The role of β-bulky alkyl substituents in aldol reactions of boron enolates of methylketones with aldehydes

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INTRODUCTION

Recently, we described that the levels of 1,5-syn selectivities in aldol reactions involving boron enolates of β-alkoxy methylketones, where the β-alkoxy protecting group is TBS, are dependent on the volume of the alkyl substituent in β-position (Scheme 1).

Scheme 1. Aldol reactions.

Based on these results, we prepared methylketone 5 in order to assess the steric contribution of the β-alkyl substituent in reactions of the corresponding boron enolates with achiral aldehydes.

RESULTS AND DISCUSSION

Our studies began with the preparation of methylketone 5. Treatment of acid 6 with LiAlH4 (69%) followed by Swern oxidation (96%) provided 7. Aldol reaction between 7 and 8 (99%) followed by treatment with TBSOTf (85%) lead to the formation of 9. Finally, treatment of 9 with MeLi gave methylketone 5 in 99% yield (Scheme 2).

Scheme 2. Preparation of methylketone 5.

The aldol reactions of methylketone 5 with aldehydes 10a-g were investigated using (c-Hex)3BCl and Et3N in Et2O, providing the 1,5-syn and 1,5-anti aldol adducts (Scheme 3, Table 1).

Scheme 3. Aldol reactions of 5 with RCHO.

Table 1. Aldol reactions of 5 with RCHO.

* Ratio was determined by 1H and 13C NMR analysis of the diastereoisomeric mixture of aldol adducts. † Isolated yields of both isomers after SiO2 gel flash chromatography.

These boron-mediated aldol reactions were found to proceed with good yields and excellent levels of remote 1,5-syn stereinduction. The relative stereochemistry for aldol adducts 11a-g and 12a-g was unambiguously established on the basis of Kishi methodology.

CONCLUSION

The stereoinduction observed in these reactions shows that the levels of 1,5-syn selectivities in aldol reactions are really dependent on the volume of the alkyl substituent at the β position.

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REFERENCES


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