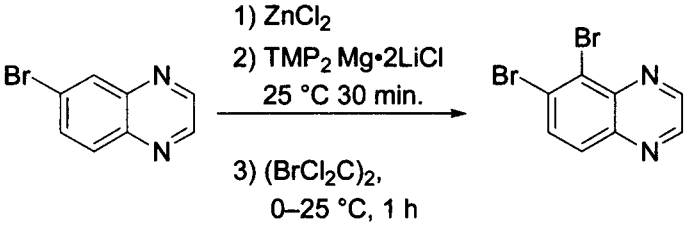
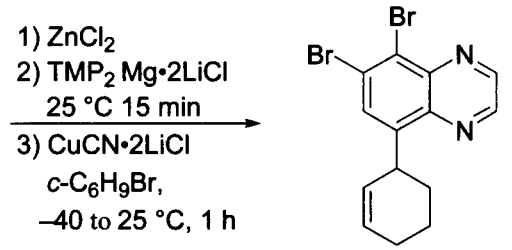
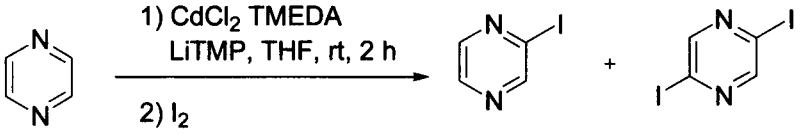
position to that substituent. A second functionalization would occur at the first available site to the benzo-fused ring.





Difunctionalization of pyrazines to form 2,5-diiodopyrazine was an important synthetic goal because of the multiple applications of this type of molecule. The first dihalogenation of pyrazine was accomplished using cadmium ion salt in moderate yield.[50] This reaction is controllable to the point that modifying the equivalence of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) to provide the selective formation of either the monohalogenated or dihalogenated aromatic ring.



TMEDA (eq)	% Recovered	% Recovered
0.33	63%	0%
1.00	0%	58%

12.4 Coupling Reactions

12.4.1 Transition-metal coupling reactions

Direct arylation of aromatic compounds by C–H activation with aryl halides by transition metal catalysis has become an important synthetic process.[51] However until recently the reported procedures were limited to only electron-rich aromatic rings and heteroaromatic compounds. Biaryl compounds containing pyrazine were isolated in moderate to high yields when potassium