EJ52-1999-825

Journal of the Chinese Chemical Society, **1999**, *46*, 825-826

Organocopper Mediated Conjugate Addition of Vinyl Grignard Reagent to α,β-Unsaturated Acylsilane

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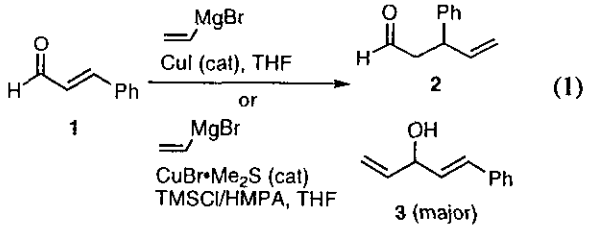
Vinyl Grignard reagent added to *trans*-cinnamaldehyde in the presence of cuprous iodide to give conjugate addition product in good yield.

INTRODUCTION

Conjugate addition of organocopper related reagents to α,β-unsaturated carbonyl compounds is one of the most important synthetic methods,[1] in which, conjugate addition to α,β-unsaturated aldehydes is usually difficult. Due to the high reactivity of the formyl group, 1,2-addition is often a severe competing reaction. However, it was reported that with the addition of chlorotrimethylsilane/hexamethylphosphoric triamide (HMPA) the regiochemical problem can be solved.[2] Also, $Me_5Cu_3Li_2$ is found to be very successful in conjugate methylation of enals.[3]



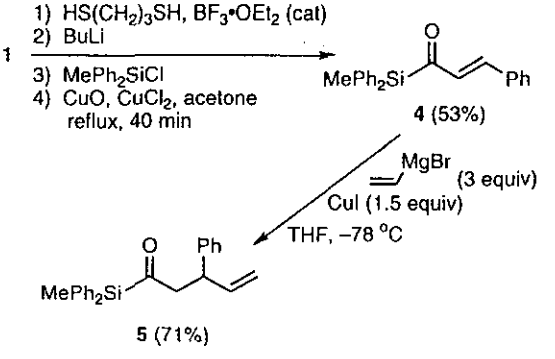
(1)

RESULTS AND DISCUSSION

Recently, we needed to perform a conjugate addition of a vinyl moiety to *trans*-cinnamaldehyde (**1**). As shown in Eq. 1, the reaction of vinyl magnesium bromide with aldehyde **1** catalyzed by copper with or without the use of TMSCl/HMPA all gave 1,2-addition product **3** in major amount. It is known that α,β-unsaturated acylsilanes are excellent Michael acceptors.[4] However, copper mediated conjugate addition of Grignard reagents to these compounds has not been reported. Therefore, we decided to explore this possibility.

As shown in Scheme I, we prepared acylsilane **4** using the methodology developed by Danheiser and Fink.[4] Thus, silylation of the dithioacetal derived from *trans*-cinnamaldehyde (**1**) followed by hydrolysis[5] of the resulting 2-silyl-1,3-dithiane gave acylsilane **4** in 53% yield. Addition of the acylsilane **4** to a mixture of vinyl magnesium bromide (3 equiv) and cuprous iodide (1.5 equiv) in THF at -78 °C (2.5 h) afforded the conjugate addition product **5** in 71% yield. It is well established that acylsilanes can be converted to the corresponding aldehydes.[4,6] Therefore, this methodology successfully complements the conjugate addition chemistry of α,β-unsaturated aldehydes. In addition, due to the versatile synthetic utilities of acylsilanes,[6,7] this process provides a useful entry to the synthesis of acylsilanes.

Scheme I



EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded at 200 or 300 MHz; ^{13}C NMR spectra were recorded at 50 or 75 MHz. Chloroform (δ = 7.24 ppm) was used as internal standard, and $CDCl_3$ was used as the solvent. THF was distilled from sodium benzophenone ketyl under N_2. Acetone was distilled over sodium carbonate. All reactions were performed under a blanket of N_2 or Ar.

Dedicated to Professor Kung-Tsung Wang on the occasion of his 70th birthday.

***trans*-1-(Methyldiphenylsilyl)-3-phenyl-2-propen-1-one (4)**

To a solution of 5.00 g (37.8 mmol) of *trans*-cinnamaldehyde and 4.01 g (37.8 mmol) of 1,3-propanedithiol in 6 mL of chloroform was added two drops of borontrifluoride etherate. The resulting mixture was stirred at room temperature for 24 h and then partitioned between ether (100 mL) and water (100 mL). The ether layer was washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo to give 8.00 g of a yellow liquid. Part of the liquid (1.00 g) was dissolved in 10 mL of THF followed by the addition of 3.55 mL (5.40 mmol) of a 1.52 M solution of *n*-butyllithium in hexane over a period of 5 min at -78 °C. The resulting solution was stirred at the same temperature for 20 min followed by the addition of 0.900 mL (4.50 mmol) of chloromethyldiphenylsilane in one portion. The reaction mixture was stirred at the same temperature for 2 h and then partitioned between ether (100 mL) and water (100 mL). The ether layer was washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo to give 2.20 g of a yellow liquid. The liquid was stirred with 1.43 g (18.0 mmol) of copper oxide and 1.21 g (9 mmol) of copper dichloride in refluxing acetone (16 mL) for 40 min. The resulting mixture was filtered, and the filtrate was partitioned between ether (100 mL) and water (100 mL). The ether layer was washed with brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo to give 1.50 g of a yellow liquid. The liquid was chromatographed over silica gel (eluted with ethyl acetate/hexane, 1/99) to give 780 mg (53%) of **4** as a yellow oil: IR (neat) 1630, 1616 cm^{-1}; ^1H NMR (300 MHz) δ 0.74 (s, 3H), 6.87 (d, J = 16.5 Hz, 1H), 7.19 (d, J = 16.5 Hz, 1H), 7.22-7.50 (m, 12H), 7.50-7.61 (m, 3H); ^{13}C NMR (50 MHz) δ -4.3, 128.3, 128.8, 130.1, 130.5, 131.7, 133.6, 134.7, 135.1, 144.5, 232.2; HRMS calcd for $C_{22}H_{20}OSi$ *m/z* 328.1284, found 328.1288.

1-(Methyldiphenylsilyl)-3-phenyl-4-penten-1-one (5)

To a mixture of 120 mg (0.914 mmol) of cuprous iodide in 1 mL of THF cooled at 0 °C was added 1.26 mL (1.26 mmol) of a 1 M THF solution of vinyl magnesium bromide, and the resulting mixture was cooled to -78 °C. A solution of 100 mg (0.420 mmol) of **4** in 1 mL of THF was added to the above mixture and stirred at the same temperature for 2.5 h. The reaction mixture was partitioned among 3 mL of saturated ammonium chloride solution, 25 mL of brine, and 25 mL of ether. The organic layer was dried ($MgSO_4$) and concentrated in vacuo to give 139 mg of a yellow oil. The oil was chromatographed over silica gel (eluted with ethyl acetate/hexane, 2/98) to give 71 mg (71%) of **5** as a yellow oil: IR (neat) 1635 cm^{-1}; ^1H NMR (200 MHz) δ 0.68 (s, 3H), 2.95-3.18 (m, 2H), 3.97 (q, J = 7.0 Hz, 1H), 4.75-4.98 (m, 2H), 5.85 (ddd, J = 17.1, 10.4, 7.0 Hz, 1H), 6.95-7.24 (m, 6H), 7.24-7.58 (m, 9H); ^{13}C NMR (50 MHz) δ -5.5, 42.7, 54.4, 114.3, 126.3, 127.6, 128.0, 128.2, 128.4, 129.5, 130.1, 132.4, 134.0, 135.0, 136.1, 140.7, 143.1, 242.5. Anal. Calcd for $C_{24}H_{24}OSi$: C, 80.85; H, 6.78. Found: C, 80.40; H, 6.93.

ACKNOWLEDGMENT

We thank the National Science Council of the Republic of China for financial support.

Received February 25, 1999.

Key Words

Conjugate addition; α,β-Unsaturated acylsilane.

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