Novabiochem®

Resins for solution phase organic synthesis

Scavenger resins

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Polymer-supported reagents

Polymer-supported reagents

Reagent type	Product No.	Product Name	Page
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$RCO_2H \rightarrow RCOCl$ $ROH \rightarrow RCl$ $RCONH_2 \rightarrow RCN$ $RCONHR \rightarrow R(Cl)=NHR$ $ROH + RXH \rightarrow RXR$	855032	Triphenylphosphine polystyrene	38

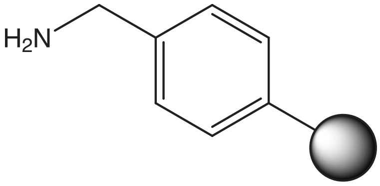
Converting mesh sizes to µm

For your convenience a table which converts the mesh sizes for resin beads to their average diameter in µm is given below.

Mesh	µm
20	850
25	710
35	500
50	300
60	250
70	212
100	150
140	106
200	75
325	45
400	38

Resins for solution phase organic chemistry

Product No.	Product	Quantity	Price
855076	**Aminomethylated polystyrene EHL (200-400 mesh), 2% DVB** AM resin EHL (200-400 mesh), 2% DVB NBC No.: 01-64-0177 Loading: 2.00 - 3.00 mmole/g resin, by photometric determination of the Fmoc-chromophore liberated upon treatment with DBU/DMF. ⚠ Prolonged storage: ≤ -20°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

Aminomethylated polystyrene is a useful tool for scavenging activated carboxylic acids, sulfonyl halides and isocyanates [1 - 4]. Typically, 1.5 - 3 equivalents of resin (based on reactive nitrogen content) relative to electrophiles such as isocyanates are employed. With acid and sulfonyl chlorides, unless an additional tertiary base is present, the excess used should be doubled to ensure complete neutralization of the HCl generated. The reaction is normally carried out at room temperature in polar non-hydroxylic solvents, such as DCM, DMF or THF, and is complete in 1 - 4 h.

This resin has also been used to scavenge alkylating reagents such as alkyl bromides [6, 7] and mesylates [8].

REFERENCES

[1] D. L. Flynn, et al. (1997) *J. Am. Chem. Soc.*, **119**, 4874.

[2] J. Chen, et al. (1999) *Tetrahedron Lett.*, **40**, 9195.

[3] S. W. Kaldor, et al. (1996) *Bioorg. Med. Chem. Lett.*, **6**, 7193.

[4] J. Habermann, et al. (1998) *J. Chem. Soc., Perkin Trans 1*, 3127.

[5] J. Parlow & D. Flynn (1998) *Tetrahedron*, **54**, 4013.

[6] W. Xu, et al. (1998) *Bioorg. Med. Chem. Lett.*, **8**, 1089.

[7] M. Caldarelli, et al. (1999) *J. Chem. Soc., Perkin Trans 1*, 107.

[8] J. Habermann, et al. (1999) *J. Chem. Soc., Perkin Trans 1*, 1253.

Properties

Reactivity:

removes acid chlorides, sulfonyl chlorides, isocyanates, isothiocyanates, acids

Polymer type:

copoly(styrene-2 % DVB), 200-400 mesh

Loading:

2.00 - 3.00 mmole/g resin, by photometric determination of the Fmoc-chromophore liberated upon treatment with DBU/DMF.

Solvent compatibility:

DCM, DCE, THF, toluene, DMF

Typical reaction conditions:

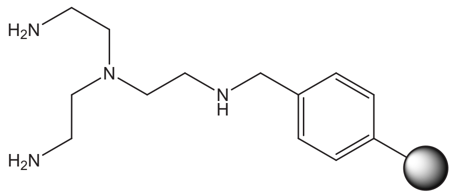
1.5 - 3 eq. relative to isocyanate; 3 - 6 eq. relative to acid chloride; sulfonyl chloride; 1 - 4 h, 20 °C

Use of aminomethylated polystyrene

1. Add amine resin (6 eq. relative to excess acid or sulfonyl chloride; 3 eq. relative to isocyanate) to the reaction mixture containing excess acylating reagent.
2. Agitate gently for 4 h at rt.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

For help selecting the most appropriate resin see Table 1, page 45.

Product No.	Product	Quantity	Price
855023	**Tris-(2-aminoethyl)amine polystyrene** Polyamine resin NBC No.: 01-64-0170 Loading: ≥ 2.20 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-bound amine reagent has been used to scavenge acid chlorides [1 - 4], sulfonyl chlorides [1], isocyanates [1, 3, 5], acid anhydrides [5], isothiocyanates [1], and α,β-unsaturated ketones [2]. Typically, 1.5 - 3 equivalents of resin (based on reactive nitrogen content) relative to electrophiles such as isocyanates are employed. With acid and sulfonyl chlorides, unless an additional tertiary base is present, the excess used should be doubled to ensure complete neutralization of the HCl generated. The reaction is normally carried out at room temperature in polar non-hydroxylic solvents, such as DCM, DMF or THF, and is complete in 1 - 4 h.

This resin has been used to scavenge the reactants of a multi-component-reaction by participating as the amine component in the thiazolidinone-forming reaction [6](Figure 1).

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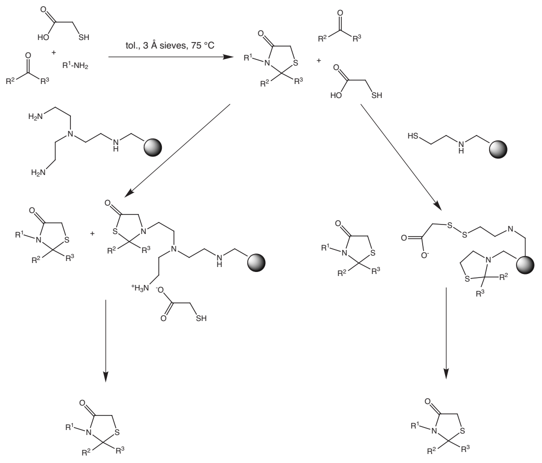


Fig. 1: Synthesis of a thiazolidinone using polymer-supported purification [6].

Properties

Reactivity:

removes acid chlorides, sulfonyl chlorides, isocyanates, isothiocyanates, acids

Polymer type:

copoly(styrene-1 % DVB), 200-400 mesh

Loading:

≥ 2.20 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate

Solvent compatibility:

DCM, DCE, THF, toluene, DMF

Typical reaction conditions:

1.5 - 3 eq. relative to isocyanate; 3 - 6 eq. relative to acid chloride, sulfonyl chloride; 1 - 4 h, 20 °C

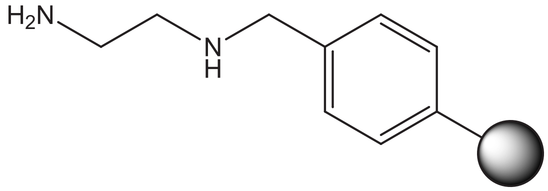
Use of tris-(2-aminoethyl)-amine polystyrene

1. Add tris-(2-aminoethyl)-amine polystyrene (6 eq. relative to excess acid or sulfonyl chloride; 3 eq. relative to isocyanate) to the reaction mixture containing excess of acylating reagent.
2. Agitate gently for 4 h at rt.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] R. J. Booth & J. C. Hodges (1997) *J. Am. Chem. Soc.*, **119**, 4882.
[2] M. W. Creswell, et al. (1998) *Tetrahedron*, **54**, 3983.
[3] C. Blackburn, et al. (1998) *Tetrahedron Lett.*, **39**, 3635.
[4] M. Takayanagi, et al. (2000) *J. Org. Chem.*, **65**, 3811.
[5] K. C. Nicolaou, et al. (2000) *J. Am. Chem. Soc.*, **122**, 9968.
[6] S. E. Ault-Justus, et al. (1998) *Biotechnol. & Bioeng. (Comb. Chem.)*, **61**, 17.

Product No.	Product	Quantity	Price
855077	**N-(2-Aminoethyl)aminomethyl polystyrene** Ethylenediaminemethyl polystyrene NBC No.: 01-64-0178 Loading: ≥ 2.00 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate.	5 g 25 g 100 g	



Description, Methods, Applications

N-(2-Aminoethyl)aminomethyl polystyrene is an effective polymer-bound quench for activated carboxylic acids, sulfonyl halides, isocyanates and isothiocyanates [1, 2]. Typically, 1.5 - 3 equivalents of resin (based on reactive nitrogen content) relative to electrophiles such as isocyanates are employed. With acid and sulfonyl chlorides, unless an additional tertiary base is present, the excess used should be doubled to ensure complete neutralization of the HCl generated. The reaction is normally carried out at room temperature in polar non-hydroxylic solvents, such as DCM, DMF or THF, and is complete in 1 - 4 h.

It has been employed in DCM to remove excess aldehyde from a Grignard reaction [3] (Figure 1).

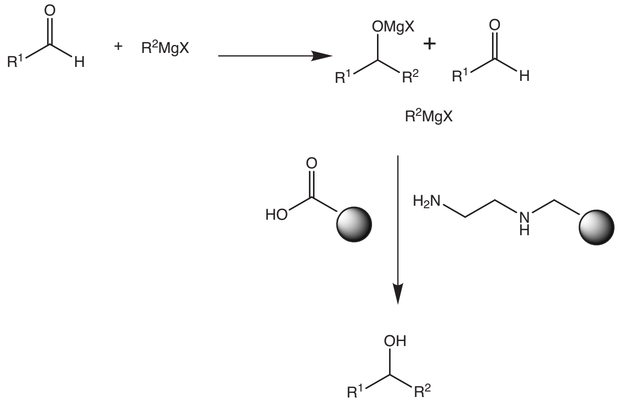


Fig. 1: Use of N-(2-aminoethyl)aminomethyl polystyrene [3].

Properties

Reactivity:

removes acid chlorides, sulfonyl chlorides, isocyanates, isothiocyanates, acids

Polymer type:

copoly(styrene-1 % DVB), 200-400 mesh

Loading:

≥ 2.00 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenyl-isocyanate

Solvent compatibility:

DCM, DCE, THF, toluene, DMF

Typical reaction conditions:

1.5 - 3 eq. relative to isocyanate; 3 - 6 eq. relative to acid chloride; sulfonyl chloride; 1 - 4 h, 20 °C

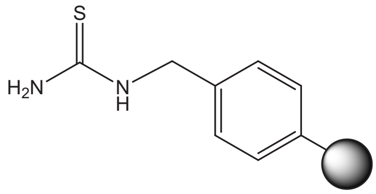
Use of N-(2-aminoethyl)aminomethyl polystyrene

1. Add amine resin (6 eq. relative to excess acid or sulfonyl chloride; 3 eq. relative to isocyanate) to the reaction mixture containing excess acylating reagent.
2. Agitate gently for 4 h at rt.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] R. J. Booth & J. C. Hodges (1997) *J. Am. Chem. Soc.*, **119**, 4882.
[2] P. López-Cremades, et al. (2000) *Synlett*, **10**, 1411.
[3] D. L. Flynn, et al. (1997) *J. Am. Chem. Soc.*, **119**, 4874.

Product No.	Product	Quantity	Price
855078	**Methylthiourea polystyrene** Thiocarbamoyl AM resin (200-400 mesh), 2% DVB NBC No.: 01-64-0181 Loading: ≥ 2.50 mmole/g resin, as determined by elemental analysis of sulfur. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry.	5 g 25 g 100 g	



Description, Methods, Applications

Methylthiourea polystyrene is an effective, highly-loaded support for scavenging activated electrophilic reagents such as bromomethylcarbonyl compounds [1], benzyl halides, allyl halides, and aryl fluorides [2]. In a synthesis of ICE inhibitors, this resin was found to completely remove Z-Asp-CH_2Br from a mixture with Z-Asp-OMe in DMF by heating for 3 hours at 60 °C (Figure 1) [1]. Under these conditions, the use of mercaptoethylaminomethyl polystyrene led to hydrolysis of the bromomethylketone.

	% removed	
Halide	4 h	o/n
Benzyl bromoacetate	71	100
Cinnamyl bromide	83	100
1-Bromodecane	12	15

Conditions: 2 eq. methylthiourea polystyrene in THF at 55 °C.

Table 1: Removal of various bromides using methylthiourea polystyrene.

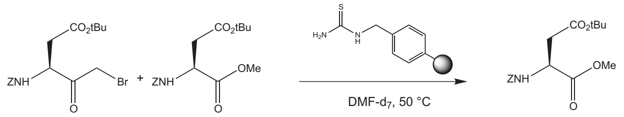


Fig. 1: Scavenging of a bromoketone using methylthiourea polystyrene [1].

Properties

Reactivity:

removes benzyl and allyl halides, bromomethylcarbonyl compounds

Polymer type:

copoly(styrene-2 % DVB), 200-400 mesh

Loading:

≥ 2.50 mmole/g resin, as determined by elemental analysis of sulfur

Solvent compatibility:

DCM, DCE, DMF, THF, toluene

Typical reaction conditions:

3 eq. relative to alkyl halide; o/n, 60 °C

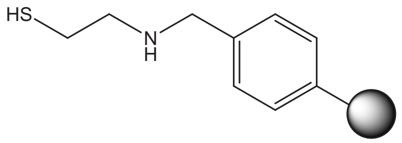
Use of methylthiourea polystyrene

1. Add thiourea resin (3 eq. relative to excess alkyl halide) to the reaction mixture.
2. Heat at 60 °C; o/n.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] J. S. Warmus, et al. (1998) *Bioorg. Med. Chem. Lett.*, **8**, 2309.
[2] B. Raju, et al. (2002) *J. Comb. Chem.*, **4**, 320.

Product No.	Product	Quantity	Price
855025	**N-(2-Mercaptoethyl)aminomethyl polystyrene** Cysteamine methyl polystyrene (200-400 mesh) NBC No.: 01-64-0180 Loading: ≥1.40 mmole/g resin, as determined by elemental analysis of sulfur. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

N-(2-Mercaptoethyl)aminomethyl resin can serve both as a polymer-supported nucleophilic scavenger for electrophilic reagents, and as a base. It is particularly suited to the sequestration of aldehydes and ketones as the 1,2-disposition of the heteroatoms favors the formation of stable thiazolidines with these electrophiles [1] (Figure 1). This support may be used to remove activated electrophilic reagents such as bromomethylcarbonyl compounds, benzyl halides and allyl halides. No additional base is needed to remove the acid generated in this reaction since the resin contains its own built-in base. The effectiveness of this resin in removing benzyl bromoacetate from DMF is demonstrated in Figure 2. When employed in a large excess, it may also be used to scavenge the dibenzofulvene by-product released on Fmoc group removal [2]. Since the reaction is reversible, the resin can be regenerated by treatment with piperidine in DMF.

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Halide	% removed 4 h	 o/n
Benzyl bromoacetate	88 (100^a)	100
Cinnamyl bromide	76	100
1-Bromodecane	6	15

Conditions: 2 eq. N-(2-mercaptoethyl)aminomethyl polystyrene in THF at 55 °C; ^{a}2 eq. N-(2-mercaptoethyl)aminomethyl polystyrene in DMF-d_7 at 60 °C for 3 h.

Table 1: Removal of various bromides using N-(2-mercaptoethyl)-aminomethyl polystyrene.

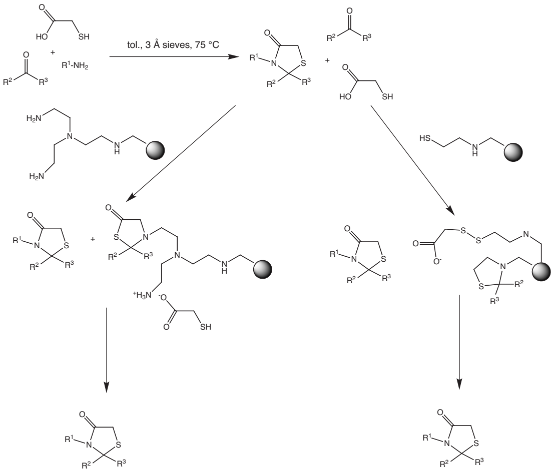


Fig. 1: Synthesis of a thiazolidinone using polymer-supported purification [1].

Properties

Reactivity:

removes benzyl and allyl halides, bromomethylcarbonyl compounds, aldehydes, ketones

Polymer type:

copoly(styrene-1 % DVB), 200-400 mesh

Loading:

≥1.40 mmole/g resin, as determined by elemental analysis of sulfur

Solvent compatibility:

DMF, THF, toluene

Typical reaction conditions:

2-3 eq. relative to alkyl halide; 4 h - o/n, 60 °C

For help selecting the most appropriate resin see Table 1, page 45.

Use of N-(2-Mercaptoethyl)aminomethyl polystyrene

1. Add thiol resin (2 eq. relative to excess alkyl halide or aldehyde) to the reaction mixture.
2. Heat at 60 °C for 4 h.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

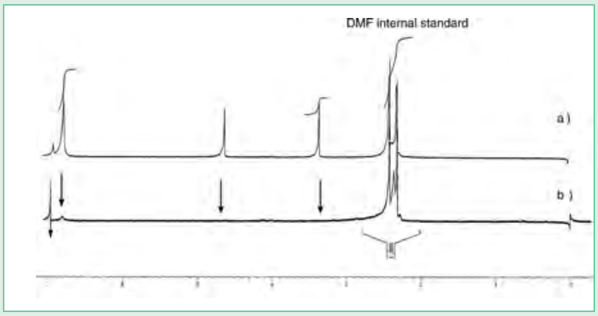
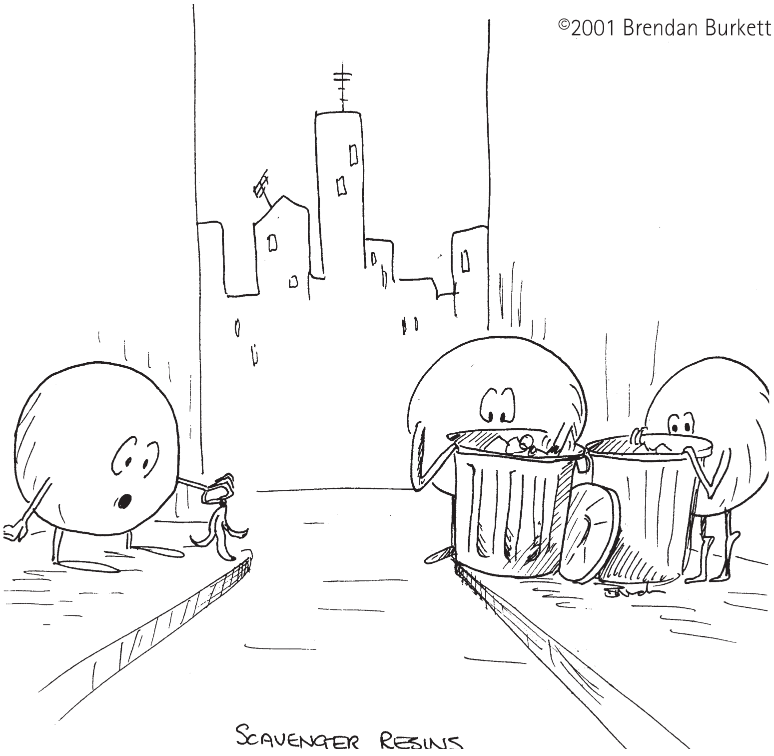


Fig. 2: a) ^{1}H nmr spectrum of a sample of benzyl bromoacetate (0.06 mmole) in DMF-d_7 containing DMF; b) after heating at 60 °C for 3 h with N-(2-Mercaptoethyl)aminomethyl polystyrene (0.12 mmole).

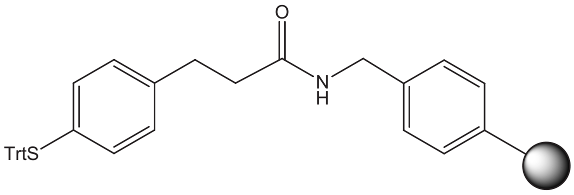
REFERENCES

[1] S. E. Ault-Justus, et al. (1998) *Biotechnol. & Bioeng. (Comb. Chem.)*, **61**, 17.

[2] J. Sheppeck II, et al. (2000) *Tetrahedron Lett.*, **41**, 5329.



Product No.	Product	Quantity	Price
855091	**3-[4-(Tritylmercapto)phenyl]propionyl AM resin** NBC No.: 01-64-0301 Loading: 0.70 - 1.00 mmole/g resin, as determined by elemental analysis of sulfur. ⚠ Prolonged storage: +15 to +25°C; keep dry and under argon.	5 g 25 g	



Description, Methods, Applications

This aryl thiol-based scavenger is an extremely effective tool for scavenging reagents such as alkyl halides, mesylates, tosylates and α,β-unsaturated carbonyl compounds. It is far more reactive than similar scavengers based on alkyl mercaptans, particularly with relatively unreactive compounds such as long chain alkyl halides. Before use the resin must be treated with 50% TFA in DCM to unmask the protected arylthiol group. Sequestration of alkyl halides is best carried out in mixtures of THF or DMF and EtOH (the presence of EtOH accelerates the reaction) using 2 eq. of resin. Pre-treatment of the resin with 2 eq. of TMSOK, NaOMe or NaHMDS in THF can be used to generate the resin-bound thiophenolate, in which case no additional base needs to be added to the reaction mixture. Alternatively, a tertiary base such as DIPEA can be added to neutralize the HBr generated during thioether formation.

A similar thiophenol resin has been used to immobilize esters of hydroxymaleimide to produce polymer-supported N-hydroxysuccinimide esters for the purpose of fluorescence labeling [1].

	% removed	
Halide	4 h	o/n
Benzyl bromoacetate	100	-
Cinnamyl bromide	100	-
1-Bromodecane	78	87

Conditions: 2 eq. sodium salt of 3-(4-(tritylmercapto)phenyl)propionyl AM resin in THF at 55 °C.

Table 1: Removal of various bromides using 3-[4-(Mercapto)-phenyl]propionyl AM resin.

Properties

Reactivity:

removes alkyl halides, bromomethylketones, mesylates, tosylates, α,β-unsaturated carbonyl compounds

Polymer type:

copoly(styrene-1 % DVB), 100-200 mesh

Loading:

0.70 - 1.00 mmole/g resin, as determined by elemental analysis of sulfur

Solvent compatibility:

DCM, DMF, THF

Typical reaction conditions:

2 - 3 eq. relative to alkyl halide; 1 - 4 h at rt

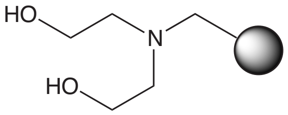
Use of 3-[4-(Tritylmercapto)phenyl]propionyl AM resin

1. Suspend resin in TFA/DCM (1:1) for 5 min. Drain resin and repeat until filtrates remain colorless.
2. Isolate the resin by filtration and wash with DCM and THF. Treat resin with NaOMe (2 eq.) in THF/MeOH 9:1 or NaHMDS (2 eq.) in THF. Wash with THF.
3. Add resin (2 eq. relative to excess alkyl halide) to reaction mixture, followed by EtOH (3 ml/g of resin). Stir o/n at rt.
4. Remove resin by filtration and wash with THF (3 x).
5. Evaporate combined filtrates to dryness.

REFERENCES

[1] M. Katoh & M. Sodeoka (1999) *Bioorg. Med. Chem. Lett.*, 9, 881.

Product No.	Product	Quantity	Price
855110	**N,N-Diethanolaminomethyl polystyrene** NBC No.: 01-64-0433 Loading: 1.50 - 2.50 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromophenyl boronic acid ⚠ Prolonged storage: +2 to +8°C; keep dry and under argon.	1 g 5 g	



Description, Methods, Applications

N,N-Diethanolaminomethyl polystyrene can serve both as a polymer-supported protecting group and a scavenger resin for boronic acids [1 - 3]. The resin reacts rapidly at room temperature with boronic acids in non-hydrolytic solvents to form a bicyclic diethanolamine boronate. It may also be used with hydrolytic solvents provided a greater excess of resin is employed; however, it is not compatible with aqueous or semi-aqueous reaction media.

This resin has been used recently to prepare a supported 2-pyridylboron reagent for Suzuki couplings [4].

This product was developed at the University of Alberta, Edmonton, and is protected by US patent application 09/943,465 and International patent application PCT/CA01/01172.

Properties

Application:
Scavenger for boronic acids; immobilization of boronic acids and their modification; resin to resin transfer

Reactivity:
removes boronic acids

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
1.50 -2.50 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromophenyl boronic acid

Solvent compatibility:
DCE, DCM, DMF, THF

Use of Diethanolaminomethyl polystyrene

For scavenging

1. Add resin (2 - 3 eq. relative to excess boronic acid) to reaction mixture. When used with alcoholic solvents, the excess of resin may need to be increased.
2. Stir for 1- 4 h at rt.
3. Remove resin by filtration and wash with THF (3 x).
4. Evaporate combined filtrates to dryness.

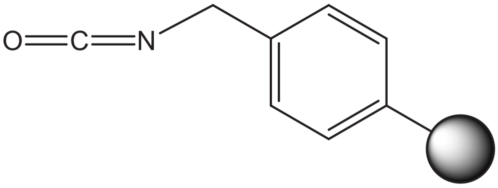
For immobilization of boronic acids [1]

1. Weigh 1 eq. resin into a reaction vessel.
2. Add 1.3 eq. $RB(OH)_2$ and THF.
3. Shake at rt for 1 h.
4. Drain and wash 3x with dry THF.

REFERENCES

[1] M. Gravel, et al. (2002) J. Org. Chem., 67, 3.
[2] D. G. Hall, et al. (1999) Angew. Chem. Int. Ed., 38, 3064.
[3] M. Gravel, et al. (2000) J. Comb. Chem., 2, 228.
[4] P. Gros, et al. (2004) *Tetrahedron Lett.*, **45**, 6239.

Product No.	Product	Quantity	Price
855022	**Methylisocyanate polystyrene** NBC No.: 01-64-0169 Loading: ≥ 1.50 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromobenzylamine. ⚠ Prolonged storage: ≤ -20°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

Methylisocyanate polystyrene reacts rapidly with nucleophiles without releasing any by-products, making it an excellent tool for the sequestration of nucleophilic reagents during solution-phase parallel synthesis [1 - 8]. With primary and secondary aliphatic amines, the reaction occurs at room temperature and is usually complete in 1 - 18 h, using a 1.5 - 3.0 fold excess of resin (relative to nucleophile) in solvents such as DCM, THF and DCE. Alcohols are unreactive under these conditions, offering the possibility of selectively removing an amine in the presence of compounds containing hydroxyl groups. Aromatic amines react slowly at room temperature but may be removed during prolonged treatments at elevated temperatures [see Table 1].

By utilizing methylisocyanate polystyrene in combination with tris-(2-aminoethyl)-amine or TBD-methyl polystyrene, excess amine and acid chloride can be removed simultaneously from coupling reactions, leaving only the pure amide product in solution [5].

The use of methylisocyanate polystyrene is exemplified below in the synthesis of 1-allyl-3-phenethyl-thiourea.

	% removed		
Amine	1 h	3 h	o/n
Propylamine	85	90	100
Diethylamine	79	82	100
p-Anisidine[a]	-	100	100

Conditions: 1.5 eq. methylisocyanate polystyrene in $CDCl_3$ at rt or [a]60 °C.

Table 1: Removal of various amines using methylisocyanate polystyrene.

Properties

Reactivity:

removes amines, hydrazines

Polymer type:

copoly(styrene-2 % DVB), 200-400 mesh

Loading:

≥ 1.50 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromobenzylamine

Solvent compatibility:

DCE, DCM, DMF, THF, toluene

Typical reaction conditions:

3 eq. relative to nucleophile; 3 - 18 h at rt (amines), 18 h at 60 °C (anilines)

Use of methylisocyanate polystyrene

1. Add resin (3 eq. relative to excess amine) to reaction mixture.
2. Stir for 3 h at rt for aliphatic primary and secondary amines, or 18 h at 60 °C for anilines.
3. Remove resin by filtration and wash with THF (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] S. W. Kaldor, et al. (1996) *Tetrahedron Lett.*, **37**, 7193.

[2] S. W. Kaldor, et al. (1996) *Bioorg. Med. Chem. Lett.*, **6**, 3041.

[3] R. J. Booth & J. C. Hodges (1997) *J. Am. Chem. Soc.*, **119**, 4882.

[4] B. A. Dressman, et al. (1998) *Tetrahedron Lett.*, **39**, 3631.

[5] M. W. Creswell, et al. (1998) *Tetrahedron*, **54**, 3983.

[6] C. Hulme, et al. (1999) *Tetrahedron Lett.*, **40**, 7925.

[7] I. Stevenson, et al. (2000) *Bioorg. Med. Chem. Lett.*, **10**, 2697.

[8] N. Baindur, et al. (2003) *J. Comb. Chem.*, **5**, 653.

Synthesis of 1-allyl-3-phenethyl-thiourea

2-Phenylethylamine (0.72 mmole) and allylisothiocyanate (0.6 mmole) were stirred together in d^2-DCM for 2 h. A sample was removed, diluted with $CDCl_3$ and a ^1H nmr spectrum recorded (Figure 1a). To the residue was added methylisocyanate polystyrene (0.24 mmole) and the mixture stirred for 2 h. A further sample was removed, diluted with $CDCl_3$ and a ^1H nmr spectrum recorded (Figure 1b), which indicated quantitative conversion of the isothiocyanate to the thiourea and complete removal of excess amine.

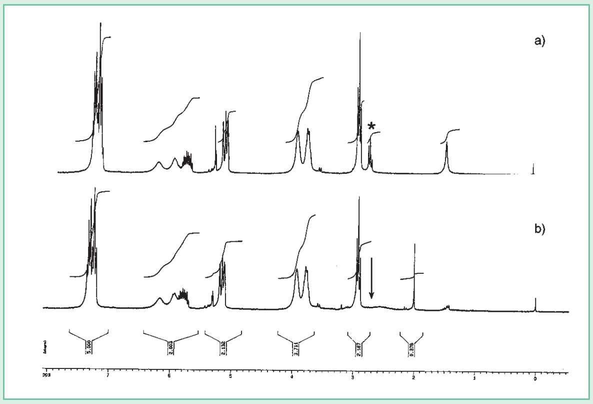
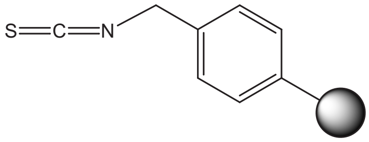


*Fig. 1: a) ^1H nmr spectrum of crude reaction mixture, * residual phenylethylamine; b) after addition of methylisocyanate resin.*

Product No.	Product	Quantity	Price
855088	**Methylisothiocyanate polystyrene** NBC No.: 01-64-0289 Loading: ≥1.50 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 4-chlorobenzylamine. ⚠ Prolonged storage: +15 to +25°C; keep dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

Methylisothiocyanate polystyrene reacts with nucleophiles without releasing any by-products, making it an excellent tool for the sequestration of amines during solution phase parallel synthesis [1].

To our knowledge there are no publications describing the use of methylisothiocyanate polystyrene as a scavenger resin, however, it is believed to have similar properties to the analogous oxygen-containing support and is likely to be less moisture sensitive.

Properties

Reactivity:
removes amines, hydrazines

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
≥1.50 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 4-chlorobenzylamine

Solvent compatibility:
DCE, DCM, DMF, THF, toluene

Typical reaction conditions:
3 eq. relative to nucleophile; 3 - 18 h at rt (amines), 18 h at 60 °C (anilines)

Use of methylisothiocyanate polystyrene

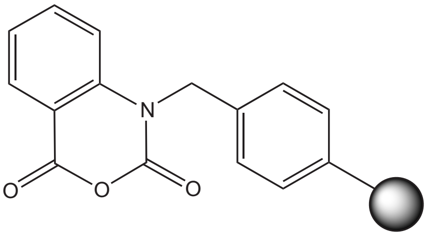
1. Add resin (3 eq. relative to excess amine) to reaction mixture.
2. Stir for 3 h at rt for aliphatic primary and secondary amines, or 18 h at 60 °C for anilines.
3. Remove resin by filtration and wash with THF (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] R. J. Booth & J. C. Hodges (1999) *Acc. Chem. Res.*, **32**, 18.

For help selecting the most appropriate resin see Table 1, page 45.

Product No.	Product	Quantity	Price
855095	**N-Methylisatoic anhydride polystyrene** NBC No.: 01-64-03017 Loading: ≥ 1.80 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromobenzylamine. ⚠ Prolonged storage: +15 to +25°C; keep dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

N-Methylisatoic anhydride polystyrene can be used in similar applications to methylisocyanate resin, as it reacts cleanly with primary and secondary amines releasing only carbon dioxide (Figure 1) [1]. The reaction is typically conducted in DCM, THF, or DMF at room temperature using 3 equivalents of resin relative to nucleophile. This reagent can be prepared with a higher level of functionality than methylisocyanate polystyrene and is likely to be more stable during long term storage.

	% removed	
Amine	3 h	o/n
Propylamine	100	-
Diethylamine	87	100
p-Anisidine[a]	74	100

Conditions: 1.5 eq. N-methylisatoic anhydride polystyrene in $CDCl_3$ at rt or [a]60 °C in DMF-d_7.

Table 1: Removal of various amines using N-Methylisatoic anhydride polystyrene.

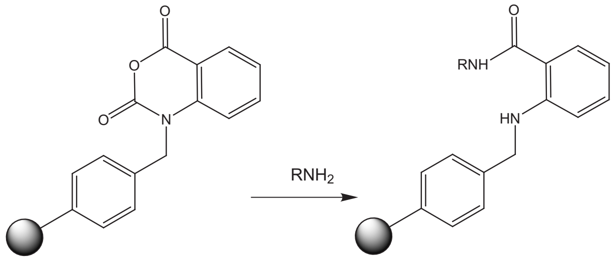


Fig. 1: Amine quenching by N-Methylisatoic anhydride resin.

Properties

Reactivity:

removes amines, hydrazines

Polymer type:

copoly(styrene-2 % DVB), 200-400 mesh

Loading:

≥ 1.80 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with 4-bromobenzylamine

Solvent compatibility:

DCE, DCM, DMF, THF, toluene

Typical reaction conditions:

3 eq. relative to nucleophile; 3 - 18 h at rt (amines), 18 h at 60 °C (anilines)

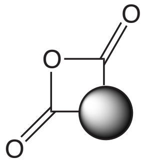
Use of N-Methylisatoic anhydride polystyrene

1. Add resin (3.0 eq. relative to excess amine) to reaction mixture.
2. Stir for 3 h at rt for aliphatic primary and secondary amines, or 18 h at 60 °C for anilines.
3. Remove resin by filtration and wash with THF (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] G. M. Coppola (1998) *Tetrahedron Lett.*, **39**, 8233.

Product No.	Product	Quantity	Price
855108	**MP-anhydride resin** NBC No.: 01-64-0422 Loading: ≥ 5.00 mmole/g resin, as determined by elemental analysis of nitrogen, after derivatization with benzylamine. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry.	5 g 25 g 100 g	



Description, Methods, Applications

MP-anhydride resin is an ultra-high load macroporous resin for scavenging of primary and secondary amines [1, 2]. The resin reacts with amines at a substitution of 5 mmole/g through ring-opening of the anhydride and amide bond formation. If the amine to be removed is strongly basic, an additional 5 mmole/g of amine can be scavenged through ion exchange interactions, making a total capacity of 10 mmole/g. The low swelling of this resin (2.4 ml/g) and its high capacity make it the most volume efficient amine scavenger available. It has a reactive density of 2.1 mmole/ml (covalent binding only), 8 times that of methylisocyanate polystyrene and twice that of isocyanate silica supports.

As the base matrix is macroporous, the resin is compatible with all commonly used solvents. Primary and seconday amines are generally scavenged in 2 - 4 hours using a 2-fold excess of resin. Electron-rich anilines can be removed under similar conditions but require the use of elevated temperatures to effect complete scavenging.

Properties

Reactivity:

removes amines, hydrazines

Polymer type:

macroporous resin, 15-50 mesh

Loading:

≥ 5.00 mmole/g resin, as determined by elemental analysis of nitrogen, after derivatization with benzylamine

Solvent compatibility:

DCE, DCM, DMF, MeOH, THF

Typical reaction conditions:

2 - 3 eq. relative to nucleophiles; 2 - 18 h at rt (amines), 4 - 18 h at 60 °C (anilines)

Use of MP anhydride resin

1. Add resin (3 eq. relative to excess amine) to reaction mixture.
2. Stir for 3 h at rt for aliphatic primary and secondary amines, or 18 h at 60 °C for anilines.
3. Remove resin by filtration and wash with THF (3 x).
4 Evaporate combined filtrates to dryness.

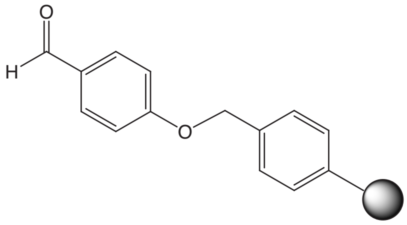
REFERENCES

[1] M. Sanna, et al. in "Proceedings of ECSOC-5, The Fifth International Electronic Conference on Synthetic Organic Chemistry", http://www.mdpi.net/ecsoc-5/b0006/b0006.htm.

[2] N. D. Hone, et al. (2003) *Tetrahedron Lett.*, **44**, 8169.

For help selecting the most appropriate resin see Table 1, page 45.

Product No.	Product	Quantity	Price
855026	**4-Benzyloxybenzaldehyde polystyrene** Aldehyde Wang HL resin NBC No.: 01-64-0182 Loading: 2.40 - 3.50 mmole/g resin, as determined by elemental analysis of sulfur, after derivatization with tosylhydrazide. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

4-Benzyloxybenzaldehyde polystyrene is an excellent polymer-supported scavenger reagent for removing amines, hydrazines, hydroxylamines and 1,2-aminothiols [1]. It can selectively sequester primary amines in the presence of secondary amines [2], making it especially useful during the work-up of reductive alkylation reactions, as exemplified below in the synthesis of N-isobutyl-5-methoxytryptamine.

Properties

Reactivity:

removes primary amines, hydrazines, hydroxylamines, 1,2-aminothiols, Grignard reagents, organolithiums

Polymer type:

copoly(styrene-2 % DVB), 200-400 mesh

Loading:

2.40 - 3.50 mmole/g resin, as determined by elemental analysis of sulfur, after derivatization with tosylhydrazide

Solvent compatibility:

DCE, DCM, DMF, THF, toluene

Typical reaction conditions:

3 eq. relative to nucleophile; 4 - 18 h at 50 °C (amines and hydrazines); 1 h at rt (organometallics)

Use of 4-benzyloxybenzaldehyde polystyrene

1. Add resin (3 eq. relative to excess amine, hydrazine or organometallic) to reaction mixture.
2. With primary amines and hydrazines stir for 3 h at 50 °C; the reaction may be catalyzed by the addition of AcOH. For organometallics the reaction can be conducted at rt.
3. Remove resin by filtration and wash with THF (3 x).

Synthesis of N-isobutyl-5-methoxytryptamine

5-Methoxytryptamine (95 mg, 0.5 mmole), methanol (1 ml) and isobutyryl aldehyde (0.032 ml, 0.35 mmole) were shaken at rt for 3 h. Borohydride resin (0.5 g, 1.25 mmole, 2.5 mmole/g) was added and the reaction mixture was left to shake at rt for 16 h.

4-Benzyloxybenzaldehyde polystyrene (0.4 g, 1.0 mmole, 2.45 mmole/g) and DCM (3 ml) were added and the reaction mixture was left to shake at rt for 6 h. The reaction mixture was filtered and the resin washed with DCM (2 ml), THF (2 ml) and methanol (2 ml). The filtrate was evaporated *in vacuo* to give the title compound (90 mg, 74 % yield, 95 % purity by silica gel LC) as a pale yellow solid.

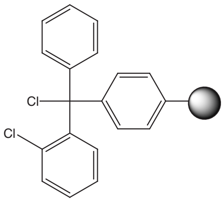
Results kindly provided by Jon Roffey, Cerebrus Ltd.

REFERENCES

[1] M. W. Creswell, et al. (1998) *Tetrahedron*, **54**, 3983.

[2] R. J. Booth & J. C. Hodges (1999) *Acc. Chem. Res.*, **32**, 18.

Product No.	Product	Quantity	Price
855017	2-Chlorotrityl chloride resin (100-200 mesh), 1% DVB NBC No.: 01-64-0114 Loading: 1.00 - 1.60 mmole/g resin, as determined from the substitution of the Fmoc-Ala-Leu loaded resin. ⚠ Prolonged storage: +15 to 25°C; bottle must always be kept tightly closed when cold and must be allowed to reach room temperature before opening; use only with dried solvents in dry glassware and apparatus.	1 g 5 g 25 g	



Description, Methods, Applications

2-Chlorotrityl chloride resin is a useful reagent for scavenging of carboxylic acids and thiols from solution. The reaction is conducted using 2 - 3 fold excess of resin in the presence of DIPEA (5 eq.), or an excess of polymer-supported base such as piperidinomethyl polystyrene, and is normally complete within 1 - 2 h. DIPEA hydrochloride salt generated can be easily removed by treating the mixture with bicarbonate resin to liberate the free base, which then can be removed by evaporation.

Properties

Reactivity:
removes thiols and carboxylic acids

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
1.00 - 1.60 mmole/g resin, as determined from the substitution of the Fmoc-Ala-Leu loaded resin

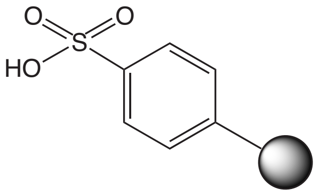
Solvent compatibility:
DCE, DCM, DMF, THF, toluene

Typical reaction conditions:
3 eq. relative to nucleophile, 1 - 2 h

Scavenging of carboxylic acids and thiols

1. Add DIPEA (6 eq. relative to excess thiol or carboxylic acid) to reaction mixture.
2. Add 2-chlorotrityl chloride resin (3 eq. relative to residual thiol or carboxylic acid) and stir at rt for 1 - 2 h.
3. Add (Polystyrylmethyl)trimethylammonium bicarbonate (4 eq. relative to residual thiol or carboxylic acid) and agitate gently for 3 h at rt.
4. Remove resins by filtration and wash with DCM.
5. Evaporate combined filtrates to dryness.

Product No.	Product	Quantity	Price
855109	**Sulfonic acid resin MP** NBC No.: 01-64-0432 Loading: 2.50 - 3.50 mmole/g resin, as determined by elemental analysis of sulfur.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-supported version of toluene-sulfonic acid can be used as an amine scavenger or to promote reactions requiring strong acid catalysis.

Properties

Application:
Strong acid catalyst and amine scavenger

Polymer type:
macroporous copoly(styrene-DVB), 70-90 mesh

Loading:
2.50 - 3.50 mmole/g resin, as determined by elemental analysis of sulfur

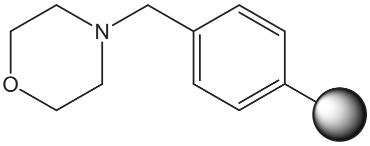
Solvent compatibility:
DCM, DCE, THF, toluene, DMF

Typical scavenging reaction conditions:
2-3 eq. relative to amine for 3 h

Use of Sulfonic acid resin MP

1. Add resin (2 eq. relative to amine) to reaction mixture.
2. Stir at rt for 1 - 2 h.
3. Remove resin by filtration and wash with DCM.
4. Evaporate combined filtrates to dryness.

Product No.	Product	Quantity	Price
855024	**Morpholinomethyl polystyrene** NBC No.: 01-64-0171 Loading: ≥ 3.20 mmole/g resin, as determined by elemental analysis of nitrogen.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-bound tertiary amine is ideal for applications requiring addition of a tertiary base as its use eliminates the need to separate product from amine salts at the end of the reaction. By using these reagents in combination with polyamine and isocyanate resins, the synthesis of amides and sulfonamides can be accomplished utilizing filtration as the only purification step [1 - 6].

Care should be exercised when using these supports in conjunction with chloroformates as these highly electrophilic reagents can cleave the benzylic amine, releasing the corresponding carbamate into solution.

Sold under license from Warner-Lambert Company.

Properties

Application:
tertiary amine base

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
≥ 3.20 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:
DMF, THF, DCM, DCE

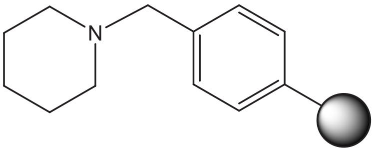
Typical reaction conditions:
3 eq. relative to electrophile

REFERENCES

[1] R. J. Booth & J. C. Hodges (1997) *J. Am. Chem. Soc.*, **119**, 4882.
[2] M. W. Creswell, et al. (1998) *Tetrahedron*, **54**, 3983.
[3] C. Blackburn, et al. (1998) *Tetrahedron Lett.*, **39**, 3635.
[4] M.-O. Contour-Galcéra, et al. (2001) *Bioorg. Med. Chem. Lett.*, **11**, 741.
[5] M. Takayanagi, et al. (2000) *J. Org. Chem.*, **65**, 3811.
[6] F. Palacios, et al. (2002) *J. Org. Chem.*, **67**, 7283.

For help selecting the most appropriate resin see Table 2, page 47.

Product No.	Product	Quantity	Price
855082	**Piperidinomethyl polystyrene** NBC No.: 01-64-0212 Loading: 3.00 - 5.00 mmole/g resin, as determined by elemental analysis of nitrogen.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-bound tertiary amine is ideal for applications requiring addition of a tertiary base as its use eliminates the need to separate product from ammonium salts at the end of the reaction. By using these reagents in combination with polyamine and isocyanate resins, the synthesis of amides and sulfonamides can be accomplished utilizing filtration as the only purification step [1, 2].

The use of piperidinomethyl polystyrene resin is exemplified in the synthesis of N-phenylethyl-toluenesulfonamide.

Properties

Application:
tertiary amine base

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
3.00 - 5.00 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:
DMF, THF, DCM, DCE

Typical reaction conditions:
3 eq. relative to electrophile

REFERENCES

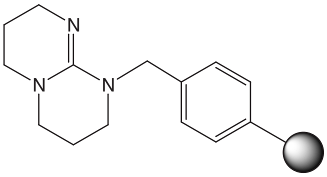
[1] R. J. Booth & J. C. Hodges (1997) *J. Am. Chem. Soc.*, **119**, 4882.

[2] N. Baindur, et al. (2003) *J. Comb. Chem.*, **5**, 653.

Synthesis of N-phenylethyl-toluenesulfonamide

2-Phenylethylamine (0.72 mmole) and piperidinomethyl polystyrene (1.2 mmole) were stirred together in DCM (0.5 ml). Tos-Cl (0.6 mmole) was added and the mixture gently magnetically stirred o/n. The spent resin was removed by filtration and washed with DCM. Methylisocyanate polystyrene (0.24 mmole) was added and the mixture stirred for 2.5 h. The resin was removed by filtration and washed with DCM. The combined filtrates were evaporated to give the desired product in quantitative yield.

Product No.	Product	Quantity	Price
855033	**TBD-methyl polystyrene** NBC No.: 01-64-0332 Loading: 2.00 - 3.00 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with chloroacetic acid. ⚠ Prolonged storage: +15 to +25°C; keep cool and dry and under argon.	5 g 25 g	



Description, Methods, Applications

TBD-methyl polystyrene is a polymer-bound version of the strong and highly hindered organic base 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD). It has been used to mediate the esterification of carboxylic acids [1], the alkylation of active methylene compounds [2, 3], secondary amines [4], phenols [5, 6] and thiols [7], and the cleavage from REM resins [8]; and to sequester auxiliary nucleophiles from amide-bond forming reactions [9]. This reagent was shown to be a good catalyst for the nitroaldol (Henry) reaction and the addition of dialkyl phosphites to a variety of carbonyl compounds and imines [10], and for mediating the 1,3-cycloaddition of t-butyl isocyanoacetate to nitrostyrenes [11].

The use of TBD-methyl resin is exemplified below in the synthesis of 2-(3-Methoxyphenoxy)-1-phenylethanone. As can be seen from this example, contrary to [5], this resin does not appear to be an effective scavenger for phenols.

TBD-methyl polystyrene also effectively cleaves the Fmoc group from protected amines; however, the reagent does not scavenge the dibenzofulvene by-product.

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[1] K. Iijima, et al. (1992) *J. Macromol. Sci., Pure Appl. Chem.*, **A29**, 249.
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[9] J. J. Weidner, et al. (1999) *Tetrahedron Lett.*, **40**, 239.
[10] D. Simoni, et al. (2000) *Tetrahedron Lett.*, **41**, 1607.
[11] M. Caldarelli, et al. (1999) *J. Chem. Soc., Perin Trans. 1*, 107.

Properties

Application:
strong tertiary amine base

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
2.00 - 3.00 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with chloroacetic acid

Solvent compatibility:
DMF, THF, DCM, DCE

Typical reaction conditions:
3 eq. relative to acidic component

Synthesis of 2-(3-Methoxyphenoxy)-1-phenylethanone

To phenacyl bromide (1.0 mmole) and 3-methoxyphenol (1.2 mmole) in THF/MeCN (4:1) was added TBD-methyl polystyrene (2.5 mmole). The mixture was stirred o/n at rt. After this time, HPLC analysis (Figure 1) indicated almost quantitative conversion of the phenylacylbromide. Residual phenol was only partially removed by the resin.

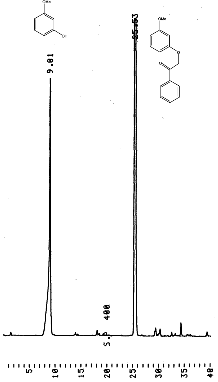
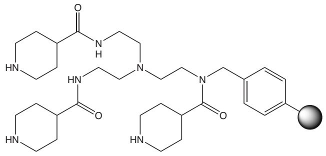


Fig. 1: HPLC profile of reaction mixture.

Product No.	Product	Quantity	Price
855083	**Piperidine-4-carboxylic acid polyamine resin** Tris-(isonipecotylaminoethyl)-amine polystyrene HL resin (200-400 mesh), 1% DVB NBC No.: 01-64-0256 Loading: 1.3 - 2.5 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-bound base can be used in place of piperidine as a Knoevenagel catalyst [1]. It also cleaves Fmoc protecting groups in solution [2], but the dibenzofulvene produced is not scavenged and remains mostly in solution. This may be removed by employing a large excess of N-(2-mercaptoethyl)-aminomethyl polystyrene [3].

Properties

Application:
secondary amine base

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
1.3 - 2.5 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate

Solvent compatibility:
DMF, THF, DCM, DCE

REFERENCES

[1] J. Simpson, et al. (1999) *Tetrahedron Lett.*, **40**, 7031.
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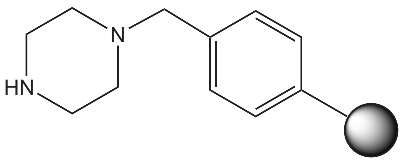
Product No.	Product	Quantity	Price
855092	**Piperazinomethyl polystyrene** NBC No.: 01-64-0310 Loading: 0.80 - 1.50 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate.	5 g 25 g	



Description, Methods, Applications

This polymer-bound secondary amine is an efficient solid phase Knoevenagel catalyst (Figure 1) [1]. Its use eliminates the problems associated with separating product from piperidine salts and piperidine related by-products during work-up. Furthermore, the use of this resin minimizes side reactions due to transesterification when reactions are carried out in alcoholic solvents.

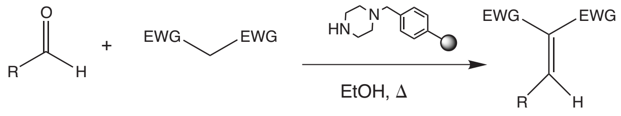


Fig. 1: Knoevenagel reaction using Piperazinomethyl polystyrene.

Properties

Application:
secondary amine base

Polymer type:
copoly(styrene-1 % DVB), 100-200 mesh

Loading:
0.80 - 1.50 mmole/g resin, as determined by elemental analysis of chlorine, after derivatization with 3,4-dichlorophenylisocyanate

Solvent compatibility:
DMF, THF, DCM, DCE, EtOH

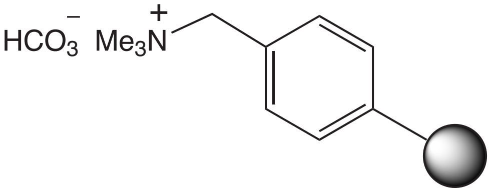
Use of piperazinomethyl polystyrene

1. Dissolve aldehyde (1 eq.) and active methylene compound (1 eq.) in ethanol.
2. Add piperazinomethyl polystyrene (0.075 eq.) and reflux for 2 h.
3. Remove resin by filtration.
4. Evaporate filtrate to dryness.

REFERENCES

[1] J. Simpson, et al. (1999) *Tetrahedron Lett.*, **40**, 7031.

Product No.	Product	Quantity	Price
855040	(Polystyrylmethyl)trimethylammonium bicarbonate NBC No.: 01-64-0419 Loading: ≥ 3.50 mmole/g resin, as determined photometrically from the remaining p-nitrophenol after scavenging.	5 g 25 g 100 g	



Description, Methods, Applications

(Polystyrylmethyl)trimethylammonium bicarbonate is a general purpose polymer-supported base for scavenging of acidic molecules, such as carboxylic acids, HCl and HBr, and for the neutralization of amine salts [1 - 3].

Its use greatly simplifies the work-up of reactions which generate salts of volatile amines, such as those involving neutralization of HCl or HBr with DIPEA or TEA. Treatment of the reaction mixture with bicarbonate resin liberates the free amine, enabling the amine then to be simply removed by evaporation, with the chloride or bromide remaining bound as the counterion to the resin.

Removal of excess carboxylic acids and phenols generally requires the use of 3 - 4 equivalents of resin and takes typically 1 - 3 hours; although for hindered systems the excess may need to be increased and the reaction time extended.

Properties

Application:
polymer-supported inorganic base

Polymer type:
macroporous copoly(styrene- DVB), 20-50 mesh

Loading:
≥ 3.50 mmole/g resin, as determined photometrically from the remaining p-nitrophenol after scavenging.
Solvent compatibility:
DCM, MeCN, THF

Typical reaction conditions:
4 eq. relative to acidic component; 1 - 3 h.

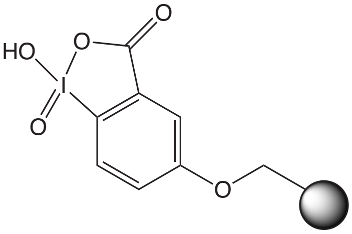
Use of bicarbonate resin in removing salts of volatile amines

1. Add bicarbonate resin (4 eq. relative to expected amine salt) to reaction mixture and gently agitate at rt for 1 - 3 h.
2. Remove resin by filtration and wash with DCM.
3. Evaporate combined filtrates and dry *in vacuo*.

REFERENCES

[1] J. Parlow, et al. (1997) *Tetrahedron Lett.*, **38**, 7959.
[2] S. V. Ley, et al. (1999) *J. Chem. Soc., Perkin Trans. I*, 1251.
[3] S. R. Stauffer & J. A. Katzenellenbogen (2000) *J. Comb. Chem.*, **2**, 318.

Product No.	Product	Quantity	Price
855043	**IBX-polystyrene** NBC No.: 01-64-0301 Loading: 0.90 - 1.50 mmole/g resin, as determined by elemental analysis of iodine. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry.	1 g 5 g 25 g	



Description, Methods, Applications

This polymer-bound version of IBX cleanly converts primary and secondary alcohols to the corresponding aldehydes and ketones [1].

Benzylic and allylic alcohols are most readily oxidized, and this may be used to effect selective oxidation in polyhydroxylic compounds. The reagent is compatible with a wide-range of non-hydroxylic functionalities, such as ethers, thioethers, and secondary amides, and has been used to convert peptide alcohols to the corresponding aldehydes [2].

Table 1 shows conversion yields for the oxidation of various primary and secondary alcohols with IBX-polystyrene.

Table 1: Yields of aldehydes prepared with IBX-polystyrene.

	Yield of aldehyde or ketone		
Alcohol	2 eq.	3 eq.	4 eq.
4-Bromobenzyl alcohol	100	-	-
Cinnamyl alcohol	98.6	99.2	-
2-Phenyl-1-ethanol	-	77	80
1-Phenyl-1-ethanol	98.8	-	-
2-Phenyl-1-propanol	-	90	95
3-Phenyl-1-propanol	-	70	-
5-Phenyl-1-propanol	-	68	71

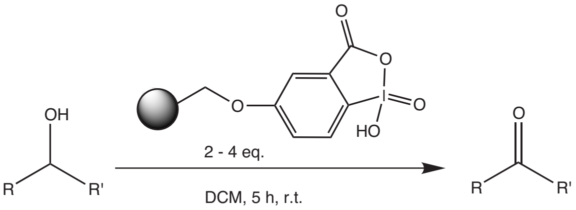


Fig. 1: Oxidation of alcohols with IBX-polystyrene.

Properties

Application:
oxidizes alcohols to aldehydes and ketones

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
0.90 - 1.50 mmole/g resin, as determined by elemental analysis of iodine

Solvent compatibility:
DMF, THF, DCM, DCE

Use of IBX-polystyrene

1. Dissolve alcohol (1 eq.) in DCM.
2. Add IBX-polystyrene (2 - 4 eq.).
3. Agitate and follow reaction by HPLC.
3. Remove resin by filtration.
4. Evaporate filtrate to dryness.

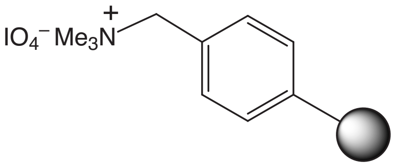
REFERENCES

[1] G. Sorg, et al. (2001) *Angew. Chem. Int. Ed.*, **40**, 4395.

[2] G. Sorg, et al. (2005) *J. Pept. Sci.*, **11**, 147.

For help selecting the most appropriate resin see Table 2, page 47.

Product No.	Product	Quantity	Price
855100	**(Polystyrylmethyl)trimethylammonium metaperiodate** NBC No.: 01-64-0374 Loading: 2.00 - 2.50 mmole/g resin, as determined by elemental analysis of iodine. ⚠ Prolonged storage: ≤ -20°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-supported metaperiodate is an effective reagent for the oxidative cleavage of 1,2-diols, conversion of sulfides to sulfoxides, and catechols and quinols to quinones [1].

Under conditions given in the method below trans-cyclohexane-1,2-diol gave adipaldehyde in 97% yield (Figure 1).

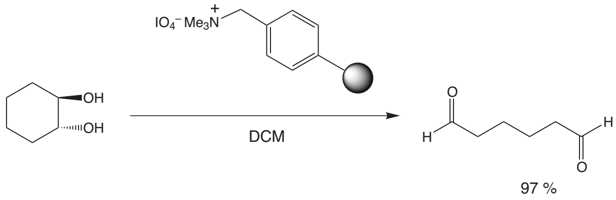


Fig. 1: Synthesis of adipaldehyde using (polystyrylmethyl)-trimethylammonium metaperiodate.

Properties

Application:
oxidation of 1,2-diols, 1,2-aminoalcohols, thioethers, catechols, quinols

Polymer type:
macroporous copoly(styrene-DVB), 20-50 mesh

Loading:
2.00 - 2.50 mmole/g resin, as determined by elemental analysis of iodine

Solvent compatibility:
DCE, DCM, DMF, THF

Typical reaction conditions:
2 eq. relative to diol

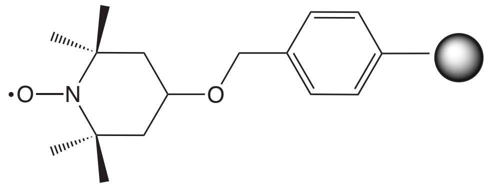
Use of (Polystyrylmethyl)trimethylammonium metaperiodate

1. Add resin (2 eq.) to the diol or sulfide in DCM.
2. Stir for 2 h (catechols and quinols) or o/n (sulfides and 1,2-diols) at rt.
3. Remove resin by filtration and wash with DCM (3 x).
4. Evaporate combined filtrates to dryness.

REFERENCES

[1] P. Hodge & D. C. Sherrington in "Polymer-supported reactions in organic synthesis", Chichester, J. Wiley & Sons, 1980, pp. 88.

Product No.	Product	Quantity	Price
855107	**TEMPO polystyrene** 4-(Polystyrylmethyloxy)-2,2,6,6-tetramethyl-piperidin-1-yloxy free radical NBC No.: 01-64-0414 Loading: 1.50 - 2.00 mmole/g resin, as determined by elemental analysis of nitrogen. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

Oxidation of TEMPO polystyrene with N-chlorosuccinimide yields the corresponding polymer-bound oxoammonium salt (Figure 1) [1]. This powerful oxidant cleanly converts primary alcohols to aldehydes and secondary alcohols to ketones (Figure 2). In cases where the initial product is easily enolizable, such as benzyl methyl ketone or cholesterol, further oxidation can occur which leads to generation of the 1,2-diketone. Similarly, terminal diols are further oxidized to lactones and β-naphthol is converted to a mixture of naphthoquinones (Table 1).

TEMPO polystyrene may also be used to catalyze the oxidation of alcohols with oxone in the presence of a phase-transfer agent such as tetrabutylammonium bromide (TBA-Br) [2]. The efficacy of this approach was examined using 4-bromobenzyl alcohol as a model (Table 2).

Alcohol	Product	Yield (%)
benzyl alcohol	benzaldehyde	>95
piperonol	piperonal	>95
3-phenylpropanol	3-phenylpropanal	90
cinnamyl alcohol	cinnamaldehyde	>95
cyclohexanol	1,2-dioxocyclohexane	85
1,4-butanediol	g-butyrylactone	65
1-phenylpropanol	phenylpropan-1-one	>95

Table 1: Oxidation of alcohols with polymer-supported oxoammonium salts [1].

Reaction conditions[a]	% Conversion (HPLC)
Oxone	0
Oxone + TBA-Br	60 - 75
Oxone + TEMPO-PS	0
Oxone + TEMPO-PS + TBA-Br	97.5 - 98[b]

Table 2: Oxidation of 4-bromobenzyl alcohol with oxone catalyzed by TEMPO polystyrene [2].

[a] Alcohol (188 mg,1 mmole) in DCM (5 ml) o/n at rt, with or without addition of TEMPO-PS (30 mg, 0.06 mmole), TBA-Br (13 mg, 0.04 mmole) and oxone (1.35 g, 2.2 mmole); [b] 1-2% acid also generated.

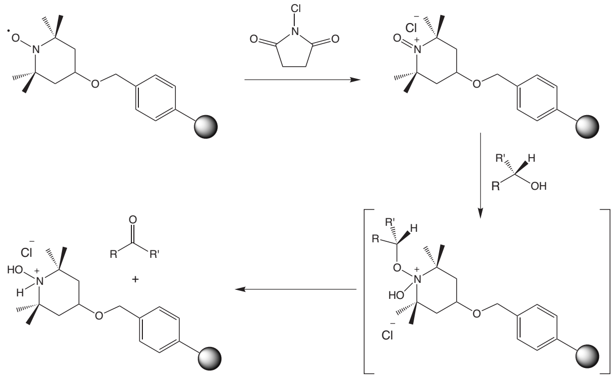


Fig. 1: Mechanism of TEMPO-mediated oxidation of alcohols.

For help selecting the most appropriate resin see Table 2, page 47.

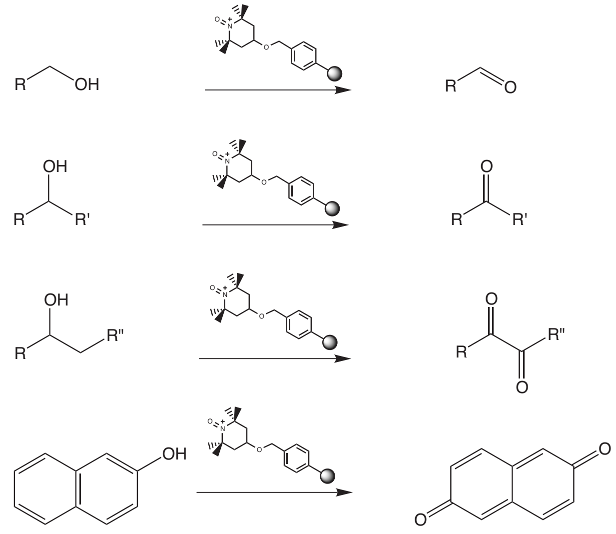


Fig. 2: Applications of oxoammonium resin.

Properties

Application:
oxidation of alcohols

Reactivity:
converts primary alcohols to aldehydes and secondary alcohols to ketones

Polymer type:
copoly(styrene-1 % DVB), 100-200 mesh

Loading:
1.50 - 2.00 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:
DCE, DCM, THF

Typical reaction conditions:
3 - 5 eq. resin relative to alcohol in DCM

Conversion to oxoammonium salt

1. Dissolve N-chlorosuccinimide (5 eq.) in dry DCM. Add 4M HCl in dioxane (6 eq.) and stir for 5 min.
2. Add to TEMPO resin (1 eq.), pre-swollen in DCM.
3. Agitate gently for 15 min.
4. Isolate resin by filtration and wash with dry DCM.

Oxidation of alcohols with oxammonium resin

1. Dissolve alcohol (1 eq.) in dry DCM.
2. Add freshly prepared resin (5 eq.) pre-swollen in DCM and agitate for 1 h (primary alcohols) or 2 h (secondary alcohols).
3. Remove resin by filtration and wash with DCM.
4. Evaporate combined filtrates to dryness.

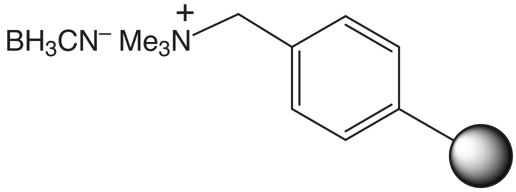
Oxidation of benzyl alcohol using TEMPO polystyrene

N-Chlorosuccinimide (524 mg, 3.92 mmole, 5 eq.) was dissolved in DCM containing 4N HCl in dioxane (1.2 ml, 4.7 mmole, 6 eq.). After 5 min the solution was added to TEMPO polystyrene (0.5 g, 0.87 mmole, 1 eq.) pre-swollen in DCM. The mixture was agitated for 15 min, and then the resin was isolated by filtration and washed with dry DCM.
This material was added to a solution of benzyl alcohol (16 µl, 0.157 mmole) dissolved in DCM. The solution was agitated for 1h at rt, and then the resin was removed by filtration, washed with DCM. The combined filtrates were evaporated to dryness to provide benzaldehyde.

REFERENCES

[1] S. Weik, et al. (2001) *Angew. Chem. Int.Ed.*, **40**, 1436.
[2] C. Bolm, et al. (2000) *Org. Lett.*, **2**, 1173.

Product No.	Product	Quantity	Price
855034	(Polystyrylmethyl)trimethylammonium cyanoborohydride NBC No.: 01-64-0337 Loading: 3.50 - 5.00 mmole/g resin, as determined by elemental analysis of boron. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-supported cyanoborohydride reagent is an excellent tool for mediating the reductive amination of aldehydes and ketones [1 - 3] and aza-Wittig reactions [4]. Furthermore, unlike the corresponding soluble reagent, the use of this material does not lead to contamination of the product by cyanide ions since the cyanide is retained on the resin throughout the reaction in organic solvents.

The use of this resin is exemplified below in the synthesis of dibenzylmethylamine (Figure 1).

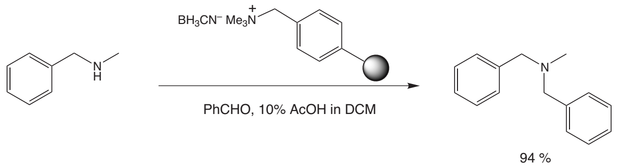


Fig. 1: Synthesis of dibenzylmethylamine.

Properties

Application:
reducing agent for reductive aminations

Polymer type:
macroporous copoly(styrene-DVB), 20-50 mesh

Loading:
3.50 - 5.00 mmole/g resin, as determined by elemental analysis of boron

Solvent compatibility:
DCE, DCM, DMF, THF, MeOH

Typical reaction conditions:
2 eq. relative to imine

Application:

Synthesis of dibenzylmethylamine

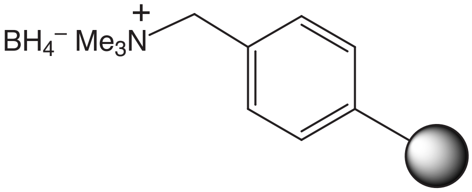
N-Methyl benzylamine (26 µl, 0.2 mmole) and a 1:10 mixture of AcOH : DCM (2ml) was shaken at rt. Benzaldehyde (60 µl, 0.6 mmole) was added followed by (polystyrylmethyl)trimethylammonium cyanoborohydride (0.12 g, 0.4 mmole, 3.35 mmole/g) and the reaction mixture was left to shake at rt for 16 h. The reaction mixture was poured onto a SCX-ion exchange column and washed with methanol (10 ml), then eluted with a 2M solution of NH_3 in methanol (4 ml).
The filtrate was evaporated *in vacuo* to give the title compound (40 mg, 94 % yield, 97.5 % purity by silicagel LC) as a colorless oil.
Results kindly provided by Jon Roffey, Cerebrus Ltd.

REFERENCES

[1] R. O. Hutchins, et al. (1978) *J. Chem. Soc., Chem. Commun.*, 1088.
[2] S. V. Ley, et al. (1998) *J. Chem. Soc., Perkin Trans 1*, 2239.
[3] J. Habermann, et al. (1998) *J. Chem. Soc., Perkin Trans1*, 3127.
[4] K. Hemming, et al. (2000) *Synlett*, 11, 1565.

For help selecting the most appropriate resin see Table 2, page 47.

Product No.	Product	Quantity	Price
855097	**(Polystyrylmethyl)trimethylammonium borohydride** NBC No.: 01-64-0349 Loading: 3.00 - 4.50 mmole/g resin, as determined by elemental analysis of boron. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g 100 g	



Description, Methods, Applications

The applications of polymer-supported borohydride have been reviewed [1, 2].

Polymer-supported borohydride has been used primarily to reduce aldehydes, ketones, and imines, and unlike sodium borohydride, it can also reduce α,β-unsaturated carbonyl compounds to the corresponding α,β-unsaturated alcohols without competing reduction of the double bond.

In model studies related to the reduction of acetophenone in DCM, 2 eq. of borohydride resin effected 84% reduction overnight. When 3 and 5 eq. were used, the extent of reaction increased to 96% and 98%, respectively.

This reagent can selectively reduce the double bond of nitroalkenes, and aryl azides and sulfonyl azides are reduced to the corresponding anilines and sulfonamides. It has also been used to reduce diphenyl diselenides to selenolates [3].

The reactivity of polymer-supported borohydride can be enhanced by using it in combination with certain transition metal salts. In the presence of $Ni(OAc)_2$, this resin reduces alkyl azides to amines, alkyl iodides to alkanes, nitro compounds to amines, and benzyl alcohols and benzaldehydes to the corresponding toluene derivatives. In the recent synthesis of epibatidine, the use of polymer-supported borohydride in conjunction with $NiCl_2$ was crucial in effecting the reduction of the key nitro group without concurrent dechlorination of the 2-chloropyridine moiety [4]. With $CuSO_4$, aldehydes and ketones are reduced to alcohols, nitro and azido compounds to amines, and bromo compounds to hydrocarbons.

The utility of this resin in the synthesis of an N-alkyltryptamine is given below in the synthesis of N-isobutyl-5-methoxytryptamine.

Properties

Application:
reducing agent

Polymer type:
macroporous copoly(styrene-DVB), 20-50 mesh

Loading:
3.00 - 4.50 mmole/g resin, as determined by elemental analysis of boron

Solvent compatibility:
DCE, DCM, DMF, MeOH, THF

Typical reaction conditions:
2 - 5 eq. relative to carbonyl compound

Synthesis of N-isobutyl-5-methoxytryptamine

5-Methoxytryptamine (95 mg, 0.5 mmole), methanol (1 ml) and isobutyryl aldehyde (0.032 ml, 0.35 mmole) were shaken at rt for 3 h. Borohydride resin (0.5 g, 1.25 mmole, 2.5 mmole/g) was added and the reaction mixture was left to shake at rt for 16 h.

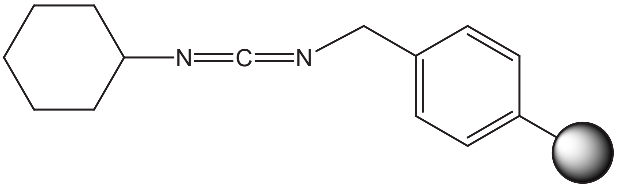
4-Benzyloxybenzaldehyde polystyrene (0.4 g, 1.0 mmole, 2.45 mmole/g) and DCM (3 ml) were added and the reaction mixture was left to shake at rt for 6 h. The reaction mixture was filtered and the resin washed with DCM (2 ml), THF (2 ml) and methanol (2 ml). The filtrate was evaporated *in vacuo* to give the title compound (90 mg, 74 % yield, 95 % purity by silica gel LC) as a pale yellow solid.

Results kindly provided by Jon Roffey, Cerebrus Ltd.

REFERENCES

[1] D. H. Drewry, et al. (1999) *Med. Res. Rev.*, **19**, 97.
[2] A. Kirschning (2000) *J. Prakt. Chem.*, **342**, 1.
[3] C. Millois & P. Diaz (2000) *Org. Lett.*, **2**, 1705.
[4] J. Habermann, et al. (1999) *J. Chem. Soc., Perkin Trans. 1*, 1253.

Product No.	Product	Quantity	Price
855029	**N-Cyclohexylcarbodiimide, N'-methyl polystyrene** NBC No.: 01-64-0211 Loading: ≥1.30 mmole/g resin, as determined by HPLC, after reaction of Z-Phe-OH with cyclohexylamine. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon; hygroscopic.	5 g 25 g 100 g	



Description, Methods, Applications

N-Cyclohexylcarbodiimide,N'-methyl polystyrene [1] is an ideal tool for mediating solution phase coupling reactions. Typically, the amine and carboxylic acid are treated with a 2-3 fold excess of resin in DCM or DMF [2, 3]; a slight excess of carboxyl component over amine component is often used to help drive the reaction to completion. As excess acid and urea by-products remain attached to the resin at the end of the reaction, the product can normally be isolated pure by filtration and evaporation of the reaction mixture. Reactions can be accelerated by the addition of auxiliary nucleophiles such as HOBt; these can be removed using polyamine- or TBD-polystyrene. This resin has also been used in conjunction with DMAP to mediate ester formation [4].

The use of this resin is exemplified below.

Properties

Application:
coupling reagent

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
≥1.30 mmole/g resin, as determined by HPLC, after reaction of Z-Phe-OH with cyclohexylamine

Solvent compatibility:
DCE, DCM, DMF, THF

Typical reaction conditions:
1.5 - 3 eq. relative to acid

Synthesis of N-phenylethyl-4-bromophenyl-acetamide & N-isobutyl-phenoxyacetamide

4-Bromophenylacetic acid (0.365 mmole) and phenylethylamine (0.24 mmole) were dissolved in dry, acid free DCM (~ 1 ml). N-Cyclohexylcarbodiimide,N'-methyl polystyrene (0.73 mmole) was added, followed by sufficient DCM to swell the resin and keep the reaction mobile, and the mixture gently magnetically stirred o/n. The spent resin was removed by filtration and washed with DCM. Evaporation of the filtrate provided the product in quantitative yield. The product was clean by ^{1}H nmr (Figure 1) and HPLC (Figure 2). The same procedure repeated with phenoxyacetic acid and isobutylamine gave N-isobutyl-phenoxyacetamide in 94% yield, which was also clean by ^{1}H nmr (Figure 3) and HPLC (Figure 4).

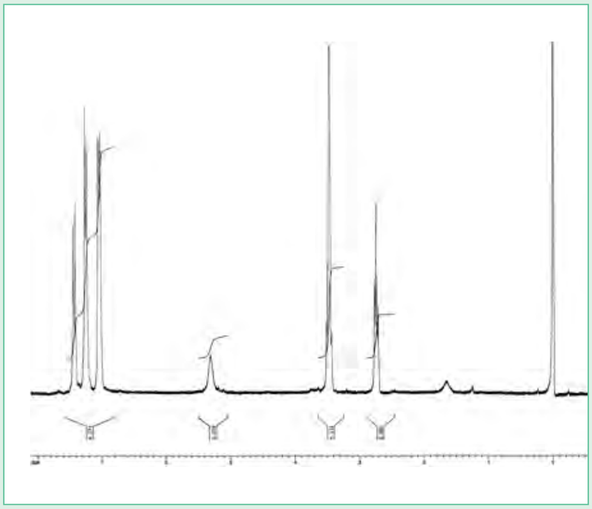


Fig. 1: ^{1}H nmr spectrum of total crude N-phenylethyl-4-bromophenylacetamide.

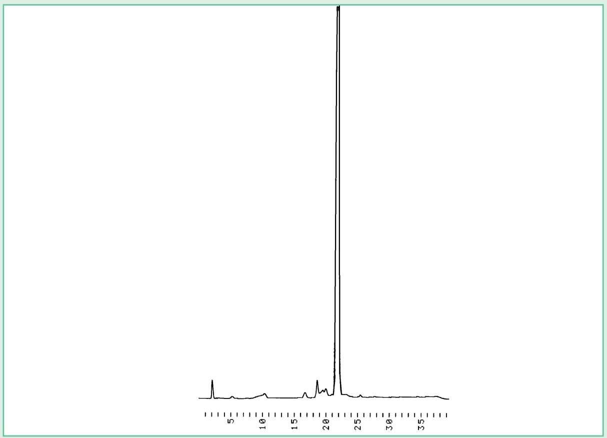


Fig. 2: HPLC elution profile of total crude N-phenylethyl-4-bromophenylacetamide.

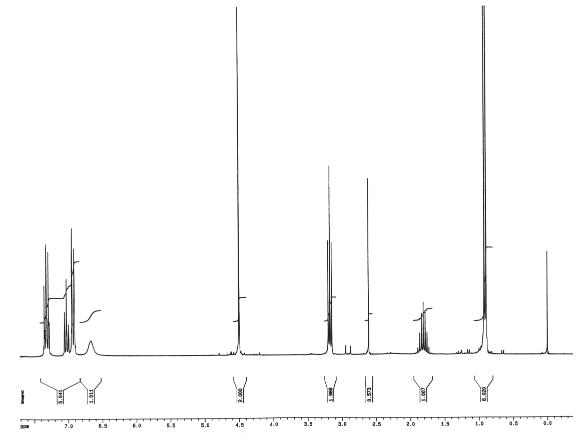


Fig. 3: ^{1}H nmr spectrum of total crude N-isobutyl-phenoxyacetamide.

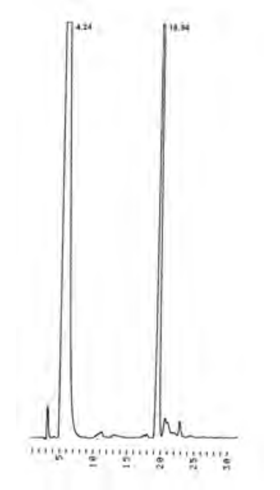
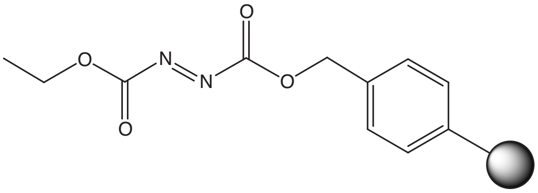


Fig. 4: HPLC elution profile of total crude N-isobutyl-phenoxyacetamide.

REFERENCES

[1] G.M Weinshenker, et al. (1988) *Org. Synth.*, Coll. Vol. VI, 951.
[2] Y. Guan, et al. (2000) *J. Comb. Chem.*, **2**, 297.
[3] K. Senten, et al. (2003) *J. Comb. Chem.*, **5**, 336.
[4] M. Cano, et al. (2002) *J. Org. Chem.*, **67**, 129.

Product No.	Product	Quantity	Price
855036	**Ethoxycarboxylazocarboxymethyl polystyrene** NBC No.: 01-64-0371 Loading: 0.70 - 1.10 mmole/g resin, as determined by elemental analysis of nitrogen. ⚠ Prolonged storage: ≤ -20°C; keep cool and dry and under argon; prevent exposure to light.	5 g 25 g 100 g	



Description, Methods, Applications

This immobilized azodicarboxylate [1] facilitates Mitsunobu coupling without generation of difficult to remove diethyl hydrazinodicarboxylate. The reaction is best carried out in THF using an excess of polymer-supported azodicarboxylate to alcohol and acidic components. Any unreacted alcohol is scavenged by excess azodicarboxylate [2].

In cases where the product is soluble in ether, triphenylphosphine by-products can be removed by ether precipitation or removed by passing the reaction mixture through a plug of silica. Alternatively, a water-soluble phosphine can be employed which can then be removed by extraction. A novel approach has been described by P. Lan, et al., which employs an anthracene-tagged phosphine that can be removed by Diels-Adler reaction with a polymer-supported maleimide [2].

In the esterification of benzoic acid the method described below gave the results given in Table 1.

Alcohol	Conversion (%)
1-Phenylethanol	56
Benzyl alcohol	69
4-Methoxybenzyl alcohol	88
4-Penten-2-ol	78
Isopropanol	85

Table 1: Esterification of benzoic acid with various alcohols.

Properties

Application:
redox-based coupling reagent

Polymer type:
copoly(styrene-1 % DVB), 100-200 mesh

Loading:
0.70 - 1.10 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:
DCE, DCM, DMF, THF

Typical reaction conditions:
2 eq. relative to alcohol

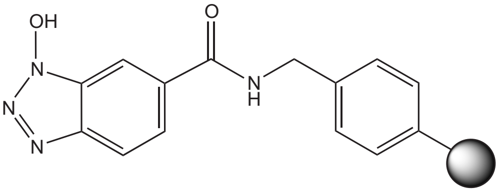
Use of Ethoxycarbonylazocarboxymethyl polystyrene

1. Dissolve alcohol (1.15 eq.) and acidic component (1 eq.), triphenylphosphine (1 eq.) in dry THF under Ar. Add azodicarboxylate resin (1.15 eq.) and gently agitate mixture for 48 h.
2. Add water (1 eq.) and stir for 10 min.
3. Remove resin by filtration, wash with THF and evaporate the combined filtrates to dryness.
4. Warm residue with ether and cool in ice-bath. Remove triphenylphosphine oxide by filtration, or filter through silica plug to remove $OPPh_3$.
5. Evaporate filtrate to dryness.

REFERENCES

[1] L. D. Arnold, et al. (1989) *J. Am. Chem. Soc.*, **111**, 3973.
[2] P. Lan, et al. (2003) *J. Comb. Chem.*, **5**, 660.

Product No.	Product	Quantity	Price
855041	**HOBt-6-carboxamidomethyl polystyrene** NBC No.: 01-64-0425 Loading: 1.00 - 1.50 mmole/g resin, as determined by elemental analysis of sulfur, after derivatization with thiophene-2-carboxylic acid. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry.	5 g 25 g 100 g	



Description, Methods, Applications

Acylation of this supported HOBt reagent generates a polymer-bound active ester which, due to the electron-withdrawing 6-carboxy substituent on the benzotriazole ring, might have similar reactivity to an HOAt ester. Treatment of acylated resin with an amine provides the corresponding amide without formation of soluble by-products. Following use, the resin can be recycled by treating with a simple amine to destroy any residual active ester. With analogous supports, the initial loading has been performed using symmetrical anhydrides in the presence of pyridine and with carboxylic acids activated with PyBrOP in DMF [1] or DIPCDI in DCM [2 - 5].

Properties

Application:
generation of active esters

Polymer type:
copoly(styrene-2 % DVB), 200-400 mesh

Loading:
1.00 - 1.50 mmole/g resin, as determined by elemental analysis of sulfur, after derivatization with thiophene-2-carboxylic acid

Solvent compatibility:
DCE, DCM, DMF, THF

Typical reaction conditions:
1 eq. relative to activated carboxylic acid

Use of HOBt resin

PyBrOP® method

1. Dissolve acid (2 eq.), PyBrOP® (2 eq.) in DMF. Add DIPEA (4 eq.), mix and add immediately to resin. Leave to react for 5 h with gentle agitation.
2. Wash resin with DMF and repeat reaction with fresh reagents.
3. Wash resin with DMF.
4. Suspend resin in DMF or DCM, add amine (0.8 eq.) and allow to react with gentle agitation o/n.
5. Remove resin by filtration, wash with DCM and evaporate the combined filtrates to dryness.

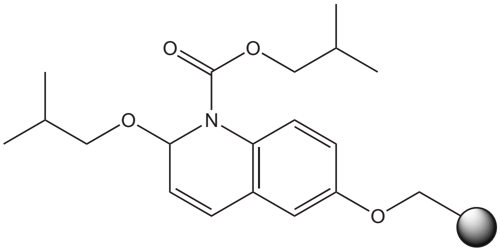
DIPCDI method [5]

1. Dissolve acid (1.5 eq.) in DCM/DMF (4:1) and add to resin. Add DIPCDI (4.4 eq.) and mix. Leave to react for 2 h with gentle agitation.
2. Wash resin with DMF and repeat reaction with fresh reagents if necessary.
3. Wash resin with DMF.
4. Suspend resin in DMF or DCM, add amine (1 eq.) and allow to react with gentle agitation o/n.
5. Remove resin by filtration, wash with DCM and evaporate the combined filtrates to dryness.

REFERENCES

[1] I. E. Pop (1997) *J. Org. Chem.*, **62**, 2594.
[2] K. G. Dendrinos & A. G. Kalivretenos (1998) *Tetrahedron Lett.*, **39**, 1321.
[3] K. G. Dendrinos & A. G. Kalivretenos (1998) *Chem. Commun.*, 499.
[4] Y. - T. Chang & P. G. Schulz (1999) *Bioorg. Med. Chem. Lett.*, **9**, 2479.
[5] O. W. Gooding, et al. (2002) *J. Comb. Chem.*, **4**, 576.

Product No.	Product	Quantity	Price
855046	**IIDQ-polystyrene** NBC No.: 01-64-0469 Loading: 1.50 - 1.90 mmole/g resin, as determined by HPLC, after reaction of 3-phenylpropionic acid with cyclohexylamine. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	5 g 25 g	



Description, Methods, Applications

IIDQ-polystyrene (IIDQ-PS) [1] is a polymer-supported version of the IIDQ coupling reagent [2]. IIDQ has many advantages over conventional carbodiimide- or uronium-based reagents: no preactivation step is required, and acid, amine and coupling reagent can be added in any order; in contrast to uronium-based reagents like HBTU, it cannot form guanidinium by-products; and it is totally stable to base.

The treatment of a carboxylic acid with IIDQ-PS in DCM or MeCN rapidly generates *in situ* the corresponding isobutoxycarbonyl mixed anhydride [3]. Attack by nucleophiles preferentially takes place at the less hindered and more electrophilic carbonyl of the carboxylic acid moiety, releasing only volatile carbon dioxide and isobutanol as by-products (Figure 1). If reaction is carried out in the presence of an amine, amide bond formation occurs concurrently with generation of the anhydride. Alternatively, addition of $NaBH_4$ or polymer-supported borohydride to the anhydride will lead directly to the corresponding alcohol.

IIDQ-PS appears to be particularly effective for mediating the acylation for anilines, and has also been found to couple peptide fragments without epimerization. In a comparative study, IIDQ-PS was found to give higher yields and greater purities than HATU, EDC-PS or DCC-PS (Table 1) [4]. Occasionally, with some secondary amines the formation of isobutyl carbamate by-products has been observed, resulting from attack by the amine at the carbonyl group.

IIDQ-PS can be regenerated from spent resin by treatment with isobutyl chloroformate/DIPEA in DCM.

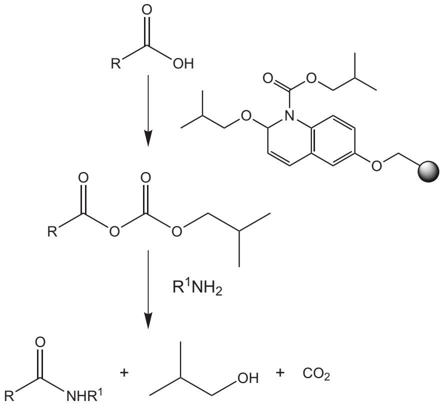


Fig. 1: Generation of mixed anhydrides with IIDQ resin.

Properties

Application:
coupling reagent

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
1.50 - 1.90 mmole/g resin, as determined by HPLC, after reaction of 3-phenylpropionic acid with cyclohexylamine

Solvent compatibility:
DCM, MeCN

Typical reaction conditions:
2 eq. relative to acid

For help selecting the most appropriate resin see Table 2, page 47.

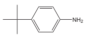
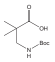
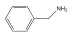
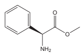
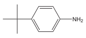
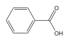
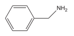
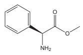
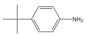
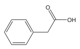
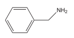
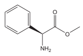
		IIDQ-PS		HATU		EDC-PS		DCC-PS	
Amine	Acid	Yield	Purity	Yield	Purity	Yield	Purity	Yield	Purity
		69	100	42	100	15	100	16	100
		66	100	45	93	39	87	17	94
		64	100	48	100	24	95	24	86
		60	100	43	100	68	100	41	100
		80	100	69	100	48	100	25	100
		61	100	77	92	49	100	35	100
		89	100	45	100	44	100	28	100
		85	100	68	100	48	81	24	95
		75	100	54	100	33	100	24	100

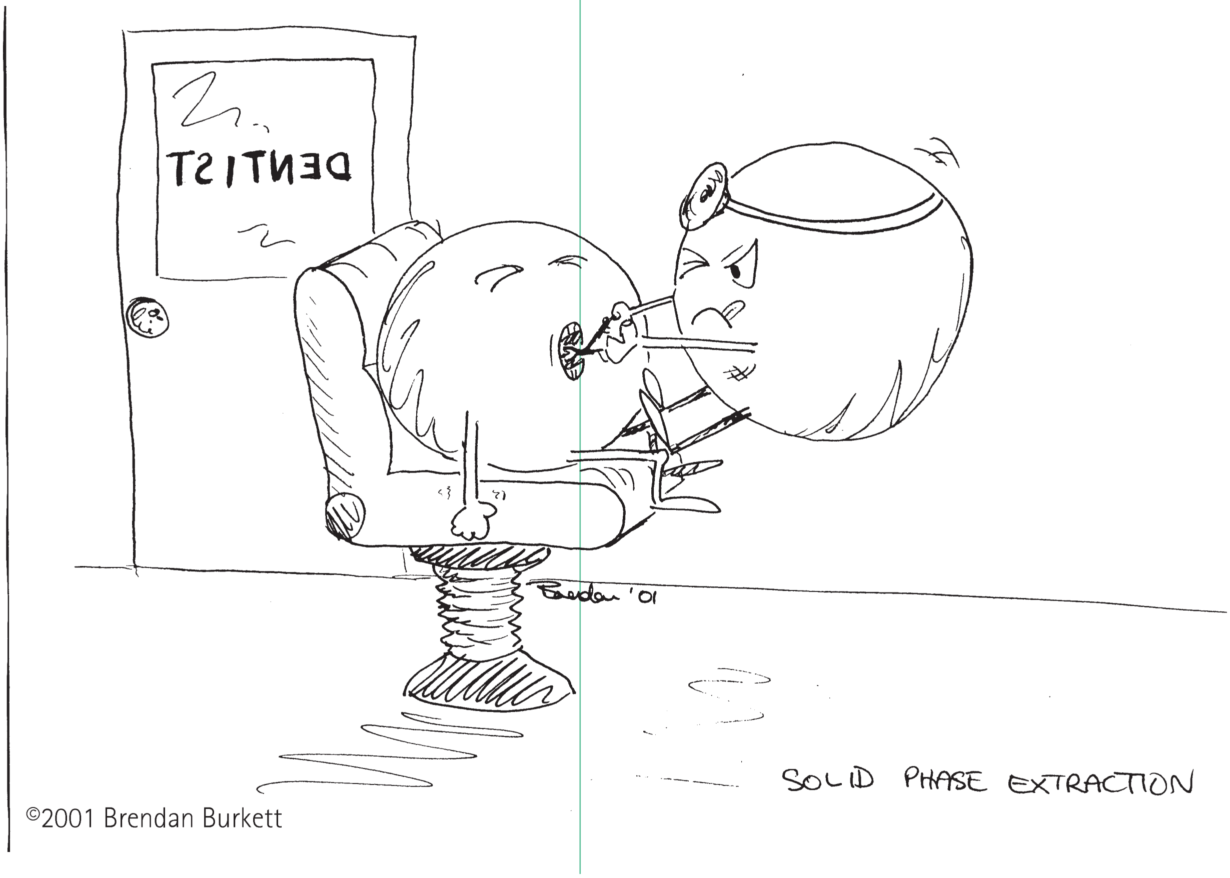
Table 1: Comparison of IIDQ-PS with other commonly used coupling reagents [4].

Use of IIDQ-polystyrene

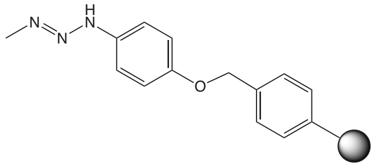
1. Dissolve amine (1 eq.) and acid (1 eq.) in minimum volume of MeCN.
2. Swell IIDQ-resin (2 eq.) in MeCN for 10 min.
3. Add amine and acid solution to resin and gently agitate for 24 h.
4. Remove resin by filtration and wash with DCM and MeOH.
5. Evaporate filtrate to dryness.

REFERENCES

[1] E. Valeur & M. Bradley (2005) *Chem. Commun.*, 1164.
[2] Y. Kiso, et al. (1973) *Chem. Pharm. Bull.*, **21**, 2507.
[3] J. R. Vaughan (1951) *J. Am. Chem. Soc.*, **73**, 3547.
[4] E. Valeur & M. Bradley, unpublished results.



Product No.	Product	Quantity	Price
855106	**4-(Methylaminoazo)phenoxymethyl polystyrene** Methyltriazene resin NBC No.: 01-64-0413 Loading: 1.0 - 2.5 mmole/g resin, as determined by elemental analysis of nitrogen. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry; prevent exposure to light.	1 g 5 g 25 g	



Description, Methods, Applications

This polymer-bound version of diazomethane cleanly converts acids to methyl esters without the use of hazardous or toxic reagents (Figure 1) [1, 2]. The reaction conditions are extremely mild, enabling even very labile substrates such as penicillin V to be esterified in good yield.

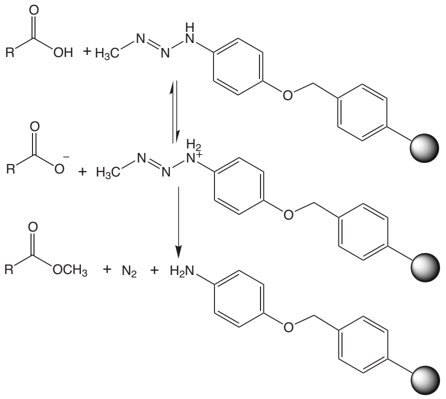


Fig. 1: Formation of methyl esters with 4-(methylaminoazo)-phenoxymethyl polystyrene.

Properties

Application:
protection of carboxylic acids

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
1.0 - 2.5 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:
DCM, DCE, THF, toluene

Typical reaction conditions:
2 - 5 eq. relative to carboxylic acid; 6 h, 20 °C

REFERENCES

[1] J. Rademann, et al. (2001) *Angew. Chem. Int. Ed.*, **40**, 381.
[2] J. Smerdka, et al. (2004) *J. Pept. Sci.*, **10**, 603.

Protection of Boc-Phe-OH using 4-(methylazoamino)phenoxymethyl polystyrene

Boc-Phe-OH (490 mg; 1.85 mmole) was dissolved in dry THF (10 ml). 4-(Methylazoamino)phenoxymethyl polystyrene (2.2 g; 4.2 mmole) was added and the solution agitated o/n at rt. The resin was removed by filtration and washed with THF. The combined filtrates were evaporated to dryness to afford the desired product in a yield of 89% (544.7 mg) with a HPLC purity of 95.7% (Figure 1). The ^{1}H nmr spectrum and HPLC elution profile of the total crude product are shown in Figures 1 and 2 respectively.

Fig. 1: HPLC elution profile of total crude Boc-Phe-OMe.

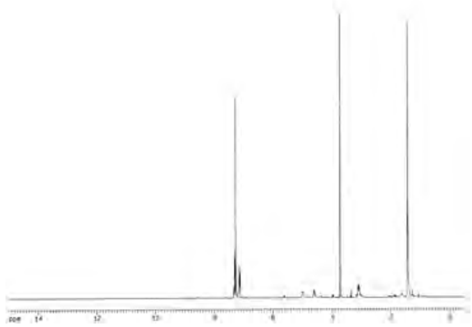
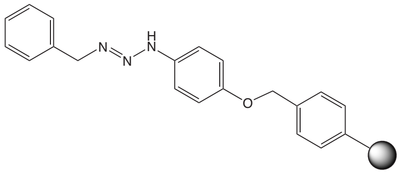


Fig. 2: ^{1}H nmr of total crude Boc-Phe-OMe.

For help selecting the most appropriate resin see Table 2, page 47.

Product No.	Product	Quantity	Price
855113	**4-(Benzylaminoazo)phenoxymethyl polystyrene** Benzyltriazene resin NBC No.: 01-64-0441 Loading: (most recent lot) 1.40 mmole/g resin, as determined by elemental analysis of nitrogen. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry; prevent exposure to light.	1 g 5 g 25 g	



Description, Methods, Applications

This polymer-bound alkylation reagent cleanly converts acids to benzyl esters without the use of hazardous or toxic reagents (Figure 1) [1, 2]. The reaction conditions are extremely mild, tolerating nitrogen containing heterocycles such as pyridine and pyrazole [1].

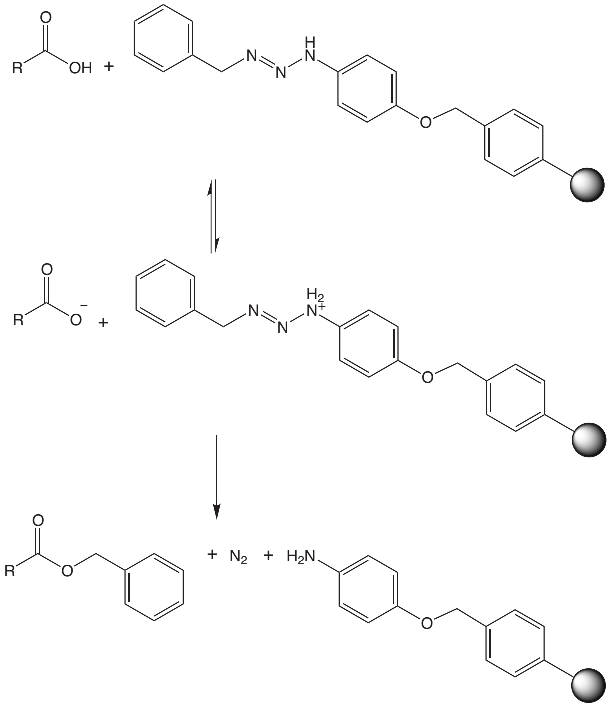


Fig. 1: Formation of benzyl esters with 4-(benzylaminoazo)-phenoxymethyl polystyrene.

Properties

Application:
protection of carboxylic acids

Polymer type:
copoly(styrene-1 % DVB), 200-400 mesh

Loading:
(most recent lot) 1.40 mmole/g resin, as determined by elemental analysis of nitrogen

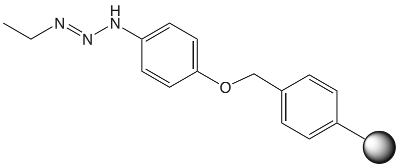
Solvent compatibility:
DCM, DCE, THF, toluene

Typical reaction conditions:
2 - 5 eq. relative to carboxylic acid; 6 h, 20 °C

REFERENCES

[1] J. Rademann, et al. (2001) *Angew. Chem. Int. Ed.*, **40**, 381.
[2] J. Smerdka, et al. (2004) *J. Pept. Sci.*, **10**, 603.

Product No.	Product	Quantity	Price
855112	**4-(Ethylaminoazo)phenoxymethyl polystyrene** Ethyltriazene resin NBC No.: 01-64-0438 Loading: (most recent lot) 1.30 mmole/g resin, as determined by elemental analysis of nitrogen. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry; prevent exposure to light.	1 g 5 g 25 g	



Description, Methods, Applications

This alkylation reagent cleanly converts acids to ethyl esters without the use of hazardous or toxic reagents (Figure 1) [1, 2]. The reaction conditions are extremely mild, tolerating nitrogen containing heterocycles such as pyridine and pyrazole [1].

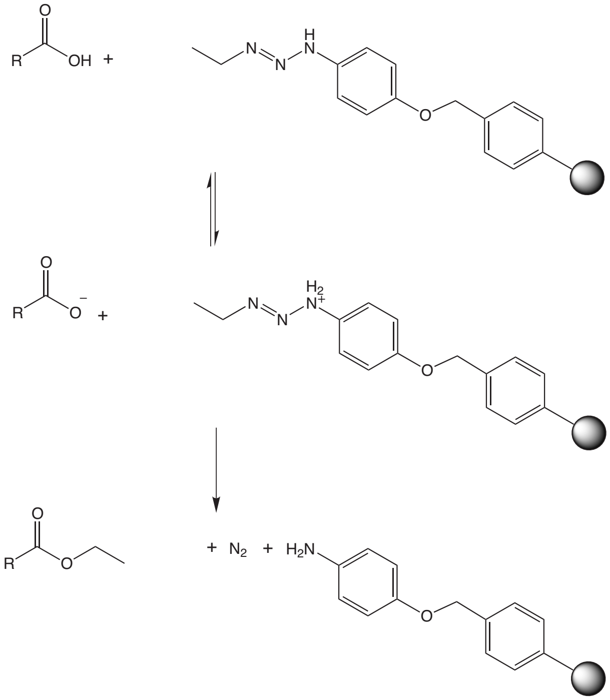


Fig. 1: Formation of ethyl esters with 4-(ethylaminoazo)-phenoxymethyl polystyrene.

Properties

Application:

protection of carboxylic acids

Polymer type:

copoly(styrene-1 % DVB), 200-400 mesh

Loading:

(most recent lot) 1.30 mmole/g resin, as determined by elemental analysis of nitrogen

Solvent compatibility:

DCM, DCE, THF, toluene

Typical reaction conditions:

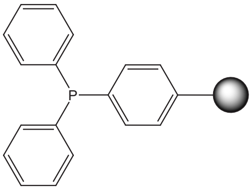
2 - 5 eq. relative to carboxylic acid; 6 h, 20 °C

REFERENCES

[1] J. Rademann, et al. (2001) *Angew. Chem. Int. Ed.*, 40, 3811.
[2] J. Smerdka, et al. (2004) *J. Pept. Sci.*, **10**, 603.

For help selecting the most appropriate resin see Table 2, page 47.

Product No.	Product	Quantity	Price
855032	**Triphenylphosphine polystyrene** Diphenylphosphinopolystyrene NBC No.: 01-64-0308; CAS No.: 39319-11-4 Loading: 1.00 - 2.00 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with benzylbromide. ⚠ Prolonged storage: ≤ -20°C; keep dry and under argon.	5 g 25 g	



Description, Methods, Applications

Polymer-bound triphenylphosphine has been utilized in conjunction with tetrachlorocarbon or trichloroacetonitrile for the conversion of alcohols to alkyl chlorides, acids to acid chlorides, primary amides to nitriles, secondary amides to imidoyl chlorides, and to directly couple acids to amides [1, 2]. The intermediate supported triphenylphosphine dichloride may also be generated from this support by treatment with triphosgene, and used in a similar manner [3].

Polymer-bound triphenylphosphine diiodide, generated *in situ* with I_2, has been used to convert alcohols to iodides. The reaction proceeds without generation of HI and so acid sensitive protecting groups, such as Boc and Z, are well tolerated. This reagent in DMF also converts primary and secondary alcohols to their corresponding formate esters [2].

The use of polymer-supported triphenylphosphine in the Wittig reaction has been well studied [1, 4, 5]. Generation of the resin-bound alkyl phosphonium salt is achieved by heating the resin with the appropriate alkyl bromide in THF or DMF. Treatment with a suitable base, such as NaHMDS or BuLi, generates the appropriate ylide. Excess base and salts are then washed away and the resin is reacted with appropriate aldehyde or ketone to release the desired alkene. By removing the alkali metal salts prior to addition of the carbonyl components the production of the Z isomer can be moderately enhanced. Similarly, triphenylphosphine resin has been used in aza-Wittig reactions [6, 7] and to promote the isomerization of Z-nitro olefins [8].

The use of this resin in the Mitsunobu reaction has also been reported [9], in which it was utilized to mediate the coupling of phenols and alcohols.

Polymer-supported triphenylphosphine has also many applications in organometallic reactions. For example, it has been employed to generate polymer-supported iridium [10], nickel [11, 12], rhodium [10, 11] and ruthenium [11] catalysts for use in hydrogenation [10, 11, 13, 14], alkene dimerization [12] and cyclooligomerization [9], and hydroformylation [11, 15] reactions. In most instances the catalyst could be used several times without loss of activity.

Properties

Application:

Wittig, Mitsunobu and halogenation reactions; as a polymer-bound ligand for use in transition metal mediated coupling reactions; as a scavenger for alkyl halides and palladium

Polymer type:

copoly(styrene-1 % DVB), 100-200 mesh

Loading:

1.00 - 2.00 mmole/g resin, as determined by elemental analysis of bromine, after derivatization with benzylbromide

Solvent compatibility:

DCE, DCM, DMF, THF

Wittig reaction

1. Heat alkyl bromide (5 eq.) in DME at 60 °C with TPP-PS resin o/n. Isolate resin by filtration and wash with THF and DCM and dry *in vacuo*.
2. Suspend the resin in dry THF under Ar. Add 1 M NaHMDS in THF (4 eq.) and gently agitate for 1 h at rt. Wash resin thoroughly with THF.
3. Add THF containing carbonyl compound (0.5 eq.) and agitate gently at rt for 24 h under Ar.
4. Remove the resin by filtration and wash with THF. Evaporate the combined filtrates to dryness.

Mitsunobu reaction

1. Dissolve alcohol (1.5 eq.) and phenol (1 eq.) in DCM.
2. Add TPP-PS resin (1.5 eq.) followed by DEAD (1.5 eq.). Stir under Ar at rt for 12 h.
3. Remove resin by filtration and wash with DCM.
4. Wash combined organic filtrates with 1 M KOH, 1 M $KHSO_4$, sat. NaCl, dry over $MgSO_4$, and evaporate to dryness.

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[1] P. Hodge and G. Richardson (1975) *J. Chem. Soc., Chem. Commun.*, 622.

[2] D. H. Drewry, et al. (1999) *Med. Res. Rev.*, **19**, 97.

[3] A. Wells (1994) *Synth. Commun.*, **24**, 1715.

[4] M. Bernard & W. T. Ford (1983) *J. Org. Chem.*, **48**, 326.

[5] I. Hughes (1996) *Tetrahedron Lett.*, **37**, 7595.

[6] P. López-Cremades, et al. (2000) *Synlett*, **10**, 1411.

[7] K. Hemming, et al. (2000) *Synlett*, **11**, 1565.

[8] P. Stanetty & M. Kremslehner (1998) *Tetrahedron Lett.*, **39**, 811.

[9] A. R. Tunoori (1998) *Tetrahedron Lett.*, **39**, 8751.

[10] J. P. Collman, et al. (1972) *J. Am. Chem. Soc.*, **94**, 1789.

[11] C. U. Pittman Jr., et al. (1975) *J. Am. Chem. Soc.*, **97**, 1742.

[12] C. U. Pittman Jr. & L. R. Smith (1975) *J. Am. Chem. Soc.*, **97**, 341.

[13] R. H. Grubbs & L. C. Kroll (1971) *J. Am. Chem. Soc.*, **93**, 3062.

[14] C. U. Pittman Jr., et al. (1975) *J. Am. Chem. Soc.*, **97**, 4774.

[15] C. U. Pittman Jr., et al. (1976) *J. Am. Chem. Soc.*, **98**, 5402.

[16] A. Grieder & A. W. Thomas (2003) *Synthesis*, **11**, 1707.

Synthesis of 2,4-dimethoxystilbene

Triphenylphosphine polystyrene (1g, 1.12 mmole) was swollen in dry DME (10 ml). Benzyl bromide (0.67 ml, 5.6 mmole) was added and the mixture agitated at 65 °C o/n. The resin was washed with THF, MeCN, toluene, ether and hexane and dried *in vacuo* o/n.

This resin was then swollen in THF under Ar. 1 M NaHMDS (4.3 ml, 4.3 mmole) was added and the mixture agitated for 1 h at rt. The resin was washed with dry THF and resuspended in THF (4 ml). 2,4-Dimethoxybenzaldehyde (90 mg, 0.54 mmole) was added and the mixture agitated o/n under Ar. The resin was removed by filtration and the filtrate evaporated to afford the product (Z:E isomer, 75:25) in a yield of 72% with a crude purity of 95% (Figure 1). The identity of the product was confirmed by ^1H nmr (Figure 2).

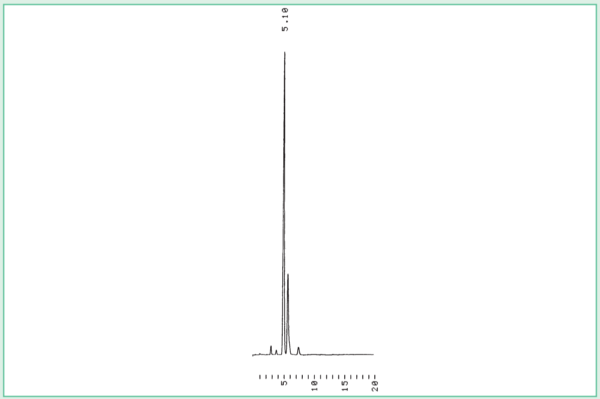


Fig. 1: HPLC elution profile of total crude dimethoxystilbene.

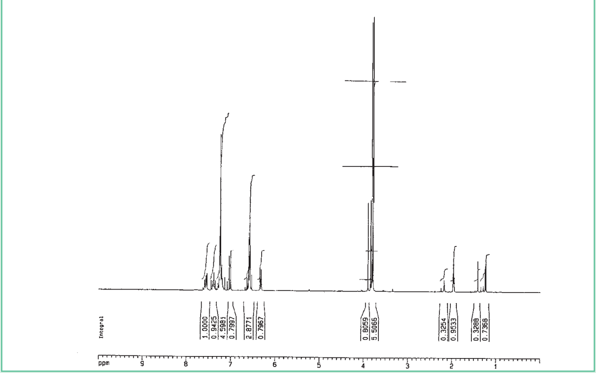
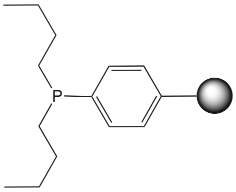


Fig. 2: ^1H nmr spectrum of total crude dimethoxystilbene.

Product No.	Product	Quantity	Price
855105	**Di(n-butyl)phenylphosphine polystyrene** Dibutylphosphinopolystyrene NBC No.: 01-64-0402 Loading: 0.40 - 1.00 mmole/g resin, as determined by elemental analysis of bromine, after coupling with benzylbromide. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry and under argon.	1 g 5 g	



Description, Methods, Applications

Dibutylphenylphosphine polystyrene is a polymer-bound analogue of tributylphosphine. In solution tributylphosphine is an extremely useful reagent for the reduction of disulfides [1]. It can be utilized as a replacement for PPh_3 in Mitsunobu reactions, and when used in conjunction with tetramethylazodicarboxamide, it was found to mediate the esterification of hindered secondary alcohols [2] and the alkylation of less acidic nucleophiles more effectively than DEAD-PPh_3 [3]. PBu_3 can also be employed in a similar manner to DMAP as a hypernucleophilic catalyst in acylation reactions [4, 5].

Properties

Application:
Mitsunobu reactions and for reducing disulfides

Polymer type:
copoly(styrene-1 % DVB), 100-200 mesh

Loading:
0.40 - 1.00 mmole/g resin, as determined by elemental analysis of bromine, after coupling with benzylbromide

Solvent compatibility:
DCE, DCM, DMF, THF

REFERENCES

[1] J. Maclaren, et al. (1966) *Aust. J. Chem.*, **19**, 2355.
[2] T. Tsunoda, et al. (1995) *Tetrahedron Lett.*, **36**, 2529.
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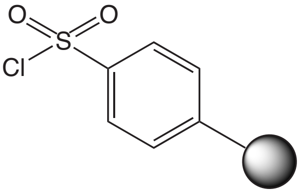
[5] E. Vedejs, et al. (1993) *J. Org. Chem.*, **58**, 7286.

Product No.	Product	Quantity	Price
855042	**Sulfonyl chloride polystyrene** Polystyrylsulfonyl chloride NBC No.: 01-64-0430 Loading: (most recent lot) 3.80 mmole/g resin, as determined by elemental analysis of nitrogen, after reaction with benzylamine. ⚠ Prolonged storage: +2 to +8°C; keep cool and dry; hygroscopic.	5 g 25 g 100 g	



Description, Methods, Applications

This polymer-supported equivalent to p-toluenesulfonic chloride is a highly versatile reagent with numerous applications in organic synthesis. It can be converted by reaction with the appropriate nucleophile into polymer-supported versions of useful sulfonyl-based reagents, such as sulfonyl hydrazine [1, 2] and sulfonyl azide [3, 4]. In a strategy known as "catch and release", it can be reacted with alcohols to generate polymer-supported tosylates, which can then be cleaved with nucleophiles to generate secondary and tertiary amines, thioethers and N-alkylimidazoles (Figure 1) [5 - 7]. This approach has been employed to prepare oxazolidinones by a cyclative cleavage strategy involving intramolecular aminolysis of the polymer-bound tosylate (Figure 2) [8].

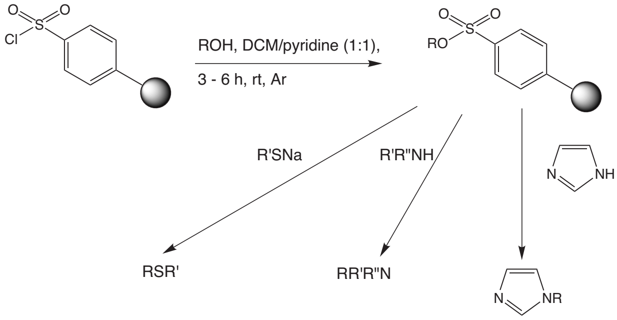


Fig. 1: Catch and release synthesis using sulfonyl chloride resin.

Sulfonyl chloride resin may also be employed as a polymer-supported scavenger for amines, hydrazines, alcohols and Grignard reagents, provided a base is added to neutralize HCl generated from the reaction. In the case of amines and hydrazines, this can be a polymer-supported base such as piperidinomethyl polystyrene or bicarbonate resin. For alcohols and anilines, it is better to use pyridine since this also acts as a catalyst for the reaction. Any pyridinium chloride generated can be easily removed by first converting it to pyridine with bicarbonate resin (855040), which then can be removed by evaporation.

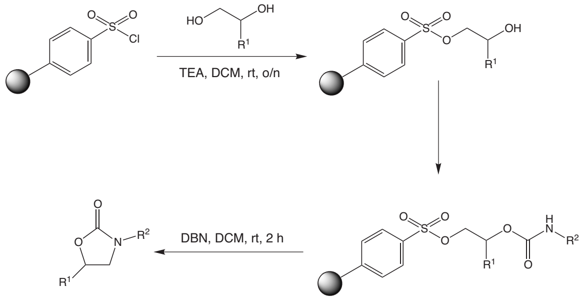


Fig. 2: Synthesis of oxazolidinones using sulfonyl chloride resin.

Properties

Application:
scavenger resin for amines, hydrazines, alcohols and Grignard reagents; catch and release of alcohols

Reactivity:
amines, alcohols

Polymer type:
copoly(styrene-1 % DVB), 100-200 mesh

Loading:
(most recent lot) 3.80 mmole/g resin, as determined by elemental analysis of nitrogen, after reaction with benzylamine

Solvent compatibility:

DCM, DCE, THF, toluene, DMF

For help selecting the most appropriate resin see Table 2, page 47.

Synthesis of tertiary amines

1. Add sulfonyl chloride resin (1 eq.) to a solution of alcohol (5 eq.) in DCM/pyridine (1:1).
2. Gently agitate mixture for 3 - 6 h at rt under Ar.
3. Isolate resin by filtration and wash with DCM, THF, THF/water, THF, DCM.
4. Suspend resin in a solution of secondary amine (2 eq.) in MeCN, DMF, DCM or THF containing DIPEA (5 eq.) and heat at 60 °C o/n.
5. Add methylisocyanate polystyrene (3 eq.) and agitate gently for 3 h to remove excess secondary amine.
6. Remove resins by filtration and wash with DCE or THF.
7. Evaporate combined filtrates to dryness.

Scavenging of alcohols and amines

1. Add pyridine (20 - 50% by volume) to reaction mixture containing unreacted amine or alcohol.
2. Add sulfonyl chloride resin (3 eq. relative to residual alcohol or aniline) and stir at rt for 5 - 8 h.
3. Add bicarbonate resin (4 eq. relative to residual alcohol or aniline) and agitate gently for 3 h at rt.
4. Remove resins by filtration and wash with DCM.
5. Evaporate combined filtrates to dryness.

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7: Solution phase organic synthesis using polymer-supported reagents

1. Introduction

Supported reagents have been employed in organic synthesis for over 50 years. However, despite the pioneering efforts of Fréchet, Hallensleben, Patchornik, and others in the '60s and '70s, the field has, until recently, attracted little interest. The situation has now changed dramtically, prompted by the need to simplify work-up and reaction procedures in high-throughput parallel synthesis. This in turn has led to a general reappraisal of the technique amongst mainstream organic chemists.

A number of excellent reviews of the subject are available [1-4], the most comprehensive of which is that from the group of Steven Ley [5].

The use of polymer-supported reagents in organic synthesis offers a number of benefits:

- i) Excess immobilized reagents can be employed to drive reactions to completion, since unreacted material can be simply removed by filtration;
- ii) Resin-bound toxic or hazardous compounds can be handled safely without risk to users or the environment;
- iii) Polymer-bound catalytic reagents can be easily removed and recycled;
- iv) Supported versions of reagents that are incompatible can be used simultaneously to achieve one-pot reactions not possible in solution.

In addition, special functionalized supports known as scavenger resins can be employed to chemoselectively remove excess reagents and by-products from crude products. Conversely, in a technique known as catch and release, resins can be utilized to extract products from crude reaction mixtures, so that they may be washed free of impurities before being released from the resin in a purified state.

Thus, by choosing an appropriate combination of scavenger resins and immobilized reagents, it is possible to perform multistep syntheses without the classical purification of intermediates. In this way the advantages of solid phase synthesis, i.e. the ability to use an excess of reagents to drive reactions to completion and the ease of product isolation, become applicable to solution synthesis. Polymer-supported reagents and scavengers have been successfully applied to multi-step syntheses to yield complex products in high purities and yields [6-12]. Attention is particularly drawn to the synthesis of epothilone C [12], which represents the most ambious and complex synthesis with polymer-supported reagents described to date. Two examples from the literature are shown in Figures 1 & 2.

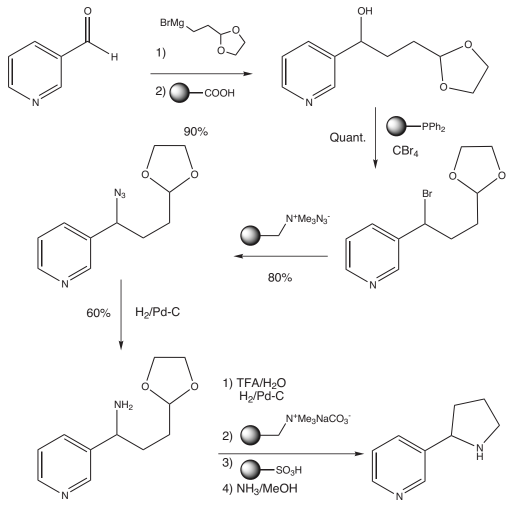

Fig. 1: Synthesis of nornicotine using polymer-supported reagents [10].

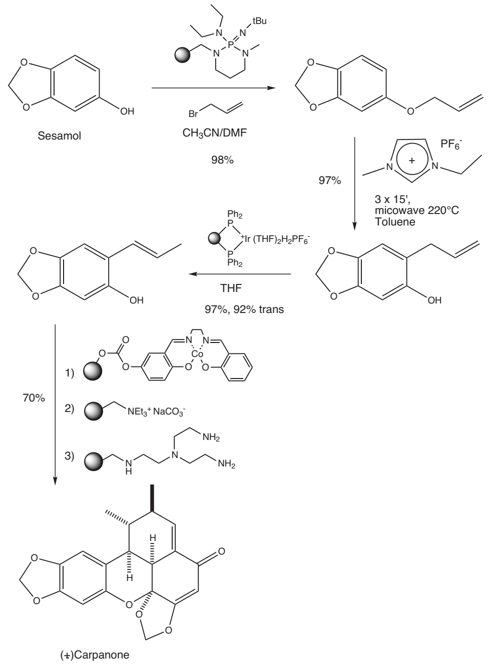

Fig. 2: Synthesis of carpanone using polymer-supported reagents [11].

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8. I. R. Baxendale, et al. (2002) *Angew. Chem. Int. Ed.*, **41**, 2194.
9. R. I. Storer, et al. (2003) *Angew. Chem. Int. Ed.*, **42**, 2521.
10. I. R. Baxendale, et al. (2002)*J. Chem. Soc., Perkin Trans. 1*, 143.
11. I. R. Baxendale, et al. (2002)*J. Chem. Soc., Perkin Trans. 1*, 1851.
12. R. I. Storer, et al. (2004) *Chem. Eur. J.*, **10**, 2529.

2. Practical considerations

The majority of supported reagents are based on divinylbenzene (DVB) cross-linked polystyrene. Resins produced with low levels of DVB cross-linker are microporous (gel-type) and must be swollen in an appropriate solvent before use to enable solvent and reagent penetration of the resin particles; recommended solvents are given under properties with each product entry in the product listing. Resins prepared with high levels of DVB are produced in the presence of a porogen, which results in materials containing permanent porosity. These materials do not require to be swollen before use and are compatible with most solvents. When using polymer-supported reagents, it is important to appreciate that reactions are often much slower than under homogeneous conditions. This is due in part to the higher reaction volume associated with the swollen resin and the restricted movement of the immobilized reactant.

The agitation of gel resins is best effected using vortexing, shaking or nitrogen-bubbling. For macroporous resins, gentle shaking, nitrogen bubbling and column washing are appropriate. In both cases, gentle magnetic stirring can also be employed provided it is not for long periods and a small flea is used.

3. Scavenger resins

The use of scavenger resins is a valuable strategy for product purification in parallel organic synthesis. For the approach to be effective, the material to be scavenged must contain a functional group not present in the target molecule, which can be utilized as a handle to chemoselectively immobilize the compound to a resin bearing a complementary functionality. Both covalent and ionic bonding can be utilized for compound sequestration, although the former is preferred since there is less risk of leaching during resin wash steps. In cases where the desired product is contaminated with only excess starting materials, purification using scavenger resins may just involve treatment of the crude reaction mixture with the appropriate resins, filtration and evaporation. Unlike conventional purification methods, scavenger resins can be used for the purification of intentional mixtures of related compounds. Furthermore, a single set of conditions can often be applied to the purification of a diverse set of compounds obtained through parallel synthesis. When using this approach, it is important to use pure solvents and reagents since these can be the source of impurities that may later require removal by chromatography.

Scavenger resins are most frequently used for the removal of electrophiles and nucleophiles, and many supports are designed such that the immobilization reaction does not liberate any soluble by-products or require any additional reagents. Due to site isolation effects, it is possible to use simultaneously scavenger resins which contain incompatible functional groups. Many of these aspects of using scavenger resins are illustrated in references [1-3].

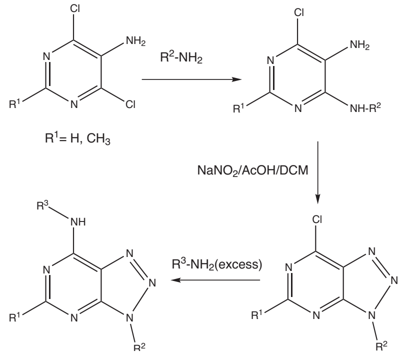

Fig. 3: Synthesis of a trisubstituted triazole pyrimidines [3].

In the example shown in Figure 3, a library of 3,5,7-trisubstituted pyrimidines was made from dichloroaminopyrimidines. Purification of the final products was unnecessary as all reactions were driven to completion by use of excess amine, which was later removed by scavenging with methylisocyanate polystyrene in the presence of a polymer-supported piperidine [3]

The properties of Novabiochem's scavenger resins are shown in Table 1. The use of scavenger resins in organic synthesis has been reviewed [4 - 6].

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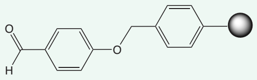
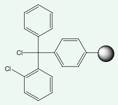
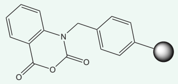
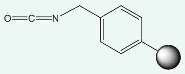
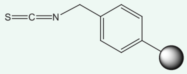
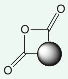
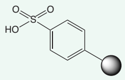
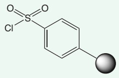
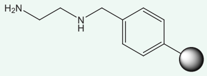
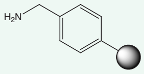
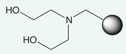
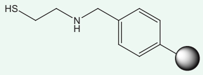
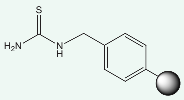
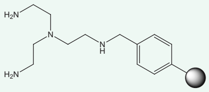
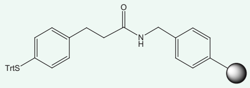
Table 1: Scavenger resins.

Resin	Structure	Loading	Reacts with
Electrophilic scavenger resins			
4-Benzyloxybenzaldehyde polystyrene 855026		2.4 - 3.5	$RNHNH_2$, NH_2OR, RNH_2, NH_2RSH, NH_2ROH
2-Chlorotrityl chloride resin 855017		1.0 - 1.6	RCO_2H, RSH
N-Methylisatoic anhydride polystyrene 855095		> 1.8	RNH_2, RR'NH, $RNHNH_2$
Methylisocyanate polystyrene 855022		> 1.5	RNH_2, RR'NH, $RNHNH_2$
Methylisothiocyanate polystyrene 855088		> 1.5	RNH_2, RR'NH, $RNHNH_2$
MP-anhydride resin EHL 855108		> 5.0	RNH_2, RR'NH, $RNHNH_2$
Sulfonic acid resin MP 855109		2.5 - 3.5	RNH_2, RR'NH,
Sulfonyl chloride polystyrene 855042		~ 3.8	RNH_2, RR'NH, ROH
Nucleophilic scavenger resins			
N-(2-Aminoethyl)aminomethyl polystyrene 855077		> 2.0	RCOCl, RSO_2Cl, RNCS, RNCO, H^+
Aminomethylated polystyrene 855076		2.0 - 3.0	RCOCl, RSO_2Cl, RNCS, RNCO, H^+
N,N-Diethanolaminomethyl polystyrene 855110		1.5 - 2.5	$RB(OH)_2$
N-(2-Mercaptoethyl)aminomethyl polystyrene 855025		> 1.4	RHalide, RCHO
Methylthiourea polystyrene 855078		> 2.5	RHalide
Tris-(2-aminoethyl)amine polystyrene 855023		> 2.2	RCOCl, RSO_2Cl, RNCS, RNCO, H^+
3-[4-(Tritylmercapto)phenyl]propionyl AM resin 855091		0.7 - 1.0	RHalide

4. Immobilized reagents

There are three principle modes of using supported reagents:

1) Stoichiometric. An excess of polymer-bound reagent is used to drive a synthetic transformation to completion. Excess or spent reagent is removed by filtration at the end of the reaction.

This approach is most useful in cases where the corresponding soluble reagent, or its by-products, are difficult to remove. For example, the use of a polymer-bound base can eliminate the need for an aqueous work-up, or an immobilized carbodiimide can obviate the requirement for chromatography to remove urea by-products.

Like scavenger resins, mutually incompatible polymer-bound reagents can be used simultaneously. Heterogeneous reactions between multiple supported components are even possible, provided the reaction operates through a soluble intermediary. For instance, β-elimination of tertiary amines from supported quarternary ammonium salts can be mediated by weakly basic ion-exchange resins if a small amount of amine is present in solution (Figure 4) [1].

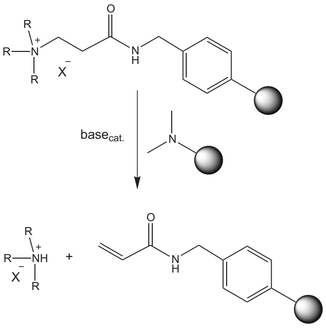


Fig. 4: Elimination of supported tertiary amines by a polymer-bound base [1].

2) Catalytic. This involves using a sub-stoichiometric amount of supported reagent, often in conjunction with a co-reagent, to carry out a transformation. At the end of the reaction the catalyst can be removed and recycled. A typical application of this kind is the oxidation of alcohols using polymer-supported TEMPO, where the resin-bound oxoammonium reactive immediate can be regenerated *in situ* using oxone in the presence of a phase-transfer reagent (Figure 5) [2].

3) Catch and release. This approach is a hybrid of solution and solid phase synthesis and involves the capture from solution of a product, or starting material, to generate a polymer-bound reactive intermediate. By-products or excess starting materials can be then washed away, before in the final step the desired product is cleaved from the support.

An example of this kind of approach is the critical condensation between a sulfamylbenzoic acid derivative and aminopyrazole in the convergent supported-reagent mediated synthesis of Sildenafil reported by Baxendale & Ley (Figure 6) [3]. The formation of the supported OBt ester serves not only to activate the benzoic acid but also allows removal of contaminating impurities.

The properties of Novabiochem's supported reagents are given in Table 2.

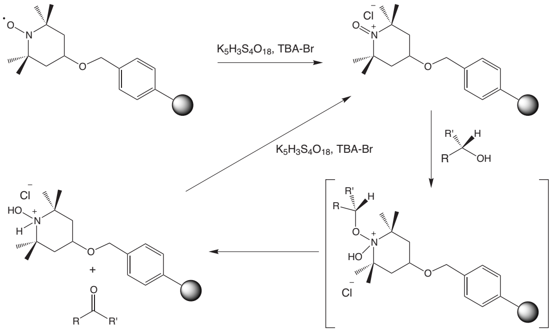


Fig. 5: Mechanism of TEMPO-mediated oxidation of alcohols with oxone [2].

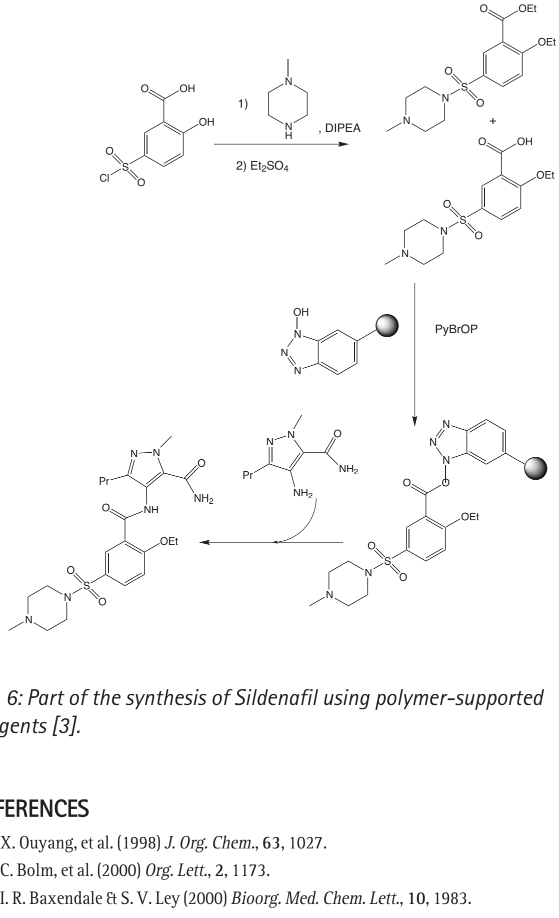


Fig. 6: Part of the synthesis of Sildenafil using polymer-supported reagents [3].

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3. I. R. Baxendale & S. V. Ley (2000) *Bioorg. Med. Chem. Lett.*, **10**, 1983.

Table 2: Immobilized reagents.

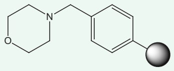
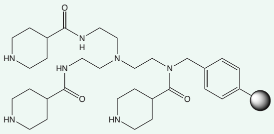
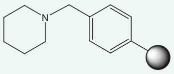
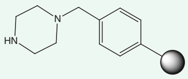
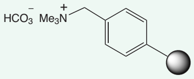
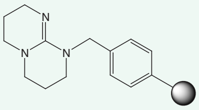
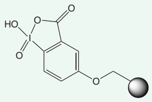
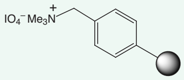
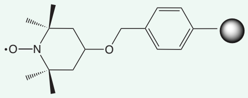
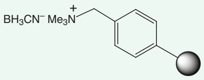
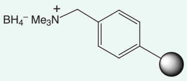
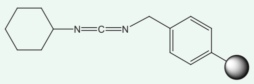
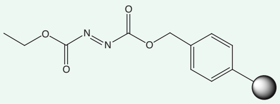
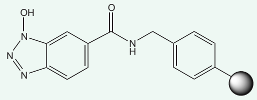
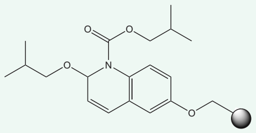
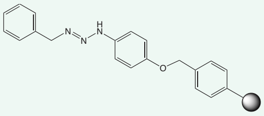
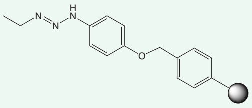
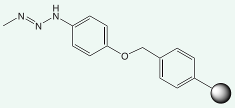
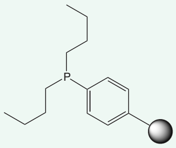
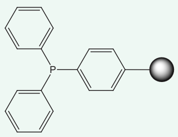
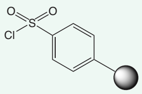
Resin	Structure	Loading	Application
Polymer-bound bases			
Morpholinomethyl polystyrene 855024		> 3.2	base
Piperidine-4-carboxylic acid polyamine resin 855083		1.3 - 2.5	immobilized secondary amine
Piperidinomethyl polystyrene 855082		3.0 - 5.0	base
Piperazinomethyl polystyrene 855092		0.8 - 1.5	immobilized secondary amine
(Polystyrylmethyl)trimethylammonium bicarbonate 855040		> 3.5	base
TBD-methyl polystyrene 855033		2.0 - 3.0	strong base
Polymer-bound oxidizing agents			
IBX polystyrene 855043		0.9 - 1.5	$RCH_2OH \rightarrow RCHO$ $RCHOHR \rightarrow RCOR$
(Polystyrylmethyl)trimethylammonium metaperiodate 855100		2.0 - 2.5	$RCH{=}CHR \rightarrow 2RCHO$ $RSR \rightarrow RSOR$ $Ar(OH)_2 \rightarrow$ quinone
TEMPO polystyrene 855107		1.5 - 2.0	$RCH_2OH \rightarrow RCHO$
Polymer-bound reducing agents			
(Polystyrylmethyl)trimethylammonium cyanoborohydride 855034		3.5 - 5.0	$RCH{=}NR \rightarrow RCH_2NHR$
(Polystyrylmethyl)trimethylammonium borohydride 855097		3.0 - 4.5	$RCHO \rightarrow RCH_2OH$ $RCOR \rightarrow RCHOHR$ $RCOCl \rightarrow RCH_2OH$

Table 2: Immobilized reagents.

Resin	Structure	Loading	Application
Polymer-bound coupling reagents			
N-Cyclohexylcarbodiimide,N'-methyl polystyrene 855029		> 1.3	$RCO_2H + RNH_2 \rightarrow RCONHR$
Ethoxycarbonylazocarboxymethyl polystyrene 855036		0.7 - 1.1	Mitsunobu reaction
HOBt-6-carboxamidomethyl polystyrene 855041		1.0 - 1.5	$RCOA + RNH_2 \rightarrow RCONHR$
IIDQ-polystyrene 855046		1.5 - 1.9	$RCOA + RNH_2 \rightarrow RCONHR$
Reagents for introduction of protecting groups			
4-(Benzylazoamino)phenoxymethyl polystyrene 855113		~ 1.4	$RCO_2H \rightarrow RCO_2Bzl$
4-(Ethylazoamino)phenoxymethyl poly-styrene 855112		~ 1.3	$RCO_2H \rightarrow RCO_2Et$
4-(Methylazoamino)phenoxymethyl poly-styrene 855106		1.0 - 2.5	$RCO_2H \rightarrow RCO_2Me$
Polymer-bound phosphines			
Di(n-butyl)phenyl polystyrene 855105		0.4 - 1.0	$RSSR \rightarrow 2RSH$
Triphenylphosphine polystyrene 855032		1.0 - 2.0	$RCO_2H \rightarrow RCOCl$ $ROH \rightarrow RCl$ $RCONH_2 \rightarrow RCN$ $RCONHR \rightarrow R(Cl){=}NHR$ $ROH + RXH \rightarrow RXR$ Ligand for Pd, Rh, Ru
Miscellaneous reagents			
Sulfonyl chloride polystyrene 855032		~ 3.8	$ROH + R'R''NH \rightarrow RNR'R''$

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