

Preliminary communication

Effects of the nature of halides on the alkyl group isomerization in the nickel-catalyzed cross-coupling of secondary alkyl Grignard reagents with organic halides

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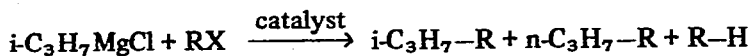
SUMMARY

The extent of alkyl group isomerization accompanying the nickel-catalyzed cross-coupling of secondary alkyl Grignard reagents with organic halides depends upon the nature of halides.

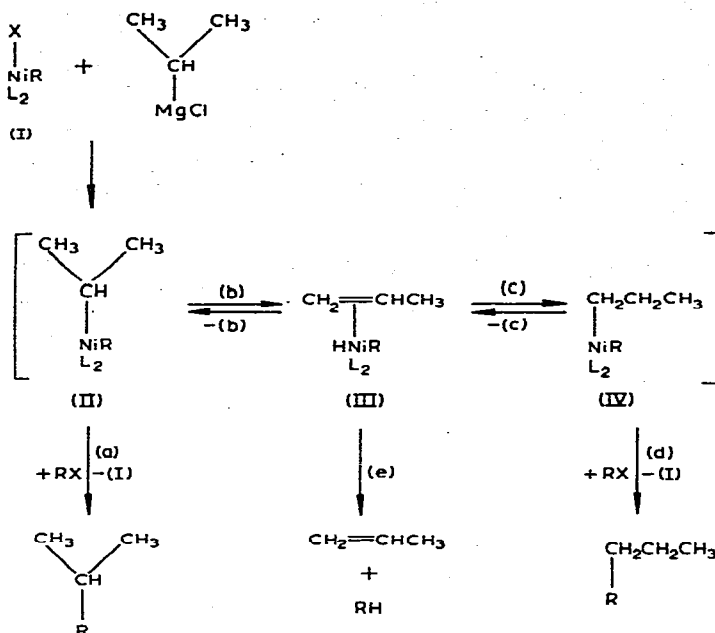
We have recently reported that nickel–phosphine complexes exhibit extremely high catalytic activity for selective cross-coupling of Grignard reagents with aromatic and olefinic halides¹, and that the reactions of secondary Grignard reagents with chlorobenzene are accompanied by alkyl group isomerization from secondary to primary, the extent of which is strongly dependent upon the electronic nature of the phosphine ligands in the catalyst².

For alkyl group isomerization a mechanism involving σ – π rearrangement of σ -alkylnickel intermediates to a hydrido-olefin nickel intermediate (Scheme I) has been proposed². This communication describes the influence of organic halides on the extent of alkyl group isomerization from secondary to primary.

Table 1 summarizes the results from the reactions of isopropylmagnesium chloride with various halides in the presence of $\text{Ni}(\text{Me}_2\text{PCH}_2\text{CH}_2\text{PMe}_2)\text{Cl}_2$, one of the most effective catalysts for the isomerization². Three significant features can be seen from these data.



Firstly, the extent of isomerization is practically independent of the lability of leaving halide, as indicated by the results with a series of fluoro-, chloro- and bromobenzenes; the comparable reactivity of fluorobenzene is particularly noteworthy. With



SCHEME I

TABLE 1

PRODUCTS FROM THE REACTION OF $i\text{-C}_3\text{H}_7\text{MgCl}$ WITH VARIOUS HALIDES IN THE PRESENCE OF $Ni(\text{Dmpe})\text{Cl}_2$ ^a

Halide		Total yield ^b (%)	Product distribution ^b (%)		
R	X		$\begin{array}{c} \text{Y} \\ \\ R \end{array}$	$\begin{array}{c} \text{R} \\ \wedge \end{array}$	RH
C_6H_5	F	62	12	84	<i>c, d</i>
C_6H_5	Cl	88	12	78	<i>6 d</i>
C_6H_5	Br ^e	83	10	69	<i>8 f</i>
<i>p</i> -MeC ₆ H ₄	Cl	45	5	84	11
<i>p</i> -MeOC ₆ H ₄	Cl	24	6	65	29
<i>m</i> -CF ₃ C ₆ H ₄	Cl	81	13	74	13
<i>p</i> -CF ₃ C ₆ H ₄	Cl ^g	100	46	44	10
<i>o</i> -CF ₃ C ₆ H ₄	Cl	40	51	33	16
$\alpha\text{-C}_{10}\text{H}_7$	Br ^g	100	73	19	8

^a To a mixture of the halide (5 mmoles) and the catalyst (0.025 mmole) in 3 ml of ether was added an isopropyl Grignard solution (7 mmoles) at 0°. The mixture was refluxed, unless otherwise indicated, for 40 h, hydrolyzed, and then analyzed by GLC. Dmpe refers to Me₂PCH₂CH₂PMe₂. ^b Determined by GLC using an internal standard. ^c Benzene could not be determined, since the retention time on GLC coincided with that of fluorobenzene. ^d Biphenyl (4%) was also formed. ^e Refluxed for 20 h. ^f Biphenyl (13%) was also formed. ^g Refluxed for 13 h.

iodobenzene only small amounts of cross-coupling occur, and benzene and biphenyl are the major products.

Secondly, the isomerization is strongly influenced by the electronic nature of the substituents on the aromatic ring in such a sense that the electron-releasing substituents facilitate the isomerization to give *n*-propyl derivatives preferentially, while electron-withdrawing substituents retard the isomerization and give rise to isomeric mixtures enriched in isopropyl derivatives.

Finally, α -naphthyl bromide also strongly retards the isomerization. Further important information was obtained from the reaction of 2-pentylmagnesium chloride with vinyl chloride in the presence of the same catalyst, forming 3-methyl-1-hexene only. Thus, vinyl chloride can completely inhibit the isomerization.

The electronic effects of substituents on the aromatic ring are in keeping with those noted for the phosphine ligands². Thus, an increase in electron density on nickel in the intermediate (II) (Scheme I) due to electron-releasing substituents facilitates the σ - π rearrangement, resulting in the preferential formation of primary alkyl coupling products. The observed constancy of the isomerization ratio with variation in leaving halide seems to be consistent with this idea. The negligibly small effect of the *m*-CF₃ group suggests that resonance effects are rather more important than inductive effects.

Although it should be noted that in Scheme I step (a) may be regarded as a bimolecular substitution process^{1,3} while the σ - π rearrangement [step (b)] is unimolecular⁴, and hence that the halides may play an important role also in step (a), the mechanistic details have yet to be satisfactorily elucidated.

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