First substoichiometric version of the catalytic enantioselective addition of an alkyllithium to an aldehyde.

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Supplementary Information

Typical procedure of the catalytic substoichiometric enantioselective nucleophilic 1,2-addition of methyllithium onto ortho-tolualdehyde.

Methyllithium (0.30 mmol, 1.2 equiv., 1.6 M in diethylether) was added to a solution of 3APH (0.25 mmol, 0.33 equiv.) in THF (15 mL) at -20°C under an atmosphere of argon. After stirring for 20 min., a second aliquot of MeLi (0.90 mmol, 1.2 equiv. 1.6 M in diethylether) was added dropwise to the preformed solution of lithium amide (3APLi). The resulting mixture was stirred for 30 min. at -20°C. The mixture was cooled to -78°C and let for 30 min. at this temperature. A solution of o-tolualdehyde (0.75 mmol, 1 equiv.) and LiCl (0.33 equiv., 0.3 M in THF) in THF (4 mL) was added at -78°C over a 1h period and the mixture was stirred at -78°C for another hour. The medium was then quenched at the same temperature with a 3 M aqueous HCl solution (3 mL) and was extracted with diethylether (3 x 10 mL) at room temperature. The combined organic layers were washed with aqueous NaHCO3 (saturated, 10 mL) then brine (10 mL), dried with MgSO4 and concentrated under reduced pressure. The residue was purified by column chromatography (Et2O / cyclohexane, 3:7) to give 1-o-tolylethanol in 80% yield. The analytical data are in full agreement with data in literature: Li, W.; Sun, X.; Zhou, L.; Hou, G.; Yu, S.; Zhang, X. J. Org. Chem. 2009, 74, 1397-1399.
NMR spectra of o-TolCH(CH₃)OLi / LiCl mixed aggregate

Addition of lithium chloride on the lithium (R)-1-o-tolylethanolate. Enlargement of 1D ¹H and 1D ⁶Li spectra recorded in THF at 195K. a) ⁶LiCl polluted by solvents. b) lithium (R)-1-o-tolylethanolate. c) Addition of 0.33 eq. of ⁶LiCl. d) Addition of 0.66 eq. of ⁶LiCl. e) Addition of 1 eq. of ⁶LiCl. f) Addition of 2 eq. of ⁶LiCl.