



Synthesis of enantioenriched 3-substituted phthalides using chiral organomagnesiates

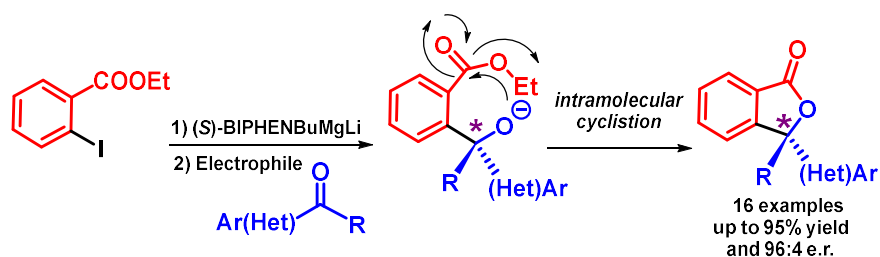
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The synthesis of new functionalised (hetero)aromatic compounds is an omnipresent challenge for the synthetic chemist due to their multiple and varied applications. Indeed aromatics and heterocycles moieties are everywhere in day life. Thus, novel methodologies are continually being sought for their synthesis. Many methodologies exist already but metallation reactions, deprotonation or metal-halogen exchange, are powerful method for it. In recent years, it has been discovered that heterobimetallic reagents composed of a polar organometallic (e.g. an organolithium) and a “soft” organometallic (e.g. organomagnesium) can performed metalation reactions with an increased selectivity and reactivity compared to the monometallic reagent.[1]

Our laboratory has been focusing on developing chemistry using bimetallic ate complexes and reported their preparation and use for the asymmetric synthesis of pyridyl and pyrazyl carbinols.[2] The X-Ray and NMR characterization of the BIPHEN-based magnesiate and resulting azinylorganometallic intermediate revealed a perfectly controlled arrangement of the ligands around the central metal[3] as a single compound allowing for a high level of enantiocontrol along the reaction of azinylmagnesiates with aldehydes.

Based on these precedents, we decided to explore the reactivity of chiral organomagnesiates for the synthesis of chiral 3-substituted isobenzofuranones. We have obtained the proof of concept that a BIPHEN-based chiral monobutylmagnesiates ((S)-BIPHENBuMgLi) can efficiently promote the enantioselective magnesiationlactonization of 2-iodobenzoates opening access to chiral 3-substituted Isobenzofuranones.[4] The reaction was found to be effective with aromatics with electron-withdrawing and electron-releasing substituents, heteroaromatic and aliphatic (enolizable) aldehydes. Moreover, the reaction has been performed using recovered and recrystallized (S)-BIPHEN H2 that furthermore improves the enantioselectivity of the reaction.



References

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