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A newly-designed PE-supported arsine for efficient and practical catalytic Wittig olefination†

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A newly designed PE-supported arsine has been developed as an excellent catalyst for catalytic Wittig-type olefination. Simple ketones, in particular inactive ketones prove to be suitable substrates for the first time. This reaction provides an easy access to di-, tri-, and tetra-substituted olefins in high yield.

Wittig reaction¹ and its variants² are important synthetic tools due to their unambiguous positioning and good stereoselectivity of the double bonds.³ The catalytic Wittig reaction process, which provides an atom economic pathway by avoiding the use of stoichiometric phosphines,⁴ has been paid much attention.^{5–7} Recently, O'Brien and coworkers documented the first catalytic Wittig olefination of aldehydes by using 3-methyl-1-phenyl-phospholane-1-oxide catalyst.⁷ Although great progress has been achieved on aldehydes^{5–7} and activated ketones,^{5a} to date, no catalytic Wittig olefination of inactive ketones has been reported. In this communication, we present our original breakthrough on developing a highly efficient and practical catalytic Wittig olefination of general ketones and aldehydes, employing newly designed recoverable and reusable PE-supported arsine catalysts⁸ in low loading.

Initially, we examined all of the documented catalyst systems for catalytic Wittig-type reactions of both cyclohexanone and benzophenone under the reported optimal conditions respectively (entries 1–9, Table 1). Unfortunately, all of these catalysts gave no reaction (entries 5, 7 and 9, Table 1) or trace amount of desired products (entries 1, 2 and 8, Table 1) for both substrates except for ⁿBuTe-PEG-TeBuⁿ, which gave only 19% conversion for cyclohexanone (entry 6, Table 1). Although AsPh₃ was reported as a catalyst for the Wittig olefination of trifluoromethyl arylketone,^{5a} only 31% yield was obtained for cyclohexanone even when 100 mol% of triphenylarsine was employed (entry 4, Table 1). To our delight, when a newly-designed PE-supported^{9,10} arsine (**PE-1**, *M_n*: 34 kg mol⁻¹, arsine incorporation ratio in polyethylene: 5.2 mol%) was utilized, the catalytic olefination of cyclohexanone could proceed smoothly with 100% conversion

(entry 10, Table 1). In particular, when polymethylhydrosiloxane (PMHS), a much cheaper, more easy to handle and more environmentally friendly reducing agent was used instead of diphenylsilane, the reaction was promoted effectively, affording the desired product in 98% isolated yield (entry 11). In contrast, other catalysts such as AsBu₃, AsPh₃ and phosphine oxide could not give satisfying results under current conditions (entries 12–14).

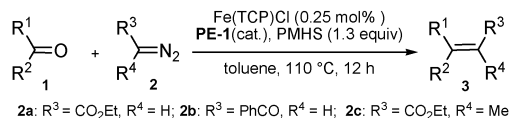
Under the optimized conditions, we investigated the substrate scope of the catalytic Wittig olefination of ketones.

Table 1 Ylide olefination of ketones using different catalysts^a

Entry	Catalyst (mol%)	Substrates	Conv. ^{b,c} (%)
1 ^{5b}	As(<i>n</i> -Bu) ₃ (20)		Trace
2 ^{5b}	As(<i>n</i> -Bu) ₃ (20)		Trace
3 ^{5a}	AsPh ₃ (20)		< 5
4 ^{5a}	AsPh ₃ (100)		31 (31)
5 ^{5a}	AsPh ₃ (20)		0
6 ⁶	ⁿ BuTe-PEG-TeBu ⁿ (2.0)		19
7 ⁶	ⁿ BuTe-PEG-TeBu ⁿ (2.0)		0
8 ⁷			Trace
9 ⁷			0
10 ^d	PE-1 (2.0)		100
11 ^e	PE-1 (2.0)		100 (98)
12 ^e	AsBu ₃ (2.0)		41
13 ^e	AsPh ₃ (2.0)		53
14 ^e			0

^a Under the optimal literature reaction conditions (for details, see ESI).^b Determined by ¹H NMR. ^c Isolated yields in brackets. ^d Ketone (3.0 mmol), EDA (2.0 equiv.), Fe(TCP)Cl (0.25 mol%), Ph₂SiH₂ (1.3 equiv.), 110 °C, toluene (3.0 mL), 12 h. ^e The same as footnote d but using PMHS (*M_n*: 1700–3200 g mol⁻¹, 1.3 equiv.) instead of Ph₂SiH₂.^a State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China. E-mail: tangy@sioc.ac.cn^b Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China

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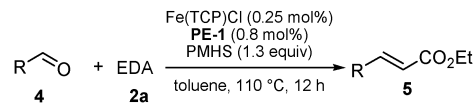
Table 2 The PE-1 catalyzed Wittig reaction of ketones^a

Entry	1	2 (equiv.)	PE-1 (mol%)	Yield (%)	<i>E/Z</i> ^b
1		2a (2.0)	2.0	97	>99/1
2		2a (2.0)	2.0	98	—
3		2a (2.0)	2.0	95	—
4 ^c		2a (2.5)	3.0	93	—
5 ^d		2a (3.0)	4.0	81	60/40
6 ^d		2a (3.0)	4.0	83	63/37
7 ^d		2a (3.0)	4.0	81	83/17
8 ^e		2a (4.0)	8.0	64	—
9 ^f		2b (2.5)	4.0	98	95/5
10 ^g		2c (3.0)	4.0	94	93/7
11 ^g		2c (3.0)	4.0	84	—
12 ^g		2c (3.0)	4.0	85	—

^a Ketone (3.0 mmol), toluene (3 mL). ^b Determined by ¹H NMR. ^c 15 h. ^d 18 h. ^e 48 h. ^f 38 h. ^g 36 h.

As summarized in Table 2, PE-1 could catalyze the olefination of simple ketones with diazoacetate (EDA)¹¹ very well, affording the desired 1,1,2-trisubstituted alkenes in excellent yields. For example, trifluoromethyl phenyl ketone gave (*E*)-ethyl 4,4,4-trifluoro-3-phenylbut-2-enoate in 97% yield with >99/1 *E*-selectivity (entry 1, Table 2). Both cyclic and acyclic aliphatic ketones were suitable substrates in the presence of a catalytic amount of PE-1. For instance, cyclohexanone, cyclopentanone, and hex-5-en-2-one reacted with EDA, giving the corresponding olefins in high yields (entries 2, 4 and 6, Table 2). Even for benzophenone, inert in the reported catalytic systems, 64% yield was obtained when 8 mol% of PE-1 was employed (entry 8, Table 2). Other diazo compounds, such as diazo acetophenone and ethyl 2-diazopropanoate, were also suitable substrates for the current Wittig-type olefination, providing an efficient access to tri- and tetra-substituted alkenes (entries 9–12, Table 2).

PE-1 can promote the catalytic Wittig olefination of simple ketones very well, suggesting that the reduction of the PE-1 loading for the reaction of aldehydes is possible. As expected, with only 0.8 mol% of PE-1 as the catalyst, both electron-withdrawing and -donating aromatic aldehydes worked well, giving 1,2-disubstituted alkenes in higher than 94% yields (entries 1–16, Table 3). Furan-2-carbaldehyde gave 98% yield (entry 17, Table 3). Aliphatic aldehydes were also favorable substrates affording the corresponding unsaturated esters in

Table 3 The PE-1 catalyzed Wittig reaction of aldehydes^a

Entry	R	Yield ^b (%)	Entry	R	Yield ^b (%)
1	1-Naphthyl 4a	99	17	2-Furyl 4q	98
2	2-NO ₂ C ₆ H ₄ 4b	95	18	PhCH/CH 4r	96
3	2,6-Cl ₂ C ₆ H ₃ 4c	98	19	PhCH ₂ CH ₂ 4s	97
4	2,4-Cl ₂ C ₆ H ₃ 4d	99	20	C ₆ H ₅ (CH ₃)CH 4t	98
5	4-ClC ₆ H ₄ 4e	99	21	Cyclohexyl 4u	98
6	4-BrC ₆ H ₄ 4f	99	22	CH ₃ (CH ₂) ₆ 4v	94
7	4-CF ₃ C ₆ H ₄ 4g	96	23	BnO(CH ₂) ₃ 4w	93
8	4-NO ₂ C ₆ H ₄ 4h	99			
9	4-CNC ₆ H ₄ 4i	99	24 ^c		87
10	3-NO ₂ C ₆ H ₄ 4j	98	25 ^d		99
11	3-ClC ₆ H ₄ 4k	99			
12	2-ClC ₆ H ₄ 4l	98	26 ^e	4-ClC ₆ H ₄ 4e	98
13	4-MeC ₆ H ₄ 4m	99	27 ^f	4-ClC ₆ H ₄ 4e	94
14	4-MeOC ₆ H ₄ 4n	97	28 ^e	CH ₃ (CH ₂) ₆ 4v	95
15	3,4-Me ₂ C ₆ H ₃ 4o	94	29 ^{f,g}	CH ₃ (CH ₂) ₆ 4v	94
16	Ph 4p	99	30 ^h	1-Naphthyl 4a	87

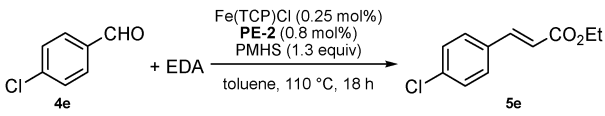
^a Aldehyde (3.0 mmol), EDA (1.6 equiv.), toluene (3 mL). ^b *E/Z* > 99/1. ^c 100% ee. ^d 94% ee. ^e With 1.5 equiv. of 2b and 1.0 mol% of PE-1. ^f With 2.0 equiv. of 2c and 1.0 mol% of PE-1, 15 h. ^g *E/Z* = 79 : 21. ^h 4a (24 mmol), EDA (3.0 equiv.), PE-1 (0.05 mol%), Fe(TCP)Cl (0.03 mol%), toluene (6 mL), 98 h.

very high yields (entries 18–25, Table 3). The reaction conditions were mild enough and no racemization was observed when optically active aldehydes such as 4x and 4y were employed (entries 24 and 25, Table 3). Diazo acetophenone and ethyl 2-diazopropanoate proved to react with aldehydes smoothly under the reaction conditions (entries 26–29, Table 3). In all cases described above, the stereoselectivity is excellent and the *E/Z* ratio is >99/1 except for the reaction of capryl aldehyde with 2c (entry 29, Table 3). Thus, it provides a facile way for the synthesis of di-, tri- α,β -unsaturated carbonyl compounds with excellent *E*-selectivity. Remarkably, the loading of PE-1 could be further reduced down to 0.05 mol% when the reaction was scaled up (entry 30, Table 3).

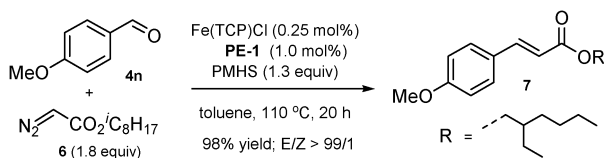
The influence of the arsine content in the PE chain on the catalytic efficiency is nearly negligible. As shown in Table 4, for example, PE-2 with 0.39 mol% incorporation ratio of arsine was very efficient as well. Moreover, the PE-supported arsine proves to be a temperature-controlled recoverable and reusable catalyst. In the PE-2 catalyzed reaction between 4-chlorobenzaldehyde and EDA, the desired olefin could be obtained in 98% yield and >99 : 1 *E/Z* selectivity even after 5 runs (entry 5, Table 4).

The current reaction is practically useful. For instance, (*E*)-heptan-3-yl 3-(4-methoxyphenyl) acrylate 7,¹² which is useful as the UV-light absorbing ingredient in commercially available sunscreens, could be readily synthesized from *p*-methoxybenzaldehyde in 98% yield in the presence of 0.25 mol% of Fe(TCP)Cl and 1.0 mol% of PE-1 (Scheme 1).

In summary, a new catalyst has been developed for highly efficient catalytic Wittig-type reactions. The substrate scope is universal and the catalytic olefination of inactive ketones was

Table 4 PE-2 as a recoverable and reusable catalyst for Wittig reaction


Run	Yield (%)	E/Z	Run	Yield (%)	E/Z
1	99	> 99 : 1	4	96	> 99 : 1
2	99	> 99 : 1	5	98	> 99 : 1
3	94	> 99 : 1			

**Scheme 1** Synthesis of UV-light absorbing reagent 7.

realized for the first time. Even for diphenylketone and hex-5-en-2-one, high yields were obtained. Both aromatic aldehydes and aliphatic aldehydes work well for such an olefination with excellent yields and stereoselectivities. EDA, diazo acetophenone, and ethyl 2-diazopropanoate are good reagents for the olefination. Thus it provides an easy access to 1,2-disubstituted alkenes, 1,1,2-trisubstituted alkenes, and 1,1,2,2-tetrasubstituted alkenes with high stereoselectivity. The loading of PE-supported catalyst could be reduced down to 0.05 mol% in the presence of the cheap reducing agent PHMS and the PE-supported arsine was recoverable and reusable, making the current reaction atom-economic and potentially practically useful in organic synthesis.

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