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ASYMMETRIC NICKEL-CATALYZED CROSS-COUPLING REACTION OF ALLYLIC SUBSTRATES WITH GRIGNARD REAGENTS

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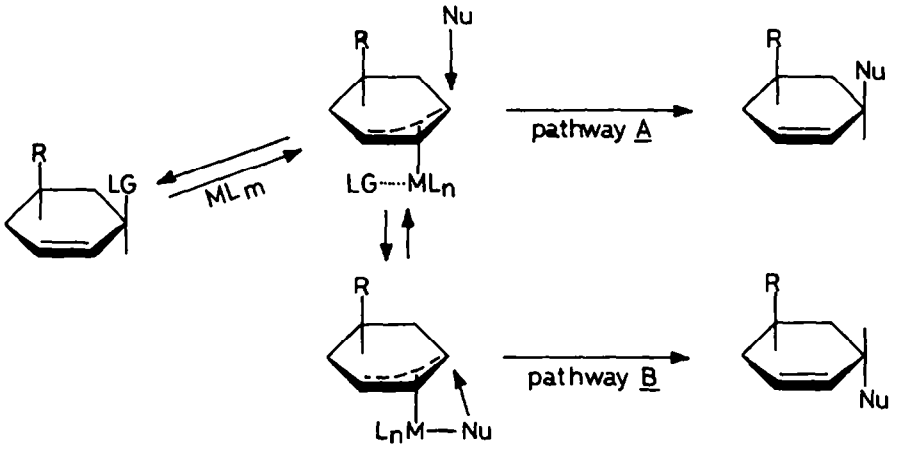
Abstract - Two possible routes for the synthesis of optically active olefinic compounds through cross-coupling reaction between allylic electrophiles and Grignard reagents catalyzed by nickel complexes containing chiral diphosphine ligands were investigated: i) the reaction of chiral racemic (or prochiral) allylic compounds with achiral Grignard reagents and ii) the reaction of chiral Grignard reagents with allyl electrophiles. Optical yields higher than 90% were obtained for the first reaction route (compound 11) and up to 58% (compound 34) were obtained for the second route, using a C_2 chiral ligand, namely (S,S)-1,2-dimethyl-1,2-ethanediylbis(diphenylphosphine).

It has long been known that olefinic compounds oxidized at the allylic position such as alcohols, ethers or esters are activated toward nucleophilic substitution by palladium or nickel compounds mostly containing phosphine ligands. [1,2] Stereochemical investigations have found either retention or inversion of configuration for these reactions depending on the incoming nucleophile.[3] Indeed, the stereochemistry of the reaction products is a consequence of an "anti" attack of the metal catalyst on the allylic substrate followed by an external attack (with respect to the metal) when the incoming nucleophile is soft (e.g., stabilized enolates) or by an internal attack (i.e., mediated by the metal) by less soft or hard nucleophiles (e.g., organometallics of the main group elements). [4-7] (Scheme 1). Using stabilized carbon nucleophiles and palladium catalysts, an asymmetric carbon-carbon bond formation was realized using chiral phosphine ligands as cocatalyst.[8] An influence of the size of the nucleophile on the optical yield has been observed.[8] Optical yields as high as 86% were then reported, [9,10] but only using allylic substrates having suitable substituents (e.g., three phenyl groups). Comparison of pathways A and B in Scheme 1 leads to the expectation of a more effective steric control by the chiral ligand when pathway B is followed, i.e., when the nucleophile first attacks at the metal and then is transferred to the allylic moiety (compare,e.g., ref. 11). In fact we have reported in a preliminary account of this work the achievement of quite good optical yields[12] in the reaction of Grignard reagents with almost sterically unbiased allyl phenyl ethers as the substrate using [(S,S)-1,2-dimethyl-1,2-ethanediylbis(diphenylphosphine)]nickel(II)chloride [13](2') as catalyst precursor. In the present paper we report a reevaluation of the highest (97%) optical yield calculated on the basis of literature data in the preliminary communication (which appears to be in fact lower ($\sim$ 60%)) and a more detailed study of the reaction of chiral or prochiral allylic electrophiles with Grignard reagents using chiral nickel catalysts containing optically active homologues of 1,2-ethanediylbis(diphenylphosphine). Palladium complexes containing the same ligands are either practically unactive (as also reported by other authors[14]) or bring about extensive formation of secondary products. Furthermore, some results of the cross-



ML_m or ML_n = Metal with ligands. R = Substituent, e.g. alkyl group, $COOCH_3$ etc. LG = Leaving group, e.g. C_6H_5O, CH_3COO etc. Nu = Nucleophilic reagent, e.g. $NaCH(COOCH_3)_2$, RMgX etc.

Scheme 1

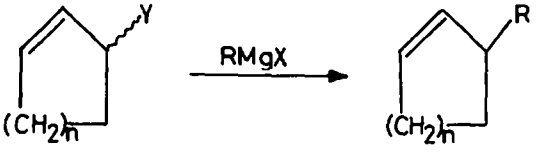
coupling reaction of chiral (racemic) Grignard reagents with allylic electrophiles are also reported.

Results

The allylation reactions have been carried out in ether solvents using as the catalyst precursor (P-P)$NiCl_2$(1'-6') complexes, where P-P are the following chiral ligands: (R)-1,2-propanediylbis(diphenylphosphine)(prophos[15])(1'),(S,S)-1,2-dimethyl-1,2-ethanediylbis(diphenylphosphine)(chiraphos[16])(2'),(R)-1-phenyl-1,2-ethanediylbis(diphenylphosphine) (phenphos[17]) (3'),(R)-1-cyclohexyl-1,2-ethanediylbis(diphenylphosphine)(cyphos[18])(4'),(R,R)-1,2-ethanediylbis(phenyl-o.methoxyphenylphosphine) (dipamp[19])(5') and (R,R)-bicyclo(2.2.1)hept-5-ene-2,3-diylbis(diphenylphosphine)norphos[20])(6').

a) Reactions of achiral Grignard reagents

In Table 1 the results are reported of the alkylation of 2-cyclohexen-1-ol(1) with either CH_3MgBr (12) or CH_3MgI(13) in the presence of different catalytic system and at different conversion of the allylic alcohol[21] (Scheme).



	n	Y
1	2	OH
2	2	OC_6H_5
3	2	S-t.C_4H_9
4	2	Br
5	1	OC_6H_5

	n	R
6	2	CH_3
7	2	C_2H_5
8	2	C_6H_5
9	2	CH_2=CH
10	1	CH_3
11	1	C_2H_5

Scheme 2

Under the reaction conditions used, enantiomer selection of the substrate always takes place. The relative topicity[22] of the chiral ligand and of the less reactive alcohol is of the ul type. No regular correlation seems to exist between the topicity of the alkylation product and that of the ligand used; however, the only ligand, for which an exception to the ul relative topicity is observed (chiraphos) , results in a low asymmetric induction. The best optical yield for 2-methyl-cyclohexene (6) has been obtained with phenphos ligand. The extent of conversion to the alkylation product influences the optical purity of the unreacted material (as expected[23]) but not that of recovered 6. The same trend is shown by the halide of the Grignard reagent. It was noted that the reaction times for the

Table 1. Alkylation of 2-cyclohexen-1-ol (1) with CH_3MgX to 2-methylcyclohexene (6) using (P-P)$NiCl_2$ as the catalyst precursor in ethyl ether.[a]

P - P	CH_3MgX X=	Reaction time [h]	Conversion [%]	Unreacted 1, Optical purity [%], (abs.conf.)	6, Optical purity [%], (abs.conf.)
(R)-Prophos	I	76	63	3.6(S)	4.3(S)
(S,S)-Chiraphos	I	80	70	13.8(R)	2.0(S)
(R)-Phenphos	I	18	30	2.2(S)	15.8(S)
(R)-Phenphos	I	32	50	3.5(S)	15.9(S)
(R)-Phenphos	Br	240	30	0.5(S)	15.7(S)
(R)-Cyphos	I	67	70	~ 0	0.2(S)

[a] at the boiling point of the reaction mixture (34-36°C).

reaction of allylic alcohols are quite often irreproducible due to the casual formation of a heterogeneous reaction mixture.

Table 2 shows the influence of the chiral ligand and of the leaving group in the reaction of ethyl magnesium bromide (14) with different cyclohexene-2-derivatives (Scheme 2). Chemical yields of the alkylation product 7, at 100% conversion, are 60-85% due to some competing reduction of the electrophile.[24]

Table 2. Asymmetric ethylation of 2-cyclohexene-derivatives with C_2H_5MgBr (14) to 2-ethylcyclohexene (7) in ethyl ether[a] solution using (P-P)$NiCl_2$ as the catalyst precursor

P - P	cyclo-C_6H_9Y Y =	Reaction time [h]	Yield [%]	7, Optical purity % , (abs.conf.)
(R)-Phenphos	OH	120	75	28.4(S)
(S,S)-Chiraphos	OH	160	65	49.5(R)
(R)-Prophos	OC_6H_5	35	80	29.7(S)
(R)-Cyphos	OC_6H_5	40	80	16.2(S)
(R,R)-Norphos	OC_6H_5	15	80	48.1(S)
(R,R)-Dipamp	OC_6H_5	44	80	11.2(R)
(R)-Phenphos	OC_6H_5	24	80	26.5(S)
(S,S)-Chiraphos	OC_6H_5	91	60	51.2(R)
(S,S)-Chiraphos	S-t.C_4H_9	48	72	51.0(R)
(S,S)-Chiraphos	Br	24	85	15.1(R)

[a] at the boiling point of the reaction mixture (34-36°C); conversion was almost complete in each case.

The relative topicity of the recovered ethylation product and that ot the chiral ligand is of the ul type, the only exception being the product obtained with dipamp ligand. For optically pure (+) (R)-2-ethylcyclohexene (7) $[\alpha]_D^{25}$ ($CHCl_3$) + 83.34 (maximum value) was taken for the calculation of the optical yield, and not the previously used value $[\alpha]_D^{25}$ + 49.35 (minimum value), that we have confidently extrapolated from literature data.[25,26] This value (+ 83.34) has been extrapolated from the enantiomeric excess of dimethyl 2-ethyl-adipate (15) obtained from the above olefin via oxidation with KIO_4-$KMnO_4$[27] and esterification with CH_2N_2 (see experimental part). Racemization during such oxidation should be limited;[28] in fact our value (+ 83.34) accords in a narrow range with a

very recent new value (+ 76.5) reported by the same authors.[25,26]

Optical yields for the ethylation are substantially higher than in the corresponding methylation reaction. Using either phenphos or chiraphos ligands there is practically no influence of the leaving group on the optical yield, unless a competition with the non-catalyzed alkylation exists, as in the case of 2-bromocyclohexene (4).[29]

The results presented in Table 3 show that there is a certain influence of the ether solvent. In fact the optical yield is a little bit lower in diethyl ether than in tetrahydrofuran or in t.butyl-methyl ether.

Table 3. Asymmetric ethylation of 2-phenoxycyclohexene (2) with C_2H_5MgBr (14) using [(S,S)-Chiraphos]$NiCl_2$ (2') in different ether solvents.[a]

Ether solvent	Reaction time [h]	Yield [%]	7, Optical purity [%],(abs.conf.)
$(C_2H_5)_2O$	76	80	52.0(R)
THF	22	90	57.9(R)
$t.C_4H_9OCH_3$	48	80	59.5(R)

[a]The reactions were carried out at room temperature; complete conversion was obtained in each case.

Table 4 reports results obtained in the reaction of 2 and 5 using phenphos or chiraphos ligands with different Grignard reagents (13, 14, CH_2=CHMgBr(16) and C_6H_5MgBr(17)). Asymmetric induction

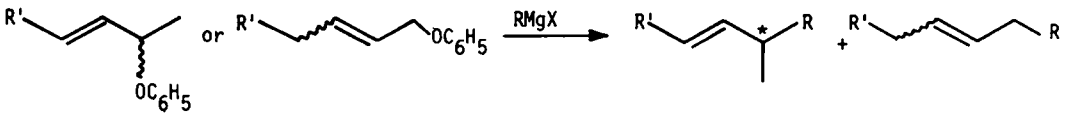
Table 4. Asymmetric allylation of some Grignard reagents by 2-phenoxy-cyclohexene (2) or 2-phenoxy-cyclopentene (5) in the presence of (P-P)$NiCl_2$.[a]

Allylic substrate	RMgBr R =	P - P	Reaction time [h]	Yield[c] [%]	Product (6-11) opt.purity [%], (abs. config.)
2	CH_3	(S,S)-Chiraphos	17	70	1.3(S)
		(R)-Phenphos	20	80	13.3(S)
2	C_2H_5	(S,S)-Chiraphos	91	60	51.2(R)
		(R)-Phenphos	24	80	20.8(S)
2	CH_2=CH [b]	(S,S)-Chiraphos	137	35[d]	24.2(S)
		(R)-Phenphos	168	20[e]	7.4(R)
2	C_6H_5 [b]	(S,S)-Chiraphos	150	80	5.8(S)
		(R)-Phenphos	120	85	<0.1(S)
5	/ CH_3 [b]	(S,S)-Chiraphos	17	60	13.5(R)
		(R)-Phenphos	18	70	5.1(R)
5	C_2H_5	(S,S)-Chiraphos	5	60	90.4(R)
		(R)-Phenphos	3	78	37.4(S)

[a]in ethyl ether (unless otherwise stated) at 34-35°C; [b]THF as the solvent; [c]conversion was complete (unless otherwise stated); [d]conversion 45%; the recovered ether had (R) prevailing absolute configuration and 11.4% optical purity; [e]conversion 25%

depends strongly on the structure of the organometallic compound and on the size of the ring of the electrophilic reagent. In all cases, with one exception, chiraphos ligand gives better asymmetric induction than phenphos ligand.

In Table 5 are presented the results of the ethylation or of the phenylation of some acyclic phenyl ethers (Scheme 3) using chiraphos ligand. Due to their structure, regioisomers are possible for the



R'=H, 18 R'=H,E,20 R'=H,R=C_2H_5 22 and 23
R'=CH_3, 19 R'=H,Z,21 R'=H,R=C_6H_5 24 and 25
R'=CH_3,R=C_2H_5 26

Scheme 3

first three substrates; two regioisomers are indeed formed and their ratio is strongly influenced by the entering group, but not by the isomeric structure of the reacting electrophile. Also the optical yield for the chiral reaction products depends on the Grignard reagent used but not on the structure of the electrophile. In spite of the different descriptor for the absolute configurations of 3-phenyl-but-1-ene(24) and 3-methyl-pent-1-ene(22), both products arise from the same prochiral face of the allylic substrate. It should be noted that the optical yield in the ethylation of (E) 2-phenoxy-pent-3-ene (19) is much lower than in the case of 5 (34% vs. 90%).

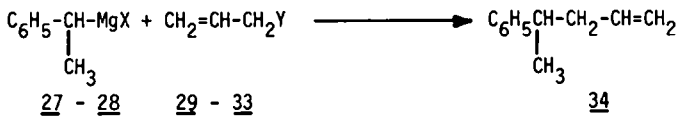
Table 5. Asymmetric allylation of Grignard reagents in THF as the solvent using [(S,S)-Chiraphos]$NiCl_2$ as the catalyst precursor.[a]

Allylic substrate	RMgBr R=	Reaction time [h]	R [%]	R [%]	R' R		
					R'=	[%]	opt.purity [%] (abs.conf.)
18	C_2H_5	24	61	1	H	38	17.5(S)
	C_6H_5	60	35	0	H	65	60.0(R)
20	C_2H_5	24	63	1	H	36	22.3(S)
	C_6H_5	120	35	0	H	65	58.0(R)
21	C_2H_5	35	63	1	H	36	18.5(S)
	C_6H_5	100	36	0	H	64	58.5(R)
19	C_2H_5	48	-	-	CH_3	100[b]	34.1(S)[b]

[a]at 20°C; the conversion was complete in each case; [b]4-methyl-hex-2-ene (26) (E/Z=97:3) (the optical purity refers to the (E)diastereomer).

b) Reaction of chiral Grignard reagents

The results obtained in the allylation of C_6H_5-CH(CH_3)MgX(X=Cl,(27); X=Br,(28)) to 4-phenylpent-1-ene (34) (Scheme 4) are reported in Table 6. Again chiraphos ligand brings the best optical and chemical yields; the relative topicity being of the ul type. There is a small influence of the nature of the halide



27 - 28 29 - 33 34

Y	OC_6H_5	$PO(C_2H_5)_2$	$PO(C_6H_5)_2$	OC_2H_5	SCH_3
	29	30	31	32	33

Scheme 4

Table 6. Asymmetric allylation of 1-phenylethylmagnesium halide in diethyl ether catalyzed by (P-P)$NiCl_2$ complexes.[a]

C_6H_5CHMgX CH_3 X=	Y=	P - P	Reaction time [h]	β Hydrogen[b] elimination [%]	Yield [%]	34, Optical purity [%], (abs.conf.)
Cl	OC_6H_5	(R)-Prophos	24	11	81	14.0(S)
Cl	OC_6H_5	(R)-Phenphos	20	25	36	10.1(S)
Cl	OC_6H_5	(S,S)-Chiraphos	2	5	87	58.3(R)
Br	OC_6H_5	"	2	13	87	47.0(R)
Cl	$PO(OC_2H_5)_2$	"	1	5	65	37.2(R)
Cl	$PO(OC_6H_5)_2$	"	2	2	75	13.4(R)
Cl	OC_2H_5	"	2	13	55	47.3(R)
Cl	SCH_3	"	20	16	70	56.8(R)
Br	SCH_3	"	24	30	55	46.2(R)

[a]at 20°C; [b]percent of styrene with respect to the sum of styrene (35) and 4-phenyl-pent-1-ene(34)

of the Grignard reagent both on the optical yield and on the selectivity of the reaction, the chloro reagent giving the best results. Optical yields are definitely lower for allylic electrophiles, which react with the Grignard reagent even in the absence of a catalyst, as the phosphates.[30] However the optical yield is also a little bit lower in the case of the coupling of the Grignard reagent with allyl ethyl ether. Otherwise, the optical yield does not seem to be influenced by the leaving group of the allyl electrophile although the extent of β-hydrogen elimination is.

Discussion

An asymmetric cross-coupling reaction between allylic electrophiles and organometallic reagents can be realized[31] either starting with chiral racemic (or prochiral) allylic substrates[8-10] and/or with chiral racemic organometallic reagents[8,32,33] (compare Scheme 1). Stabilized metal enolates have been asymmetrically allylated;[8-10,34] recently it has been shown that even the non-metallated precursors can be used.[35] The total involvement of a η-allylic intermediate in these reactions[8,9] has been called into question.[36,37] Such an intermediate, however, appears to be the most probable

in our case, based on following observations: a) it is possible to convert a racemic material (e.g. 5)to practically a single alkylation enantiomer 11 (Scheme 2 and Table 3) and b) the optical purity of 6 formed from 1 and methyl Grignard reagents (Table 1) does not depend on the degree of conversion, whereas that of the unreacted substrate does. In fact, we assume that the key intermediate in these reactions is a complex having a structure similar to that of Fig. 1, which is based on the crystal structure reported for (n-methallyl) [1,2-ethanediylbis(diphenylphosphine)]nickel (II)bromide (36)[38]. Following the report that bis-(1,5-cyclooctadiene)nickel (37) reacts with allyl phenyl ether in the presence of triphenylphosphine to yield the (n-allyl)(phenoxo)nickel(II) (triphenylphosphine complex (38)[39,40] attempts were made to prepare analogously complexes containing chelating diphosphines such as diphos or chiraphos. However, we isolated the nickel-bischelate complex from the reaction mixture. Similar products are formed in the reaction of the aforementioned phenoxocomplex with the diphosphine and also in the reduction by s.butyl-magnesium bromide of the nickel diphosphine dichloro [13] complexes in the presence of allyl phenyl ether. Comparison of the stereochemical course of the nickel[6] and palladium[5,7] catalyzed allylation of hard nucleophiles as well as model studies on palladium allyl complexes[4,5] strongly suggests that the intermediate of Fig. 1 is formed through alkylation of a preformed allyl complex. However we cannot rule out an activation of the Grignard reagent preceeding the activation of the allylic electrophile, [41] since the [Chiraphos]$NiCl_2$(2')catalyst precursor, reduced with i.propyl-magnesium bromide, does not cause appreciable isomerization of 3-phenoxy-but-1-ene (18) in 130 hrs at room temperature. By contrast, this substrate is ethylated or phenylated completely in 24 and 60 hrs respectively. For chiral (or prochiral) allylic electrophiles asymmetric induction should be determined during the reductive elimination step [41-43] from the intermediate in Fig.1.This is, in fact, confirmed by the low influence (if any) of the leaving group on the optical yield in the asymmetric ethylation of cyclohexen-2-derivatives, when the substrate does not react directly with the Grignard reagent (Table 2). In the case of chiral Grignard reagents asymmetric induction could be determined during the enantiomer discriminating alkylation of the transition metal complex(es).[44] Transalkylation reaction can be indeed largely stereospecific;[45] however sterically labile s.alkyl nickel complexes have been recently described.[46]

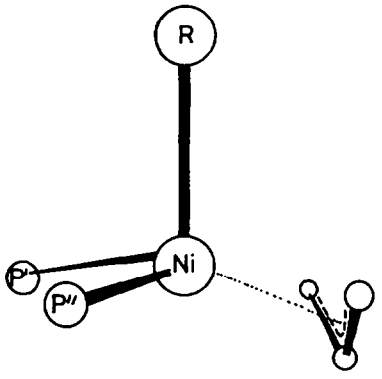


Fig.1

In contrast with the results obtained in the asymmetric cross-coupling reaction between phenyl halides and s.butyl-magnesium halides using the same catalytic system,[44] there is a large influence of the chiral ligand on the optical yield of the allylation product. For all the cases examined, with the exception of the methylation of the cyclohexene derivatives, the chiraphos ligand always gives the best optical yield. This has been rationalized considering the geometry of the reaction intermediate which gives rise to the alkylation product.[12] The use of chiral ligands with C_2 symmetry such as chiraphos reduces the number of possible diastereomeric reaction intermediates (compare the structure in (Fig.1)); in fact this represents a better premise for achieving high asymmetric induction. A lower number of reaction intermediates could also be responsible for a more efficient enantiomer selection of 1-phenylethyl Grignard reagents in the synthesis of 34 (Table 6). It should be noted that enantiomer selection of these Grignard reagents in the cross-coupling with vinyl halides is much lower[47] (10-20 e.e.) with the same [Chiraphos]$NiCl_2$ (2') catalyst precursor. The fact that the ligand dipamp (which also has a C_2 symmetry) causes the lowest asymmetric induction (Table 2) can be understood on the basis of the two possible diaste-

reomeric conformation of the chelation ring,[16] which in this case should not be very different in energy. The large influence of the entering group on the optical yield is difficult to rationalize. By contrast, the lower optical yield observed in the ethylation of (E)-2-phenoxy-pent-3-ene (19) compared with the cyclic substrates might be due to a different orientation of the substituents on the allylic moiety (at least one of the methyl group in the acyclic substrate must be in the anti position when the alkylation product is formed) and/or to the doubled number of the possible intermediates, due to the above syn-anti isomerism. For the isomeric phenoxybutenes the geometry of the starting material does not influence either the isomeric composition or the enantiomeric composition of the reaction products. Therefore very rapid syn-anti isomerization and enantioface equilibration (with respect to the formation of the products) take place in the allylic intermediates. It is worth noting that the rapid isomerization and enantioface equilibration of the allylic intermediates does not appearto be a common feature of nickel complexes. In the methylation [42] of (Z)- and (E)-pent-2-en-1-ol (39) and of pent-1-en-3-ol (40) with (R,R)-[Diop]$NiCl_2$ (41) [48] as the catalyst precursor, the recovered 3-methyl-pent-1-ene (22) showed different enantiomeric excess for the three different substrates. Furthermore, in the phenylation of (S)-but-1-en-3-ol (42) in the presence of $(PPh_3)_2NiCl_2$ (43)the (R)-3-phenyl-but-1-ene (44)showed 25% retention of the optical activity.[49]

Conclusions

The results presented in this paper confirm that the allylation reaction can be an useful method for asymmetric carbon-carbon bond formation.[10] The control of the stereochemical evolution of this reaction remains elusive, in spite of the rather high optical yield one can achieve in some cases. In fact, the large number of possible diastereomeric intermediates, the lack of detailed knowledge of the reaction mechanism and particularly the fact that we do not know[50] whether alkylation implies simply attack of the entering group on the η-allyl moiety or it is a consequence of reductive elimination from an η^1-allyl intermediate, means that it is only possible to speculate on the origin of the asymmetric induction.[42] Indeed, there are even exceptions to the prevailing ul relative topicity of the chiral ligand used and the absolute configuration of the chiral carbon atom of the allylic moiety (in the intermediate in Fig. 1) undergoing alkylation. However, a rationale seems to emerge from the present results, i.e., the possible significance of having asymmetric metal atoms in the catalytic species [51,52] and, as a consequence, of the symmetry of the chiral ligand. It might be expected that such a concept is valid also for other catalytic reactions and therefore is useful for devicing other chiral ligands.

Experimental

Materials. Tetrahydrofuran, diethylether and t.butyl-methyl ether were distilled from $LiAlH_4$ under nitrogen. Nickel dichloride diphosphine complexes used as the catalyst precursors were prepared as described elsewhere.[13] Cyclohex-2-en-1-ol (1) was prepared through reduction with diisobutylaluminium hydride from cyclohex-2-en-1-one (45)(Fluka product).[53] 2-Phenoxy-cyclohexene (2),[54] 2-t.butyltio-cyclohexene (3),[55] 2-phenoxy-cyclopentene (5), [54] 1-phenylethylchloride [56],(46) and 1-phenylethylbromide (47), [57] were synthesized according to described procedures. (E)- and (Z)-1-phenoxy-but-2-ene (20) were prepared from the corresponding chloride [54,58]; the pure isomeric alcohols were obtained through rectification of the commercial (E)- and (Z)-mixture (EGA product) on an autoannular still Perkin-Elmer 251. (E)-2-phenoxy-pent-3-ene (19) was analogously synthesized from the commercial alcohol (Fluka). Allyl phenyl ether (29), allyl ethyl ether (32) and allyl methyl sulfide (23) were Fluka products. Allyl phosphates (30) and (31) were prepared according to published procedures.[59]

Methods. GC analyses (2 or 4 mx0.29 cm columns packed with 15% carbowax 20M on chromosorb A, 2.5% silicone gum on AW-DMCS chromosorb G 80-100 mesh, diethyleneglycol+$AgNO_3$ on chromosorb R 60-80 mesh and dimethylsulfolane on kieselguhr 60-100 mesh) were carried on a Perkin-Elmer 900 or an a Perkin-Elmer Sigma 4 with flame ionization detectors. Preparative GC's were carried out on a Perkin-Elmer F21 using 5 columns 90 x 0.95 cm packed with 20% silicone gum SE 52 on chromosorb A 60-80 mesh. Mass spectra were run on a Hitachi/Perkin-Elmer RMU-6L. NMR spectra were recorded on WH 90 or AM 300 WB Bruker spectrometers. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. Optical purity for the reaction products was calculated on the basis of following values for maximal optical rotation (values are referred to (S)products):

2-ethyl-cyclohexene(7) $[\alpha]_D^{25}$-83.34(c=1,$CHCl_3$) α_D^{25} (l=1)-60.45°(neat)(vide infra); 2-methyl-cyclohexene(6)$[\alpha]_D^{25}$-89.4(c=4.1,CCl_4),[60] 2-vinyl-cyclohexene(9)$[\alpha]_D^{25}$+267(c=1,$CHCl_3$);[25,26] 2-phenylcyclohexene(8)$[\alpha]_D^{29}$-159.6(c=0.53, benzene);[61] 2-methyl-cyclopentene(10)$[\alpha]_D^{20}$-174.5 (±4.5)(neat);[62] 2-ethyl-cyclopentene(11)$[\alpha]_D^{24}$-123.2(c=7.5, $CHCl_3$) α_D^{25}(l=1)-84.4° (neat)[63](this value has been recently confirmed by P.A. Ramaiah and E. Gil-Av through complexation to platinum (II) complexes (compare ref. 64); we are very grateful to Prof. V. Schurig (Tubingen, West Germany) for this information)); 3-methyl-pent-1-ene(22)$[\alpha]_D^{17}$-38.2 (neat);[65] 3-phenyl-but-1-ene(24)$[\alpha]_D^{25}$+6.84 (neat);[66](E)-4-methyl-hex-2-ene(26)$[\alpha]_D^{25}$+44.2 (neat);[67] 4-phenyl-pent-1-ene(34)$[\alpha]_D^{25}$+19.8 (neat);[66] 2-cyclohexene-1-ol(1)$[\alpha]_D^{20}$-112.0(c=0.6, $CHCl_3$);[68] 2-phenoxy-cyclohexene(2) α_D^{25}(l=1)-181° (neat) (this work); 3-phenoxy-but-1-ene(18) α_D^{25} (l=1)+15.2° (neat) (this work).

2-Methylcyclohexene(6) from 2-cyclohexen-1-ol(1). 50mg of the catalyst precursor were suspended under nitrogen in 30 ml diethyl ether and 7.8 g (0.08 mol) of 1. The suspension was cooled down at -30° and a threefold excess of the Grignard reagent (12 or 13) was slowly added (total volume 90 ml). When addition was complete the suspension was warmed up at 35° and then refluxed for the reported time. Conversion was determined by GC using an internal standard. The suspension was hydrolyzed successively with water and 10% H_2SO_4, washed with water to neutrality and dried over Na_2SO_4. After removing the bulk of ether through distillation, excess methanol was added and 6 was separated as an azeotropic mixture with methanol and recovered, after washing with water, through distillation over $LiAlH_4$. The compound was purified through preparative GC for the determination of the optical purity. Unreacted 1 was recovered from the above residue in methanol through distillation under vacuum. Yields are reported in Table 1.

Alkylation procedures

Ethylation of 2-phenoxycyclohexene (2) to 2-ethylcyclohexene (7). To a suspension of 30-35 mg of the catalyst precursor (1'-6') and 0.04 mol of 2, in 36 ml diethyl ether, the solution of C_2H_5MgBr (14) was slowly added. The molar ratio of 2 : 14 was 1:1.2 and the total volume was 65 ml. Then the reaction mixture was hydrolyzed with water and 10% H_2SO_4, washed with 10% NaOH, with water and dried over Na_2SO_4. After the removal of the solvent, 7 was recovered through fractional distillation and purified by preparative GC before the determination of the optical rotation. In some cases the above scale of reaction was doubled. When conversion was incomplete, the olefin was previously recovered as an azeotropic mixture with methanol and then purified as reported in the previous examples; the unreacted substrate 2 was obtained by distillation. The isomeric purity of 2-ethyl-cyclohexene (7) was determined by ^{13}C-NMR in $CDCl_3$ (22.63 MHz) (δ in ppm and multiplicity): 132.3(d), 126.9(d), 37.3(d), 29.4(t), 29.1(t), 21.9(t), 11.5(q), 27.7(t).
The reaction of the other cyclic allylic derivatives (3, 4 and 5) with the other Grignard reagents (12, 13, 14, 16 and 17) leading to the olefinic compounds 6 - 11 were similarly carried out. For the reactions of acyclic allyl derivatives (18-21) with (14 and 17), both the ratio between the catalyst and the reactions and the total volume of the solution was as reported for the cyclic substrates. After hydrolysis aliphatic olefins (22, 23 and 26) were recovered as an azeotropic mixture with methanol, then washed with water, dried and separated by fractional distillation; aromatic olefins (24 and 25) were directly recovered by distillation after hydrolysis.

4-Phenylpent-1-ene (34). 60 mg of the nickel catalyst precursor (1'-3') were suspended in an ether solution containing 0.05 mol of the allyl derivative (29 - 33) and the solution of the Grignard reagent (27 or 28) was added at 0°. The total volume was kept at 70 ml. At the end of the reaction, the mixture was hydrolyzed with water and 10% H_2SO_4 and the organic phase was washed with water and 10% NaOH, dried and concentrated, 4-phenyl-pent-1-ene (34) was recovered by distillation. Yields are reported in Table 6.

Evaluation of the maximum rotary power of 2-phenoxy-cyclohexene (2). A sample of (-) (S)-cyclohex-2-en-1-ol (1) ($[\alpha]_{578}^{20}$+10.2 (c=0.9,$CHCl_3$), optical purity 6.1%) was obtained by reduction of cyclohex-2-1-one (45) by $LiAlH_4$ modified with quinine.[69] Successive reaction with phenol, triphenylphosphine and diethylazodicarboxylate[70] gave, after work-up, (-) (S)-2-phenoxy-cyclohexene (2) having α_D^{25} (l=1) -11.1° (neat).

Evaluation of the maximum rotatory power of 3-phenoxy-but-1-ene (18). A sample of 18 having α_D^{25}(l=1)+0.761° (neat) was recovered from a cross-coupling reaction of the same substrate with C_6H_5MgBr[12], at 45% conversion, and purified by preparative GC. This sample was hydrogenated in benzene with $RhCl(PPh_3)_3$ as previously reported.[71] The (+) (S)-2-phenoxy-butane (48) was recovered through vacuum distillation and purified by preparative GC: α_D^{25}(l=1)+2.71° (neat), optical purity 5.0%.[72]

Evaluation of the maximum rotatory power of 2-ethyl-cyclohexene (7).

3 g of (S)-2-ethyl-cyclohexene (7) ($[\alpha]_D^{25}$ -20.33(c=1, $CHCl_3$), $[\alpha]_D^{25}$(l=1)-14.75° (neat)) were slow-

ly added, under nitrogen, to a solution of 23.5 g $NaIO_4$ in 81 ml acetone and 100 ml water. To this stirred solution, at 5°, 0.73 g $KMnO_4$ in 28 ml water and 28 ml acetone were simultaneously added over 1 hour.[27] Stirring was continued overnight at 5°. The resulting suspension was filtered through celite and acetone was removed under vacuum. The solution was acified with 10% H_2SO_4 and continuosly extracted with ether. The ether extract was treated with 5% NaOH and the water solution, after extractions with ether, was acified with 10% H_2SO_4. 2-Ethyl-adipic acid was recovered by extractions with ether, esterified with CH_2N_2 and the diester 15 purified by distillation. NMR analysis of this compound in the presence of $Eu(hfc)_3$ showed an e.e. = 24.4%. A maximum rotatory power $[\alpha]_D^{25}$ 83.3 was so determined for 2-ethyl-cyclohexene (7). This value was further confirmed by the following chemical correlation. 3 g of 7 ($[\alpha]_D^{25}$ -25.77 (c=1, $CHCl_3$)) were dissolved in 20 ml methanol and ozonized at -50°. The reduction of the crude ozonide, after removal of the solvent, was carried out with 14 g $LiAlH_4$ in 150 ml dry ether to give 2-ethyl-1,6-hexane-diol (49). The corresponding dimethylate 50, obtained in the usual manner, was reduced with $LiAlH_4$ in ether to afford 0.5 g of (S)-3-methyl-heptane (51) $[\alpha]_D^{25}$ +2.89 (neat) (o.p. 31%).[73]

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