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จุฬาลงกรณ์มหาวิทยาลัย

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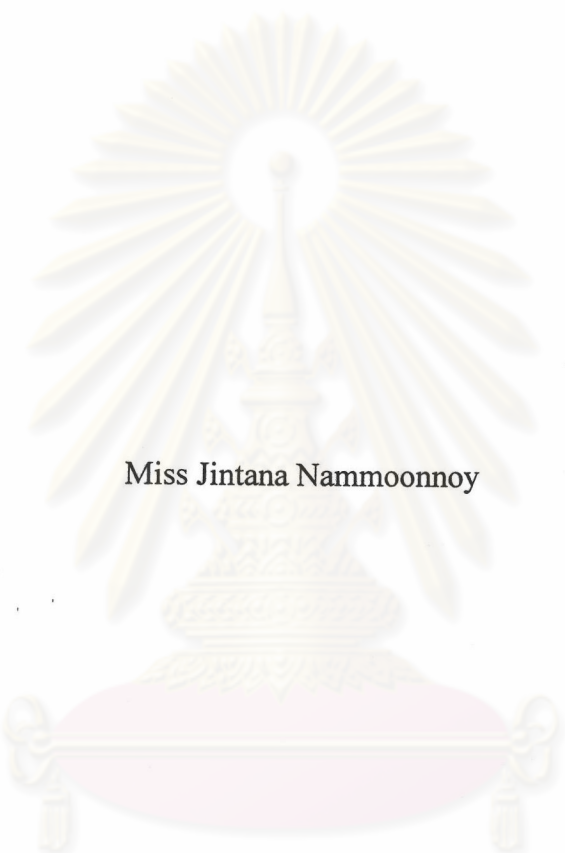
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SYNTHESIS OF α -HYDROXYPHOSPHONIC ACID DERIVATIVES



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ศูนย์วิทยทรัพยากร
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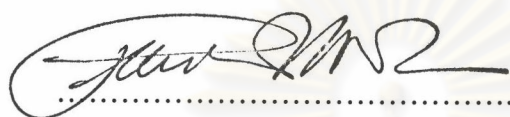
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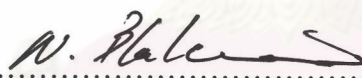
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ได้เตรียมแอลฟาไฮดรอกซีฟอสโฟเนตจากปฏิกิริยาระหว่างแอลดีไฮด์กับไดอัลคิลฟอสไฟต์โดยใช้ตัวเร่งปฏิกิริยาหลายชนิดได้แก่ ไตรเอทิลามีน อะลูมินา ทีเทเนียมไอโซโพรพอกไซด์ และลิเทียมอะลูมิเนียมไฮไดรด์พบว่าตัวเร่งปฏิกิริยาที่เหมาะสมที่สุดในการเตรียมแอลฟาไฮดรอกซีฟอสโฟเนตได้แก่ ลิเทียมอะลูมิเนียมไฮไดรด์ โดยให้เปอร์เซ็นต์ผลิตภัณฑ์ประมาณ 43-84 % นอกจากนี้ยังได้ศึกษาปฏิกิริยาคะตะลิติกอะซิเมตริกไฮโดรฟอสโฟนิเลชันของแอลดีไฮด์กับไดอัลคิลฟอสไฟต์โดยใช้ตัวเร่งปฏิกิริยาที่เป็นสารประกอบเชิงซ้อนของลิเทียมอะลูมิเนียมไฮไดรด์กับลิแกนด์ต่างๆได้แก่ ลิแกนด์กลุ่มซิฟเบส เปปไทด์ซิฟเบสและกลุ่มเอ็นซาลิซิลเบตาอะมิโนแอลกอฮอล์ จากผลการทดลองพบว่าตัวเร่งปฏิกิริยาระหว่างอัลดีไฮด์กับไดอัลคิลฟอสไฟต์ที่มีประสิทธิภาพที่สุดคือตัวเร่งปฏิกิริยาที่เตรียมได้จากปฏิกิริยาระหว่างลิเทียมอะลูมิเนียมไฮไดรด์กับลิแกนด์กลุ่มเอ็นซาลิซิลเบตาอะมิโนแอลกอฮอล์โดยให้เปอร์เซ็นต์ผลิตภัณฑ์ประมาณ 50-75 % และสามารถให้สารที่มีเปอร์เซ็นต์ไอแนนซิโอเมอริกเอ็กเซสปานกลางคือประมาณ 32-70 % ซึ่งเปอร์เซ็นต์ไอแนนซิโอเมอริกเอ็กเซสวิเคราะห์โดยใช้เทคนิคแก๊สโครมาโตกราฟีบนโครลคอลลัมน์ จากการศึกษาพบว่าความเกะกะของหมู่แทนที่ในส่วนที่เป็นเอ็นซาลิซิลและเบตาอะมิโนแอลกอฮอล์จะมีผลต่อการเหนี่ยวนำให้เกิดซีเล็กติวิตี นอกจากนี้ยังพบว่าปฏิกิริยาของอะลิฟาติกอัลดีไฮด์จะให้ไอแนนซิโอซีเล็กติวิตีสูงกว่าของอะโรมาติกอัลดีไฮด์

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จุฬาลงกรณ์มหาวิทยาลัย

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JINTANA NAMMOONNOY: SYNTHESIS OF α -HYDROXYPHOSPHONIC ACID DERIVATIVES

THESIS ADVISOR: ASSISTANT PROFESSOR WORAWAN BHANTHUMNAVIN, Ph.D.
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The synthesis of α -hydroxyphosphonates by the reaction between dialkyl phosphites and aldehydes using various catalysts such as triethylamine, alumina, titanium isopropoxide, and lithium aluminium hydride were studied. The use of lithium aluminium hydride as catalyst resulted in the desired products in moderate to high yields (43-84%). The asymmetric synthesis of α -hydroxyphosphonates by asymmetric hydrophosphonylation reaction of aromatic aldehyde with dialkyl phosphites in the presence of a catalytic amount of complexes of lithium aluminium hydride and chiral ligands was carried out. The ligands of interest are chiral Schiff's base, peptide Schiff's base, and *N*-salicyl- β -aminoalcohol ligands. The reaction of aldehydes and dialkyl phosphites in the presence of Li-Al-*N*-salicyl- β -aminoalcohol complexes proceeded efficiently to give the corresponding α -hydroxyphosphonate in moderate yields (50-75%) and moderate enantioselectivity (32-70% *ee*). The enantiomeric excess was observed by chiral gas chromatography. The bulkiness of substituents on the salicyl and β -amino alcohol moiety plays a significant role in the induction of enantioselectivities. In addition, the aliphatic aldehydes gave product in higher enantiomeric excess than aromatic aldehydes.

Department.....Chemistry.... Student's signature.....*Jintana Nammoonnoy*.....
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List of Abbreviations

Ar	aromatic	m	multiplet
bs	broad singlet	Me	methyl
Bu	butyl	MHz	megaHertz
°C	degree Celsius	mg	milligram(s)
CDA	chiral derivatizing agent	mL	milliliter(s)
CDCl ₃	deuterated chloroform	mmol	millimole
CLSR	chiral lanthanide shift reagent	m.p.	melting point
CSA	chiral solvating agent	MS	molecular sieves
d	day(s)	MTPA	α -methoxy- α -(trifluoro
d	doublet (NMR)		methyl)phenylacetic acid,
DBU	1,8-diazabicyclo[5,4,0]undec-		Mosher's acid
	7-ene	NMR	nuclear magnetic resonance
DCC	dicyclohexylcarbodiimide	Tf	trifluoromethanesulfonyl
DMAP	4- <i>N,N</i> -dimethylamino	Ph	phenyl
	pyridine	ppm	parts per million
DEHP	diethyl phosphite	Pr	propyl
DMHP	dimethyl phosphite	rt	room temperature
dd	doublet of doublet (NMR)	s	singlet
<i>de</i>	diastereomeric excess	t	triplet
<i>dr</i>	diastereomeric ratio	THF	tetrahydrofuran
<i>ds</i>	diastereoselectivity	TBD	1,5,7-triazabicyclo[4,4,0]dec-
<i>ee</i>	enantiomeric excess		5-ene
equiv	equivalent	TMG	trimethylguanidine
Et	ethyl	μ L	microliter
g	gram	δ	chemical shift
h	hour(s)	%	percent
Hz	Hertz		
<i>J</i>	coupling constant		
K	Kelvin		
lit.	literature		
LAH	lithium aluminium hydride		