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**SYNTHESIS OF SULFUR-CONTAINING CHIRAL LIGANDS FOR
TRANSITION METAL-CATALYZED ASYMMETRIC NUCLEOPHILIC
ADDITION TO CARBONYL COMPOUNDS**

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A Dissertation Submitted in Partial Fulfillment of the Requirements
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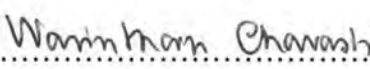
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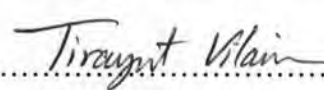
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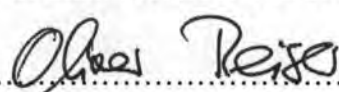
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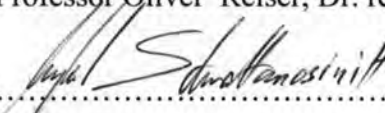
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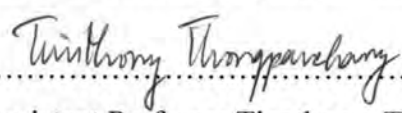
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ได้สังเคราะห์ชุดของไทโอเลท-บีตา-อะมิโนแอลกอฮอล์ และ บีตา-อะมิโนแอลกอฮอล์ที่มีโครงสร้างพื้นฐานเป็นวงไทโอพีนด้วยปฏิกิริยาออกเค็นเซชันระหว่างแอลดีไฮด์ที่มีอะตอมซัลเฟอร์เป็นองค์ประกอบกับไครัลอะมิโนแอลกอฮอล์ที่เหมาะสมตามด้วยปฏิกิริยารีดักชันด้วยโซเดียมโบโรไฮไดรด์ ปฏิกิริยาเหล่านี้ให้ชุดของไครัลไทโอเลท-บีตา-อะมิโนแอลกอฮอล์ในเปอร์เซ็นต์ผลิตภัณฑ์ที่สูง (73-89 เปอร์เซ็นต์) และให้ไครัลบีตา-อะมิโนแอลกอฮอล์ที่มีโครงสร้างพื้นฐานเป็นวงไทโอพีนในปริมาณผลิตภัณฑ์ 49-95 เปอร์เซ็นต์ จากนั้นได้นำสารเหล่านี้ไปศึกษาความสามารถในการเป็นลิแกนด์สำหรับตัวเร่งปฏิกิริยาการเติมในโครมีเทนเข้าที่อะตอมคาร์บอนของแอลดีไฮด์แบบอสมมาตร (ปฏิกิริยาในโตร-แอลคอก หรือ ปฏิกิริยาเฮนรี) เมื่อมีตัวเร่งปฏิกิริยาที่เตรียมจากคอปเปอร์ (II) อะซิเตตที่ 13.5 โมลเปอร์เซ็นต์และลิแกนด์ที่ 15 โมลเปอร์เซ็นต์ให้ผลิตภัณฑ์เป็นบีตาไนโตรแอลกอฮอล์ โดยมีปริมาณผลผลิตที่สูงและอเนนซิโอเมอร์อีกเฮส (ee) สูงได้ถึง 88 เปอร์เซ็นต์ เมื่อใช้ไครัลลิแกนด์ที่มีโครงสร้างพื้นฐานเป็นวงไทโอพีนและมีหมู่แทนที่เป็นวงพีนิลอยู่ในตำแหน่งบีตาของอะมิโนแอลกอฮอล์ นอกจากนี้ยังสามารถลดปริมาณของตัวเร่งปฏิกิริยาเหลือเพียง 5 โมลเปอร์เซ็นต์ซึ่งยังคงมีประสิทธิภาพดีในการเร่งปฏิกิริยาตลอดจนการเหนี่ยวนำให้เลือกเกิดผลิตภัณฑ์ที่ต้องการ จากการพิสูจน์แอมโซลูทคอนฟิกูเรชันของผลิตภัณฑ์พบว่า ปฏิกิริยาที่ใช้ลิแกนด์ที่มีคอนฟิกูเรชันเป็น R จะให้ผลิตภัณฑ์ที่มีคอนฟิกูเรชันเป็น S และได้เสนอแบบจำลองแทรนซิชันสเตตเพื่อทำนายอเนนซิโอซีเลคตีวิตีของปฏิกิริยา นอกจากนี้ยังได้ศึกษาการนำลิแกนด์ระบบดังกล่าวไปใช้เป็นตัวเร่งปฏิกิริยาอื่นๆ เช่น ปฏิกิริยารีดักชันคีโตนและอนุพันธ์ด้วยโซเดียมโบโรไฮไดรด์แบบอสมมาตร ปฏิกิริยารีดักชันอะซีโตฟีโนนด้วยบอเรนแบบอสมมาตร ไคเนติกเรโซลูชันของราซีมิกไฮโดรเบนโซอินและปฏิกิริยาการเติมอินโดลเข้าที่เบนซิลไดนามาโลเนต

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WORALUK MANSAWAT: SYNTHESIS OF SULFUR-CONTAINING CHIRAL
LIGANDS FOR TRANSITION METAL-CATALYZED ASYMMETRIC NUCLEOPHILIC
ADDITION TO CARBONYL COMPOUNDS.

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A series of thiolated β -amino-alcohols and thiophene-based β -amino-alcohols had been synthesized by condensation between an aldehyde containing sulfur atom and an appropriate chiral amino-alcohol followed by reduction with sodium borohydride. The reactions provided a series of chiral thiolated β -amino-alcohol ligands in 73-89% and chiral thiophene-based β -amino-alcohols in 49-95% yield. These synthesized compounds were evaluated as ligands for asymmetric addition of nitromethane to carbon atom of aldehydes (nitro-aldol or Henry reaction) in the presence of 13.5 mol% of Cu(II) acetate and 15 mol% of ligand to give the β -nitroalcohol product in moderate to excellent yields and in up to 88% ee when chiral thiophene-based β -amino-alcohol possessing phenyl substituent at the β position of amino-alcohol was used as a ligand. In addition, the catalyst loading was successfully reduced to 5 mol% while the enantioselective induction is still very effective. The absolute configuration of all products from the reactions where the (*R*)-ligand was employed, was confirmed to be *S*. A transition state model to explain the enantioselectivity of the reaction is proposed. Moreover, this group of chiral catalysts showed their catalytic ability not only in an asymmetric nitro-aldol reaction but also in an asymmetric borohydride reduction, asymmetric borane reduction, asymmetric benzoylation as well as asymmetric Michael addition of indole to benzylidene malonate.

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List of Abbreviations

Å	angstrom	mL	milliliter (s)
Ar	aromatic group	mmol	millimole
acac	acetylacetonate	mp	melting point
br	broad	NMR	nuclear magnetic resonance
°C	degree celsius	OAc	acetate
CDCl ₃	deuterated chloroform	OTf	trifluoromethane-sulfonate
CuTC	copper(I) thiophene-2-carboxylate	Ph	phenyl
d	doublet (NMR)	ppm	part per million
dd	doublet of doublet (NMR)	q	quartet (NMR)
ee	enantiomeric excess	rt	room temperature
equiv	equivalent	s	singlet (NMR)
g	gram (s)	t	triplet (NMR)
h	hour (s)	[α] _D	specific rotation
Hz	hertz	μL	microliter
<i>J</i>	coupling constant	μm	micrometer
lit	literature	δ	chemical shift
m	multiplet (NMR)	%	percent
min	minute		