The "Resin-Capture – Release" Hybrid Technique: A Merger between Solid- and Solution-Phase Synthesis

Andreas Kirschning,*[a] Holger Monenschein,[b] and Rüdiger Wittenberg[a]

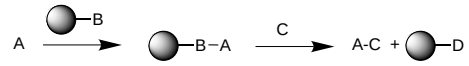
Abstract: A polymer-assisted organic synthesis that combines the concept of solid-phase synthesis with the idea of polymer-supported scavenging reagents has recently appeared on the chemistry scene. This technique has frequently been termed the "resin-capture – release" methodology and is initiated by the immobilization of a small molecule on a polymeric support. This intermediate is subjected to a second transformation by adding a new reaction partner in solution. This reactant plays two roles: a) the chemical alteration of the polymer-bound intermediate and b) the simultaneous release of this reaction product from the resin back into solution. This new concept is presented and future prospects are discussed.

Keywords: combinatorial chemistry · functionalized polymers · reagents · solid-phase synthesis

Introduction

R. B. Merrifield[1] and the solid-phase synthesis based on his concepts revolutionized polypeptide and polynucleotide synthesis and more than ten years ago it set the stage for combinatorial chemistry. Todays driving force for this still rapidly growing technique is associated with the need to rapidly generate libraries of compounds.[2] As an alternative, the utilization of functionalized polymers as reagents and catalysts has recently appeared on this scene after an incubation time of more than 25 years.[3] Here, it is not the substrate which remains attached to the solid support during a multistep synthesis but the polymer-bound reagent or catalyst promotes a chemical transformation of a substrate which is present in solution. One advantage of this polymer-assisted solution-phase synthesis is the possibility to monitor the reaction using known analytical techniques.[4] Besides the use of stoichiometric reagents another technique for polymer-assisted solution-phase purification has often been employed recently. Polymer-bound scavengers are resins which are added after a chemical reaction to remove excess reactants and by-products.[5]

However, the true potential of polymers in organic synthesis will fully be exploited if the whole orchestra of techniques are combined. And in fact, a hybrid technique that combines the concept of solid-phase synthesis with the idea of polymer-supported scavenging reagents has seen increased interest in polymer-assisted synthesis. Often, this method which is only one example among other polymer-assisted combinations has been termed the "resin-capture – release" methodology and we shall use this terminology throughout this report. The functionalized polymers which have been developed for this technique allow the trapping of a small molecule as an activated polymer intermediate. After washing to remove soluble by-products, this intermediate is subjected to a second transformation by adding a new reaction partner in solution. This reactant not only chemically alters the polymer-bound intermediate but at the same time provokes release of the product from the resin back into solution (Scheme 1). Sometimes the second transformation is



Scheme 1. The "resin-capture – release" methodology.

only used to modify the immobilized intermediate and it is a third transformation which leads to release of the product from the resin. However, it needs to be pointed out that due to the fact that this methodology is located in between two distinct polymer-assisted techniques a clear cut is not always possible and therefore, some of the sequences given in this article could well be defined as examples for solid-phase synthesis. Nevertheless, it is the intention of this report to familiarize the reader with methodologies that merge various

[a] Prof. Dr. A. Kirschning, R. Wittenberg
Institut für Organische Chemie
Universität Hannover
Schneiderberg 1B
30167 Hannover (Germany)
Fax: (+49) 511-762 3011
E-mail: andreas.kirschning@oci.uni-hannover.de

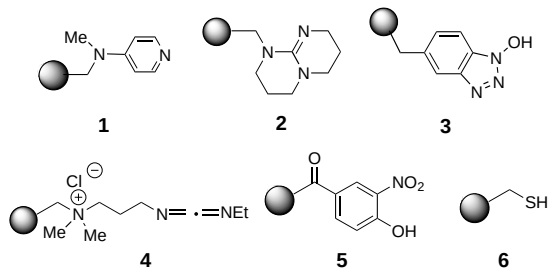
[b] H. Monenschein
Institut für Organische Chemie
Technische Universität Clausthal
Leibnizstrasse 6
38678 Clausthal-Zellerfeld (Germany)

  0947-6539/00/0624-4445 $ 17.50+.50/0

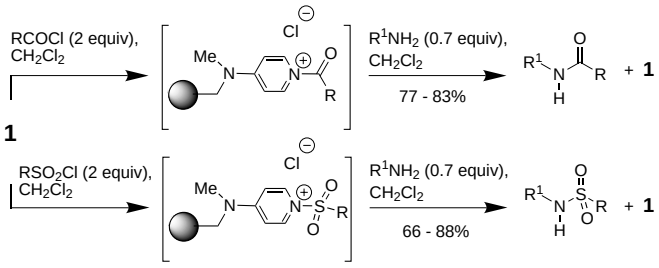
polymer-assisted techniques. The "resin-capture – release" methodology even if the terminology will not prevail in the longrun is one important group of polymer-assisted techniques in organic synthesis which clearly illustrates this development. The transformations given here though some of them showing reminiscence to solid-phase synthesis are easily incorporated into a multistep polymer-assisted synthesis in solution where polymer-supported reagents or catalysts are employed prior or after the "resin-capture – release" transformation.

Functional polymers for "capture – release" techniques

Acyl and sulfonyl transfer protocols: Probably the most widely employed applications of the "resin-capture – release" methodology are acylation and sulfonylation reactions using polymer-supported amines such as poly-DMAP **1**, poly(4-vinylpyridine),[6] and poly-TBD (TBD: 1,5,7-triazabicyclo[4.4.0]-dec-5-ene) **2**. Reagent **1** is well suited for trapping acyl



chlorides as well as sulfonyl chlorides[7] which then react with amines to the corresponding amides and sulfonamides (Scheme 2).[8]

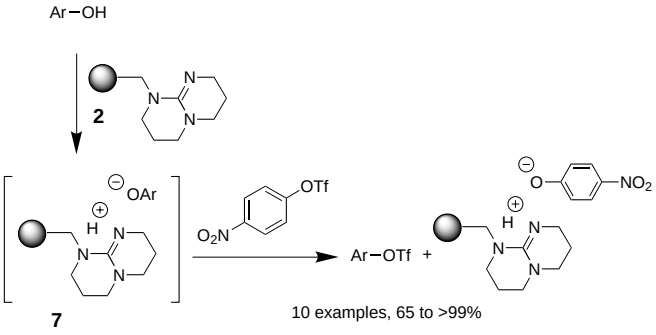


Scheme 2. Capture – release resins in acylation reactions.

Weakly nucleophilic heterocyclic amines have efficiently been acylated utilizing solid-supported reagent **5**.[9] Here, the electron-deficient phenol group allows for intermediate anchoring of an acyl chloride onto the resin which then is released upon treatment with various 2-aminopyridines and 2-aminothiazoles. Traces of unreacted starting material were then conveniently removed by addition of the acidic ion-exchange resin Amberlite IRA-120.

Likewise, polymer-anchored 1-hydroxybenzotriazole (HOBt) **3** was originally developed as a highly reactive *N*-acylating agent for the formation of peptide bonds in solution.[10] Recently, it was shown that this functionalized polymer also performs coupling of acids and amines, including the transfer of protecting groups (Fmoc, Cbz, Boc)[11] and the synthesis of *N*-hydroxysuccinimide esters[12] in a "resin-capture – release" mode. In a similar fashion, an acylsulfonamide library was constructed by immobilizing and activating carboxylic acids on functionalized diimide resin **4**[13] which reacted further to acylsulfonamides with sulfonamides.[14]

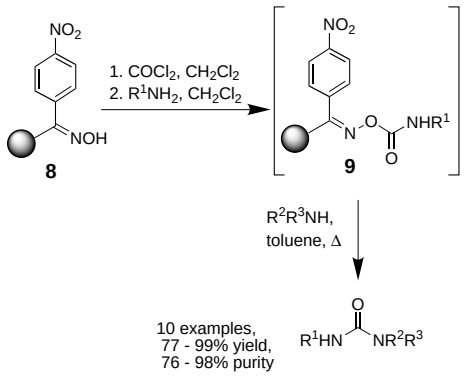
The use of basic poly-TBD **2** allows for the rapid synthesis of aryl triflates (Scheme 3).[15] Phenols were immobilized on resin **2** to afford intermediate polymer **7**. This resin was treated with 4-nitrophenyl triflate which plays the role of a triflate transfer reagent thereby releasing the desired aryltriflate into solution.



Scheme 3. Preparation of aryl triflates promoted by PTBD **2**.

In an earlier example of the "resin-capture – release" methodology trifluoracetylation of amines was achieved using polymer-bound benzyl thiol **6**. Trifluoracetic anhydride was employed in the capturing process while addition of amines to the intermediate polymer-bound thioester released the desired trifluoracetamide from the resin.[16]

Finally, polymer-supported oxime **8** has served as a reagent for trapping primary amines after treatment with phosgene[17] to furnish intermediate oxime carbamates **9** (Scheme 4).[18] Thermolysis in the presence of amines results in release of ureas into solution.

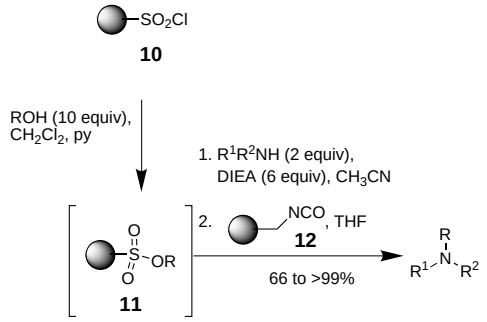


Scheme 4. Polymer-assisted preparation of substituted urethanes using polymer-anchored oxime **8**.

Alkylation protocols: In an opposite manner to bases such as **1** and **2** in terms of reactivity, polymer-supported tosyl chloride equivalent **10** is able to capture alcohols as polymer-bound sulfonates **11** which are released as secondary

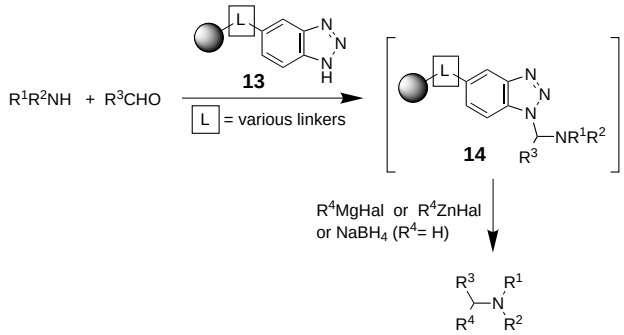
0947-6539/00/0624-4446 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 24

amines, sulfides and alkylated imidazoles with primary amines, thiols, and imidazoles as nucleophiles in a substitution process (Scheme 5).[19] This technique has further been extended for the preparation of tertiary amines.[20] Excess of amine was scavenged by polymer-supported isocyanate **12**.[21, 22]



Scheme 5. Polymer-supported sulfonyl chloride **10** as a capture–release resin.

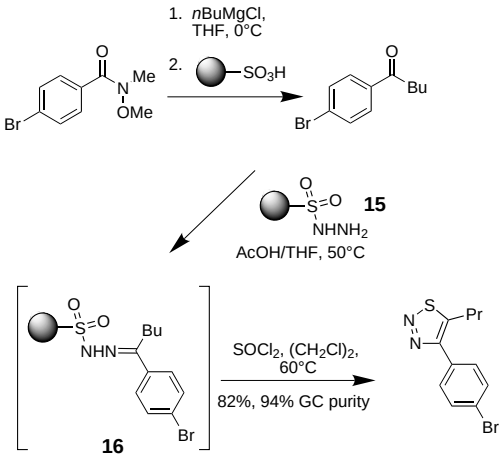
Recently, three research groups independently disclosed that benzotriazoles **13** attached through various linkers to a polymeric support react with aldehydes and amines to form polymer-anchored Mannich-type adducts **14** (Scheme 6).[23] These intermediates are cleaved under reducing conditions and in the presence of organomagnesium or organozinc reagents to provide libraries of secondary and tertiary amines in moderate yield (11–65%) and with acceptable purity (13–>99%).[23]



Scheme 6. Preparation of tertiary amines assisted by polymer-bound benzotriazoles.

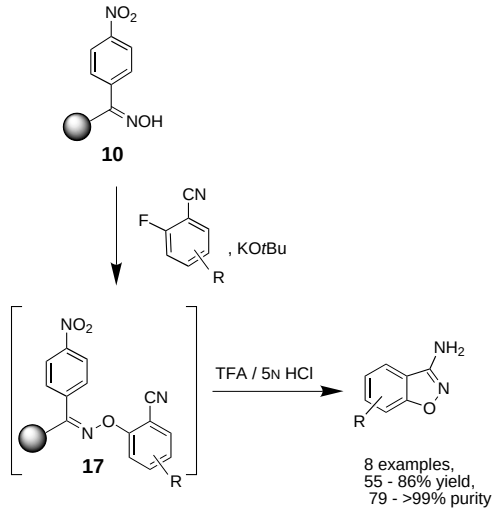
Cleavage protocols with simultaneous ring closure: In various cases, the release step is accompanied by a cyclization leading to heterocycles. It should be noted that under these conditions parts of the linker can become part of the product which is released into the solution.

Thus, gel-type polystyrene-sulfonyl-hydrazide resin **15** which originally was developed for carbonyl scavenging applications[24] can also serve as a linker for carbonyl compounds in solid-phase synthesis and gives access to support-bound sulfonyl hydrazones **16**.[25] Treatment with thionyl chloride initiated the Hurd–Mori reaction and cleavage from the resin which afforded 1,2,3-thiadiazoles (Scheme 7). In order to generalize this strategy noncommercially available ketones were first generated by reacting a set of Weinreb-amides with Grignard reagents followed by immobilized sulfonic acid-mediated decomposition of the tetrahedral intermediate. Additional diversifications of resin-bound sulfonylhydrazones **16** such as Stille coupling or Shapiro olefin synthesis are possible.



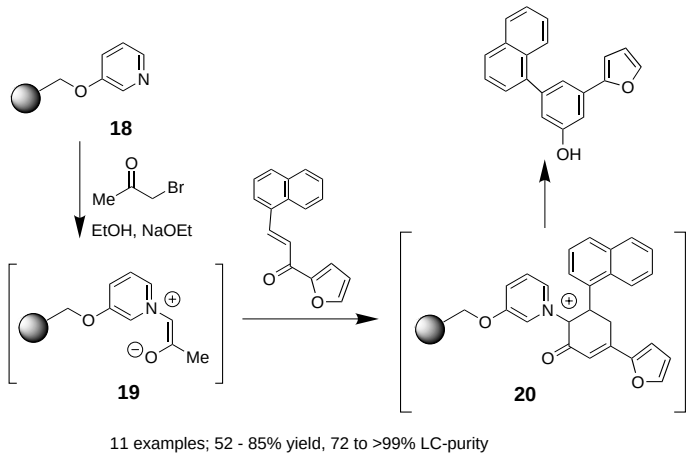
Scheme 7. Polymer-assisted preparation of 1,2,3-thiadiazoles.

Polymer-supported oxime **8** (see also Scheme 4) may also serve as a nucleophile in S_NAr reactions (Scheme 8).[26] This procedure afforded aryl oxime adducts **17** which were released as 3-aminobenzoisoxazoles by means of an acid-promoted cyclization.



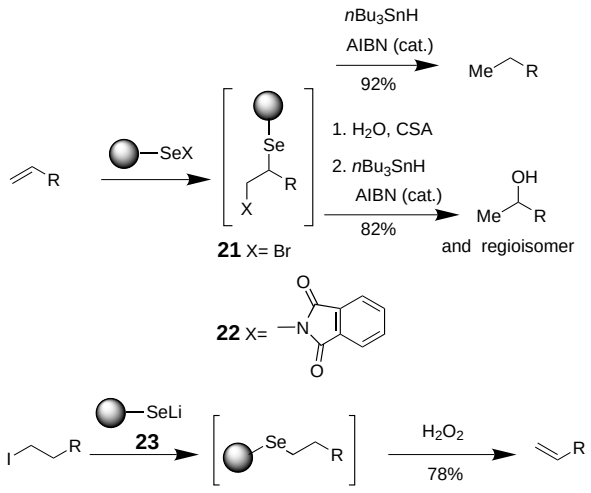
Scheme 8. Polymer-assisted synthesis of 3-aminobenzoisoxazoles.

Katritzky and co-workers devised a very elegant polymer-assisted "cyclization–cleavage" approach which starts from functionalized polymer **18**. It allows the synthesis of variously substituted phenols (Scheme 9).[27] Base-catalyzed reaction between polymer-bound acetonyl building block **19** and an α,β-unsaturated ketone resulted in a tandem addition/annulation reaction to afford immobilized intermediate **20**. This sequence was followed by elimination and rearrangement to the corresponding phenol.



Scheme 9. Polymer-assisted preparation of complex phenols.

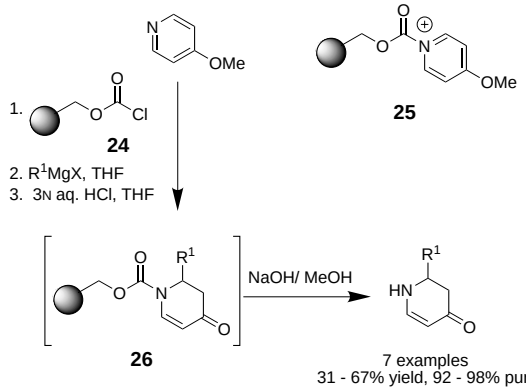
Selenium-based polymer-assisted synthesis: Another example of the "resin-capture–release" technique which should see widespread applications in the future is the selenium-mediated functionalization of organic compounds. Polymer-supported selenium-derived reagents[28] are very versatile because a rich chemistry around the carbon–selenium bond has been established in solution and the difficulties arising from the odor and the toxicity of low-molecular selenium compounds can be avoided. Thus, reagent **21** (X = Cl) was first prepared by Michels, Kato, and Heitz[29] and was employed in reactions with carbonyl compounds. This treatment yielded polymer-bound α-seleno intermediates which were set free back into solution as enones from hydrogen peroxide induced elimination. Recently, new selenium-based functionalized polymers **21** (X = Br)–**23** were developed which have been utilized in syntheses according to Scheme 10.[30]



Scheme 10. Applications of organoselenium reagents covalently bound to polymers.

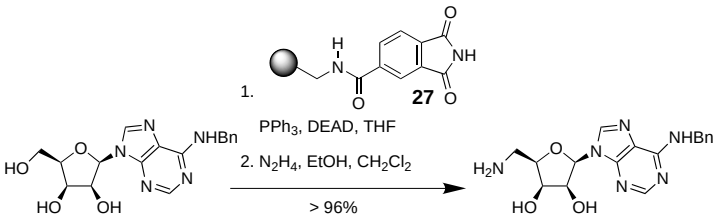
The reactivity of functionalized polymer **21** was elegantly exploited for the cyclization of alkenyl-substituted β-dicarbonyls by Nicolaou and co-workers which gave access to the core structure of garsubellin A.[31]

Miscellaneous applications: An extended application of the "resin-capture–release" technique is depicted in Scheme 11. With the help of reagent **24**, a functionalized pyridine was captured as an acyl pyridinium cation **25** on a solid support which was followed by Grignard addition and hydrolysis under acidic conditions to afford polymer-supported *N*-acylated dehydropyridinones **26**.[32] Advantageously, any unreacted acylium complex collapses to the parent resin upon workup. These heterocycles, which ideally can serve as scaffolds, are then released under basic conditions.



Scheme 11. Preparation of dehydropyridinones utilizing the capture–release technique.

A very interesting variant of the polymer-supported Mitsunobu reaction was recently disclosed by Gelb and Aronov (Scheme 12).[33] Polymer-bound phthalimide **27** was designed which is able to trap alcohols such as nucleosides under Mitsunobu conditions. After purification by washing the loaded resin the corresponding amine was subsequently released into solution in high yield by hydrazinolysis.

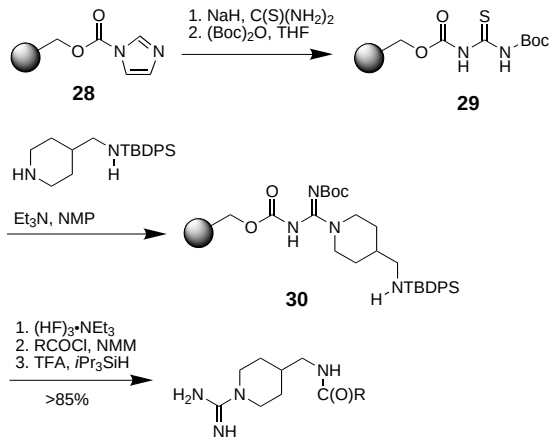


Scheme 12. A polymer-based Mitsunobu-reaction.

Guanidines were prepared by treatment of polymer-bound bis-urethane protected thiourea **29** with primary and secondary amines.[34] Thiourea **29** could be prepared from the carbonylimidazole resin **28** (from Wang resin) using thiourea followed by capping as *tert*-butylcarbamate. As shown in Scheme 13 silyl-protected diamine was loaded onto polymer **29** to furnish polymer-bound guanidine **30**. Desilylation and acylation paved the way for cleavage to release the functionalized guanidine into solution.

Other synthetic applications of this technique are the immobilization of vinylboronates by means of a Suzuki-coupling. Release from the resin by a second transformation afforded substituted styrenes including tamoxifen and ana-

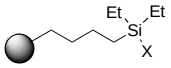
0947-6539/00/0624-4448 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 24



Scheme 13. Polymer-assisted guanidation of amines.

logues derived therefrom, a drug to be used clinically for treatment of estrogen dependent breast cancers.[35] In a related purely for purification designed version[36, 37] of the "resin-capture–release" technique β-amino alcohols were captured by PEG-supported dialkylborane.[38] Purification of the target molecules was achieved after precipitation, washing and release under mildly acidic conditions.

In this context, an interesting new class of functionalized polymers has been introduced namely silanes such as **31**.[39] They can easily be converted into polymer-bound silyl triflate **32**, silyl cyanide **33**,[40] or silyl azide **34**.[40] Functionalized polymers **32** and **34** are able to trap reaction partners from solution.[41] For example, enones are captured by silyl triflate **32**,[39] to form electron-rich polymer-bound dienes which were released after Diels–Alder cycloaddition followed by treatment with traces of trifluoroacetic acid to result in cyclohexenes.[42] We believe that soon more examples that combine solid-phase synthesis with polymer-assisted solution-phase synthesis will be disclosed which are based on the use of functionalized polymers such as **31**–**34**.



31 X = H
32 X = OTf
33 X = CN
34 X = N_3

Outlook

Here, we gave a brief description of a hybrid technique in the realm of polymer-assisted synthetic methodologies which merges scavenger protocols with solid-phase synthesis. This singular strategy is part of a broader development in this field. Indeed, the true potential of polymers in organic synthesis will fully be exploited if the whole orchestra of techniques is combined.[43] Hybrid techniques will play an increasingly important role that combine both solid phase organic synthesis followed by derivatization of functional groups with polymer-supported reagents after release and cleavage of the substrate from the polymer or vice versa. These developments will also enhance the utility of soluble polymers in automated parallel synthesis. Thus, soluble polymers may be loaded with substrates which are processed by polymer-anchored reagents or catalysts.

In summary, the "resin-capture–release" hybrid methodology will become one important instrument in this orchestra of techniques.

[1] R. B. Merrifield, *J. Am. Chem. Soc*. **1963**, *85*, 2149–2154.
[2] a) F. Z. Dörwald, *Organic Synthesis on Solid Phase*, Wiley VCH, Weinheim, **2000**; b) N. K. Terrett, *Combinatorial Chemistry*, Oxford University Press, **1998**; c) D. Obrecht, J. M. Villalgordo, *Solid-supported combinatorial and parallel synthesis of small-molecular-weight compound libraries*, Pergamon, Elsevier Science, Oxford, **1998**; d) S. R. Wilson, A. W. Czarnik, *Combinatorial Chemistry, Synthesis, Application*, Wiley, New York, **1997**.
[3] Recent reviews on polymer-supported reagents: a) D. H. Drewry, D. M. Coe, S. Poon, *Med. Res. Rev.* **1999**, *19*, 97–148; b) S. J. Shuttleworth, S. M. Allin, P. K. Sharma, *Synthesis* **1997**, 1217–1239; c) C. U. Pittman, Jr., *Polym. News* **1998**, *23*, 416–418; d) S. W. Kaldor, M. G. Siegel, *Curr. Opin. Chem. Biol*. **1997**, *1*, 101–106; e) P. Laszlo, *Preparative Chemistry using Supported Reagents*, Academic Press, San Diego, **1987**.
[4] For reviews on polymer-supported catalysts refer to ref. [3] and a) B. Jandeleit, D. J. Schaefer, T. S. Powers, H. W. Turner, W. H. Weinberg, *Angew. Chem*. **1999**, *111*, 2648–2689; *Angew. Chem. Int. Ed.* **1999**, *38*, 2476–2514; b) E. Lindner, T. Schneller, F. Auer, H. A. Mayer, *Angew. Chem*. **1999**, *111*, 2288–2309; *Angew. Chem. Int. Ed.* **1999**, *38*, 2154–2174; c) J. H. Cameron in *Solid state organometallic chemistry: Methods and applications* (Eds.: M. Gielen, R. Willem, B. Wrackmeyer), Wiley, Chichester, **1999**, p. 473–519; c) J. H. Clark, D. J. Macquarrie, *Chem. Soc. Rev.* **1996**, 303–310; d) D. C. Bailey, S. H. Langer, *Chem. Rev*. **1981**, *81*, 109–148.
[5] For reviews on scavenger techniques refer to: a) D. L. Flynn, R. V. Devraj, J. J. Parlow in *Solid Phase Organic Synthesis* (Ed.: K. Burgess), Wiley, New York, **2000**, pp. 149–194; b) J. J. Parlow, R. V. Devraj, M. S. South, *Curr. Opin. Chem. Biol*. **1999**, *3*, 320–336; c) J. C. Hodges, *Synlett* **1999**, 152–158; d) D. L. Flynn, R. V. Devraj, J. J. Parlow, *Curr. Opin. Drug Discovery Dev.* **1998**, *1*, 41–50; e) L. M. Gayo, *Biotechnol. Bioeng.* **1998**, *61*, 95; f) R. J. Booth, J. C. Hodges, *Acc. Chem. Res.* **1999**, *32*, 18–26; g) D. L. Flynn, R. V. Devraj, N. Naing, J. J. Parlow, *Med. Chem. Res.* **1998**, *8*, 219–243.
[6] J.-G. Rodríguez, R. Martín-Villamil, S. Ramos, *New J. Chem.* **1998**, 865–868.
[7] J. G. Keay, E. F. V. Scriven, *Chem. Ind*. **1994**, *53*, 339–350.
[8] L. L. Tamanaha, J. A. Porco, Jr., *Synthesis & Purification* **1999**, *2*, 1–4 (Catalogue of Argonaut Technologies)
[9] K. Kim, K. Le, *Synlett* **1999**, 1957–1959.
[10] a) R. Kalir, A. Warshawsky, M. Fridkin, A. Patchornik, *Eur. J. Biochem*. **1975**, *59*, 55–61; b) M. Stern, R. Kalir, A. Patchornik, A. Warshawsky, M. Fridkin, *J. Solid-Phase Biochem*. **1977**, *2*, 131–139; c) I. E. Pop, B. P. Déprez, A. L. Tartar, *J. Org. Chem*. **1997**, *62*, 2594–2603; d) K. Dendrinos, J. Jeong, W. Huang, A. G. Kalivretenos, *Chem. Commun.* **1998**, 499–500.
[11] K. G. Dendrinos, A. G. Kalivretenos, *J. Chem. Soc. Perkin Trans I* **1998**, 1463–1464. A similar functionalized polymer, based on *N*-hydroxysuccinimide was disclosed by M. Adamczyk, J. R. Fishpaugh, P. G. Mattingly, *Tetrahedron Lett*. **1999**, *40*, 463–466.
[12] K. G. Dendrinos, A. G. Kalivretenos, *Tetrahedron Lett.* **1998**, *39*, 1321–1324.
[13] Other applications of reagent **4** include the preparation of amides: M. C. Desai, L. M. Stephens Stramiello, *Tetrahedron Lett*. **1993**, *34*, 7685–7688 and thiol esters: M. Adamczyk, J. R. Fishpaugh, *Tetrahedron Lett*. **1996**, *37*, 4305–4308.
[14] C. F. Sturino, M. Labelle, *Tetrahedron Lett*. **1998**, *39*, 5891–5894.
[15] S. Boisnard, J. Chastanet, J. Zu, *Tetrahedron Lett*. **1999**, *40*, 7469–7472.
[16] P. I. Svirskaya, C. C. Leznoff, M. Steinman, *J. Org. Chem*. **1987**, *52*, 1362–1364.
[17] M. A. Scialone, S. W. Shuey, P. Soper, Y. Hamuro, D. M. Burns, *J. Org. Chem*. **1998**, *63*, 4802–4807.

[18] S. Kobayashi, T. Furuta, K. Sugita, O. Okitsu, H. Oyamada, *Tetrahedron Lett*. **1999**, *40*, 1341 – 1344.
[19] J. K. Rueter, S. O. Nortey, E. W. Baxter, G. C. Leo, A. B. Reitz, *Tetrahedron Lett*. **1998**, *39*, 975 – 978. Polymer-bound arylsulfonate esters can undergo various reactions at remote functionalities prior to cleavage from the resin with diethyl amine: E. W. Baxter, J. K. Rueter, S. O. Nortey, A. B. Reitz, *Tetrahedron Lett*. **1998**, *39*, 979 – 982.
[20] F. Hu, J. A. Porco, *Synth. Pur. Lett*. **1999**, *1*, 1 – 5.
[21] a) S. W. Kaldor, J. E. Fritz, J. Tang, E. R. McKinney, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 3041 – 3044; b) M. W. Creswell, G. L. Bolton, J. C. Hodges, M. Meppen, *Tetrahedron* **1998**, *54*, 3983 – 3998.
[22] B. Raju, J. M. Kassir, T. P. Kogan, *Bioorg. Med. Chem. Lett*. **1998**, *8*, 3043 – 3048.
[23] a) K. Schiemann, H. D. H. Showalter, *J. Org. Chem*. **1999**, *64*, 4972 – 4975; b) A. R. Katritzky, S. A. Belyakov, D. O. Tymoshenko, *J. Comb. Chem*. **1999**, *1*, 173 – 176; c) A. Paio, A. Zaramella, R. Ferrito, N. Conti, C. Marchioro, P. Seneci, *J. Comb. Chem*. **1999**, *1*, 317 – 325.
[24] a) O. Galioglu, A. Akar, *Eur. Polym. J.* **1989**, *25*, 313 – 316; b) D. W. Emerson, R. R. Emerson, S. C. Joshi, E. M. Sorensen, J. M. Turek, *J. Org. Chem*. **1979**, *44*, 4634 – 4640; c) H. Kamogawa, A. Kanzawa, M. Kadoya, T. Naito, M. Nanasawa, *Bull. Chem.Soc. Jpn*. **1983**, *56*, 762 – 765.
[25] Y. Hu, S. Baudart, J. A. Porco, Jr., *J. Org. Chem*. **1999**, *64*, 1049 – 1051.
[26] S. D. Lepore, M. R. Wiley, *J. Org. Chem*. **1999**, *64*, 4547 – 4550.
[27] A. R. Katritzky, S. A. Belyakov, Y. Fang, J. S. Kiely, *Tetrahedron Lett*. **1998**, *39*, 8051 – 8054.
[28] For various examples of immobilized selenium reagent refer to a) Y. Okamoto, K. L. Chelleppa, R. Hornsang, *J. Org. Chem*. **1973**, *38*, 3172 – 3175; b) E. J. Goethals, *Eur. Polym. J.* **1974**, *10*, 847 – 849; c) K. Kondo, *J. Polym. Sci. Polym. Lett. Ed*. **1974**, *12*, 679 – 683; d) M. Kato, R. Michels, W. Heitz, *J. Polym. Sci. Polym. Lett. Ed*. **1976**, *14*, 413 – 415; e) K.-i. Fujita, K. Watanabe, A. Oishi, Y. Ikeda, Y. Taguchi, *Synlett* **1999**, 1760 – 1762.
[29] R. Michels, M. Kato, W. Heitz, *Makromol. Chem*. **1976**, *177*, 2311 – 2320.
[30] K. C. Nicolaou, J. Pastor, S. Barluenga, N. Wissinger, *Chem. Commun*. **1998**, 1947 – 1948.
[31] K. C. Nicolaou, J. A. Pfefferkorn, G.-Q. Cao, S. Kim, J. Kessabi, *Org. Lett*. **1999**, *1*, 807 – 810.
[32] a) C. Chen, I. A. McDonald, B. Munoz, *Tetrahedron Lett*. **1998**, *39*, 217 – 220; b) B. Munoz, C. Chen, I. A. McDonald, *Biotechnol. Bioeng. (Comb. Chem.)* **2000**, *71*, 78 – 84. For the preparation of resin-bound chloroformate refer to J. R. Hauske, P. Dorff, *Tetrahedron Lett*. **1995**, *36*, 1589 – 1592.
[33] A. M. Aronov, M. H. Gelb, *Tetrahedron Lett*. **1998**, *39*, 4947 – 4950.
[34] J. J. Josey, C. A. Tarlton, C. E. Payne, *Tetrahedron Lett*. **1998**, *39*, 5899 – 5902.
[35] a) S. D. Brown, R. W. Armstrong, *J. Org. Chem.* **1997**, *62*, 7076 – 7077; b) D. Brown, R. W. Armstrong, *J. Am. Chem. Soc*. **1996**, *118*, 6331 – 6332.
[36] An early example of this concept, using polystyrylboronic acid for separating and purifying 1,2-*cis* diols from *cis/trans*-mixtures was presented by E. Seymour, J. M. J. Fréchet, *Tetrahedron Lett*. **1976**, 3669 – 3672.
[37] S. Sunami, T. Sagara, M. Ohkubo, H. Morishima, *Tetrahedron Lett*. **1999**, *40*, 1721 – 1724.
[38] M. H. Kim, K. D. Janda, *J. Org. Chem.* **1998**, *63*, 889 – 894.
[39] Y. Hu, J. A. Porco, Jr., J. W. Labadie, O. W. Gooding, B. M. Trost, *J. Org. Chem*. **1998**, *63*, 4518 – 4521.
[40] A. Missio, C. Marchioro, T. Rossi, M. Panunzio, S. Selva, P. Seneci, *Biotechnol. Bioeng*. **2000**, *71*, 38 – 43.
[41] a) Y. Hu, J. A. Porco, Jr., *Tetrahedron Lett*. **1998**, *39*, 2711 – 2714. b) Y. Hu, J. A. Porco, Jr., *Tetrahedron Lett*. **1999**, *40*, 3289 – 3292.
[42] E. M. Smith, *Tetrahedron Lett*. **1999**, *40*, 3285 – 3288.
[43] X. Ouyang, R. W. Armstrong, M. M. Murphy, *J. Org. Chem*. **1998**, *63*, 1027 – 1032.

  0947-6539/00/0624-4450 $ 17.50+.50/0