Keywords
Solid Phase Extraction, Metal Removal, Palladium, Suzuki-Miyaura Coupling, Screening

Background
The diversity and reliability of organometallic reactions has increased greatly over the last few decades, and it is commonplace to see such reactions in high throughput and process chemistry environments[1]. The removal of active metal species containing Palladium in particular, is essential to provide clean and safe compounds for screening. There are several products on the market that are effective in scavenging metal species, but they require long residency time in the reactions in order to reduce the metal concentrations to an acceptable level of <5ppm. Polymer Laboratories has developed a highly effective thiol containing polymeric SPE media, which can reduce the concentration of certain metal species to less than 1ppm after just one pass through the SPE device under gravity.

PL-Thiol SPE: Effective Removal of Palladium Species
Polymer Laboratories has developed a specially engineered polymeric SPE media, which has been further modified with a thiol-functionalized linker. In order to gain optimal flow characteristics, the polymeric SPE media is monodisperse, giving a very narrow particle size distribution. The resulting particle size of 45 microns results in a flow rate of around 0.5 mL per minute for most common non-viscous organic solvents. One of the key advantages of this SPE device is that the media is self-indicating when in the presence of palladium, thus clearly identifying when the device is nearing completion.

Removal of Palladium Residues from Suzuki-Miyaura Reactions
The Suzuki-Miyaura reaction is one of the most commonly used palladium catalyzed coupling reactions in modern drug discovery [2,3]. The ability to form diversely functional biaryl species under mild conditions makes it ideal for the high throughput chemist. One of the major problems associated with this coupling reaction is that the catalyst used, typically Palladium Tetrakis-triphenylphosphine Pd(PPh₃)₄, is very difficult to remove. Most polar organic molecules will act as excellent ligands for palladium, and the interactions can even survive preparative HPLC.

In the reaction below, the palladium content of the crude reaction products was determined using Inductively Coupled Plasma Mass Spectroscopy (ICP-MS). The crude material was then re-suspended in methanol and passed through a pre-conditioned PL-Thiol MP SPE cartridge. The palladium content after SPE treatment is shown in brackets.

In the second Suzuki-Miyaura reaction, Pd EnCat® 30 catalyst was used. The catalyst is a Palladium encapsulated polyurea polymer, which is highly effective in a range of cross coupling conditions [4,5]. Pd EnCat has a much lower level of palladium residues compared to a solution phase catalyst, 16.2 vs 95.4ppm for the Tetrakis-triphenylphosphine Palladium. After treatment with PL-Thiol SPE, the residual palladium left was 0.9 ppm.
The Removal of Palladium Species from Organic Solutions Using PL-Thiol MP SPE Devices

Typical Procedure

- Pre-condition SPE tube with MeOH (1mL)
- Add the Pd containing solution to the SPE tube.
- Allow the solution to pass through the SPE media under gravity.
- Once all of the solution has passed through, wash the SPE tube with 1-2 mL of a suitable solvent (MeOH, H2O etc.)
- Take the organic solution and remove the solvent in vacuo to yield desired compound free of metal contamination

References

Ordering Information

PL-Thiol MP SPE  500mg
Thiol functionalized resin
Loading 1.5mmol (nominal)
(Pack of 50 pre packed 6mL tubes)  3582-CM89

Polymer Laboratories manufactures SPE material in bulk quantities: Please contact us for a quotation

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