105. Nickel-catalyzed Asymmetric Alkylation of Some Chiral and Achiral Allylic Alcohols

Preliminary communication

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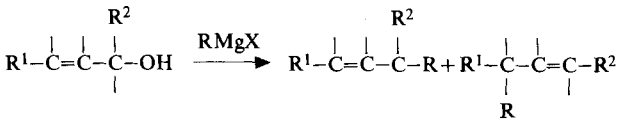
Summary

[(−)(*R*)-1,2-bis(Diphenylphosphino)-1-phenylethane]nickel(II) chloride was found to catalyze the asymmetric alkylation of some chiral and achiral allylic alcohols with *Grignard* reagents, leading to the formation of optically active olefins. Enantiomer discrimination of the substrate takes place in the alkylation of chiral allylic alcohols.

Allylic alcohols react with an excess of *Grignard* reagents in the presence of catalytic amounts of nickel(II)complexes to afford alkenes [1] [2] *(Scheme).*



(1)

The reaction rate appears to depend on the degree of substitution of the substrate; in fact it has been reported that 2-cyclohexen-1-ol is not alkylated by CH_3MgBr in the presence of catalytic amounts of $(Ph_3P)_2NiCl_2$ [1].

Owing to our interest in catalytic asymmetric C,C bond formation [3] we have studied the alkylation of some chiral and achiral allylic alcohols by *Grignard* reagents in the presence of [(−)(*R*)-1,2-bis(diphenylphosphino)-1-phenylethane]-nickel(II) chloride (**1**). The preliminary results we have obtained are shown in the *Table*. They show that:

i) Enantiomer differentiation of secondary *Grignard* reagents takes place; *e.g.*, in the alkylation of 2-propen-1-ol by *sec.* butyl magnesium iodide optically active 4-methyl-1-hexene is formed with a low enantiomeric excess. The chemical yield in the alkylation product is very poor (~10%), probably due to reduction of the substrate [2]. A very small amount of isomerization of the alkyl group of the *Grignard* reagent from the secondary to the primary structure, leading to the formation of 1-heptene, is also observed;

ii) Cyclic allylic alcohols are alkylated in the presence of **1** not only by CH_3MgI or CH_3MgBr but also by C_2H_5MgI which contains available β-hydrogen

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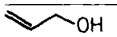
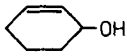
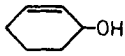
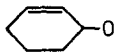
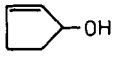
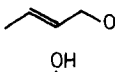
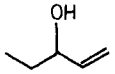
Table. *Asymmetric Alkylation of Some Allylic Alcohols by* Grignard *Reagents Catalyzed by* (1)

Substrate	*Grignard* Reagent	Reaction Time (hrs)	Conversion (%)	Unreacted Substrate $[\alpha]_D^{20}$	Unreacted Substrate Optical purity (configuration)	Chiral Alkylation Product Yield	Chiral Alkylation Product $[\alpha]_D^{25}$	Chiral Alkylation Product Optical purity (configuration)
	Bu^sMgI	120	≈100	–	–	10	+ 0.17[a])	1.3(*R*)[b])
	MeMgBr	240	30	−0.56[c])	0.5(*S*)[d])	28	−14.00[e])	15.7(*S*)[f])
	MeMgI	18	30	−2.46[c])	2.2(*S*)[d])	29	−14.20[e])	15.9(*S*)[f])
	EtMgI	120	~95	n.d.[g])	n.d.[g])	84	−23.46[e])	n.d.[g])[h])
	MeMgI	160	85	n.d.[g])	n.d.[g])	80	+ 6.07[i])[j])	4.5(*R*)[k])
	EtMgI	45	70	–	–	24[k])	− 1.58[i])[m])	4.1(*R*)[n])
	MeMgI	235	40	−2.03[i])	5.8(*R*)[o])[p])	24[q])	+ 0.49[i])[m])	1.3(*S*)[n])

[a]) In heptane. [b]) Based on data reported by *P. Pino, L. Lardicci & L. Centoni*, Gazz. chim. It. *91*, 428 (1961). [c]) In $CHCl_3$. [d]) Based on data reported by *S. Yamada, N. Takamura & T. Mizoguchi*, Chem. Pharm. Bull. *23*, 2539 (1975). [e]) In CCl_4. [f]) Based on data reported by *J.A. Berson, P.B. Dervan, R. Malherbe & J.A. Jenkins*, J. Amer. chem. Soc. *98*, 5937 (1976). [g]) Not determined. [h]) Unknown product. [i]) Neat. [j]) At 20°. [k]) *V. Schurig & E. Gil-Av*, Isrl. J. Chem. *15*, 91 (1976/77). [l]) ~40% of 2-hexene is formed. [m]) At 17°. [n]) Based on data reported by *P. Pino, L. Lardicci & L. Centoni*, J. org. Chem. *24*, 1399 (1959). [o]) Based on data reported by *J. Kenyon & D.R. Snellgrove*, J. chem. Soc. *127*, 1169 (1925). [p]) Based on data reported in *Beilsteins* Handbuch der Organischen Chemie, EIV, *1*, 2117 (1974). [q]) ~15% of 3-hexene is formed.

atoms. In the latter case hydrogenolysis of 2-cyclohexen-1-ol to cyclohexene takes place to a very limited extent (< 10%). The reaction rate is higher for alkylation with CH_3MgI than with CH_3MgBr;

iii) Enantiomer differentiation (kinetic resolution [4]) takes place in the alkylation of chiral allylic alcohols. The extent of differentiation appears to depend on the structure of the allylic alcohol and on the halide of the *Grignard* reagent;

iv) The optical purity of the alkylation product of chiral allylic alcohols is not related to that of the unreacted substrate. The optical purity of 3-methyl-1-cyclohexene remains practically the same by changing the halide of the *Grignard* reagent;

v) In the alkylation of 2-buten-1-ol and of 1-penten-3-ol with EtMgI or MeMgI, isomeric olefinic products are formed, the ratios of 3-methyl-1-penten to *n*-hexenes formed being about 0.6 or 1.6, respectively. In these two cases the 3-methyl-1-pentene has the opposite prevailing absolute configuration.

For the alkylation of allylic alcohols catalyzed by nickel complexes, a π-allylic nickel intermediate has been proposed [1] [2] [5]. On the basis of the allylic intermediate, a different mechanism for asymmetric induction should be operating in the formation of the alkylation products. (Possible conformers [6] arising from rotation of the π-system about the metal allyl axis are not considered for the sake of simplicity.)

In the case of 2-propen-1-ol, the enantiomeric excess of 4-methyl-1-hexene should arise from the preferential reaction of either enantiomer of the *Grignard* reagent, as already observed in the asymmetric alkylation of unsaturated halides [3].

As far as the cyclic allylic alcohols examined are concerned, asymmetric induction should arise from a preferential alkylation of either diastereotopic position in the intermediate nickel allylic complex.

From *trans*-2-buten-1-ol, four diastereomeric allylic complexes are possible, owing to the *syn-anti*-isomerism and to the nonequivalence of the two faces of the allylic moiety [6]. When chelate ligands are present in the catalytic system, interconversion of the *syn*- and *anti*-isomers should be rapid in comparison with alkylation rate [2]. Both diastereomerism phenomena can influence the optical yield.

Similar remarks can also be made for 1-penten-3-ol. However, in this case, the observed enantiomer differentiation of the substrate may influence the selection of the two faces of the allylic moiety and, therefore, the asymmetric induction.

It has very recently been reported that diphosphine-palladium complexes [7] are active catalysts for reaction (1) and that different allylic derivates [8] [9] can also be used as the substrates. These observations, together with our results, display the potential usefulness of this reaction for the synthesis of optically active products.

Further investigations are in progress to examine the influence of the type of the diphosphine ligand on the phenomena of asymmetric induction reported and the stereochemistry of the reaction.

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Experimental Part

(−)(*R*)-1,2-bis(Diphenylphosphino)-1-phenylethane was prepared as recently described [10]. The corresponding nickel dichloride complex was prepared in ethyl alcohol [11]. Allylic alcohols were commercial products purified through distillation or rectification before use.

The alkylation reactions were carried out in diethyl ether solutions at the boiling point of a mixture containing in 120 ml 0.07 mol allylic alcohol, 0.25 mol *Grignard* reagent and 1.10^{-4} mol nickel complex. Conversions and yields were determined by GC. using internal standards. The reaction mixtures were hydrolyzed with H_2O and diluted sulfuric acid. The olefin was separated from the unreacted alcohol by distillation or rectification. Products were purified through prep. GC. before determination of the optical rotation.

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