

A NOVEL FIVE-CARBON HOMOLOGATION LEADING TO 3,4-ALKADIENOIC ACIDS BY  $S_N2'$   
REACTION OF  $\beta$ -ETHYNYL- $\beta$ -PROPIOLACTONE WITH GRIGNARD REAGENTS  
IN THE PRESENCE OF COPPER(I) CATALYST

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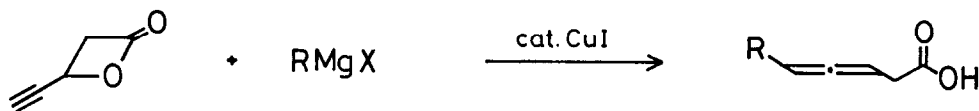
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*Summary:  $\beta$ -Ethynyl- $\beta$ -propiolactone reacts regioselectively with Grignard reagents in the presence of copper(I) catalyst to afford 3,4-alkadienoic acids in high yields. Synthetic utility of this reaction is demonstrated in the simple synthesis of pellitorine.*

Allene-forming 1,3-substitution reaction ( $S_N2'$ ) of propargylic derivatives have been of synthetic and mechanistic interest for years.<sup>1,2</sup> One of the most valuable method for synthesis of allene has been the  $S_N2'$  reaction of diorganocuprates with propargylic derivatives such as an alcohol,<sup>2a</sup> ether,<sup>2b</sup> acetate,<sup>2c</sup> tosylate,<sup>2d</sup> halide,<sup>2e</sup> sulfinate,<sup>2f</sup> and carbamate.<sup>2g</sup> Recently, it was found that highly regioselective reaction of  $\beta$ -propiolactone with diorganocuprates<sup>3</sup> or with Grignard reagents in the presence of copper(I) catalyst<sup>4</sup> affords  $\beta$ -substituted propionic acids in high yields. On the other hand,  $\beta$ -ethynyl- $\beta$ -propiolactone, prepared easily by 1,2-cycloaddition of ketene and propinal,<sup>5</sup> corresponds to a propargylic ester. If  $\beta$ -ethynyl- $\beta$ -propiolactone could undergo selectively  $S_N2'$  reaction with organometallic reagents, it will provide a new five-carbon homologation leading to the corresponding 3,4-alkadienoic acids. In this communication, we wish to report highly regiocontrolled alkylation of  $\beta$ -ethynyl- $\beta$ -propiolactone with Grignard reagents in the presence of copper(I) catalyst<sup>6</sup> to afford 3,4-alkadienoic acids<sup>7</sup> in high yields.

When butylmagnesium bromide (1.2 equiv) was added into a THF-Me<sub>2</sub>S (20 : 1) solution of  $\beta$ -ethynyl- $\beta$ -propiolactone (1 equiv) and copper(I) iodide (2 mol%) at -78 °C and stirred for 1 h at that temperature, the  $S_N2'$  product, 3,4-nonadienoic acid was obtained in a high yield of 97% without any accompanying product through

$S_N2$  pathway. However, addition of the lactone into a mixture of butylmagnesium bromide and copper(I) iodide decreased the yield of 3,4-nonadienoic acid (61%). Ether, instead of THF was employed as a solvent to result in decreasing the yield (80%).



The copper-catalyzed reaction of several representative Grignard reagents with  $\beta$ -ethynyl- $\beta$ -propiolactone was examined as shown in Table I. Grignard reagents of primary, secondary, or tertiary alkyl group attacked regioselectively almost only at the terminal acetylene carbon of the lactone to furnish 3,4-alkadienoic acids in high yields. When Grignard reagents with  $sp^2$  carbon such as phenyl or vinyl group were employed, the yields of the corresponding acids were slightly decreased. However, allylmagnesium bromide gave only a small

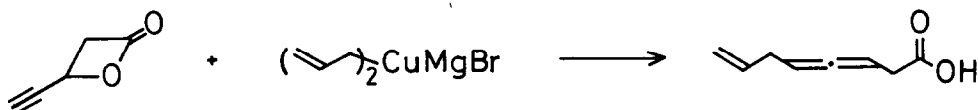
Table I. Reaction of  $\beta$ -Ethynyl- $\beta$ -Propiolactone with Grignard Reagents in the Presence of CuI (2 mol%)<sup>a</sup>

RMgX	Product	Yield(%)
MeMgBr		97 <sup>b</sup>
BuMgBr		97 <sup>b</sup>
s-BuMgCl		90 <sup>b</sup>
t-BuMgCl		85 <sup>b</sup>
PhMgBr		78 <sup>c</sup>
CH <sub>2</sub> =CHMgBr		72 <sup>c</sup>
CH <sub>2</sub> =CHCH <sub>2</sub> MgBr		11 <sup>c</sup>
(CH <sub>2</sub> =CHCH <sub>2</sub> ) <sub>2</sub> CuMgBr <sup>d</sup>		54 <sup>c</sup>

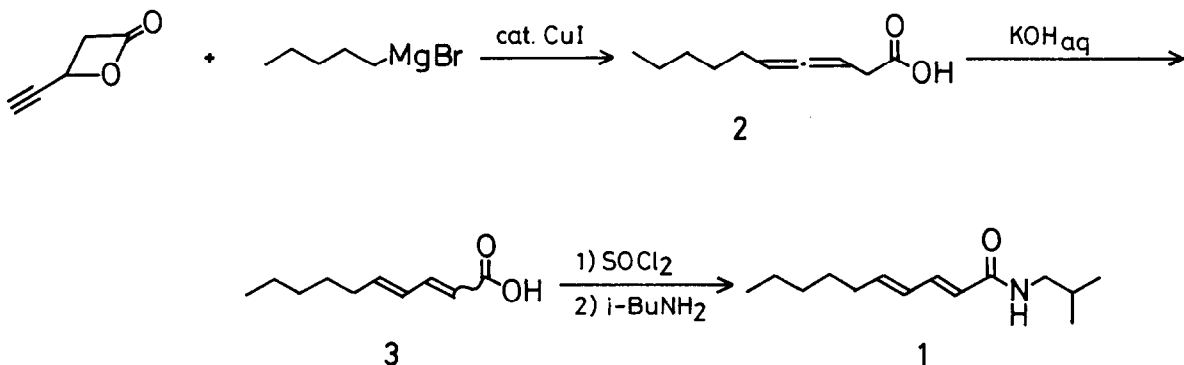
<sup>a</sup> All reactions were performed on 2 mmol scales in THF-Me<sub>2</sub>S (20 : 1) at -78 °C for 1 h. The molar ratio of RMgX and the lactone is 1.2 : 1.0. All products were identified by IR and NMR spectra. <sup>b</sup> Isolated by bulb-to-bulb distillation. <sup>c</sup> Isolated by silica gel TLC. <sup>d</sup> In this case, diallylcuprate was used, and the reaction was carried out at -50 °C for 1 h.

amount of 3,4,7-octatrienoic acid.

Since the reaction of diallylcuprate<sup>3</sup> has been found to be superior to copper-catalyzed reaction of allyl Grignard reagent in the case of allylation of  $\beta$ -propiolactone,<sup>4</sup> diallylcuprate was employed for the reaction with  $\beta$ -ethynyl- $\beta$ -propiolactone. When the lactone was treated with diallylcuprate, prepared from allylmagnesium bromide (2 equiv) and copper(I) iodide (1 equiv), in THF-Me<sub>2</sub>S (10 : 1) at -50 °C for 1 h, the yield of 3,4,7-octatrienoic acid was expectedly increased to 54%.



3,4-Alkadienoic acids has been employed as useful precursors of several natural products.<sup>7a,8</sup> Here a simple synthesis of N-isobutyl-E,E-2,4-decadienamide, pellitorine (1) utilizing the regioselective reaction of  $\beta$ -ethynyl- $\beta$ -propiolactone was demonstrated. Pellitorine is an insecticidal compound isolated from *Anacyclus Pyrethrum* roots, and a number of synthesis of pellitorine proceeded via E,E-2,4-decadienoic acid or its ester as the key intermediates.<sup>9</sup> Our synthetic route is outlined in the following scheme.



The starting 3,4-decadienoic acid (2) was prepared in 90% yield by the copper-catalyzed reaction of  $\beta$ -ethynyl- $\beta$ -propiolactone with n-amylylmagnesium bromide at -78 °C for 1 h; bp 131 ~ 133 °C / 1.8 mmHg; NMR (CCl<sub>4</sub>)  $\delta$  0.99 (3H, t, J=6Hz, CH<sub>3</sub>), 1.05 ~ 1.70 (6H, m, CH<sub>2</sub>), 1.70 ~ 2.30 (2H, m, CH<sub>2</sub>C=C), 3.08 (2H, dd, J=5Hz, CH<sub>2</sub>CO<sub>2</sub>), 4.80 ~ 5.40 (2H, m, olefinic), and 10.41 (1H, s, CO<sub>2</sub>H); IR (film) 3080 (OH), 1960 (C=C=C), and 1700 (C=O) cm<sup>-1</sup>. 3,4-Decadienoic acid 2 was isomerized to 2,4-decadienoic acid (3) (EZ:EE=41:59) in 94% yield in refluxing aqueous 2N KOH solution for 1 h. Treatment of 3 with 5 mol% of thiophenol and 1 mol% of 2,2'-azobis(isobutyronitrile) (AIBN) at 80 °C for 2 h gave isomer

equilibration to predominantly the E,E isomer (EZ:EE=22:78). Pure E,E-2,4-decadienoic acid obtained by recrystallization from hexane was transformed to pellitorine **1** in 93% yield by subsequent treatment with SOCl<sub>2</sub> and i-BuNH<sub>2</sub>; NMR (CCl<sub>4</sub>) δ 0.70 ~ 1.10 (3H, t, J=6Hz, CH<sub>3</sub>, 6H, d, J=6Hz, CH<sub>3</sub>), 1.70 ~ 2.40 (2H, m, CH<sub>2</sub>C=C), 3.03 (2H, t, J=5.5Hz, NCH<sub>2</sub>), 5.70 ~ 6.30 (3H, m, olefinic), 6.70 ~ 7.30 (1H, m, olefinic), 8.10 (1H, t, J=5.5Hz, NH); IR (KBr pellet) 3300 (NH), 3080 (NH) (NH), 1660 (C=C), 1620 (C=O), and 995 (CH=CH) cm<sup>-1</sup>.

#### References and Notes

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