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Microwave-Assisted Cross-Coupling Reaction of Alkynylstibanes with Aryl Iodides in the Presence of Ammonium Salt

Naoki KAKUSAWA and Jyoji KURITA*

Faculty of Pharmaceutical Sciences, Hokuriku University; Kanagawa-machi, Kanazawa 920–1181, Japan.

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The scope of microwave-assisted coupling reaction of alkynylstibane and aryl iodides to form diarylalkynes is presented. Highly efficient reaction took place smoothly in dimethyl sulfoxide in the presence of cetyltrimethylammonium bromide with much shorter time (1 min) and lower catalyst loading (0.5 mol%) than the conventional method (heating for 24 h with 10 mol% catalyst).

Key words microwave; cross-coupling; alkynylstibane; aryl iodide; palladium catalyst; phase transfer catalyst

The use of microwave (MW) oven as a new tool for synthetic chemistry is a fast-growing area, and the technique has been accepted as a method for reducing reaction times and for increasing yields of product, as well as for improving selectivity compared to conventional methods.[1,2] As a result, this has opened up the possibility of optimizing various reactions in a short time.[3—6] We have recently reported that ethynylstibanes ($Ph_2Sb{\equiv}R$) resulted in cross-coupling reaction to afford ethynylketones ($R{\equiv}COR^1$) on heating with acyl chlorides (R^1COCl) in the presence of a Pd catalyst [$PdCl_2(PPh_3)_2$].[7] However, the ethynylation of aryl halides (Ar-X) proceeded sluggishly under the same reaction conditions; the reaction needs greater loading of the Pd catalyst (10 mol%) and longer reaction time (24 h at 80 °C), and the yield of the coupling product ($R{\equiv}Ar$) is low (16% yield). Thereafter, we also demonstrated that the same reaction of $Ph_2Sb{\equiv}R$ with Ar-X or vinyl halides proceeded more efficiently in amine solvents, in that Sb···N intermolecular coordination would facilitate the coupling reaction.[8,9] Taking these results and knowing that MW irradiation is highly effective for a variety of transition metal-catalyzed reaction into consideration,[10—16] the reaction of diphenyl(phenylethynyl)stibane **1** with aryl halides **2** was performed under MW irradiation to improve the reaction. In this note we report the results of our investigations on the Pd-catalyzed coupling reaction in the presence of ammonium salts as an aid for effective MW absorption in a polar solvent. Under optimal reaction conditions, the reaction took place quite effectively in extremely short time (1 min) to afford the coupling products diarylacetylene **3** along with 1,4-diphenyl-1,3-butadiyne **4** in good yields even when only 0.5 mol% of the palladium catalyst was employed.

Initial attempts for the reaction of **1** with iodobenzene **2a** in the presence of 5 mol% of $PdCl_2(PPh_3)_2$ under MW irradiation in 1,2-dichloroethane (DCE) gave cross-coupling product **3a** (9%) and homo-coupling product **4** (20%) in low yields. The MW effect is known to be operative in a highly polarized medium, so it is preferable to carried out the reaction in solvents with higher dielectric constant.[1] Other approach is the coexistence of an appropriate MW coupler such as ammonium salt[17—21] or ionic liquid[4,22—28] as an additive. We therefore attempted the reaction using several solvents in the absence or presence of ammonium salt. As can be seen in Table 1, a survey of suitable solvents for this reaction showed that dimethyl sulfoxide (DMSO) was superior to other solvents. Thus, coupling products **3a** and **4** were obtained in 47% and 33% yields, respectively, when the reaction of **1** with **2a** (1.5 eq) was carried out in DMSO under MW irradiation at 80 °C for 3 min. Also apparent was that the coexistence of tetra-alkylammonium salts facilitates the formation of the coupling products. Detailed study on ammonium salts as additives revealed that cetyltrimethylammonium bromide (CTMAB) is the best choice among three kinds of ammonium salts examined here for the present reaction, and no noticeable difference in the yields of the coupling products was observed even when only 0.5 mol% of the Pd catalyst was used with CTMAB (Table 2). The reaction of **1** and **2a** in the absence of Pd catalyst under the same conditions gave the

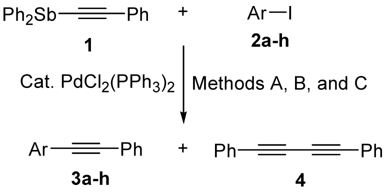

Chart 1

Table 1. Palladium-Catalyzed Coupling Reaction of **1** with **2a** in Various Solvents under MW Irradiation[a)]

Entry: Solvent	Max. Temp./°C	Yield/%[b)]	
		3a	**4**
1: DCE	83	9	20
2: benzene	80	6	10
3: THF	66	4	9
4: triethylamine	88	20	10
5: DMSO	80	47	33

a) A mixture of **1** (1 mmol), **2a** (1.5 mmol), and Pd cat. (5 mol%) in solvent (3 ml) was irradiated using CEM Discover MW system for 3 min. *b)* GC yields.

Table 2. Palladium-Catalyzed Coupling Reaction of **1** with **2a** in the Presence of Ammonium Salt[a)]

Entry: R_4NBr/(mol eq)	Solvent	Pd cat. /mol%	Yield/%[b)]	
			3a	**4**
1: None	Neat	5	27	14
2: TBAB[c)] (0.5)	Neat	5	48	18
3: BTEAB[d)] (0.5)	Neat	5	50	22
4: CTMAB[e)] (0.5)	Neat	5	53	28
5: CTMAB (0.5)	DMSO	5	55	27
6: CTMAB (1)	DMSO	5	62	21
7: CTMAB (1)	DMSO	1	63	23
8: CTMAB (1)	DMSO	0.5	63	23

a) A mixture of **1** (1 mmol), **2a** (1.5 mmol), and Pd cat. (5 mol%) in DMSO (3 ml) was irradiated using the MW system (300 W, Max. Temp. 130 °C) for 3 min. *b)* GC yields. *c)* Tetrabutylammonium bromide. *d)* Benzyltriethyl-ammonium bromide. *e)* Cetyltrimethylammonium bromide.

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* To whom correspondence should be addressed. e-mail: j-kurita@hokuriku-u.ac.jp

Table 3. Palladium-Catalyzed Coupling Reaction of **1** and **2** under Various Reaction Conditions

		Yields of the products/%a)					
2	Ar	Method A (conventional)b)		Method B (MW-Irrn.)c)		Method C (MW-Irrn.)d)	
		3	**4**	**3**	**4**	**3**	**4**
a	C_6H_5	49	21	47	33	63	23
b	*o*-$NO_2C_6H_4$	77	11	—	—	76	21
c	*m*-$NO_2C_6H_4$	73	20	64	21	75	14
d	*p*-$NO_2C_6H_4$	89	5	79	21	83	14
e	*p*-$CH_3COC_6H_4$	46	7	59	29	75	19
f	*o*-$CH_3C_6H_4$	30	20	30	25	57	16
g	*p*-$CH_3C_6H_4$	32	20	32	34	48	26
h	*p*-$CH_3OC_6H_4$	35	25	59	25	48	41

a) GC yields. *b*) Method A: A mixture of **1** (1 mmol), **2** (1.5 mmol), and Pd cat. (10 mol%) in Et_2NH (5 ml) was refluxed (55 °C) for 24 h under argon atmosphere. *c*) Method B: A mixture of **1** (1 mmol), **2** (1.5 mmol), and Pd cat. (5 mol%) in DMSO (3 ml) was irradiated using the MW system (300 W, Max. Temp. 130 °C for **2a**, **e**—**g**, and 80 °C for **2b**—**d**) for 3 min. *d*) Method C: A mixture of **1** (1 mmol), **2** (5 mmol), CTMAB (1 mmol), and Pd cat. (0.5 mol%) in DMSO (3 ml) was irradiated using the MW system (300 W, Max. Temp. 130 °C for **2a**, **e**—**g**, and 80 °C for **2b**—**d**) for 1 min.

products **3a** (21%) and **4** (4%) in poor yields, indicating the presence of the catalyst is not essential in the present reaction. However, prolonged MW irradiation (10 min) of the reaction mixture did not show noticeable improvement in the yields of **3a** (29%) and **4** (8%).

To study the scope of this MW-assisted coupling reaction, we finally performed the coupling reaction of **1** with a variety of aryl iodides **2a**—**h** using 5 eq of **2** with shorter reaction time (1 min) (Method C), and the results are summarized in Table 3 (***Caution***).29) The results obtained from the conventional methods (Method A)9) and under the condition employed in entry 5 in Table 1 (Method B) are also shown for ready comparison with those of Method C. In most cases, superior results were obtained in terms of yields of the coupling products and reaction time, when the reaction was run in DMSO in the presence of CTMAB. Thus, MW irradiation of a mixture of **1** and **2a** in DMSO with 1 eq. of CTMAB with respect to the stibane **1** for 1 min afforded **3a** and **4** in 63% and 23% yields, respectively. This reaction is sensitive to the electronic nature of the substituent on aryl iodides. Aryl iodides with electron-attracting groups gave coupling products in better yields than those with electron-donating groups. Noticeable increase in the yield of the homo-coupling product **4** was also observed under MW irradiation conditions, especially when the reaction was performed with **2** having electron-donating groups. The result implies that the product **4** should be a thermodynamically controlled product. Use of bromobenzene instead of aryl iodides as a coupling partner resulted in significant decrease in the yields of **3a** (5%) and **4** (8%). It has been well documented that aryl bromides and chlorides are less reactive than the corresponding aryl iodides in a wide range of transition metal-catalyzed coupling reactions.30—33)

In summary, we have demonstrated an efficient MW-assisted coupling reaction between ethynylstibane and aryl iodides in the presence of tetra-alkylammonium salt to form diarylalkynes. It should be reemphasized that the reaction proceeds in greatly reduced time by use of 0.5 mol% of Pd catalyst with CTMAB.

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29) The microwave apparatus used here should have a protective cage around it in case of explosion, especially when aryl iodides having nitro group **2b**—**d** is used at over 120 °C. *Typical Procedure*: A vial (10 ml: designed for CEM Discover MW system) containing a solution of **1** (188 mg, 0.5 mmol), **2a** (510 mg, 2.5 mmol), CTMAB (182 mg, 0.5 mmol), and PdCl$_2$(PPh$_3$)$_2$ (1.8 mg, 2.5 μmol) in DMSO (3 ml) was firmly sealed with silicon septa and aluminum cap. The mixture was heated at 130 °C for 1 min by the system (300 W, Max. Temp. 130 °C), then diluted with ether. The organic layer was washed with brine, filtered through a bed of celite and dried over anhydrous MgSO$_4$. The yields of the products were determined by GLC analysis (5% SE-30, 1.6 m, column temp. 210 °C) using biphenyl (t_R=1.25 min) as an internal standard. Diphenylacetylene (55.9 mg, 63%, t_R=2.99 min). 1,4-Diphenyl-1,4-butadiyne (11.4 mg, 23%, t_R=10.67 min).

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