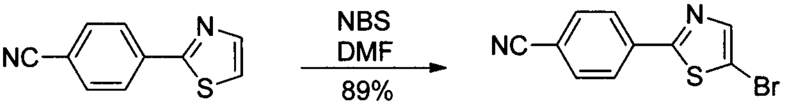
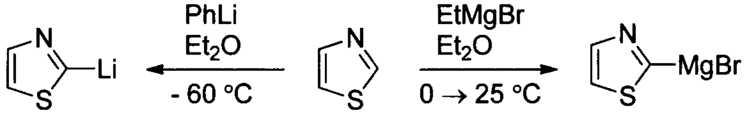
This reaction has also been used in the syntheses toward diamidino 2,5-bis(aryl)thiazoles exhibiting antiprotozoal activity against *Trypanosoma brucei rhodensiense* (T. b. r.) and *Plasmodium falciparum (P. f.),* shown below. Here, the synthesis involved conversion of derivatized thiazoles to bromothiazoles as substrates for Suzuki cross-couplings.[34]

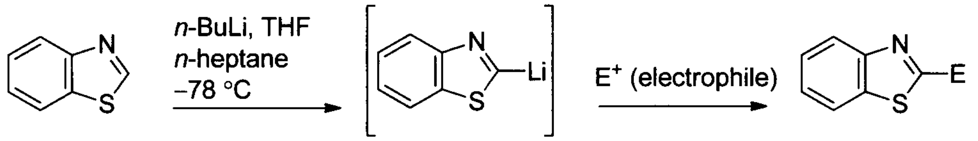


7.2.2 C-Metalation

The proton on the C2 position of the thiazole ring possesses higher kinetic and thermodynamic acidity than the ones on C4 and C5.[35] Organolithiates and Grignard reagents attack thiazoles and benzothiazoles thereby acting as strong bases *via* deprotonation. Deprotonation of thiazoles and benzothiazoles at the C2 position is well understood and has been employed in combination with various electrophiles. For example, thiazole deprotonation with *n*-butyl lithium at low temperatures and the reaction of its corresponding lithiate with an aldehyde is well known.[36]



Benzothiazoles undergo reactions similarly at the 2-position through deprotonation in the presence of a base such as *n*-butyl lithium.[37]



Florio et al. have found that 2-lithio-4-methylthiazole can be conveniently generated almost quantitatively by the deprotonation of 4-methyl-thiazole with lithium diisopropylamide (LDA) in THF at −78 °C. Addition of α-chloroacetone to the solution yields the corresponding chlorohydrins.[38]