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Utilization of  $\text{Me}_3\text{SiSnBu}_3$  in organic synthesisI. Generation of a stannyl anion from  $\text{Me}_3\text{SiSnBu}_3$  and  $\text{R}_4\text{NX}$ Miwako Mori <sup>a</sup>, Naotake Kaneta <sup>a</sup>, Naohiro Isono <sup>a</sup> and Masakatsu Shibasaki <sup>b</sup><sup>a</sup> Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060 (Japan)<sup>b</sup> Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113 (Japan)

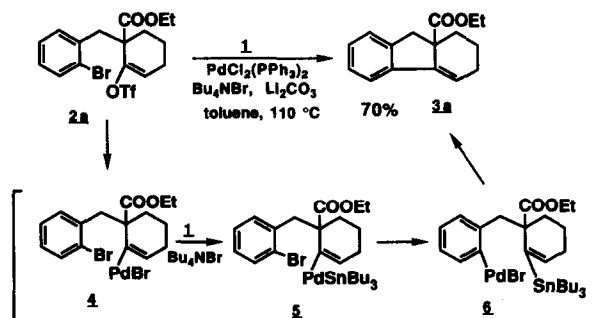
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## Abstract

A metal free stannyl anion generated from  $\text{Me}_3\text{SiSnBu}_3$  and  $\text{R}_4\text{NX}$  in DMF reacted with an aryl halide bearing carbonyl group to produce an aryl anion *via* the so-called halogen–metal exchange process, which reacted with a carbonyl group to afford a cyclized product in good yield.

## 1. Introduction

$\text{Me}_3\text{SiSnBu}_3$  (**1**), a bimetallic reagent that possesses a metal–metal bond, is quite interesting because each group plays an important role in synthetic organic chemistry. The reactivity of the Si–Sn bond of  $\text{Me}_3\text{SiSnBu}_3$  has been studied by several groups [1]. We have found that the stannyl group or the silyl group of  $\text{Me}_3\text{SiSnBu}_3$  can be transmetalated with an aryl palladium halide or vinyl palladium triflate [2]. Using these results, we developed a new palladium catalysed tandem transmetalation–cyclization reaction [2]. An aryl bromide, **2a**, having a vinyl triflate in a molecule was treated with  $\text{Me}_3\text{SiSnBu}_3$ ,  $\text{Bu}_4\text{NBr}$ ,  $\text{Li}_2\text{CO}_3$  and a catalytic amount of  $\text{PdCl}_2(\text{PPh}_3)_2$  in toluene at 110°C for 1.5 h to produce the cyclized product **3a** in 70% yield. The reaction should proceed through an intramolecular transmetalation followed by intermolecular transmetalation of the stannyl group to palladium(II) as shown in Scheme 1. The intermediary vinyl palladium bromide (**4**), which was produced by oxidative addition of vinyl triflate to palladium(0) followed by conversion of the triflate anion to bromide anion, was converted to vinylpalladium stannane (**5**) by transmetalation of the stannyl group of  $\text{Me}_3\text{SiSnBu}_3$  to

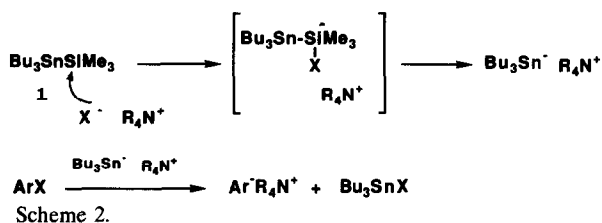


Scheme 1.

palladium. Reductive elimination of vinyl stannane from **5** was followed by oxidative addition of the aryl bromide to palladium(0) to produce compound **6**. The intramolecular transmetalation of the stannyl group of vinyl stannane to palladium(II) was then followed by reductive elimination to give the cyclized product **3a**.

During the course of this study, we found that a stannyl anion was generated from  $\text{Me}_3\text{SiSnBu}_3$  and  $\text{R}_4\text{NX}$ . The stannyl anion, which was a synthetically useful reagent, was usually prepared from  $\text{Bu}_3\text{SnH}$  and LDA or  $\text{Bu}_3\text{SnSnBu}_3$  and  $\text{RLi}$  [3]. Recently, Chenard reported that the reaction of  $\text{Me}_3\text{SiSnBu}_3$  with an  $\alpha,\beta$ -unsaturated ketone in the presence of a naked cyanide ion afforded a 1,4-addition product [1b]. We now want to report that a stannyl anion was formed

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from  $\text{Me}_3\text{SiSnBu}_3$  [4\*] and  $\text{R}_4\text{NX}$  in DMF (Scheme 2) and the stannyl anion generated,  $\text{Bu}_3\text{SnNR}_4$ , was treated with an aryl halide to produce an aryl anion [5].

## 2. Results and discussion

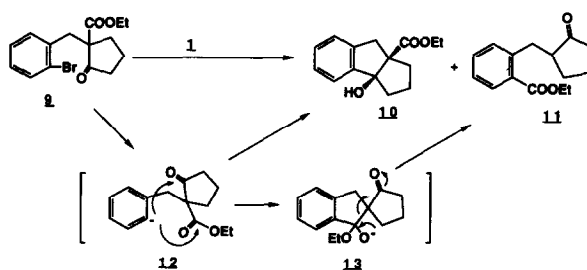
### 2.1. New reaction of an aryl halide with ester in the presence of $\text{Me}_3\text{SiSnBu}_3$ - $\text{R}_4\text{NX}$

When compound **2b** was treated with  $\text{Me}_3\text{SiSnBu}_3$  (1.1 equiv.),  $\text{Bu}_4\text{NBr}$  (3 equiv.), and  $\text{Li}_2\text{CO}_3$  (1.0 equiv.) in the presence of  $\text{PdCl}_2(\text{PPh}_3)_2$  (3 mol%) in toluene at  $110^\circ\text{C}$  for 1.5 h, only a small amount of the desired compound **3b** was obtained. The reaction was carried out in DMF instead of toluene as solvent and it was very surprising to find that another cyclized product **7** was obtained in 31% yield.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra indicated that the vinyl triflate skeleton remained unchanged and a new infrared absorption due to a keto-carbonyl group appeared instead of the disappearance of the ester-carbonyl group. When the product was treated with  $\text{HCOOH}$ - $^i\text{Pr}_2\text{NEt}$  in the presence of a catalytic amount of  $\text{Pd}(\text{OAc})_2$  and  $\text{PPh}_3$  [6] in DMF, the spiro-ketone **8** was obtained in 93% yield (Scheme 3). The structure of **8** was confirmed by  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and mass spectral data. The results indicate that the C-C bond was formed between the carbon of an aryl halide and the carbonyl carbon of the ester group. To reconfirm whether the C-C bond formation occurs between the aryl halide and the carbonyl carbon, compound **9** was treated in a

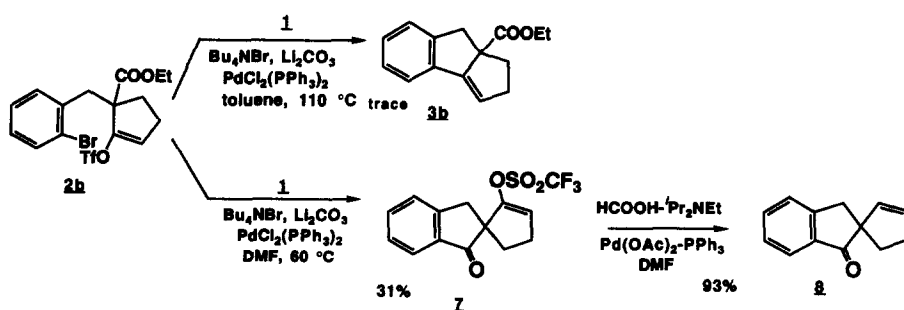
TABLE 1. Reaction of **9** with **1**

Run	$\text{Me}_3\text{SiSnBu}_3$ (equiv.)	$\text{PdCl}_2(\text{PPh}_3)_2$ (mol%)	$\text{PPh}_3$ (mol%)	Time (h)	<b>10</b> (%)	<b>11</b> (%)	<b>9</b> (%)
1	1.1	3	—	9	13	0	77
2	1.1	3	6	1	22	4	45
3	1.1	3	30	24	38	11	47
4	2.0	3	30	8	47	10	28
5	1.1	—	—	8	45	16	39
6	2.0	—	—	8	50	27	23

similar manner in DMF. The desired cyclized product was obtained but the yield was low (13% yield). (Table 1, run 1). The yield was improved when a large amount of  $\text{PPh}_3$  (30 mol%) was used in this reaction (Table 1, runs 2–4). In these cases, another product **11** was obtained. The IR spectrum of compound **11** shows the absorption of the five-membered keto-carbonyl ( $1738\text{ cm}^{-1}$ ) and the ester carbonyl ( $1716\text{ cm}^{-1}$ ). On the basis of the other spectral data, compound **11** can be obtained by the reaction of an aryl bromide with the ester carbonyl. The reaction should proceed by ring opening of the five-membered ring of compound **13** as shown in Scheme 4. It was very surprising that the reaction proceeded without using a palladium catalyst (runs 5 and 6). In the reaction of compound **2b** with  $\text{Me}_3\text{SiSnBu}_3$ , it was also confirmed that the reaction proceeded without using a palladium catalyst (Table 2, run 2) and none of the cyclized product was obtained without  $\text{Me}_3\text{SiSnBu}_3$  (run 3). These results suggest that



Scheme 4.



Scheme 3.

\* Reference number with asterisk indicates a note in the list of references.

TABLE 2. Reaction of **2b** with **1**

Run	Me <sub>3</sub> SiSnBu <sub>3</sub> (equiv.)	Solvent	Temperature (°C)	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> (mol%)	<b>7</b> (%)	<b>2b</b> (%)
1	1.1	DMF	60	3	31	—
2	—	DMF	60	3	—	95
3	1.1	DMF	60	—	38	34

an aryl anion is formed under these reaction conditions and it reacted with the keto- or ester-carbonyl group.

## 2.2. The halide effect of ammonium salt in the cyclization reaction

A stannyl anion plays an important role in the formation of an aryl anion from an aryl bromide. If a hypervalent silicate is formed by coordination of the bromide ion of Bu<sub>4</sub>NBr to the silyl group of Me<sub>3</sub>SiSnBu<sub>3</sub> and the stannyl anion is formed from the silicate, the halide effect of the ammonium salt should be observed because the silyl group is harder than the stannyl group, and the hardness is greater for the lighter member of a periodic family. Thus, the cyclization of **9** into **10** or **11** was carried out under constant conditions (at 60°C, for 1 h, in DMF) using various ammonium salts (Table 3, runs 1, 2 and 3). The chloride ion was most effective for this reaction (runs 1, 2 and 3) but the use of Bu<sub>4</sub>NF did not afford a good result in spite of the rapid disappearance of the starting material on TLC. The reaction proceeded even at room temperature (run 6) and Li<sub>2</sub>CO<sub>3</sub> was not required for this reaction (run 4). HMPA could be used as the solvent (run 7) and the use of a catalytic amount of R<sub>4</sub>NX did not give a good result (run 8). The fact that the harder chloride ion was more effective for this reaction indicates that the halide ion of the ammonium salt coordinates to the silyl group of Me<sub>3</sub>SiSnBu<sub>3</sub> to form the hypervalent silicate.

TABLE 3. Effect of ammonium salt halide anion on the cyclization reaction of **9**

Run	Bu <sub>4</sub> NX X =	Li <sub>2</sub> CO <sub>3</sub> (equiv.)	Solvent	Temperature (°C)	<b>10</b> (%)	<b>11</b> (%)	SM (%)
1	F	1	DMF	60	32	—	—
2	Cl	1	DMF	60	46	16	9
3	Br	1	DMF	60	20	6	37
4	Cl	—	DMF	60	52	12	—
5	None	—	DMF	60	—	—	85
6	Cl	—	DMF	20	53	19	—
7	Cl	—	HMPA	20	48	15	—
8	Cl <sup>a</sup>	—	DMF	20	4	13	60

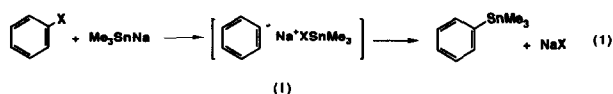
<sup>a</sup> Reaction was carried out in the presence of a catalytic amount (10 mol%) of Bu<sub>4</sub>NCl at room temperature for 72 h.

TABLE 4. Effect of aromatic halides in the cyclization reaction of **14**

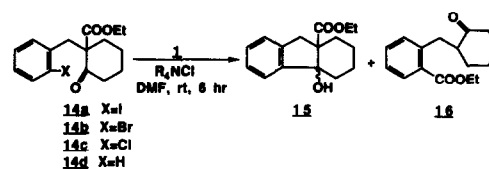
Run	ArX X =	R <sub>4</sub> NCl	Yields of products (%)			Recovery of SM (%)
			<b>15</b>	<b>16</b>	<b>14d</b>	
1	I	Bu <sub>4</sub> NCl	21	30	15	—
2	I	BnEt <sub>3</sub> NCl	30	33	19	2
3	Br	BnEt <sub>3</sub> NCl	32	18	17	24
4	Cl	BnEt <sub>3</sub> NCl	—	—	—	98

## 2.3. The effect of halogen variation of the aromatic ring

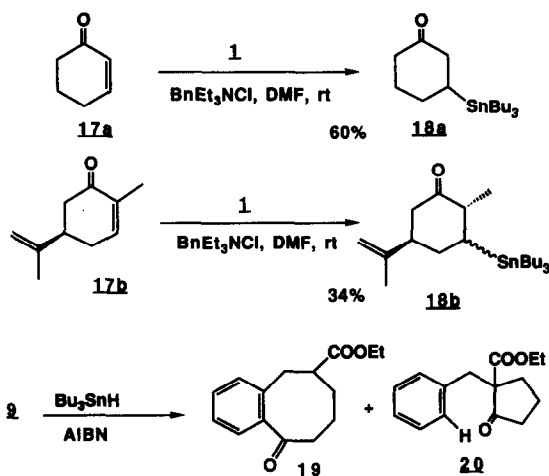
Kuivila *et al.* [7] reported that the reaction of an aryl halide with a stannyl anion proceeds *via* a halogen-metal exchange process to form complex **I** (eqn. (1)).



They estimated that the reaction between an aryl halide and an organostannyl sodium results in the formation of the caged species **I**, which reacts to form a substitution product, ArSnR<sub>3</sub> or diffuses from the cage as ArNa and R<sub>3</sub>SnX. Reaction of an aryl bromide bearing intramolecular traps such as a keto-carbonyl or hydroxy group with Me<sub>3</sub>SnNa supports the mechanism proposed. The order of reactivities of the aryl halides is ArI > ArBr > ArCl > ArF [7]. In our reaction, if the halide ion of an ammonium salt coordinates with the silyl group of Me<sub>3</sub>SiSnBu<sub>3</sub>, a stannyl anion is formed, which reacts with an aryl halide to form ArSnR<sub>3</sub> or Ar<sup>−</sup>NR<sub>4</sub><sup>+</sup>. In these processes, the effect of halogen variation of the aromatic ring is observed. Thus, the reaction of the various aryl halides **14** with stannyl anion generated from Me<sub>3</sub>SiSnBu<sub>3</sub> and R<sub>4</sub>NCl was examined (Table 4). As expected, the reaction of the aryl iodide **14a** with Me<sub>3</sub>SiSnBu<sub>3</sub> in the presence of R<sub>4</sub>NCl in DMF gave a good result and the starting material was recovered completely unchanged from the reaction of the aryl chloride **14c** with Me<sub>3</sub>SiSnBu<sub>3</sub> (run 4). The cationic part of the ammonium salt did not significantly affect this reaction (runs 1 and 2). These results suggest that the order of the reactivities of the aryl halide with the stannyl anion generated from Me<sub>3</sub>SiSnBu<sub>3</sub> and R<sub>4</sub>NCl was the same as that of ArX and the organostannyl sodium reported by Kuivila. Thus, the aryl anion (Ar<sup>−</sup>R<sub>4</sub>N<sup>+</sup>) is formed under



Scheme 5.



Scheme 6.

these reaction conditions and it attacks the carbon of the carbonyl group to produce the cyclized product. In these processes, the solvent (DMF or HMPA) plays an important role such as stabilization of the hypervalent silicate.

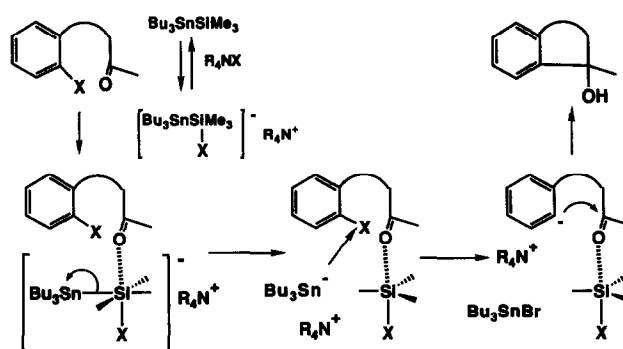
#### 2.4. Further evidence for the generation of stannyl anion

Generation of the stannyl anion from  $\text{Me}_3\text{SiSnBu}_3$  in the presence of  $\text{R}_4\text{NX}$  in DMF was also supported by the following results. Still [8] has already reported that the reaction of 2-cyclohexenone with  $\text{Me}_3\text{SnLi}$  in THF, which was prepared from  $\text{Me}_3\text{SnSnMe}_3$  and  $\text{MeLi}$  or  $\text{BuLi}$ , gave a 1,4-addition product, namely, 3-trialkylstannyl-cyclohexanone. When a DMF solution of 2-cyclohexenone (**17a**) and  $\text{Me}_3\text{SiSnBu}_3$  in the presence of  $\text{BnEt}_3\text{NCl}$  was stirred at room temperature for 6 h, 3-tributylstannylcyclohexanone (**18a**) was obtained in 63% yield. In a similar manner, carbone (**17b**) afforded 3-stannylated carbone (**18b**) in 34% yield.

Additionally, as previously mentioned, the reaction of compound **9** with  $\text{Me}_3\text{SiSnBu}_3$  and  $\text{Bu}_4\text{NBr}$  gave the cyclized product **10** (50%) along with **11** (27%). On the other hand, Beckwith has reported that compound **9** treated with  $\text{Bu}_3\text{SnH}$  in the presence of AIBN in benzene afforded compound **19** (14%) and the dehalogenation product **20** (75%) [9]. In the latter case, the reaction proceeded *via* a radical mechanism. These results suggest that the stannyl anion is generated from  $\text{Me}_3\text{SiSnBu}_3$  and  $\text{R}_4\text{NX}$  in DMF.

#### 2.5. A possible reaction mechanism

On the basis of these results, a possible reaction mechanism is shown in Scheme 7. The key step in the proposed mechanism is the generation of the stannyl anion. The coordination of  $\text{Cl}^-$  on silicon of  $\text{Me}_3\text{SiSnBu}_3$  in DMF affords the hypervalent silicate,



Scheme 7. A possible reaction course.

which is followed by the concerted attack of the carbonyl group on silicon [10] with the formation of the hypervalent silicate. This gives rise to generation of the metal free stannyl anion. The so-called halogen-metal exchange [11\*] of an aryl halide with the stannyl anion then provides an aryl anion [12], which attacks the carbonyl group activated by the silyl group. In this reaction, solvents such as DMF or HMPA must play an important role in the stabilization of the hypervalent silicate or of the stannyl anion.

The remarkable characteristics of this reaction are as follows. The hypervalent silicate was formed from  $\text{Me}_3\text{SiSnBu}_3$  even with the bromide ion in DMF, resulting in the generation of the metal free stannyl anion. The generated metal free stannyl anion reacted with an aryl halide to provide an aryl anion, which does not react with stannyl halide in the cage and it diffused from the cage to attack carbonyl groups such as aldehyde [13\*], ketone and even ester groups to give the cyclized products [7].

### 3. Experimental section

All manipulations were performed under an argon atmosphere using standard Schlenk techniques, and all the reaction solutions were degassed through a freeze-pump-thaw cycle. Solvents were distilled under an argon atmosphere from sodium benzophenone (THF,  $\text{Et}_2\text{O}$ , dioxane),  $\text{CaH}_2$  (HMPA, DMF,  $\text{Et}_3\text{N}$ ,  $t\text{-BuOH}$ ), Na (toluene), or  $\text{P}_2\text{O}_5$  ( $\text{CH}_2\text{Cl}_2$ ,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ ). All other reagents and solvents were purified when necessary using standard procedures. NMR spectra were recorded on a JEOL JNM-FX100 spectrometer. IR spectra were recorded on a JASCO A-300 spectrophotometer. Mass spectra were obtained from a JEOL JMS-DX303 or JEOL JMS-HX110. Melting points were determined by Yanagimoto Special No. 815 or Ishii Melting point apparatus and were not corrected.  $\text{Me}_3\text{SiSnBu}_3$  was prepared by the method reported [1,3a]. Ethyl 1-(2-bromobenzyl)-2-oxocyclopentane-1-

carboxylate (**9**) [9] and ethyl 1-(halobenzyl)-2-oxocyclohexane-1-carboxylate (**14a–c**) [2] were prepared according to the literature methods.

### 3.1. 5-(2-Bromobenzyl)-5-ethoxycarbonylcyclopent-1-en-1-yl triflate (**2b**)

To a dichloroethane (20 ml) solution of **9** (1.27 g, 3.92 mmol) and 2,6-di-*t*-butyl-4-methylpyridine (1.75 g, 7.73 mmol) was slowly added Tf<sub>2</sub>O at 0°C. The solution was warmed to 80°C for 9 h. After the mixture was cooled, Et<sub>2</sub>O was added, and the white precipitate was collected by filtration. The filtrate was concentrated and the residue was purified by chromatography on silica gel (hexane/EtOAc, 10:1) to give **2b** (1.74 g, 97%). IR (neat) 1740, 1655, 1595, 1425, 1210 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.28 (t, *J* = 7.3 Hz, 3H); 1.8–2.5 (m, 4H); 4.16 and 4.60 (ABq, *J* = 14 Hz, 2H); 4.22 (q, *J* = 7.3 Hz, 2H); 6.72 (brd, 1H); 7.0–7.2 (m, 3H); 7.5–7.6 (m, 1H). MS: *m/z* 459, 457 (M<sup>+</sup> + 1), 385, 383 (M<sup>+</sup> – COOEt), 377 (M<sup>+</sup> – Br), 279, 277, 171, 169 (bp). HR-MS calcd. for C<sub>16</sub>H<sub>17</sub>BrF<sub>3</sub>O<sub>5</sub>S (M<sup>+</sup> + 1): 456.9933. Found: 456.9922.

### 3.2. Cyclization of aryl halide (**2b**)

To a solution of the triflate **2b** (108 mg, 0.237 mmol), Bu<sub>4</sub>NBr (230 mg, 0.714 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (5.1 mg, 3 mol %), and Li<sub>2</sub>CO<sub>3</sub> (19 mg, 0.26 mmol) in DMF (2 ml) was added Bu<sub>3</sub>SnSiMe<sub>3</sub> (95 mg, 0.26 mmol) and the solution was warmed to 60°C under argon for 2 h. After cooling the reaction mixture, ethyl acetate and 10% aq. HCl solution were added. The aqueous layer was extracted with EtOAc and the organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc, 10:1) to afford the ketone **7** (24 mg, 31%). IR (neat): 1720, 1655, 1610, 1420, 1215 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.9–2.2 (m, 1H); 2.3–2.8 (m, 3H); 3.12 and 3.52 (ABq, *J* = 16 Hz, 2H); 5.98 (m, 1H); 7.2–7.8 (m, 4H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 26.7, 35.2, 38.1, 60.1, 118.8, 120.7, 124.7, 126.4, 128.0, 135.0, 135.6, 148.6, 152.2, 205.0. MS: *m/z* 333 (M<sup>+</sup> + 1), 269, 199 (bp), 181, 171, 153, 128, 115, 105, 91. FD-MS 332.

### 3.3. Reaction of vinyl triflate **7** with HCOOH and Pd(OAc)<sub>2</sub>

A solution of vinyl triflate **7** (25 mg, 0.074 mmol), HCOOH (7 μl, 0.16 mmol), <sup>1</sup>Pr<sub>2</sub>NEt (40 μl, 0.23 mmol), Pd(OAc)<sub>2</sub> (0.6 mg, 0.0027 mmol) and PPh<sub>3</sub> (1.5 mg, 0.0057 mmol) in DMF (200 μl) was heated to 60°C under argon for 5 min. Water was added and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by preparative

thin layer chromatography on silica gel (hexane/EtOAc, 4:1) to afford the detriflated product **8** (13 mg, 93%). IR (neat): 1715, 1605 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.6–2.1 (m, 1H); 2.25–2.8 (m, 3H); 3.19 (s, 2H); 5.5 (m, 1H); 6.0 (m, 1H); 7.2–7.8 (m, 4H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 32.7, 36.1, 41.5, 63.1, 124.4, 126.4, 127.5, 133.5, 134.4, 134.8, 136.0, 152.9, 209.7. MS: *m/z* 184 (M<sup>+</sup>, bp), 169, 155, 141, 128, 115, 102, 91.

### 3.4. Cyclization of ethyl 1-(2-bromobenzyl)-2-oxocyclopentane-1-carboxylate (**9**)

To a solution of **9** (50 mg, 0.16 mmol) and Bu<sub>4</sub>NCl (130 mg, 0.467 mmol) in DMF (1 ml) was added Bu<sub>3</sub>SnSiMe<sub>3</sub> (114 mg, 0.315 mmol); the mixture was stirred at room temperature under argon for 1 h. Then 10% NH<sub>4</sub>OH solution was added and the mixture was stirred for 30 min. The whole mixture was extracted with EtOAc. The organic layer was washed with 10% HCl, brine, saturated NaHCO<sub>3</sub> and brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by preparative thin layer chromatography on silica gel (hexane/EtOAc, 5:1) to afford **10** (20 mg, 53%), **11** (7.2 mg, 19%) and debrominated product (1 mg, 2%).

**10**: IR (neat): 3500, 1715, 1610, 1598 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz): δ 1.28 (t, *J* = 7.0 Hz, 3H); 1.2–1.4 (m, 1H); 1.7–1.9 (m, 2H); 2.1–2.4 (m, 2H); 2.45–2.65 (m, 1H); 2.85 and 3.72 (ABq, *J* = 17 Hz, 2H); 2.93 (s, 1H); 4.21 (q, *J* = 7.0 Hz, 2H); 7.1–7.4 (m, 4H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.3, 23.2, 37.9, 41.3, 42.6, 60.9, 61.6, 94.7, 123.9, 124.5, 127.6, 128.8, 141.5, 145.9, 175.8. MS: *m/z* 246 (M<sup>+</sup>), 228 (M<sup>+</sup> – H<sub>2</sub>O), 172, 155 (bp), 145, 128, 115. HR-MS calcd. for C<sub>15</sub>H<sub>16</sub>O<sub>2</sub> (M<sup>+</sup> – H<sub>2</sub>O): 228.1150. Found: 228.1139.

**11**: IR (neat): 1738, 1716, 1601 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz): δ 1.39 (t, *J* = 7.0 Hz, 3H); 1.5–1.8 (m, 2H); 1.9–2.1 (m, 2H); 2.12 (ddd, *J* = 18.3, 10.0, ~0 Hz, 1H); 2.35 (ddd, *J* = 18.3, 9.5, ~0 Hz, 1H); 2.4–2.6 (m, 1H); 2.77 (dd, *J* = 13.2, 9.5 Hz, 1H); 3.59 (dd, *J* = 13.2, 4.4 Hz, 1H); 4.36 (q, *J* = 7.0 Hz, 2H); 7.2–7.3 (m, 2H); 7.41 (dd, *J* = 7.5, 2.0 Hz, 1H); 7.89 (dd, *J* = 7.0, 1.5 Hz, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.3, 20.5, 29.3, 33.8, 38.0, 50.9, 61.0, 126.3, 130.4, 130.7, 131.5, 131.7, 141.7, 167.7, 219.6. MS: *m/z* 246 (M<sup>+</sup>), 200 (M<sup>+</sup> – OEt), 172, 145 (bp), 135, 115, 91, 83, 77. HR-MS calcd. for C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>: 246.1313. Found: 246.1284.

### 3.5. 3-Tributylstannylcyclohexanone (**18a**)

To a solution of 2-cyclohexen-1-one (50 mg, 0.52 mmol) and BnEt<sub>3</sub>NCl (287 mg, 1.04 mmol) in DMF (1 ml) was added Bu<sub>3</sub>SnSiMe<sub>3</sub> (374 mg, 1.03 mmol) and the solution was stirred at room temperature under argon for 6 h. A 10% NH<sub>4</sub>OH solution was added and the mixture was stirred for 1 h. The whole mixture was extracted with ether. The organic layer was washed

with brine, 10% HCl and brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by chromatography on silica gel (hexane then hexane/EtOAc, 20:1) to afford **18a** (120 mg, 60%). IR (neat): 1710 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.7–1.0 (m, 15H); 1.0–2.5 (m, 21H). MS: *m/z* 383, 385, 387 (M<sup>+</sup>), 327, 329, 331 (M<sup>+</sup> – Bu), 287, 289, 291 (SnBu<sub>3</sub>), 97. HR-MS calcd. for C<sub>18</sub>H<sub>36</sub>OSn: 388.1789. Found: 388.1786.

### 3.6. 5-Isopropenyl-2-methyl-3-tributylstannylcyclohexanone (**18b**)

To a solution of (–)-carvone (24 mg, 0.16 mmol) and BnEt<sub>3</sub>NCl (73 mg, 0.32 mmol) in DMF was added Bu<sub>3</sub>SnSiMe<sub>3</sub> (114 mg, 0.315 mmol) and the solution was stirred at room temperature under argon for 6 h. A 10% NH<sub>4</sub>OH solution was added and the mixture was stirred for 1 h. The whole mixture was extracted with ether. The organic layer was washed with brine, 10% HCl and brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by chromatography on silica gel (hexane then hexane/EtOAc = 20:1 then hexane/EtOAc, 10:1) to afford **18b** (26 mg, 37%) and to recover carvone (7.9 mg, 33%). IR (neat): 1720, 1645 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.70–0.98 (m, 15H); 1.06 (d, *J* = 6.4 Hz, 3H); 1.15–1.64 (m, 12H); 1.75 (brs, 3H); 2.02–2.56 (m, 6H); 2.64–2.92 (m, 1H); 4.73 (brs, 1H); 4.77 (q, *J* = 1.4 Hz, 1H). MS: *m/z* 442 (M<sup>+</sup>), 385 (M<sup>+</sup> – Bu, bp). HR-MS calcd. for C<sub>22</sub>H<sub>42</sub>OSn: 442.2258. Found: 442.2249.

### 3.7. Cyclization of ethyl 1-(2-iodobenzyl)-2-oxocyclohexane-1-carboxylate (**14a**)

To a solution of **14a** (61 mg, 0.16 mmol) and BnEt<sub>3</sub>NCl (73 mg, 0.32 mmol) in DMF (1 ml) was added Bu<sub>3</sub>SnSiMe<sub>3</sub> (114 mg, 0.315 mmol) and the solution was stirred at room temperature under argon for 6 h. Then a 10% NH<sub>4</sub>OH solution was added and the mixture was stirred for 30 min. The whole mixture was extracted with EtOAc. The organic layer was washed with 10% HCl, brine, saturated NaHCO<sub>3</sub> and brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by chromatography on silica gel (hexane/EtOAc, 20:1 then 10:1 then 5:1) to afford **15** (12 mg, 30%), **16** (14 mg, 33%) and de-iodinated product (7.6 mg, 19%).

**15**: IR (neat): 3455, 1720, 1605 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.25 (t, *J* = 7.1 Hz, 3H); 1.44–2.36 (m, 8H); 2.73 and 3.54 (ABq, *J* = 15.6 Hz, 2H); 4.24 (q, *J* = 7.1 Hz, 2H); 7.18–7.40 (m, 4H). MS: *m/z* 260 (M<sup>+</sup>), 242

(M<sup>+</sup> – H<sub>2</sub>O), 215 (M<sup>+</sup> – OEt), 186 (M<sup>+</sup> – COOEt + 1), 169 (M<sup>+</sup> – COOEt – H<sub>2</sub>O, bp). HR-MS calcd. for C<sub>16</sub>H<sub>20</sub>O<sub>3</sub>: 260.1413. Found: 260.1392.

**16**: IR (neat): 1720, 1710, 1600 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.37 (t, *J* = 7.1 Hz, 3H); 1.40–1.88 (m, 6H); 1.92–2.18 (m, 2H); 2.24–2.44 (m, 1H); 2.65 (dd, *J* = 16.4, 7.3 Hz, 1H); 3.58 (dd, *J* = 16.4, 8.3 Hz, 1H); 4.34 (q, *J* = 7.1 Hz, 2H); 7.18–7.50 (m, 3H); 7.84–7.96 (m, 1H). MS: *m/z* 260 (M<sup>+</sup>), 214 (M<sup>+</sup> – OEt + 1), 186 (M<sup>+</sup> – COOEt, bp). HR-MS calcd. for C<sub>16</sub>H<sub>20</sub>O<sub>3</sub>: 260.1412. Found: 260.1400.

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