

Conjugate Addition of α -(Trialkylstannyl)alkyl Groups to α,β -Enones: Preparation of γ -Stannyl Ketones

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Synopsis. The title reaction was examined under various conditions. The corresponding cuprates underwent 1,4-addition satisfactorily to afford γ -stannyl ketones.

As a continuation of our study on organotin compounds containing a cationic center within the same molecule,¹⁾ we intended to examine the chemistry of γ -stannyl ketones **3** under acidic conditions.²⁾ In view of the successful preparation of β -stannyl ketones by the conjugate addition of trialkylstannyl anions to α,β -enones,³⁾ we investigated the conjugate addition of α -(trialkylstannyl)alkyl groups **2** to α,β -enones **1**.

Unlike the case for the preparation of β -stannyl ketones, where the stannyl lithium compounds added to α,β -enones in a 1,4-fashion as smoothly as stannyl cuprates,⁴⁾ the reaction of (trimethylstannyl)methyl lithium **4**, prepared from bisstannyl compound **5**⁵⁾ did not give any clear-cut products with α,β -enones (Charts 1 and 2). After several attempts, we found that cuprates **6k** or **7k**,⁶⁾ prepared from **5** through successive treatment with *n*-BuLi or MeLi and CuCN, underwent 1,4-addition smoothly in the presence of BF₃-etherate.⁷⁾ The results with several enones are shown in Table 1. We designate **3ak**, as an example, for the product obtained from **1a** with **7k**. The use of **8**⁸⁾ with BF₃-etherate was also applicable (Run 2), although a small amount of 3-(2-thienyl)cyclohexanone (5%) involving the dummy ligand was identified.⁹⁾ Although the preparation of **6k** or **7k** from **5** was generally acceptable,

Table 1. Conjugate Addition of α -(Trialkylstannyl)alkyl Group to **1**

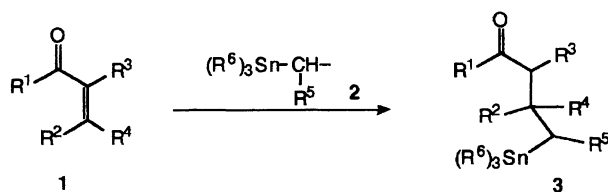
Run	Starting material	Reagent	Product	Yield %	D.r. ^{a)}
1	1a	7k	3ak	77	—
2	1a	8k	3ak	56 ^{b)}	—
3	1a	10m	3am	69	3 : 1
4	1a	10n	3an	66	1 : 0
5	1b	7k	3bk	68	—
6	1b	8k	3bk	47	—
7	1b	10n	3bn	40	1 : 0
8	1c	7k	3ck	70	1 : 0
9	1d	6k	3dk	64	1.4 : 1
10	1e	10l	3el	66	—
11	1e	8k	3ek	16	—
12	1e	10m	3em	85	1.2 : 1
13	1e	10n	3en	88	1 : 0
14	1f	7k	3fk	44	—

a) Diastereomer ratio. b) 3-(2-Thienyl)cyclohexanone was also identified (5%).

the method was not applicable for the preparation of **6l**—**6n**, mainly due to the low yields of the corresponding bisstannylalkanes **9**. The requirement of six moles of Grignard reagent for R⁶ and two tin atoms to prepare each mole of the reagent was also a drawback.

In our previous paper,¹⁰⁾ we reported that reagent **10n** was prepared from the corresponding iodide **11** by activating iodine with copper–zinc, followed by treating with CuCN. It was found that reagents **10l**—**10n**, prepared in the same way, added to α,β -enones smoothly in the presence of trimethylsilyl chloride.¹¹⁾ The results with several enones have been included in Table 1. As is obvious from comparison of Runs 2, 6, and 11, the yields from the same reagent **8k** were dependent upon the substrates. Although we have not made a systematic evaluation of each reagent, the reagents **10** afford reasonable results with the substrates used in the present study, as compared with other reagents.

The diastereomer ratios of the products can be determined from ¹³C NMR and/or GLC analyses. Although the stereochemistry of the products has not been elucidated, we tentatively assigned 3,5-*trans*- and 2,3-*trans*- structures for **3ck** and **3dk**, respectively, in view of the generally accepted reaction pattern of conjugate addition of stannyl lithium,¹²⁾ and the *erythro* configuration for the products obtained from **10m** and **10n**, in analogy with the structure assignment of **3an**, discussed in our previous paper.¹⁰⁾



	R ¹	R ²	R ³	R ⁴
a	—	-(CH ₂) ₃ -	H	H
b	—	-(CH ₂) ₃ -	H	Me
c	—	-CH ₂ CHMeCH ₂ -	H	Me
d	—	-(CH ₂) ₃ -	Me	H
e	—	-(CH ₂) ₂ -	H	H
f	Me	Me	H	Me

Chart 1.

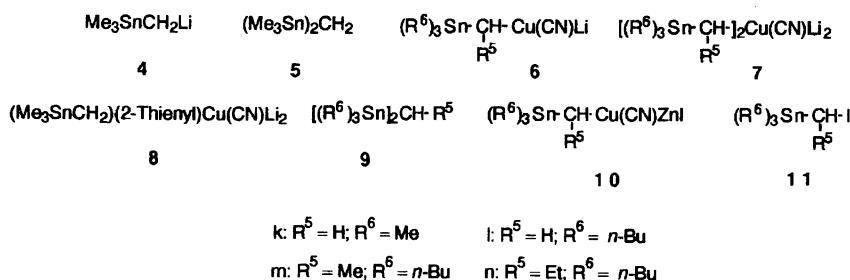


Chart 2.

Experimental

Unless otherwise stated, the mass spectra were obtained by the EI method at 70 eV, the ^1H NMR data on a 60 MHz or 90 MHz machine with CCl_4 solutions, ^{13}C NMR data on a 22.5 MHz machine with CDCl_3 solutions, using samples purified by column chromatography. The purity of the samples was checked by GLC equipped with a capillary column (SE 30) and/or ^{13}C NMR analyses.

Preparation of Tin Reagents: Trimethylstannyl-lithium **4**,⁵ bis(trimethylstannyl)methane **5**,⁵ (tributylstannyl)iodomethane **10l**,¹³ 1-(tributylstannyl)-1-iodoethane **10m**,¹⁰ and 1-(tributylstannyl)-1-propane **10n**¹⁰ were prepared according to the reported methods.

General Procedure for the Reactions Using **6k or **7k**:** To a suspension of CuCN (0.96 mmol) in ether (3 cm^3) was added a THF solution of **4**, prepared from bis(trimethylstannyl)methane **5** (0.94 mmol) and $n\text{-BuLi}$ or MeLi (0.94 mmol) at -78°C .⁵ A clear solution was obtained by raising the temperature to -40°C — -30°C , while stirring for 30 min. After lowering the temperature to -78°C again, BF_3 -etherate (0.96 mmol) and enones **1** (1.03 mmol) were added, and the solution was stirred for 20 min. The reaction was quenched by adding a solution of sat NH_4Cl -aq NH_3 (9:1) and extracted with ether. After evaporating the solvent, the residue was purified by silica-gel column chromatography (AcOEt /hexane). When $n\text{-BuLi}$ was used as a lithiation reagent, a few percent of the corresponding butyldimethylstannyl compounds also formed. Reagent **7k** was prepared in a similar way by using double amounts of **5** and MeLi .

3ak: IR (neat) 2923, 1713, and 1224 cm^{-1} ; MS m/z (rel intensity) 276 (M^+ , 5), 261 (53), 165 (100), and 135 (52); ^1H NMR $\delta=0.05$ (s, 9H), 0.85 (m, 2H), and 1.0—2.5 ppm (m, 9H). Found: m/z 276.0508. Calcd for $\text{C}_{10}\text{H}_{20}\text{OSn}$: M, 276.0536. Butyldimethylstannyl derivative: MS m/z 303 ($\text{M}^+ - \text{Me}$, 21), 261 ($\text{M}^+ - \text{Bu}$, 100), 207 (21), 151 (77), and 135 (58).

3bk: MS m/z 290 (M^+ , 5), 275 (44), 219 (18), 205 (33), 165 (100), and 135 (43); ^1H NMR $\delta=0.04$ (s, 9H), 0.93 (s, 5H), 2.07 (s, 2H), and 1.34—2.35 (m, 6H). Found: m/z 290.0729. Calcd for $\text{C}_{11}\text{H}_{22}\text{OSn}$: M, 290.0693. Butyldimethylstannyl derivative: MS m/z 317 ($\text{M}^+ - \text{Me}$, 21), 275 ($\text{M}^+ - \text{Bu}$, 100), 257 (30), 205 (55), 151 (85), and 135 (75).

3ck: ^1H NMR $\delta=0.03$ (s, 9H), 0.83 (s, 2H), 0.93 (d, $J=8\text{ Hz}$, 3H), 0.99 (s, 3H), and 1.1—2.4 (m, 7H); ^{13}C NMR $\delta=-8.39$, 22.19, 24.39, 29.50, 32.53, 38.92, 48.19, 49.06, 56.05, and 210.62.

3dk (diastereomer mixture): The product showed two peaks (ratio, 1.4:1) on GLC, which showed identical mass spectra. MS $m/z=290$ (M^+ , 7.5), 275 (100), 248 (50), 236

(43), 221 (38), and 165 (82); ^1H NMR $\delta=0.13$ (s, 9H), 1.2—1.8 (m, 2H), [$\{1.00$ (d, $J=7\text{ Hz}$), 1.05 (d, $J=7\text{ Hz}\}$], 3H], and 1.25—2.67 (m, 8H). Found: m/z 275.0477. Calcd for $\text{C}_{10}\text{H}_{19}\text{OSn}$: M—Me, 275.0458.

3fk: ^1H NMR $\delta=0.18$ (s, 9H), 1.12 (s, 6H), 1.13 (s, 2H), 2.10 (s, 3H), and 2.36 (s, 2H).

General Procedure for the Reactions Using **8k:** To a suspension of CuCN (3.08 mmol) in ether (6 cm^3) was added a solution of 2-thienyllithium⁸ (1.0 M, 3.1 cm^3) (1 M = 1 mol dm^{-3}), and the solution was stirred for 1 h at 0°C (Solution A). A solution of **4**, prepared from **5** (1.063 g, 3.11 mmol) and MeLi (1.05 M, 3.0 mmol) in another flask at -78°C was transferred into solution A at -78°C , and the mixture was stirred for 30 min at -50°C . The solution was cooled again to -78°C , and BF_3 -etherate (0.39 cm^3 , 3.1 mmol) and enones **1** (3.1 mmol) were added. After 30 min, the reaction was quenched in the same way as described above.

General Procedure for the Reactions Using **10l—**10n**:** To a suspension of Cu-Zn^{14} (105 mg, 1.5 mmol) in benzene (0.8 cm^3) and HMPA (0.27 cm^3 , 1.5 mmol) was added the corresponding iodide **11** (0.75 mmol), and the solution was stirred for 1.5 h at 60°C . After being cooled to room temperature, the solution was added to a suspension of CuCN (68.5 mg, 0.75 mmol) in THF (2 cm^3) at -20°C . The solution was stirred for 5 min at this temperature, and then for 30 min at 0°C . The solution was cooled again to -20°C , and a solution of enones **1** (0.5 mmol) and TMSCl (0.16 cm^3 , 1.2 mmol) in THF (1 cm^3) was added. The mixture was stirred for 2 h at 0°C and then overnight at room temperature. The reaction mixture was quenched with NH_4Cl aq and extracted with ether. The extract was washed with dil HCl and NaHCO_3 aq, and dried over MgSO_4 . The residue obtained by evaporation of the solvent was purified on a silica-gel column (hexane/ether).

3am (diastereomer mixture): ^1H NMR $\delta=0.85$ —1.2 (m) and 1.2—2.3 (m). ^{13}C NMR¹⁵ $\delta=[9.21, 9.30^*]$, 13.66, [14.98, 15.81 *], 25.52, 27.55, 29.33, [31.05, 32.53 *], [41.28, 41.37 *], [44.53, 44.94 *], [48.17 * , 48.64], and [211.48 * , 211.64], (3:1).

3an: ^1H NMR $\delta=0.85$ —1.1 (m), 1.1—1.9 (m), 1.9—2.4 (m); ^{13}C NMR $\delta=10.00$, 13.67, 14.45, 23.03, 25.62, 27.59, 29.37, 32.56, 37.30, 41.45, 41.90, 48.42, and 211.41. Found: m/z 430.2221. Calcd for $\text{C}_{21}\text{H}_{42}\text{OSn}$: M, 430.2239.

3bn: ^1H NMR $\delta=0.8$ —1.1 (m), 1.3—2.1 (m), and 2.1—2.4 (br); ^{13}C NMR $\delta=11.23$, 13.58, 16.04, 21.26, 22.15, 25.12, 27.55, 29.28, 38.26, 40.99, 42.91, 45.84, 53.66, and 211.55.

3el: ^1H NMR $\delta=0.6$ —1.0 (m, 16H), 1.0—1.5 (m, 16H), and 1.9—2.4 (m, 4H); ^{13}C NMR $\delta=9.35$, 13.65, 16.14, 27.39, 29.23, 33.90, 36.13, 39.11, 48.96, and 219.29. Ethylene ketal:

^1H NMR δ =0.85—1.1 (m, 16H), 1.1—1.75 (m, 16H), 1.75—2.1 (m, 4H), and 3.71 (s, 4H).

3em (diastereomer mixture): ^1H NMR δ =0.85—1.2 (m), 1.2—2.3 (m); ^{13}C NMR δ =9.02, 13.67, [16.15, 17.00*], [25.70, 26.29*], 27.55, 29.36, 29.80, 30.75*, [38.93, 39.11*], [43.12, 43.41*], [45.52*, 46.17], and 218.47. (1.2:1). Ethylene ketal (two peaks on GLC): ^1H NMR δ =0.85—1.2 (m), 1.2—2.3 (m), and 3.80 (s, 4H).

3en: MS m/z 359 ($\text{M}^+ - \text{Bu}$, 100), 291 (36), 235 (74), and 179 (77); ^{13}C NMR δ =9.75, 13.65, 14.11, 24.13, 27.57, 29.36, 30.95, 35.77, 39.11, 40.23, 45.59, and 218.85. Found: (CI) m/z 417.2168. Calcd for $\text{C}_{20}\text{H}_{41}\text{OSn}$: $\text{M} + \text{H}$, 417.2179.

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