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COPPER-CATALYSED REACTIONS OF ALLYLIC GRIGNARD REAGENTS WITH EPOXIDES.

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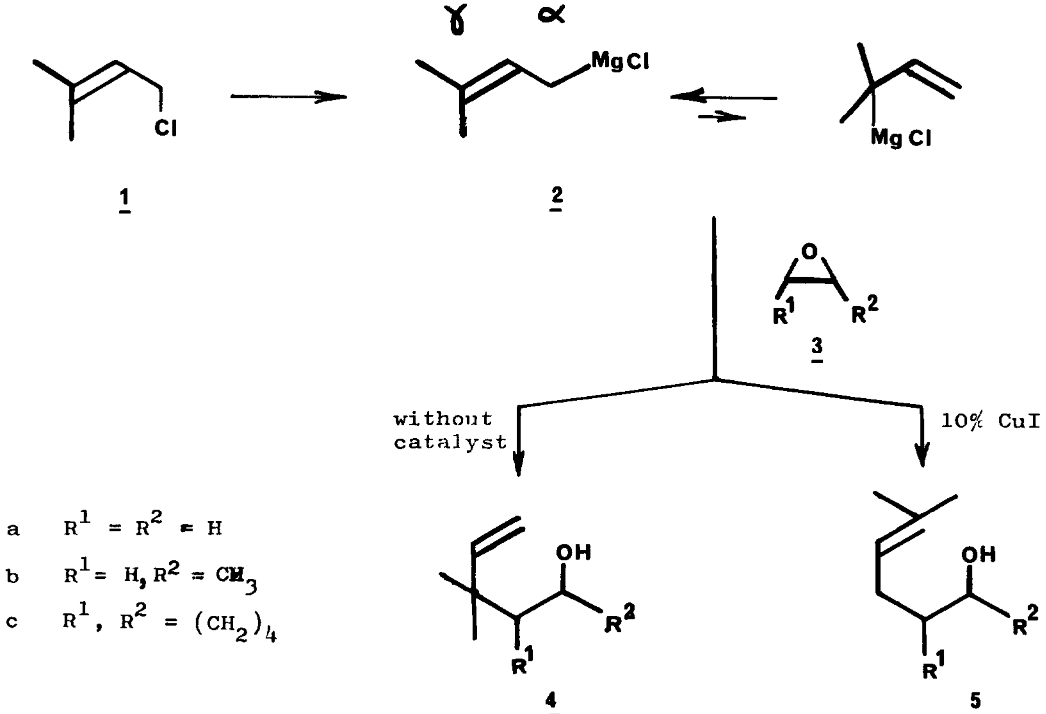
Most of the reactions of unsymetrical allylic Grignard reagents show the tendancy to react on the internal carbon of the allyl system rather than on the terminal carbon[1,2]. The mechanism of this reaction with electrophilic substrates has been studied[3,4].

We recently described the copper-catalysed regioselective alkylation of the allylic magnesium reagents[5]. We now report the regioselective reactions of these organometallic species with epoxides[6]. The ''prenyl'' Grignard reagent <u>2</u> , 3-methylbut-2-enyl-magnesium chloride, which is a potentially useful synthetic ''isoprene unit'' was studied in greater detail.



a $R^1 = R^2 = H$
b $R^1 = H, R^2 = CH_3$
c $R^1, R^2 = (CH_2)_4$

4:5 ratios* and overall yields** (%) in the reaction of reagent 2 with epoxides 3:

	without catalyst		with 10% CuI	
	4 : 5	yield	4 : 5	yield
a	98 : 2	84	2 : 98	75
b	99 : 1	70	3 : 97	68
c	92 : 8	86	1 : 99	86

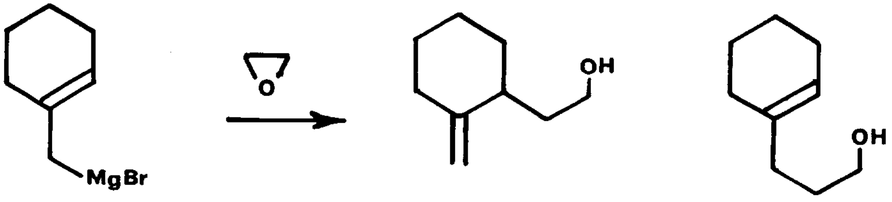
*) measured by glpc

**) yields are given for distilled products.

When this reagent 2 was treated in THF[7] with various epoxides 3, the ''γ products'' 4[8] were obtained in high yield and purity, in agreement with previous results with butenyl magnesium bromide[3,9]. However, when treated with 10% copper iodide, the reagent 2 gave the ''α products'' 5[8] with very small amount (1 to 3%) of ''γ products'' 4 [10]. Moreover, while 3c did not react significantly with 2 at 0°, but gave 4c after 2 hr at 20° without catalyst, it gave 5c within 1.5 hr at -30° with the catalyst.

By reaction with monosubstituted epoxides such as 3b, attack occured on the less substituted carbon of the epoxide: under uncatalysed conditions, 4b was formed in 70% yield (99% purity); with 10% copper iodide, 5b was obtained (68%) in 97% purity.

The Grignard reagent 6 which has a secondary substituted γ site showed the same high regioselectivity with ethylene oxide: without catalyst, it gave the alcohol 7; with 10% CuI, the alcohol 8 was obtained (81%) in 97% purity.

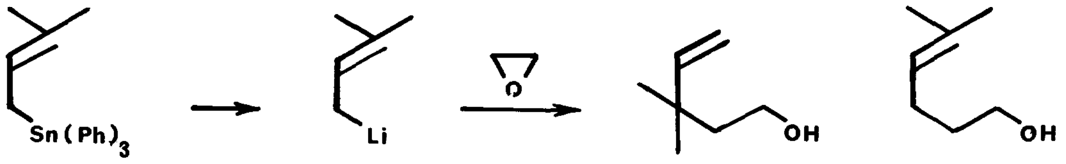


6 7 8

				Yield (%)
without CuI	99	:	1	89
10% CuI	3	:	97	81

When the stoichiometric dialkyl cuprate of the Grignard 2 was prepared (with 50% copper iodide) and treated with epoxides, the α products 5 were obtained in good yields, no rearranged products 4 were detected. However, with 3c, which is less reactive, the γ product 5c was formed in lower yield (50%) and contaminated by 20% of trans-2-iodo-cyclohexanol.

The prenyl lithium reagent 10, obtained from dimethylallyltriphenyltin 9[11] (by reaction with phenyl lithium)[12], and treated with epoxides 3, gave the rearranged products 4 in good yield (70-85%). However, the corresponding cuprate[13] (prepared by reaction with 50% copper iodide) treated with ethylene oxide, gave a mixture (55:45) of alcohols 4a and 5a.



9 **10** **4a** **5a**

without CuI	98	:	2
50% CuI	55	:	45

These results illustrate the greater utility and mechanistic interest of copper-catalysed reactions of allylic Grignard reagents over the stoichiometric (formed with 50% copper iodide) lithium cuprate reagents, high regioselectivity and high yields were observed.

Typical procedure: To 190 mg of copper iodide and 0.98g (10 mmol) of epoxide 3c in anhydrous THF (20 ml), 28 ml (1.5 equiv., 0.55 N in THF) of the Grignard reagent 2 were added dropwise (10 mn) at -30°. After 1.5 hr at -30°, work-up in the usual manner and distillation gave 1.44g (86%) of alcohol 5c.

References and Notes

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6) For reactions of organocopper reagents with epoxides, see: G.H. POSNER, *Organic Reactions*, 22, 253 (1975), and a recent report: P.R. McGUIRK, A. MARFAT andP. HELQUIST, *Tetrahedron Letters*, 2465 (1978).

7) In THF/HMPA, a mixture of alcohols 4 and 5 was formed: 70:30 of 4a and 5a from 3a, 30:70 of 4c and 5c from 3c.

8) All new compounds were identified by satisfactory analytical and spectral data.

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