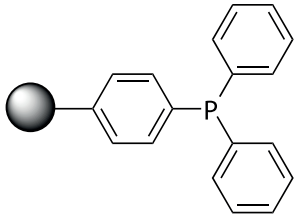
Biotage® PS-Triphenylphosphine

Solid-Supported Phosphine



Key Facts

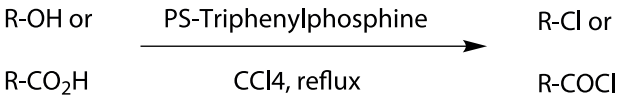
Stoichometric | Shelf Life | Capacity (mmol/g) | BSE/TSE | Scalable | Particle Size (µm) | Thermally & Mechanically Stable | Good Laboratory Practice | Bulk Density (g/L)

Specifications

Chemical Name:	Diphenylphosphino-polystyrene
Resin Type:	1% Cross-linked poly(styrene-co-divinylbenzene)
Application:	Chlorination of acids and alcohols, Wittig and Mitsunobu reactions, scavenging of alkyl halides
Typical Chlorination Conditions:	0.5 equivalent of acid or alcohol in CCl_4, 3 h, reflux
Typical Mitsunobu Reaction Conditions:	1.0 equivalent of alcohol, 1.5 equivalent of phenol, 2.2 equivalents of resin, and 1.6 equivalent of di-tert-butyl azodicarboxylate (DBAD) at room temperature for 16 h
Typical Wittig Reaction Conditions:	2.0 equivalents of ylide resin, 8.0 equivalent of sodium bis (dimethylsilyl)amide/tetrahydrofuran (NaHMDS/THF), resin washed with THF, followed by 1.0 equivalent of carbonyl compound in THF at room temperature for 16 h
Typical Alkyl Halide Scavenging Conditions:	3.0 equivalent of resin, DMF, 10 mL/g resin, 20 °C, 16 h

Biotage® PS-Triphenylphosphine is a diphenylphosphinated polystyrene resin that is a solid-supported equivalent of triphenylphosphine. The capacity of the resin is determined by the quantitation of benzyl bromide uptake in DMF (GC, internal standard method). The resin can readily convert alcohols or carboxylic acids to the corresponding chlorides or acid chlorides in carbon tetrachloride (Scheme 1).[1–3] Reaction conditions are relatively mild and the products are formed in high yield and purity.

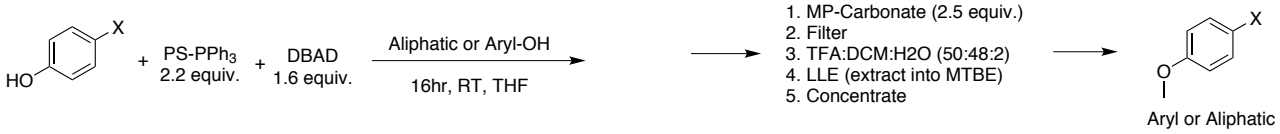
PS-Triphenylphosphine can also be used in Mitsunobu reactions to prepare aryl ethers in good-to-excellent yields and in high purities (Scheme 2).[4] The procedures described provide pure products without the need for laborious silica gel chromatography. Removal of excess phenol is accomplished



Scheme 1. Chlorination using PS-Triphenylphosphine.

with MP-Carbonate, while removal of excess DBAD (di-tert-butyl azodicarboxylate)-based hydrazide by-products may be accomplished by addition of TFA, followed by separation with silica or by liquid-liquid extraction (LLE). Reactions may be carried out at room temperature. Comparative studies suggest that there is no significant advantage to degassing the reaction mixture with nitrogen contrary to previous recommendations.[6] However, the order of addition of the substrates is critical in minimization of side products.

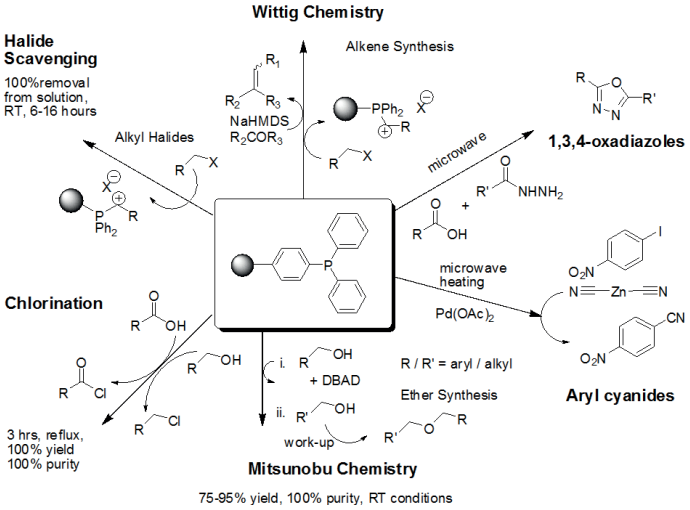
PS-Triphenylphosphine resin can also be used to synthesize olefins via the Wittig reaction (Scheme 3)[5,6] or as a scavenger for alkyl halides (Scheme 4).



Scheme 2. Mitsunobu reaction using PS-Triphenylphosphine.

Application Areas:

- Mitsunobu chemistry - in the synthesis of aryl or alkyl ethers[1]
- Chlorination - for the ready conversion of alcohols and acids to the corresponding halides or acid chlorides[2]
- Wittig chemistry - for C=C double bond formation in the synthesis of olefins[3]
- Scavenging - of alkyl halides in solution
- Cyanation - of aryl halides to form aryl cyanides[4]
- Cyclisation (condensation) to form 1,3,4-oxadiazoles[5]



Representative Procedures

Mitsunobu Reaction (Table 1, Entry 3)

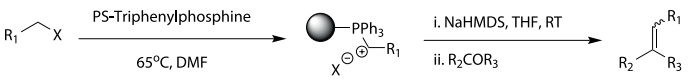
To a reaction vessel containing PS-Triphenylphosphine resin (311 mg, 0.66 mmol) was added a solution of p-methoxyphenol (0.45 mmol in 1 mL anhydrous THF). The suspension was allowed to stand for 5 minutes and then a solution of DBAD (di-tert-butyl azodicarboxylate) (1 mL, 0.48 mmol in anhydrous THF) was added. A further 0.5 mL of THF was added and the solution agitated at room temperature for 30 min. A solution of benzyl alcohol (1 mL, 0.3 mmol in anhydrous THF) was added and the reaction stirred overnight. In order to scavenge any excess phenols, MP-Carbonate resin (274 mg, 0.75 mmol) was then added and the mixture was stirred for a further 2 h. The resin was filtered and washed with THF (2 x 2 mL). To the filtrate was added 5 mL of a TFA/DCM/water (50:48:2) solution, and the mixture was stirred at RT for 2 h. The product was then extracted with MTBE, washed with water, and the MTBE layer concentrated to afford the product in 81% yield and 100% purity.

Chlorination (Table 2, Entry 4)

To a suspension of PS-Triphenylphosphine resin in CCl_4 (1 g, 2.12 mmol in 8 mL) was added a solution of piperonyl alcohol in CCl_4 (152 mg, 1 mmol in 2 mL). The reaction was heated at reflux for 3 h after which the mixture was filtered and the filtrate concentrated to give pure piperonyl chloride in 100% theoretical yield and purity.

Wittig Reaction (Table 3, Entry 2)

1-Iodobutane (0.53 mL, 8.52 mmol) was added to a suspension of PS-Triphenylphosphine (3.0 g, 4.26 mmol) in 30 mL DMF and the reaction was stirred for 48 h at 65 °C. The resulting phosphonium resin was washed with DMF (4 x 40 mL), toluene (4 x 40 mL), DCM (4 x 40 mL), and diethyl ether (4 x 40 mL) and dried in vacuo for 12 h. The dried phosphonium resin (0.2 g, 0.2 mmol) was added to a reaction vessel, followed by the addition of THF (2 mL). To the suspension of phosphonium resin was added a solution of sodium bis(dimethylsilyl)amide (2.0 M NaHMDS in THF, 0.4 mL, 0.8 mmol) at room temperature and the reaction stirred for 1 h. The ylide resin was washed with THF (5 x 4 mL) to remove excess base. To the suspension of ylide resin in anhydrous THF (2 mL) was added a solution of p-methoxybenzaldehyde (0.2 mL, 0.1 mmol) in THF (2 mL) and the mixture was stirred for 16 h. The reaction mixture was diluted with 2 mL hexane and directly applied to a silica SPE cartridge[8] followed by washing with hexane/ether (2:1, 2 x 4 mL). The solvent was concentrated to provide the olefin in 94% yield (GC purity 91%).



Scheme 3. Wittig reaction using PS-Triphenylphosphine.

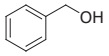
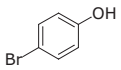
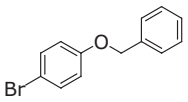
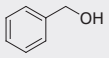
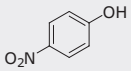
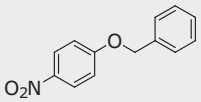
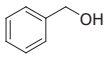
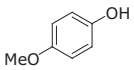
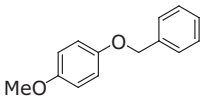
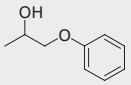
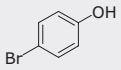
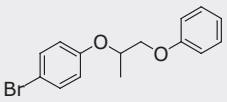
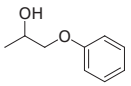
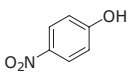
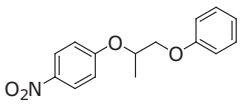
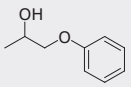
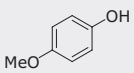
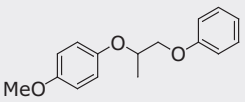
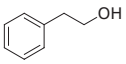
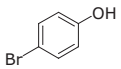
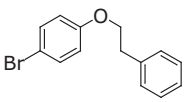
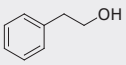
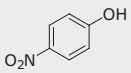
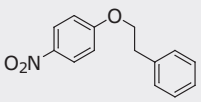
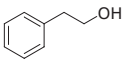
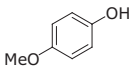
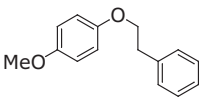
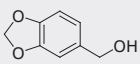
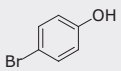
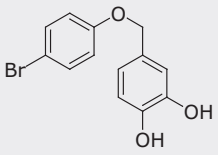
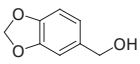
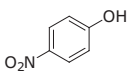
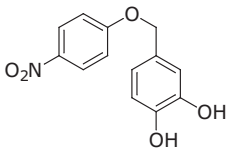
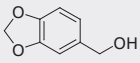
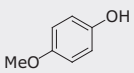
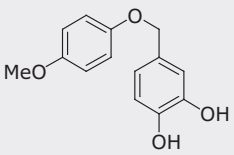
Entry	Alcohol	Phenol	Aryl Ether	% Yield	% Purity
1				80	100
2				73	98
3				81	100
4				87	97
5				92	100
6				84	100
7				81	100
8				76	100
9				91	96
10				86	100[a]
11				94	100[a]
12				92	100[a]

Table 1. Mitsunobu reaction using PS-Triphenylphosphine resin.
[a]Conversion 100%. The product was comprised of a mixture of hydrolyzed and un-hydrolyzed acetal protecting group. The product may be purified by LLE using aqueous base and MTBE.

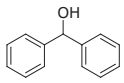
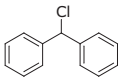
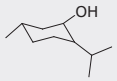
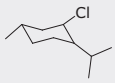
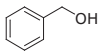
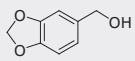
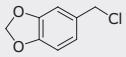
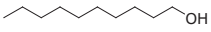
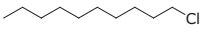
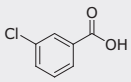
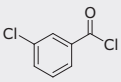
Entry	Alcohol	Product	% Isolated Yield	% Purity[a]
1			98	95
2			74[b]	64[c]
3			100	100
4			100	100
5			100	100
6			73	95

Table 2. Chlorination of acids and alcohols using PS-Triphenylphosphine.
[a]GC analysis: HP-5 phenylmethylsilicone column 100–250 ºC, 15 ºC/min, 10 min hold.
[b]Not isolated.
[c]Rate of reaction slower for hindered aliphatic secondary alcohols, 28% conversion after 3 h, 64% conversion after 16 h reflux. Determined by ^{1}H NMR.

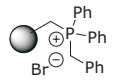
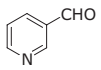
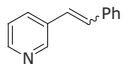
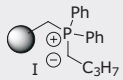
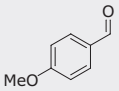
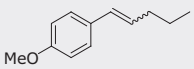
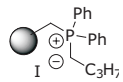
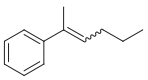
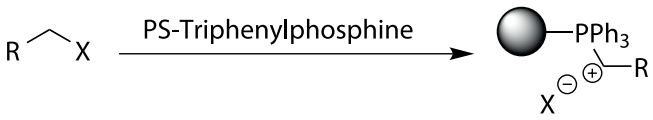
Entry	Phosphonium Resin	Carbonyl Compound	Olefin	% Isolated Yield (cis:trans)[a]	% GC Purity[b]
1				81 (5:1)	95
2				94 (2:3)	91
3				88 (2:1)	94

Table 3. Wittig reaction using PS-Triphenylphosphine.
[a]Ratio determined by ^{1}H NMR analysis.
[b]GC analysis: HP-5 phenylmethylsilicone column 100–250 ºC, 15 ºC/min, 10 min hold.

Scavenging of Alkyl Halide (Table 4, Entry 2)

PS-Triphenylphosphine (3.0 equivalents) was added to a solution of benzyl bromide (1.0 equivalent) in DMF (10 mL/g resin added) and the reaction stirred at room temperature for 5–16 h. Results by GC analysis indicate >80% scavenging after 6 h and 100% scavenging after 16 h.



Scheme 4. Scavenging of alkyl halides using PS-Triphenylphosphine

Entry	Material Scavenged	Solvent	Temp °C	% Scavenged[a]	Time (h)
1	Ethyl bromoacetate	DMF	20	100	6 h
2	Benzyl bromide	DMF	20	100	16 h
3	Cinnamyl chloride	THF:DMF	50	100	10 h
4	Cinnamyl bromide	DMF	20	100	16 h

Table 4. Scavenging of alkyl halides with PS-Triphenylphosphine resin (3.0 equiv.)
[a]GC analysis: HP-5 phenylmethylsilicone column 100–250 °C, 15 °C/min, 10 min hold.

Ordering Information

Part Number	Quantity
800510	3 g
800378	10 g
800379	25 g
800380	100 g
800381	1000 g

References

1. Relles, H. M.; Schluenz, R. W. *J. Am. Chem. Soc.* 1974, 96, 6469.
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6. Bernard, M.; Ford, W. T. *J. Org. Chem.* 1983, 48, 326.
7. Bolli, M. H.; Ley, S. V. *J. Chem. Soc., Perkin Trans.* 1. 1998, 15, 2243.
8. Part Number 440-0100-C. Compatible Solvents: DMF (3.5 mL/g), THF (4.1 mL/g), DCM (5 mL/g), benzene (3.1 mL/g).

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