CHEMISTRY LETTERS, pp. 1257-1260, 1977. Published by the Chemical Society of Japan

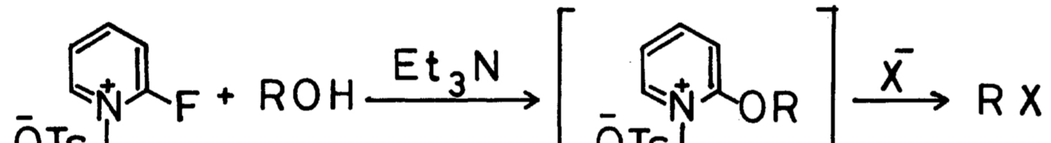
A NEW ONE-POT CROSS COUPLING REACTION OF THE GRIGNARD REAGENTS AND ALLYL ALCOHOLS VIA 2-ALLYLOXYPYRIDINIUM SALTS

Teruaki MUKAIYAMA, Masanori IMAOKA, and Toshio IZAWA
Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

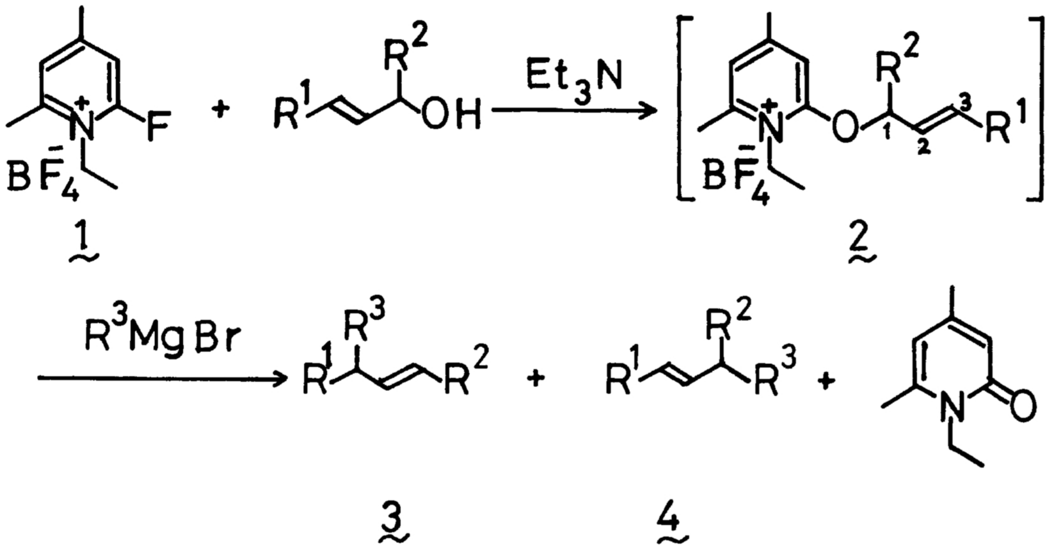
A new one-pot cross coupling reaction of the Grignard reagents and allyl alcohols via 2-allyloxypyridinium salt was investigated. 2-Allyloxy-1-ethyl-4,6-dimethylpyridinium salts, prepared in situ from allyl alcohols and 1-ethyl-2-fluoro-4,6-dimethylpyridinium tetrafluoroborate, reacted easily with the Grignard reagents to afford the corresponding cross coupling products in good yield.

Concerning the cross coupling reaction of the Grignard reagents and alcohols, many reports have been proposed, but, in most cases, the reaction was completed by two-steps procedure via the corresponding halides, tosylate, etc.,[1)] and no report has appeared on the direct coupling of free alcohols with the Grignard reagents.[2)]

Recently we have reported many useful synthetic reactions utilizing the onium salts of azaaromatics.[3)] For example, direct conversion of various alcohols to the corresponding substituted products was achieved by successive treatment with the onium salts and with various nucleophiles, e.g., I^-, Cl^-, N_3^-, $Me_2NCS_2^-$, etc.[4)]



In the present communication we wish to report a useful method for the carbon-carbon bond formation by one-pot cross coupling of allyl alcohols with the Grignard reagents chosen as an appropriate nucleophile.

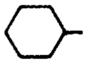
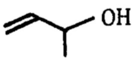


As shown in the above scheme, allyl alcohol reacted with 1-ethyl-2-fluoro-4,6-dimethylpyridinium tetrafluoroborate, **1**, in the presence of an equimolar amount of triethylamine to form 2-allyloxypyridinium salt, **2**, which was subsequently converted to the corresponding cross coupling products in good yields by treatment with various Grignard reagents.

The typical procedure is described for the reaction of cinnamyl alcohol with phenethylmagnesium bromide; to a dichloromethane (1 ml) solution of **1** (175 mg, 0.73 mmol) under argon atmosphere was added a mixture of cinnamyl alcohol (81 mg, 0.60 mmol) and triethylamine (75 mg, 0.74 mmol) in dichloromethane (1.5 ml) at -20°C, and the mixture was stirred for 30 min. To the resulting mixture, a THF solution (2.3 ml) of phenethylmagnesium bromide (1.98 mmol) was added dropwise. Thirty minutes after, the cooling bath was off and stirred continuously at room temperature for additional one hour. The reaction mixture was quenched with 2N hydrochloric acid, extracted with ether, and dried over anhydrous sodium sulfate. After removal of the solvent, 3,5-diphenyl-1-pentene was separated in 99% yield by thin layer chromatography on silica gel.

In a similar manner, various allyl alcohols were coupled with various Grignard reagents to afford the corresponding coupling products in good yields as summarized in the following Table.

Table. The cross coupling reaction of allyl alcohols and the Grignard reagents

Alcohol	R^3	Products (%) a)	
		3	4
	n-Bu-	84 b)	
	$PhCH_2CH_2$-	99 b)	
		84 b)	
	Ph-		95 b)
	$PhCH_2CH_2$-	94 b)	
	Ph-		84 b)
	$PhCH_2CH_2$-	76	

a) The nmr and ir spectra of all the products well agreed with the assigned structures.

b) By glc analysis, each product was found to be contaminated by trace amount of an unidentified compound.

As shown in the Table, primary and secondary alkylmagnesium bromide coupled with 2 at C-3 carbon (S_N2' reaction) exclusively to give 3. On the other hand, in the case of phenylmagnesium bromide, the mode of action was dramatically changed to S_N2 reaction (C-1 carbon attack) exclusively. For example, cinnamyl alcohol coupled with phenylmagnesium bromide to produce 1,3-diphenyl-1-propene in 95% yield and no 3,3-diphenyl-1-propene was obtained.

It is noted that allyl alcohols were regioselectively coupled with the Grignard reagents under very mild conditions by simple one-pot procedures.

REFERENCES AND NOTE

1) a) H. Gilman and J. Robinson, Org. Synth., Coll. Vol. II, John Wiley and Sons, New York, N. Y., 1966, p. 47.
   b) J. Gore and J. P. Dulcere, J. Chem. Soc., Chem. Commun., 1972, 866.
   c) G. Stork, P. A. Grieco, and M. Gregson, Tetrahedron Lett., 1969, 1393.
   d) F. Derguini-Boumechal, R. Lorne, and G. Linstrumell, Tetrahedron Lett., 1977, 1181.

2) Recently Murahashi et al. reported a coupling reaction of lithium allyloxyalkylcuprates by the use of some phosphonium salt; Y. Tanigawa, H. Kanamaru, A. Sonoda, and S. Murahashi, J. Am. Chem. Soc., 99, 2361 (1977).

3) For example : K. Narasaka, T. Masui, and T. Mukaiyama, Chem. Lett., 1977, 763. T. Mukaiyama, N. Usui, E. Shimada, and K. Saigo, ibid., 1975, 1045. T. Mukaiyama, Y. Aikawa, and S. Kobayashi, ibid., 1976, 57. M. Shiono, Y. Echigo, and T. Mukaiyama, ibid., 1976, 1397.

4) S. Kobayashi, M. Tsutsui, and T. Mukaiyama, Chem. Lett., 1976, 373. T. Mukaiyama, S. Shoda, and Y. Watanabe, ibid., 1977, 383. K. Hojo, S. Kobayashi, K. Soai, S. Ikeda, and T. Mukaiyama, ibid., 1977, 635. K. Hojo, H. Yoshino, and T. Mukaiyama, ibid., 1977, 437.

(Received July 29, 1977)