Synthesis of Oxopyrazolidine-1-carboximidamides from Morita Baylis-Hillman adducts

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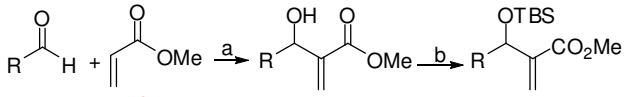
INTRODUCTION

Pyrazolidin-3-ones derivatives, including 5-oxopyrazolidine-1-carboximidamides, are an important class of compounds, which possess widespread pharmacological properties such as analgesic, antipyretic and anticancer. Several synthetic approaches have been developed to access pyrazolidin-3-one rings. In this work we disclose a facile and diastereoselective synthetic approach to prepare oxopyrazolidine-1-carboximidamides derivatives from Morita-Baylis-Hillman (MBH) adducts. Our approach is based on a tandem sequence involving a Michael addition reaction and cyclization, which forms in a single step a new cycle and controls the relative stereochemistry of two centers.

RESULTS AND DISCUSSION

The MBH adducts were prepared according to a methodology we described some years ago. In brief, aldehydes were treated with methyl acrylate to provide the corresponding MBH adducts (**7-11**) in good yield. Treatment of MBH adducts **7-11** with TBS trifluoromethanesulfonate gave the corresponding silylated derivatives (**12-16**) in excellent yields (Table 1).

Table 1. Preparation of silylated MBH adducts



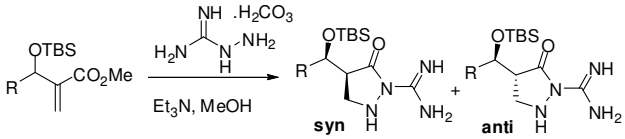
1-5 6 7-11 12-16

Reagents and conditions: a. DABCO, ultrasound; b. TBSOTf, Et_3N, CH_2Cl_2, r.t.

Entry	R	Adduct (a)	Silylation (b)
1	3-Cl-Ph	7, 91%	12, >99%
2	2-F-Ph	8, 87%	13, 94%
3	4-OMe-Ph	9, 72%	14, >99%
4	Py	10, 81%	15, 93%
5	4-NO_2-Ph	11, 97%	16, 97:%

Having the MBH adducts in our hands, we react them with aminoguanidine carbonate (1.5 eq.) in the presence of triethylamine. Some oxopyrazolidine-1-carboximidamides were easily prepared in good yield and high diastereoselectivity (Table 2). We rationalize that the diastereoselectivity is resulting from the control exerted by the voluminous silyl group. Our previous results support this proposition.

Table 2. Oxopyrazolidine-1-carboximidamides from MBH adducts.



12-16 17-21

Silylated adduct	R	Yield	Prod./Diast
12	3-Cl-Ph	79	17, 5:1
13	2-F-Ph	77	18, 6:1
14	4-OMe-Ph	81	19, 5:1
15	Py	57	20, 5:1
16	4-NO_2-Ph	80	21, 3:1

*Diastereoselectivity was determined by ^{1}H NMR, by measuring the coupling constant of the carbinolic proton.

CONCLUSION

In summary, we have demonstrated that oxopyrazolidine-1-carboximidamides can be prepared in good yields and diastereoselectivity from MBH adducts.

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