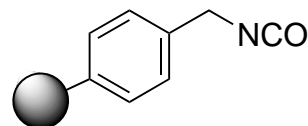


PS-Isocyanate

Nucleophile Scavenger



Chemical Name: Polystyrene methylisocyanate

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

Capacity: 1.0–1.8 mmol/g (based on benzylamine uptake)

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

Application: Scavenging nucleophiles, including amines and alkoxides

Typical Scavenging Conditions: 2–3 equiv relative to nucleophile, 1–16 h, 20 °C

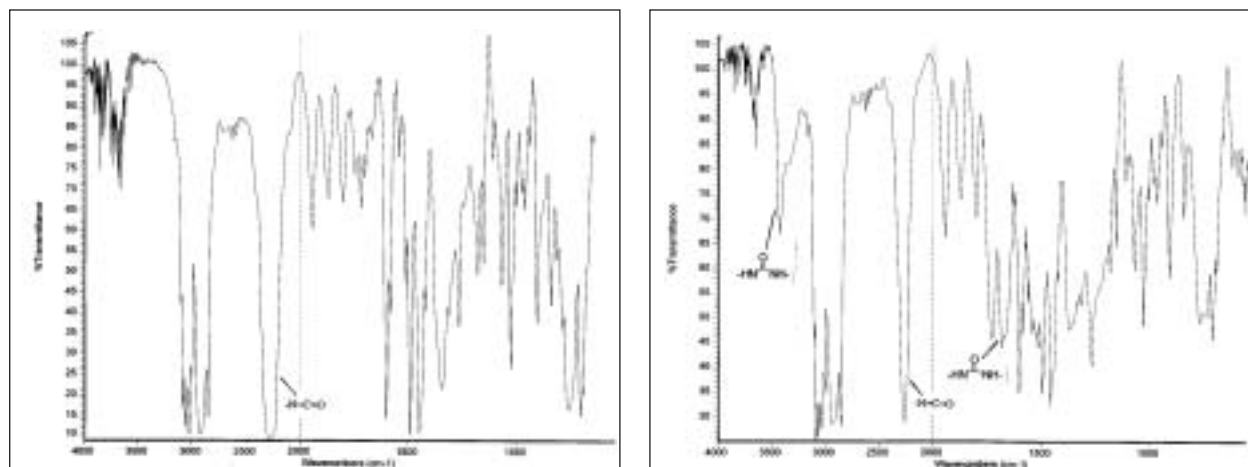
Compatible Solvents: DCM (9.5 mL/g), DCE (7.2 mL/g), THF (8.2 mL/g), toluene (7.8 mL/g)

PS-Isocyanate is a 1% cross-linked poly(styrene-*co*-divinylbenzene) which has pendent benzylisocyanate functionality. The resin is produced from aminomethyl resin by a superior process which gives high conversion with minimal urea formation as determined by IR spectroscopy (**Figure 1**). The resin can readily scavenge excess nucleophiles from solution, which are often used to drive reactions to completion. This facilitates workup and purification.^{1–5} The reaction of nucleophiles with the isocyanate moiety occurs without liberation of small molecule byproducts.

Removal of nucleophiles from solution generally requires 2–3 equiv of PS-Isocyanate depending on substrate reactivity. Comparative scavenging of amines (0.2–0.05 M) of varying reactivity was tested as a function of time and temperature (**Table 1**). Typical aliphatic amines are completely sequestered by 3 equiv of PS-Isocyanate within 1 h. Three equiv of PS-Isocyanate sequestered 100% aniline at room temperature over 16 h. A less reactive aromatic amine, 2-aminobenzophenone, was not completely sequestered even at elevated temperatures. The use of DIEA as a catalyst did not improve the scavenging efficiency of PS-Isocyanate towards aromatic amines. Alcohols were not reactive towards PS-Isocyanate at room temperature, suggesting that aliphatic amines can be selectively sequestered in the presence of alcohol functionality. More nucleophilic alcohols may be removed at elevated temperatures.

PART NUMBER	QUANTITY
800260	10 g
800261	25 g
800262	100 g
800311	1000 g

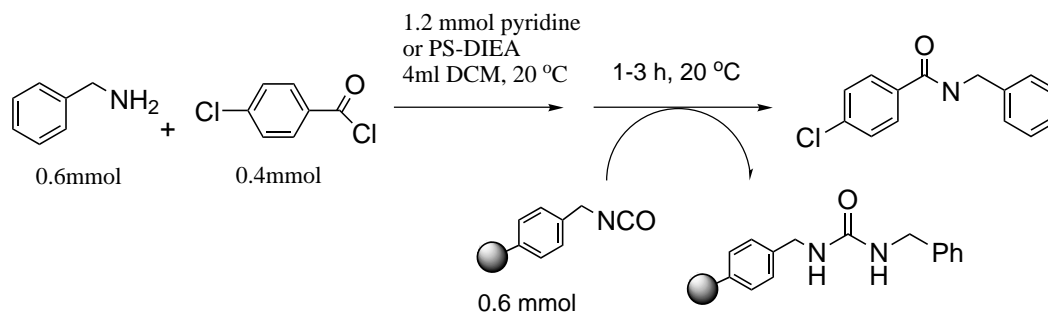
Figure 1. FT-IR Spectra of (a) PS-Isocyanate, 1.2 mmol/g; (b) polystyrene methylisocyanate, 0.9 mmol/g, prepared by the procedure described in reference 4.



Upon completion of the scavenging, the product is washed away from the resin with a suitable solvent. Suitable solvents include those which dissolve the product and swell polystyrene, but are not nucleophilic enough to react with the resin. DCM, dichloroethane, THF, and toluene are all good choices with DCM being preferred.

PS-Isocyanate was tested in an amide bond forming application where 4-chlorobenzoyl chloride was allowed to react with excess benzylamine in the presence of PS-DIEA resin as the base (**Scheme 1, Table 2**). Upon completion of the reaction, the excess benzylamine was scavenged using 3 equiv PS-Isocyanate resin. The product was then isolated by washing it free of the resin followed by concentration. The yields were determined gravimetrically and the purities by GC. PS-Isocyanate was also used to sequester excess secondary amines in the preparation of tertiary amines using PS-TsCl.

Scheme 1:



REPRESENTATIVE PROCEDURE

Amide Formation Reaction:

4-chlorobenzoyl chloride was allowed to react for 1 hour with 1.5 equiv of benzylamine in DCM with 3 equiv of PS-DIEA resin as the base.

Reaction Workup:

The excess benzylamine was scavenged by adding PS-Isocyanate resin (3 equiv relative to excess amine). The beads were removed by filtration, washed 2 x with DCM and the combined filtrate was concentrated to afford the benzyl 4-chlorobenzamide as the sole product in 87% yield.

REFERENCES

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Table 1. Comparative Scavenging of Nucleophiles in Dichloromethane

Nucleophile Scavenged	PS-Isocyanate (equiv)	Temp (°C)	% Scavenged	
			1 h	16 h
piperidine	3.0	20	100	–
benzyl amine	3.0	20	100	–
aniline	3.0	20	–	100
aniline	3.0	60 ¹	92	100
2-aminobenzophenone	3.0	60 ¹	–	81

¹Dichloroethane solvent

Table 2. Amide Bond Formation

Base	Scavenging Time	% Yield	% Purity
PS-DIEA	1 hr	87.0	96.7
PS-DIEA	3 hr	87.4	94.5

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