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Preliminary communication

DIRECT ALKYLATION OF ALLYLIC ALCOHOLS WITH ALLYLIC REARRANGEMENT USING A NEW ALKYLATING REAGENT, RCu:BF_3 *

YOSHINORI YAMAMOTO* and KAZUHIRO MARUYAMA
Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606 (Japan)

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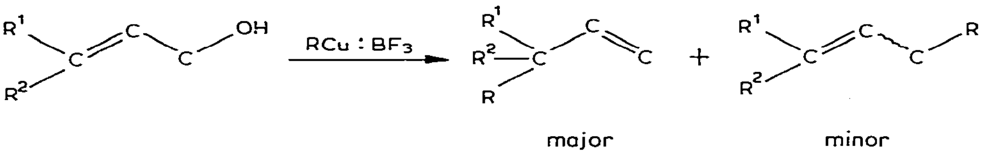
Summary

Direct alkylation of allylic alcohols with allylic rearrangement can be realized with a new alkylating reagent, RCu:BF_3. This is the first example of direct displacement of a hydroxyl group by hydrocarbon groups using an organocopper reagent.

Carbon—carbon bond formation, one of the most fundamental operations in organic chemistry, is often accomplished by the substitution reaction of an organometallic reagent with an organic substrate which has a suitable leaving group. The current reagent of choice is an organocopper derivative, which enables substitution of halogens and of alcohol derivatives by various hydrocarbon groups in many different types of organic substrates [1]. To our knowledge, however, a hydroxyl group cannot be replaced directly by hydrocarbon groups using an organocopper reagent [2]. We have found that the direct alkylation of allylic alcohols, with allylic rearrangement, can be realized with a new alkylating reagent, RCu:BF_3 (eq. 1).



(1)

We recently reported that the substitution of allylic halides with complete allylic rearrangement can be achieved by using RCu:BF_3 [3]. It appeared desirable to examine if other allylic substrates, such as acetates and ethers, could react with this new reagent to give the corresponding alkylation products. Indeed, the

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*The authors dedicate this contribution to Professor Herbert C. Brown, on the occasion of his 66th birthday and in honor of his distinguished contributions to chemistry.

reaction proceeded quite smoothly with allylic acetates but sluggishly with allylic ethers. For example, the reaction of allyl phenyl ether with 3 equivalents of n-$C_4H_9Cu:BF_3$ produced 1-heptene (26%) and 72% of the allyl phenyl ether was recovered. The most surprising observation was that allylic alcohols also were alkylated with allylic rearrangement. The results are summarized in Table 1.

TABLE 1

DIRECT ALKYLATION OF ALLYLIC ALCOHOLS WITH $RCu:BF_3$ [a]

Entry	Allylic alcohol	$RCu:BF_3$ R (mmol)	Product ratio (%) [b,c]		Yield (%) [b]
			γ-Alkylation	α-Alkylation	
1	$C_6H_5CH{=}CHCH_2OH$	n-C_4H_9 (1)	83	17	17
2	$C_6H_5CH{=}CHCH_2OH$	n-C_4H_9 (2)	91	9	66
3	$C_6H_5CH{=}CHCH_2OH$	n-C_4H_9 (3)	91	9	97
4	$C_6H_5CH{=}CHCH_2OH$	CH_3 (3)	95	5	96
5	$CH_3CH{=}CHCH_2OH$	n-C_4H_9 (3)	86	14	99
6	$CH_2{=}CHCH(OH)CH_3$	n-C_4H_9 (2)	90 [d]	10	44
7	$CH_2{=}CHCH(OH)CH_3$	n-C_4H_9 (3)	94 [d]	6	85
8	$C_6H_5CH{=}CHCH_2OH$	n-C_4H_9Cu (2)	—	—	— [e]
9	$C_6H_5CH{=}CHCH_2OH$	$(n\text{-}C_4H_9)_2CuLi$ (2)	—	—	— [e]

[a] All reactions were performed on a 1 mmol scale as previously described [3], except that allylic alcohols instead of allylic halides were added to an ether solution of $RCu:BF_3$. Utilization of THF as the solvent led to poor results. [b] By GLC analysis. [c] The stereochemistry of the minor products was not determined precisely, except where otherwise indicated. [d] *cis*/*trans* 45/55. [e] Not detected.

Although the reaction of cinnamyl alcohol with an equivalent amount of n-$C_4H_9Cu:BF_3$ did produce the alkylation products (entry 1), the best result was obtained when 3 molar equivalents of the reagent were used (entries 3—5, 7). As expected, the corresponding alkylcopper and cuprate reagents did not give the desired products (entries 8, 9). The reaction of cinnamyl acetate with 3 molar equivalents of n-$C_4H_9Cu:BF_3$ also gave the alkylation products in 92% yield, but the regioselectivity was low (γ/α 62/38).

It is known that 1/1 and/or 2/1 addition complexes are formed between alcohols and BF_3 [4]. Therefore, it might be thought these complexes can react with an alkylcopper reagent. To test this possibility, a pre-mixed ether solution of cinnamyl alcohol (1 mmol) and $BF_3:OEt_2$ (1 mmol) was added to an ether solution of n-C_4H_9Cu (2 mmol) at –30 ~ –40°C. GLC analysis revealed that the alkylation products were obtained in only 8% yield (γ/α 58/42), which suggests that the reactive species in our reactions is not RCu but rather $RCu:BF_3$ (or $R\bar{B}F_3\overset{+}{C}u$). It is not possible at present to completely eliminate a possibility that $RCu:BF_3$ reacts with the allyl alcohol—BF_3 complex instead of with the alcohol itself.

The following procedure for the synthesis of 3-phenyl-1-heptene is representative. A 200-ml flask, equipped with a magnetic stirrer and maintained under nitrogen, was charged with 5.7 g (30 mmol) of CuI and 60 ml of dry ether. n-Butyllithium in hexane (1.3 *M*, 30 mmol) was added at –30°C, and the resulting mixture was stirred at this temperature for 5 min. The mixture then was cooled to –70°C, and $BF_3:OEt_2$ (47%, 3.9 ml, 30 mmol) was added. After the mixture had been stirred for a few minutes, cinnamyl alcohol (1.34 g, 10 mmol) in ether was added, and the mixture was allowed to warm slowly to room temperature with stirring. The product was filtered through a column of alumina using petroleum ether. The olefin thus obtained in essentially pure form was distilled under reduced pressure: 1.56 g, 90%, b.p. 65—66°C (5 mmHg).

The reaction of allylic halides (γ-attack > 98—99%) [3] proceeds with greater regioselectivity than that of allylic alcohols. Unfortunately, however, allylic halides often are highly reactive and there is a difficulty of obtaining these halides in pure form under normal conditions. On the other hand, allylic alcohols are easily handled and hence the present development greatly enhances the possibilities of the route to carbon—carbon bond formation via $RCu{:}BF_3$.

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