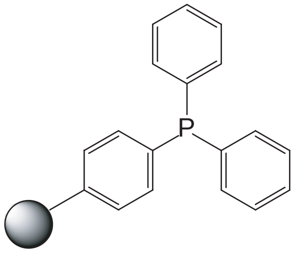
*Technical Note 508*

# PS-Triphenylphosphine

## Resin-Bound Phosphine



***Chemical Name:*** Diphenylphosphino-polystyrene

***Resin Type:*** 1% Cross-linked poly(styrene-co-divinylbenzene)

***Loading:*** Typical loading 2.2 mmol/g (minimum loading 1.8 mmol/g) based on uptake of benzyl bromide

***Bead Size:*** 75–150 microns, 100–200 mesh (95% within)

***Application:*** Chlorination of acids and alcohols, Wittig and Mitsunobu reactions, scavenging of alkyl halides

***Typical Chlorination Conditions:*** 0.5 equiv of acid or alcohol in $CCl_4$, 2 h, 80 ˚C

***Typical Mitsunobu Reaction Conditions:*** 1.0 equiv of alcohol, 1.0 equiv of phenol, 1.0 equiv of resin, and 1.0 equiv of diethylazodicarboxylate (DEAD) at room temperature for 16 h

***Typicl Wittig Reaction Conditions:*** 2.0 equiv of ylide resin, 8.0 equiv of sodium bis(dimethylsilyl)amide/ tetrahydrofuran (NaHMDS/THF), resin washed with THF, followed by 1.0 equiv of carbonyl compound in THF at room temperature for 16 h

***Typical Alkyl Halide Scavenging Conditions:*** 3.0 equiv of resin, DMF, 10 mL/g resin, 20 ˚C, 16 h

***Compatible Solvents:*** DMF (3.5 mL/g), THF (4.1 mL/g), DCM (4.9 mL/g), benzene (3.1 mL/g) and other solvents that swell gel-type polystyrene

PS-Triphenylphosphine is a phosphinated polystyrene resin that is a resin-bound equivalent of triphenylphosphine. The capacity of PS-Triphenylphosphine is determined by the quantitation of benzyl bromide uptake in DMF (GC, internal standard method). This resin can readily convert acids or alcohols to the corresponding acyl or alkyl chlorides in $CCl_4$ (**Scheme 1**).[1–3] The conditions are mild and products are formed in high purity (**Table 1**).

**Scheme 1. Chlorination using PS-Triphenylphosphine**

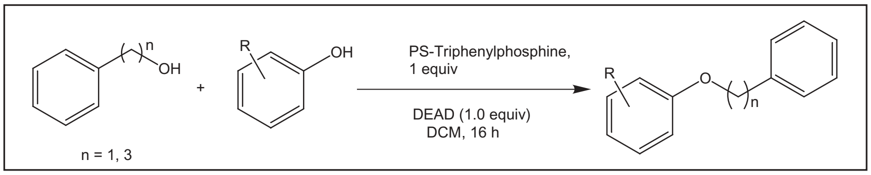
$$\begin{array}{c}\text{ROH or}\\ \text{RCOOH}\end{array} \xrightarrow[\text{CCl}_4,\ 80\ ^\circ\text{C}]{\text{PS-Triphenylphosphine (2 equiv)}} \begin{array}{c}\text{RCl or}\\ \text{RCOCl}\end{array}$$

| PART NUMBER | QUANTITY |
|---|---|
| 800378 | 10 g |
| 800379 | 25 g |
| 800380 | 100 g |
| 800381 | 1000 g |

Biotage

PS-Triphenylphosphine may also be utilized for Mitsunobu reactions to prepare aryl ethers in high purity (**Scheme 2, Table 2**).[4] Removal of hydrazide byproducts is readily accomplished using a silica SPE cartridge. PS-Triphenylphosphine resin can be utilized to synthesize olefins via the Wittig reaction (**Scheme 3, Table 3**).[5,6] The resin gave superior results for Wittig reactions when compared with another resin-bound triphenylphosphine (2% cross-linked), in which case starting materials were recovered. PS-Triphenylphosphine may also be used as a scavenger for alkyl halides (**Table 4**).

**Scheme 2. Mitsunobu Reaction using PS-Triphenylphosphine**



## REPRESENTATIVE PROCEDURE

**Chlorination (Entry 1, Table 1):**

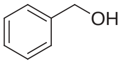
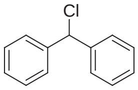
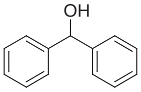
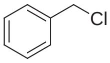
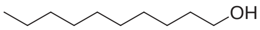
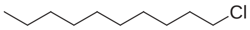
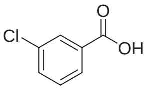
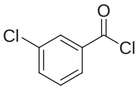
A 2.2 mL solution of benzyl alcohol (15.4 mg, 0.14 mmol) in $CCl_4$ was added under nitrogen to a reaction vessel containing 214.2 mg of PS-Triphenylphosphine resin (1.35 mmol/g, 0.29 mmol). The mixture was stirred and heated under reflux for 2 h at 80 ˚C. The product was filtered and the resin was washed with DCM (3 x 3 mL). GC quantitation (using biphenyl as internal standard) showed that benzyl chloride was produced from the resin in 100% yield and 98% purity.

## REPRESENTATIVE PROCEDURE

**Mitsunobu Reactions (Entry 3, Table 2):**

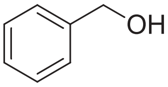
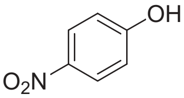
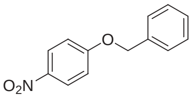
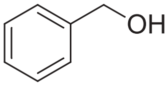
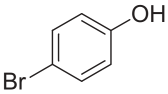
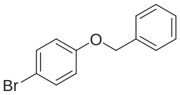
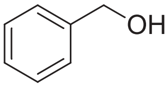
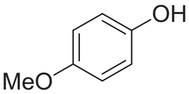
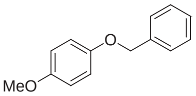
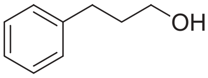
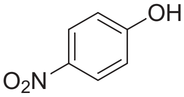
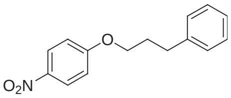
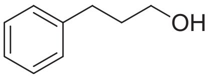
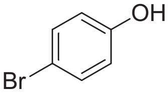
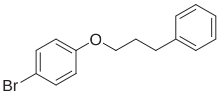
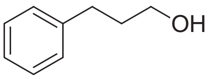
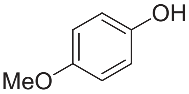
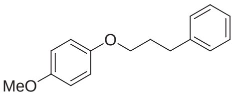
To a reaction vessel containing 1 mL DCM was added a solution of p-methoxyphenol (0.35 mL, 0.175 mmol) in 2 mL DCM , a solution of benzyl alcohol (0.35 mL, 0.175 mmol) in 2 mL DCM and 130 mg of PS-Triphenylphosphine resin (1.35 mmol/g, 0.175 mmol). The reaction mixture was stirred for 0.5 h at room temperature and cooled to 0 ˚C. A solution of DEAD (0.35 mL, 0.175 mmol) in 2 mL DCM was added to the reaction mixture at 0 ˚C and then stirred for 16 h at room temperature. The reaction mixture was washed with aq. KOH solution (5%, 4 mL), followed by 5 % aq. HCl (4 mL). The DCM extract was filtered into a vial and the resin was washed further with DCM (2 x 4 mL). The solvent was concentrated and the product was purified by filtration through a SPE cartridge (6 mL/2 g ISOLUTE® Silica Gel, part number 460-0200-C) with 10:1 of hexane/ether. The solvent was concentrated to provide *p*-methoxyphenyl benzyl ether in 88% yield (GC purity 96%). $^{1}$H NMR ($CDCl_3$ , 300 MHz): ∂ 7.45–7.30 (m, 5H,Ar-H), 6.95–6.83 (m, 4H,Ar-H), 5.03 (s, 2H, $CH_2$ ), 3.78 (s, 3H, $CH_3$ ) ppm; $^{13}$C NMR ($CDCl_3$ , 75 MHz): d 154.01, 152.98, 128.49, 127.82, 127.41, 115.88, 114.65, 70.73, 55.68 ppm.

**Table 1. Chlorination of Acids and Alcohols Using PS-Triphenylphosphine Resin**

| Entry | ROH or RCOOH | RCl or RCOCl | Yield | GC Purity[a] |
|---|---|---|---|---|
| 1 |  |  | 100% | 98% |
| 2 |  |  | 98% | 95% |
| 3 |  |  | 100% | 100% |
| 4 |  |  | 73% | 98% |

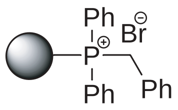
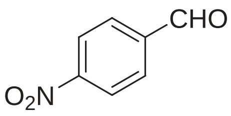
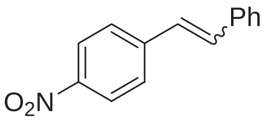
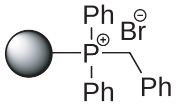
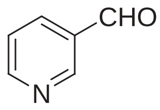
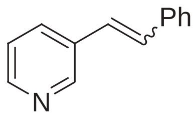
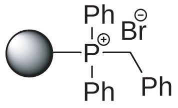
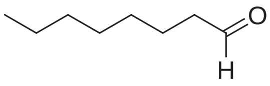
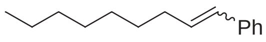
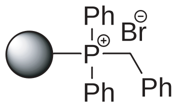
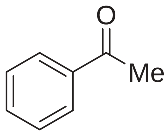
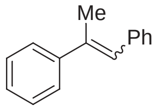
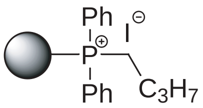
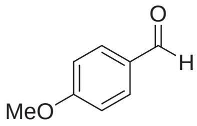
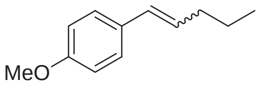
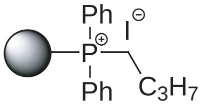
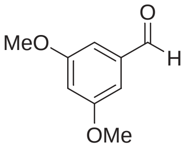
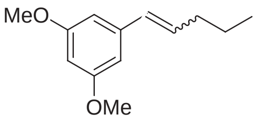
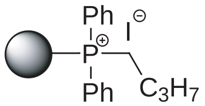
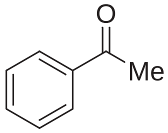
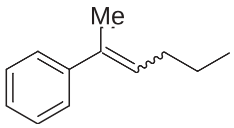
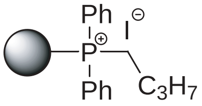
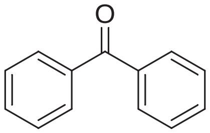
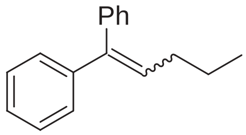
[a] GC analysis: HP-5 phenylmethylsilicone column 100–280 ˚C, 15 ˚C/min, 1 min hold

**Table 2. Mitsunobu Reaction Using PS-Triphenylphosphine Resin**

| Entry | Alcohol | Phenol | Aryl ether | % Yield (isolated) | GC Purity [a] |
|---|---|---|---|---|---|
| 1 |  |  |  | 79 | 98% |
| 2 |  |  |  | 80 | 92% |
| 3 |  |  |  | 88 | 98% |
| 4 |  |  |  | 62 | 100% |
| 5 |  |  |  | 68 | 96% |
| 6 |  |  |  | 75 | 100% |

[a] GC analysis: HP-5 phenylmethylsilicone column 100–280 ˚C, 15 ˚C/min, 10 min hold

**Table 3. Wittig Reaction Using PS-Triphenylphosphine Resin**

| Entry | Phosphonium Resin | Carbonyl Compound | Olefin | % Isolated Yield (cis:trans)[a] | GC Purity[b] |
|---|---|---|---|---|---|
| 1 |  |  |  | 98%<br>(3:1) | 96% |
| 2 |  |  |  | 81%<br>(5:1) | 95% |
| 3 |  |  |  | 96%<br>(1:1) | 81% |
| 4 |  |  |  | 88%<br>(2:1) | 87% |
| 5 |  |  |  | 94%<br>(2:3) | 91% |
| 6 |  |  |  | 87%<br>(1:3) | 98% |
| 7 |  |  |  | 88%<br>(2:1) | 94% |
| 8 |  |  |  | 82% | 99% |

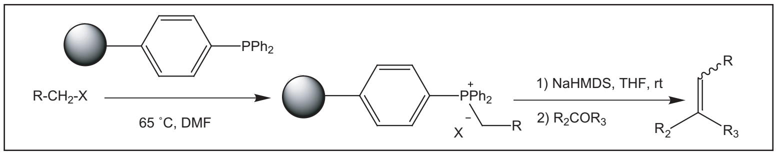
[a] Ratio determined by $^1$H NMR analysis.[b] GC analysis: HP-5 phenylmethylsilicone column 100–250 ˚C, 15 ˚C/min, 10 min hold

### Table 4. Comparative Scavenging of Alkyl Halides with PS-Tripheylphosphine Resin (3.0 equiv)

| Entry | Material Scavenged | Equiv | Solvent | Temp ˚C | % Scavenged [a] | Time (h) |
|---|---|---|---|---|---|---|
| 1 | Ethyl bromoacetate | 1.0 | DMF | 20 | 100 | 6 h |
| 2 | Benzyl bromide | 1.0 | DMF | 20 | 100 | 16 h |
| 3 | Cinnamyl chloride | 1.0 | THF:DMF | 50 | 68 | 10 h |
| 4 | Cinnamyl bromide | 1.0 | DMF | 20 | 100 | 16 h |

[a] GC analysis: HP-5 phenylmethylsilicone column 100–250 ˚C, 15 ˚C/min, 10 min hold

### Scheme 3. Wittig Reaction Using PS-Triphenylphosphine Resin



## REPRESENTATIVE PROCEDURE

**Wittig Reactions (Entry 5, Table 3):**

1-Iodobutane (0.53 mL, 8.52 mmol) was added to a suspension of PS-Triphenylphosphine (1.42 mmol/g, 3.0 g) in 30 mL DMF and the reaction was stirred for 48 h at 65 ˚C. The 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 addition of 2 mL THF. 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 mixture was 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 2 mL anhydrous THF was added a solution of *p*-methoxy-benzaldehyde (0.2 mL, 0.1 mmol) in 2 mL THF and stirred for 16 h. The reaction mixture was diluted with 2 mL hexane and directly applied to a silica SPE cartridge (6 mL/1 g silica gel, ISOLUTE SI, part number 460-0100-C), followed by washing twice with 4 mL of 2:1 hexane/ether. The solvent was concentrated to provide the olefin in 94% yield (GC purity 91%).

## REPRESENTATIVE PROCEDURE

**Alkyl Halide Scavenging (Entry 2, Table 4):**

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

## REFERENCES

1. Relles, H. M.; Schluenz, R.W. *J. Am. Chem. Soc.* 1974, *96*, 6469.
2. Regen, S. L.; Lee, D. P. *J. Org. Chem.* 1975, *40*, 1669.
3. Landi, J. J. Jr.; Brinkman, H. R. *Synthesis* 1992, 1093.
4. Tunoori, A. R.; Dutta, D.; Georg, G. I. *Tetrahedron Lett.* 1998, *39*, 8751.
5. Bernard, M.; Ford, W.T. *J. Org. Chem.* 1983, *48*, 326.
6. Bolli, M. H.; Ley, S.V. *J. Chem. Soc., Perkin Trans. 1.* 1998, *15*, 2243.

041-702

Biotage

**United Staes and Canada**
T: + 1 434 979 2319
Toll-Free: +1 800 446 4752
ordermailbox@biotage.com

**United Kingdom, EIRE**
Biotage
T: + 44 1443 811811
eurosales@eu.biotage.com

**Sweden**
Biotage
T: + 46 18 56 59 00
order@eu.biotage.com

**Japan**
Biotage
T: + 81 422 281233
order@biotage.co.jp