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COMMUNICATION

Cobalt-catalyzed conjugate addition of silylacetylenes to α , β -unsaturated ketones†‡

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Catalytic addition of silylacetylenes to α , β -unsaturated ketones proceeded in the presence of a cobalt complex coordinated with a bisphosphine ligand to give high yields of β -alkynylketones.

Catalytic conjugate addition of terminal alkynes to α,β -unsaturated carbonyl compounds and related compounds is one of the most straightforward methods to prepare functionalized internal alkynes.¹ There have been several reports on the metal-catalyzed conjugate addition of terminal alkynes to α , β -unsaturated carbonyl compounds. The conjugate addition to β-unsubstituted enones (vinyl ketones) or enoates (acrylates), which are more reactive than β -substituted ones, has been reported by use of Rh,² Ru,³ and Pd⁴ catalysts. The asymmetric conjugate alkynylation of β -substituted α , β -unsaturated carbonyl compounds has also been recently developed: the asymmetric alkynylation of Meldrum's acid derived acceptors (Cu⁵ and Rh),⁶ oxazepanedione acceptors (Zn),⁷ and α , β -unsaturated thioamides (Cu).^{8,9} In this context, we recently reported rhodium-catalyzed reactions which realize the asymmetric conjugate addition of silylacetylenes to enones,¹⁰ enals,¹¹ and nitroalkenes.^{12,13}

Cobalt-catalyzed reactions have received particular attention in the area of carbon–carbon coupling reactions displaying their unique reactivity and selectivity.¹⁴ Cobalt complexes have also been reported to catalyze the conjugate addition of malonate esters¹⁵ or alkyl and aryl halides under reductive conditions.^{16,17} Recently, Li and co-workers reported that the addition of terminal alkynes to iminium ions, *in situ* generated from aldehydes and secondary amines, is efficiently catalyzed by cobalt complex CoCl₂(PPh₃)₂.¹⁸ Meanwhile, there have been no reports on the cobalt-catalyzed conjugate alkynylation of enones to the best of our knowledge. Here we report the cobaltcatalyzed addition of silylacetylenes to α , β -unsaturated ketones and some preliminary results of its asymmetric variant.

Cheng and co-workers^{14e,19} have extensively studied a catalytic system of CoX_2 /bisphosphine/Zn generating a Co(1) species in

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E-mail: tnishi@kuchem.kyoto-u.ac.jp, thayashi@kuchem.kyoto-u.ac.jp; *Fax:* +81 75 753 3988; *Tel:* +81 75 753 3983 reductive coupling reactions. Based on their reports, we examined the catalytic activity of cobalt(1) complexes in the addition of a silylacetylene to an enone. It was found that the conjugate alkynylation is catalyzed by cobalt complexes, where significant effects of a solvent, a catalyst precursor, and a ligand were observed (Table 1). Thus, treatment of 1-phenyl-2-buten-1-one (**1a**) with 2 equiv.²⁰ of (triisopropylsilyl)acetylene (**2m**) in the presence of Co(OAc)₂·4H₂O (5 mol%), 1,2-bis(diphenylphosphino)ethane (dppe) (5 mol%), and zinc powder (50 mol%) in dimethylsulfoxide (DMSO) at 80 °C for 10 h gave the alkynylation product **3am** in 81% yield (Table 1, entry 1). The reactions in polar solvents, *N*,*N*-dimethylformamide (DMF)

 Table 1
 Cobalt-catalyzed conjugate addition of alkyne 2m to enone 1a^a



$$n = 1$$
, dppm $n = 3$, dppp
 $n_2 P P P h_2$ $n = 2$, dppe $n = 4$, dppb

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Entry	Catalyst	Ligand	Solvent	$\operatorname{Yield}^{b}(\%)$
1	Co(OAc) ₂ ·4H ₂ O	dppe	DMSO	81
2	Co(OAc) ₂ ·4H ₂ O	dppe	DMF	24
3	Co(OAc) ₂ ·4H ₂ O	dppe	CH ₃ CN	8
4	Co(OAc) ₂ ·4H ₂ O	dppe	Toluene	0
5	Co(OAc) ₂ ·4H ₂ O	dppe	1,4-Dioxane	0
6	$Co(OAc)_2$	dppe	DMSO	75
7	CoCl ₂	dppe	DMSO	29
8	CoBr ₂	dppe	DMSO	21
9	CoI ₂	dppe	DMSO	19
10	Co(OAc)2·4H2O	dppm	DMSO	0
11	Co(OAc) ₂ ·4H ₂ O	dppp	DMSO	63
12	Co(OAc) ₂ ·4H ₂ O	dppb	DMSO	0
13	Co(OAc)2·4H2O	rac-binap	DMSO	0
14		dppe	DMSO	0
15	Co(OAc)2·4H2O		DMSO	0
16^{c}	Co(OAc) ₂ ·4H ₂ O	dppe	DMSO	0
17^d	Co(OAc)2·4H2O	dppe	DMSO	97

^{*a*} Reaction conditions: **1a** (0.30 mmol), (triisopropylsilyl)acetylene (**2m**) (0.60 mmol), cobalt catalyst (5 mol%), ligand (5 mol%), Zn (50 mol%), solvent (0.5 mL) at 80 °C for 10 h. ^{*b*} Yield of **3am** determined by ¹H NMR. ^{*c*} Performed without Zn. ^{*d*} For 20 h. binap: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl.

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Table 2Cobalt-catalyzed conjugate alkynylation of enones 1^a

0 R ¹ H—	R^{3} R^{2} R^{2} R^{3} R^{3} R^{3}	Co(0 dppe Zn (DM\$ 80 °	DAc); e (5 n 50 m 50 C, 20	₂ [.] 4H₂O (5 mc nol%) ol%) ⊢h	$\xrightarrow{R^{1}} R^{1} \xrightarrow{Q} R^{2}$	SiR3		
Entry	\mathbf{R}^1		\mathbf{R}^2	R ³	SiR ₃	$\operatorname{Yield}^{b}(\%)$		
1	Ph		Н	Me (1a)	Si(<i>i</i> -Pr) ₃ (2m)	97 (3am)		
2	4-MeOC ₆ H ₄		Н	Me (1b)	$Si(i-Pr)_3$ (2m)	92 (3bm)		
3	4-ClC ₆ H ₄		Н	Me (1c)	$Si(i-Pr)_3$ (2m)	74 (3cm)		
4	2-furyl		Η	Me (1d)	Si(<i>i</i> -Pr) ₃ (2m)	93 (3dm)		
5	(E)-PhCH=	CH	Н	Me (1e)	$Si(i-Pr)_3$ (2m)	80 (3em)		
6	Ph		Н	Et (1f)	$Si(i-Pr)_3$ (2m)	88 (3fm)		
7^c	Ph		Н	<i>i</i> -Pr (1g)	$Si(i-Pr)_3$ (2m)	65 (3gm)		
$8^{d,e}$	Me		Н	Me (1h)	$Si(i-Pr)_3$ (2m)	92 (3hm)		
$9^{d,e}$	PhCH ₂ CH ₂		Н	Me (1i)	$Si(i-Pr)_3$ (2m)	87 (3im)		
$10^{d,e}$	Me		Н	C_5H_{11} (1j)	$Si(i-Pr)_3$ (2m)	67 (3jm)		
11^e	Ph		Me	H (1k)	$Si(i-Pr)_3$ (2m)	73 (3km)		
12	Et		Н	H (11)	$Si(i-Pr)_3$ (2m)	77 (3lm)		
13	Ph		Н	Me (1a)	$SiPh_2(t-Bu)$ (2n)	95 (3an)		
14^{f}	Ph		Н	Me (1a)	$SiMe_2(t-Bu)$ (20)	70 (3ao)		
15 ^f	Ph		Η	Me (1a)	SiEt ₃ (2p)	40 (3ap)		
^{<i>a</i>} Reaction conditions: 1 (0.30 mmol), alkyne 2 (0.60 mmol), Co(OAc)- $4H_{2}O$ (5 mol%) dppe (5 mol%) Zn (50 mol%) DMSO								

Co(OAc)_{2'}4H₂O (5 mol%), dppe (5 mol%), Zn (50 mol%), DMSO (0.50 mL) at 80 °C for 20 h. ^{*b*} Isolated yield of **3**. ^{*c*} Performed with **2m** (3 equiv.) at 60 °C for 60 h. ^{*d*} Alkyne **2m** (4 equiv.). ^{*e*} For 40 h. ^{*f*} Alkyne **2** (5.0 equiv.).

and acetonitrile, took place to give 3am in 24% and 8% yield, respectively (entries 2 and 3), whereas the addition product was not formed at all in toluene or 1,4-dioxane (entries 4 and 5). The use of anhydrous Co(OAc)₂ gave **3am** in 75% yield (entry 6), while cobalt(II) halides, which are often used as catalyst precursors combined with zinc in the cobalt-catalyzed reactions,¹⁴ were lower in their catalytic activity than Co(OAc)₂ (entries 7-9). Of common bisphosphine ligands other than dppe such as dppm, dppp, dppb, and binap (entries 10-13), only dppp displayed a catalytic activity to give 3am in 63% yield (entry 11). The alkynylation in the absence of the cobalt catalyst (entry 14), dppe (entry 15), or zinc (entry 16) did not take place at all.^{21,22} The highest yield (97%) was obtained in the reaction using Co(OAc)₂·4H₂O (5 mol%), dppe (5 mol%), and zinc (50 mol%) for a prolonged reaction time (20 h) (entry 17).

Table 2 summarizes the results obtained for the reaction of several enones 1 with alkynes 2. The reaction of 1-propenyl ketones 1a–1e, substituted with aryl groups or a styryl group on the carbonyl, proceeded well to give the corresponding β -alkynylketones 3am–3em in high yields (entries 1–5). The addition to linear enones bearing ethyl (1f) and isopropyl (1g) at the β position gave the corresponding addition products 3fm and 3gm in 88% and 65% yield, respectively (entries 6 and 7). Alkyl alkenyl ketones 1h–1j are also good substrates to give the corresponding addition products 3hm–3jm in 67–92% yields, although their reactivities were lower than those of aryl ketones (entries 8–10). It should be noted that the reaction of α -substituted enone 1k gave the addition product 3km in 73% yield (entry 11), whereas the formation of only 2% of 3km was observed under the standard reaction conditions



Scheme 1 Asymmetric addition of alkyne 2m to enone 1a.

of the rhodium catalysis.^{10,23} The present cobalt-catalyzed conjugate alkynylation can introduce bulky silylacetylenes **2m–2p** (entries 1, 13–15), but the addition of phenylacetylene or 1-octyne to **1a** did not take place.²⁴

The asymmetric variant of the present alkynylation is promising for the synthesis of chiral internal alkynes because the catalytic system can be applied to the addition to β-substituted enones, which can create stereogenic center at the β -position by the alkynylation. The preliminary results of the asymmetric alkynylation are shown in Scheme 1 and Table 3. The chiral bisphosphine ligand (S,S)-chiraphos²⁵ was attempted as a first choice, because dppe was a good ligand for the cobalt-catalyzed alkynylation. Unfortunately, however, the enantioselectivity of the asymmetric alkynylation of enone 1a catalyzed by the cobalt/(S,S)-chiraphos catalyst was very low giving **3am** of 1% ee. The use of (S,S)-bdpp,²⁶ which was successfully used in the cobalt-catalyzed asymmetric arylation of aldehydes by Cheng and co-workers,²⁷ displayed high enantioselectivity (87% ee), where a higher catalyst loading (10 mol%) was required to give 3am in high yield (93%).²⁸ As summarized in Table 3, the asymmetric addition of alkyne 2m to enones 1a-1d and 1f gave the corresponding β-alkynyl ketones in good yields, with enantioselectivities ranging from 79 to 91% ee (Table 3, entries 1-5).

In summary, we have developed a cobalt-catalyzed addition of silylacetylenes to α , β -unsaturated ketones giving β -alkynylketones in high yields. We have also demonstrated that the

Table 3 Cobalt-catalyzed asymmetric conjugate alkynylation of enones $\mathbf{1}^{a}$



^{*a*} Reaction conditions: **1** (0.30 mmol), **2m** (0.60 mmol), Co(OAc)₂·4H₂O (10 mol%), (*S*,*S*)-bdpp (10 mol%), Zn (50 mol%), DMSO (0.50 mL) at 80 °C. ^{*b*} Isolated yield. ^{*c*} Determined by chiral HPLC analysis.

asymmetric variant of the present catalysis is achieved by use of a chiral bisphosphine ligand. Studies on development of more efficient and stereoselective systems of the cobaltcatalyzed alkynylation are underway.

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