OPINION

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Syn-anti epimerization of aldols by aldolate dianions

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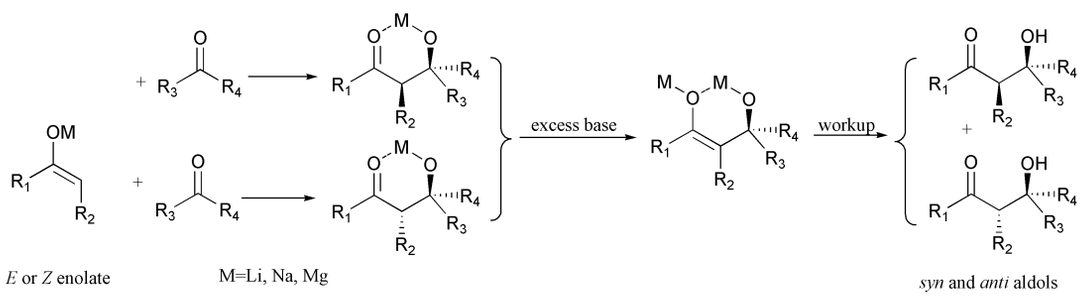
A proposed mechanism based on distal aldolate dianions is illustrated in this paper to explain the outcome of the directed aldol reaction when one uses more than 2 equivalents of base.

The aldol addition[1] is a powerful and general method for stereocontrolled construction of carbon-carbon bonds. The most important stereochemical question in the directed aldol reaction concerns the formation of *threo* and/or *erythro* isomers of aldols or ketols.

One may use several mole equivalents of Li (or Na, Mg, *etc.*) enolates of the ketone and only 1 mole equivalent aldehyde to obtain the best yield of the desired condensation product. However, undesired products were usually obtained, along with the expected ones. One may explain the results through a rapid equilibration between the starting *E*- and *Z*-enolates based on the classic retro-aldol aldol process.[1]

During our studies on the total synthesis of brassinolide,[2] we observed an interesting phenomenon, which we think can be well-explained through the formation of aldolated dianions, but not by the retro-aldol aldol process. A proposed mechanism is illustrated in Scheme 1 based on distal aldolate dianions[3] when excess strong base was used during the aldol condensation.

In summary, in our experiments *syn*- and *anti*-aldols were produced at the same time, whether the starting enolate was the *Z*- or *E*-enolate, in the directed aldol condensation when using an excess amount of strong base, as explained by the above-proposed mechanism.



Scheme 1 The proposed mechanism based on the distal aldolate dianions.

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References

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3 For reports on the isomerization of aldols *via* an enol or enolate mechanism, see: (*a*) V. A. Martin, D. H. Murray, N. E. Pratt, Y. Zhao and K. F. Albizati, *J. Am. Chem. Soc.*, 1990, **112**, 6965; (*b*) D. E. Ward, M. Sales and P. K. Sasmal, *Org. Lett.*, 2001, **3**, 3671 and references cited therein.

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