Tetrahedron: Asymmetry Vol. 1, No. 3, pp. 199-214, 1990
Printed in Great Britain

0957-4166/90 $3.00+.00
Pergamon Press plc

ASYMMETRIC DIELS-ALDER REACTION CATALYSED BY SOME CHIRAL LEWIS ACIDS

F. REBIERE , O. RIANT , H. B. KAGAN*

Laboratoire de Synthèse Asymétrique
ICMO (URA CNRS N° 255)
Université Paris Sud, 91405 Orsay, France

(*Received* 19 *January* 1990)

ABSTRACT : Diels-Alder reaction between cyclopentadiene and various dienophiles (mainly methacrolein) at -78°C was catalysed by various chiral aluminum alcoholates. The catalysts were prepared by reaction of $EtAlCl_2$ with several families of diol (or their monoether monoalcohol derivatives) . The most enantioselective catalyst is derived from diol **5a**. A detailed investigation in that case gives some light on the experimental parameters of the system, especially the reproductible preparation of the catalyst. Enantiomeric excess up to 86% (in exo cycloadduct **2a**) could be achieved. Tentative structures are proposed for the transition state of the reaction.

INTRODUCTION

The Diels-Alder reaction is one of the most powerful methods for the stereoselective elaboration of rings with an array of asymmetric centers. Good control of relative stereochemistry is obtained in many cases of thermal or Lewis acid catalysed Diels-Alder reactions. Highly enantioselective Diels-Alder reactions have been achieved with the help of a *chiral auxiliary* bound to diene or dienophile[1-4].

Asymmetric catalysis is the most promising process to propagate chirality from small amount of a chiral auxiliary[5]. The use of chiral Lewis acids for controlling enantioselectivity of Diels-Alder reaction has proved to be difficult[6]. The first significant result was published in 1979 by Koga[8] with a chiral catalyst *in situ* prepared from (-) menthol and ethylaluminum dichloride. This catalyst (15% mol equiv) has been used for the condensation at -78°C between cyclopentadiene and methacrolein. Adduct **2a** (mainly exo stereoselectivity) was isolated with ee's up to 72%. The reaction is difficult to control and for almost 8 years there were no further reports of this interesting system. In 1987 Koga confirmed and developed his pionneer work[9]. Menthoxy dichloroaluminum displays some catalytic activity in the hetero Diels-Alder reaction (ee's up to 16%)[10]. Very recently, Yamamoto described spectacular results (ee's up to 97%) in some hetero Diels-Alder reactions catalysed by a bulky chiral organo aluminum complex prepared from (R)-3,3'-bis(tris-arylsilyl)binaphtol and trimethylaluminum[11]. Corey also had excellent results with an aluminum complex prepared from trimethylaluminum and a chiral

disulfonamide in the Diels-Alder reaction between a cyclopentadiene derivative and 3-acryloyl-1,3-oxazolidine-2-one[12].

Titanium complexes prepared from chiral diols have been used as chiral Lewis acids for the Diels-Alder reactions. Stoichiometric amounts of titanium complex are usually needed, and enantiomeric excesses in the range of 90-95% have been obtained by various authors in the condensation of cyclopentadiene and some specific acrylamides[13-15]. Catalytic use of titanium complexes is a recent developement. Reetz *et al.*[16] found that the formation of adduct **2** (16% ee) could be catalysed by 1,1-binaphtoxy dichlotitanium. Narasaka *et al* [17-18] made the interesting observation that 4Å molecular sieves allow the use of catalytic amounts of a dialkoxy dichlorotitane (prepared from a chiral diol) keeping the enantioselectivity at the level of 90% ee. The same authors found that 1,3,5-trialkylbenzenes are excellent solvents for enhancing the enantioselectivity.

Chiral boron complexes have also been investigated in Diels-Alder reactions. A chiral boron complex prepared from juglone and a disubstituted 1,1'-binaphtol stoichiometrically react with various dienes to give Diels-Alder adducts with ee's to 98%[19]. Catalysts of type $RBBr_2$ (R= pinanyl) catalysed at -78°C the formation of adduct **2** (28% ee)[20]. Very recently, Yamamoto *et al.* found that a boron complex *in situ* formed from mono-acyl tartaric acid and diborane is an excellent asymmetric catalyst for the Diels-Alder reaction of cyclopentadiene and acrylic acid (78% ee)[21] or of cyclopentadiene and methacrolein (96% ee)[22].

The last class of chiral Lewis acids to have been investigated comprises that of europium complexes. These complexes catalysed asymmetric hetero Diels-Alder reactions with enantiomeric excesses up to 60%[23-24], but they are not active in the usual Diels-Alder reaction.

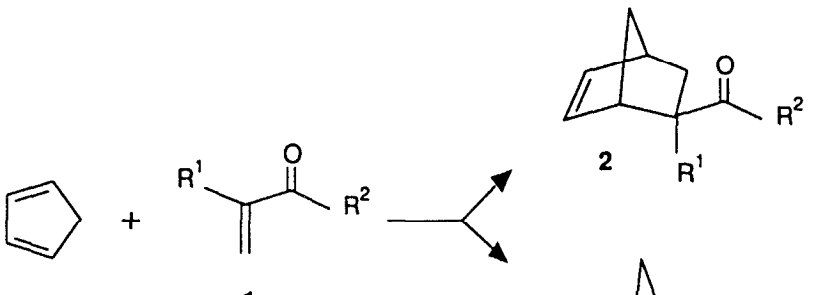
We have investigated over several years various possibilities of asymmetric catalysis of the Diels-Alder reaction. We wish to present herein results concerning the condensation of cyclopentadiene and some dienophiles (mainly methacrolein) to form adducts **2**. We selected as chiral catalysts aluminum complexes which are easily prepared from reactions of ethylaluminum dichloride and various chiral alcohols or diols.

RESULTS

The basic hypothesis at the initial stage of this work was to elaborate more sophisticated aluminum alcoholates than the catalyst discovered by Koga[8,9]. We envisaged complexes where an oxygen is in the vicinal position of the alkoxide moiety, with the hope to take benefit of chelation, as depicted in **4**, for a better control of asymmetric catalysis. As a model reaction, we selected the cycloaddition between methacrolein **1a** and cyclopentadiene. Some reactions were also performed with acrolein **1b** and methyl acrylate **1c**.

We first prepared, for comparison, menthoxy dichloaluminum from (-) menthol and ethylaluminum dichloride. This chiral catalyst (0.1 equiv.) mainly gave exo cycloaddduct **2a** with 56% enantiomeric excess (in good agreement with the results of Koga[9]). The reaction was performed in dichloromethane at -78°C and results were very reproducible by following a specific experimental procedure for the preparation of the catalyst (*vide-infra*). The enantiomeric excess of **2a** was

measured by ^1H NMR analysis of the formyl proton in the presence of $Eu(hfc)_3$ or by isolation of pure **2a** and determination of its optical purity (taking $[\alpha]_D$ -23.3° (EtOH) as the maximum specific rotation[25]).

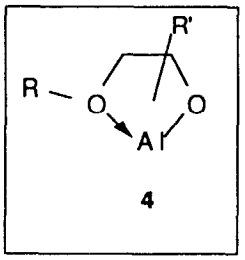


a : R^1 = Me R^2 = H

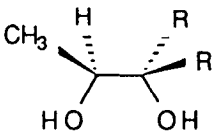
b : R^1 = H R^2 = H

c : R^1 = H R^2 = OMe

In our standard conditions for the synthesis of **2a**, we compared the behaviour of various catalysts prepared from some chiral diol monoethers (**10** , **11**). These ethers were synthesized from the corresponding diols (see experimental section). The chiral diols were prepared by addition of an excess of organometallics on (S)-ethyl lactate, (S)-ethyl mandelate or (R)-ethyl β-hydroxy-butyrate. For some Grignard reagents it was necessary to protect first the secondary alcohol through benzylation. All details are given in the experimental section.

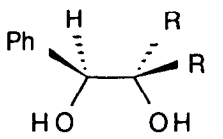


4



5

a : R = Ph
b : R = p-Tol
c : R = 1-Napht
d : R = CH_2Ph



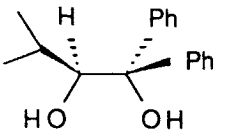
6

a : R = Ph
b : R = Me
c : R,R = -$(CH_2)_5$-

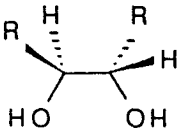
Enantiomeric excesses of cycloadduct **2a** were disappointingly low (Table 1) when alcohol monoethers (**10**, **11**) were used to prepare aluminum catalysts, either with the hydroxy group on the asymmetric center or on the vicinal position. We

then investigated the efficiency of chiral aluminum diolates by taking a 2:1 ratio between ethylaluminum dichloride and diol but optical yields remained very low (Table 1). In a third set of experiments the catalyst was prepared with a 1:1 ratio of ethylaluminum dichloride and diol which leaves one free hydroxy group per aluminum atom (results are listed in Table 2). This stoichiometry gave many cases of enantiomeric excesses below 20%, but quite high enantiomeric excesses were observed with diols **5** (44-73% ee, entries 1-3 Table 2).

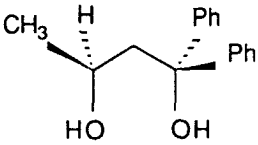
Since diol **5a** is the most easy to prepare and also leads to the highest enantiomeric excess (73% ee, exo/endo = 98:2), we selected this case for a detailed study.



7

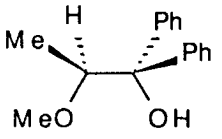


8

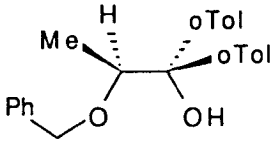


9

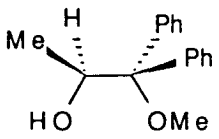
a : R = Me
b : R = Ph
c : R = CO_2Et



10a



10b



11

TABLE 1

Diels-Alder reaction between methacrolein and cyclopentadiene catalysed by Cl_2AlOR^* (R*OH=**10**, **11**, **5a**).

	Chiral alcohol[a]	Isolated yield[b]	Exo/endo	ee of **2a**[c]
1	**10a**	90%	95:5	20 (+)
2	**10b**	90%	95:5	20 (+)
3	**11**	90%	92:8	0
4	**5a**[d]	95%	95:5	0

a) Catalyst prepared by reaction between R*OH and $EtAlCl_2$ (1:1), unless stated. b) 0.1 mol equiv catalyst, reaction at -78°C in CH_2Cl_2. c) Measured by H^1 NMR with $Eu(hfc)_3$. d) 2 mol equiv of $EtAlCl_2$.

TABLE 2

Diels-Alder reaction between methacrolein and cyclopentadiene catalyzed by Cl_2AlOR^* (R*OH=chiral diols **5-9**)

	Chiral diol[a]	Isolated yield[b]	exo/endo	ee of **2a**[c]
1	**5 a**	90%	98:2	73% (-)
2	**5 b**	90%	98:2	55% (-)
3	**5 c**	80%	98:2	44% (-)
4	**5 d**	30%	96:4	0
5	**6 a**	40%	93:7	6% (-)
6	**6 b**	90%	96:4	0
7	**6 c**	90%	95:5	0
8	**7**	90%	92:8	18% (-)
9	**8 a**	90%	90:10	0
10	**8 b**	90%	90:10	0
11	**8 c**	80%	98:4	18% (+)
12	**9**	90%	98:2	20% (+)

a) Catalyst prepared at room temperature in CH_2Cl_2 from chiral diol and $EtAlCl_2$ (1:1). b) 0.1 mol equiv catalyst, reaction at -78°C for 20 h in CH_2Cl_2. c) Measured by ^1H NMR with $Eu(hfc)_3$.

Study of experimental parameters with chiral aluminum catalyst prepared from diol **5a**

1/ *Catalyst preparation :*

(S)-diol **5a** in dichloromethane reacts at -78°C with one mol equiv of $EtAlCl_2$. The soluble aluminum complex was then immediately used at -78°C as catalyst for the Diels-Alder reaction or the solution was kept at room temperature for an ageing period. The enantiomeric excess of cycloadduct **2a** has been found to be *highly dependent of ageing time* (Table 3). The best procedure was to wait for 2-3 hours at room temperature before to start the catalytic Diels-Alder reaction at -78°C. Under these conditions, very reproducible results have been obtained, with ee=73% ±1%. The ageing period corresponds to a chemical modification of the system, as established by polarimetry and ^1H NMR studies of the solution. We have no information about the structural changes occuring during the warm-up from -78°C to room temperature. The slow decrease of specific rotation by standing at room temperature could be correlated with modifications in ^1H NMR spectrum, and this point will be discussed later. In view of the deleterious effect of traces of water during catalytic reactions involving titanium alcoholates[17,18,26] we briefly explored the influence of molecular sieves. In our standard conditions (-78°C) there was an

important decrease of enantioselectivity by addition of molecular sieves or by introduction of 1 mol equiv of water (entries 7,8 Table 3).

TABLE 3

Influence of the ageing time or addition of molecular sieves or water on the enantioselectivity of aluminum catalyst prepared from $EtAlCl_2$ and (S)-**5a** in the synthesis of (-)-**2a** by Diels-Alder reaction.

	Ageing time[a]	α of solution[b] (l = 1 dm)	Isol. yield	Exo/endo	ee of **2a**
1	0	-	90%	93:7	6% (-)
2	0.5 h	-13.1°	90%	98:2	66% (-)
3	1 h	-11.5°	90%	98:2	69% (-)
4	3 h	-11.4°	90%	98:2	73% (-)
5	5 h	-8.58°	90%	98:2	60% (-)
6	20 h	-0.26°	90%	98:2	17% (-)
7	3 h[d]	-	90%	98:2	45% (-)
8	3 h[e]	-	50%	98:2	55% (-)

a) Catalyst was prepared at -78°C in CH_2Cl_2 and was kept at room temperature for a ageing time. b) Measured in CH_2Cl_2 at 365 nm. c) Reaction : 20h at -78°C. d) Addition of 4 Å molecular sieves. e) Addition of 1 mol equiv H_2O.

TABLE 4

Preparation of achiral aluminum catalyst from $EtAlCl_2$ or i-$PrOAlX_2$ and (S)-**5a**, and use in the asymmetric synthesis of (S)-**2a**.

	Precursor[a,b]	Exptl. conditions[c]	Isolated yield	Exo/endo	ee[d]
1	$EtAlCl_2$	CH_2Cl_2	90%	98:2	73%
2	$EtAlCl_2$	toluene	80%	98:2	72%
3	*i*-$PrOAlCl_2$	CH_2Cl_2	70%	98:2	60%
4	*i*-$PrOAlCl_2$	toluene[d]	55%	98:2	73%
5	*i*-$PrOAlBr_2$	toluene[d,e]	0		

a) Reaction with 1 mol equiv of (S)-**5a** at -78°C, ageing period: 3h at room temperature. b) Catalyst: 0.1 mol equiv by respect to methacrolein. c) Reaction : 20h at -78°C. d) Elimination of isopropanol by evaporation e) Catalyst is insoluble.

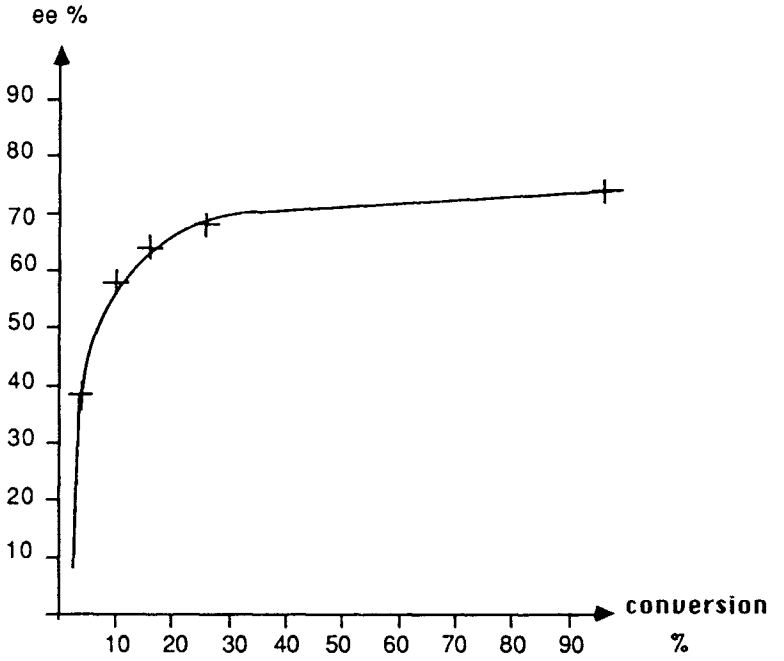
Replacement of dichloromethane by toluene does not influence optical yields (see entries 1,2 in Table 4).

The chiral catalyst could be prepared by a procedure avoiding $EtAlCl_2$. This method involves the reaction between diol (S)-**5a** and *i*-$PrOAlCl_2$, in dichloromethane or toluene. In this last case it is necessary to remove isopropanol by evaporation. Some representative results are given in Table 4.

2/ *Influence of catalytic ratio on conversion extent :*

A decrease of the catalytic ratio from 0.1 to 0.01 does not stop the reaction performed under the standard conditions at -78°C. The isolated yield is 50% after 20 h (instead of 90%). The ee of (-)-**2a** is not changed (73%). Increasing the amount of catalyst too much is not beneficial on the ee : catalyst ratio of 0.5 or 1 give ee's of 64% and 51% respectively (after 20 h).

The standard reaction (catalyst ratio = 0.05) could be followed from its early beginning (5% conversion). There is a progressive increase in the ee of the cycloadduct **2a** from 38% to 73% (Figure 1). This significant change means that the chiral catalyst (prepared with 3 h ageing at room temperature) is modified at -78°C in presence of the reactants. At the beginning of the reaction the catalytic species is not very enantioselective. A rough calculation allows an estimation of the enantioselectivity in the final stages of the Diels-Alder reaction. the correction for the initial low enantiomeric excess gives a value of 75% in the final turnovers of the reaction.



Asymmetric synthesis of (-)-**2a** with a chiral catalyst (0.05 mol equiv) prepared from $EtAlCl_2$ and (S)-**5a** (1:1). Reaction performed in CH_2Cl_2 at -78°C.

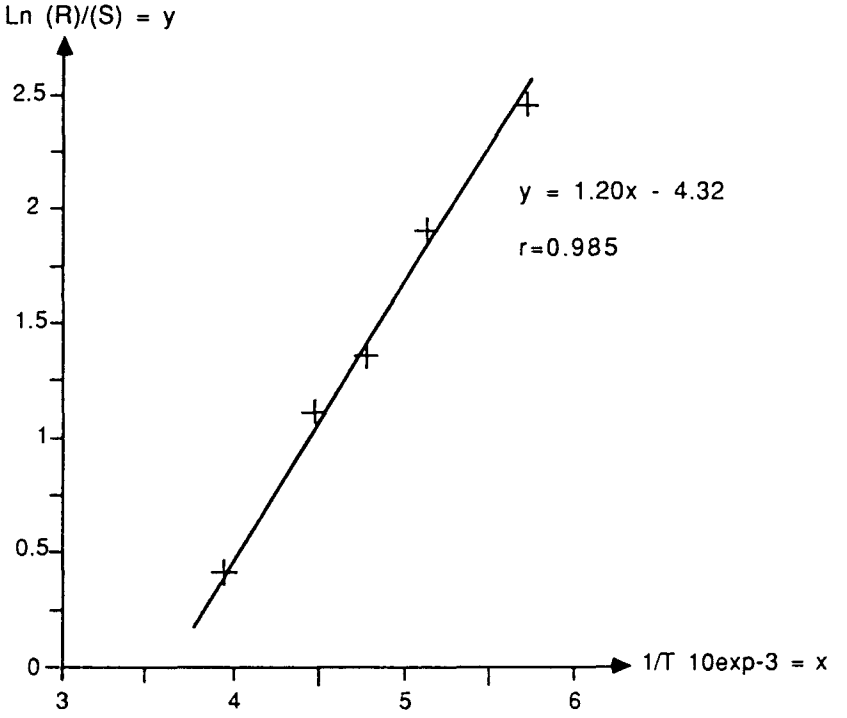
Figure 1

The dependency of ee with concentration of reactants has not been studied thoroughly. A decrease of methacrolein concentration parallels a decrease of enantioselectivity.

3/ *Influence of temperature:*

Comparative experiments were performed between -20°C and -100°C with the standard system (catalyst ratio = 0.1). There is an important increase in the optical yield when decreasing the temperature. At the lowest temperature (-)-**2a** was prepared with 86% ee. The plot Ln[R]/[S] versus 1/T (T absolute temperature) gives a straight line (Figure 2) with an excellent correlation coefficient (r=0.985). From the equation of the line , and using the relation $Ln[R]/[S] = -\Delta H /RT + \Delta S /R$ it is possible to calculate ΔH = -2.46 kcal mol^{-1} and ΔS = -8.9 eu.

At -78°C the observed enantioselectivity arises from an enthalpic control since ΔG = -0.74 kcal mol^{-1}, ΔH = -2.46 kcal mol^{-1} and $-T\Delta S$ = +1.73 kcal mol^{-1}. A more negative entropy characterises the preferred transition state and opposes to the enantioselectivity of the reaction. Lowering of temperature significantly decreases the $-T\Delta S$ term. Calculations indicate that 99% ee should be attained for T = 123 K (-150°C).



Influence of temperature on the asymmetric Diels-Alder reaction giving (-)-**2a** in CH_2Cl_2 at -78°C (0.1 mol equiv catalyst prepared from $EtAlCl_2$ and (S)-**5a** (1:1). Details are in experimental section.

Figure 2

4/ Diels-Alder reaction with acrolein or methyl acrylate :

The standard catalyst ($EtAlCl_2$/(S)-**5a** = 1:1, catalyst ratio = 0.1) was used for the cycloaddition between cyclopentadiene and some dienophiles other than methacrolein. Results are indicated in Table 5. Diastereoselectivity and enantioselectivity are poor. The same trend has been already observed when methacrolein is replaced by acrolein in various asymmetric Diels-Alder reactions[9].

TABLE 5

Diels-Alder reaction between acrolein or methyl acrylate and cyclopentadiene catalysed by $EtAlCl_2$ / **5a** combination

Dienophile	Solvent[a], temperature	Isolated yield (%)	Exo/endo[b]	ee[c] (%)
Acrolein	CH_2Cl_2, -78°C	70%	30:70	exo: 23 endo:29
Acrolein	Toluene,-78°C	70%	16:84	endo: 25
Methyl acrylate	CH_2Cl_2, -20°C	40%	16:84	endo: 36

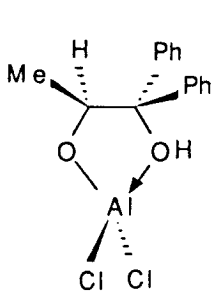
a) 0.1 mol equiv catalyst. b) Measured by ^1H NMR. Diastereomers were not separated. c) Measured by ^1H NMR with $Eu(hfc)_3$.

DISCUSSION

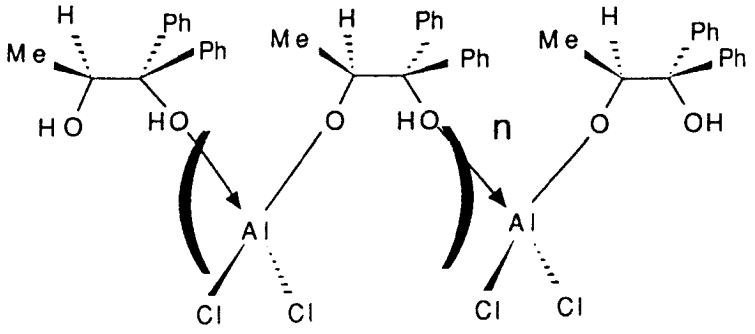
After a large screening of chiral diols and their monoethers it has been possible to devise a simple and efficient chiral catalyst. It is obtained by interaction between (S)-**5a** and $EtAlCl_2$ at -78°C in dichloromethane.

The actual structure of the aluminum alcoholate is not known, but we wish to discuss some likely possibilities. The primary species obtained at -78°C should be the *monoalcoholate* **12**, formed after deprotonation of the less hindered hydroxy group. The ageing at room temperature could be related to oligomerisation process such as **12-13** or to a deeper chemical modification of **12**. ^1H NMR spectroscopy at room temperature (in dichloromethane) clearly shows a structural evolution. The quadruplet at 5.15 ppm (H on the asymmetric center) and the doublet at 1.2 ppm (CH_3) decrease and completely disappear after a long standing at room temperature. This could be indicative of a process leading ultimately to 1,1-diphenylacetone under the Lewis acidity of the medium. This hypothesis (which was not further explored) fits with the simultaneous loss of optical activity and loss

of enantioselectivity in catalysis. The monoalcohol **12**, prepared in dichloromethane at -78°C, has been mixed with two equivalents of methacrolein prior to warming up to room temperature. In this case ^1H NMR again shows a doublet at 1.2 ppm (H at asymmetric center) and a quadruplet at 5.15 ppm (CH_3). There is no modification of the spectrum, even after a long standing (12 h). Presence of the aldehyde, acting as a Lewis base, protects the aluminum complex against degradation.



12



13

After ageing for 2-3h at room temperature the catalyst has the optimum enantioselectivity (see *infra*) and starts to precipitate at -78°C (in dichloromethane). Addition of methacrolein at this temperature results in dissolution after 20 min, presumably by complexation of aluminum by a carbonyl group. Enantioselectivity is always highest when cyclopentadiene is added at -78°C after full homogeneisation of the medium, and not immediately after introduction of methacrolein. In the later case catalysis starts with an aluminum complex of lower enantioselectivity. In the experimental section, a detailed procedure allowing the best enantioselectivity is described.

Even with good control of the ageing periods (at room temperature and then at -78°C with methacrolein) further modification remains a parameter in the reaction. Optical yield is not the same at low conversion (38% ee) or at total conversion (75% ee). This is assigned to a change in the structure of the catalyst, influenced by complexation to reactants or to the cycloadduct.

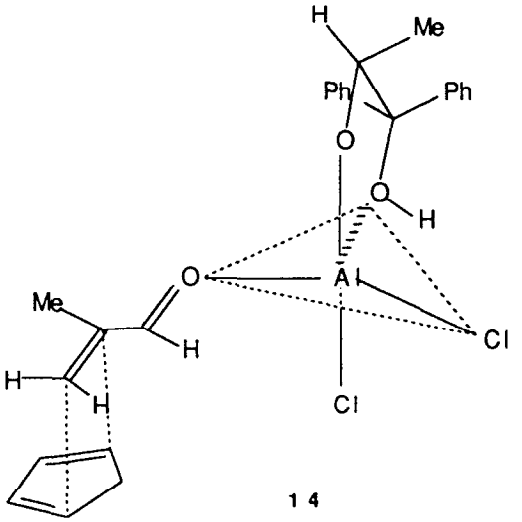
It would be useful to propose a model allowing a correlation of the absolute configuration of the chiral ligand to the absolute configuration of the product **2a**. Catalytic activation occurs by coordination of carbonyl of methacrolein to aluminum. Usually organoaluminum complexes prefer tetracoordination[27]. However several five-coordinate aluminum complexes have been recently described[28], and some six-coordinate aluminum are also known[29]. Consequently we will discuss catalytic properties of **12** or its oligomer **13** on the basis of two models. If the Lewis acidity of **12** (or **13**) is great enough, activation should occur through complex **14**. Decoordination of the OH group in **12** prior to coordination to methacrolein would give the four-coordinate complex **15** (written with two anti conformations along C-C bonds). In the both cases it is the back side of C=C which is less hindered (*si* face), and which will react with cyclopentadiene, in agreement

with experimental data. Model **15** is similar to a model proposed by Koga[9] to explain asymmetric induction by dichloro(-)menthylaluminum. We have no evidence in favour of **14** with respect to **15** or vice-versa.

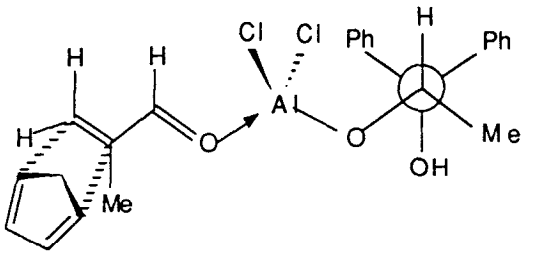
Nonlinear correlations between enantiomeric excess of chiral auxiliary and enantiomeric excess of a product can give some mechanistic informations in asymmetric catalysis[30]. Diol (S)-**5a** of 50% ee was prepared and used to form the aluminum catalyst. Under the standard conditions cycloadduct (-)-**2a** was obtained with 36% ee, this value is exactly half the standard value (73% ee). Hence we conclude that there is no nonlinear effect in our system.

In conclusion, models **14** or **15** accomodate most of the experimental data. The poor behaviour of catalysts prepared from monoalcohols **10b** or **11** are not easily explained by the above models, but may be the replacement of hydroxy group in **14** by an OMe moiety (as in **11**) prevents the chelate formation because of steric interference with the vicinal phenyl groups.

Protection of the catalyst in presence of methacrolein and increase in enantioselectivity during the reaction could be related to the increase of coordination number in complexes **14** or **15** by an additional molecule of methacrolein as ligand.



14



15

CONCLUSION

Quite high enantioselectivity (86% ee) has been reached in the catalytic Diels-Alder reaction between methacrolein and cyclopentadiene, after a careful screening of various chiral aluminum alcoholates. The catalyst issued of **5a** is very specific for the enantioselective formation of **2a**. The detailed investigation needed to improve the optical yield revealed many experimental parameters in order to start the catalytic reaction from the appropriate aluminum species. Presumably these factors should be useful to consider in the future for the devise of new chiral aluminum catalysts.

Acknowledgments

We thank CNRS for a financial support. One of us (O.R.) acknowledges ENS Lyon for a fellowship.

EXPERIMENTAL

Apparatus ^{1}H NMR spectra were recorded on Bruker AM 250 MHz and Bruker AM 200 MHz spectrometers in deuteriochloroform using tetramethylsilane as internal standard. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Melting points were determined on Reichert apparatus and are uncorrected. Microanalysis was performed at the Service microanalyse du CNRS (Gif sur Yvette).

Chemicals Dichloromethane was distilled over calcium hydride and stored under argon. Tetrahydrofuran and toluene were distilled over sodium/ benzophenone ketyl before use. (S) ethyl lactate ($[\alpha]_D$ -11°, neat l=1) was purchased from Fluka. Ethylaluminum dichloride was used as a molar solution in hexanes (Aldrich). (+) $Eu(hfc)_3$ was purchased from Aldrich. All dienophiles were distilled and stored under argon and over 4Å molecular sieves at -20°C before use. Cyclopentadiene was prepared from dicyclopentadiene and used immediately.

(S) 1,1-diphenyl 1,2-dihydroxypropane **5a**

Prepared from (S) ethyl lactate and 3 mol equiv of PhMgBr in ether according to refs[31,32]. Yield: 70%; mp 91-93° (lit. 94°); $[\alpha]_D$ -101°(c= 2.1, MeOH) (lit. $[\alpha]_D$ -97.2°, EtOH); ^{1}H NMR δ 1.12 (3H, d, J=5.6 Hz), 1.84 (1H, s), 2.98 (1H, s), 4.84 (1H, m, J=5.6 Hz), 7.1-7.8 (10H, m).

(S) 1,1-di-*p*-tolyl 1,2-dihydroxypropane **5b**

Prepared as above with *p*-tolylMgBr. Yield: 45% after crystallisation in hexane; mp 91-92°; $[\alpha]_D$ -85° (C=2, MeOH); ^{1}NMR δ 1.11 (3H, d, J=5Hz), 1.64 (1H, s), 2.29 (3H, s), 2.33 (3H, s), 2.86 (1H, s), 4.76 (1H, m, J=5 Hz), 7.0-7.6 (8H, m).

(S) 1,1-di-(1-naphthyl) 1,2-dihydroxypropane **5c**

(S) ethyl lactate was transformed into its O-benzyl ether (Ag_2O, then benzyl bromide) according to ref.[33].

The O-benzyl ether (20 mmol) in THF was treated at room temperature with 3 mol equiv of Grignard reagent prepared from 1-bromonaphthalene and magnesium in THF. O-benzyl ether was isolated as an oil. This crude material was deprotected in THF by 5 mol equiv sodium naphtalenide at 0°C for 15 min giving **5c** with 25% yield after purification by flash-chromatography on silica (cyclohexane/AcOEt= 4:1); mp 102-105°; $[\alpha]_D$ -174° (c=1, MeOH); ^1H NMR δ 0.95 (3H, m), 2.25 (1H, bs), 3.48 (1H, s), 5.75 (1H, m), 7.0-8.5 (14H, m); MS (NH_3, CI) m/e 328 (M^+, 99%), 183 (40), 155 (100), 144 (40), 127 (40). Anal. calcd for $C_{23}H_{20}O_2$: C, 83.20; H, 7.56; O, 9.23. Found C,82.18; H, 7.42; O, 8.06.

(S) 1,1-dibenzyl 1,2-dihydroxypropane **5d**

Prepared as above with $PhCH_2MgBr$. Yield: 85% oil, after flash-chromatography on silica (cyclohexane/AcOEt=2:1); $[\alpha]_D$ +1.16° (c= 4, EtOH); ^1H NMR δ 1.30 (3H, d, J=5Hz), 2.80 (2H, m), 2.86 (2H, m), 3.62 (1H, m, J=5Hz), 7.1-7.4 (10H, m); MS (NH_3, CI) m/e 274 ($M+NH_4^+$, 80%), 256 (M^+, 8), 147 (44), 115 (24), 108 (100), 105 (24). Anal. calcd for $C_{17}H_{20}O_2$: C, 79.66; H, 7.86; O, 12.48. Found C, 78.89; H, 8.10; O, 13.04.

(S) 1,1,2-triphenyl 1,2-dihydroxypropane **6a**

To (S) ethyl mandelate in ether was added 3 mol equiv of PhMgBr according to ref.[34]. Yield: 68% after crystallisation in hexane; mp 127-128° (lit. 126°)[34]; $[\alpha]_D$ -206° (c=1.5, MeOH) (lit. $[\alpha]_D$ -213.°, MeOH)[34]; ^1H NMR δ 2.4 (1H, s), 3.15 (1H, s), 5.65 (1H, s), 7-7.8 (15H, m).

(S) 1-phenyl 2,2-dimethyl 1,2-dihydroxypropane **6b**

Similar procedure than for preparation of **6a**. Yield: 55% oil, after flash-chromatography on silica (cyclohexane/AcOEt= 2:1); $[\alpha]_D$ -16.5°, (C= 1.6, EtOH) (lit. $[\alpha]_D$ - 16.5°, c= 2 MeOH)[35]; ^1H NMR δ 1.1 (3H, s), 1.25 (3H, s), 4.5 (1H, s), 7.3-7.5 (5H, m)

(S) 1-phenyl 2,2-pentamethylene 1,2-dihydroxypropane **6c**

The Grignard reagent derived from 1,5-dibromopentane was added as above to (S) ethyl mandelate. Yield: 15% oil, after flash-chromatography on silica (cyclohexane/AcOEt= 2:1), $[\alpha]_D$ +8.9 ° (c= 2 , MeOH); ^1H NMR δ 1.2-1.7 (4H, m), 2.0 (2H, m), 3.7 (1H, m), 4.45 (1H, d), 4.9 (2H, m), 5.75 (1H, m), 7.25-7.45 (5H, m); MS (NH_3, CI) m/e 224 ($M+NH_4^+$, 31%), 206 (M^+, 13), 190 (31), 108 (100), 105 (31); Anal. calcd for $C_{13}H_{18}O_2$: C, 75.7; H, 8.79; O, 15.51. Found C, 75.06; H, 9.25; O, 15.47.

(S) 1,1-diphenyl 3-methyl 1,2-dihydroxybutane **7**

7 was synthetised from (S) ethyl 2-hydroxy-isovalerate. This ester has been prepared by nitrous deamination of (S)-valine (according to the general procedure described in ref.[36]). (S) 2-hydroxy-isovaleric acid was obtained in 35% yield after crystallisation in pentane/ether; $[\alpha]_D$ 14.5° (c=1.8, $CHCl_3$). Esterification by ethanol in toluene gave ethyl ester in 70% yield, $[\alpha]_D$ -1.87 (neat, l=1). Addition of 3 mol equiv of PhMgBr in ether gave **7**. Yield: 60 % after crystallisation in cyclohexane, mp 106 ° (lit 102°)[35], $[\alpha]_D$ -164° (c= 0.8, benzene) (lit $[\alpha]_D$ -164°, benzene)[37].^1H NMR δ 0.9 (6H, d.d), 1.7 (1H, m), 4.5 (1H, d), 7.1-7.7 (10H, m).

(S) 1,1-diphenyl 1,3-dihydroxybutane **9**

(S) Ethyl 3-hydroxybutyrate (90% ee) was prepared by Baker's yeast reduction of ethyl acetoacetate according to ref.[38]. Reaction with 3 mol equiv of

PhMgBr in ether gave **9** in 45% yield after crystallisation in cyclohexane; mp 79° (lit. 80-82°), $[\alpha]_D$ +58.5° (c= 1, $CHCl_3$) (lit.$[\alpha]_{Hg}$ +65.4°, $CHCl_3$). **9** has previously been described in refs[39,40]. ^1H NMR δ 1.2 (3H, d), 2.4 (2H, m), 3.9 (1H, m), 7.1-7.5 (10H, m).

(S) 1,1-diphenyl 1-hydroxy 2-methoxypropane **10a**

Prepared in THF by using 1.2 mol equiv NaH and 1.2 mol equiv of MeI at room temperature for 24h. After crystallisation in pentane **10a** was isolated in 80% yield: mp 69° (lit. 72°)[41], $[\alpha]_D$ -131° (c=1.05, $CHCl_3$) (lit.$[\alpha]_D$ -91°, MeOH)[41]; ^1H NMR δ 1.03 (3H, d, J=6.6Hz), 3.4 (3H, s), 4.32 (1H, m), 7.1-7.6 (10H, m).

(S) 1,1-di-o-tolyl 1-hydroxy 2-benzyloxypropane **10b**

Prepared as for **5e** from (S) ethyl lactate O-benzyl ether and 2 mol equiv of o-tolylMgBr in ether. Yield: 60% after flash-chromatography on silica (cyclohexane/AcOEt=2:1) and crystallisation in hexane; mp 72-74°, $[\alpha]_D$ -60 ° (c= 2, MeOH); ^1H NMR δ 1.05 (3H, d), 2.0 (3H, s), 4.6 (1H, m), 4.65 (2H, m), 7.0-7.5 (13H, m). Anal. calcd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56; O, 9.20. Found: C, 82.20; H, 7.5; O, 8.1.

(S) 1,1-diphenyl 1-methoxy 2-hydroxypropane **11**

11 was prepared in two steps from diol (S)-**5a**: O-benzylation of the secondary alcohol in a similar procedure as for the alcohol **10a**. Yield: 98%. The resulting ether **10c** (mp 75°, $[\alpha]_D$ -45.5° (C=1.5, $CHCl_3$)) was O-methylated (1 molar equiv *n*-BuLi in THF at 0°C for 1h, then 1.2 molar equiv MeI for 3 days at room temperature) in 76% yield into *(S)-1,1-diphenyl 1-methoxy 2-benzyloxypropane* as an oil ; ^1H NMR δ 1.1 (3H, d, J=8.2Hz), 3.14 (3H, s), 4.50 (1H, m), 4.64 (2H, m), 7.1-7.5 (15H, m); MS (NH_3, CI) m/e 225 (100%), 197 (78), 105 (42). Anal. calcd for $C_{23}H_{24}O_2$: C, 79.34; H, 7.44; O, 13.22. Found C, 79.79; H, 7.45; O, 12.82.

The diether compound was debenzylated under hydrogen (1 atm) in presence of Pd(10%)/C at room temperature for 3 days. The oily monoether **11** was recovered in 40% yield after purification by flash-chromatography on silica (cyclohexane/AcOEt= 5:1); $[\alpha]_D$ -7.8° (c=3.5 in $CHCl_3$). ^1H NMR δ 1.09 (3H, d, J=6.6Hz), 2.12 (1H, d, J=5Hz), 3.04 (3H, s) 4.73 (1H, m), 7.25-7.5 (10H, m); MS (NH_3, CI) m/e 260 ($M+NH_4^+$, 0.3%), 228 (47), 211 (90), 197 (100). Anal. calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.44; O, 13.22. Found C, 79.79; H, 7.45; O, 12.86.

Catalysed Diels-Alder reaction between methacrolein and cyclopentadiene

The following standard procedure has been applied with a catalyst derived from $EtAlCl_2$ and (S)-**5a**.

0.46 g of (S)-**5a** (2 mmol) dissolved in 20 mL dichloromethane under argon is cooled to -78°C. To this solution is added at -78°C 1 mmol $EtAlCl_2$ (1 mL of 1 N hexane solution). After 3 h stirring at room temperature and cooling again to -78°C (some precipitation occurs), 0.8 mL freshly distilled methacrolein were added. After 0.5 h stirring at -78°C (homogen isation occured) 1.1 mL cyclopentadiene (15 mmol) was introduced. After standing at -78°C for 18 h the reaction was quenched by addition of 20 mL water. An ether extraction, washing by saturated NaCl solution and drying on $MgSO_4$ yielded 1.8 g oily **2a**. Isolated yield: >95%, exo/endo=98:2, ee=73% (measured by ^1H NMR on formyl proton after addition of 1 molar equiv Eu(hfc)$_3$, 44 Hz separation between the 2 enantiomers). Purification by flash-chromatography on silica (CH_2Cl_2/cyclohexane= 3:2) gave 1.3 g (95% yield) of (-)-**2a**, $[\alpha]_D$ -17.0° (c=1, EtOH 95%). ee=73%.

^{1}H NMR and MS are in agreement with structure **2a**.

The catalyst has also been prepared from i-PrOAlCl$_2$ or i-PrOAlBr$_2$ and (S)-**5a**:

In a dry Schlenck tube were placed 7.5 mmol (i-PrO)$_3$Al (1.53 g) and 23 mL dry toluene. 15 mmol AlX$_3$ (2g sublimed AlCl$_3$ or 4g AlBr$_3$) were slowly added. The resulting solution was stirred 48 h under argon at room temperature, and 1 mL of this 1 M solution is added to a solution of 0.46 g (S)-**5a** (2 mmol) in 20 mL toluene at -78°C. After warm to room temperature and standing for 3 h, the isopropanol was evaporated. The catalyst (as a powder) was cooled to -78°C and can be used as above.

Catalysed Diels-Alder reaction between acrolein and cyclopentadiene

The reaction was performed in standard conditions as above (catalyst prepared from EtAlCl$_2$ and (S)-**5a**), furnishing 1.6 g crude adducts (85% yield), exo/endo=30:70 (measured by ^{1}H NMR after addition of 1 mol equiv Eu(hfc)$_3$ (40 Hz separation on formyl proton). **2b**: 23% ee, **3b**: 29% ee.

Catalysed Diels-Alder reaction between methyl acrylate and cyclopentadiene

The reactions were run under standard conditions (catalyst prepared from EtAlCl$_2$ and (S)-**5a**) at -20°C for 24 h.; 0.55 g (37% yield) of purified adducts **2c**, **3c** was obtained after flash-chromatography on silica (CH_2Cl_2/hexane= 3:1). Exo/endo= 16:84 (^{1}H NMR). **3c**: 40% ee (^{1}H NMR, 0.1 mol equiv Eu(hfc)$_3$, 20 Hz separation on methoxy).

REFERENCES AND NOTES

(1) For reviews on asymmetric Diels-Alder reactions see refs[2-4].

(2) Paquette, L. A. in *"Asymmetric Synthesis"*, Morrison, J. D. ed. , Vol 3B, p.455, Academic Press, N. Y., **1984**.

(3) Oppolzer, W. ; *Angew. Chem. Int. Ed. Eng.l* , **1984**, 23, 876-889.

(4) Helmchen, G. ; Karge, R. ; Weetman, J. in *Modern Synthetic Methods 1986*, Scheffold, R. ed, Vol 4, 262

(5) Bosnich, B. ; *"Asymmetric Catalysis"*, NATO ASI Series, Martiners Nijhoff Publishers, Dordrecht, **1986**.

(6) BF_3 complex with (-)-menthyl ethyl ether catalyses the Diels-Alder reaction between cyclopentadiene and methyl acrylate giving a product with a very small optical activity[7].

(7) Guseinov, M. M. ; Akhmedov, I. M. ; Mamedov, E. G. ; *Azerb. Khem. Zh.* , **1976**, (1), 46. *Chem. Abstr.* **1976**, 85, 176295z.

(8) Hashimoto, S. ; Komeshima, N. ; Koga, K. ; *J. Chem. Soc. Chem. Comm.* , **1979**, 437.

(9) Takahashi, I. ; Hashimoto, S. ; Ikota, N. ; Tomioka, K. ; Koga, K. ; *Tetrahedron Lett.* , **1987**, 28, 5687-5690.

(10) Quimpère, M. ; Jankowski, K. ; *J. Chem. Soc. Chem. Comm.* , **1987**, 676-677.

(11) Maruoka, K. ; Itoh, T. ; Shirasaka, T. ; Yamamoto, H. ; *J. Am. Chem. Soc.* , **1988** ,110 , 310-312.

(12) Corey, E. J. ; Imwinkelried, R. ; Pikul, S. ; Xiang, Y. B. ; *J. Am. Chem. Soc.* , **1989**, 111 , 5493-5495.

(13) Narasaka, K. ; Inoue, M. ; Okada, N. ; *Chem. Lett.* , **1986**, 1109-1111.

(14) Chapuis, C. ; Jurczak, J. ; *Helv. Chim. Acta* , **1987**, 70, 436-440.
(15) Seebach, D. ; Beck, A. K. ; Imwinkelried, R. ; Roggo, S. ; Wonnacott, A. ; *Helv. Chim. Acta* , **1987**, 70, 954.
(16) Reetz, M. T. ; Kyung, S. H. ; Bolm, C. ; Zierke, T. ; *Chem. Ind.* (London), **1986**, 824.
(17) Narasaka, K. ; Inoue, M. ; Yamada, T. ; *Chem. Lett.* , **1986**, 1967-1968.
(18) Narasaka, K. ; Inoue, M. ; Yamada, T. ; Sugimori, J. ; Ywasawa, N. ; *Chem. Lett.* , **1987**, 2409-2412.
(19) Kelly, T. R. ; Whiting, A. ; Chandrakumar, N. S. ; *J. Am. Chem. Soc.* , **1986**, 108, 3510-3513.
(20) Kauffman, D. ; Bir, G. ; *Tetrahedron Lett.* , **1987**, 28, 777-780.
(21) Furuta, K. ; Miwa, Y. ; Iwanaga, K. ; Yamamoto, H. ; *J. Am. Chem. Soc.* , **1988**, 110, 6254-6255.
(22) Furuta, K. ; Simizu, S. ; Miwa, Y. ; Yamamoto, H. ; *J. Org. Chem.*, **1989**, 54, 1481-1483.
(23) Bednarski, M. ; Maring, C. ; Danishefski, S. ; *Tetrahedron Lett.* , **1983**, 24, 3451.
(24) Bednarski, M. ; Danishefski, S. ; *J. Am. Chem. Soc.* , **1983**, 105, 3716.
(25) Berson, J. A. ; Walla, J. S. ; Remanick, A. ; Susuki, S. ; Reynolds-Warnhoff, P. ; Willner, D. ; *J. Am .Chem. Soc.*, **1961**, 83, 3986.
(26) Hanson, R. M. ; Sharpless, K. B. ; *J. Org. Chem.*, **1986**, 51, 1922.
(27) Kagan, H. B. in *Comprehensive Organometallic Chemistry*, (Wilkinson, G. ed), **1982**, Vol 8, 463.
(28) Sierra, M. L. ; Srini, V. ; de Mel, J. ; Oliver, J. P. ; *Organometallics*, **1989**, 8, 2486-2488, and references quoted therein.
(29) Leman, J. T. ; Barron, A. R. , *Organometallics*, **1989**, 8, 1828-1829.
(30) Puchot, C. ; Samuel, O. ; Dunach, E. ; Zhao, S. ; Agami, C. ; Kagan, H. B. ; *J. Am .Chem. Soc.*, **1986**, 108, 2353-2 .
(31) Tiffeneau, M. ; *C. R. Acad. Sci.* (Paris), **1908**, 29, 5821.
(32) Taker, K. ; Vasi, I. G. ; *J. Sci. Indust. Res.* , **1961**, 20B, 66.
(33) Mislow, K. ; O'Brien, R. E. ; Schaeffer, H. ; *J Am. Chem. Soc.* , **1962**, 84, 1940-1944.
(34) Devant, R. ; Mahler, U. ; Braon, M. , *Chem. Ber.* , **1988**, 121, 397-406.
(35) Fuganti, C. ; Ghiringhelli, D. ; *Gazz. Chim. Ital.* , **1969**, 99, 316-322.
(36) Seebach, D. ; Hungerbuhler, E. ; in *Modern Synthetic Methods 1980*, Scheffold, R. ed, Salle + Sauerlander, 160-1 .
(37) Vigneron, J. P. ; Dhaenens, M. ; Horeau, A. ; *Tetrahedron*, **1977**, 33, 507-510.
(38) Seebach, D. ; Sutter, M. A. ; Weber, R. H. ; Zuger, M. F. ; *Organic Synth.* , **1983**, Vol 63, 1.
(39) Walborsky, H. M. ; Murari, M. P. ; *Canad. J. Chem.* , **1984** , 62, 2464-2470.
(40) Najera, C. ; Yus, M. ; Seebach, D. ; *Helv. Chim. Acta*, **1984**, 67, 289-300.
(41) Gacek, M. ; Undheim, K. ; *Acta Chem. Scand.*, Ser. B, **1975**, B-29(2), 206-212.
(42) Hamon, D. P. G. ; Massy-Westropp, R. A. ; Pipithakol, T. ; *Aust. J. Chem.* , 1974, 27, 2199-2204.