CHAPTER IV

CONCLUSION

1,3,5-Triacetyl-2,4,6-trihydroxybenzene **(53)** was synthesized in one-pot, one step process in high purity up to 91% yield from excessive acetylations of phloroglucinol dihydrate upon treatment with excess acetyl chloride and $AlCl_3$. The synthesis had been extended to use other acid chlorides such as cinnamoyl chloride, *N,N*-dimethylcarbamoyl chloride and chloroacetyl chloride. It was found that only chloroacetyl chloride could give the expected hexasubstituted benzene product **60** in 54% yield, although the ^{1}H-NMR data showed the ratio of the peak area of phenolic hydroxy protons and methylene protons were observed to be approximately 1:3 rather than the expected 1:2. It was possible that the integration of hydroxyl protons might not be fully included. The acetylations and chloroacetylations were repeated with 1,3,5-trimethoxybenzene. The desired hexasubstituted benzene products were not found in these cases. Phenol derivatives **63** and **64** were formed instead, presumably by initial demethylations followed by acetylations.

1,3,5-Triformyl-2,4,6-trihydroxybenzene **(51)** has been successfully synthesized either by Duff reaction or Reimer-Tiemann reaction. Compound **51** was found to be relatively unstable and speculated that its oxidation could have readily happened to yield the corresponding tricarboxylic acid **59**. Excessive methylations of compound **51** were immediately performed giving the expected product **66**, which was still not stable enough to be used in subsequent transformations. Phloroglucinol could be coupled with excess *p*-tolyl aromatic diazonium salt to create the corresponding tris-diazo compound **69** in quantitative yield.

The arrangements into the facially segregated hexasubstituted benzene (*ababab* geometry) were achieved by triple *O*-alkylations on phenolic hydroxy groups with alkylating agents. The reaction of compound **53** with dimethyl sulfate, benzyl bromide or 1,5-dibromopentane generated the symmetric compounds **70**, **71** and **72** in 93%, 72% and 77% yield, respectively. Compound **70** was further brominated with

NBS at α-carbon atoms providing the desired tribromo product **73** in 17% yield. However, the major product of the reaction was compound **74** from the repeatedly brominated three times at the same α-carbon of the starting material. Exhaustive iodination of compound **53**, **70** and **71** were performed on methyl ketone moieties. The yellow precipitate of CHI_3 was observed in the reactions of compound **53** and **70** expecting that their corresponding tricarboxylic acids were formed. Nevertheless, the products could not be confirmed the structures by NMR and Mass spectroscopy. Functionalization on the carbonyl groups was achieved when treating compound **70** with hydroxylamine hydrochloride to produce compound **75** in 53% yield. Unfortunately, many other attempts on the carbonyl functionalizations of compound **53** and **70** were not successful and the condensed products seemed to be easily converted back to their starting materials. Mixture of various products and unreacted starting material were often encountered.

Tripodal ligands based on compound **53** as the core structure were synthesized. Tripodal ligand **86** has been prepared in three steps. Triple *O*-alkylations by 1,5-dibromopentane generated the symmetric intermediate **72**. The subsequent substitutions with sodium azide followed by reduction achieved the tris-amine **86** in overall 59% yield starting from compound **53**. Moreover, intermediate **72** could be converted to chiral tripodal ligand **94** by aminations with (*R*)-(+)-1-phenylethylamine in basic condition in 34% overall yield. Tripodal ligand **100** has also been produced in three steps from compound **53**. Alkylations of compound **53** with dimethyl sulfate obtained compound **70**, which was condensed with hydroxylamine to generate compound **75** followed by substitutions with Boc-L-Pro-OSu. Ligand **100** was obtained in 18% overall yield, although it appeared to be in unsymmetric form.