10356 J. Am. Chem. Soc. 1993, 115, 10356–10357

Communications to the Editor

Highly Chemoselective Allylation of Carbonyl Compounds with Tetraallyltin in Acidic Aqueous Media

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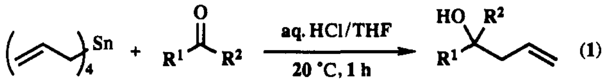
Received May 5, 1993

The addition of an allylmetal reagent to carbonyl compounds is a useful process in organic synthesis.[1] However, this highly reactive reagent sometimes causes lack of chemoselectivity. For example, not only Grignard and lithium reagents[2,3] but also titanium reagent[4] often fail to discriminate between aldehydes and ketones. Herein, we disclose a new allylation reaction of carbonyl compounds by tetraallyltin *in acidic aqueous media* which shows exclusive chemoselectivity toward aldehydes.

Reaction of 4 equiv of carbonyl compounds **2** with tetraallyltin (**1**, 1 equiv) in a 1:8 mixture of 2 N HCl (1 equiv) and THF at 20 °C exclusively afforded the corresponding homoallyl alcohol **3** (eq 1). Selected results with various carbonyl compounds are shown in Table I.[5] Several characteristic features of the reaction have been noted: (1) Reaction of aldehydes **2a**–**2d** resulted in quantitative yields (entries 1–4). Pivalaldehyde (**2e**) reacted relatively slowly, very likely for a steric reason (entry 5). (2) Ketones were inert under the standard reaction conditions except for cyclohexanone (**2i**), which showed a relatively high reactivity (entries 6–10). Heating was effective to accelerate the reaction of ketone (entry 6). (3) No reaction occurred with ester **2k** or acid chloride **2l** (entries 11 and 12). (4) In the reaction with α,β-unsaturated aldehyde **2c**, the 1,2-addition reaction proceeded preferentially (entry 3). (5) Noteworthy are the facts that tetraallyltin (**1**) decomposed relatively slowly in acidic aqueous media[6,7] and that four of the allyl groups on tin metal reacted with carbonyl compounds in the presence of 1 equiv of hydrochloric acid.[8,10] (6) None of the organic tin compound was produced, and thus the workup of the reaction proceeded quite smoothly.



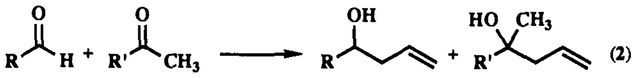
1 **2** **3**

Table I. Allylation of Various Carbonyl Compounds **2** with Tetraallyltin (**1**)[a]

entry	carbonyl compound	R^1	R^2	product	yield, %[b]
1	**2a**	$^nC_7H_{15}$	H	**3a**	>99
2	**2b**	Ph	H	**3b**	88
3	**2c**	(*E*)-PhCH=CH	H	**3c**	87
4	**2d**	$^cC_6H_{11}$	H	**3d**	84
5	**2e**	^{t}Bu	H	**3e**	48 (81)[c]
6	**2f**	$^nC_5H_{11}$	CH_3	**3f**	1 (33)[d]
7	**2g**	Ph	CH_3	**3g**	<1
8	**2h**	$-(CH_2)_4-$		**3h**	<1
9	**2i**	$-(CH_2)_5-$		**3i**	55
10	**2j**	$-CH=CH(CH_2)_3-$		**3j**	<1
11	**2k**	Ph	OCH_3	**3k**	<1
12	**2l**	Ph	Cl	**3l**	<1[e]

[a] The reaction was carried out using tetraallyltin (**1**, 1 equiv) and a carbonyl compound (**2**, 4 equiv) in a 1:8 mixture of 2 N HCl (1 equiv) and THF at 20 °C for 1 h. [b] Isolated yield based on the amount of **2**. [c] The reaction was carried out using 2 equiv of pivalaldehyde at 20 °C for 5 h. [d] Performed at 80 °C for 4 h. [e] After the reaction, unreacted benzoyl chloride (**2l**) was recovered as ethyl benzoate in 29% yield by esterification ($EtOH/Et_3N$).

The above results suggested a possibility of chemoselective addition of tetraallyltin to aldehydes in the presence of ketones. Indeed, in a competitive reaction of benzaldehyde (**2b**, 4 equiv) and acetophenone (**2g**, 4 equiv) with tetraallyltin (**1**, 1 equiv), only the aldehyde adduct **3b** was obtained with 99.98% selectivity[11] (eq 2). No chemoselectivities were observed for allyl Grignard reagent or allyllithium. Allyltitanium reagent was reported to show a moderate chemoselectivity (**3b**:**3g** = 84:16).[4] Using



R = Ph (**2b**); R' = Ph (**2g**):	**3b** : **3g**
$H_2C=CHCH_2MgBr$	46 : 54
$H_2C=CHCH_2Li$	51 : 49
$H_2C=CHCH_2Ti(O^iPr)_3$	84 : 16[4]
$H_2C=CHCH_2Ti(O^iPr)_4MgCl$ (4)	98 : 2[12a]
	32 : 68 (**2b**/**2g**=1/10)
$(H_2C=CHCH_2)_4Sn/HCl$	>99.98 : <0.02
	99.4 : 0.6 (**2b**/**2g**=1/10)
R = $^nC_7H_{15}$ (2a); R' = $^nC_5H_{11}$ (2f):	**3a** : **3f**
$H_2C=CHCH_2SnBu_3/BF_3\cdot OEt_2$	80 : 20
$(H_2C=CHCH_2)_4Sn/HCl$	>99 : <1

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[1] Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1.

[2] (a) Nützel, K. In *Houben-Weyl*: *Methoden der Organischen Chemie*; Müller, E., Eds.; Thieme Verlag: Stuttgart, 1973; Vol. 13/2a, p 47. (b) Schöllkopf, U. In *Houben-Weyl*: *Methoden der Organischen Chemie*; Müller, E., Eds.; Thieme Verlag: Stuttgart, 1970; Vol. 13/1, p 87.

[3] A recent excellent solution to this problem: Reetz, M. T.; Harmat, N.; Mahrwald, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 342.

[4] Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer-Verlag: Berlin, 1986; p 80.

[5] General experimental procedure: to a solution of tetrallyltin (**1**, 283 mg, 1 mmol) and carbonyl compounds **2** (4 mmol) in THF (4 mL) was added at 20 °C an aqueous HCl solution (2 N, 0.5 mL, 1 mmol). The mixture was stirred for 1 h at this temperature. A saturated $NaHCO_3$ aqueous solution (10 mL) was added to the mixture, and the aqueous layer was extracted with ether (10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (hexane–ethyl acetate) to afford the homoallyl alcohol **3**.

[6] Allylation of carbonyl compounds in aqueous media has been restricted to a Barbier-type reaction: (a) Nokami, J.; Otera, J.; Sudo, T.; Okawara, R. *Organometallics* **1983**, *2*, 191. (b) Nokami, J.; Wakabayashi, S.; Okawara, R. *Chem. Lett.* **1984**, 869. (c) Uneyama, K.; Matsuda, H.; Torii, S. *Tetrahedron Lett.* **1984**, *25*, 6017. (d) Uneyama, K.; Kamaki, N.; Moriya, A.; Torii, S. *J. Org. Chem.* **1985**, *50*, 5396. (e) Pétrier, C.; Luche, J.-L. *J. Org. Chem.* **1985**, *50*, 910. (f) Petrier, C.; Einhorn, J.; Luche, J.-L. *Tetrahedron Lett.* **1985**, *26*, 1449. (g) Wada, M.; Ohki, H.; Akiba, K. *J. Chem. Soc., Chem. Commun.* **1987**, 708. (h) Minato, M.; Tsuji, J. *Chem. Lett.* **1988**, 2049. (i) Wilson, S. R.; Guazzaroni, M. E. *J. Org. Chem.* **1989**, *54*, 3087. (j) Waldmann, H. *Synlett* **1990**, 627. (k) Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017. (l) Oda, Y.; Matsuo, S.; Saito, K. *Tetrahedron Lett.* **1992**, *33*, 97. (m) Kanagawa, Y.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1992**, *57*, 6988.

[7] Tetraallyltin exists stably in a neutral or basic aqueous solution. The ratio of H_2O to THF is voluntary. For example, in a 1:1 mixture of H_2O and THF, the reaction proceeds equally well.

[8] Allyltributyltin, which is commonly used for Lewis acid-promoted carbonyl allylation,[9] does not react at all in the presence of HCl. On the other hand, intramolecular allylstannane–aldehyde condensation reactions were successfully accomplished by Brønsted acids: (a) Denmark, S. E.; Weber, E. J.; Wilson, T. M.; Willson, T. M. *Tetrahedron* **1989**, *45*, 1053. (b) Gevorgyan, V.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 1313.

[9] Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; p 216.

[10] One equivalent of HCl was requisite to obtain nearly quantitative yields. Yields of the alcohol **3b** obtained by the reaction of benzaldehyde (**2b**) with tetraallyltin (**1**) in the presence of catalytic amount of HCl were, for 0.1 equiv, 12%; for 0.5 equiv, 57%.

[11] The **3b**/**3g** ratio was determined by GC analysis.

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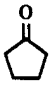
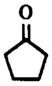
Table II. Chemoselective Carbonyl Allylation of Aldehydes with Tetraallyltin[a]

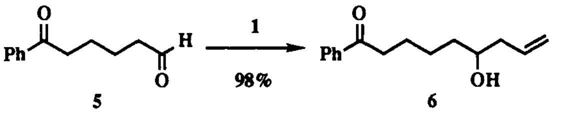
Entry	Carbonyl compounds			Yield, %[b]	Ratio[c]
1	$^{n}C_7H_{15}CHO$	+	$^{n}C_5H_{11}COCH_3$	98	>99 : <1
2	$^{n}C_7H_{15}CHO$	+	$PhCOCH_3$	98	>99 : <1
3	PhCHO	+	$^{n}C_5H_{11}COCH_3$	94	>99 : <1
4	$^{c}C_6H_{11}CHO$	+	$^{n}C_5H_{11}COCH_3$	>99[d]	>99 : <1
5	$^{t}BuCHO$	+	$^{n}C_5H_{11}COCH_3$	46	>99 : <1
6	$^{n}C_7H_{15}CHO$	+		85	>99 : <1
7	$^{n}C_7H_{15}CHO$	+		99	>99 : <1
8		+		80[e]	99 : 1
9	(*E*)-PhCH=CHCHO	+	$PhCOCH_3$	95	>99 : <1
10	PhCHO	+		87	>99 : <1
11	$^{c}C_6H_{11}CHO$	+	$PhCO_2CH_3$	94	>99 : <1
12	PhCHO	+	PhCOCl	96[f]	>99 : <1

[a] The reaction was carried out using tetraallyltin (**1**, 1 equiv) and two carbonyl compounds (4 equiv, respectively) in a 1:8 mixture of 2 N HCl (1 equiv) and THF at 20 °C for 1 h. [b] Combined isolated yields of the allylation products. [c] Determined by ^1H NMR or GLC analysis. [d] Two equivalents each of two carbonyl compounds were used. [e] The reaction was carried out at 20 °C for 5 h. [f] The reaction was carried out at 20 °C for 5 min, and unreacted benzoyl chloride was recovered as ethyl benzoate in 42% yield by esterification ($EtOH/Et_3N$).

allyltitanium ate complex **4**, however, 98% aldehyde selectivity was achieved.[12] In the reaction of octanal (**2a**, 1 equiv) and 2-heptanone (**2f**, 1 equiv) with allyltributyltin (1 equiv) in the presence of $BF_3{\cdot}OEt_2$, a lower aldehyde selectivity (80:20) was observed.[13] In sharp contrast, exclusive aldehyde selectivity (>99:1) was obtained for tetraallyltin. Even in the presence of a large excess (10 equiv) of acetophenone (**2g**), tetraallytin (**1**) reacted nearly exclusively (**3b**:**3g** = 99.4:0.6) with benzaldehyde (**2b**), whereas allyltitanium ate complex **4** afforded the ketone adduct **3g** as the major product (**3b**:**3g** = 32:68).[14]

Table II summarizes the general aspects of the new chemoselective allylation process; exclusive formation of aldehyde adduct was observed in all experiments. It was surprising that tetraallyltin reacted exclusively with aldehyde in the presence of acid chloride (entry 12). Furthermore, even ketone/ketone discrimination is possible. For example, a higher selectivity (99:1, entry 8) was observed for the competitive reaction of cyclohexanone and cyclopentanone than for the reaction with the allyltitanium ate complex **4** (88:12).[15]

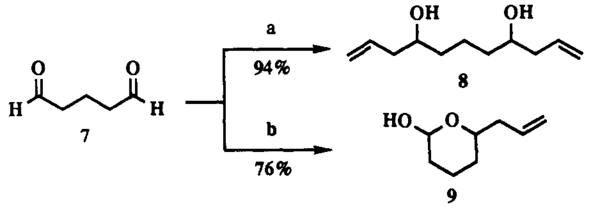
Intramolecular discrimination of carbonyl groups is also possible with tetraallyltin under acidic media. Thus, reaction of keto aldehyde **5**[16] with tetraallyltin (**1**) resulted in complete chemoselectivity (>99%) toward aldehyde (eq 3).



(3)

Water-soluble aldehyde was used without any difficulty. Thus, treatment of an aqueous solution of glutaraldehyde (**7**) with 1 equiv of tetraallyltin in the presence of excess acid afforded the diallylated product **8** in 94% yield. Monoallylated cyclic hemiacetal **9** was selectively obtained by dilution method using 0.25 equiv of tetraallyltin (Scheme I).

Scheme I[a]



[a] (a) Tetraallyltin (**1**, 1 equiv), 2 N HCl (10 equiv)/THF (1:8), 20 °C, 1 h; (b) Tetraallyltin (**1**, 0.25 equiv), 2 N HCl (1 equiv)/THF (1:16), 20 °C, 3 h.

Acknowledgment. Financial support from the Ministry of Education, Science and Culture of the Japanese Government is gratefully acknowledged.

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[12] (a) Reetz, M. T.; Wenderoth, B. *Tetrahedron Lett.* **1982**, *23*, 5259. We reexamined the competitive reaction of benzaldehyde (**2b**, 1 equiv) and acetophenone (**2g**, 1 equiv) using allyltitanium ate complex **4** to result in lower chemoselectivities (**3b**:**3g** = 74:26 ~ 72:28). Aldehyde selective allylation reactions were also achieved using Cr(II)/allyl bromide: (b) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179.

[13] Similar aldehyde selectivity (70:30) was reported: Naruta, Y.; Ushida, S.; Maruyama, K. *Chem. Lett.* **1979**, 919.

[14] The **3b**/**3g** ratio of the products obtained by the reaction of a 1:10 mixture of benzaldehyde (**2b**) and acetophenone (**2g**) with allyl bromide/$CrCl_2$ was 93:7.[12b]

[15] Reetz, M. T.; Westermann, J.; Steinbach, R.; Wenderoth, B.; Peter, R.; Ostarek, R.; Maus, S. *Chem. Ber.* **1985**, *118*, 1421.

[16] Antonioletti, R.; D'Auria, M.; Mico, A. D.; Piancatelli, G.; Scettri, A. *Synthesis* **1983**, 890.