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Catalytic asymmetric vinylogous Mukaiyama (CAVM) reactions: aldehyde activation versus enolate activation

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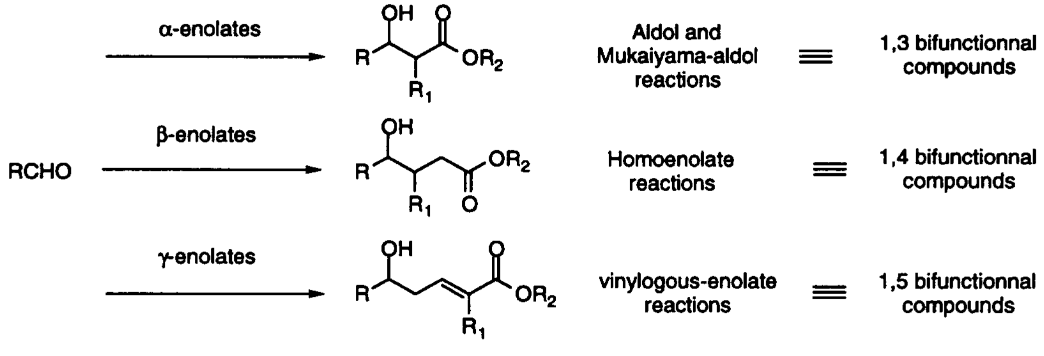
Abstract

The catalytic asymmetric vinylogous Mukaiyama (CAVM) reactions of various aldehydes using either aldehyde or enolate activations are described. © 1999 Elsevier Science Ltd. All rights reserved.

Reactions of aldehydes with α (aldol reactions), β (homoenolate reactions) and γ (vinylogous-enolates) enolates (Scheme 1) have found an increasing number of applications in the construction of natural products.[1] Furthermore, impressive results have been obtained in asymmetric homoenolate[2] and aldol[3] reactions. More recently, highly efficient catalytic asymmetric Mukaiyama-aldol reactions have been described.[4] However, to the best of our knowledge,[5–7] an asymmetric version of the vinylogous-aldol reaction has not yet been described.[8]



Scheme 1.

We would like to report herein our preliminary results on the development of a catalytic asymmetric system for the vinylogous Mukaiyama reaction.[9] To this end, we envisioned two types of catalytic systems (Scheme 2): the activation of the aldehyde using an enantiomerically pure Lewis acid, and the activation of the enolate using a chiral salt.

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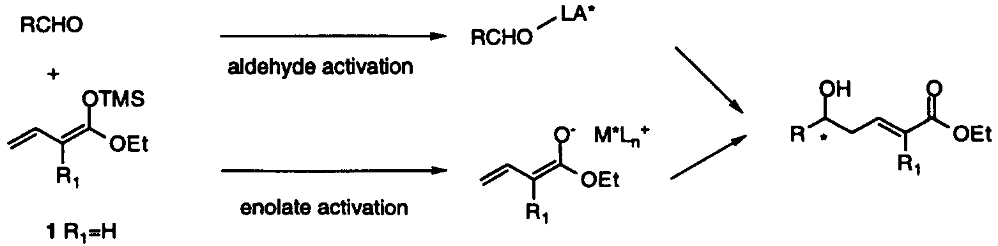
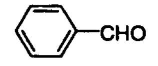
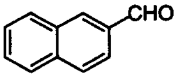
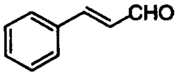
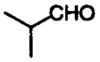


1 R$_1$=H
2 R$_1$=Me

Scheme 2.

Results obtained in the CAVM reactions of various aldehydes and vinylogous enolate **2**[10] using either (*R*)-binol-Ti(*i*PrO)$_4$ (aldehyde activation) or CuF_2((*S*)-tol-binap)[7] (enolate activation) are summarized in Table 1.

Table 1
CAVM reactions of aldehydes using aldehyde activation (A) and enolate activation (B)

Entry	Aldehyde	Conditions	Yield (%)	Ee (%)
1		A	45	75[a]
2		B	80	70[a]
3		A	25	75[b]
4		B	70	48[b]
5		A	45	60[c]
6		B	35	56[c]
7		A	18	70[d]
8		B	68	77[d]

Conditions : A : $Ti(OiPr)_4$ / (R)-binol 20%, DCM, rt. B : ((S)-tol-binap)-CuF_2 10%, THF, rt. HPLC : a) DAICEL-OJ (hex-iPrOH 95:5) ; b) DAICEL-OD (hex-iPrOH 90:10) ; c) DAICEL-OD (hex-iPrOH 80:20) ; d) DAICEL-OD (hex-iPrOH 98:2).

In both activation modes, the γ-aldol products were obtained in 18–80% yield, and 48–77% enantiomeric excesses, particularly impressive in the case of the enolate activation since the chiral moiety is supposed to be far away from the prochiral aldehyde.

In conclusion, the conceptually new asymmetric enolate activation appears to be an ideal complement to the traditional Lewis-acid aldehyde activation in the development of catalytic asymmetric vinylogous Mukaiyama reactions.

Further developments, determination of the absolute configuration, and the application of this strategy to the synthesis of natural products are currently in progress and will be published in due course.

Acknowledgements

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