

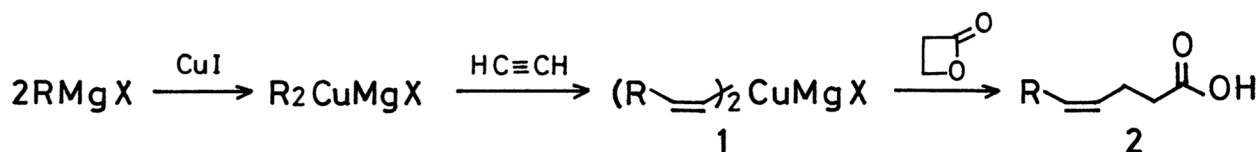
ONE-POT SYNTHESIS OF (Z)-4-ALKENOIC ACIDS

Tamotsu FUJISAWA,* Toshio SATO, Tatsuo KAWARA, and Kouichi NARUSE
Chemistry Department of Resources, Mie University, Tsu, Mie 514

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-methoxycarbonyl-propylidene phosphorane 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⁾



(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 mmHg⁶⁾ 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

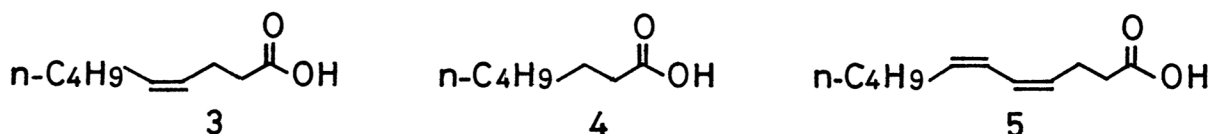


Table. One-pot Synthesis of (Z)-4-Alkenoic Acids

R in Cuprate 1	Molar Ratio HC≡CH/R ₂ CuMgBr	Product 2	Yield ^a (%)
C ₂ H ₅	4.1		87
n-C ₄ H ₉	4.1		90
n-C ₅ H ₁₁	6.2		83
n-C ₆ H ₁₃	5.2		87
n-C ₇ H ₁₅	5.7		90
n-C ₈ H ₁₇	5.7		80
n-C ₉ H 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⁾

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