CHEMISTRY LETTERS, pp. 1123-1124, 1980.

ONE-POT SYNTHESIS OF (*Z*)-4-ALKENOIC ACIDS

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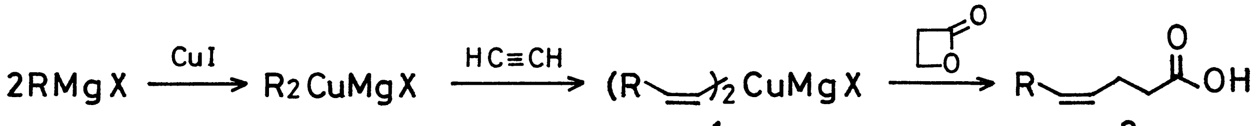
The reaction of β-propiolactone with di-(*Z*)-1-alkenylcuprates, prepared from Grignard reagents, copper(I) iodide and acetylene, gave (*Z*)-4-alkenoic acids in high yields in one-pot operation.

We wish to report here a general method for one-pot synthesis of various (*Z*)-4-alkenoic acids (**2**) by the ring-opening reaction of β-propiolactone with di-(*Z*)-1-alkenylcuprates (**1**). Although (*Z*)-4-alkenoic acids and their esters are known as a component of perfumes and flavors,[1] there have been only a few studies on the stereoselective synthesis of them: 1) the conjugate addition to ethyl acrylate with (*Z*)-1-alkenylcuprates, prepared from (*Z*)-1-alkenyl bromide, lithium metal and copper(I) iodide,[2] and 2) the Wittig reaction of 3-methoxycarbonylpropylidenephosphorane with alkanals.[3]

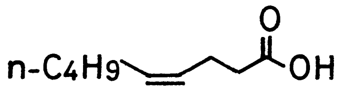
One-pot synthesis of (*Z*)-4-alkenoic acids described in this letter was effected through the following steps: 1) the preparation of di-(*Z*)-1-alkenylcuprates (**1**) by the *cis* addition of dialkylcuprates to acetylene,[4] and 2) the regioselective ring-opening of β-propiolactone with diorganocuprates.[5]



1 **2**

(*Z*)-4-Heptenoic acid was easily obtained in a high yield by the following procedure. Acetylene (300 ml, 12.4 mmol) was introduced into a solution of bromomagnesium diethylcuprate, prepared from ethylmagnesium bromide (6 mmol) and CuI (3 mmol) in a mixed solvent of THF (20 ml) and dimethyl sulfide (1 ml), at -78 °C for 30 min. The reaction mixture was stirred at -30 °C for 30 min. Then, β-propiolactone (2 mmol) in THF (8 ml) was added dropwise at -45 °C for over 15 min, and the reaction mixture was stirred at -30 °C for 3 h. A usual work-up furnished (*Z*)-4-heptenoic acid of bp 97~99 °C/15 mmHg[6] in 87% yield.

On the other hand, when the reaction of β-propiolactone with bromomagnesium di-(*Z*)-1-hexenylcuprate, prepared from butylmagnesium bromide, copper(I) iodide and acetylene, was carried out by the similar procedure described above, (*Z*)-4-nonenoic acid (**3**) was obtained in a yield of 53% accompanied by heptanoic acid (**4**, 17%) and



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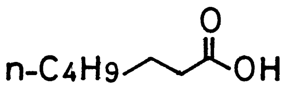

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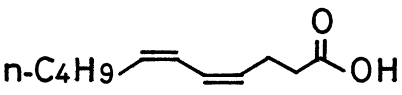

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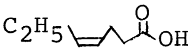
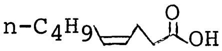
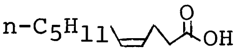
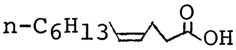
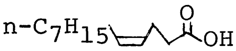
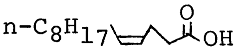
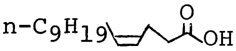
Table. One-pot Synthesis of (*Z*)-4-Alkenoic Acids

R in Cuprate 1	Molar Ratio $HC{\equiv}CH/R_2CuMgBr$	Product 2	Yield[a] (%)
C_2H_5	4.1		87
n-C_4H_9	4.1		90
n-C_5H_{11}	6.2		83
n-C_6H_{13}	5.2		87
n-C_7H_{15}	5.7		90
n-C_8H_{17}	5.7		80
n-C_9H_{19}	6.6		81

[a] The yields were based on β-propiolactone.

a small amount of (*Z*,*Z*)-4,6-undecadienoic acid (5). The former by-product is due to the direct reaction of β-propiolactone with dibutylcuprate, which did not react with acetylene. However, the yield of 3 was increased to 90%, when four molar amounts of acetylene was introduced to the solution of bromomagnesium dibutylcuprate in ten portions at 10 min intervals at -45 °C.

Furthermore, (*Z*)-4-alkenoic acids with longer alkyl substituents were also obtained in high yields by the reaction of β-propiolactone with bromomagnesium di-(*Z*)-1-alkenylcuprates, and the result is summarized in the Table. In these cases, it is necessary to introduce an excess (5.2~6.6 molar amounts) of acetylene into a solution of the corresponding dialkylcuprate at -30 °C in the same manner as that described for the synthesis of (*Z*)-4-nonenoic acid.

Thus, the regioselective ring-opening of β-propiolactone with di-(*Z*)-1-alkenylcuprates offered a convenient and general synthetic method for various (*Z*)-4-alkenoic acids from easily available reagents such as copper(I) iodide, Grignard reagents, acetylene and β-propiolactone in one-pot operation.[7]

References

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7) For a related independent investigation, see: J. F. Normant, A. Alexakis, and G. Cahiez, *Tetrahedron Lett.,* 21, 935 (1980).

(Received July 8, 1980)