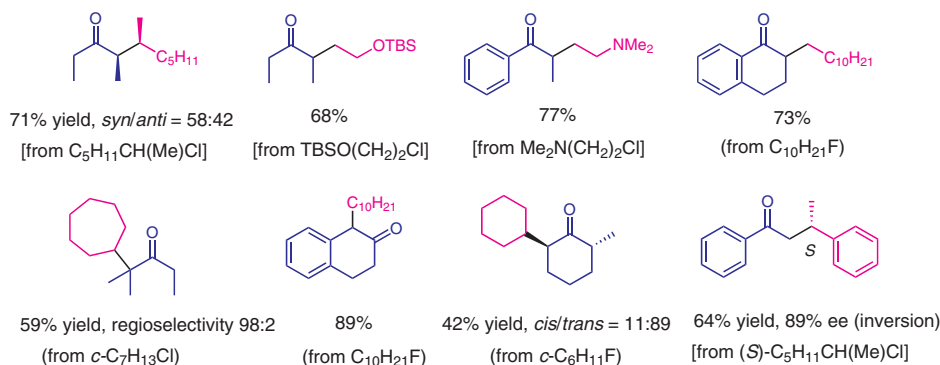
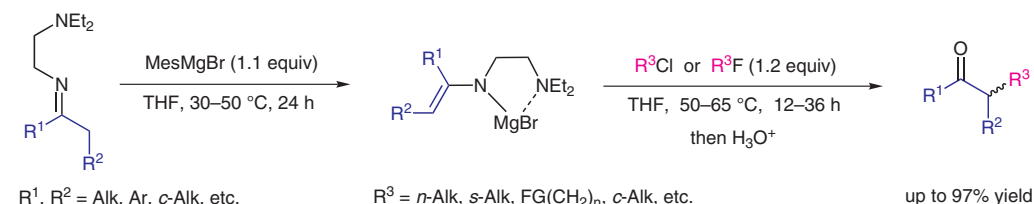


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Regioselective α -Alkylation of Ketones with Alkyl Chlorides and Fluorides via Highly Nucleophilic Magnesium Enamides

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Regioselective α -Alkylation of Ketones via Magnesium Enamides



Significance: Alkylation of ketones via their metal enolates is one of the fundamental C–C bond-forming reactions in organic chemistry. However, the scope and selectivity of this process is often not satisfactory. The authors report herein a great improvement of this reaction, allowing to use usually unreactive primary and secondary alkyl chlorides and fluorides as electrophiles, with excellent regio- and often good stereoselectivity. Use of enantiopure benzyl halides afforded products with good enantioselectivities.

Comment: This elegant approach is based on the formation of highly nucleophilic magnesium enamides with inner coordination N–Mg bond. The imines are prepared by the usual way from the corresponding ketones. A large variety of electrophiles are now suitable for the alkylation. The reaction of α -phenylethyl chloride proceeds mostly with inversion, though racemization may take place under harsh conditions. Probably, an enantioselective version of this reaction can be developed using a chiral amine auxiliary.

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