

A practical catalytic Wittig-type reaction

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Soluble PEG-supported telluride **2** was synthesized and found to be an effective catalyst for the catalytic Wittig-type reaction to give a variety of α,β -unsaturated esters in high yields with excellent *E*-stereoselectivity in the presence of sodium bisulfite as well as triphenyl phosphite.







In the past decades, highly efficient catalysis has become one of the most important frontiers in exploratory organic synthetic research.¹ Although the ylide reaction is one of the most useful approaches in both constructing C–C double bonds² and forming small ring compounds,³ surprisingly, relatively few catalytic ylide reactions, in particular Wittig-type reactions, were reported in literature.⁴ The first example of catalytic Wittig-type reactions appeared in 1989, in which Huang *et al.* found tributylarsine could be used as the catalyst in the presence of triphenyl phosphite.⁵ Later on, they described the catalytic ylide olefination, epoxidation, and cyclopropanation reactions mediated by *n*-butyl telluride or isobutyl telluride.⁶ Dai *et al.* also reported the first catalytic ylide aziridination and provided a facile way to the synthesis of vinyl-type aziridines.⁷ Aggarwal *et al.* realized excellent catalytic asymmetric ylide epoxidation, cyclopropanation and aziridination reactions by a carbene approach.⁸ In this process, the ylide was formed directly from phenyldiazomethane in the presence of a catalytic amount of both chiral sulfide and rhodium acetate. In all of the reactions described above, however, the amount of catalyst used was 20

mol%. Reduction of the catalyst means low yield even if the reaction time was prolonged.⁹ Needless to say, these processes need to be improved before it can be considered as a useful synthetic tool. In our continuing studies on the application of ylides in organic synthesis,¹⁰ we focused on the economy of ylide reactions. In this paper, we wish to report a highly effective Wittig-type olefination catalyzed by the soluble poly(ethyleneglycol) (PEG)-supported telluride **2** (PEG–Te–Bu).¹¹

When *p*-chlorobenzaldehyde was mixed with ethyl bromoacetate in the presence of triphenyl phosphite and 1 mol% of compound **2** in toluene at 80 °C, we found that the Wittig-type reaction product was afforded in 88% yield with excellent stereoselectivity.[†] This meant that the catalytic efficiency of this reaction was improved greatly compared with other catalytic ylide reactions reported to date. By optimizing the reaction conditions, the desired olefin could be obtained in quantitative yield when 2 mol% of telluride **2** was used. To determine the generality of this reaction, a variety of structurally different aldehydes were employed. Some results are summarized in Table 1 (entries 1, 3, 5, 7, 9, 11, 13, 15 and 17). From Table 1, both aliphatic and aromatic aldehydes worked well with high stereoselectivity in reasonable yields.

To make this reaction more practical, we tried to use inorganic reducing reagents instead of triphenyl phosphite and found excellent results were achieved when sodium bisulfite

Table 1 Olefination of aldehydes catalyzed by PEG-supported telluride

Entry	Aldehyde	R'	t/h	Cocatalyst	Yield (%) ^a	<i>E/Z</i> ^b
1	<i>p</i> -CH ₃ OC ₆ H ₄ CHO ^c	Et	43	P(OPh) ₃	94	> 99:1
2		Bu ^t	43	NaHSO ₃	87	> 99:1
3	<i>p</i> -CH ₃ C ₆ H ₄ CHO	Et	23	P(OPh) ₃	93	90:10
4		Bu ^t	24	NaHSO ₃	96	94:6
5	<i>trans</i> -C ₆ H ₄ CH=CHCHO ^c	Et	48	P(OPh) ₃	74	> 99:1
6		Bu ^t	23	NaHSO ₃	88	> 99:1
7	C ₆ H ₅ CHO	Et	18	P(OPh) ₃	98	> 99:1
8		Bu ^t	11	NaHSO ₃	92	> 99:1
9	<i>p</i> -ClC ₆ H ₄ CHO	Et	7	P(OPh) ₃	98	> 99:1
10		Bu ^t	48	NaHSO ₃	93	> 99:1
11	<i>p</i> -CF ₃ C ₆ H ₄ CHO	Et	12	P(OPh) ₃	74	> 99:1
12	<i>p</i> -NO ₂ C ₆ H ₄ CHO	Bu ^t	11	NaHSO ₃	77	> 99:1
13		Et	12	P(OPh) ₃	96	> 99:1
14		Bu ^t	11	NaHSO ₃	88	> 99:1
15		Et	48	P(OPh) ₃	70	> 99:1
16		Bu ^t	48	NaHSO ₃	76	> 99:1
17	<i>n</i> -C ₉ H ₁₉ CHO	Et	48	P(OPh) ₃	74	86:14
18		Bu ^t	72	NaHSO ₃	84	95:5
19		Bu ^t	24	NaHSO ₃	74	> 99:1
20 ^d		Bu ^t	48	NaHSO ₃	69	> 99:1

^a Isolated yields. ^b The ratio of *E*:*Z* isomers was determined by ¹H NMR. ^c 5 mol% catalyst used. ^d The aldehyde used in this reaction was the crude product by Swern oxidation of 2,3-epoxy-5-benzoyloxypentane-1-ol. The yield refers to the total yields of oxidation reaction and Wittig-type reaction based on 2,3-epoxy-5-benzoyloxypentane-1-ol.

was used as the cocatalyst. Both aromatic aldehydes and aliphatic aldehydes could react with *tert*-butyl bromoacetate to afford the corresponding products in high yields with high stereoselectivity (entries 2, 4, 6, 8, 10, 12, 14, 16 and 18) in the presence of sodium bisulfite. It was noteworthy that phthalaldehyde could react with bromoacetate under these conditions and both aldehyde groups could be olefinated in high yield (entry 19 in Table 1). γ,δ -Epoxy- α,β -unsaturated ester, a useful building block, could also be synthesized by the current method in moderate yield with excellent stereoselectivity (entry 20 in Table 1).

This modification simplified the purification greatly and realized a phosphorus-free catalytic reaction. One could get the product just by filtering off the solid inorganic compounds and precipitating the catalyst after the reaction was completed.

Further study showed that α,β -unsaturated esters can be mass-produced under these reaction conditions and the catalyst could be recovered in quantity but lost its activity partially through multiple cycles. 2-Furaldehyde (10.85 mmol) was reacted with *tert*-butyl bromoacetate in the presence of sodium bisulfite and the desired product was obtained in 90% yield when 2 mol% of PEG-telluride was used. The catalyst was recovered in 100% yield by filtering off the solid of the reaction mixture, followed by addition of ether and collection of the precipitate. The recovered catalyst could be used in the second run but only 69% yield was obtained probably due to the decomposition of PEG-telluride during the catalytic olefination.¹²

Despite the advantages of easy separation and purification of products, the uses of polymer-supported catalysts suffered from lowered catalytic activity and stereoselectivity due to the restriction of polymer matrix that resulted in limited mobility and the accessibility of the active site. The PEG-telluride for catalytic ylide olefination reported here represents a novel, highly efficient polymer-supported catalyst that shows higher catalytic activity as compared to the free corresponding catalysts. Thus, we have developed an effective catalytic ylide olefination, which involves a simple procedure, mild reaction conditions, the use of catalytic PEG-telluride, and in particular, the use of sodium bisulfite as cocatalyst. The high catalytic efficiency, together with the ability to easily purify the product, demonstrates our method to be practical for the synthesis of α,β -unsaturated esters. The extension of our method to other olefination, epoxidation, cyclopropanation and aziridinations is in progress in our laboratory.

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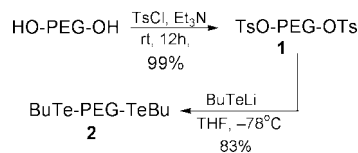
Notes and references

† Typical procedure for the synthesis of α,β -unsaturated esters. A, P(OPh)₃ as the cocatalyst: a mixture of catalyst **2** (0.0680 g, 2 mol%), ethyl bromoacetate (0.06 mL, 0.5 mmol), P(OPh)₃ (0.36 mL, 1.4 mmol) in toluene (3.0 mL) was stirred at 80 °C for 10 min and then K₂CO₃ (0.1796 g, 1.3 mmol) was added. The resulting suspension was stirred for 1 min, followed by addition of a mixture of aldehyde (1.0 mmol) and ethyl bromoacetate (0.1 mL, 0.90 mmol) in toluene (1.0 mL) in portions in 3.5 h. After the reaction was completed (monitored by TLC), the mixture was filtered rapidly through a glass funnel with a thin layer of silica gel and washed with ethyl acetate. The filtrate was concentrated and the residue was purified by flash column chromatography to afford the desired product.

B, NaHSO₃ as the cocatalyst: a mixture of catalyst **2** (0.0680 g, 2 mol%), *tert*-butyl bromoacetate (0.06 mL, 0.4 mmol), NaHSO₃ (0.1664 g, 1.6

mmol) and in THF (3.0 mL) was refluxed for 10 min and then H₂O (0.04 mL) was added. The resulting mixture was stirred for 10 min, followed by addition of K₂CO₃ (0.2760 g, 2.0 mmol). After being stirred for 1 min, to this suspension was added a mixture of aldehyde (1.0 mmol), *tert*-butyl bromoacetate (0.12 mL, 0.8 mmol) and water (0.03 mL) in THF (1.0 mL) in portions in 3.5 h. The reaction was quenched by anhydrous MgSO₄ after the reaction was complete (monitored by TLC). The resulting mixture was filtered rapidly through a glass funnel with a thin layer of silica gel and washed with ethyl acetate. The combined filtrate was concentrated and the residue was purified by flash column chromatography to afford the desired product.

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- PEG-supported telluride **2** was prepared readily from PEG 4,000 (MW Av. 3,000) in two steps by the sequential tosylation of PEG and the substitution of tosylate **1** with lithium butyltelluride in high yield as shown in the following scheme.



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