

NICKEL-PHOSPHINE COMPLEX-CATALYZED GRIGNARD COUPLING OF β -BROMOVINYL ETHYL ETHER:
A NEW TYPE OF FUNCTIONALIZED TWO-CARBON HOMOLOGATION OF GRIGNARD REAGENTS

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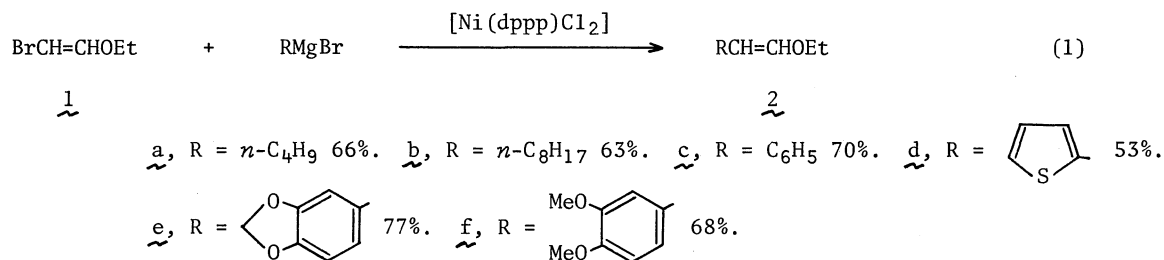
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β -Bromovinyl ethyl ether smoothly couples with Grignard reagents in the presence of $[\text{Ni}(\text{dppp})\text{Cl}_2]$ as a catalyst to give the corresponding alkylated and arylated vinyl ethers in good yields. This reaction provides a new one-step, functionalized two-carbon homologation of Grignard reagents.

In the presence of a catalytic amount of nickel-phosphine complexes, $[\text{NiL}_2\text{X}_2]$, Grignard reagents react with aromatic and vinylic $\text{C}(\text{sp}^2)$ -halides to give the cross-coupling products selectively.¹ Despite the widespread applicability, such a Grignard coupling reaction has a serious limitation that the substituents on the organic halides and on the Grignard reagents are restricted to those which cannot react with the reagents. In view of the characteristic features of the nickel catalyzed Grignard coupling and the important roles played by carbonyl compounds in synthetic organic chemistry, appropriately masked halocarbonyl compounds may be the substrates of the first choice in order to overcome the problems mentioned above. Accordingly, we have applied the Grignard coupling to readily available β -bromovinyl ethyl ether (1).² We were primarily apprehensive for low reactivity of 1, because there is some tendency for electron donating substituent(s) on the organic halides to decrease their reactivity toward the nickel catalyzed Grignard coupling.¹

Contrary to such anxiety, this halide readily participates in the Grignard coupling to give the corresponding β -alkylated and β -arylated vinyl ethers (2) (eq. 1). General procedure is as follows. To a suspension of a catalytic quantity (ca. 1 mole %) of $[\text{Ni}(\text{dppp})\text{Cl}_2]$ ³ in ether or THF was added a Grignard solution at 0°C. This was followed by dropwise addition of 1 at 0°C and an exothermic reaction occurred. The reaction mixture was stirred at room temperature or heated to 40 - 50°C overnight to ensure the reaction. Hydrolysis, usual workup and distillation in vacuo gave the homologated vinyl ethers (2).

The coupling reaction seemed to be nonstereospecific with respect to the C=C bond. Thus, the coupling of Z -1⁴ with $\text{C}_6\text{H}_5\text{MgBr}$ in refluxing ether gave a 58:42 mixture of Z - and E -2c. Previously we established that the nickel-catalyzed Grignard coupling of monohaloolefins proceeds stereo-



specifically.⁵ The absence of the stereospecificity in the coupling of 1 may be attributable to the presence of the β -ethoxy group, but the mechanistic details should wait for further work.

This coupling reaction provides a new type of one-step, functionalized two-carbon homologation of a Grignard reagent. While such process has usually been achieved by the reaction of Grignard reagents with ethylene oxide, the present reaction affords a one-step route to various homologated vinyl ethers, very useful synthetic intermediates.⁶

The alkylated vinyl ethers are readily hydrolyzed to give aldehydes; *e.g.*, treatment of 2b with 2,4-dinitrophenylhydrazine in 0.1M phosphoric acid afforded the corresponding hydrazone in higher than 90% yield. Therefore the present coupling reaction can be regarded as the formylmethylation of Grignard reagents. Unfortunately, we have not yet found suitable conditions for hydrolysis of the arylated vinyl ethers. Further work is now in progress.

Coupling reaction of bromoketene diethyl acetal, BrCH=CH(OEt)_2 ,⁷ with a phenyl Grignard reagent proceeded rather sluggishly under similar conditions to give, after acid hydrolysis, only 20% yield of ethyl phenylacetate.

Improvement and extension of the present coupling reaction are now under investigation.

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REFERENCES AND NOTES

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2. G. Stork and M. Tomasz, *J. Amer. Chem. Soc.*, 86, 471 (1964).
3. $\text{dppp} = \text{Ph}_2\text{P}(\text{CH}_2)_3\text{PPh}_2$. $[\text{Ni}(\text{dppp})\text{Cl}_2]$ has been found one of the most effective catalysts for the Grignard coupling.¹
4. A stereoselective preparation of *Z*-1 (*Z* > 99%) was achieved by treatment of a bromine adduct of ethyl vinyl ether with triethylamine at $-10^\circ\text{C} \sim \text{room temperature}$ followed by filtration and distillation, while the Stork's method gave a mixture of *Z:E* = 84:16.
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