **18** or a C-2 symmetry axis, such as D-threitol **3** or D-mannitol **13** led, with good yields, to the corresponding lactone obtained in a racemic mixture.

Only one exception was observed when D-ribitol **5**, having a plane of symmetry, was oxidized with 0.2 eq of catalyst and 4 eq of benzalacetone at 60°C for 5 hours. D,L-Ribono-1,4-lactone **6** and D,L-arabinono-1,4-lactones **7** were isolated in 47% and 18% yield respectively. Similar epimerisation at C-2 was already observed in the oxidation of 2-acetamido-2-deoxy-D-mannopyranose with the same oxidizing system.[8]

When the oxidation of D-ribitol was performed at 80°C with 0.4 eq of $RhH(PPh_3)_4$ the overall yield increased to 94% but the ratio **6**/**7** remained equal to 2.5:1.

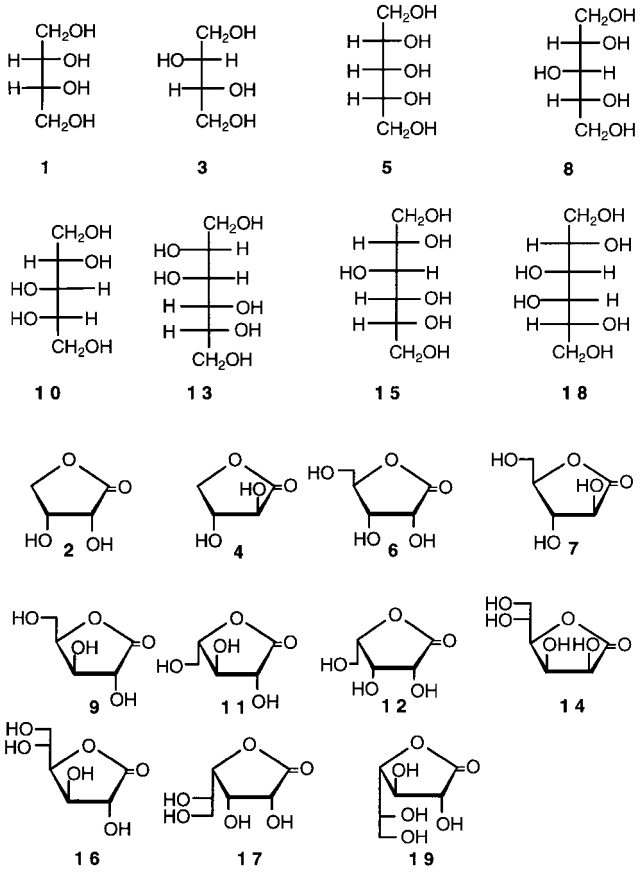


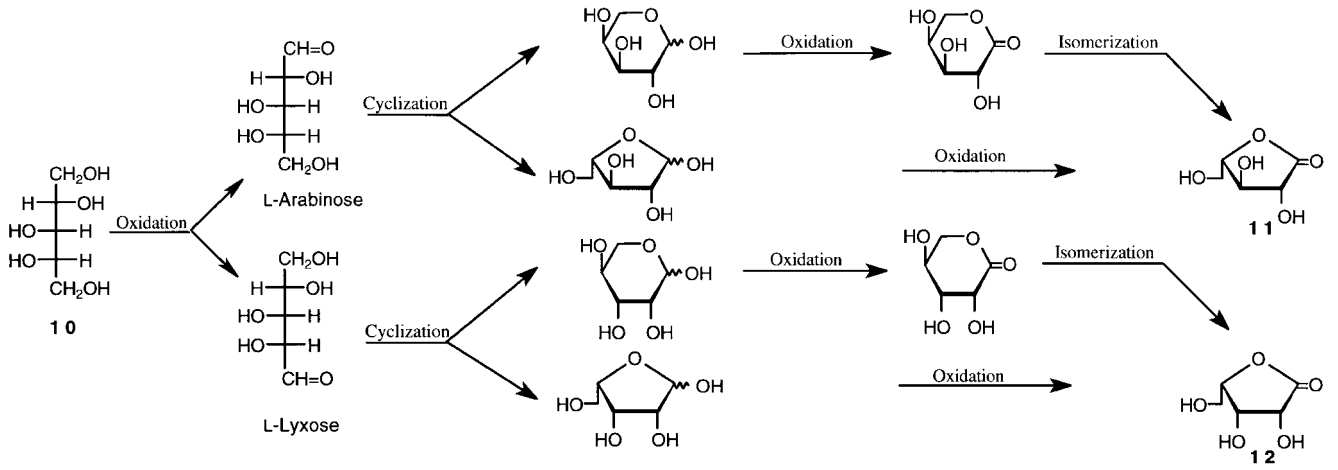
Table. Oxidation of unprotected itols by $RhH(PPh_3)_4$-Benzalacetone[a]

Substrate	Product (% yield)	Substrate	Product (% yield)
1	**2** (95)	**10**	**11+12** (72)
3	**4** (90)	**13**	**14** (90)
5	**6+7** (94)	**15**	**16+17** (96)
8	**9** (85)	**18**	**19** (60)

[a][Itol]=2.5 mmol, Benzalacetone (4 eq), $RhH(PPh_3)_4$ (0.2-0.4 eq), DMF, 60-80°C

The oxidation of L-arabinitol which has no symmetry led to the two expected L-arabinono-1,4-lactone **11** and L-lyxono-1,4-lactone **12** in 72% overall yield and in ratio **11**/**12**=1.25:1.

As explained in Scheme 2, after an oxidation at C-1 of L-arabinitol, the L-arabinopyranose or furanose formed was oxidized to give the L-arabinono-1,4-lactone **11**. The rare L-lyxono-1,4-lactone **12** is obtained *via* the L-lyxose resulting from the oxidation at the C-5 of the starting itol.



Scheme 2

In earlier work,[9] we have shown that $RhH(PPh_3)_4$ induced an intramolecular esterification of a dialdehyde derivative. In the case of itols, it was difficult to assume that a dialdehyde might be the intermediate, as this hypothesis required the simultaneous oxidation of the two primary alcohol functions.

Similarly the non symmetric D-glucitol was oxidized to give D-glucono-1,4-lactone **16**, as major product, and the L-gulono-1,4-lactone **17** isolated in 96% overall yield in a ratio **16**/**17**=2.2:1.

In conclusion, we have shown that oxidation of unprotected itols by catalytic hydrogen transfer using $RhH(PPh_3)_4$ as catalyst and benzalacetone as hydrogen acceptor, afforded preparation of glycono-1,4-lactones under mild conditions in good yields.

Typical procedure

The $RhH(PPh_3)_4$ catalyst was prepared using the Levinson and Robinson[10] method.

To a solution of itol (2.5 mmol) and $RhH(PPh_3)_4$ (0.2-0.4 eq) in anhydrous DMF (3 mL) at 60-80°C, under argon atmosphere, was added a solution of benzalacetone (4 eq) in DMF (2 mL). The reduction of benzalacetone was controlled by GCP (DEGS, 5%, 10 feet, 160°C). After total consumption of the itol [TLC ($CHCl_3$-MeOH)], concentration under vacuum gave the crude mixture which was poured into water and washed with chloroform. The water was evaporated and chromatography on silica gel (eluent: AcOEt) gave glycono-1,4-lactone. All products were identified according to their literature data or their ^1H, ^{13}C NMR spectra and their elemental analyses data.

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