CHAPTER IV
CONCLUSION

The investigation had been carried out to search for novel chiral ligands containing soft donor atom complexing with transition metal for catalytic asymmetric nucleophilic addition to carbonyl compounds. The work had focused on the utilization of various optically active catalysts including those derived from chiral amino alcohols with appropriate metals as well as reaction conditions. It was found that the enantiomeric composition of the resulting β-nitroalkanols could be monitored by chiral HPLC. The results described herein indicated that the simple thiolated amino-alcohols ligand (**69**) as well as thiophene-based amino-alcohol ligands (**70**) was suitable for asymmetric nitro-aldol reaction under relatively mild conditions at room temperature. The copper(II) acetate complexing of amino-alcohol ligands bearing *N*-(2-alkylthio)benzyl substituents (**69**) provided only modest enantioselectivities (22-46% ee) while those carrying *N*-2-thienylmethyl substituents, (*R*)-**70b** complexed with copper(II) acetate provided better enantioselectivities (up to 75% ee). Attempts to increase the steric bulk of the thiophene unit resulted in no major improvement in enantioselectivity. Similar attempts on the amino alcohol moiety also proved unsuccessful. Furthermore, in order to investigate the necessity and the role of the thiophene moiety in chiral thiophene-based amino-alcohol ligand on the stereochemical outcome of the reaction, other non-thiophene amino-alcohol ligands including five-membered heteroaromatic rings and some benzo-fused analogues, were synthesized and used in place of the thiophene. The results showed that enantioselectivity of the product was not as good as those obtained with the original thiophene-based ligand, (*R*)-**70b**. Moreover, other types of chiral amino-alcohol based ligands forming bidentate complexes with copper(II) were also employed in nitro-aldol reaction. The results revealed that a moderate degree of selectivity was obtained when (*R*)-**73a** having a phenyl ring in place of thiophene ring (52% ee). In addition, substrate generality investigation revealed that a range of aromatic aldehydes were acceptable for the nitro-aldol reaction with nitromethane, giving moderate to good enantioselectivities (61-88% ee) using chiral ligand (*R*)-**70b**.

To expand the utilization of these chiral amino-alcohol ligands in other asymmetric reactions, the ligands were also tested for enantioselective reactions. This includes asymmetric borohydride reduction, asymmetric borane reduction, asymmetric benzoylation, and 1,4-additions of indole to benzylidene malonate. Some of the selected chiral ligands were tested using the optimized conditions. For borohydride reduction, the C_2-symmetrical diamine ligand (**49**) could induce the enantioselectivity of secondary alcohol up to 76% ee while other type of ligands of interest failed to do so. As for asymmetric borane reduction, it was found that the ligands of interest were not suitable for this reaction system since bidentate ligands were generally found to give low enantioselectivities. Successful kinetic resolution of (±)-hydrobenzoin was achieved by benzoylation in the presence of copper(II) chloride and the C_2 symmetrical ligands, (*R*)-**70l** and **49a**. In addition, a preliminary study on the possibility to use this type of ligands in asymmetric Michael addition, a selection of ligands as well as a variety of metal salts were tested. These chiral ligands complexing with various metal salts could indeed induce the enantioselectivity of the Michael reaction, however, to an unsatisfactory degree especially when compared to those reported previously. There is, however, an opportunity for further improvement under a more thorough study in the future.