



Preparation and preliminary evaluation of new organometallic bases from *cis*-2,6-dimethylpiperidine

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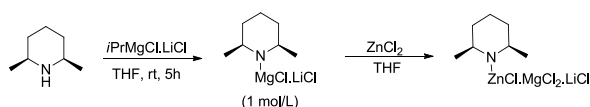
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INTRODUCTION

Recently, magnesiate and zincate reagents have proven their synthetic importance for the functionalization of arenes.¹ In addition, mixed Li/Mg and Li/Zn amides prepared from 2,2,6,6-tetramethylpiperidine (TMPH) are highly soluble and active bases that allow smoothly metalation of various aromatic and heteroarenes with an excellent functional group tolerance.² In this work, we have been investigating the preparation and the reactivity of mixed metal bases from *cis*-2,6-dimethylpiperidine (DMPH) as alternative for TMP-metal bases.

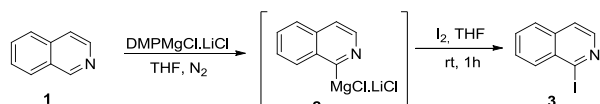
RESULTS AND DISCUSSION

The mixed lithium/magnesium base DMPMgCl.LiCl was prepared in THF through the direct reaction of the *cis*-2,6-dimethylpiperidine (DMPH) with the turbo Grignard *i*-PrMgCl.LiCl. Titration against benzoic acid using 4-(phenylazo)-diphenylamine as indicator indicated that the desired base was produced with the concentration of 1 mol/L. On the other hand, the zinc base DMPZnCl.LiCl was prepared through the reaction of DMPMgCl.LiCl with ZnCl₂ in THF (Scheme 1).



Scheme 1

In order to investigate the reactivity of the base DMPMgCl.LiCl, we have used isoquinoline as a model substrate (Scheme 2).



Scheme 2

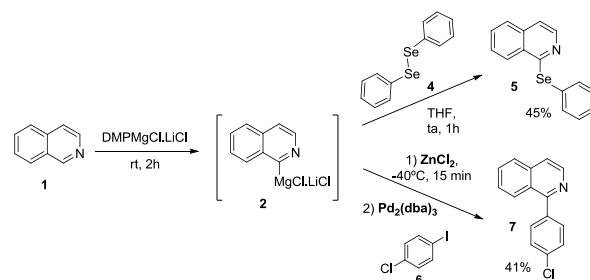
The metalation was monitored by CG analysis of the aliquots of the reaction mixture that were quenched with iodine. Results are presented in Table 1. As observed, the best conversion was obtained when 2 equiv. of the base was used, leading to the iodide **3** with 89% isolated yield. This strategy has been applied to the synthesis of other functionalized isoquinoline, some examples are presented in the below (Scheme 3).

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Table 1. Tests of reaction conditions for the direct metallation with isoquinoline DMPMgCl.LiCl

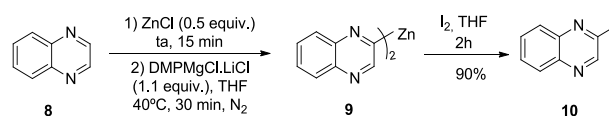
Entry	Base (Eq)	Reaction time	Temperature	Conversion GC
1	1.1	1h	r.t.	35,14 %
2	1.1	3h	r.t.	4,91%
3	1.3	1h	r.t.	59,24 %
4	1.5	1h	r.t.	88,48 %
5	1.5	1h	0°C	4,66 %
6	1.8	1h	r.t.	92 %
8	2	1h	r.t.	> 98%

*r.t. = room temperature



Scheme 3

The zinc base DMPZnCl.LiCl presented low reactivity against the substrate tested. However, organozinc reagents of type **9** could be prepared by using the strategy presented below (Scheme 4).



Scheme 4

CONCLUSION

The base DMPMgCl.LiCl has been prepared and presented good reactivity for the functionalization of the heterocyclic substrates such as isoquinoline and quinoxaline. The scope of the methodology is now under investigation in our laboratories.

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