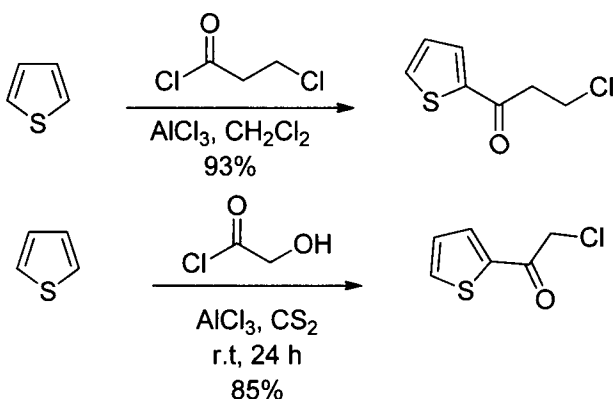
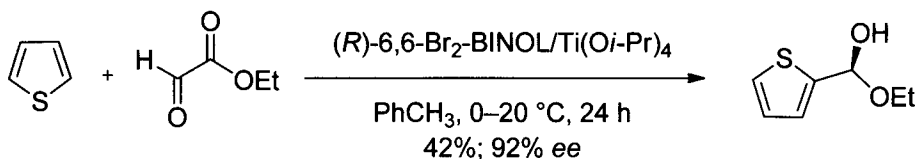


The following acylation reactions of thiophenes are regioselective (*C2*) and high yielding. Both reactions are key C–C bond forming reactions that have been used in the synthesis of duloxetine.^{79,80}



Jurczak and co-workers have developed an enantioselective variation of the Friedel–Crafts reaction to produce hydroxyl(thiophene-2-yl)acetates from the reaction of thiophenes with glyoxylates in the presence of a chiral BINOL–titanium catalyst.⁸¹ The desired thiophenes can be produced in high enantiomeric excess and can be utilized as a key intermediates in the synthesis of duloxetine.



Vilsmeier–Haack Reaction

The Vilsmeier–Haack reaction has been used in the synthesis of thiophenes with potential anti-inflammatory properties. The electron-rich ring of the thiophene system makes it an ideal nucleophile for the Vilsmeier–Haack