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Sila-Morita−Baylis−Hillman Reaction of Arylvinyl Ketones: Overcoming the Dimerization Problem

Alexander Trofimov and Vladimir Gevorgyan*

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061

vlad@uic.edu

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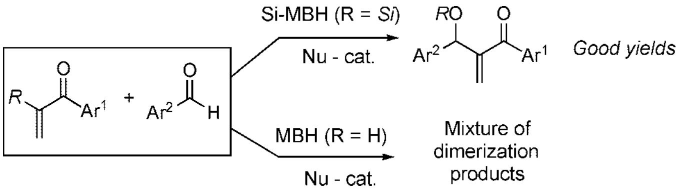
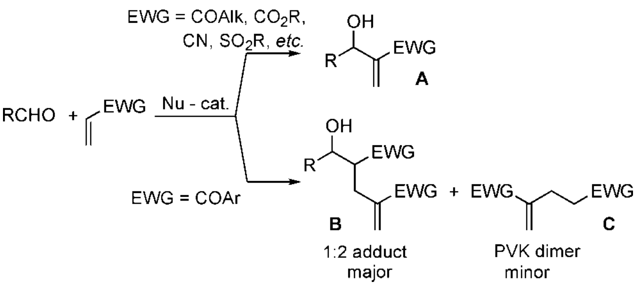
ABSTRACT

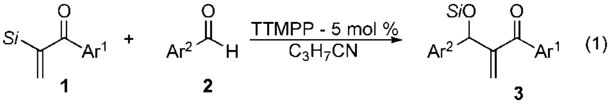


Arylvinyl ketones, under Morita−Baylis−Hillman (MBH) reaction conditions, produce a mixture of dimerization products. We propose a solution to this problem: a sila-MBH reaction. This cascade reaction involves addition of phosphine catalyst to arylvinyl ketones, trapping of the forming β-silylenolate with aldehyde, followed by a 1,3-Brook rearrangement to give the Si-MBH adducts in good to excellent yields.

The Morita−Baylis−Hillman (MBH) reaction is one of the mildest yet most powerful and general methods for C−C bond formation.[1] This reaction was shown to be highly efficient with a variety of Michael acceptors such as ketones, esters, cyanides, etc. to produce allylic alcohols **A** (Scheme 1). Unfortunately, because of high reactivity, the MBH reaction is not efficient with arylvinyl ketones. In this case, the formation of a 1:2 adduct **B** is the major reaction path together with simple dimerization of the substrate to give **C**.[2] Most importantly, this approach completely fails to produce the normal MBH reaction adduct **A**. Herein we wish to report a sila-MBH reaction of α-silylated vinyl aryl ketones **1** with aldehydes **2** in the presence of catalytic amounts of TTMPP (tris(2,4,6-trimethoxyphenyl)phosphine) to produce **3** in good to excellent yields (eq 1).

Scheme 1





1 **2** **3**

Previously, we reported the TTMPP-catalyzed sila-MBH reaction of cyclopropenes. In that case, unusually high reactivity

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(1) For recent reviews, see: (a) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4614. (b) Shi, Y.-L.; Shi, M. *Eur. J. Org. Chem.* **2007**, *18*, 2905. (c) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811. For recent advances, see: (d) Jellerichs, B. G.; Kong, J.-R.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 7758. (e) Wang, L.-C.; Luis, A. L.; Agapiou, K.; Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2402. (f) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404. (g) Thalji, R. K.; Roush, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 16778. (h) Krafft, M. E.; Haxell, T. F. N. *J. Am. Chem. Soc.* **2005**, *127*, 10168.

(2) (a) Shi, M.; Li, C.-Q.; Jaing, J.-K. *Molecules* **2002**, *7*, 721. (b) Shi, M.; Li, C.-Q.; Jaing, J.-K. *Helv. Chim. Acta* **2002**, *85*, 1051.

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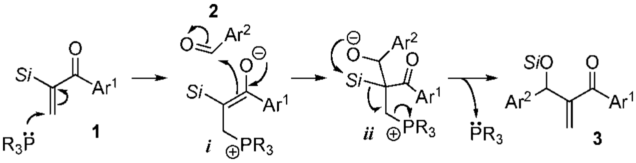
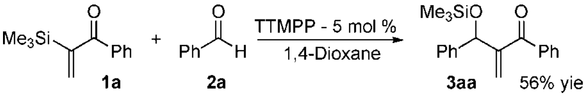
of a non-Michael acceptor-type double bond was attributed to the strain of a cyclopropene ring.[3] We intended to test this tandem transformation on acyclic silylated arylvinyl ketones.[4] It was anticipated that zwiterionic enolate ***i***,[5] produced upon addition of nucleophilic catalyst to enone **1**, would undergo an addition to the carbonyl group of aldehyde **2**[6] to generate alkoxide ***ii***. The latter is perfectly set for the subsequent 1,3-Brook rearrangement[7]/elimination cascade to furnish siloxymethylene enone **3** and release the catalyst (Scheme 2).

Scheme 2



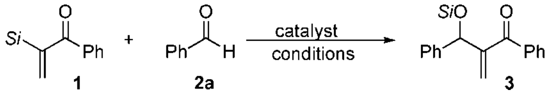
We were pleased to find that employment of 5 mol % of TTMPP[8] in dioxane was effective for the reaction of silylated vinylphenyl ketone **1a** and benzaldehyde **2a** to produce the corresponding adduct **3aa** in 56% yield (eq 2).



(2)

Next, the optimization of the reaction conditions was performed (Table 1). Screening other N- or P-based nucleophiles revealed TTMPP as superior catalysts for this transformation (entries 1−6). Switching solvent from dioxane to butyronitrile allowed for the substantial increase of the yield, producing **3aa** in 73% yield (entry 12). Changing the catalyst loading (entries 13 and 14) or nature of the silyl group[9] (entries 15 and 16) did not lead to the more efficient reaction. Notable improvement of the yield (81%) was obtained when 2 equiv of enone **1a** was used (entry 17).

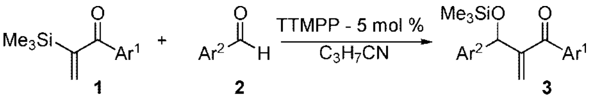
Table 1. Optimization of the Reaction Conditions[a]

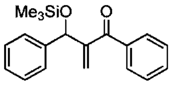
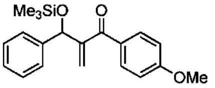
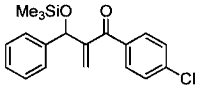
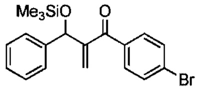
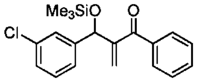
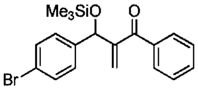
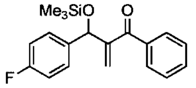
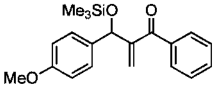
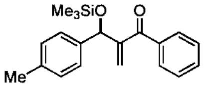
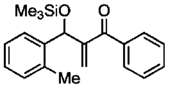
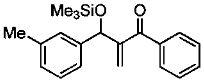
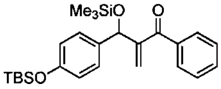


entry	Nu[b]	mol %	solvent	Si	time, h	yield, %[c]
1	TTMPP	5	1,4-dioxane	Me_3Si	12	56
2	TDMPP	5	1,4-dioxane	Me_3Si	12	51
3	DABCO	5	1,4-dioxane	Me_3Si	12	0
4	DMAP	5	1,4-dioxane	Me_3Si	12	5
5	PPh_3	5	1,4-dioxane	Me_3Si	12	0
6	$P^{t}Bu_3$	5	1,4-dioxane	Me_3Si	12	0
7	TTMPP	5	DMF	Me_3Si	12	52
8	TTMPP	5	pyridine	Me_3Si	12	46
9	TTMPP	5	toluene	Me_3Si	12	66
10	TTMPP	5	DMSO	Me_3Si	12	48
11	TTMPP	5	diglyme	Me_3Si	12	42
12	TTMPP	5	C_3H_7CN	Me_3Si	12	73
13	TTMPP	10	C_3H_7CN	Me_3Si	5	71
14	TTMPP	1	C_3H_7CN	Me_3Si	12	0
15	TTMPP	5	C_3H_7CN	$PhMe_2Si$	12	32[d]
16	TTMPP	5	C_3H_7CN	$^{t}BuMe_2Si$	12	0
17	**TTMPP**	**5**	C_3H_7CN	$\mathbf{Me_3Si}$	**12**	**81**[d,e]

[a] 0.1 mmol scale; 1 M concentration; room temperature; 1.5 equiv of benzaldehyde. [b] TDMPP = tris(2,6-dimethoxyphenyl)phosphine; DABCO = 1,4-diazabicyclo[2.2.2]octane; DMAP = 4-(dimethylamino)pyridine. [c] GC yield. [d] Isolated yield. [e] Slow addition of 2.0 equiv of phenylvinylketone **1a**.

Table 2. Sila-Morita−Baylis−Hillman Reaction



no.	Ar^1	Ar^2	product	yield %[a]
1	C_6H_5 **1a**	C_6H_5 **2a**		**3aa** 81
2	p-$MeOC_6H_4$ **1b**			**3ba** 69[b]
3	p-ClC_6H_4 **1c**			**3ca** 72
4	p-BrC_6H_4 **1d**			**3da** 77
5	C_6H_5 **1a**	p-ClC_6H_4 **2b**		**3ab** 99
6		m-ClC_6H_4 **2c**		**3ac** 84
7		p-BrC_6H_4 **2d**		**3ad** 88
8		p-FC_6H_4 **2e**		**3ae** 91
9		p-$MeOC_6H_4$ **2f**		**3af** 55
10		p-MeC_6H_4 **2g**		**3ag** 73
11		o-MeC_6H_4 **2h**		**3ah** 100
12		m-MeC_6H_4 **2i**		**3ai** 72
13		p-$TBSOC_6H_4$ **2j**		**3aj** 84

[a] Isolated yield. [b] Reaction was performed at room temperature with 1.5 equiv of benzaldehyde **2a** and 1 equiv of enone **1b** (1 M).

With optimized conditions in hand, the scope of this transformation was examined (Table 2). Remarkably, the reaction was found to be quite general with respect to the alkene component. Electronically different arylvinyl ketones **1a−d** reacted smoothly with benzaldehyde **2a**, producing the corresponding silylated MBH adducts **3aa−da** in good yields (entries 1−4). Next, a series of differently substituted aryl adlehydes **2b−j**[10] in the reaction with phenylvinyl ketone **2a** were tested (entries 5−13). Both electron-rich and -deficient aryl aldehydes reacted well under the reaction conditions. Methoxy, siloxy, and halogen substituents were well tolerated in this transformation.

In summary, we have developed a sila-Morita–Baylis–Hillman reaction of readily available and stable[11] α-silylvinylaryl ketones[12] with aryl aldehydes. This protocol proceeds via a 1,3-Brook rearrangement/elimination cascade[13] and allows for the mild and efficient synthesis of syloxymethylene aryl enones, structural units unavailable via a traditional MBH reaction.

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Supporting Information Available: Preparative procedures and analytical and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(3) Chuprakov, S.; Malyshev, D.; Trofimov, A.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 14868.

(4) For the Michael addition/Peterson olefination tandem of α-silylenones, see: (a) Tanaka, J.; Kobayashi, H.; Kanemasa, S.; Tsuge, O. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1193. (b) Iqbal, M.; Evans, P. *Tetrahedron Lett.* **2003**, *44*, 5741.

(5) For spectroscopic characterization of analogous phosphonium intermediates, see: Zhu, X.-F.; Henry, C. E.; Kwon, O. *J. Am. Chem. Soc.* **2007**, *129*, 6722.

(6) For reactions of α-silylenolates with alkyl and carbonyl electrophiles, see: (a) Demuth, M. *Helv. Chim. Acta* **1978**, *61*, 3136. (b) Inoue, T.; Sato, T.; Kuwajima, I. *J. Org. Chem.* **1984**, *49*, 4671. (c) Tsuge, O.; Kanemasa, S.; Suzuki, T.; Matsuda, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2851. (d) Tsuge, O.; Kanemasa, S.; Otsuka, T.; Suzuki, T. *Bull. Chem. Soc. Jpn.* **1986**, *61*, 2851.

(7) For a review on Brook rearrangement, see: (a) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065. For recent advances, see: (b) Takeda, K.; Sawada, Y.; Sumi, K. *Org. Lett.* **2002**, *4*, 1031. (c) Xin, L.; Nicewicz, D. A.; Johnson, J. S. *Org. Lett.* **2002**, *4*, 2957. (d) Fleming, I.; Lawrence, A. J.; Richardson, R. D.; Surry, D. S.; West, M. C. *Helv. Chim. Acta* **2002**, *85*, 3349. (e) Jankowski, P.; Plesniak, K.; Wicha, J. *Org. Lett.* **2003**, *5*, 2789. (f) Sawada, Y.; Sasaki, M.; Takeda, K. *Org. Lett.* **2004**, *6*, 2277. (g) Liu, G.; Sieburth, S. M. *Org. Lett.* **2003**, *5*, 4677. (h) Okugawa, S.; Takeda, K. *Org. Lett.* **2004**, *6*, 2973. (I) Clayden, J.; Watson, D. W. *Tetrahedron* **2005**, *61*, 3195. (j) Sasaki, M.; Hashimoto, A.; Tanaka, K.; Kawahata, M.; Yamaguchi, K.; Takeda, K. *Org. Lett.* **2008**, *10*, 1803.

(8) For TTMPP-catalyzed processes, see: (a) Yoshimoto, K.; Kawabata, H.; Nakamichi, N.; Hayashi, M. *Chem. Lett.* **2001**, 934. (b) Kawabata, H.; Hayashi, M. *Tetrahedron Lett.* **2002**, *43*, 5645. (c) Roper, S.; Wartchow, R.; Hoffmann, H. M. R. *Org. Lett.* **2002**, *4*, 3179. (d) Weeden, J. A.; Chisholm, J. D. *Tetrahedron Lett.* **2006**, *47*, 9313.

(9) For Brook rearrangement of different silyl groups, see for example: Bräuer, N.; Michel, T.; Schaumann, E. *Tetrahedron* **1998**, *54*, 11481.

(10) Employment of aliphatic aldehydes under these reaction conditions was not efficient.

(11) α-Silylated aryl vinyl ketones are stable compounds in contrast to their nonsilylated counterparts.

(12) Sato, S.; Matsuda, I.; Izumi, Y. *Tetrahedron Lett.* **1983**, *24*, 3855.

(13) This reaction appeared to be quite sensitive to the substitution at the β-position of the alkene moiety, thus ruling out possible involvement of an alternative mechanism proceeding via TTMPP activation of a silyl group[14] followed by trapping of the forming allenolate with aldehyde. See Supporting Information for details.

(14) For TTMPP activation of a silyl group, see: (a) Matsukawa, S.; Saijo, M. *Tetrahedron Lett.* **2008**, *49*, 4655. (b) Matsukawa, S.; Okano, N.; Imamoto, T. *Tetrahedron Lett.* **2000**, *41*, 103. (c) Matsukawa, S.; Obu, K. *Chem. Lett.* **2004**, *33*, 1626. (d) Matsukawa, S.; Kitazaki, E. *Tetrahedron Lett.* **2008**, *49*, 2982. (e) Kobayashi, S.; Tsuchiya, Y.; Mukaiyama, T. *Chem. Lett.* **1991**, *4*, 537.