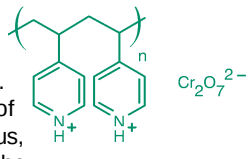
Polymeric Regeants and Supports for SPOS

The importance of solid phase organic synthesis (SPOS) and combinatorial chemistry in the discovery of new drugs has spurred renewed interest in both polymeric reagents and solid supports. SPOS offers distinct advantages over solution phase chemistry: (1) reactions may be driven to completion using excess reagents; (2) byproducts and excess reagents can often be removed by washing or filtering the resin, thus simplifying workups; and (3) polymeric reagents are often more convenient to use and easier to handle. Aldrich provides a variety of polymeric reagents and solid supports for your convenience, a few of which are highlighted below. For reagents and supports not listed here, please visit our Web site at **www.sigma-aldrich.com/combichem** or email our Technical Services Department: **aldrich@sial.com**.

Polymer-Bound Dichromate and Perbromide

Employed in Parlow's groundbreaking work in which three synthetic transformations were carried out *simultaneously* in one reaction vessel using three different polymeric reagents. The substrate was simply added to a slurry of the three polymeric reagents in cyclohexane. Thus, *sec*-phenethyl alcohol was oxidized to acetophenone with polymer-bound dichromate. The ketone was then α-brominated with polymer-supported tribromide. Displacement with a polymer-bound pyrazol-3-ol gave the desired product in 48% yield after simple filtration. No isolation of the intermediates was required. The synthesis takes advantage of the ability of polymers to isolate reactive species, thereby allowing their coexistence in the same reaction vessel.



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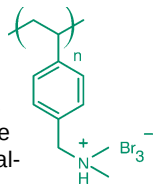


33,809-5

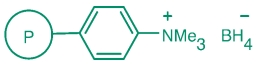
Parlow, J.J. *Tetrahedron Lett.* **1995**, *36*, 1395.

23,746-9 **Poly(4-vinylpyridinium dichromate),** cross-linked **25g; 100g**

33,809-5 **Tribromide, polymer-supported** (tribromide on Amberlyst® A-26), ~1mmol Br_3^-/g resin **5g; 25g**

Borohydride Exchange Resin (BER)

Borohydride exchange resin (borohydride on Amberlite® IRA-400) has been used to reduce a wide variety of functional groups with the added advantage that boron species remain bound to the polymer, greatly simplifying workups. For instance, BER selectively reduces α,β-unsaturated carbonyl compounds to allylic alcohols.[1] It also reduces aryl azides and aryl sulfonyl azides to arylamines and arylsulfonamides.[2] In combination with $Ni(OAc)_2$, BER selectively reduces both aryl and alkyl nitro groups in the presence of other functional groups,[3] and also selectively dehalogenates alkyl bromides and iodides, and α-halo amides and esters.[4] Reductive amination of aldehydes and ketones occurs in good yields with BER[5] and was recently reported in a novel solution phase approach to combinatorial libraries.[6]

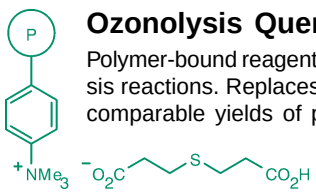


33,809-5

(1) Sande,A.R. et al. *Tetrahedron Lett.* **1984**, *25*, 3501. (2) Kabalka, G.W. et al. *Synth. Commun.* **1990**,*20*, 293. (3) Yoon, N.M.; Choi, J. *Synlett* **1993**, 135. (4) Yoon, N.M. et al. *J. Org. Chem.* **1994**, *59*, 4687. (5)Yoon,N.M.etal. *Synth.* Commun. **1993**, *23*,1595. (6) Kaldor, S.W. et al. *Tetrahedron* Lett.**1996**, *37*, 7193.

32,864-2 **Borohydride, polymer-supported** (borohydride on Amberlite® IRA-400) 2.5mmol BH_4^-/g resin **25g; 100g**

Ozonolysis Quench Reagent



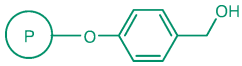
45,901-1

Polymer-bound reagent for the reductive quenching of ozonolysis reactions. Replaces volatile dimethyl sulfide and provides comparable yields of product. Simple filtration removes the sulfur-containing byproducts.

Appell, R.B. et al. *Synth. Commun.* **1995**, *25*, 3589.

45,901-1 **3,3'-Thiodipropionic acid, polymer-bound,** contains ~2.5meq S/g resin **10g; 50g**

Wang Resin



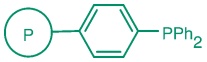
47,063-5

The Wang resin (4-benzyloxybenzylalcohol, polymer-bound) has become a very useful tool in SPOS and combinatorial chemistry due to its ability to support a diverse range of reactions. Recently, this resin has been employed in the preparation of pyridines and pyrido-[2,3-*d*]pyrimidines via Knoevenagel and Hantzsch condensation reactions.[1] Dihydropyrimidines can be prepared via the multicomponent Biginelli condensation using a Wang resin-linked GABA urea.[2] The resin has also been successfully employed in palladium-mediated Heck reactions between aryl halides and olefins.[3] Additionally, the Wang resin has been utilized in the solid-phase synthesis of lavendustin A, a potent tyrosine kinase inhibitor, and in the combinatorial synthesis of sixty structurally related lavendustin A analogs.[4]

(1) Gordeev, M.F. et al. *Tetrahedron Lett.* **1996**, *37*, 4643. (2) Wipf, P.; Cunningham, A. *ibid.* **1995**, *36*, 7819. (3) Yu, K.-L. et al. *ibid.* **1994**, *35,* 8919. (4) Green, J. *J. Org. Chem.* **1995**, *60*, 4284.

47,063-5 **4-Benzyloxybenzyl alcohol, polymer-bound,** ~0.5 -1.0 mmol OH/g resin, 200-400 mesh **5g; 25g**

Polymer-Bound Triphenylphosphine



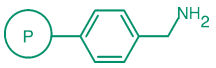
36,645-5

Polymer-bound phosphonium salts, which are readily prepared from polymer-bound triphenylphosphine, have been shown to be efficient, traceless linkers for SPOS.[1] The phosphonium salts have been manipulated in a number of ways to liberate products lacking polar functionality. Additionally, the phosphine resin complexed with iodine yields a convenient peptide coupling reagent, giving peptides in high yields with no detectable racemization.[2]

(1) Hughes, I. *Tetrahedron Lett.* **1996**, *37*, 7595. (2) Caputo, R. et al. *Synthesis* **1995**, 141.

36,645-5 **Triphenylphosphine, polymer-supported,** ~3mmol P/g resin **1g; 5g**

Aminomethylated Polystyrene



34,391-9

Aminomethylated polystyrene, a versatile resin for SPOS, has recently been employed in the synthesis of 1,4-benzodiazepines via the Stille reaction; a number of examples using a traceless silicon-based linker were reported.[1,2] Moore and co-workers reported the solid-supported synthesis of phenylacetylene oligomers via the Heck reaction.[3] The resin has also been used as a solid phase scavenger for excess isocyanates, acid chlorides, chloroformates, and sulfonyl chlorides in solution phase chemistry.[4]

(1) Plunkett, M.J.; Ellman, J.A. *J. Am. Chem. Soc.* **1995**, *117*, 3306. (2) Idem *J. Org. Chem.* **1995**, *60*, 6006. (3) Young, J.K. et al. *J. Am. Chem. Soc.* **1994**, *116*, 10841. (4) Kaldor, S.W. et al. *Tetrahedron Lett.* **1996**, *37*, 7193.

34,391-9 **Poly(styrene-*co*-divinylbenzene), aminomethylated,** 1% cross-linked, 200-400 mesh, 1mmol N/g resin **1g; 5g**

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