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SYNTHESIS OF CONFORMATION-RESTRICTED TRIPODAL LIGANDS FOR
MOLECULAR RECOGNITION

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A Dissertation Submitted in Partial Fulfillment of the Requirements
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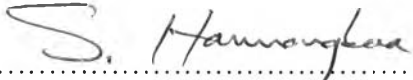
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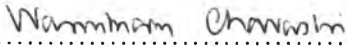
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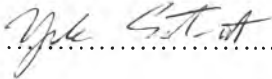
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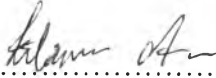
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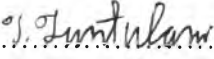
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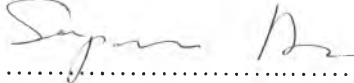
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1,3,5-ไตรแอซิทิล-2,4,6-ไตรแอลคอกซีเบนซีนเป็นอนุพันธ์ของเบนซีนที่มีการจัดเรียงตัวของหมู่แทนที่ทั้งหกตำแหน่งในลักษณะสลับขึ้น-ลงของระนาบวงเบนซีนซึ่งสามารถนำไปใช้ประโยชน์เป็นลิแกนด์สามขาได้ สารตั้งต้น 1,3,5-ไตรแอซิทิล-2,4,6-ไตรไฮดรอกซีเบนซีน (53) สังเคราะห์ได้จากกระบวนการแอซิทิลเลชันของฟลูออโรลูซีนอลในภาวะเดียวให้ผลิตภัณฑ์สูงถึง 91% การทำแอลคิเลชันที่หมู่ไฮดรอกซีทำให้ได้โครงสร้าง 70-72 มีปริมาณในช่วง 72-93% ซึ่งมีการจัดเรียงตัวของหมู่แทนที่รอบวงเบนซีนที่ชี้ออกไปทั้งสองด้านของระนาบวงเบนซีนในลักษณะ *ababab* สารตั้งต้น 53 ทำปฏิกิริยาการแทนที่กับสารประกอบ 1,5-ไดโบรโมเพนเทนได้สารประกอบ 72 ซึ่งเมื่อทำปฏิกิริยาต่อกับเกลือเฮไลด์และตามด้วยกระบวนการรีดักชันจะได้ลิแกนด์เอมีนสามขา 86 เป็นผลิตภัณฑ์ในปริมาณรวม 59% และเมื่อนำสารประกอบ 72 ทำปฏิกิริยาต่อกับสารประกอบ (*R*)-(+)-1-ฟีนิลเอทิลเอมีนจะได้ลิแกนด์สามขาที่เป็นไครัลโมเลกุล 94 เป็นผลิตภัณฑ์ในปริมาณรวม 34% สารประกอบ 70 ที่มาจากการทำเมทิลเลชันสามารถเกิดปฏิกิริยาการควบแน่นกับไฮดรอกซิลเอมีนได้เป็นสารประกอบ 75 จากนั้นทำปฏิกิริยาการแทนที่กับอนุพันธ์ที่มีหมู่ปกป้องของ L-โพรลีนทำให้ได้ลิแกนด์สามขาที่เป็นไครัลโมเลกุล 100 เป็นผลิตภัณฑ์ในปริมาณรวม 18%

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YONGSAK SRITANA-ANANT, Ph.D., CO-ADVISOR : AMARAWAN
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1,3,5-Triacetyl-2,4,6-trialkoxybenzenes are the derivatives of hexasubstituted benzene with fully alternated up-down arrangements of the binding arms to be exploited as the tripodal ligands. The precursor, 1,3,5-triacetyl-2,4,6-trihydroxybenzene (**53**), was synthesized from acetylations of phloroglucinol in one-pot process with 91% yield. Alkylations on the phenolic hydroxyl groups provided the scaffold **70-72** in the range of 72-93% yields, displaying *ababab* facial segregation of the respective substituents around the phenyl plane. Triple *O*-alkylations of the core structure **53** by 1,5-dibromopentane generated the symmetric intermediate **72** and subsequent substitutions with azide followed by reduction achieved the tris-amine ligand **86** in overall 59% yield. Chiral tripodal ligand **94** could also be obtained in overall 34% yield from the substitutions of intermediate **72** with (*R*)-(+)-1-phenylethylamine. The methylated product **70** was condensed with hydroxylamine to generate compound **75**, which was substituted with protected L-proline derivatives. Chiral tripodal ligand **100** was obtained in overall 18% yield.

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LIST OF ABBREVIATIONS

^{13}C -NMR	: carbon-13 nuclear magnetic resonance spectroscopy
^1H -NMR	: proton nuclear magnetic resonance spectroscopy
Acetone- d_6	: hexadeuterated acetone
anh.	: anhydrous
Ar	: aryl
atm	: atmosphere
bend	: bending vibration (IR)
Boc	: tertiarybutyloxycarbonyl
br	: broad peak (NMR)
CDCl_3	: deuterated chloroform
CD_3OD	: tetradeuterated methanol
cm^{-1}	: unit of wavenumber (IR)
d	: doublet (NMR)
d	: day (s)
dd	: double of doublet (NMR)
DMAP	: <i>N,N</i> -dimethylaminopyridine
DMF	: <i>N,N</i> -dimethylformamide
DMSO	: dimethyl sulfoxide
DMSO- d_6	: hexadeuterated dimethyl sulfoxide
eq	: equivalent (s)
EtOAc	: ethyl acetate
EtOH	: ethanol
FT-IR	: Fourier transform infrared spectroscopy
g	: gram (s)
h	: hour (s)
Hz	: hertz (s)
IR	: infrared spectroscopy
<i>J</i>	: coupling constant
M	: molar (s)
m	: multiplet (NMR)
m.p.	: melting point

m/z	: mass per charge ratio
MeCN	: acetonitrile
MeOH	: methanol
mg	: milligram (s)
MHz	: megahertz (s)
min	: minute (s)
mL	: milliliter (s)
mM	: millimolar (s)
mmol	: millimole (s)
MS	: mass spectrometry
NMR	: nuclear magnetic resonance spectroscopy
°C	: degree Celsius
Ph	: phenyl
ppm	: parts per million (unit of chemical shift)
q	: quartet (NMR)
R _f	: retardation factor
RT	: room temperature
s	: singlet (NMR)
st	: stretching vibration (IR)
t	: triplet (NMR)
td	: triple of doublet (NMR)
THF	: tetrahydrofuran
TLC	: thin layer chromatography
δ	: chemical shift