

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

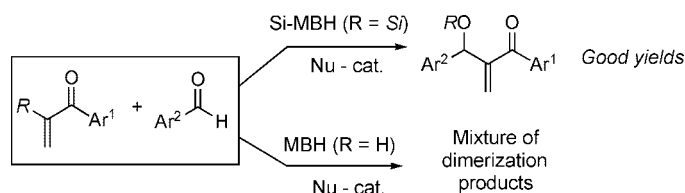
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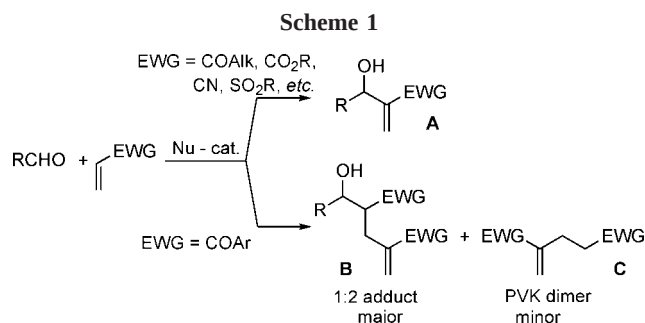
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ABSTRACT

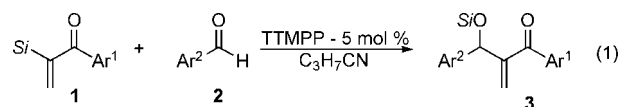


Arylvinyl ketones, under Morita–Baylis–Hillman (MBH) reaction conditions, produce a mixture of dimerization products. We propose a solution to this problem: a sila-MBH reaction. This cascade reaction involves addition of phosphine catalyst to arylvinyl ketones, trapping of the forming β -silylenolate 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).



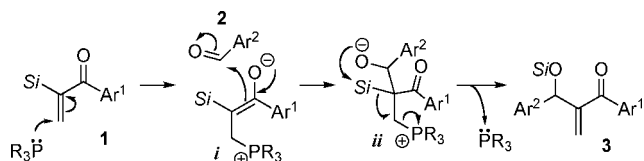
Previously, we reported the TTMPP-catalyzed sila-MBH reaction of cyclopropenes. In that case, unusually high reactivity

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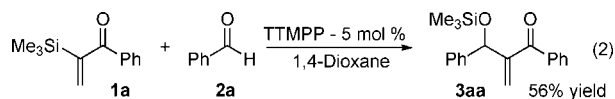
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of a non-Michael acceptor-type double bond was attributed to the strain of a cyclopropene ring.³ We intended to test this tandem transformation on acyclic silylated arylvinyl ketones.⁴ It was anticipated that zwitterionic enolate **i**,⁵ produced upon 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 rearrangement⁷/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 TTMPP⁸ 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).



Next, the optimization of the reaction conditions was performed (Table 1). Screening other N- or P-based nucleo-

Table 1. Optimization of the Reaction Conditions^a

Si		catalyst		conditions		yield,	
entry	Nu ^b	mol %	solvent	Si	time, h	% ^c	
1	TTMPP	5	1,4-dioxane	Me ₃ Si	12	56	
2	TDMPP	5	1,4-dioxane	Me ₃ Si	12	51	
3	DABCO	5	1,4-dioxane	Me ₃ Si	12	0	
4	DMAP	5	1,4-dioxane	Me ₃ Si	12	5	
5	PPh ₃	5	1,4-dioxane	Me ₃ Si	12	0	
6	P ^t Bu ₃	5	1,4-dioxane	Me ₃ Si	12	0	
7	TTMPP	5	DMF	Me ₃ Si	12	52	
8	TTMPP	5	pyridine	Me ₃ Si	12	46	
9	TTMPP	5	toluene	Me ₃ Si	12	66	
10	TTMPP	5	DMSO	Me ₃ Si	12	48	
11	TTMPP	5	diglyme	Me ₃ Si	12	42	
12	TTMPP	5	C ₃ H ₇ CN	Me ₃ Si	12	73	
13	TTMPP	10	C ₃ H ₇ CN	Me ₃ Si	5	71	
14	TTMPP	1	C ₃ H ₇ CN	Me ₃ Si	12	0	
15	TTMPP	5	C ₃ H ₇ CN	PhMe ₂ Si	12	32 ^d	
16	TTMPP	5	C ₃ H ₇ CN	^t BuMe ₂ Si	12	0	
17	TTMPP	5	C ₃ H ₇ CN	Me ₃ Si	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 ₆ H ₅	1a	C ₆ H ₅	2a	3aa 81
2	<i>p</i> -MeOC ₆ H ₄	1b			3ba 69 ^b
3	<i>p</i> -ClC ₆ H ₄	1c			3ca 72
4	<i>p</i> -BrC ₆ H ₄	1d			3da 77
5	C ₆ H ₅	1a	<i>p</i> -ClC ₆ H ₄	2b	3ab 99
6			<i>m</i> -ClC ₆ H ₄	2c	3ac 84
7			<i>p</i> -BrC ₆ H ₄	2d	3ad 88
8			<i>p</i> -FC ₆ H ₄	2e	3ae 91
9			<i>p</i> -MeOC ₆ H ₄	2f	3af 55
10			<i>p</i> -MeC ₆ H ₄	2g	3ag 73
11			<i>o</i> -MeC ₆ H ₄	2h	3ah 100
12			<i>m</i> -MeC ₆ H ₄	2i	3ai 72
13			<i>p</i> -TBSOC ₆ H 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).

philes 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 group⁹ (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).

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 aldehydes **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 stable¹¹ α -silylvinylaryl ketones¹² with aryl aldehydes. This protocol proceeds via a 1,3-Brook rearrangement/elimination cascade¹³ 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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(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 group¹⁴ followed by trapping of the forming allenolate with aldehyde. See Supporting Information for details.

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