CHAPTER IV

CONCLUSION

The work had focus on the synthesis of α-aminophosphonates *via* nucleophilic addition of diethyl phosphite to imines including asymmetric and non-asymmetric synthesis. For asymmetric synthesis, the enantiomeric composition of the resulting α-aminophosphonates could be monitored by ^{1}H NMR spectroscopy. It was found that although acceptable yield of the product was obtained, none of the chiral catalysts based on metal-salen and related ligands could induce stereoselectivity in the hydrophosphonylation of *N*-benzylidenebenzylamine. We have also investigated (*S*)-phenylglycinol as an auxiliary for asymmetric hydrophosphonylation of aldimines in the presence of achiral Lewis acids as catalyst. Among all Lewis acids tested, LiCl was found to be the best catalyst in the diastereoselective hydrophosphonylation of imines derived from (*S*)-phenylglycinol. It was also found that the aldimine derived from aromatic aldehyde gave fair yield and high diastereoselectivity whereby the aliphatic aldehydes only gave moderate yield and diastereoselectivity.

A novel synthetic method of α-aminophosphonates has also been developed by base catalyzed addition of diethyl phosphite to *N*-Boc imines generated *in situ* by the action of a suitable base on α-amidoalkylphenyl sulfones. The results indicated that the desired addition reaction took place quickly in the presence of DBU when aromatic α-amido sulfones were used to give the protected aminophosphonic acid in high yields (60-95%). In addition to Boc, other *N*-protecting groups such as formyl, acetyl, benzyloxy carbonyl, and ethoxycarbonyl also gave the desired products in good yield (50-80%). Furthermore, for the aliphatic α-amido sulfones, the suitable base was K_2CO_3 in MeCN. The reaction required longer reaction time and provided slightly lower yield than the aromatic substrates. The protecting group were removed by acid hydrolysis in hot concentrated HCl to give high yield of desired α-aminophosphonic acids in racemic form. Attempts have also been made to develop an asymmetric synthesis version of this method, although this was not yet successful.