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NICKEL-CATALYZED *cis-trans* ISOMERIZATION OF 1-ALKENYL GRIGNARD REAGENTS

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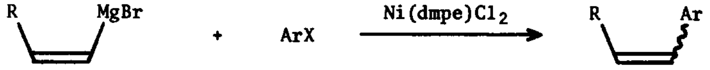
Although oxidative addition and reductive elimination of organic molecules are most important steps catalyzed by various transition metals,[1] stereochemical aspects concerning such processes with alkenyl or alkyl transition metal compounds[2] remain equivocal and controversial.[3] For example, couplings of alkenyl groups *via* transition metal complexes have been shown to proceed with retention of configuration for Cu, Ag, Fe, Co, Ni, Pd, Pt, Mo, Rh, etc.,[4] while much less stereospecificity has been observed during the couplings of alkenyl Grignard and of lithium reagents in the presence of salts of metals such as Ni, Pd, Co, Cr.[5] While nickel complexes currently hold an important position as efficient coupling agents,[6] the stereochemistry of the alkenyl-nickel species concerned seems particularly ambiguous.[5,6] To our knowledge, nobody has described metal-catalyzed *cis-trans* isomerization of alkenyl Grignard reagents.

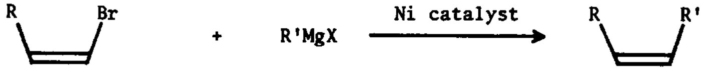
We have now found that alkenyl Grignard reagents undergo *cis-trans* isomerization very easily under the influence of catalytic amounts of nickel salts. This communication demonstrates the importance of the interaction between an alkenyl Grignard reagent and a nickel center in the *cis-trans* isomerization process.

Our first observation is the non-stereoselective nature of the cross-coupling of 1-alkenyl Grignard reagents[7] with aryl halides in the presence of $[Ni(dmpe)Cl_2]$, dmpe = $Me_2PCH_2CH_2PMe_2$, as a catalyst (eq. 1 and Table I).



(1)

These results are in marked contrast with the previously reported, highly stereospecific cross-coupling of monohalo-olefins with various Grignard reagents (eq. 2).[11]



(2)

As Table I demonstrates, the stereoselectivity is strongly dependent upon the nature of the aryl halide and the halide-to-Grignard reagent ratio. Thus, the more reactive the aryl halides and the greater the halide-to-Grignard reagent ratio, the higher the stereoselectivity. In addition, the stereoselectivity seems to be higher with bulky alkenyl Grignard reagents. These results indicate that the low stereoselectivity is attributable to a reaction distinct from and competitive with the essentially stereoselective cross-coupling (Scheme 1).

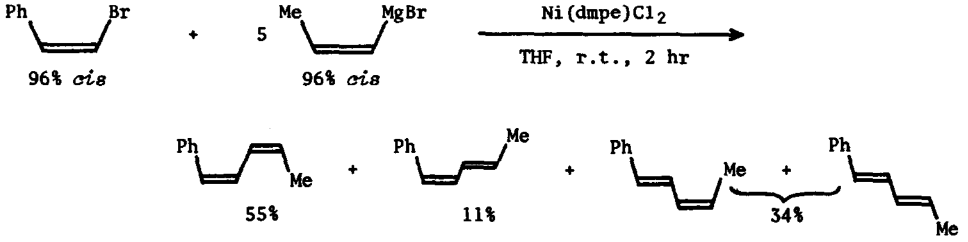
Table I. Cross-Coupling of 1-Alkenyl Grignard Reagents with Aryl Halides Catalyzed by $[Ni(dmpe)Cl_2]$[a]

RCH=CHMgBr (A)		ArX (B)	Mole ratio	RCH=CHAr	
R	*cis/trans*[b]		A/B	Yield (%)[c]	*cis/trans*[c]
Me	96/4	PhCl	1.2/1	15	0/100
Me	96/4	PhBr	1/0.8	84	27/73
Me	96/4	PhBr	1/5	66	73/27
Me	96/4	PhBr	1/20	61	95/5
Me	96/4	p-$CH_3OC_6H_4Br$	1.2/1	79	30/70
Me	96/4	p-ClC_6H_4Br	1.2/1	95	85/15
Me	96/4	α-$C_{10}H_7Br$	1.2/1	87	95/5
n-C_3H_7	100/0	PhBr	1.2/1	63	17/83
i-C_3H_7	94/6	PhBr	1.2/1	41	68/32
Ph	71/29	PhBr	1.2/1	42	1/99

[a] ArX/catalyst ≃ $1/10^{-2}$. The mixture in tetrahydrofuran was heated at 50° for 40 hr.
[b] For the determination of the *cis/trans* ratios, see footnote 7. [c] Determined by GLC.

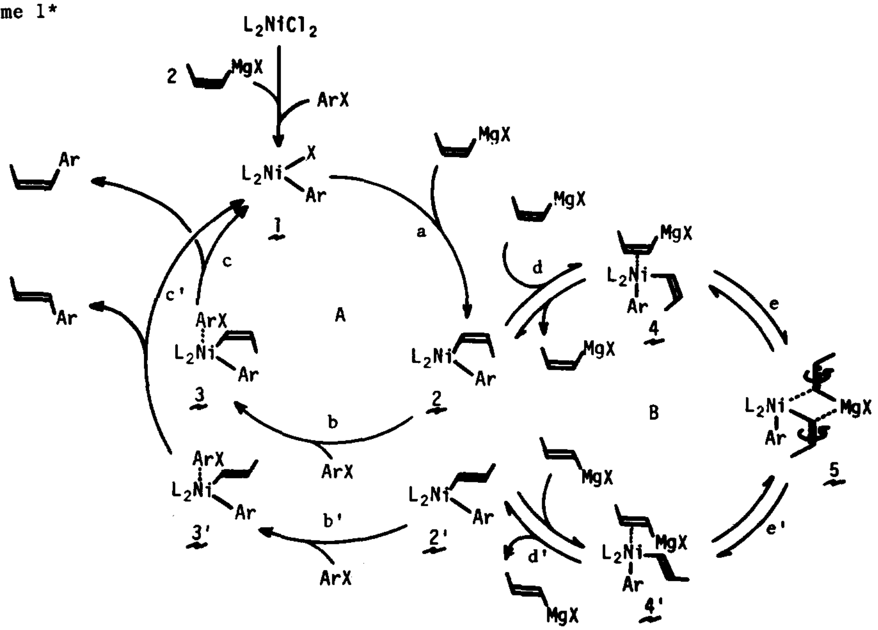
In Scheme 1, a (halo)(organo)nickel complex **1** reacts with the *cis*-alkenyl Grignard reagent to form a *cis*-alkenyl-nickel species **2**. In cases of reactive and/or excess of aryl halides, **2** may take course b to give a *cis*-olefin with retention of configuration *via* an 18-electron[12] intermediate **3** (cycle A). Alternatively, with excess of alkenyl Grignard reagent and with less reactive aryl halides, the alkenyl Grignard reagent as an olefinic component may well compete with the aryl halide for coordination onto the alkenyl-nickel **2** (cycle B). This type of interaction may be responsible for the *cis-trans* isomerization of alkenyl group(s). Although the nature of this interaction can not readily be elucidated, we suggest the possible intermediacy of species **5**, with reference to the known interaction mode between organonickel complexes and aluminum alkyls.[13] Geometric isomerization around the olefinic bond would be possible in **5**, because of the lowering of π-bond order. The resulting *trans*-alkenyl-nickel species **2'** gives a *trans*-olefin upon complexing with an aryl halide.

The relevance of such interactions as in **5** between the alkenyl Grignard reagent with the alkenyl group already attached to nickel may be supported by the partial isomerization of the



(3)

Scheme 1*



*For simplicity, we illustrate the specific case for the *cis*-alkenyl Grignard reagent.

β-styryl moiety observed in the cross-coupling of *cis*-β-bromostyrene with excess of the *cis*-propenyl Grignard reagent (eq. 3),[14] in contrast to the stereoselective reaction of the same halide with excess of the methyl Grignard reagent which contains no unsaturation (eq. 2).

Apart from the cross-coupling, the reversible cycle B strongly suggests that the *cis-trans* isomerization of an alkenyl Grignard reagent itself is catalyzed by nickel complexes under mild conditions. For example, in the presence of a small amount of $(Ph_3P)_2NiCl_2$, $NiCl_2$ or $Ni(PPh_3)_4$ (catalyst/Grignard reagent = $10^{-2}/1$), *cis*-PhCH=CHMgBr (*cis*/*trans* = 74/26 or 80/20)[7] was converted to the *trans*-rich Grignard reagent (*cis*/*trans* = 29/71 $\sim$ 17/83)[7] over 5 hr at room temperature.[15] The same *cis*-*trans* (29/71) mixture was formed also from the 88% *trans*-Grignard reagent. By contrast, no isomerization occurred in the absence of nickel catalysts. Interestingly, ferric chloride and cobaltous chloride exhibited little catalytic activity for the isomerization under the same conditions, the 80% *cis* being converted to the 71% *cis* with $FeCl_3$ and to the 76% *cis* with $CoCl_2$.

While further studies are required before the mechanism can be fully understood, the present observations may help to resolve the ambiguous stereochemical problem concerning, at least, alkenyl-nickel species.[5,16]

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7. The *cis-trans* isomer ratios were determined by ^{1}H NMR spectrum for $CH_3CH{=}CHMgBr$,[8] by trimethylsilylation for n-C_3H_7- and i-C_3H_7-$CH{=}CHMgBr$,[9] and by ^{1}H NMR spectra of PhCH=CHD quenched with D_2O for PhCH=CHMgBr.[10] The β-styryl Grignard reagent was prepared in the presence of excess of 1,2-dibromoethane in place of ethyl bromide which was used by Yoshino *et al.*,[10] in order to prevent coexistence of the ethyl Grignard reagent.
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14. The geometrical configuration of all the products was fully characterized by the IR and ^{1}H NMR spectra.
15. The preparation of the Grignard reagent and the subsequent catalytic reactions were carried out in the dark and under nitrogen. The *cis-trans* isomerization was accompanied by *ca.* 35% decomposition of the Grignard reagent by an unknown mechanism.
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