

# Changes in Stereoselectivity in the Triose Aldol Condensation with Increased Concentration of Alkaline-Earth Metal Ions

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The presence of strontium and calcium chlorides in the triose aldol condensation has been found to affect the diastereoselectivity markedly. Whereas *arabino*-2-hexulose (fructose) is the major product under ordinary conditions, high concentrations of the alkaline-earth metal ions cause a change in favour of the *xylo*- and *lyxo*-diastereomers. No such effect was observed when high concentrations of alkali-metal chlorides were used.

Product mixtures from triose aldol condensations, catalysed by various alkali- and alkaline-earth-metal hydroxides have been investigated in previous papers<sup>1,2</sup> of this series. Only small variations were observed in the proportions of the diastereomeric 2-hexuloses formed in the reactions with these catalysts. Carbohydrates with suitably oriented oxygen atoms are known to form complexes with calcium and strontium ions,<sup>3</sup> and possible complexes between these ions

and glyceraldehyde under the triose aldol condensation condition might be expected to lead to changes in the diastereoselectivity from that obtained with alkali hydroxides. The apparent lack of such differences could be due to the low metal-ion concentrations used in these reactions, in particular since cations are, to some extent, engaged in enediolate stabilisation. Hence, higher metal-ion concentrations are probably needed for the observation of possible differences in diastereo-

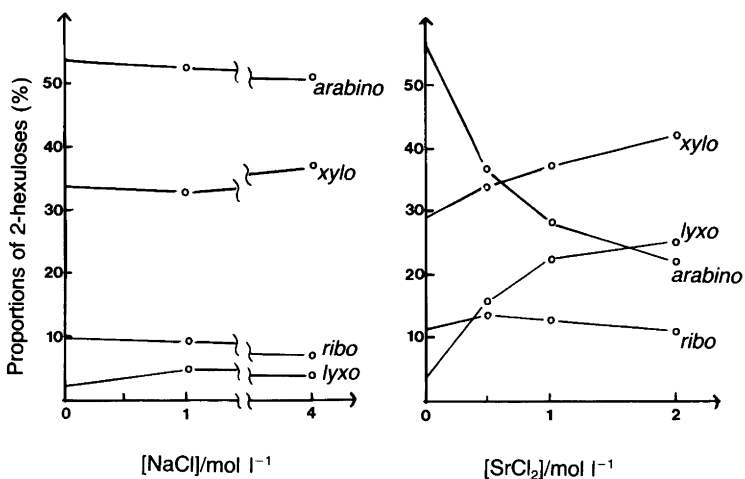


Fig. 1. Variations in the proportions of 2-hexuloses formed in the triose aldol condensation with increasing concentration of sodium chloride and strontium chloride.

Table 1. Product composition of 2-hexuloses after triose aldol condensation with different catalysts.

Catalyst or salt (concentration/mol l <sup>-1</sup> )	pH	Product composition of 2-hexuloses/%			
		<i>ribo</i>	<i>lyxo</i>	<i>arabino</i>	<i>xylo</i>
Sr(OH) <sub>2</sub> (0.01)	12.3	11	3	57	29
Ca(OH) <sub>2</sub> (0.01)	12.3	14	6	50	30
NaOH (0.02)	12.3	10	2	54	34
LiOH (0.02)	12.3	11	5	55	29
SrCl <sub>2</sub> (2)	12.0	11	25	22	42
CaCl <sub>2</sub> (3)	11.4	12	32	22	34
NaCl (4)	12.0	7	4	51	38
LiCl (4)	12.0	11	5	58	26

selectivity in these aldol condensations. The mixtures of 2-hexuloses obtained from the triose aldol condensation in the presence of varying concentrations of alkali- and alkaline-earth-metal chlorides have therefore been investigated.

## Results and discussion

No significant changes in the product composition were observed for the triose aldol condensation with increasing concentrations of sodium chloride (Fig. 1). It is also seen (Table 1) that the diastereoselectivity in the lithium hydroxide catalysed reaction is the same in 4 M lithium chloride as it is without addition of the salt. On the other hand, the diastereoselectivity of the reaction was markedly influenced by the presence of calcium or strontium chloride (Table 1). The *xylo*-isomer is the major product with both of these ions, but more remarkable is the increase, from about 5 to 32 and 25%, respectively, in the proportion of

*lyxo*-2-hexulose (tagatose) on addition of alkaline-earth metal chlorides.

In the absence of alkaline-earth metal salts, diastereomers with the *threo*-configuration at C3–C4 are formed preferentially in the triose aldol condensation.<sup>1,2,4</sup> The observed diastereoselectivity is in accordance with a pericyclic reaction mechanism and a transition state formed by an attack of a *cis*-enediolate on the aldehyde<sup>2</sup> [Fig. 2(a)]. The increase in the proportions and the ultimate predominance of compounds with a *threo*-configuration at C4–C5, on addition of alkaline-earth metal chlorides, may be explained by an attack of the enediolate from the less-hindered side of a metal–glyceraldehyde complex involving the three oxygens of the triose [Fig. 2(b)], leading to an *anti*-periplanar orientation of the carbon chain around the C4–C5 bond in the resulting transition state. Regardless of the configuration and orientation of the attacking enediolate, products with the *threo*-configuration at C4–C5 are formed. The loss of diastereoselectiv-

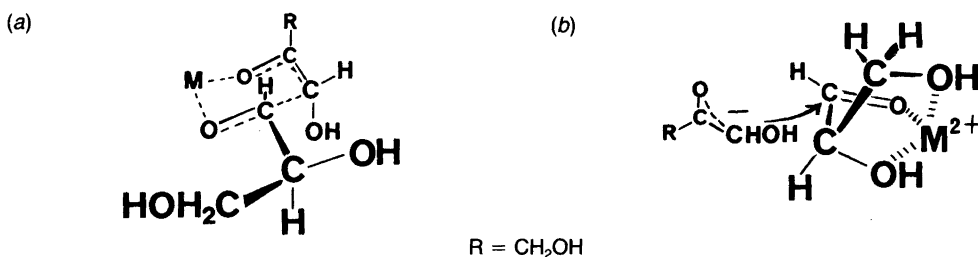


Fig. 2. (a) Transition state leading to *L*-arabino-2-hexulose (*L*-fructose) in the triose aldol condensation according to a pericyclic model; (b) attack of enediolate on a glyceraldehyde–alkaline-earth metal-ion complex leading to *xylo*- and *lyxo*-isomers.

ity in the C3–C4 bond formation is understandable, since the carbonyl oxygen of the glyceraldehyde molecule is engaged in complex formation before the attack of the enediolate, and the complexing, which is necessary for the stereoselectivity-controlling pericyclic transition state [Fig. 2(a)], is prevented.

The  $^1\text{H}$  nuclear magnetic resonance spectrum of DL-glyceraldehyde in deuterium oxide shows the presence of only a few per cent of the aldehyde form in equilibrium with other forms. The difference between sodium ions and alkaline-earth ions in their ability to form complexes with glyceraldehyde is observed in the spectra of the triose in the presence of sodium and calcium chlorides. The signal from the aldehyde proton at 9.70 ppm is not affected by the presence of sodium chloride, whereas a broad signal is observed on the addition of the calcium salt (Fig. 3).

It is obvious from previous<sup>1,5,6</sup> and present results that it is possible to influence the diastereoselectivity of the triose aldol condensation. From strongly favouring of *arabino*-2-hexulose (fructose) with anion-exchange resins, the stereoselectivity is altered to favour the *xylo*- and *lyxo*-diastereomers with metal hydroxides in the presence of calcium and strontium salts. This fact should be taken into consideration when aldol condensations between small sugars are used in syntheses.

## Experimental

**General methods.** Gas liquid chromatography (GLC) was performed with a Perkin–Elmer F 11 gas chromatograph, equipped with a flame-ionisation detector and a glass column (1.8 m  $\times$  2 mm i.d.) filled with 3% Dextsil 300 on 100/120 Supelcoport. The temperature programme was  $4^\circ \text{min}^{-1}$  from  $90 \rightarrow 170^\circ \text{C}$ . For GLC–MS analyses, a Varian Aerograph 2400 gas chromatograph was used in combination with a Micromass 12 F mass spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded with a Jeol JNM GX-270 spectrometer.

**Aldol condensations.** Solutions of DL-glyceraldehyde (10 mg) in water (1 ml) containing an alkali- or alkaline-earth-metal hydroxide in the presence or absence of salts (Table 1) were stored at room temperature for 45 min. The solutions

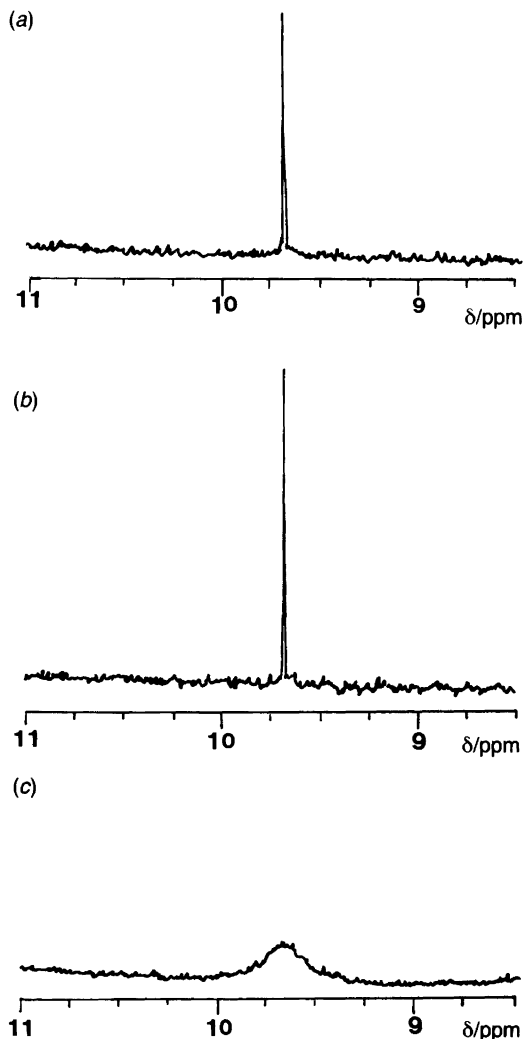


Fig. 3. The aldehyde proton region in the  $^1\text{H}$  NMR spectra recorded in deuterium oxide of (a) DL-glyceraldehyde; (b) DL-glyceraldehyde in the presence of sodium chloride; and (c) DL-glyceraldehyde in the presence of calcium chloride.

were neutralised with Dowex 50 W ( $\text{H}^+$ ) ion-exchange resin, and those containing chloride were treated with a mixture of Dowex 50 W ( $\text{H}^+$ ) and Dowex 1 ( $\text{HCO}_3^-$ ) ion-exchange resins. The solutions were filtered and concentrated under reduced pressure, and the residues were stirred with acetone containing 2% (v/v) conc. sulfuric acid (3 ml) for 2 h at room temperature. The

acetone solutions were then neutralised with solid sodium hydrogen carbonate and subjected to GLC or GLC-MS.<sup>1</sup>

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### References

1. Morgenlie, S. *Carbohydr. Res.* 80 (1980) 215.
2. Morgenlie, S. *J. Carbohydr. Chem.* 6 (1987) 661.

3. Angyal, S. J. In: *Carbohydrates in Solution*, Am. Chem. Soc., Advances in Chemistry Series 117 (1973), p. 106.
4. Fischer, H. O. L. and Baer, E. *Helv. Chim. Acta* 19 (1936) 519.
5. Morgenlie, S. *To be published.*
6. Gutsche, C. D., Redmore, D., Buriks, R. S., Nowotny, K., Grassner, H. and Armbruster, C. W. *J. Am. Chem. Soc.* 89 (1967) 1235.

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