Palladium Catalysed Addition of 1-Carboranyltributyltin to Aldehydes

Hiroyuki Nakamura, Naoki Sadayori, Masaru Sekido and Yoshinori Yamamoto*

Department of Chemistry, Faculty of Sciences, Tohoku University, Sendai 980-77, Japan

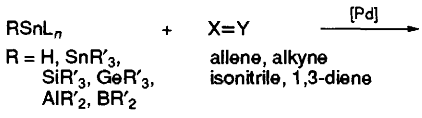
The addition of *o*-carboranyltributyltin **1** to aldehydes **2** is catalysed by $[Pd_2(dba)_3]\cdot CHCl_3$, (dba = dibenzylideneacetone) giving the corresponding adducts, 1-(*o*-carboranyl)-1-methanol derivatives **3**, in good to high yields.

The cross-coupling of organometallic reagents RM with organic halides and related electrophiles R'X, catalysed by palladium and nickel, provides a novel method for generating a C–C bond (R–R').[1] Among various organometallic reagents, organotins ($RSnL_n$) are amongst the most useful in palladium catalysed coupling reactions.[1g,h] Palladium catalysed addition reactions of $RSnL_n$ to a multiple bond (X=Y) are less common than coupling (substitution) reactions (Scheme 1).[1h] It is known that X=Y may form part of *e.g.* an allene, an alkyne, an isonitrile or a 1,3-diene, and R may be hydrogen,[2] or a fragment R'_3M in which M is another group 14 element,[3] or aluminum or boron.[3]

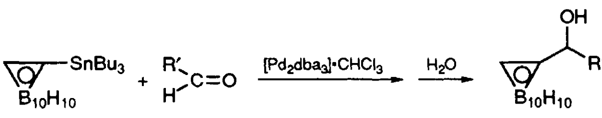
We wish to report that the addition of 1-carboranyltributyltin **1** (R=C) to aldehydes **2** (X=Y; >C=O) is catalyzed by $[Pd_2(dba)_3]\cdot CHCl_3$ (Scheme 2). The results are summarized in Table 1. The addition of **1** to benzaldehyde proceeded very smoothly even at room temp. in the presence of $[Pd_2(dba)_3]\cdot CHCl_3$–dppe catalyst (entry 1). The use of $[Pd(PPh_3)_4]$ or $[PdCl_2(PPh_3)_2]$ gave lower yields, and $[RhCl(PPh_3)_3]$ or $[RhH(CO)(PPh_3)_3]$[4] afforded the adduct in only *ca.* 10% yield. No addition took place with $[NiBr_2(PPh_3)_2]$ as catalyst. Aliphatic aldehydes and cinnamaldehyde also undergo the addition reaction in good to high yields (entries 2–11). Addition to 2-phenylpropanal produced a 3 : 1 diastereoisomeric mixture of the adducts (entry 7).[5]

A mechanistic rationale which accounts for this unprecedented addition reaction is shown in Scheme 3. The oxidative insertion of Pd^0 into the C–Sn bond of **1** would produce the palladium(II) intermediate **4**[6] and the addition of **4** to aldehydes would afford **5**, which would give **6** and palladium(0) species *via* reductive elimination. Alternatively the interaction between **1** and aldehydes might produce a pentavalent tin intermediate, which upon oxidative insertion of Pd^0 into the carbon–tin bond would give the palladium(II) intermediate **7**, which by migration of the carborane anion to the cationic centre may afford **6** and a palladium(0) species. However, the addition reaction of **1** to cyclopropyl aldehyde gave **8** in good yield without being accompanied by a ring opened product which thus precludes the latter mechanism. In order to obtain proof for the proposed mechanism, a 1 : 1 mixture of **1** and $[Pd_2(dba)_3]\cdot CHCl_3$ in THF was kept at room temp. under Ar for 1 d, and quenched by H_2O. The carborane was obtained in essentially quantitative yield. Therefore, it is clear that **4** is formed by the oxidative insertion of Pd^0 into the C–Sn bond in the absence of aldehydes.

Needless to say, palladium catalysed addition reaction between aldehydes and ordinary organotins, such as $SnBu_4$, $PhSnBu_3$, or CH_2=$CHSnBu_3$, did not take place.† The ^{13}C NMR chemical shifts of the α and β carbon atoms of **1** in $CDCl_3$ occur at δ 61.9 and 59.2, whereas that of the carborane was at δ 54.6. The ^{119}Sn NMR chemical shifts of **1**, **9** and **10** in $CDCl_3$ were at δ 22.83, −33.9 and −35.4, respectively. Judging from the ^{119}Sn chemical shift data, the tin atoms of **9** and **10** are charged more negatively in comparison with the tin atom of **1**. No reaction took place between aldehydes and **9** in the presence of palladium catalysts and no oxidative insertion



Scheme 1

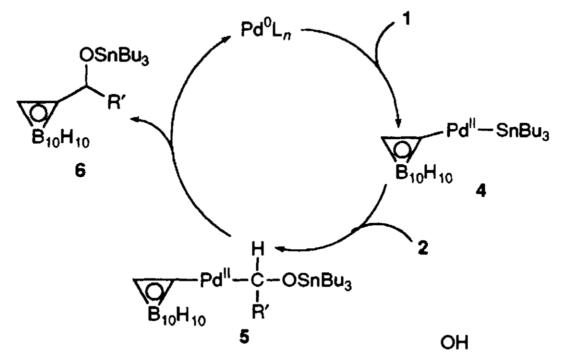


Scheme 2

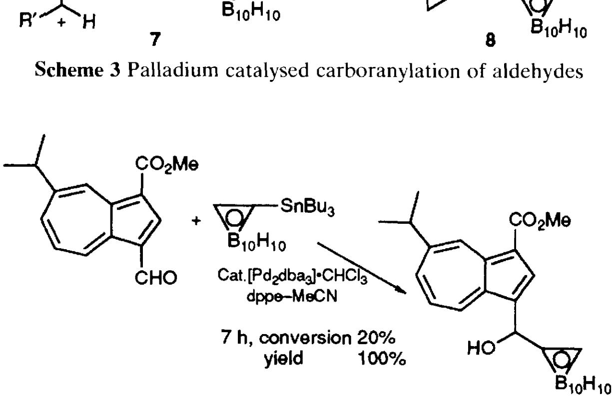
Table 1 Palladium catalysed addition of *o*-carboranyltributyltin **1** to aldehydes **2**[a]

Entry	Aldehyde **2**	Reaction conditions	Yield of **3**[b] (%)
1	PhCHO	Room temp. (1 d)	70
2	*p*-BrC_6H_4CHO	Reflux (1 h)	98
3	*p*-$NO_2C_6H_4CHO$	Reflux (2 h)	≈100
4	*p*-MeC_6H_4CHO	Reflux (1 h)	85
5	*p*-$MeOC_6H_4CHO$	Reflux (3 h)	99
6	$PhCH_2CH_2CHO$	Reflux (1 h)	97
7	PhCHMeCHO	Reflux (1 h)	63[c]
8	Bu^nCHO	Reflux (1 h)	74
9	Pr^iCHO	50 °C (12 h)	65
10	$C_6H_{11}CHO$	Reflux (1 h)	96
11	PhCH=CHCHO	Reflux (4 h)	47[d]

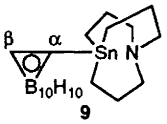
[a] All reactions were carried out under Ar in THF; **1** (0.24 mmol), **2** (0.19 mmol), $[Pd_2(dba)_3]\cdot CHCl_3$ (0.04 mmol), dppe (0.08 mmol). [b] Isolated yield using silica gel column chromatography. [c] The diastereoisomer ratio was 3 : 1. [d] No 1.4-adduct was obtained.



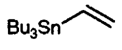
Scheme 3 Palladium catalysed carboranylation of aldehydes



Scheme 4



9



10

of Pd^{O} into the carbon–tin bond of **9** and **10** occurred. Accordingly, it seems that the presence of low negative charge on tin is essential for oxidative insertion. Interestingly, Stille coupling did not take place between organic halides and **1** (and **9**).

Although further work is needed to clarify the mechanism of the above addition reaction, it is synthetically very useful‡ for providing biologically active carborane derivatives which are important as ^{10}B carriers for neutron capture therapy.[7] The reaction of 1-carboranyltributyltin with azulene aldehyde, which is an anti-ulcer agent,[8] in the presence of $[Pd_2(dba)_3]\cdot CHCl_3$ as catalyst at room temp. gave the desired carborane–azulene condensation product in good yield (Scheme 4), whereas the reaction of 1-lithiocarborane with the same aldehyde afforded a complex mixture of products. We are now in a position to combine carboranes with tumour seeking substrates bearing an aldehyde group in the presence of palladium catalyst, without the requirement for carbanionic species.[9]

Received, 16th August 1994; Com. 4/05019C

Footnotes

† These tin compounds undergo a facile transmetallation under the Stille coupling conditions.

‡ The reaction of **1** with *p*-nitrobenzaldehyde is representative. To a dry THF (2 ml) solution of **1** (100 mg, 0.24 mmol) and the aldehyde (28 mg, 0.19 mmol) were added $[Pd_2(dba)_3]\cdot CHCl_3$ (42 mg, 0.04 mmol) and 1,2-bis(diphenylphosphino) ethane (32 mg, 0.08 mmol) under Ar. The mixture was refluxed for 1 hour and the progress of the reaction was monitored by TLC. The solvent was removed *in vacuo*, and the product was purified by silica gel column chromatography using hexane–ethyl acetate (4 : 1) as eluent. The adduct was obtained in ≈100% yield (55 mg, 0.19 mmol). ^{1}H NMR investigation of the crude product indicated formation of the Bu_3Sn derivative of the adduct. Accordingly hydrolysis of the O–Sn bond took place during work-up.[10]

References

1 Review. M = Li, Mg (*a*) M. Kumada, *Pure Appl. Chem.*, 1980, **52**, 669; (*b*) M. Kumada, in *Organotransition Metal Chemistry*, ed. Y. Ishii and M. Tsutsui, Plenum, New York, 1975, p. 211; M = B, Al (*c*) E. Negishi, *Acc. Chem. Res.*, 1982, **15**, 340; *Pure Appl. Chem.*, 1981, **53**, 2333; (*d*) E. Negishi, in *Current Trends in Organic Synthesis*, ed. H. Nozaki, Pergamon, New York, 1983, p. 269; M = Hg (*e*) R. C. Larock, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 27; *Tetrahedron*, 1982, **38**, 1713; M = Zr (*f*) J. Schwartz, *Pure Appl. Chem.*, 1980, **52**, 733; M = Sn (*g*) J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508; (*h*) T. N. Mitchell, *Synthesis*, 1992, 803.

2 J. C. Cochran, L. E. Williams, B. S. Bronk, J. A. Calhoun, J. Fassberg and K. G. Clark, *Organometallics*, 1989, **8**, 804; H. Miyake and K. Yamamura, *Chem. Lett.*, 1989, 1981; H. X. Zhang, F. Guibé and G. Balavoine, *J. Org. Chem.*, 1990, **55**, 1857; T. N. Mitchell and U. Schneider, *J. Organomet. Chem.*, 1991, **405**, 195.

3 T. N. Michell, A. Amamria, H. Killing and D. Rutschow, *J. Orgnomet. Chem.*, 1986, **304**, 257; E. Piers and R. T. Skerlj, *J. Chem. Soc., Chem. Commun.*, 1986, 626; T. N. Mitchell and U. Schneider, *J. Organomet. Chem.*, 1991, **407**, 319; B. L. Chenard, E. D. Laganis, F. Davidson and T. V. Rajan Babu, *J. Org. Chem.*, 1985, **50**, 366; T. N. Mitchell, R. Wickenkamp, A. Amamria, R. Dicke and U. Schneider, *J. Org. Chem.*, 1987, **52**, 4868; B. L. Chenard and C. M. Van Zyl, *J. Org. Chem.*, 1986, **51**, 3561; E. Piers and R. T. Skerlj, *J. Chem. Soc., Chem. Commun.*, 1987, 1025; Y. Ito, T. Bando, T. Matsuura and M. Ishikawa, *J. Chem. Soc., Chem. Commun.*, 1986, 980; M. Murakami, Y. Morita and Y. Ito, *J. Chem. Soc., Chem. Commun.*, 1990, 428; K. Nozaki, K. Wakamatsu, T. Nonaka, W. Tuckmantel, K. Oshima and K. Utimoto, *Tetrahedron Lett.*, 1986, **27**, 2007; S. Sharma and A. C. Oehlschlager, *J. Org. Chem.*, 1989, **54**, 5064.

4 This rhodium catalyst was effective for the addition of certain nucleophiles to activated imines; Y. Yamamoto, Y. Kubota, Y. Honda, H. Fukui, N. Asao and H. Nemoto, *J. Am. Chem. Soc.*, 1994, **116**, 3161.

5 In general, the addition of ordinary organometallic reagents to 1-phenylpropanal produces a 3–5 : 1 diastereoisomeric mixture of adducts; Y. Yamamoto and K. Maruyama, *J. Am. Chem. Soc.*, 1985, **107**, 6411.

6 The Stille coupling is explained by a mechanism which involves, as a key step, the transmetallation between R′PdX and $RSnL_n$ [ref. 1(*g*)]. The Suzuki coupling reaction between organoboranes (RBL_n) and organic halides (R′X) is explained also by the transmetallation mechanism between R′PdX and RBL_n: N. Miyaura, T. Ishiyama, H. Sasaki, M. Ishikawa, M. Satoh and A. Suzuki, *J. Am. Chem. Soc.*, 1989, **111**, 314. Oxidative addition of Pd^0 into a C–B bond has been proposed by us and Uemura and coworkers; H. Yatagai, Y. Yamamoto and K. Maruyama, *J. Chem. Soc., Chem. Commun.*, 1978, 702; C. S. Cho, S. Motofusa and S. Uemura, *Tetrahedron Lett.*, 1994, **35**, 1739.

7 Review: M. F. Hawthorn, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 950.

8 T. Yanagisawa, K. Kasakai, T. Tomiyama, M. Yasunami and K. Takase, *Chem. Pharm. Bull.*, 1990, **38**, 3355.

9 For synthesis of ^{10}B carriers *via* a carbanion method, see Y. Yamamoto, T. Seko, F.-G. Rong and H. Nemoto, *Tetrahedron Lett.*, 1989, **30**, 7191. For noncarbanion methods, see H. Nemoto, F.-G. Rong and Y. Yamamoto, *J. Org. Chem.*, 1990, **55**, 6065; H. Nemoto, J. Cai and Y. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1994, 577; Y. Yamamoto, T. Seko and H. Nemoto, *J. Org. Chem.*, 1989, **54**, 4734.

10 Carboranylstannane **1** was synthesized *via* the reaction of tributylstannyl chloride and lithiocarborane which was prepared by the literature procedure: T. L. Heying, J. W. Ager, Jr., S. L. Clark, R. P. Alexander, S. Papetti, J. A. Reid and S. I. Trotz, *Inorg. Chem.*, 1963, **2**, 1097. Similarly, **9** was synthesized from lithiocarborane and 1-azabicyclo[3.3.3]undecane-5-stannyl chloride: E. Vedejs, A. R. Haight, and W. O. Moss, *J. Am. Chem. Soc.*, 1992, **114**, 6556.