Directed Magnesiation of Haloaromatic Oxazolines using the mixed lithium/magnesium base TMPMgCl.LiCl

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INTRODUCTION

The metallation of aromatics is a convenient approach to the functionalization of unsaturated scaffolds. Polyfunctional aryl halides are of high importance as agrochemicals, pharmaceuticals and building blocks. Recently, mixed lithium/magnesium amides such as TMPMgCl.LiCl and TMP₂Mg.2LiCl have proven to be interesting bases for functionalization of arenes under mild conditions. In this work we wish to report the use of magnesium amides for the magnesiation of several haloaromatics oxazolines and subsequent reactions with electrophiles.

RESULTS AND DISCUSSION

The oxazolines were prepared by condensation of aldehydes with aminoalcohol, providing the products with yields ranging from 75 to 90% (Scheme 1).

Scheme 1: Preparation of oxazolines.

The mixed Li/Mg base was obtained through the direct reaction of 2,2,6,6-tetramethylpiperidine (TMPH) with i-PrMgCl.LiCl (Scheme 2).

Scheme 2: Preparation of TMPMgCl.LiCl

The magnesiation of haloaromatics oxazolines with TMPMgCl.LiCl was achieved within 2 h at room temperature. Further reaction several electrophiles led to the expected functionalized oxazolines in good yields (Scheme 3, Table 1).

Scheme 3: Magnesiation of oxazolines

Table 1. Products obtained after directed magnesiation of oxazolines

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<thead>
<tr>
<th>Compound</th>
<th>Reactant</th>
<th>Yield</th>
<th>Reaction Conditions</th>
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[a] Yield of isolated, analytically pure product.
[b] A transmetalation with ZnCl₂ (1.1 equiv.) and Pd-catalyzed cross-coupling using 2 mol% Pd(dba)₃, 4 mol% and tfp were performed.

CONCLUSION

The metallation of haloaromatic oxazolines using TMPMgCl.LiCl was successfully achieved under mild conditions. The resulting Grignard reagents can be combined with a large number of electrophiles to provide highly functionalized oxazolines in good yields.

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REFERENCES


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