Nickel Catalysed Asymmetric Coupling Reaction between Allyl Phenyl Ethers and Grignard Reagents

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The asymmetric allylation of Grignard reagents by allyl phenyl ethers in the presence of [(−)-(*S,S*)-2,3-bis(diphenylphosphino)butane]nickel(II) chloride gives rise to optically active olefins, with fair to high optical yields; asymmetric induction in the synthesis of 3-ethylcyclohex-1-ene exceeds 97%.

In spite of the considerable interest in catalytic asymmetric syntheses involving carbon–carbon bond formation, there are few examples of such reactions[1] and high optical yields have seldom been obtained.[2–5]

Recently we reported a new synthesis of optically active olefins *via* the cross-coupling reaction of Grignard reagents and allylic alcohols in the presence of [(−)-(*R*)-1,2-bis(diphenylphosphino)-1-phenylethane]nickel(II) chloride as the catalyst precursor.[6] However, the chemical and optical yields were rather low under the reaction conditions used. It is widely accepted that a π-allylic nickel intermediate is involved in this reaction.[7] For a long time it has been known that allyl phenyl ethers give these intermediates[8] and therefore it seemed likely that they would be a better starting material than the corresponding alcohols. In fact, one less equivalent of the Grignard reagent is necessary and the occasional heterogeneity (which depresses catalytic activity) observed with allylic alcohols, is avoided.

Examination of the structure proposed for the intermediate in this kind of reaction[9–11] reveals that when the chiral bidentate ligand has no C_2 axis (Figure 1), the metal becomes a centre of chirality.[12] Since there is no reason to expect a high asymmetric induction in the formation of this intermediate, the use of a chiral ligand having a C_2 axis would reduce the number of such diastereoisomeric intermediates; therefore, this would provide a method for obtaining higher optical yields in the cross-coupling reaction. We report here results obtained using this idea, and these represent a large improvement in terms of chemical and optical yields.

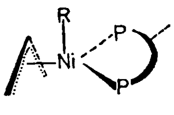


Figure 1

Allylation reactions of the Grignard reagents have been carried out in tetrahydrofuran at room temperature using [(−)-(*S,S*)-2,3-bis(diphenylphosphino)butane]nickel(II) chloride as the catalyst precursor;[13] molar ratios of Grignard reagent–allyl ether–catalyst 1.2/1/0.005.

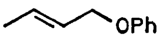
The results are reported in Table 1. They show that by varying the reaction partners it is possible to synthesize olefins with very high optical yield. Indeed asymmetric induction in the formation of 3-ethylcyclohex-1-ene is the highest ever reported in asymmetric carbon–carbon bond formation. Futhermore there is some indication of the stereochemical development of the reaction.

In fact, the very high optical yield obtained in the synthesis of 3-ethylcyclohex-1-ene starting with chiral racemic (**3**) indicates that the cyclohexenyl moiety must give rise to a symmetric reaction intermediate, *i.e.* to a η^3-allyl intermediate (we assume that the reaction for allylic phenyl ethers is

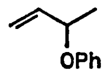
Table 1. Asymmetric allylation reaction of Grignard reagents catalysed by [(−)-(2*S*,3*S*)-2,3-bis(diphenylphosphino)butane]nickel(II) chloride.

Substrate	RMgBr R	Reaction time/h	Conversion (%)	Isolated yield (%)[a]	Regioselectivity[b]	Chiral reaction product, optical yield (%), and absolute configuration
(1)	Et	24	100	80	64(63/1):36	3-methylpent-1-ene 22.3 (*S*)[c]
	Ph	120	100	85	35:65(65/0)	3-phenylbut-1-ene 58.0 (*R*)[d]
(2)	Et	24	100	75	62(61/1):38	3-methylpent-1-ene 17.5 (*S*)[c]
	Ph[g]	40	45	78	35:65(65/0)	3-phenylbut-1-ene 58.3 (*R*)[d]
	Ph	60	100	85	35:65(65/0)	3-phenylbut-1-ene 61.0 (*R*)[d]
(3)	Et	22	100	85	—	3-ethylcyclohex-1-ene 97.7 (*R*)[e]
	Ph	22	100	90	—	3-phenylcyclohex-1-ene 5.8 (*S*)[f]

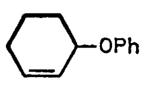
[a] With respect to the reacted allyl ether; sum of all allylation products. [b] Ratio of the percentage of the linear coupling products *vs.* the chiral coupling products; in brackets are the *E*/*Z* ratios for the linear coupling products. [c] Calculated assuming $[\alpha]_D^{17}$ +38.20° (neat) as the maximum rotatory power.[16] [d] Calculated assuming $[\alpha]_D^{25}$ −6.84° (neat) as the maximum rotatory power.[17] [e] Calculated assuming $[\alpha]_D^{25}$ +49.35° ($CHCl_3$) as the maximum rotatory power.[18] [f] Calculated assuming $[\alpha]_D^{29}$ −149.7° (benzene) as the maximum rotatory power.[19] [g] Recovered **(2)** [α_D^{25} (l = 1) +0.75° (neat)] has (*S*) absolute configuration and *ca.* 5% optical purity, as determined by hydrogenation with $RhCl(PPh_3)_3$ to the corresponding s-butyl phenyl ether.[20]



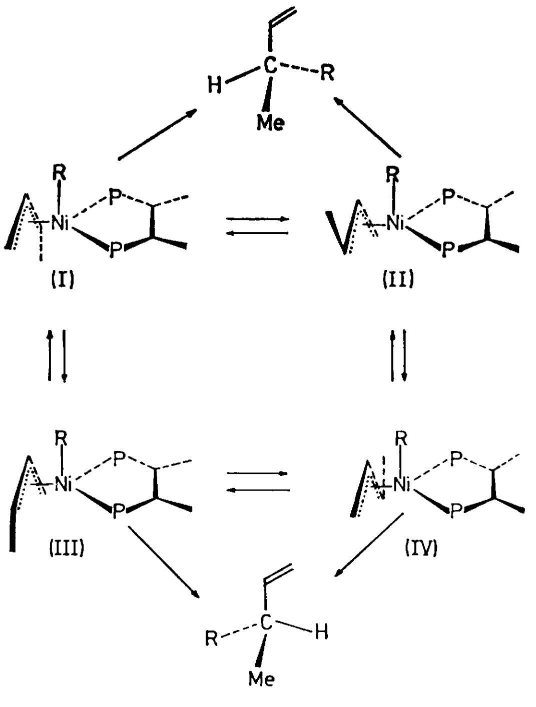
(1)



(2)



(3)



Scheme 1

stereospecific as in the case of the corresponding allylic alcohols[14]). Thus, asymmetric induction in the alkylation (or arylation) of **(3)** is determined by the difference between the reaction rates at the two diastereoisotopic positions of the allylic moiety in the intermediate (*cf.* Figure 1).

Compounds **(1)** and **(2)** give rise to the same chiral products (3-methylpent-1-ene or 3-phenylbut-1-ene). Regioselectivity in the formation of the coupling products is the same for **(1)** and **(2)** and depends only on the nature of the Grignard reagent. Within the limits of reproducibility, the optical purity of the chiral coupling products is the same whether the starting material is **(1)** or **(2)**. Furthermore, when **(2)** is the substrate, a kinetic resolution takes place (k_R/k_S = *ca.* 1.13† when C_6H_5MgBr is the Grignard reagent); however the optical purity of the coupling product is practically independent of the extent of conversion. On the basis of an allyl mechanism, **(1)** or **(2)** would give rise to the same four different intermediates owing to *syn-anti*-isomerism and to the two different faces of the allylic systems presented to the chiral nickel complex (rotational isomerism of the allylic moiety is neglected) (Scheme 1). The equal isomeric and enantiomeric composition of the coupling products when starting with **(2)** (both at low and total conversion) or **(1)** indicates that the equilibration of the intermediates (I), (II), (III), and (IV) (Scheme 1) must be rapid with respect to the formation of the coupling products. Therefore, asymmetric induction in this case is determined by the difference in the rates for the formation of the reaction products from (III) and/or (IV) with respect to (I) and/or (II). It is to be noted that intermediates (III) and/or (IV) appear more reactive with respect to (I) and/or (II), both for R = Et and Ph, as far as the formation of the chiral products is concerned. It is worthwhile to note that intermediates

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† Calculated according to a previously published formula.[21]

of type (I)—(IV) arising from allylic alcohols do not appear to interconvert very rapidly when another ligand [such as PPh_3 or 2,2-dimethyl-4,5-bis(diphenylphosphinomethyl)-1,3-dioxolan] is used with the nickel catalysts.[10,15]

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