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

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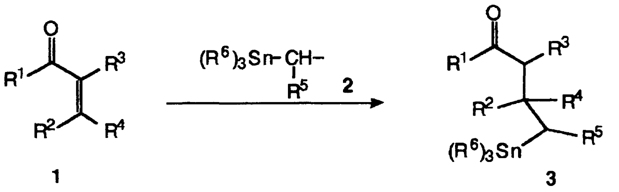
Synopsis. The title reaction was examined under various conditions. The corresponding cuprates underwent 1,4-addition satisfactorily to afford γ-stannyl ketones.

As a continuation of our study on organotin compounds containing a cationic center within the same molecule,[1] we intended to examine the chemisty 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 stannyllithium compounds added to α,β-enones in a 1,4-fashion as smoothly as stannylcuprates,[4] the reaction of (trimethylstannyl)methyllithium **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 BF$_3$-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 BF$_3$-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, 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 R^6 and two tin atoms to prepare each mole of the reagent was also a drawback.



	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.

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%).

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 ^{13}C 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 stannyllithium,[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]

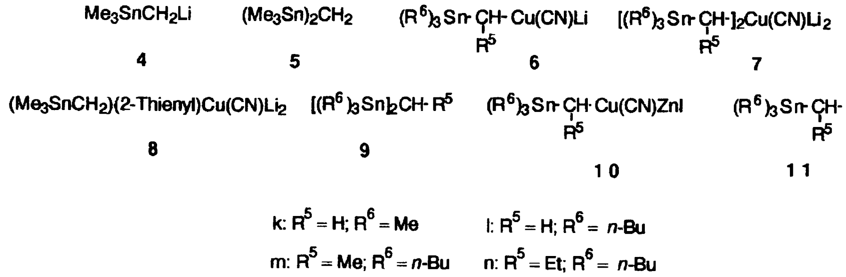


Chart 2.

Experimental

Unless otherwise stated, the mass spectra were obtained by the EI method at 70 eV, the ^{1}H 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: Trimethylstannyllithium **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*-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 chromatograpy (AcOEt/hexane). When *n*-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); ^{1}H NMR δ=0.05 (s, 9H), 0.85 (m, 2H), and 1.0—2.5 ppm (m, 9H). Found: *m/z* 276.0508. Calcd for $C_{10}H_{20}OSn$: M, 276.0536. Butyldimethylstannyl derivative: MS *m/z* 303 ($M^+ - Me$, 21), 261 (M^+ −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); ^{1}H NMR δ=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 $C_{11}H_{22}OSn$: M, 290.0693. Butyldimethylstannyl derivative: MS *m/z* 317 ($M^+ - Me$, 21), 275 ($M^+ - Bu$, 100), 257 (30), 205 (55), 151 (85), and 135 (75).

3ck: ^{1}H NMR δ=0.03 (s, 9H), 0.83 (s, 2H), 0.93 (d, *J*=8 Hz, 3H), 0.99 (s, 3H), and 1.1—2.4 (m, 7H); ^{13}C NMR δ=−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): ^{1}H NMR δ=0.13 (s, 9H), 1.2—1.8 (m, 2H), [{1.00 (d, *J*=7 Hz), 1.05 (d, *J*=7 Hz)}, 3H], and 1.25—2.67 (m, 8H). Found: *m/z* 275.0477. Calcd for $C_{10}H_{19}OSn$: M−Me, 275.0458.

3fk: ^{1}H NMR δ=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-thienyllithium[8] (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–Zu[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): ^{1}H NMR δ = 0.85—1.2 (m) and 1.2—2.3 (m). ^{13}C NMR[15] δ=[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: ^{1}H NMR δ=0.85—1.1 (m), 1.1—1.9 (m), 1.9—2.4 (m); ^{13}C NMR δ=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 $C_{21}H_{42}OSn$: M, 430.2239.

3bn: ^{1}H NMR δ=0.8—1.1 (m), 1.3—2.1 (m), and 2.1—2.4 (br); ^{13}C NMR δ=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: ^{1}H NMR δ=0.6—1.0 (m, 16H), 1.0—1.5 (m, 16H), and 1.9—2.4 (m, 4H); ^{13}C NMR δ=9.35, 13.65, 16.14, 27.39, 29.23, 33.90, 36.13, 39.11, 48.96, and 219.29. Ethylene ketal:

^{1}H 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): ^{1}H 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): ^{1}H NMR δ=0.85—1.2 (m), 1.2—2.3 (m), and 3.80 (s, 4H).

3en: MS m/z 359 ($M^+ - Bu$, 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 $C_{20}H_{41}OSn$: M+H, 417.2179.

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References

1) T. Sato, *Synthesis*, **1990**, 259.

2) Novel types of bond cleavages and 1,5-hydride shifts have been observed with the γ-stannyl ketones: T. Sato, K. Tachibana, A. Kawase, and T. Hirose, *Chem. Lett.*, **1993**, 937.

3) J. Fujiwara and T. Sato, *Bull. Chem. Soc. Jpn.*, **66**, 1258 (1993).

4) S. Sharma and A. C. Oehlschlager, *J. Org. Chem.*, **56**, 770 (1991), and references cited therein.

5) T. Sato, T. Kikuchi, H. Tsujita, A. Kaetsu, N. Sootome, K. Nishida, K. Tachibana, and E. Murayama, *Tetrahedron*, **47**, 3281 (1991).

6) As general references for cuprates, see: B. H. Lipshutz, R. S. Wilhelm, and J. A. Kozlowski, *Tetrahedron*, **40**, 5005 (1984); B. H. Lipshutz, *Synthesis*, **1987**, 325; B. H. Lipshutz, *Synlett*, **1990**, 119.

7) B. H. Lipshutz, D. A. Parker, J. A. Kozlowski, and S. L. Nguyen, *Tetrahedron Lett.*, **25**, 5959 (1984); B. H. Lipshutz, E. L. Ellsworth, and T. J. Siahaan, *J. Am. Chem. Soc.*, **110**, 4834 (1988); Y. Yamamoto, *Angew. Chem., Int. Ed. Engl.*, **25**, 947 (1986).

8) B. H. Lipshutz, J. Kozlowski, D. A. Parker, S. L. Nguyen, and K. E. McCarthy, *J. Organomet. Chem.*, **285**, 437 (1985).

9) L. Zhu, R. M. Wehmeyer, and R. D. Rieke, *J. Org. Chem.*, **56**, 1445 (1991).

10) T. Sato, A. Kawase, and T. Hirose, *Synlett*, **1992**, 891.

11) B. H. Lipshutz, E. L. Ellsworth, T. J. Siahaan, and A. Shirazi, *Tetrahedron Lett.*, **29**, 6677 (1988).

12) T. Sato, M. Watanabe, T. Watanabe, Y. Onoda, and E. Murayama, *J. Org. Chem.*, **53**, 1894 (1988).

13) D. E. Seitz, J. J. Carroll, C. P. Cartaya M., S. -H. Lee, and A. Zapata, *Synth. Commun.*, **13**, 129 (1983).

14) R. D. Smith and H. E. Simmons, "Org. Synth," ed by H. E. Baumgartens, John Wiley & Sons, N. Y. (1973), Coll Vol. 5, p. 855.

15) The figures in brackets are chemical shifts of the same carbon in a set of diastereomers, with the major signal marked with an asterisk. The figures in the parentheses refer to the average intensity ratios of the pair signals.