Boron-mediated aldol reactions of a methyl ketone containing a cyclic silicon protecting group

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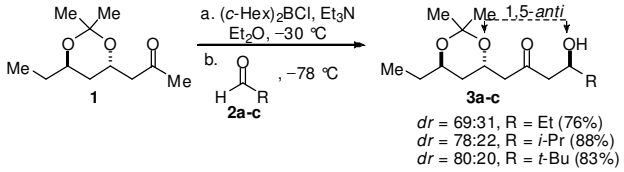
INTRODUCTION

We have showed that aldol reactions involving boron enolates of methyl ketone containing a *trans* acetonide **1** with achiral aldehydes provided the corresponding aldol adducts with moderate to good levels of diastereoselectivity, favoring the 1,5-*anti* adduct.[1]

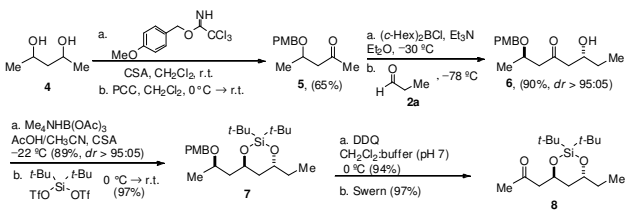
Scheme 1. Aldol reactions of methyl ketone **1**.



In this work we report the use of the boron enolate generated from methyl ketone **8**, containing a cyclic silicon protecting group in a *trans* relationship in aldol reactions with achiral aldehydes. Our intention is to evaluate the steric and eletronic effect of the silicon protecting group in the selectivity of the reactions.

RESULTS AND DISCUSSION

Treatment of **4** with PMB-acetimidate followed by oxidation with PCC resulted in **5** (65%, 2 steps). The aldol reaction between the boron enolate of methyl ketone **5** and aldehyde **2a** gave aldol adduct **6** (90%, *dr* > 95:05). Treatment of **6** with $Me_4NHB(OAc)_3$ (89%, *dr* > 95:05) followed by treatment with DTBS ditriflate resulted in **7** (97%). The compound **7** was treated with DDQ (94%) followed by Swern oxidation providing methyl ketone **8** (97%) (Scheme 2).



Scheme 2. Preparation of methyl ketone **8**.

The aldol reactions of the methyl ketone **8** with aldehydes **2a-g** were investigated using (*c*-Hex)$_2$BCl and Et_3N in Et_2O, providing the 1,5-*anti* and 1,5-*syn* aldol adducts (**10a-g** and **11a-g**) (Scheme 3, Table 1).

Scheme 3. Aldol reactions of methyl ketone **8**.

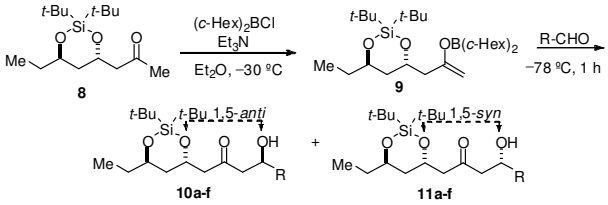


Table 1. Aldol reactions of methyl ketone **8**

ent	Aldehyde (R)	*dr*[a] (1,5-*anti*:1,5-*syn*)	Yield (%)[b]
1	Et (**2a**)	88:12	88
2	*i*-Pr (**2b**)	83:17	92
3	*t*-Bu (**2c**)	72:28	84
4	Ph (**2d**)	66:34	88
5	*p*-$NO_2C_6H_4$ (**2e**)	64:36	84
6	*p*-$OMeC_6H_4$ (**2f**)	67:33	89

[a] Ratio determined by ^1H and ^{13}C NMR analysis of the diastereoisomeric mixture of aldol adducts. [b] Isolated yields of both *anti* and *syn* isomers after SiO_2 gel flash column chromatography.

These results shown that aldol reactions involving the methyl ketone **8** provided the corresponding aldol adduct with moderate to good levels of diastereoselectivity favoring the 1,5-*anti* diastereoisomer.

The relative stereochemistry of aldol adducts **10a-f** was determined using the Kishi/Kobayashi method.[2]

CONCLUSION

We have demonstrated that the proper choice of protecting group is very important, as better selectivities were observed for less hindered aldehydes in the case of methyl ketone **8** (entries 1-3).

ACKNOWLEDGEMENTS

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REFERENCES

[1] Polo, E. C. "Controle da estereoquímica remota 1,5 em adições de enolatos de boro de metilcetonas a aldeídos"; Dissertação de Mestrado, UNICAMP, **2011**.

[2] Kobayashi, Y.; Tan, C.-H.; Kishi, Y. *Helv. Chim. Acta* **2000**, *83*, 2562.