Molecular modelling study of alkene metathesis with phosphine ligated Grubbs-type precatalysts

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Abbreviations

—□	available coordination site
ΔE_e	electronic energy difference
ΔG	Gibbs-free energy difference
λ	denotes the steric switch based on Tolman's steric parameter θ
π_p	represents the π-acidity
θ	Tolman's steric parameter
Ar	aromatic group
ATR	attenuated total reflection
BMS	borane dimethyl sulphide complex
bp	boiling point
BuLi	butyl lithium
^{13}C-NMR	carbon-13-nuclear magnetic resonance spectroscopy
$C_{a/b}$	covalent factor parameter
cc	*cisoid-cisoid* (used to indicate isomers)
CM	alkene cross-metathesis
COSMO	conductor-like screening model
COSY	homonuclear correlation spectroscopy
CPU	central processing unit
Cy	cyclohexyl group, C_6H_{11}
CyiP	1R, 2S, 4R, 5S-(+)2,5-diisopropyl-7-cyclohexylphosphabicyclo[2.2.1]heptane ligand
CyMe	1R, 2S, 4R, 5S-(+)2,5-dimethyl-7-cyclohexylphosphabicyclo[2.2.1]heptane ligand
CytB	1R, 2S, 4R, 5S-(+)2,5-ditertbutyl-7-cyclohexylphosphabicyclo[2.2.1]heptane ligand
DEPT	distortionless enhancement by polarization transfer
DFT	density functional theory
DN	double numeric
DND	double numeric plus d-functions
DNP	double numeric plus polarisation
dtbpm	bis(di-tersbutylphosphanyl)methane
E_{ar}	the QALE aromatic effect parameter
$E_{a/b}$	the ECW electrostatic factor parameter
EF	eigenvector following
EI	electron impact-ionisation
ESI	electron spray ionisation
FID	flame ionisation detector
GC	gas-chromatography, gas-chromatograph

GGA	generalized gradient approximation functional
Grubbs 1	Grubbs' first generation catalyst ($Ru(=CHPh)Cl_2(PCy_3)_2$)
Grubbs 2	Grubbs' Second generation catalyst ($(C_{21}H_{26}N_2)Ru(=CHPh)Cl_2(PCy_3)$)
^{1}H-NMR	proton nuclear magnetic resonance spectroscopy
HDD	hard disk drive
HPC	high performance computer
HSQC	heteronuclear single quantum correlation
i	iso (used to indicate isomers)
IP	isomerisation products
$IpcBH_2$	monoisopinocamphenylborane
IR	infrared spectrometry
IUPAC	International Union of Pure and Applied Chemistry
k_{init}	the initial rate constant
k_{obs}	the observed rate constant
L	ligand
LiPPh	dilithium salt of phenylphosphine
LST	linear synchronous transit
M	central metal atom
Me	methyl group, CH_3
MESP	molecular electrostatic potential
MIN	minimal basis
mp	melting point
MS	mass spectrometry
MsCl	methanesulphonyl chloride
MSD	mass selective detector
n	normal (used to indicate isomers)
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance spectroscopy
Np	neopentyl
o	*ortho* (used to indicate isomers)
OMs	bis(methanesulphonate) ester
p	*para* (used to indicate isomers)
^{31}P-NMR	phosphorous-31-nuclear magnetic resonance spectroscopy
PCy_3	tricyclohexyl phosphine
PMP	primary metathesis products
Ph	phenyl group, C_6H_5
PhiP	1R, 2S, 4R, 5S-(+)2,5-diisopropyl-7-phenylphosphabicyclo[2.2.1]heptane ligand
PhMe	1R, 2S, 4R, 5S-(+)2,5-dimethyl-7-phenylphosphabicyclo[2.2.1]heptane ligand

Phobcat	9-cyclohexyl-9-phospha-9H-bicyclononane derivative of Grubbs 1, $(Ru(=CHPh)Cl_2(C_6H_{11}PC_8H_{14})_2$
PhtB	1R, 2S, 4R, 5S-(+)2,5-ditertbutyl-7-phenylphosphabicyclo[2.2.1]heptane ligand
PPh_3	triphenyl phosphine
^iPr	isopropyl, $CH(CH_3)_2$
PW	Perdew and Wang
PYE	1H-pyridin-(2E)-ylidene
Q	functional group
QALE	quantitative analysis of ligand effects
QST	quadratic synchronous transit
R	alkyl functional group
RAM	random access memory
RCM	ring-closing metathesis
ROMP	ring-opening metathesis polymerisation
%S	selectivity towards PMP
SCF	self-consistent field
SMP	secondary metathesis products
t	ters or tertiary
^tBu	tertiary-butyl group, $C(CH_3)_3$
TEP	Tolman electronic parameter
THF	tetrahydrofuran
TS	transition state
tt	*transoid-transoid* (used to indicate isomers)
v/v	volume/volume
vdW	Van der Waals
χ	Tolman's electronic parameter
χ_d,	the corrected Tolman electronic parameter
XRD	x-ray crystal diffraction
Z-Select	Grubbs Z-selective metathesis catalyst
ZPE	zero-point energy

Summary

Keywords: Grubbs precatalyst, molecular modelling, phosphine ligands

In this study, an attempt was made to identify the electronic and steric properties of the precatalyst ligands that determine the characteristics of phosphine ligated Grubbs-type precatalysts for alkene metathesis by means of molecular modelling.

It was found from studying the literature that the possibilities for synthesising a wide range of phosphine ligands are almost unlimited. Additionally, it was found that there is no easy method to determine the electronic and steric properties of the precatalyst ligands in existence.

Molecular modelling might provide a method to study potential ligands and precatalysts before tedious synthesis methods are attempted. It was found that the theoretically calculated structures of the commercially available precatalysts compared well with the experimental data reported in literature. It is also shown that the energy profiles for alkene metathesis of simplified model systems do not compare well with non-simplified systems. Correlations between these simplified model systems and experimental work have to be regarded as serendipitous at best.

When the energy profiles of the various new and commercially available precatalysts are compared, similarities in the energy trends for 1-octene metathesis are observed. These similarities raise questions about the significance of the differences in the energy barriers. In an effort to better understand this, two low activity precatalysts were also investigated in an attempt to identify the area or trend of poor catalysis. Instead of providing the desired different result, trends very similar to that of the highly active precatalysts were observed. This led to the observation that, without a sufficiently large dataset, great care should be taken before conclusions are drawn from theoretical work.

Since the electronic investigation did not provide the desired result of finding a fast and effective method of determining which ligand merits further investigation, some steric aspects were studied. Once again, the precatalysts proved to be remarkably similar and no definitive answer for the observed differences in the various precatalysts could be determined.

A preliminary experimental study into the feasibility of the synthesis of the new potential ligands was done. The multi-step synthesis route resulted in low yields in some cases, with the need for large volumes of solvents to purify the products. The toxicity of phenylphosphine also has to be taken into account when considering these types of ligands. A new precatalyst obtained by using a

new ligand should show a remarkable improvement over the current commercially available precatalysts to justify the additional cost to synthesise a new ligand.

It would seem that for future projects more consideration should be given to the deactivation mechanism of the Grubbs-type precatalysts, since this seems to be the logical starting point to look for the answers to the experimentally observed differences. A deeper understanding of the mechanism of alkene metathesis can only be obtained if all aspects are investigated in as much detail as possible. While the results did not provide the initially expected outcome, some valuable insights were gained that challenge the current way of thinking about the alkene metathesis mechanism. It is also clear that to oversimplify a very complex reaction and using limited data will lead to false assumptions being made.

Opsomming

Sleutelwoorde: Grubbs prekatalisator, molekulêre modellering, fosfien ligande

In hierdie studie is gepoog om die elektroniese en steriese eienskappe van die prekatalisator-ligande wat die eienskappe van fosfiengebonde Grubbs-tipe-prekatalisators tydens alkeenmetatese bepaal, deur middel van molekuulmodellering te identifiseer.

Uit die literatuur is gevind dat die moontlikhede vir die sintese van ŉ wye verskeidenheid fosfienligande bykans onbeperk is. Bykomend is gevind dat daar tans geen maklike metode bestaan om die elektroniese en steriese eienskappe van die prekatalisator-ligande te bepaal nie.

Molekuulmodellering mag ŉ metode bied om potensiële ligande en prekatalisators te ondersoek voordat tydsame sintesemetodes aangepak word. Daar is gevind dat die teoreties berekende strukture van die kommersieel beskikbare prekatalisators baie goed vergelyk het met die eksperimentele data gerapporteer in die literatuur. Daar is ook bewys dat die energieprofiele van die alkeenmetatese van vereenvoudigde modelsisteme nie goed vergelyk met die nie-vereenvoudigde sisteme nie. Korrelasies tussen vereenvoudigde modelsisteme en eksperimentele werk moet hoogstens as gelukkig-toevallig beskou word.

As die energieprofiele van die reeks nuwe en die kommersiële beskikbare prekatalisators vergelyk word, word ooreenkomste in die energietendense van die metatese van 1-okteen waargeneem. Die ooreenkomste het daartoe gelei dat vrae ontstaan oor die noemenswaardigheid van die verskille in die energiegrense. ŉ Poging is aangewend om dit beter te verstaan deur ŉ paar bekende lae aktiwiteit-prekatalisators ook te ondersoek om sodoende die area of tendens van swak katalise te identifiseer. In plaas van die verlangde resultaat, is tendense wat baie soortgelyk aan dié van die hoog aktiewe prekatalisators is, waargeneem. Dit het gelei tot die waarneming dat daar sonder ŉ toereikende datastel versigtig te werk gegaan moet word alvorens gevolgtrekkings vanaf teoretiese werk gemaak word.

Die elektroniese ondersoek het nie die verlangde vinnige en effektiewe metode om te bepaal watter ligand verdere ondersoek verdien gelewer nie, en daarom is ŉ paar steriese aspekte ondersoek. Weereens het die prekatalisators merkwaardige ooreenkomste getoon en kon geen beslissende antwoord vir die waargenome verskille in die verskeie prekatalisators bepaal word nie.

ŉ Voorlopige eksperimentele studie van die uitvoerbaarheid van die sintese van die nuwe potensiële ligande is gedoen. Die multistap-sinteseroete het gelei tot lae opbrengste in sekere

gevalle en groot hoeveelhede oplosmiddels was nodig om die produkte te suiwer. Die toksiese aard van fenielfosfien moet in gedagte gehou word wanneer hierdie tipe ligande oorweeg word. Nuwe prekatalisators wat verkry word as die nuwe ligande gebruik word, moet merkwaardige verbetering oor die huidige kommersiële beskikbare prekatalisators vertoon om die addisionele koste om ŉ nuwe ligand te sintetiseer, te regverdig.

Dit wil voorkom asof toekomstige projekte meer oordenking moet verleen aan die deaktiveringsmeganisme van die Grubbs-tipe-prekatalisators, aangesien dit wil voorkom asof dit die logiese beginpunt is om vir die antwoorde vir die waargenome eksperimentele verskille te soek. ŉ Dieper insig tot die meganisme van alkeenmetatese kan slegs verkry word indien al die aspekte so breedvoerig as wat moontlik is, ondersoek word. Alhoewel die resultate nie die aanvanklike verwagte uitkoms gelewer het nie, is waardevolle insigte verkry wat die huidige denkwyse oor die alkeenmetatese meganisme in twyfel trek. Dit is ook duidelik dat te veel vereenvoudiging van ŉ baie komplekse reaksie en die gebruik van beperkte data daartoe sal lei dat verkeerde aannames gemaak word.