

Lewis Acid Catalysis of the Diels–Alder Reaction Using Niobium and Tantalum Chlorides in the Presence of Coordinating Ligands

Joshua Howarth* and Kevin Gillespie

School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland

Tel.: +353 1 7045312, Fax: +353 1 7045503, E-mail: howarthj@ccmail.dcu.ie

Received: 29 June 2000 / Accepted: 1 August 2000 / Published: 5 August 2000

Abstract: The Jacobsen and pybox type ligands effect chiral induction in the presence of niobium(V) chloride and tantalum(V) chloride in the Lewis acid catalysed Diels–Alder reaction.

Keywords: niobium, tantalum, bis-oxazoline, pybox.

Introduction

Chiral induction of the Diels–Alder reaction using Lewis acid catalysis in the presence of chiral ligands has met with a great deal of success [1]. Bis-oxazolines have been used by Corey in the presence of Mg and Fe [2, 3], and by Evans, along with pybox (Figure 1), in the presence of Cu [4]. Having an interest in chiral Lewis acids based on niobium and tantalum, we decided to investigate the potential for asymmetric induction of the bis-oxazoline and pybox classes of ligand in the presence of niobium(V)chloride or tantalum(V)chloride and compare these results with those of the *R,R* and *S,S* Jacobsen ligand (Figure 2).

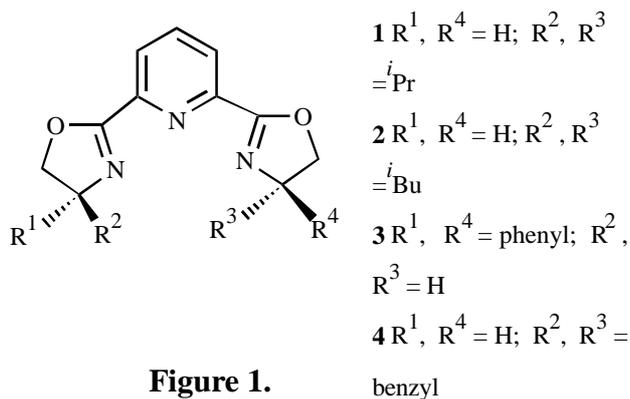


Figure 1.

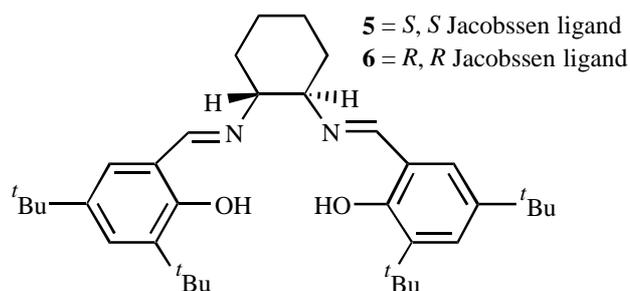
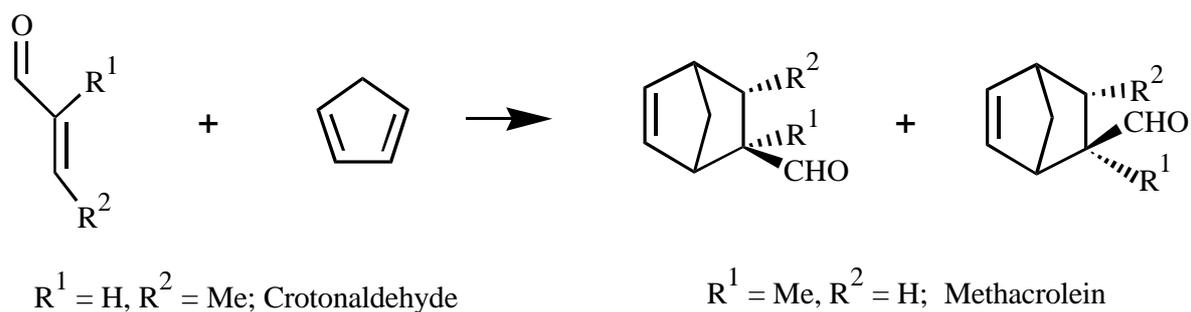


Figure 2.

The reaction we used to investigate the potential asymmetric induction was the Diels-Alder reaction between cyclopentadiene and methacrolein or crotonaldehyde, Scheme 1.



Scheme 1.

Bedekar et al [5] used a tartrate based oxazoline with the isopropylidene ring out of the plane, principally to achieve higher facial selectivity. We thought that the use of the Jacobsen ligand might provide a similar selectivity by more effectively “blocking” one side of the niobium or tantalum complex than the planar pybox ligand. The Jacobsen ligand has been used in the Lewis acid catalysis of the Diels-Alder reaction in the presence of chromium [6] and aluminium [7], the enantioselective addition of HCN to imines [8], and the enantioselective ring opening of epoxides which has been attributed to both nucleophilic delivery of a Cr-N₃ species and Lewis acid catalysis [6, 9].

Results and Discussion

The results of the Diels-Alder reaction for niobium(V) chloride, Table 1, and tantalum(V) chloride, Table 2, with the ligands 1-6 above, are shown below. The use of varying counter-ions has affected enantioselectivity in this reaction system [4] and thus results following the addition of ammonium hexafluorophosphate are included.

Table 1. Results of the Diels-Alder reaction using niobium(V) chloride.

Ligand	Dienophile	Yield (%)		Endo:Exo Ratio		Ee (%)	
		A	B	A	B	A	B
1	M	12	36	7:93	15:85	<3	10 (<i>S</i>)
	C	7	18	92:8	85:15	<3	<3
2	M	40	87	10:90	8:92	<3	10 (<i>S</i>)
	C	27	39	85:15	87:13	<3	<3
3	M	68	70	11:89	9:91	11 (<i>R</i>)	23 (<i>R</i>)
	C	25	71	89:11	88:12	<3	<3
4	M	99 ^a	56	8:92	10:90	<3	<3
	C	22	35	88:12	87:13	<3	<3
5	M	67 ^a	86	9:91	7:93	40 (<i>R</i>)	40 (<i>R</i>)
	C	39	58	89:11	76:24	25 (<i>R</i>)	19 (<i>R</i>)
6	M	49	74	10:90	6:94	38 (<i>S</i>)	42 (<i>S</i>)
	C	28	61	85:15	79:21	27 (<i>S</i>)	25 (<i>S</i>)

M = Methacrolein; C = Crotonaldehyde; A = absence of NH₄PF₆; B = presence of NH₄PF₆;

^a Reaction proceeded for 48 h instead of 24 h; n.r. = no reaction;

Table 2. Results of the Diels-Alder reaction using tantalum(V) chloride.

Ligand	Dienophile	Yield (%)		Endo:Exo Ratio		Ee (%)	
		A	B	A	B	A	B
1	M	n.r.	11		25:75		<3
	C	n.r.	7		83:17		<3
2	M	n.r.	10		16:84		
	C	n.r.	8		89:11		<3
3	M	33 ^a	84 ^a	9:91	12:88	43 (<i>R</i>)	31 (<i>R</i>)
	C	15	18	82:18	87:13	27 (<i>R</i>)	20 (<i>R</i>)
4	M	19	84	14:86	2:98	<3	<3
	C	25	45	84:16	80:20	<3	<3
5	M	n.r.	72 ^a		4:96		46 (<i>R</i>)
	C	n.r.	45 ^a		81:19		23 (<i>R</i>)
6	M	n.r.	54		2:98		47 (<i>S</i>)
	C	n.r.	19		80:20		19 (<i>S</i>)

The effectiveness of 4Å molecular sieves in enhancing selectivity in a variety of Lewis acid reactions has been reported [10]. In addition, unactivated sieves have been used in a titanium(IV) chloride catalysed reaction and proved to be substantially more effective in promoting enantioselectivity than activated sieves [11]. Therefore, the reactions with methacrolein were repeated in the presence of activated and unactivated molecular sieves, Table 3. We found however that although the addition of both activated and unactivated sieves promoted enantioselectivity in our reaction, the activated sieves gave the larger increase of enantioselectivity. Solvent effects were investigated and it was found that the reaction did not proceed at all in tetrahydrofuran (THF) and a markedly lower yield and an absence of enantioselectivity were noted in the case of acetonitrile (MeCN).

Table 3. Results using activated and unactivated sieves.

Metal	Ligand	Yield (%)		Endo:Exo Ratio		Ee (%)	
		A	U	A	U	A	U
Niobium	1	43	68	2:98	7:93	52 (<i>S</i>)	31 (<i>S</i>)
	2	35	54	6:94	6:94	20 (<i>S</i>)	<3
	3	41	44	2:98	1:99	35 (<i>R</i>)	23 (<i>R</i>)
	4	33	41	3:97	9:91	17 (<i>S</i>)	<3
	5	60	66	7:93	7:93	55 (<i>R</i>)	35 (<i>R</i>)
	6	46	34	8:92	8:92	48 (<i>S</i>)	28 (<i>S</i>)
Tantalum	5	34	32	7:93	7:93	18 (<i>R</i>)	8 (<i>R</i>)
	6	43	39	8:92	7:93	15 (<i>S</i>)	8 (<i>S</i>)

A = activated sieves added; U = unactivated sieves added

Conclusions

The Jacobson ligand provided the highest chiral induction and this may be due to the “twisted ring” structure that it possesses as opposed to the flat ring structure of the pybox ligands. A complex of NbCl₅ and the *R,R* Jacobsen ligand was isolated (crystalline, yellow needles) and the accurate mass (*m/z*

= 653.304 (ES+)) supports a species with a formula $\text{NbC}_{36}\text{H}_{52}\text{N}_2\text{O}_3$. This is further supported by microanalysis of the complex (cal (%). C 66.81; H 8.04; N 4.29, found (%) C 67.09; H 8.45; N 4.14). The ^1H NMR of the complex differed from the ligand, most notably in the aromatic region. The aromatic signals for the uncomplexed ligand lie at $\delta 6.99$ and $\delta 7.30$, in the isolated complex these signals are spread between $\delta 7.16$ and $\delta 8.40$. There is also a significant difference in the signal for the $\text{CH}=\text{N}$ proton, $\delta 8.31$ (ligand uncoordinated) to $\delta 9.43$ (isolated complex).

When this complex is used in the Diels-Alder reactions above catalysis is not observed. We currently believe that a Chloro-niobium species is involved in the catalysis and that this is hydrolysed on attempt at isolation. Coordination about Nb is likely as we observed that in this complex a $\text{C}=\text{N}$ stretch in the IR shifted from 1630 cm^{-1} (uncomplexed ligand) to 1651 cm^{-1} (Nb complexed ligand), an effect attributable to the dative bond to the metal. Our current is that the structure of the isolated complex is that shown in Figure 3. However we are currently carrying out further structural studies to unambiguously characterise the isolated complex.

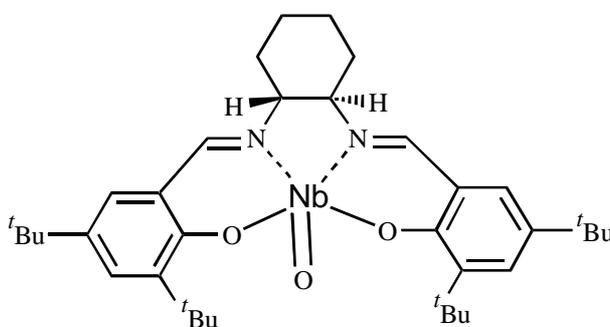


Figure 3.

Experimental

General

^1H spectra were obtained using a Bruker AM 400 NMR spectrometer and were recorded at 400 and 100 MHz respectively. All reagents and chemicals were obtained from Aldrich Chemical Company (UK) and were used as received unless otherwise noted.

Synthetic procedures

The pybox ligands were synthesised using 2,6-pyridine dicarboxyl chloride and each of the following amino alcohols; *S*-valinol, *S*-*iso*-leucinol, *R*-phenylglycinol and *S*-phenylalaninol by a combination of literature methods [5, 12]. The analyses for ip-pybox (**1**), ib-pybox (**2**), phen-pybox (**3**) and benz-pybox (**4**) were in agreement with literature values [12, 13] and the ligands were synthesised in 30–50% overall yield. The Diels-Alder reactions were carried out at -40°C under argon in dichloromethane (DCM) for 24–48 h. MCl_x (0.50 mmol) was reacted with ligand (0.55 mmol) in dry DCM under argon. The solution was stirred overnight and then cooled to -40°C . Cyclopentadiene (12.50 mmol) and dienophile (methacrolein or crotonaldehyde) (2.50 mmol) were then added and the reaction proceeded for 24–48 h, and the products were purified by distillation. The use of these Diels-Alder reactions allows compari-

son of results to other Lewis acid systems [14].

For the methacrolein adduct the endo:exo ratio was determined by comparing the aldehydic proton singlets at $\delta = 9.38$ and 9.67 in ^1H NMR. For the crotonaldehyde adduct the doublets at $\delta = 9.36$ and 9.77 were compared. Endo:exo ratios and enantiomeric excesses were calculated from the ^1H NMR after the crude adduct aldehydes were derivatised to the corresponding acetal of 2*R*, 4*R* pentanediol in the following manner: 1.5 mol equiv. of diol were placed in a small flask containing the aldehyde and a catalytic amount of *p*-toluenesulphonic acid (methacrolein adduct) or pyridinium *p*-toluenesulphonic acid (crotonaldehyde adduct) were added along with dry DCM and a small amount of Na_2SO_4 and allowed to react for 24 h. The solution was then passed through a plug of silica and the product analysed by ^1H NMR. Enantiomeric excess (ee) was determined by comparing the ratio of diastereotopic singlet protons at $\delta = 4.69$ (*R*) and 4.67 (*S*) for the methacrolein product and the doublet protons at $\delta = 4.15$ (*S*) and 4.10 (*R*) for the crotonaldehyde product.

References and Notes

1. Kagan, H.B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007.
2. Corey, E.J.; Imai, N.; Zhang, H.Y. *J. Am. Chem. Soc.* **1991**, *113*, 728.
3. Corey, E.J.; Ishimara, K. *Tetrahedron Lett.* **1992**, *33*, 6807.
4. Evans, D.A.; Murry, J.A.; von Matt, P.; Norcross, R.D.; Miller, S.J. *Angew. Chem. Int. Ed. Engl.* **1995**, *35*, 798.
5. Howarth, J.; Gillespie, K. *Tetrahedron Lett.* **1996**, *37*, 413.
6. Bedekar, A.V.; Koroleva, E.B.; Andersson, P.G. *J. Org. Chem.* **1997**, *62*, 2518.
7. Hansen, K.B.; Leighton, J.L.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1996**, *118*, 10924.
8. Schaus, S.E.; Branault, J.E.; Jacobsen, E.N. *J. Org. Chem.* **1998**, *63*, 403.
9. Sigman, M.S.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1998**, *120*, 5315.
10. Nesper, R.; Pregosin, P.S.; Puentener, K.; Woerle, M. *Helv. Chim. Acta* **1993**, *76*, 2239.
11. Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340.
12. (a) Martinez, L.E.; Leighton, J.L.; Carsten, D.H.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1995**, *117*, 5897; (b) Larrow, J.F.; Schaus, S.E.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1996**, *118*, 7420; (c) Schaus, S.E.; Larrow, J.F.; Jacobsen, E.N. *J. Org. Chem.* **1997**, *62*, 4197.
13. Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500.
14. Narasaka, K. *Synthesis*, **1991**, 1.

Sample Availability: Not available.