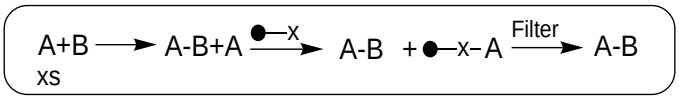
Applications

Scavenger Resins in Combinatorial Chemistry

Combinatorial chemistry has become an increasingly valuable tool for drug discovery.[1] The majority of the work in this area has concentrated on solid-phase reactions.[1] Although there have been instances of solution-phase libraries,[2] their widespread use has been limited by the ease of purification of the reaction mixtures at each step.

Within the last few years, the use of scavenger or quench reagents for solution-phase synthesis has been reported.[3] The theory behind this concept is that the scavenger/quench resins contain active groups that mimic the limiting reagent(s) in the reaction. Upon completion of the reaction, the resin is added to the reaction mixture to bind any unreacted reagent. Filtration of the resin-bound reagent yields a relatively pure product.

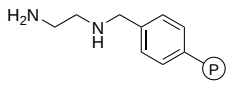
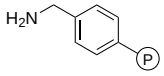
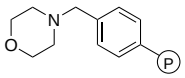
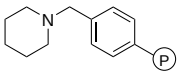
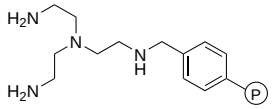
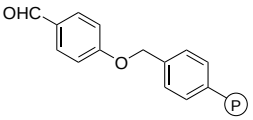
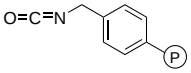
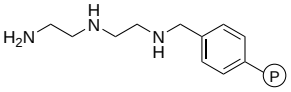


There are many advantages to using scavenger reagents. Since the reactions are run in solution, there is no need to invest time and effort in transferring and optimizing the reactions for use in the solid phase. Also, more than one scavenger resin can be used concurrently to remove multiple reagents and/or reaction byproducts, thus significantly easing reaction workup. By choosing the appropriate scavenger resin, one can eliminate the potential need for large excesses of expensive reagents. Most scavenger resins can be synthesized from commercially available materials; however, a good number of them are now commercially available. (Please see the Aldrich catalog listings provided in the table below.)

The choice of scavenger resin strongly depends on the type of reagent or byproduct that needs to be removed from the reaction mixture. Listed in the table below are some of the more common resins and the functional groups with which they react.

Some of the compound libraries synthesized by the scavenger/quench resin method are ureas,[3a,3b] thioureas,[3a] amides,[3b,3d] sulfonamides,[3a,3b,3d] carbamates,[3b] benzoxazinones[4] and dihydropyridones.

For additional information, including unit sizes and prices, please contact your local Sigma-Aldrich office or visit the Combinatorial Chemistry section of our Web site at www.sigma-aldrich.com/combichem.

Polystyrene Resin	Structure	Reacts With...
47,209-3 **Ethylenediamine, polymer-bound**		RCOCl, RSO_2Cl, RNCS, RNCO, H^+
47,366-9, 2 mmol/g; 47,367-7, 4 mmol/g **Poly(styrene-*co*-divinylbenzene), aminomethylated**[3a]		RCOCl, RSO_2Cl, RNCS, RNCO, H^+
49,381-3 **Morpholine, polymer-bound**[5]		H^+
49,461-5 **Piperidine, polymer-bound**		H^+
47,210-7 **Tris(2-aminoethyl)amine, polymer-bound**[3a,5]		RCOCl, RSO_2Cl, RNCS, RNCO, H^+
47,208-5 **4-Benzyloxybenzaldehyde, polymer-bound**[5]		$RNHNH_2$, NH_2OR, RNH_2
47,368-5 **Isocyanate, polymer-bound**[3a,3b]		RNH_2
47,978-0 **Diethylenetriamine, polymer-bound**[3c,3d]		RCHO, RCO_2H, RCOCl, anhydrides

References: (1) Review articles: (a) Hermkens, P.H.H. et al. *Tetrahedron* **1996**, *52*, 4527. (b) Idem *ibid.* **1997**, *53*, 5643. (c) Balkenhohl, F. et al. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2288. (d) Thompson, L.A.; Ellman, J. A. *Chem. Rev.* **1996**, *96*, 555. (e) Terrett, N.K. et al.. *Tetrahedron* **1995**, *51*, 8135. (2) See the solution-phase selections in refs. 1c, 1d, & 1e. (3) (a) Booth, R. J.; Hodges, J. C. *J. Am. Chem. Soc.* **1997**, *119*, 4882. (b) Kaldor, S.W. et al. *Tetrahedron Lett.* **1996**, *37*, 7193. (c) Parlow, J.J. et al. *J. Org. Chem.* **1997**, *62*, 5908. (d) Flynn, D.L. et al. *J. Am. Chem. Soc.* **1997**, *119*, 4874. (4) Parlow, J.J.; Flynn, D.L. *Tetrahedron* **1998**, *54*, 4013. (5) Cresswell, M.W. et al. *ibid.* **1998**, *54*, 3983.