An expeditious approach to tetrahydroindolizines from Morita-Baylis-Hillman Adducts

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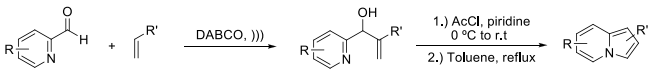
INTRODUCTION

Indolizines are important building blocks for synthesis of biomarkers, drugs and alkaloids that posses the indolizidinic core. This type of heteroaromatic skeleton can be prepared using different approaches.[1] Recently Morita-Baylis-Hillman adducts were used as building block for the synthesis of indolizidinic unity[2,3]. However, applications of these molecules remain almost unexplored.

In this communication, we disclosed our preliminary results on a simple strategy to access tetrahydroindolizines and indolizidines by partial or total hydrogenation of indolizines prepared from MBH adducts.

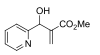
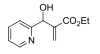
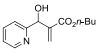
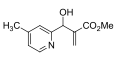
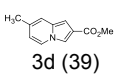
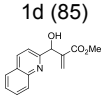
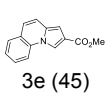
RESULTS AND DISCUSSION

The indolizines **(3a-f)** were prepared from MBH adducts **(1a-f)** according to a methodology reported on literature some years ago.

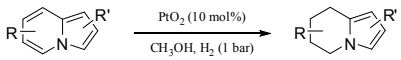


Scheme 1. Preparation of indolizines from MBH adducts

Table 1. Indolizines from MBH adducts.

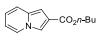
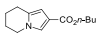
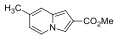
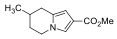
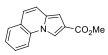
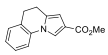
Entry	Aldehyde	Olefin	MBH Adduct (Yield %)	Indolizine (Yield)
1			 1a (93)	 3a (55)
2			 1b (96)	 3b (52)
3			 1c (93)	 3c (59)
4			 1d (85)	 3d (39)
5			 1e (88)	 3e (45)

With the indolizines in our hands, hydrogenation reactions were performed. Four protocols were tested. First, we decide to reproduce an experiment described previously where the Adam´s catalyst (PtO_2) were used under 1 atm hydrogen atmosphere. In these cases, we observed partial reduction of indolizines, affording tetrahydroindolizines as unique products in excellent yields (Table 2). The same results can be obtained using Pd/C catalyst. However, when Rh/C and Rh/Al_2O_3 catalysts were used, no reduction was observed.



Scheme 2. Preparation of tetrahydroindolizines

Table 2. Tetrahydroindolizines from indolizines

Entry	Indolizine	Tetraidroindolizine	Yield (%)
1	 3a	 4a	93
2	 3b	 4b	91
3	 3c	 4c	95
5	 3d	 4d	79
6	 3e	 4e	67[a]

[a] Reactions were carried out in 48h under 4 bar hydrogen atmosphere.

CONCLUSION

Our results clearly demonstrated that partial reduction of indolizines can be achieved in excellent yields, at low pressure, using simple reducing agents. Studies focused on partial or total asymmetric hydrogenation using homogeneous catalysts are ongoing in our laboratory.

ACKNOWLEDGEMENTS

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