Nexgen Purifications Metal Scavenging

Thiopropyl

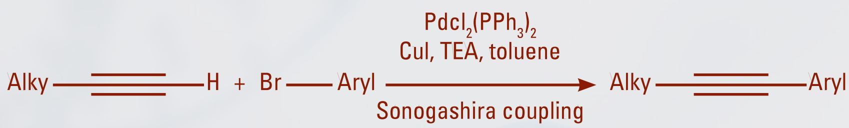
Nexgen Purifications Metal Scavenging Line is designed to retain excess organometallic catalysts commonly utilized in industrial synthesis enabling purification by simple filtration. Specific impurities are targeted including precious metals such as Pd, Pt, Ru and Rh to isolate the final desired product. Our Nexgen Purifications Metal Scavengers are highly selective in achieving the necessary purity levels for metal contamination, cost-effective, and available in cartridge format or bulk quantities.

Nexgen Purifications - Metal Scavenging Thiopropyl

Loading: 1.6 mmol/g
Surface Area: 500 m^2/g
Average Pore Size: 60Å
Pore Volume: 0.77 cm^3/g

Metals Targeted
Best Metals Scavenged: Ag, Hg, Os, Pd & Ru
Good Metals Scavenged: Cu, Ir, Pb, Rh & Sn

Case Study: Removal of Palladium from Sonogashira Coupling Reaction Using Various Metal Scavengers



Scavenger name	Pd in toluene solution (ppm)	Pd with respect to substrate (ppm)
No Scavenger (Control)	45.0	1800
Nexgen Purifications Silica Thiopropyl	< 3	< 120
Nexgen Purifications Silica Triamine	3.9	156
Competitor 1 MTcf	< 3	< 120
Competitor 1 SPM32-f	3.0	120
Competitor 1 SPM32	< 3	< 120
Competitor 1 SPM36-f	4.9	196
Competitor 1 SEM 26	4.0	160
Competitor 1 SPM36	6.7	268
Competitor 1 SEA	4.7	188
Competitor 1 STA 3	4.9	196
Competitor 2 MP	5.4	216
Competitor 2 TA	6.2	248
Competitor 2 AP	4.4	176
Competitor 3 Thiourea	< 3	< 120
Competitor 3 -Thiol	5.0	200
Competitor 3 DMT	4.0	160
Competitor 3 diamine	7.4	296
Competitor 3 triamine	5.0	200
Competitor 4 -TU	20.5	820
Competitor 4-BZA	16.2	648
Competitor 5 SA-FC Si-1	8.6	344

*All samples were incubated overnight at ambient temperature before filtration and all of them received 50 wt% loading of scavenger.

NEXGEN PURIFICATIONS

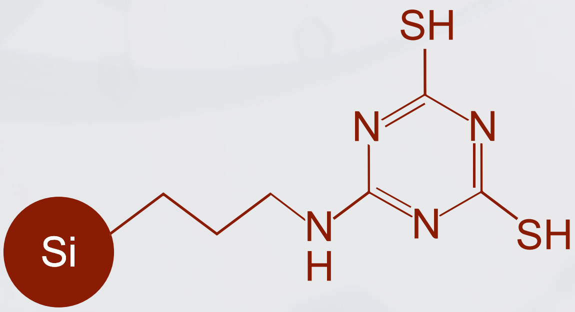
Nexgen Purifications

Metal Scavenging

Dimercaptotriazine (DMT)

Nexgen Purifications Metal Scavenging Line is designed to retain excess organometallic catalysts commonly utilized in industrial synthesis enabling purification by simple filtration. Specific impurities are targeted including precious metals such as Pd, Pt, Ru and Rh to isolate the final desired product. Our Nexgen Purifications Metal Scavengers are highly selective in achieving the necessary purity levels for metal contamination, cost-effective, and available in cartridge format or bulk quantities.

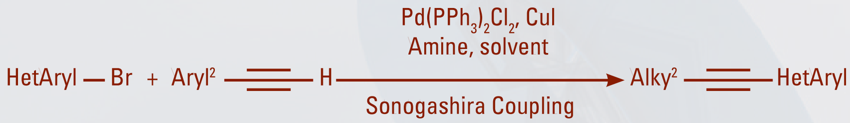
Nexgen Purifications – Metal Scavenging Dimercaptotriazine (DMT)



Loading: 0.83 mmol/g
Surface Area: 525 m^2/g
Average Pore Size: 60Å
Pore Volume: 0.79 cm^3/g

Metals Targeted
Best Metals Scavenged: Ir, Ni, Os, Pd, Pt, Rh & Ru
Good Metals Scavenged: Cd, Co, Cu, Fe, Sc & Zn

Case Study: Removal of Palladium from Sonogashira Coupling Reaction Using Various Metal Scavengers



Treated 2.6 g solution in 2-MeTHF containing about 0.5 g of product. Loadings are g/g of contained product. Pd results are estimated based on contained product.

Scavenger name	Loading (g/g)	Pd with respect to substrate (ppm)
Untreated	NA	154
Nexgen Purifications Si-DMT Lot AA	20%	20
Nexgen Purifications Si-DMT Lot AB	20%	18
Nexgen Purifications Thiopropyl	20%	59
Competitor 1 SPM32	10%	41
Competitor 1 SPM32	20%	39
Competitor 1 STA3	10%	34
Competitor 1 STA3	20%	22
Competitor 2 Si-Thiol	20%	40
Competitor 2 Si-DMT	20%	ca. 21
Competitor 3 G60 only	20%	95
10% Aq N-Ac-Cysteine (pH 3)	500%	92
10% Aq N-Ac-Cysteine (pH 11)	500%	45

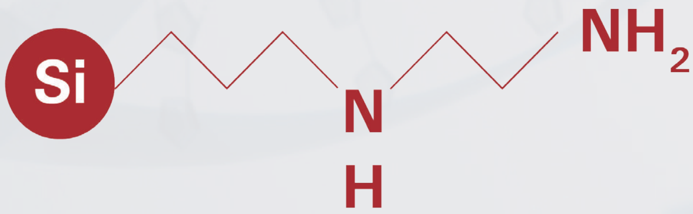
Nexgen Purifications Metal Scavenging

Primary/Secondary Amine (PSA)

Nexgen Purifications Metal Scavenging Line is designed to retain excess organometallic catalysts commonly utilized in industrial synthesis enabling purification by simple filtration. Specific impurities are targeted including precious metals such as Pd, Pt, Ru and Rh to isolate the final desired product. Our Nexgen Purifications Metal Scavengers are highly selective in achieving the necessary purity levels for metal contamination, cost-effective, and available in cartridge format or bulk quantities.

NEXGEN- METAL SCAVENGING
PRIMARY/SECONDARY AMINE (PSA)

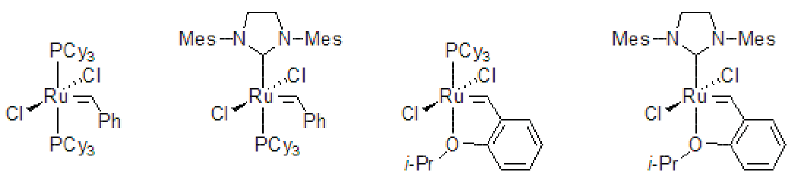
Nexgen – Metal Scavenging Primary/Secondary Amine (PSA)



Organic Loading: ≥ 0.80 mmol/gm
Surface Area: 500 m^2/g
Average Pore Size: 60Å
Pore Volume: 0.77 cm^3/g

Metals Targeted
Best Metals Scavenged: Cr, Pd, Pt, Ru, W, & Z
Good Metals Scavenged: Cd, Co, Cu, Fe, Hg, Ni, Pb, Se, & Sc

Olefin metathesis has become a well-established synthetic technique for the clean development of innumerable classes of chemical structures. Ruthenium-based catalysts are traditionally the go-to in the aforementioned reactions (ROM(P) and RCM), where a majority of the successful examples in the below reaction are achieved via Grubbs and Hoveyda-Grubbs catalysts. In order to successfully reach the maximum tolerated concentrations of residual ruthenium, various functionalized silica based sorbents were evaluated for their scavenger efficiency.



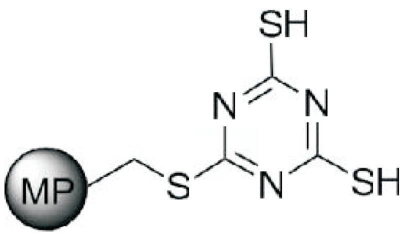
Grubbs 1st Generation — Grubbs 2nd Generation — Hoveyda-Grubbs 1st Generation — Hoveyda-Grubbs 2nd Generation

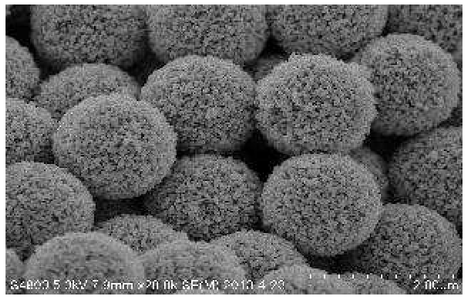
Case Study: Removal of Residual Ruthenium Concentrations Using 3 Different Metal Scavengers

Initial Ru (ppm)	Scavengers	Conditions	# of treatment	Ru (ppm)	% Yield of API
2000	Competitor 1 - Diamine	20 wt%, THF, RT, 16 h	Pass 1	950	~95.4
			Pass 2	710	
			Pass 3	600	
2000	**Nexgen PSA**	20 wt%, THF, RT, 16 h	Pass 1	800	**~99.8**
			Pass 2	**390**	
			Pass 3	340	
2000	Competitor 2- Complex Amine Resin	20 wt%, THF, RT, 16 h	Pass 1	1300	~92.8
			Pass 2	1100	

NEXGEN PURIFICATIONS

MP-TMT Highlight - Metal scavenging with resins / silicas in DMF





	Loading (mmol g)	$Pd(OAc)_2$ 3 eq (ppm)	$CuCl_2 - 2H_2O$ 3 eq (ppm)	$ZnCl_2$ 3 eq (ppm)	$CoCl_2 - 6H_2O$ 3 eq (ppm)	$Ni(OAc)_2 - 4H_2O$ 3 eq (ppm)	$FeCl_3 - 6H_2O$ 3 eq (ppm)
MP Polyamine (Nexgen)	1.71	0	0	0	0	15	0
MP-TMT (Nexgen)	1.51	0	-	-	-	-	-
Polyamine (Purolite S985)	3.1	-	-	-	-	-	-
Polyamine (Purolite S992)	1.52	-	-	-	-	-	-
Polyamine (Purolite A149)	1.7	-	-	-	-	-	-
Polyamine (Purolite A170)	0.8	-	-	-	-	-	-
MP-Thiol (Purolite S924)	7.7	-	-	-	-	-	-
Thiourea (Purolite S914)	2.5	196	-	-	-	-	-
Thiourea (Purolite TP214)	1.68	209	-	-	-	-	-
MP-Iminodiacetic (Purolite S930)	3.21	-	-	-	-	-	-
Aldoxime (Purolite S910)	6.95	-	-	-	-	-	-
QuadraPure BZA	1.3	562	0	1	0	231	27
QuadraPure BDZ	1.3	466	697	718	735	353	696
QuadraPure TU	1.3	646	0	235	307	482	505
QuadraPure DET	1	1157	1174	1176	1048	849	1033
QuadraPure IDA	1.3	1429	832	1116	982	441	886
QuadraPure AMPA	1.3	1279	1220	1044	998	374	836
SiliaMet DMT	0.62	50	22	310	214	5	442
SiliaMet Triamine	1.28	53	2	7	0	13	0
SiliaMet TAAcOH	0.44	68	61	490	244	3	286
SiliaMet TAAONa	0.45	58	0	1	0	1	0
SiliaMet Thiol	1.28	52	1226	1151	1129	392	1088
SiliaMet Thiourea	1.08	44	208	957	946	3	1079
SiliaMet Imidazole	1.16	60	11	49	53	904	127
SiliaMet Cysteine	0.35	44	278	197	84	6	20

Scavenging experimental procedure:
Resins were added to 10mL stock solutions (2000 ppm) of catalyst in DMF at room temperature and stirred for 2 hours.
Rinsed with DMF (3x2mL).
The DMF solutions were analyzed by Atomic Absorption (detection limit: 0.5 ppm)
"0 ppm" means less than the limit of detection (e.g.: 0.5 ppm).
"- ppm" means that the colored solution was still visible and wasn't analyzed.

Metal Scavenger Sample Calculations

Pd	106.42 g/mol
$Pd(OAc)_2$	224.5 g/mol

Based on known metal concentration (ppm)
For instance, if you know the palladium concentration in 950G of material is 1000ppm

Known values:
- Loading of the Scavenger (Silica Thiopropyl) = 1.6 mmol/g
- Molecular Weight of metal: Pd = 106.42 g/mol
- Residual metal concentration: 800ppm of Pd
- Amount of Pd to be scavenged = 950G

1. Determine the amount of palladium to be scavenged

$$\text{Amount of Pd (mg)} = \frac{\text{Residual metal concentration } \times \text{ Amount of Pd to be scavenged}}{1000}$$

$$\text{Amount of Pd (mg)} = \frac{\text{800ppm x 950G}}{1000} = \text{760 mg of Pd in 950 of product}$$

$$\text{Conversion in mmol of Pd} = \frac{\text{Amount of Pd in mg}}{\text{Molecular Wt of Metal}}$$

$$\text{Conversion in mmol of Pd} = \frac{\text{760 mg}}{\text{106.42 g/mol}} = \text{7.14 mmol of Pd}$$

2. Calculate the amount of scavenger (Silica Thiopropyl) to use (4 equivalents)

$$\text{Amount of Silica Thiopropyl to use} = \frac{\text{Number of mmol of metal concentration}}{\text{Silica Thiopropyl Loading}}$$

$$\text{Conversion in mmol of Pd} = \frac{\text{7.14 mmol of Pd}}{\text{1.6 mmol/g}} = \text{4.46 g of Silica Thiopropyl for 1 eq.}$$

To scavenge 800ppm of Pd, 4.46 g of Silica Thiopropyl is needed if using only one equivalent. However, it is recommended to start with a minimum of 4 equivalents at first meaning amount of Silica Thiopropyl will be 4 times higher (17.85 g). Moreover, many chemists start with very high equivalents (20 or more) to identify best scavenger to use and then optimize, thereafter. Sometimes, the residual metal concentration is unknown. In these cases, the amount (g) of Pd to be scavenged can be replaced by the amount of metal catalyst used for the reaction:

Based on amount of metal catalyst used
Known values:
- Amount of metal catalyst used: Ex. 25g of Pd(OAc)2
- Metal catalyst molecular weight: Pd(OAc)2 = 224.5 g/mol

1. Determine the amount of palladium to be scavenged

$$\text{Amount of Pd (mg)} = \frac{\text{Qty of catalyst used for the reaction x 1000}}{\text{Metal catalyst molecular weight}}$$

$$\text{Amount of Pd (mg)} = \frac{\text{25g of Pd(OAc)2 x 1000}}{\text{224.5 g/mol}} = \text{111.36 mmol of Pd (maximum to be scavenged)}$$

The amount of Silica Thiopropyl to be used can then be determined as stated above (see #2). In this particular example, one equivalent of Silica Thiopropyl corresponds to 69.6 g.

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