

Tetrahedron Letters, Vol. 37, No. 46, pp. 8405-8408, 1996 Copyright © 1996 Elsevier Science Ltd Printed in Great Britain. All rights reserved 2 0040-4039/96 \$15.00 + 0.00

n

PII: S0040-4039(96)01922-3

## Palladium Catalyzed Coupling Reactions of β-Perfluoroalkyl-Substituted Alkyl Halides with Organostannanes

Rie Shimizu and Takamasa Fuchikami\*

Sagami Chemical Research Center, 4-4-1 Nishi-Ohnuma, Sagamihara, Kanagawa 229, Japan

Abstract:  $\beta$ -Perfluoroalkyl-substituted alkyl halides reacted with organostannanes such as allyl-phenylethynyl-,  $\beta$ -phenylethenyl-, and phenyl-tributyltin in the presence of palladium-phosphine complexes to give the corresponding cross-coupling products in good yields. When the reaction was carried out under CO pressure, carbonylative coupling of the halides took place affording the corresponding fluorine-containing ketones in good yields. Copyright © 1996 Elsevier Science Ltd

Organofluorine compounds are well-known for displaying unique reactivities and selectivities in the transition-metal catalyzed functionalization reactions. For example, we have previously reported that  $\beta$ -perfluoroalkyl-substituted alkyl iodides readily undergo carbonylation and double-carbonylation reactions in the presence of transition-metal catalysts such as palladium, cobalt, and rhodium complexes to give carboxylic acids, esters,  $\alpha$ -ketoacids, and  $\alpha$ -ketoamides, <sup>1,2</sup> where these halides showed similar reactivities to phenyl or vinyl halides rather than alkyl halides. We have proposed that  $\beta$ -perfluoroalkyl-substituted alkyl-metal species, generated by the oxidative addition of these halides to low valent transition-metal complexes, can be stabilized by the internal coordination of fluorine atom(s) to metal center so that the insertion of carbon monoxide takes place more rapidly than  $\beta$ -elimination of hydrido-metal species <sup>3</sup>. If these organometallic intermediates are stable enough, it may be possible to develop new carbon-carbon bond forming reactions which have been considered to be difficult with non-fluorinated alkyl halides.<sup>4+7</sup> In the course of these working hypotheses, we have recently found that Grignard cross-coupling reaction of  $\beta$ -perfluoroalkyl-substituted alkyl halides smoothly proceeds by copper catalysts.<sup>8</sup> Here, we wish to report palladium catalyzed cross-coupling reaction and carbonylative coupling reaction of  $\beta$ -perfluoroalkyl-substituted alkyl halides with organostannanes.

$$R_{f} \xrightarrow{R} R_{r} \xrightarrow{RSnBu_{3}} R_{f} \xrightarrow{X} \frac{RSnBu_{3}, CO}{cat. Pd} R_{f} \xrightarrow{R} R (eq. 1)$$

$$R_{f} = Perfluoroalkyl R'=H, Alkyl X=I, Br$$

$$R = Ph, PhCH=CH, PhC=C, CH_{2}=CHCH_{2}$$

When  $\beta$ -(perfluorooctyl)ethyl iodide (1a) was heated with allyltributyltin (6a) (1 1 equiv) and a catalytic amount (10 mol%) of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> in benzene at 120°C for 16 h, cross-coupling product, 5-perfluorooctyl-1-pentene (7a), was obtained in 51 % yield as shown in Table 1 Thermal reaction without palladium catalyst afforded 7a in only 8% yield in addition to 92% of unchanged 1a Nickel-phosphine complex NiCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> showed a similar catalytic activity, while CuCl(PPh<sub>3</sub>)<sub>3</sub>, being an effective catalyst for

Table 1. Coupling Reaction of  $\beta$ -Perfluorooctyl-Substituted Alkyl Halides with Organostannanes.<sup>a)</sup>

R( + +	R-SnBu3	$\frac{cat}{R'} \qquad R_{f} \stackrel{K}{\frown} R'$
1a: $R_f = C_8 F_{17}$ , $R'=H$ , $X=I$ 1b: $R_f = C_8 F_{17}$ , $R'=H$ , $X=Br$ 2a: $R_f = C_7$ , $R'=H$ , $X=I$ 3a: $R_f = C_6 F_{13}$ , $R'=H$ , $X=I$ 4a: $R_f = C_8 F_{17}$ , $R'=c$ -hexyl, $X=I$ 5a: $R_f = C_3 F_7$ , $R'=C_4 H_9$ , $X=I$	6a R=CH <sub>2</sub> =CHCH <sub>2</sub> 6b R=PhC=C 6c: R=PhCH=CH 6d: R=Ph	7a. $R_f = C_8 F_{17}$ , $R = CH_2 = CHCH_2$ , $R' = H$ 7b. $R_f = C_8 F_{17}$ , $R = PhC = C$ , $R' = H$ 7c: $R_f = C_8 F_{17}$ , $R = PhCH = C'H$ , $R' = H$ 7d: $R_f = C_8 F_{17}$ , $R = Ph$ , $R' = H$ 8b. $R_f = CF_3$ , $R = PhC = C$ , $R' = H$ 9b. $R_f = C_6 F_{13}$ , $R = PhC = C$ , $R' = H$ 10b. $R_f = C_8 F_{17}$ , $R = PhC = C$ , $R' = c_{-}hexyl$ 11b. $R_f = C_8 F_{77}$ , $R = PhC = C$ , $R' = C_4 H_9$

Run	R	(equiv)	Halide	cat (mol%)	Temp Tim	e Product, yield (%) <sup>b)</sup>
1	CH <sub>2</sub> =CHCH <sub>2</sub>	(1.1)	la	none	120°C 16	h 7a: 8
2				$CuCl(PPh_3)_3$ (10)	120°C 16	n <b>7a</b> .13
3				$NiCl_2(PPh_3)_2$ (5)	120°C 16	n <b>7a</b> .57
4				$PdCl_{2}(PPh_{3})_{2}$ (10)	120°C 16	h <b>7a</b> :51
5	PhC=C	(3.0)	la	$Pd(PPh_3)_4$ (10)	120°C 16	n <b>7b</b> :97
6		(3.0)	lb	$PdCl_2(PPh_3)_2$ (10)	120°C 16	n 7 <b>b</b> 21 (53)
7		(3.0)	2a	Pd(PPh3)4 (10)	120°C 16	1 <b>8b</b> 6l
8		(3.0)	3a	Pd(PPh <sub>3</sub> ) <sub>4</sub> (10)	120°C 16	ו <b>9b</b> °79
9		(3 0)	4a	$Pd(PPh_3)_4$ (10)	1 <b>2</b> 0°C 16	n <b>TOP</b> : 53
10		(3.0)	5a	Pd(PPh <sub>3</sub> ) <sub>4</sub> (10)	120°C 16	n 11b:41
11	PhCH≔CH¢)	(1.5)	la	$PdCl_2(PPh_3)_2$ (10)	120°C 40	7 c 45(1)
12		(3.0)		$PdCl_2(PPh_3)_2$ (10)	120°C 31	n 7c. 83d)
13		(3.0)		Pd(PPh <sub>3</sub> ) <sub>4</sub> (10)	120°C 161	n 7 <b>c</b> : 97 <i>d)</i>
14	Ph	(1.1)	la	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> (10)	80°C 32	n 7d 28 (72)
15				$PdCl_2(PPh_3)_2$ (50)	80°C 16	n 7 <b>d</b> . 68 (76)

a) All reactions were carried out with halide (0.50 mmol), stannane (0.55 mmol), and catalyst in dry benzene

(1.5 ml) unless otherwise noted. b) Yields were determined by GLC. Conversion yields are shown in parentheses.

c) A mixture of (E)- and (Z)-isomers (E/Z=7/3) was used. d) Only (E)-isomer was obtained

Grignard cross-coupling reactions,<sup>8</sup> was less active in this particular coupling reaction An ethynyl moiety can be also introduced Thus, 4-perfluoroalkyl-1-phenyl-1-butynes (7b, 8b, or 9b) were obtained by the reaction of 1a, 2a, or 3a with excess amounts of (phenylethynyl)tributyltin (6b) in good yields under the identical reaction conditions. The corresponding bromide,  $\beta$ -(perfluorooctyl)ethyl bromide (1b), was less active in the present coupling reaction, affording 21% yield of 7b in addition to 60% yield of recovered 1b

	Rr	<u>_x</u>	+ CC	) + R-Snl	3u3 —	cat	-	Rf
	1a: $R_f = C_8 F_{17}$ , $X \approx I$ 6a: $R = CH_2 = CHCH_2$ 1b: $R_f = C_8 F_{17}$ , $X \approx Br$ 6b: $R = PhC = C$ 2a: $R_f = CF_3$ , $X \approx I$ 6c: $R = PhCH = CH$ 3a: $R_f = C_6 F_{13}$ , $X \approx I$ 6d: $R = Ph$			12a $R_{f} = C_{8}F_{17}$ , $R = CH_{2} = CHCH_{2}$ 12a' $R_{f} = C_{8}F_{17}$ , $R = CH_{3}CH = CH$ 12b $R_{f} = C_{8}F_{17}$ , $R = PhC = C$ 12c: $R_{f} = C_{8}F_{17}$ , $R = PhCH = CH$ 12d $R_{f} = C_{8}F_{17}$ , $R = Ph$ 13d $R_{f} = CF_{3}$ , $R = Ph$ 14d $R_{f} = C_{6}F_{13}$ , $R = Ph$				
Run	R	(equiv.)	Halide	cat	(mol%)	Temp	Time	Product, yield (%) <sup>h)</sup>
1	Ph	(1.1)	la	PdCl <sub>2</sub> (PPh <sub>3</sub> );	: (10)	120°C	16 h	12d: 97
2			lb	Pd(PPh <sub>3</sub> ) <sub>4</sub>	(10)	120°C	64 h	12d 29 (82)
3			22	PdCl <sub>2</sub> (PPh <sub>3</sub> )	(10)	120°C	16 h	<b>13d</b> : 66
4			3a	PdCl <sub>2</sub> (PPh <sub>3</sub> )	: (10)	120°C	16 h	14d 97
5	CH <sub>2</sub> =CHCH <sub>2</sub>	(1-1)	la	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	(10)	120°C	16 h	12a 16 (19), 12a* 39 (46) <sup>(2)</sup>
6				PdCl <sub>2</sub> (PPh <sub>3</sub> )	(10)	120°C	64 h	12a trace, 12a' 610
7	PhC=C	(1.1)	t a	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	(10)	80°C	16 h	<b>12b</b> 48 (61)
8	PhCH=CHd)	(3 0)	la	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	(10)	120°C	16 h	12c 79 (92) <sup>c)</sup>

Table2 Carbonylative Coupling Reaction of  $\beta$ -(Perfluorooctyl)ethyl Halides with Organostannanes  $a_{j}$ 

ab All reactions were run with halide (0.50 mmol), stannane (0.55 mmol), and catalyst in dry benzene (1.5 ml) under CO pressure (50 atm) unless otherwise noted. bb Yields were determined by GLC. Conversion yields are shown in parentheses cb Only (*E*)-isomer was obtained. ab A mixture of (*E*)- and (*Z*)-isomers (*E/Z*ab7/3) was used.

(run 6). Secondary alkyl iodides 4a and 5a, bearing a bulky group at  $\alpha$ -position, also reacted with 6b to give the cross-coupling products 10b and 11b in 53% and 41% yields, respectively When a mixture of (E)and (Z)-( $\beta$ -phenylethenyl)tributyltin (E/Z = 7/3) was used as a substrate, only (E)-1-phenyl-4-perfluorooctyl-1-butene (7c) was formed in good yield, and most of (Z)-( $\beta$ -phenylethenyl)tributyltin was recovered unchanged

In the case of the reaction with phenyltributyltin (6d), the conversion of the substrates was very low, and metallic palladium was precipitated from the reaction medium within a few hours of heating. This may be due to lower ability of 6d in the transmetallation. When the reaction of iodides 1a, 2a, or 3a with phenyltributyltin was carried out under CO atmosphere in order to prevent the deposition of palladium catalyst, the carbonylative coupling products,  $\beta$ -(perfluoroalkyl)ethyl phenyl ketones (12d, 13d, or 14d), were formed in excellent yields instead of the simple coupling products as shown in Table 2. Again, bromide 1b was found to be less reactive in this carbonylative coupling (run 2). Two products,  $\beta$ perfluorooctyl-4-oxo-1-hexene (12a) and (*E*)-6-perfluorooctyl-4-oxo-2-hexene (12a<sup>\*</sup>), were formed in the

0

reaction of 1a with allyltributyltin (6a). When heating was continued for further 48 h, the compound 12a' was obtained as a predominant product. This result suggests that the initially formed 12a may be isomerized to 12a' by the action of palladium catalyst under these reaction conditions. The similar reactions with phenylethynyl- and  $\beta$ -phenylethenyl-tributyltin (6b and 6c) also gave the corresponding carbonylated products (12b and 12c) in moderate to good yields, respectively.

In conclusion,  $\beta$ -perfluoroalkyl-substituted alkyl halides reacted with organostannanes such as allyl-, phenylethynyl-,  $\beta$ -phenylethenyl-, and phenyl-tributyltin in the presence of palladium-phosphine complexes to give the corresponding cross-coupling products in good to high yields. When the reaction was carried out under CO pressure, the carbonylative coupling reaction took place to afford the corresponding fluorinecontaining ketones. Further applications and precise mechanistic studies of the reactions are in progress.

General Procedure for Coupling Reaction (Table 1). To a mixture of 1a (0.50 mmol). Pd(PPh<sub>3</sub>)<sub>4</sub> (0.05 mmol), and dry benzene (1.5 ml) in a Pyrex<sup>®</sup> tube was added (phenylethynyl)tributyltin (6b. 1.50 mmol). The reaction mixture was stirred at 120°C for 16 h under Ar. GLC analysis revealed that 7b was formed in 97% yield. After an excess amount of KF was added, the reaction mixture was stirred for 1 day. The mixture was filtered through a sintered glass disk, and the filtrate was evaporated to be freed of solvent *in vacuo*. The product 7b was isolated by column chromatography on silica gel eluted with hexane, and identified by <sup>1</sup>H- and <sup>19</sup>F-NMR, IR, MS, and EA.

(*ieneral Procedure for Carbonylative Coupling Reaction (Table 2).* A mixture of **1a** (0.50 mmol), phenyltributyltin (**6d**, 0.55 mmol),  $PdCl_2(PPh_3)_2$  (0.05 mmol), and dry benzene (1.5 ml) was placed in an autoclave (10 ml) — The reaction mixture was stirred under CO pressure (50 atm) at 120°C for 16 h — GLC analysis revealed that **12d** was formed in 97% yield — After an excess amount of KF was added, the reaction mixture was stirred for 1 day — The mixture was filtered through a sintered glass disk, and the filtrate was evaporated to be freed of solvent *in vacuo* — The product **12d** was isolated by preparative TLC on silica gel eluted with hexane-CH<sub>2</sub>Cl<sub>2</sub> (3.1), and identified by <sup>1</sup>H- and <sup>19</sup>F-NMR, IR, MS, and EA

## REFERENCES AND NOTES

- Urata, H., Kosukegawa, O., Ishii, Y.; Yugari, H., Fuchikami, T. Tetrahedron Lett., 1989, 30, 4403-4406
- 2 Urata, H.; Ishii, Y.; Fuchikami, T. Tetrahedron Lett., 1989, 30, 4407-4410
- 3. Urata, H.; Maekawa, H., Takahashi, S., Fuchikami, T. J. Org. Chem., 1991, 56, 4320-4322.
- (a) Castle, P. L.; Widdowson, D. A., Tetrahedron Lett., 1986, 27, 6013-6016 (b) Yuan, K., Scott, W. J. Tetrahedron Lett., 1989, 30, 4779-4782
- 5 Coupling reaction of perfluoroalkyl iodides and 2,2,2-trifluoroethyl iodide with organostannanes catalyzed by Pd(PPh<sub>3</sub>)4 has been reported Matsubara, S., Mitani, M., Utimoto, K. Tetrahedron Lett., 1987, 28, 5857-5860.
- Carbonylative coupling reactions of alkyl halides with organoboron reagents have been reported. (a) Kondo, T., Tsuji, Y., Watanabe, Y. J. Organomet. Chem., 1988, 345, 397-403. (b) Ishiyama, T., Miyaura, N.; Suzuki, A. Tetrahedron Lett., 1991, 32, 6923-6926.
- 7 Carbonylative coupling reaction of alkyl halides with organostannanes under radical conditions has been reported Ryu, I., Yamazaki, H., Kusano, K.; Ogawa, A.; Kambe, N., Sonoda, N. J. Am. Chem. Soc., 1991, 113, 8558-8560
- 8 Shimizu, R.; Yoneda, E.; Fuchikami, T. Tetrahedron Lett., 1996, 37, 5557-5560.

(Received in Japan 12 August 1996; revised 20 September 1996; accepted 25 September 1996)