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สำหรับปฏิกิริยาแบบอสมมาตร โดยใช้ตัวเร่งปฏิกิริยา

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SYNTHESIS OF CHIRAL NAPHTHYL BETA-AMINOALCOHOL
LIGANDS FOR CATALYTIC ASYMMETRIC REACTIONS

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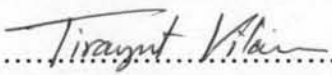
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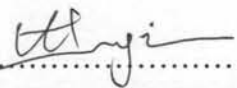
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อิทธิพล แสงสว่าง : การสังเคราะห์ไครัลลิแกนค์ในกลุ่มแนพทิลบีตาอะมิโนแอลกอฮอล์
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สามารถสังเคราะห์ไครัลลิแกนค์ในกลุ่มเอ็น-ซาลิซิล 1-แนพทิลและ 2-แนพทิลบีตาอะมิโนแอลกอฮอล์ได้ โดยเริ่มต้นจากปฏิกิริยาแอลฟาโบรมิเนชันของ 1- และ 2-อะซีโตแนพโทน ได้ผลิตภัณฑ์เป็นแอลฟาโบรมอะซีโตแนพโทนในปริมาณร้อยละผลได้เท่ากับ 98 ทั้งคู่ จากนั้นนำผลิตภัณฑ์ที่ได้ไปทำปฏิกิริยารีดักชันแบบอสมมาตรด้วย (-)-DIP-chloride ตามด้วยปฏิกิริยากับสารละลายโซเดียมไฮดรอกไซด์ ได้ผลิตภัณฑ์เป็น (R)-1-แนพทิล และ (R)-2-แนพทิลออกซิเรนในปริมาณร้อยละผลได้ 43 และ 67 และมีอีนานซีโอเมอร์อีกเศษมากกว่า 99% จากนั้นทำปฏิกิริยาการเปิดวงไครัลแนพทิลออกซิเรนที่อะตอมคาร์บอนตำแหน่งเบนซิลด้วยโซเดียมเอไซด์ ได้ผลิตภัณฑ์เป็น (S)-1-แนพทิล และ (S)-2-แนพทิล เอซิดแอลกอฮอล์ ได้ร้อยละผลได้ของผลิตภัณฑ์เท่ากับ 65 ทั้งคู่ โดยทั้งสองมีอีนานซีโอเมอร์อีกเศษมากกว่า 99 % หลังจากนั้นจึงทำปฏิกิริยารีดักชันเป็น (S)-1-แนพทิล และ (S)-2-แนพทิลอะมิโนแอลกอฮอล์ตามด้วยปฏิกิริยากับซาลิซิลลดีไฮด์ และปฏิกิริยารีดักชัน จะได้ผลิตภัณฑ์เป็นไครัลเอ็น-ซาลิซิล 1-แนพทิลและ 2-แนพทิลบีตาอะมิโนแอลกอฮอล์โดยมีเปอร์เซ็นต์ของผลิตภัณฑ์เท่ากับ 57 และ 70 เมื่อนำลิแกนค์ทั้งสองไปตรวจสอบเพื่อใช้เป็นไครัลลิแกนค์สำหรับปฏิกิริยาแอสเตรเกอร์ ปฏิกิริยาการเติมแบบไม่เกิดแบบอสมมาตร และปฏิกิริยาพุดวิกโดยใช้ตัวเร่งปฏิกิริยา พบว่า ไครัลเอ็นซาลิซิล 1-แนพทิลบีตาอะมิโนแอลกอฮอล์ มีประสิทธิภาพในการเหนี่ยวนำให้เกิดผลิตภัณฑ์ที่มีอีนานซีโอเมอร์อีกเศษในปฏิกิริยาแอสเตรเกอร์และปฏิกิริยาการเติมแบบไม่เกิด สูงถึง 97 % และ 91 % ตามลำดับ ซึ่งมีประสิทธิภาพสูงกว่าการใช้ ไครัลเอ็นซาลิซิล 2-แนพทิลบีตาอะมิโนแอลกอฮอล์เป็นลิแกนค์ โดยได้นำเสนอแบบจำลองการเลือกจำเพาะของอีนานซีโอเมอร์ในปฏิกิริยาทั้งสองด้วย แต่พบว่าลิแกนค์ทั้งสองไม่สามารถเหนี่ยวนำให้เกิดความเลือกจำเพาะของอีนานซีโอเมอร์ในปฏิกิริยาพุดวิก

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ITTIPHOL SAENGSWANG : SYNTHESIS OF CHIRAL NAPHTHYL
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N-Salicyl-1-naphthyl and *N*-Salicyl-2-naphthyl- β -aminoalcohol-based chiral ligands were synthesized. α -Bromination of 1- and 2-acetonaphthone both afforded the corresponding α -bromoacetonaphthones in 98 %. Subsequent asymmetric reduction by (-)-*B*-chlorodiisopinocampheylborane (DIP-chloride), followed by a reaction with sodium hydroxide solution resulted in optically active (*R*)-1-naphthyl and (*R*)-2-naphthyl oxiranes in 43 % and 67 % yields, respectively. The results showed that (*R*)-1-naphthyl and (*R*)-2-naphthyloxirane were obtained in higher than 99 %*ee*. The following nucleophilic ring-opening of oxiranes by sodium azide yielded benzylic-azidoalcohols in 65% and 65% yields for (*S*)-1-naphthyl and (*S*)-2-naphthyl azidoalcohols. The %*ee* values were more than 99 %. The next step is a reduction to chiral naphthylaminoalcohol, followed by a reaction with salicylaldehyde and a reduction. Through this sequence, chiral-*N*-salicyl-1-naphthyl and 2-naphthyl- β -aminoalcohols were obtained in 57% and 70%, respectively. These products had been evaluated as potential chiral ligands for catalytic asymmetric Strecker reaction, Michael reaction, and Pudovik reaction. For the Strecker and Michael reaction, chiral-*N*-salicyl-1-naphthyl- β -aminoalcohols could induce products up to 97 % and 91 %*ee*, respectively. Moreover, this ligand has been shown to be more efficient than 2-naphthyl- β -aminoalcohols. Asymmetric models of these reactions were proposed. Unfortunately, they could not induce to any enantioselections in Pudovik reaction.

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LIST OF ABBREVIATIONS

apd	apparent doublet	LiAlH ₄	lithium aluminium hydride
apt	apparent triplet	m	multiplet (NMR)
Ar	aromatic	MHz	megahertz
Bu	butyl	mg	milligram(s)
°C	degree Celcius	mL	millilitre(s)
CDCl ₃	deuterated chloroform	mmol	millimole
CSA	chiral solvating agent	m.p.	melting point
d	doublet (NMR)	NMR	nuclear magnetic resonance
dd	doublet of doublet	Ph	phenyl
ee	enantiomeric excess	ppm	part per million
eq	equivalent	q	quartet (NMR)
Et	ethyl	rt	room temperature
g	gram	s	singlet (NMR)
GC	gas chromatography	t	triplet (NMR)
h	hour(s)	THF	tetrahydrofuran
HPLC	high performance liquid chromatography	TLC	thin layer chromatography
Hz	Hertz	TMS	trimethylsilane
ⁱ Pr	isopropyl	μL	microlitre(s)
<i>J</i>	coupling constant	δ	chemical shift
k	rate constant		
lit.	literature		