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Solid-Phase Organic Reactions III[1,2]: A Review of the Literature Nov 96–Dec 97

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Abstract: This Report reviews literature published Nov 1996–Dec 97; it is the third in a series that summarises organic reactions performed on solid supports and is designed as an update to Tetrahedron Reports no. 394 and 418. The reactions are presented in a graphical abstract format and examples are given of the following reactions: amide formation, aromatic substitution (nucleophilic/electrophilic), cleavage, condensation, cycloaddition, deprotection/protection, Grignard and related reactions, heterocycle formation, immobilisation onto resin, Michael addition, miscellaneous, multiple component condensation, olefin formation, oxidation, reduction and substitution (nucleophilic/electrophilic). Solid-phase peptide or other oligomer synthesis and reactions using soluble polymeric supports are not included. This report ends with the discussion of some trends in the domain under consideration.

Introduction

This report summarises literature published during Nov 1996–Dec 1997 describing solid-phase organic reactions.

The reactions are presented in a graphical abstract format in tables according to reaction type using a similar layout to Tetrahedron Reports number 394[1] and 418[2] which taken together cover the period 1992–Nov 1996. Each graphical abstract shows abbreviated structures of polymer-bound starting materials and products and gives some information on the resin type, reaction scope, monitoring and yields. Further details of the experimental conditions are available from the primary literature references.

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Similar to the two previous Reports[1,2] this overview does not include solid-phase peptide or other oligomer synthesis. In line with the current interest in combinatorial chemistry the focus is on the synthesis of small molecules using solid-support-bound intermediates. All of the publications cited herein are from refereed journals and not from patents. This report should be used in conjunction with the two previous ones.[1,2]

In the period that is covered by this Report notable reviews on solid-phase organic chemistry[3-10] and on related aspects such as automation,[11,12] reaction monitoring,[13-15] polymer bound reagents[16,17] and aspects of combinatorial chemistry in general[18-25] have been published.

Reaction Classification

The resin-bound reactions are categorised alphabetically according to the following list:

- **Amide formation and related reactions**
- **Aromatic substitution: nucleophilic/electrophilic**
- **Cleavage**
- **Condensation**
- **Cycloaddition**
- **Deprotection/protection**
- **Grignard and related reactions**
- **Heterocycle formation**
- **Immobilisation onto resin**
- **Michael addition**
- **Miscellaneous**
- **Multiple component condensation**
- **Olefin formation**
- **Oxidation**
- **Reduction**
- **Substitution: nucleophilic/electrophilic**

This reaction classification is only a guide. It facilitates the data presentation but is unavoidably ambiguous. Moreover, it is stressed that throughout this Report only non-standard examples are given so the tables are not comprehensive. For example, the syntheses of amides and ureas are only included in the "Amide formation and related reactions" table if new reagents, resins or methods have been used; similarly, not all reductive aminations are included nor are standard solid-phase "Deprotection/protection" reactions. Some abstracts are included in more than one table; see for example the tables "Aromatic Nucleophilic Substitution" (Heck reaction[26,27]) and "Heterocycle Formation" (indoles/benzofurans[26,27]), and the tables "Miscellaneous" (Pauson–Khand reaction[28] and "Heterocycle Formation" (tetrahydrocyclopentapyridine[28]).

Trends since the previous reviews[1,2]

Nearly twice as many reactions are covered in this review than were in the previous one,[2] illustrating the continuing growth of this area. This year 57% of the references cited herein are from the pharmaceutical industry sector whilst 43% are from the university sector.

During the past year two examples of multistep solid phase synthesis of libraries of non-oligomeric natural product analogues have been published; see, for example, table "Cleavage", ref. 56, 85 and "Amide bond Formation" table, ref. 55, 56. Other striking developments are the solid phase synthesis of *Multiple Core Structure Libraries* (MCSL), featuring variations in the structure of the core as well as the substituents; see for example table "Miscellaneous", ref. 70 and the application of *Resin Capture* to extract-out the desired product with a polymer-bound reagent; see for example table "Aromatic Nucleophilic Substitution" ref. 65.

Reaction Portfolio

In the previous Report[2] we listed solid-phase reactions that can be considered as either robust, reliable or emerging. To these lists we can add now the following classes:

Robust, reliable reactions:

- N-arylation
- Deprotection (N, O-deprotection in non-oligomers)

- Formation of indoles and benzofurans (Fischer synthesis; Pd-hetero annulation)
- Pauson–Khand
- Halogenation of alcohols
- Olefin formation (Wittig, Horner–Emmons, metathesis)
- Oxidation (alcohol to aldehyde or ketone; sulfide to sulfone)
- Reduction (nitro to amine)

Emerging solid-phase reactions (for which only a limited number of examples have been published):

- Baylis–Hillman
- Aza Wittig
- Ozonolysis
- Cyclopropanation
- Organometallic reactions (Grignard)
- Asymmetric reactions
- Carbene, radical reactions (*e.g.* Miscellaneous Table)

Linkers and Cleavage step

The "Cleavage" table illustrates the attention being paid to the following:

- Cyclative cleavage featuring ring closure metathesis and heterocyclic ring formation
- Cleavage via traceless linkers (Si, Ge) or via chemical reactions (desulphurisation, decarboxylation, cycloreversion)
- Cleavage steps which liberate an increasing diversity of functional groups *e.g.* alcohols, amines, aldehydes, ketones, hydroxamic acids, amidines, and guanidines.

Soluble Polymers

Whereas in previous reviews[1,2] reactions on soluble polymers were included, these reactions are not addressed this time. For some leading contributions on this topic, see ref. 172-174. In this context the first demonstration of the suitability of a fluorous phase (third phase) method for combinatorial synthesis is also mentioned[175-180].

New resins

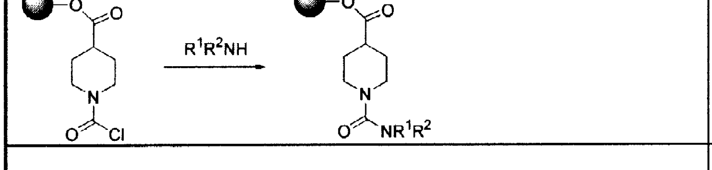
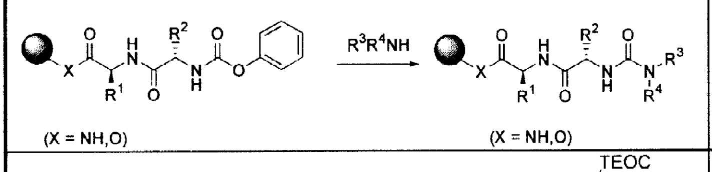
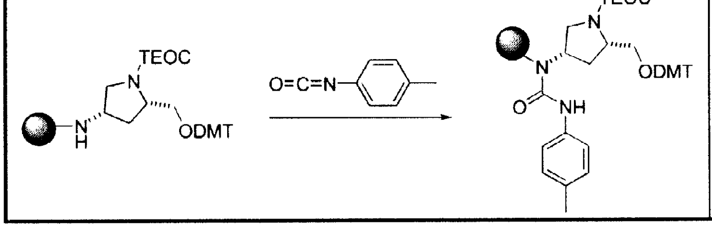
The following new resins are noted: the Bradley high loading polystyrene resin (applied in the synthesis of dendrimers, see "Michael Addition" table , ref. 151), the ArgoPore resin, which is a highly cross linked polystyrene resin with low to no swelling capacity (ref. 31) and finally resins derived from a Wang, a Sasrin or Rink resin by halogenation, which renders these resins into suitable reaction partners in nucleophilic substitutions. Several of the commercial suppliers have increased the range of resins in their catalogues (Novabiochem, Aldrich, Bachem, etc.)

Reaction Monitoring

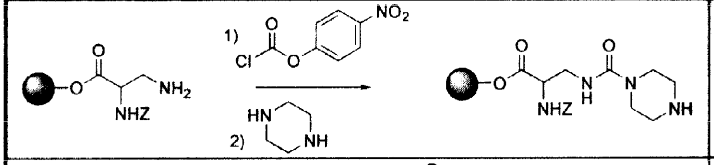
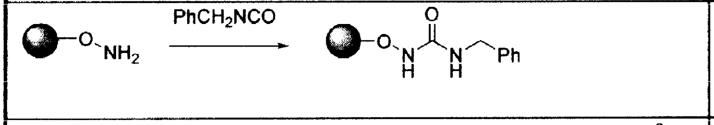
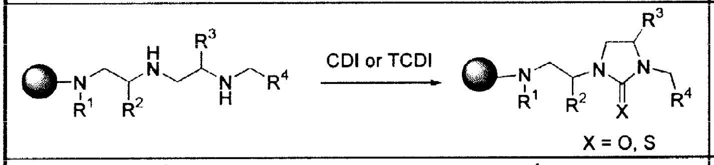
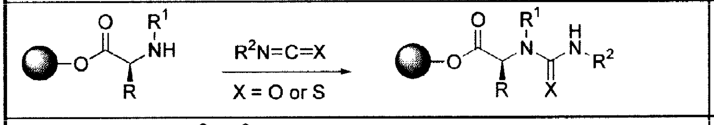
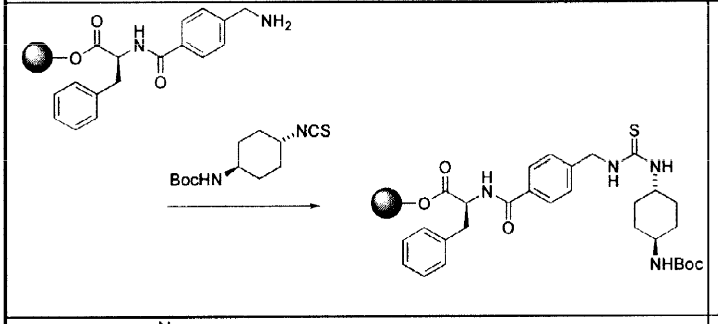
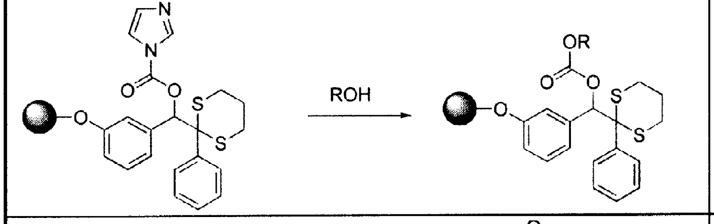
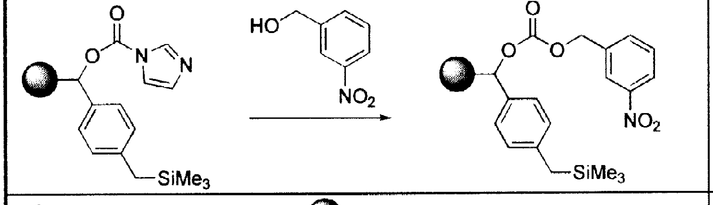
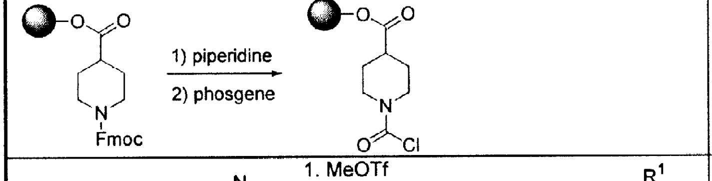
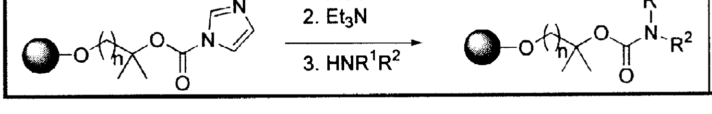
As was stated previously[1,2], this is still a non-trivial issue; as major breakthrough in this area we noticed the high-throughput NMR spectroscopy as an emerging technology[181].

Automation

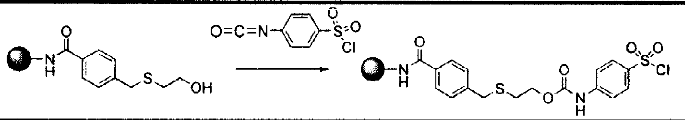
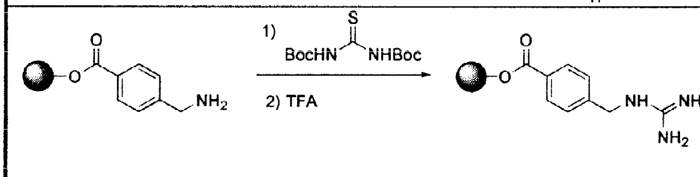
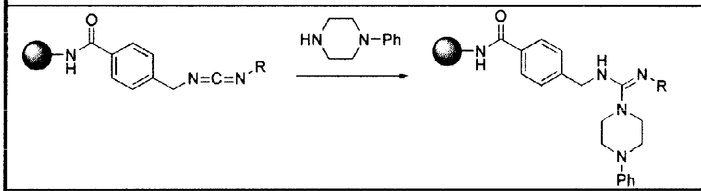
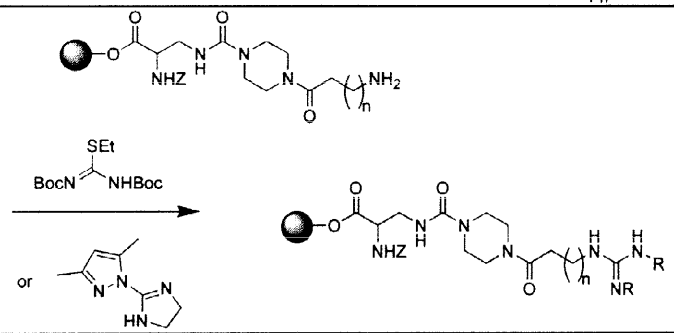
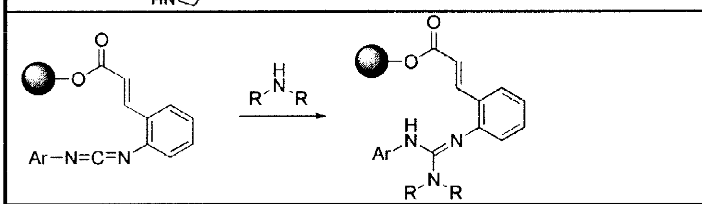
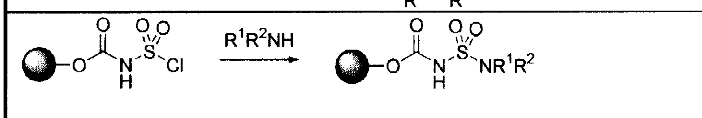
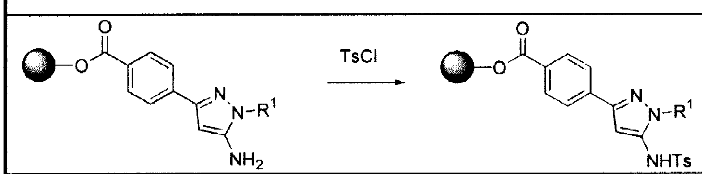
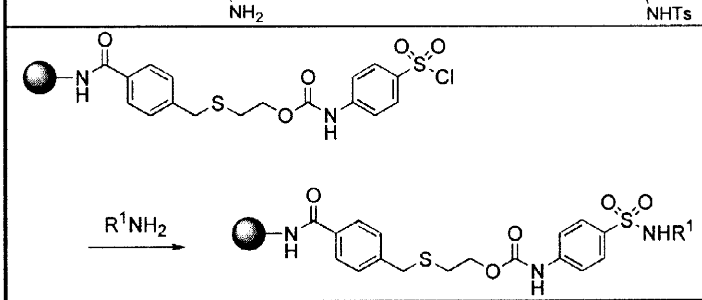
For a table on commercially available, low budget (below $30.000) solid-phase synthesis equipment the reader is referred to ref. 182.

Type of reaction: Amide formation and related reactions	Comment	Ref
	**Urea** Wang resin 24 examples	29
	**Urea** TentaGel S AM resin monitoring by UV 11 examples yield: 72-97%	30
	**Urea** ArgoGel resin 1 example overall yield reported	31

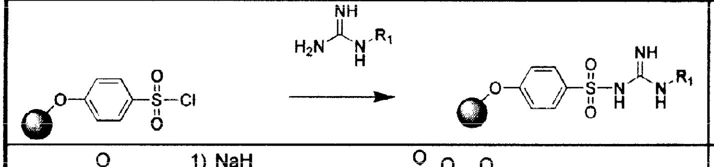
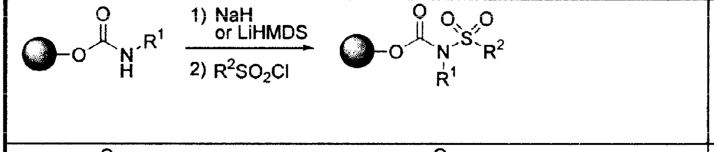
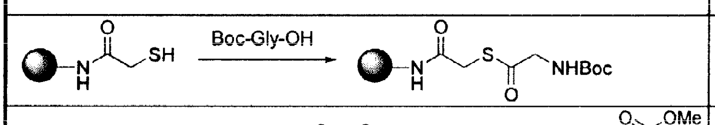
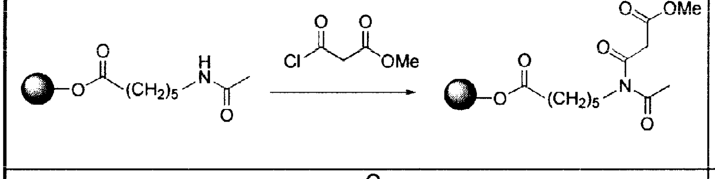
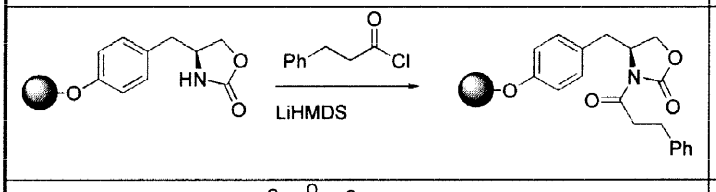
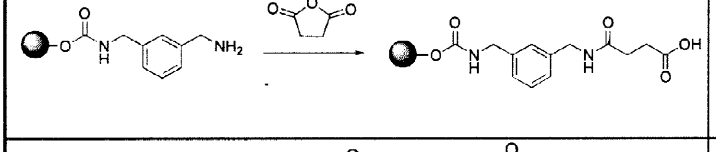
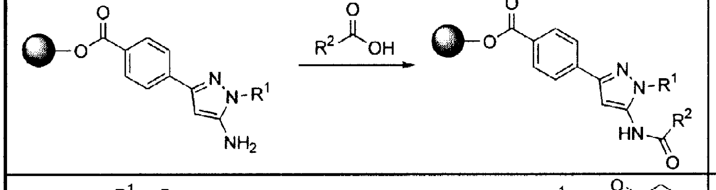
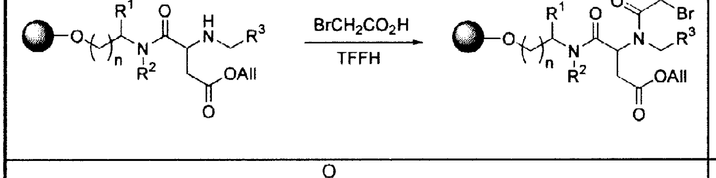
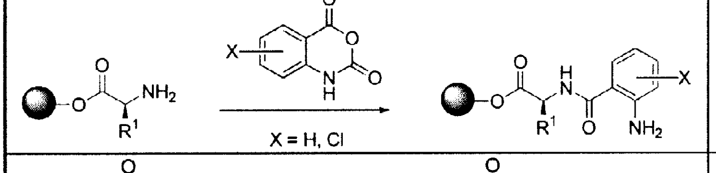
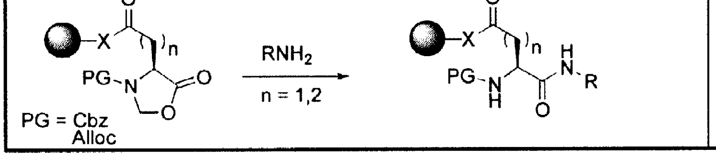
Type of reaction: Amide formation and related reactions

	**Urea** Wang resin or bromomethyl Wang resin 7 examples	32
	**N-alkoxy urea** Trityl polystyrene 1 example yield: 82%	33
	**Cyclic urea** MBHA resin library of 473,600 compounds	34
	**(Thio) urea** Wang resin 16 examples yield: 56-100%	35
	**Thiourea** PAM resin monitoring by ninhydrin test yield: 90%	36
	**Carbonate** Merrifield resin 1 example yield: 83%	37
	**Carbonate** Polystyrene resin 1 example overall yield reported	38
	**Carbamoyl chloride** Wang resin 1 example	29
	**Urethane** Merrifield resin 10 examples	39

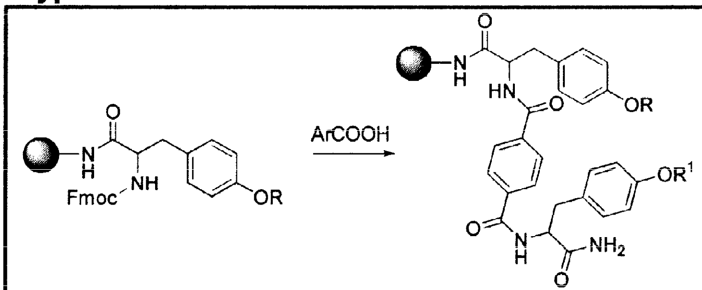
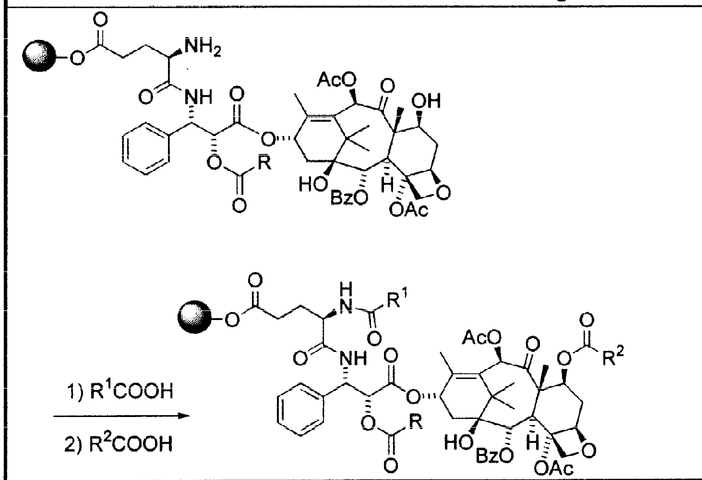
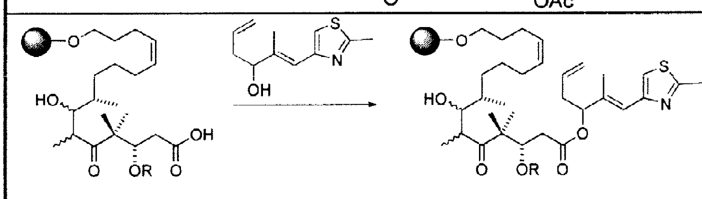
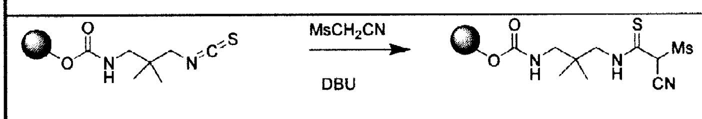
Type of reaction: Amide formation and related reactions

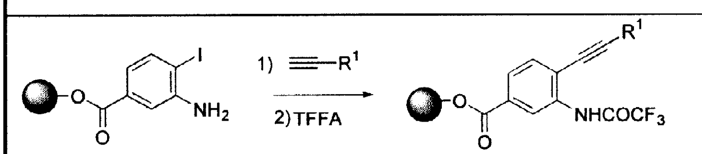
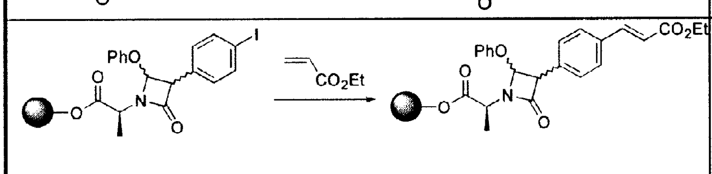
	**Urethane** MBHA resin 1 example overall yield reported	40
	**Guanidine** Wang or Rink amide resin 8 examples 2 guanylating agents yield: 0-99 %	41
	**Guanidine** Rink resin 2 examples yield:>95%	42
	**Guanidine** Wang resin or bromomethyl Wang resin several examples	32
	**Guanidine** Wang resin 8 examples	43
	**Amino sulfonylcarbamate** Wang resin 4 examples	44
	**Sulfonamide** TentaGel resin 4 examples	45
	**Sulfonamide** MBHA resin 3 examples	40

Type of reaction: Amide formation and related reactions

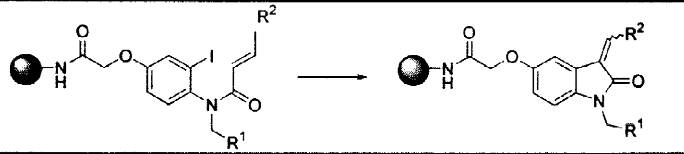
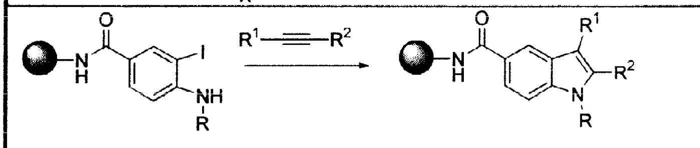
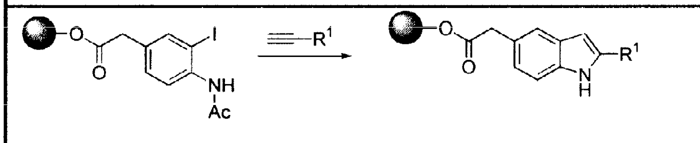
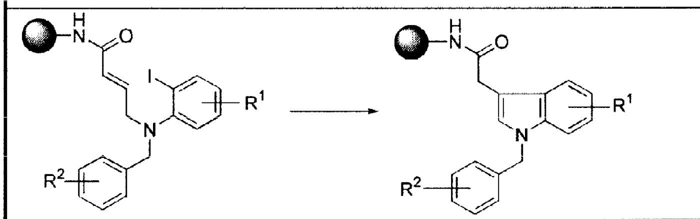
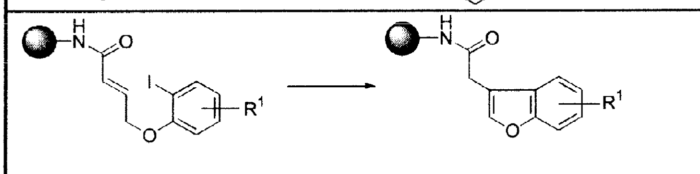
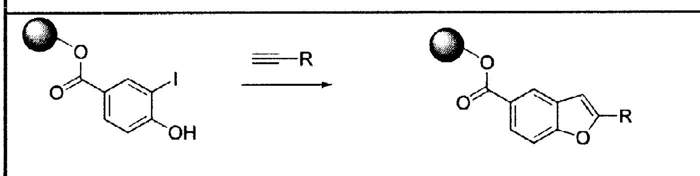
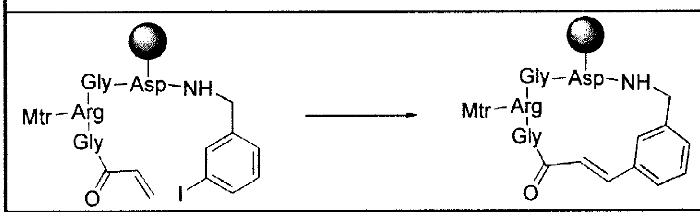
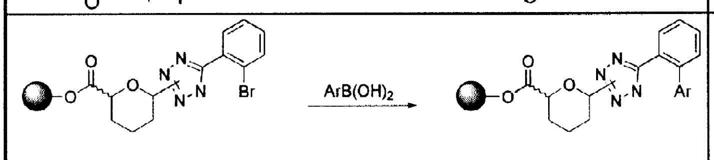
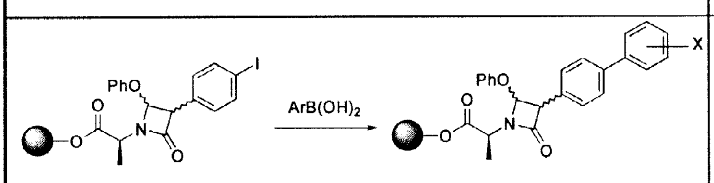
	**Sulfonamide** Merrifield resin few examples overall yield reported	46
	**Sulfonamide** Wang resin monitoring by FTIR 27 examples yield: 41-88%	47a
	**Thioester** BHA resin 2 examples	47b
	**Imide** Wang resin monitoring by FTIR overall yield reported	48
	**Imide** Chiral linker Wang resin monitoring by ^{13}C gel-phase NMR, FTIR 1 example	49
	**Amide** Wang resin monitoring by Kaiser test 2 examples	50
	**Amide** TentaGel resin 12 examples overall yield reported	45
	**Amide** secondary amine TentaGel trityl resin 36 examples	51
	**Amide** Wang resin 2 examples overall yield reported	52
	**Amide** Wang or Knorr resin monitoring by FTIR 12 examples yield: 40-95%	53

Type of reaction: Amide formation and related reactions

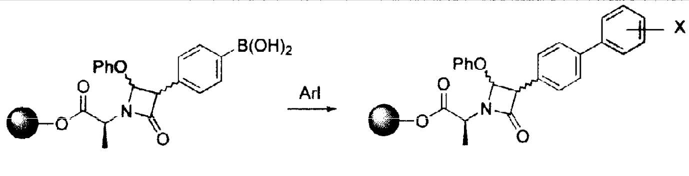
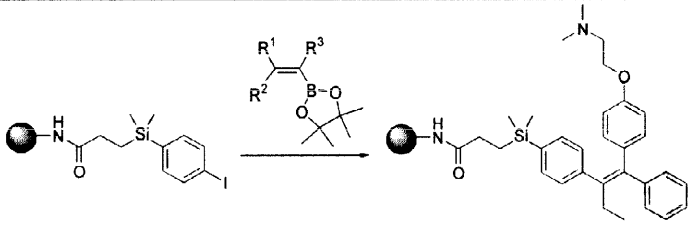
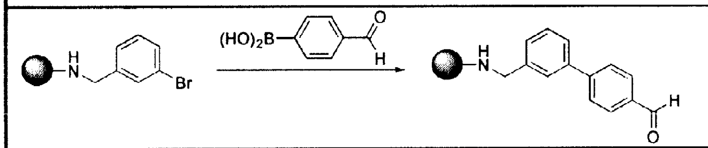
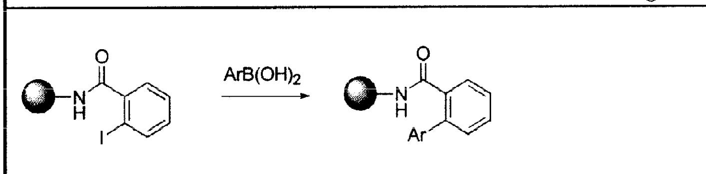
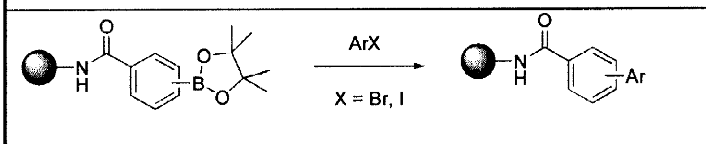
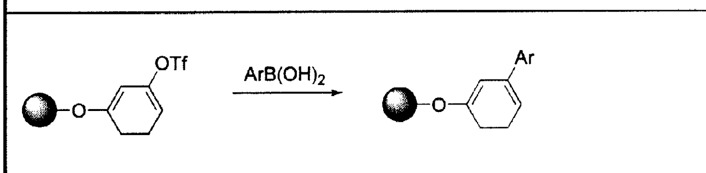
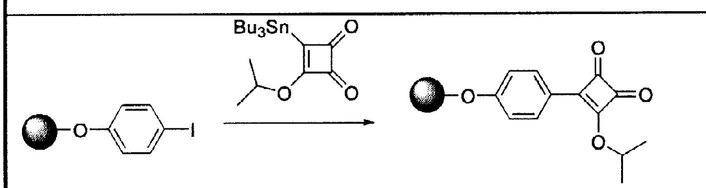
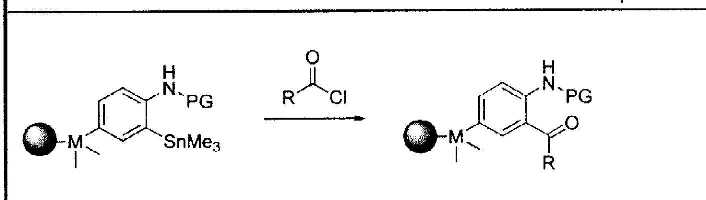
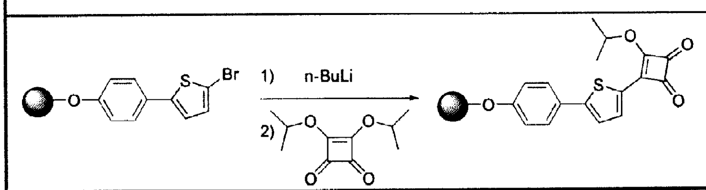
	**Amide** Rink amide resin "double combinatorial chemistry": a mixture of amines coupled to a mixture of acids 9 examples ArCOOH prepared on solid-phase	54
	**Amide and ester** Chlorotrityl resin 400 examples yield: 27-72% overall after purification split/pool radiofrequency encoded part of total synthesis	55
	**Ester** Merrifield resin 1 example yield: 80% part of total synthesis	56
	**Thioamide** Wang resin 9 examples overall yield reported	57

Type of reaction: Aromatic substitution, nucleophilic / electrophilic	Comment	Ref
	**Heck** Wang resin cat: $PdCl_2(PPh_3)_2$ 6 examples overall yield reported	58
	**Heck** ArgoGel MB-OH or Sasrin resin cat: $PdCl_2(dppf)$ 4 examples yield: 60-90 %	59

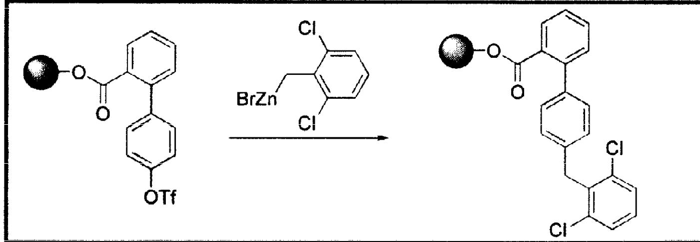
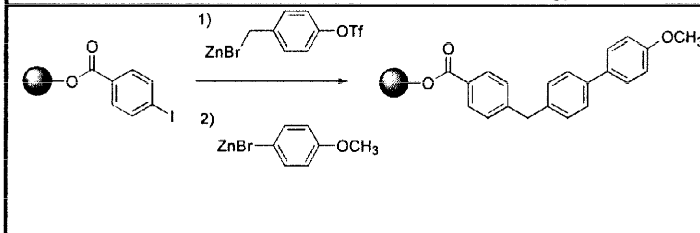
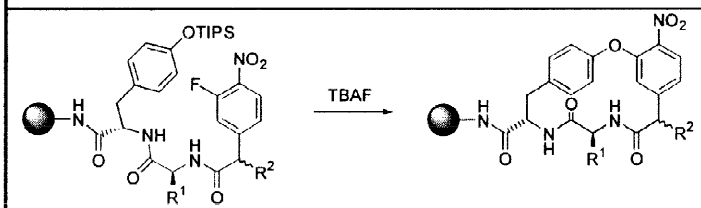
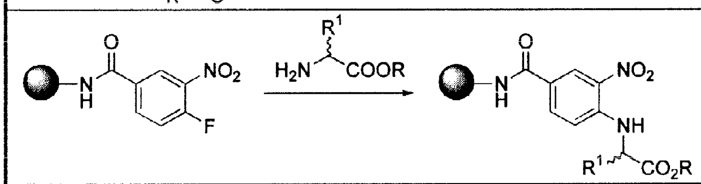
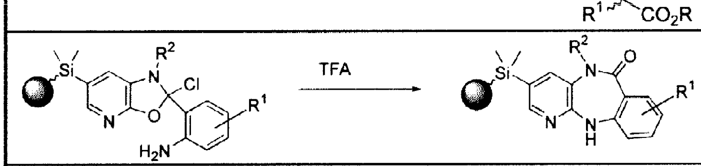
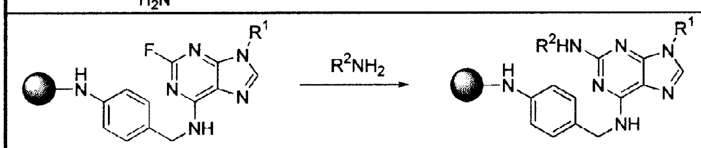
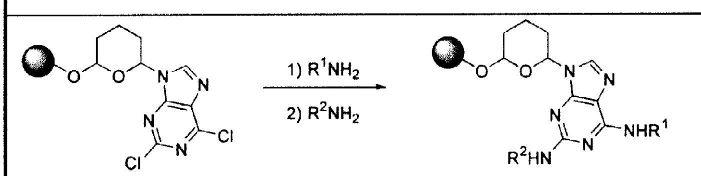
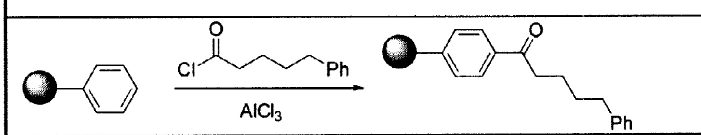
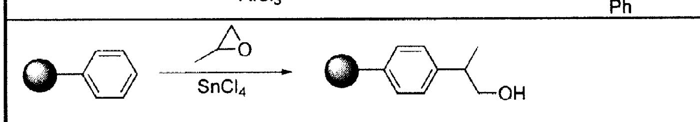
Type of reaction: Aromatic substitution, nucleophilic / electrophilic

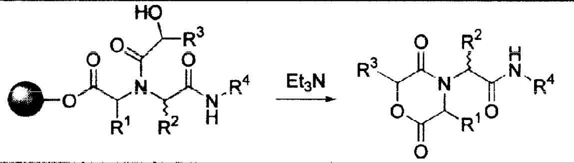
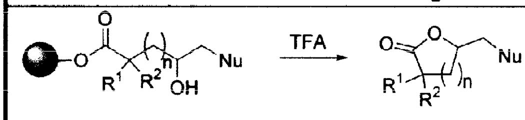
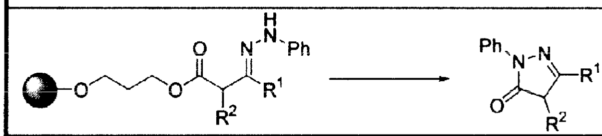
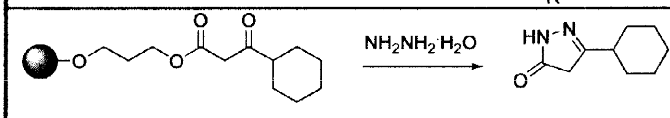
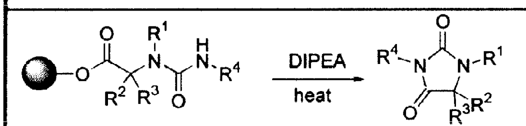
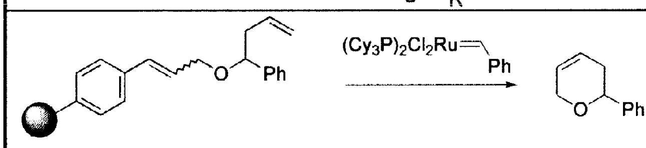
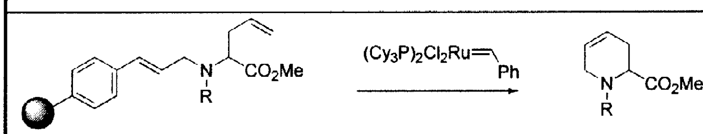
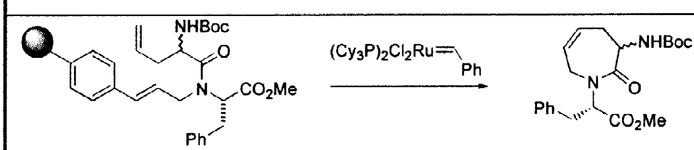
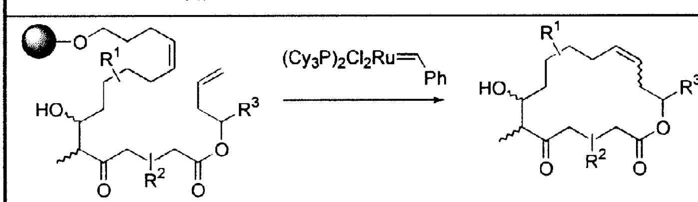
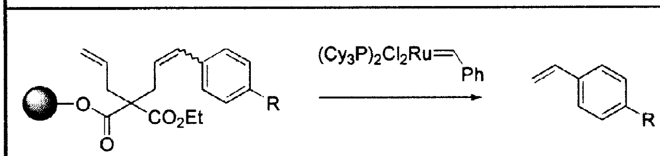
	**Heck (intramolecular)** Rink amide resin cat: $Pd(OAc)_2$ 9 examples yield: 65-92%	60
	**Heck** Rink amide resin cat: $Pd(OAc)_2$ 14 examples yield: 38-100%	27
	**Heck** TentaGel S-OH cat: $Pd(PPh_3)_2Cl_2$ 13 examples yield: 48-95%	61
	**Heck (intramolecular)** Rink amide resin cat: $Pd(PPh_3)_2Cl_2$ 15 examples yield: 67-88%	26
	**Heck (intramolecular)** Rink amide resin cat: $Pd(PPh_3)_2Cl_2$ 2 examples yield: 81-83%	26
	**Heck** TentaGel S-OH resin cat: $Pd(PPh_3)_2Cl_2$ 10 examples yield: 40-71% after cleavage	62
	**Heck (macrocyclisation)** 2-Chlorotrityl resin cat: $Pd(OAc)_2$ 1 example yield: 30% overall	63
	**Suzuki** Merrifield resin cat: $Pd(PPh_3)_4$ 2 examples yield: 53-57%	64
	**Suzuki** Sasrin and Wang resin cat: $PdCl_2(dppf)$ 7 examples yield: 65-89 %	59

Type of reaction: Aromatic substitution, nucleophilic / electrophilic

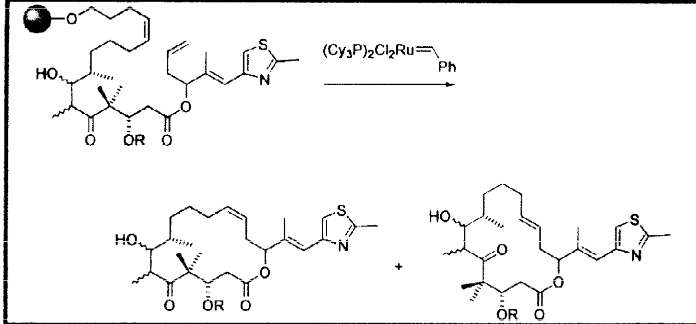
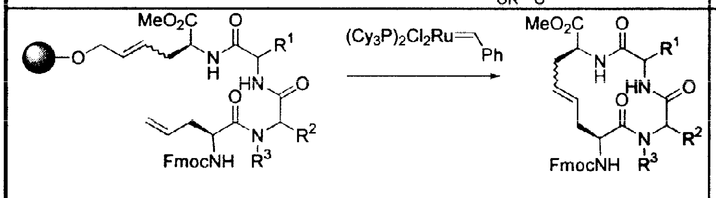
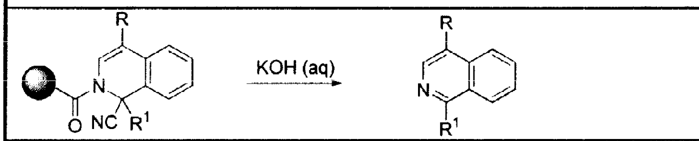
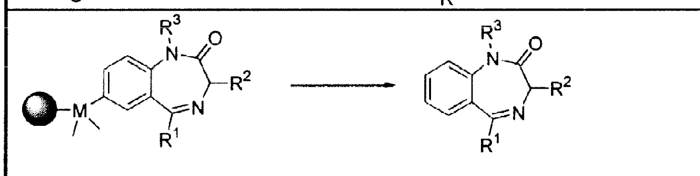
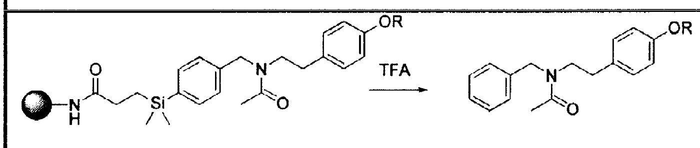
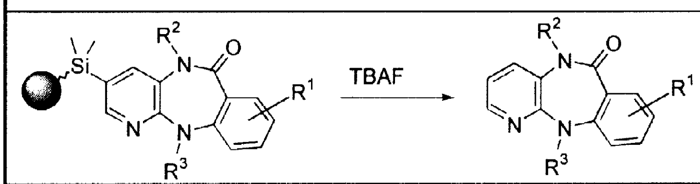
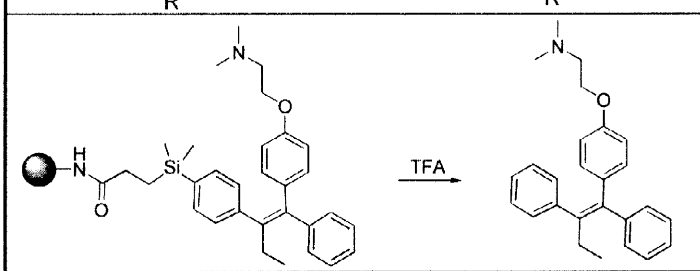
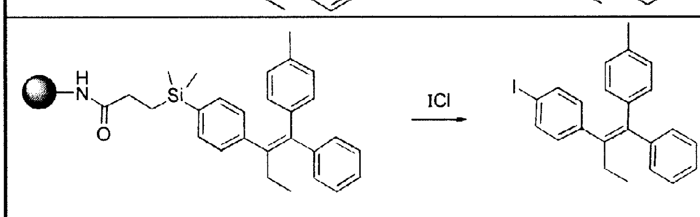
	**Suzuki** ArgoGel MB-OH resin cat: $PdCl_2(dppf)$ 3 examples yield: 60-86 %	59
	**Suzuki** ArgoGel amine resin Resin capture 25 examples yield: 13-68 % overall	65
	**Suzuki** Rink chloride resin 1 example yield: 60%	66
	**Suzuki** ArgoGel Rink resin cat: $PdCl_2(PPh_3)_2$ 8 examples yield: 62-100% automated synthesis	67
	**Suzuki** Rink amide resin cat: $Pd(PPh_3)_4$ 9 examples yield: 48-95%	68
	**Suzuki** Hydroxymethylene polystyrene resin cat: $Pd(PPh_3)_4$ 9 examples yield: 23-47%	69
	**Stille** Wang resin 1 example yield: 95%	70
	**Stille** Aminomethyl polystyrene resin cat: $Pd_2(dba)_3$ M is Si or Ge 7 examples yield: 47-68%	71
	**1,2–Addition** Wang resin 1 example overall yield reported	70

Type of reaction: Aromatic substitution, nucleophilic / electrophilic

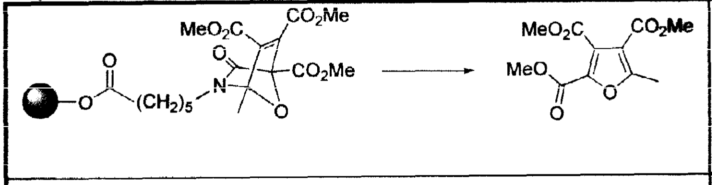
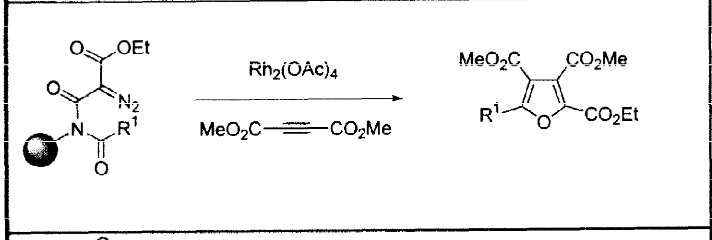
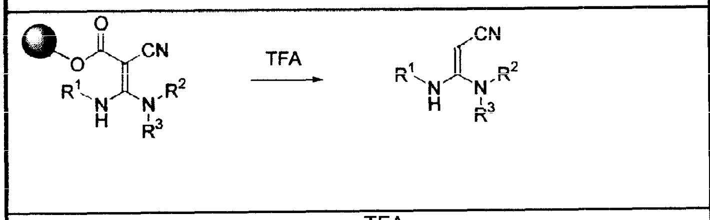
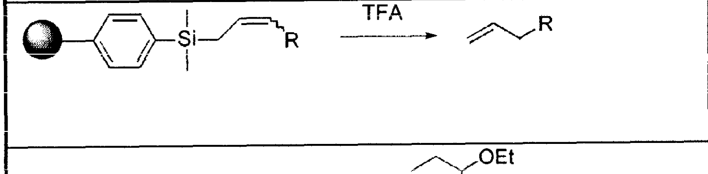
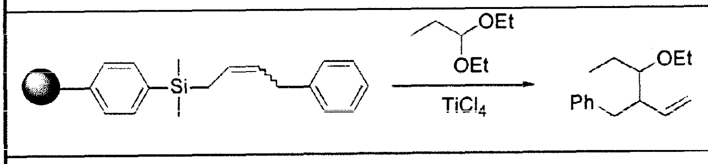
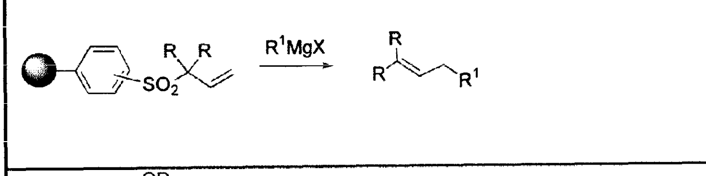
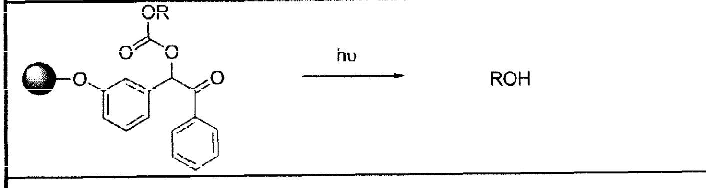
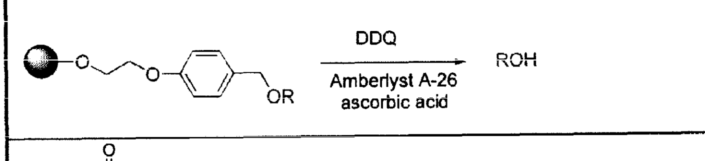
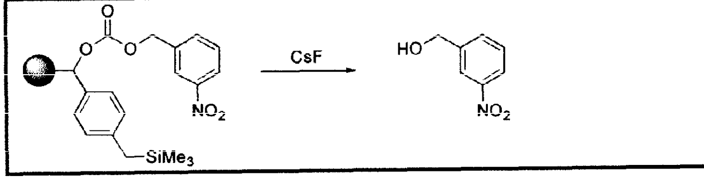
	**Cross coupling** **Wang resin** **cat: $Pd_2(dba)_3$** **2 examples** **yield: not reported**	72
	**Multiple cross coupling** Wang (or Rink MBHA) resin cat: $Pd_2(dba)_3$ several examples also ortho iodide yield: not reported	72
	**O-arylation** **Macrocyclisation** Rink resin monitoring by ^{19}F gel-phase NMR 5 examples yield: 23-59% overall	73
	**N-arylation** Rink amide resin 5 examples overall yield reported	74
	**N-arylation** Polystyrene resin 4 examples overall yield reported	75
	**N-arylation** PAL derivatised MBHA resin 28 examples yield: 51-85%	76
	**N-arylation** Merrifield resin 17 examples yield:53-96% THP linker stable at 150 °C	77
	**Friedel Crafts** Polystyrene 1 example overall yield reported	78
	**Friedel Crafts** Polystyrene resin 1 example yield not reported	79

Type of reaction: Cleavage	Comment	Ref
	**Cyclative cleavage** TentaGel S-OH resin 3 examples yield: 16-56% overall	80
	**Cyclative cleavage** Merrifield resin 12 examples yield: 45-65% overall	81
	**Cyclative cleavage** Wang resin 7 examples yield: 56-95% overall	82
	**Cyclative cleavage** Wang resin 1 example yield: 84%	82
	**Cyclative cleavage** Wang resin 18 examples yield: 82-93%	83
	**Cyclative cleavage Ring closing metathesis (RCM)** Polystyrene resin 1 example yield: 43% overall	84
	**Cyclative cleavage RCM** Polystyrene resin 2 examples yield: 22-62% overall	84
	**Cyclative cleavage RCM** Polystyrene resin 1 example yield: 16% overall	84
	**Cyclative cleavage RCM** Merrifield resin 45 examples radiofrequency tags overall yields reported	85
	**Cyclative cleavage RCM** Merrifield resin monitoring by FTIR 5 examples yield: 24-55% overall	86

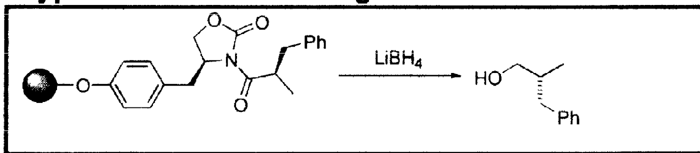
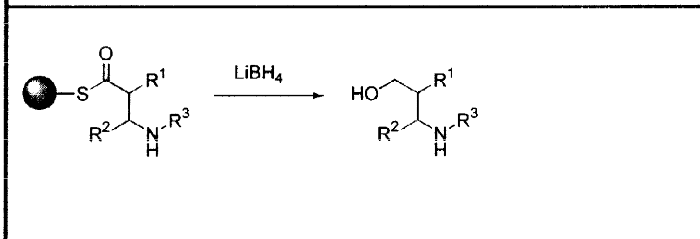
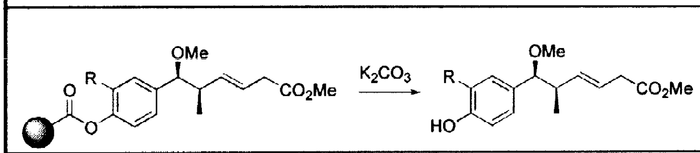
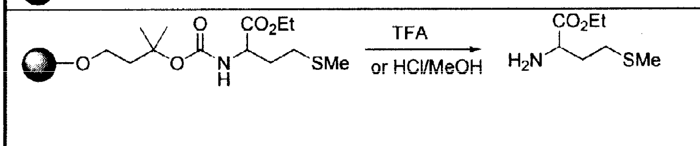
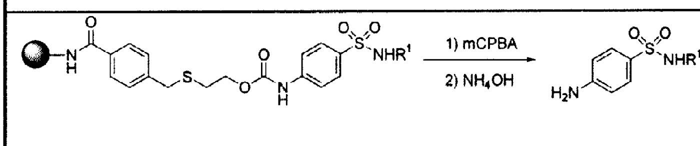
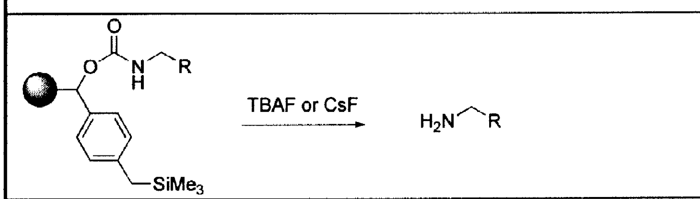
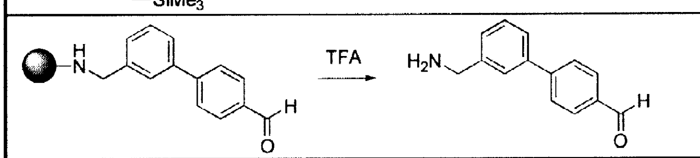
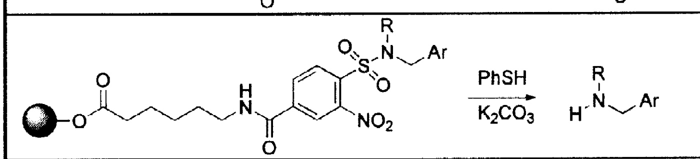
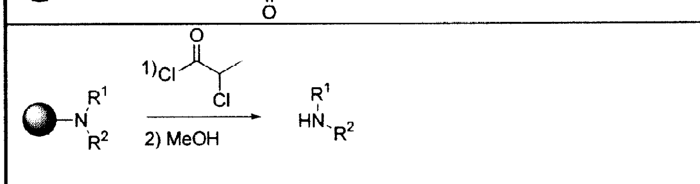
Type of reaction: Cleavage

	**Cyclative cleavage** **RCM** **Merrifield resin** **1 example** **yield:52%** **part of total synthesis**	56
	**Cyclative cleavage** **RCM** Trityl resin 6 examples yield: 30-70%	87
	**Traceless** PS carboxylic acid resin 7 examples yield: 50-59% overall	88
	**Traceless** Aminomethyl polystyrene resin M is Si or Ge 8 examples yield: 47-68%	71
	**Traceless** **Silicon linker** BHA resin 2 examples yield: 100%	89
	**Traceless** **Silicon linker** Polystyrene resin 7 examples yield: 48-65% overall	75
	**Traceless** **Silicon linker** ArgoGel amine resin 25 examples yield: 13-68 % overall Tamoxifen synthesis	65
	**Silicon linker** ArgoGel amine resin 1 example yield: 43 % overall	65

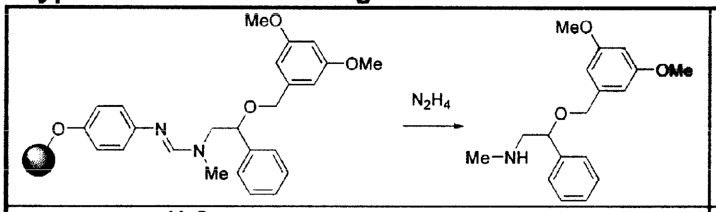
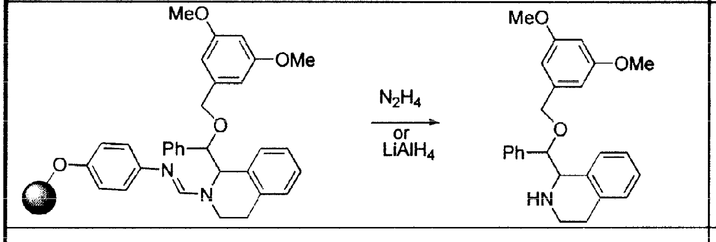
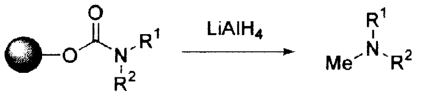
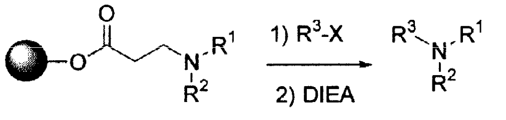
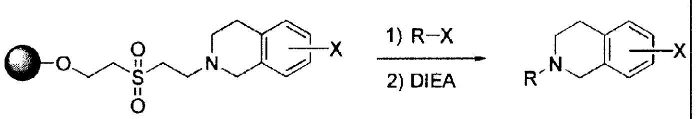
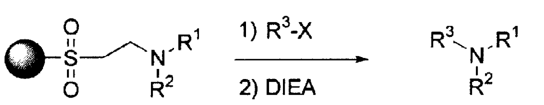
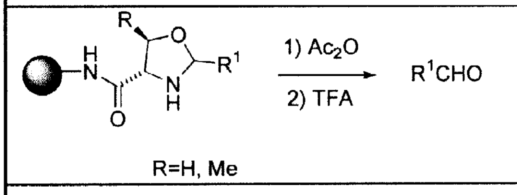
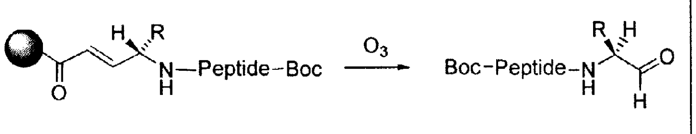
Type of reaction: Cleavage

	**Traceless Thermal cycloreversion** Wang resin 18 examples yield: 70% overall	48
	**Traceless Thermal cycloreversion** TentaGel NH_2 monitoring by ^{13}C NMR 9 examples + library of 32 yield: 50-70%	90
	**Traceless Saponification followed by decarboxylation** Wang resin 4 examples yield: 59-83% overall	91
	**Traceless Protodesilylation** Polystyrene resin 4 examples yield: not reported	92
	**Traceless C-C bond formation** Polystyrene resin 1 example yield: not reported	92
	**Alkane Nucleophilic displacement** polystyrene resin 3 examples yield:20-30% overall	93
	**Alcohol Safety Catch Photochemical** Merrifield resin 1 example yield: 72%	37
	**Alcohol Oxidative** ArgoGel-Wang resin 5 examples yield: > 70%	94
	**Alcohol Silicon induced** Polystyrene resin 7 examples yield: 3-68%	38

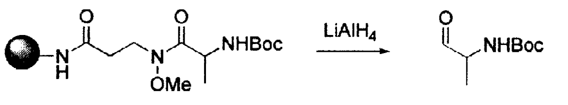
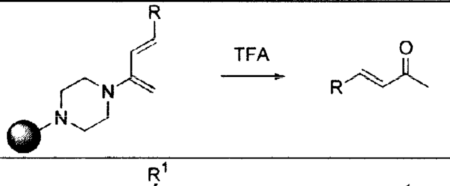
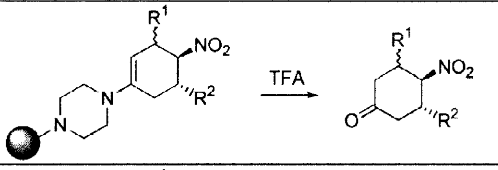
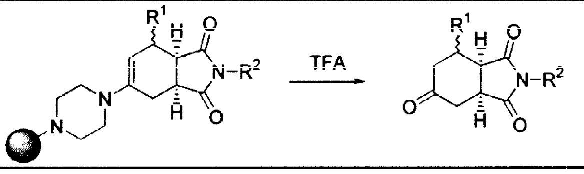
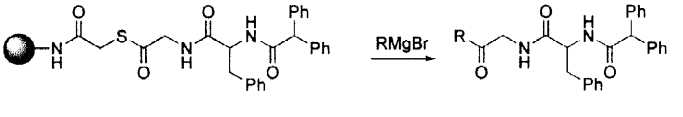
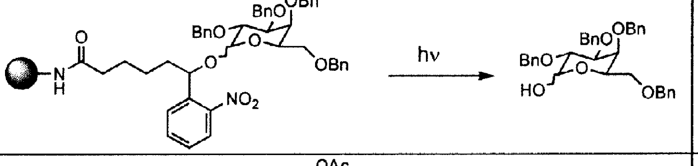
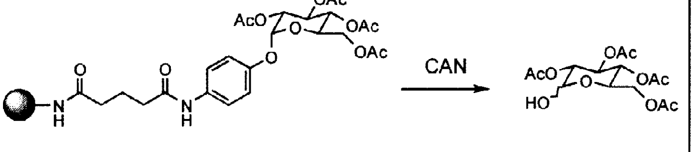
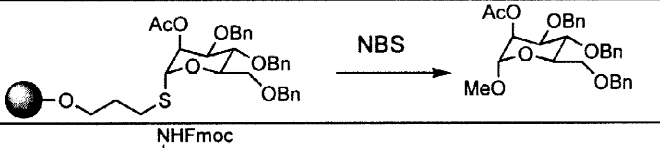
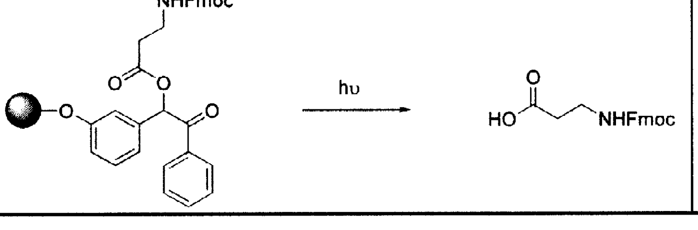
Type of reaction: Cleavage

	**Alcohol** **Reduction** Merrifield resin 1 example yield: not reported	95
	**Alcohol** **Reduction** (Chloromethylphenyl) pentyl polystyrene (CMPP), Merrifield or Wang resin 11 examples yield: 53-90% overall	78
	**Phenol** **Hydrolysis** PS carboxylic acid resin several examples yield: 37% for 10 steps	96
	**Amine** **Hydrolysis** Merrifield resin 10 examples yield: not reported	39
	**Amine (aniline)** **Safety catch** MBHA resin 3 examples yield: not reported	40
	**Amine** **Silicon induced** Polystyrene resin 2 examples yield: 82-88%	38
	**Amine** **Hydrolysis** Rink chloride resin 1 example yield: 60%	66
	***sec*-Amine** BHA resin 7 examples yield: 48-100%	97
	***sec*-Amine** **Debenzylation** Merrifield, Wang or Sasrin resin 6 examples yield:70-96%	98

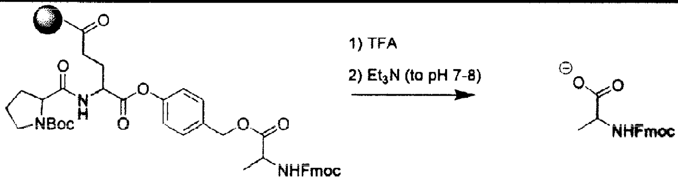
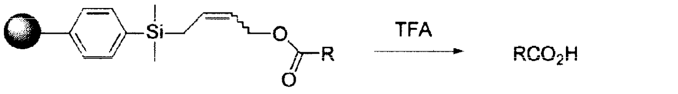
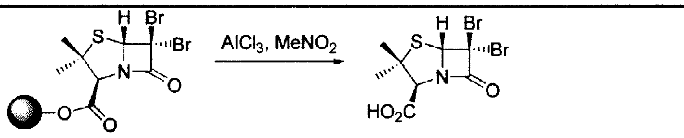
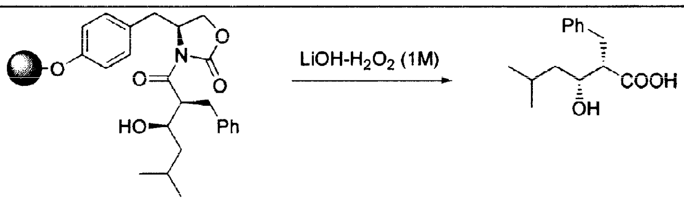
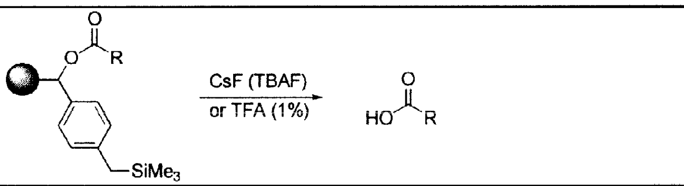
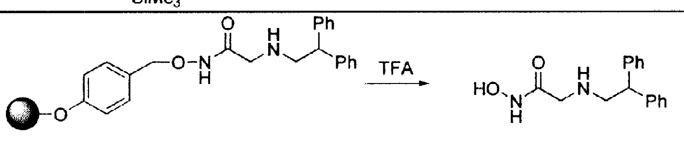
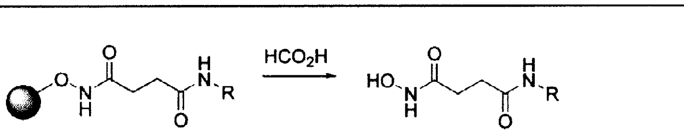
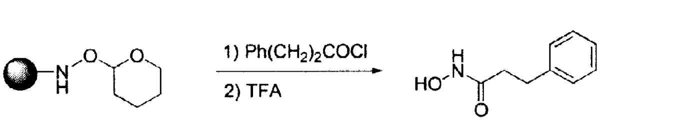
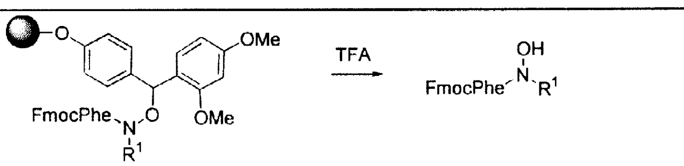
Type of reaction: Cleavage

	**Amine Nucleophilic displacement** Merrifield resin 1 example yield: 80-95%	99
	**Amine Nucleophilic displacement** Merrifield resin 3 examples yield: 60% overall	100
	***tert*-Amine Reduction** Wang resin 6 examples yield: 48-90 %	101
	***tert*-Amine Hofmann elimination** PS (REM) resin several examples monitoring by FTIR and [13]C gel-phase NMR yield: 41-88% overall recycling of resin	102
	***tert*-Amine Hofmann elimination** Hydroxymethylene resin 13 examples yield: 80-90% overall regenerate resin	103
	***tert*-Amine Hofmann elimination** Merrifield resin 5 examples (different linkers) yield: 5-83% overall regenerate resin	104
	**Aldehyde Hydrolysis** Synphase crowns peptide aldehydes 3 examples yield: not reported	105
	**Aldehyde Oxidative** Merrifield, MBHA, Expansin (Met) resin 3 examples yield: 30-83 %	106

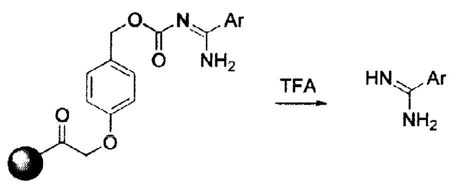
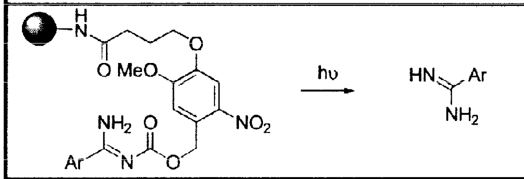
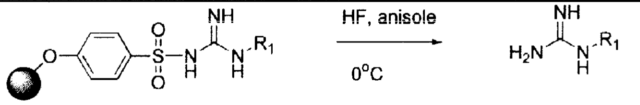
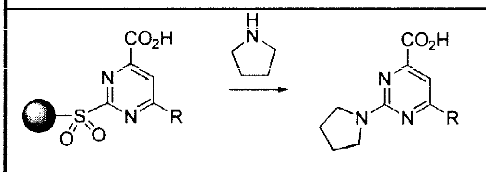
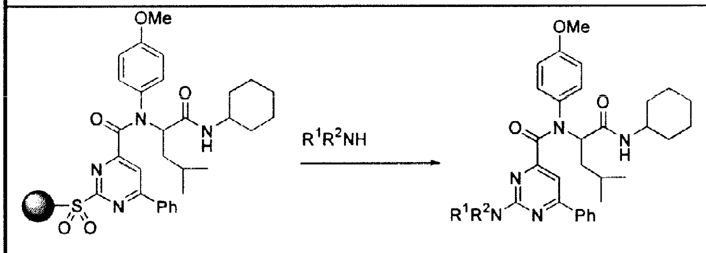
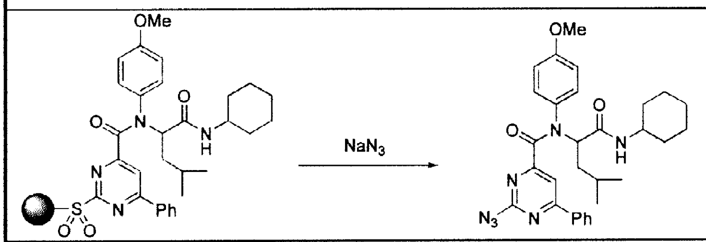
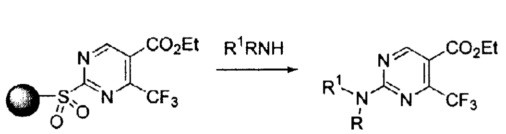
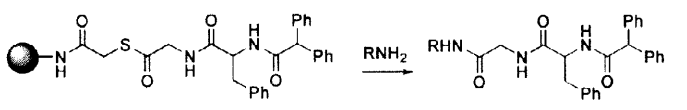
Type of reaction: Cleavage

	**Aldehyde** **Reductive** MBHA resin 6 examples Weinreb amide reduction yield: 25-40%	107
	**Ketone** **Hydrolysis** Merrifield resin 10 examples yield: 64-95%	108
	**Ketone** **Hydrolysis** Merrifield resin 7 examples yield: 31-63%	109
	**Ketone** **Hydrolysis** Merrifield resin 8 examples + library yield: 37-87%	109
	**Ketone** **Nucleophilic displacement** BHA resin 5 examples yield: 50-60%	47b
	**Glycoside** **Photochemical** amine resin 2 examples yield: 82-96 %	110
	**Glycoside** **Oxidative** Aminomethylene resin 1 example yield: 70%	111
	**Glycoside** Merrifield resin 2 examples yield: 54%	112
	**Carboxylic acid** **Safety Catch** **Photochemical** Merrifield resin monitoring by HPLC 2 examples yield: 65-75%	37

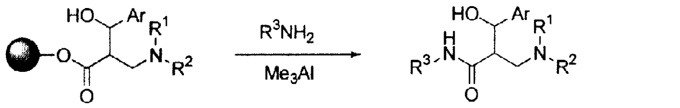
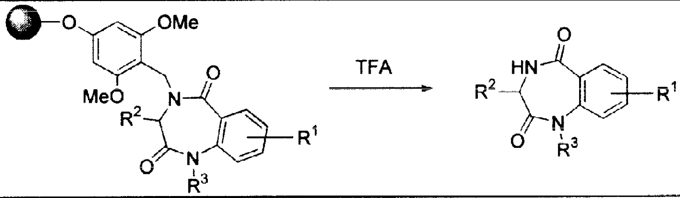
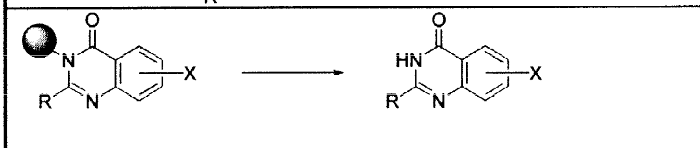
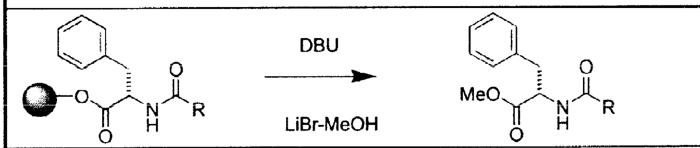
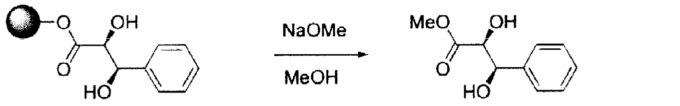
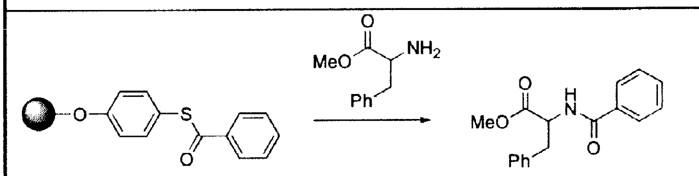
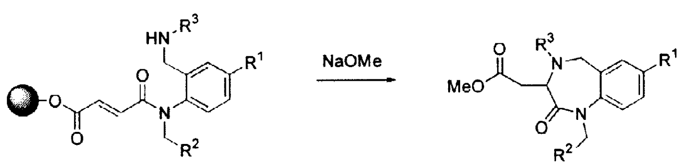
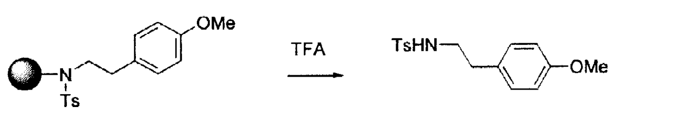
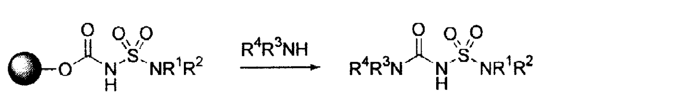
Type of reaction: Cleavage

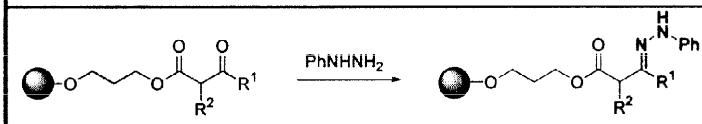
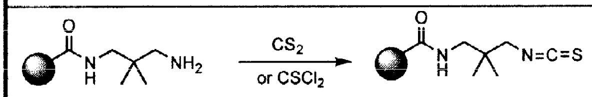
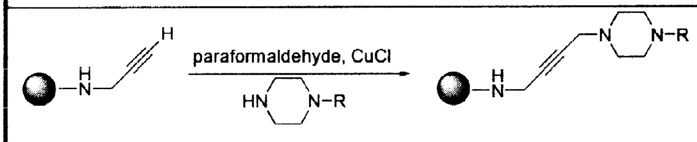
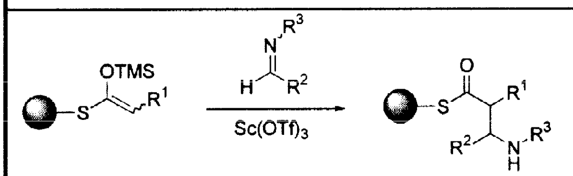
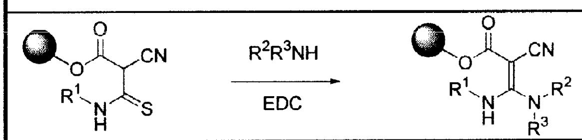
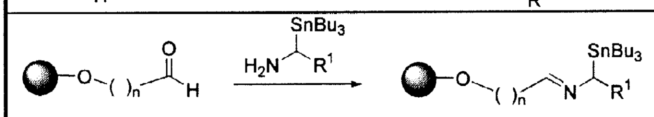
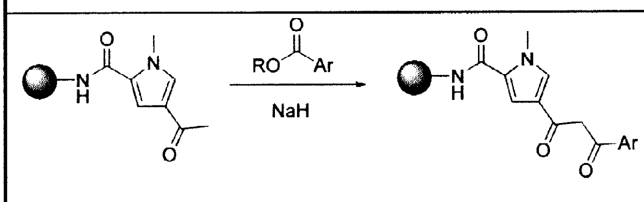
	**Carboxylic acid** **Safety Catch** TentaGel S NH_2 resin PS-PEG resin -NH_2 monitoring by UV analysis, RP-HLPC 5 examples pH cleavable linker yield: >70%	113
	**Carboxylic acid** Polystyrene resin 3 examples yield: not reported	92
	**Carboxylic acid** **Hydrolysis** Wang or Merrifield resin 15 examples yield: 66-100%	114
	**Carboxylic acid** **Hydrolysis** Chiral linker Wang resin 1 example yield: not reported	49
	**Carboxylic acid** **Silicon induced** Polystyrene resin 9 examples yield: 40-96%	38
	**Hydroxamic acid** **Hydrolysis** Rink, Sasrin and Wang resin 2 examples yield: not reported	115
	**Hydroxamic acid** **Hydrolysis** Trityl polystyrene monitoring by FTIR 9 examples yield: 48-78% overall	33
	**Hydroxamic acid** **Hydrolysis** TentaGel S-NH_2 resin 5 examples yield: 81-88 %	116
	**Hydroxamic acid** **Hydrolysis** Rink acid resin 8 examples yield: 93-100 %	117

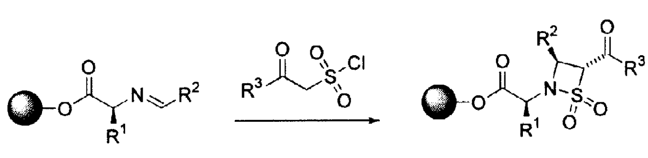
Type of reaction: Cleavage

	**Amidine Hydrolysis** aminomethyl polystyrene resin 6 examples yield: 41-71% over 2 steps	118
	**Amidine Photochemical** aminomethyl polystyrene resin 1 example yield: 20%	118
	**Guanidine** Merrifield resin 4 examples overall yield reported	46
	**Guanidine-like Nucleophilic displacement Safety catch** Merrifield resin 8 examples yield: 65-99%	119
	**Guanidine-like Nucleophilic displacement Safety catch** Merrifield resin 3 examples yield: 53-70%	119
	**Guanidine-like Nucleophilic displacement Safety catch** Merrifield resin 1 example yield: 70%	119
	**Guanidine-like Nucleophilic displacement Safety catch** TentaGel SH 6 examples yield: 50-93%	120
	**Amide Nucleophilic displacement** BHA resin 8 examples yield: 60-80%	47b

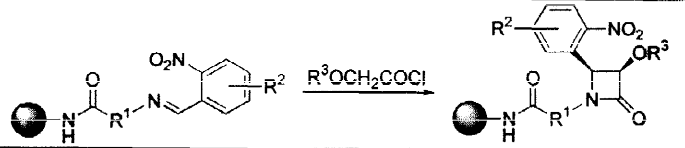
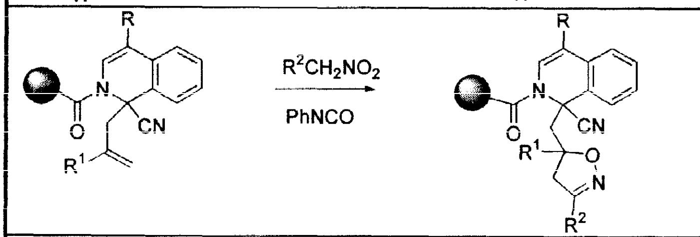
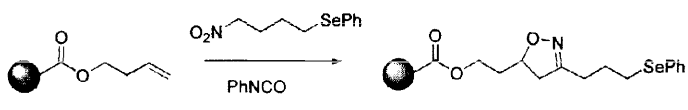
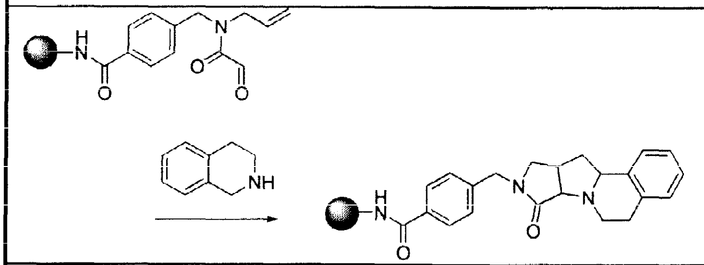
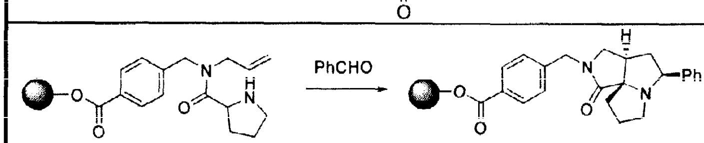
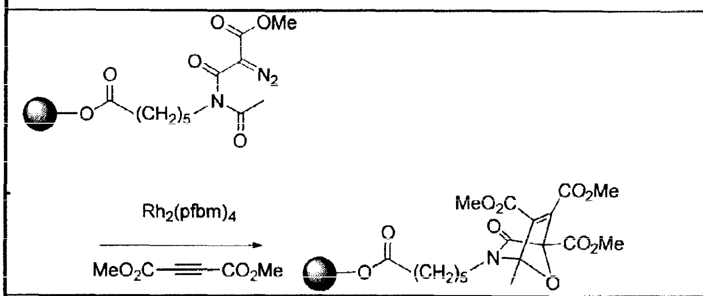
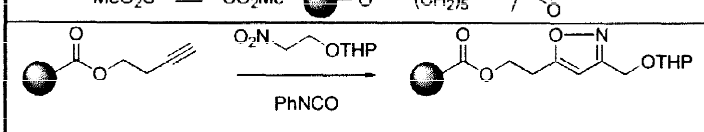
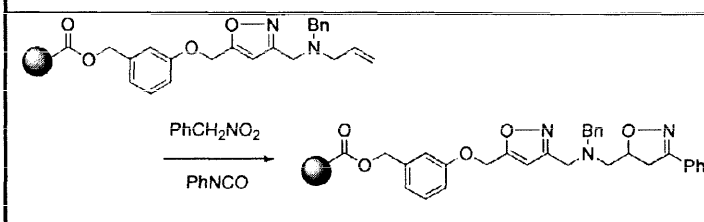
Type of reaction: Cleavage

	**Amide** **Aminolysis** Hydroxyethylene resin 18 examples yield:40-66% overall	121
	**Amide** **Debenzylation** Merrifield resin > 23 examples yield: 52-92%	122
	**Amide-like** **Hydrolysis** Rink amide resin 5 examples yield: 58-85%	52
	**Ester** **Transesterification** PAM resin	36
	**Ester** **Transesterification** Merrifield, Wang and TentaGel resin 10 examples yield: 25-85%	123
	**Ester** **Nucleophilic displacement** BHA resin 3 examples yield: 60-70%	47b
	**Ester** **Methanolysis followed by intramolecular Michael addition** Wang resin monitoring by FTIR 120 examples typical yield: 79%	124
	**Sulfonamide** **Hydrolysis** AMEBA resin (SASRIN aldehyde equivalent) 14 examples yield: 20-80% overall	125
	**Urea-like** **Nucleophilic displacement** Wang resin 28 examples yield: 26-100% over 3 steps	44

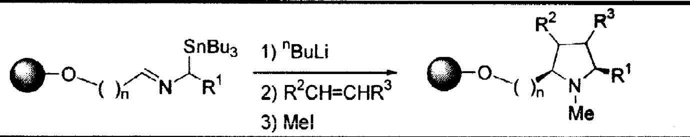
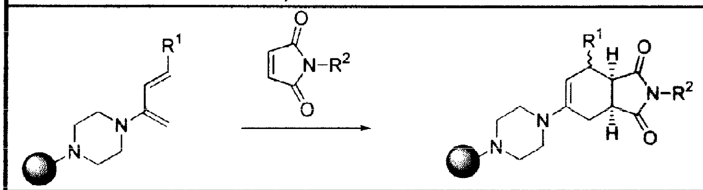
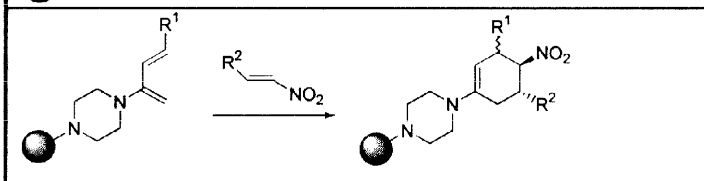
Type of reaction: Condensation	Comment	Ref
	**Hydrazone** Wang resin 7 examples overall yield reported	82
	**Isothiocyanate** Wang resin 9 examples overall yield reported	57
	**Mannich** 2-chlorotrityl chloride resin 44 examples yield: >90%	126
	**Mannich** (Chloromethylphenyl) pentyl polystyrene (CMPP), Merrifield or Wang resin 11 examples overall yield reported	78
	**Ketene aminal** Wang resin 4 examples overall yield reported	91
	**Imine** polystyrene resin 4 examples overall yield reported	127
	**Claisen** Rink amide resin split/pool only aromatic esters without α-hydrogens 140 examples yield: >95%	128

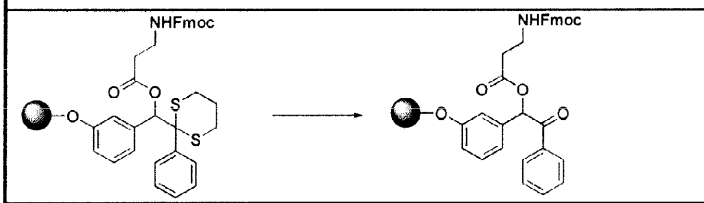
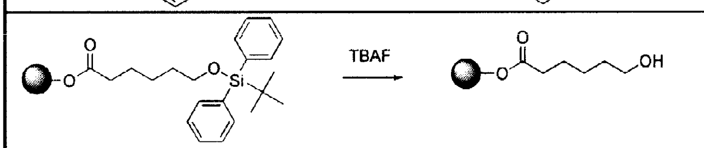
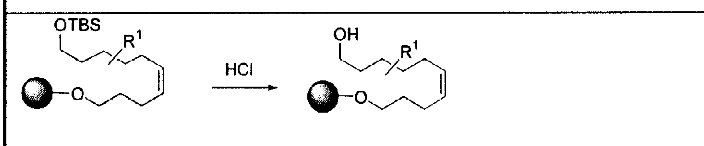
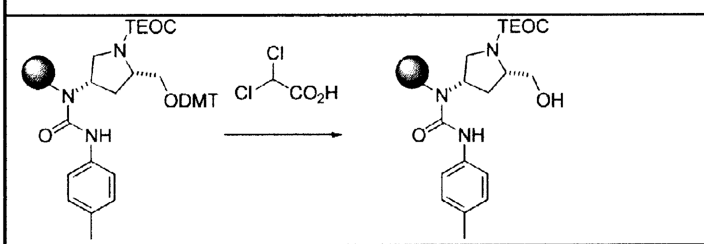
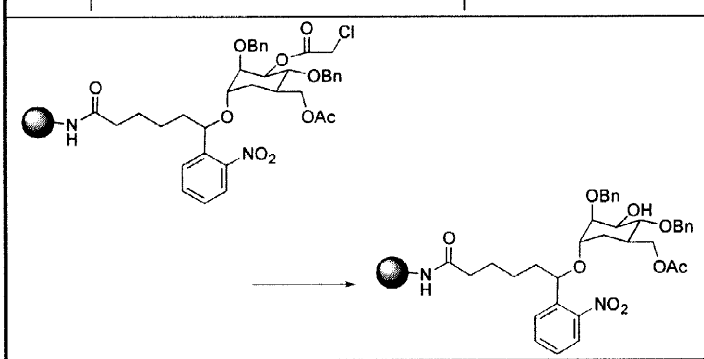
Type of reaction: Cycloaddition	Comment	Ref
	**[2+2]** TentaGel resin Photolabile linker yield: 19-39% Sasrin resin yield: 58-90% 15 examples monitoring by ^{13}C gel-phase NMR	129

Type of reaction: Cycloaddition

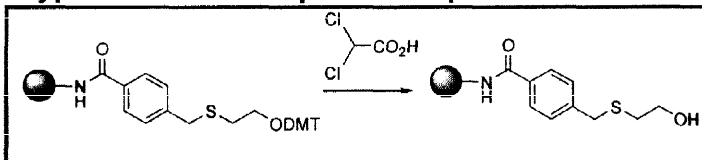
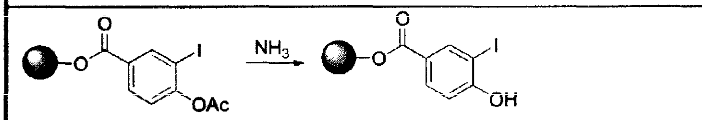
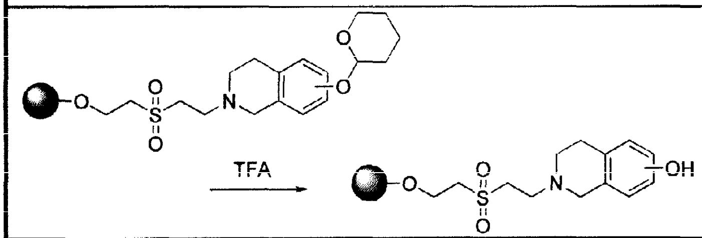
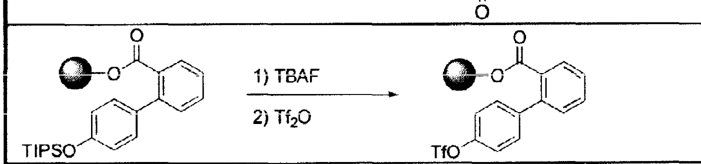
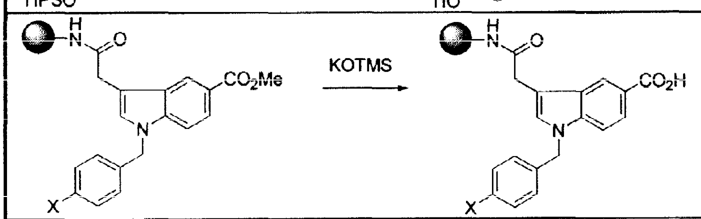
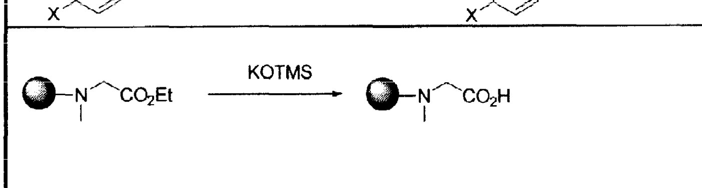
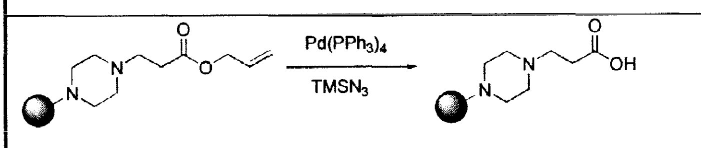
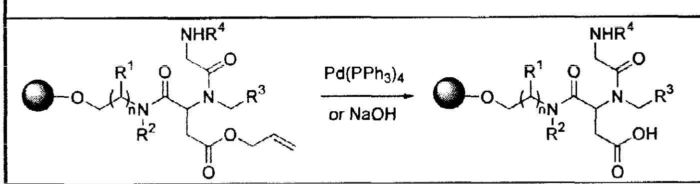
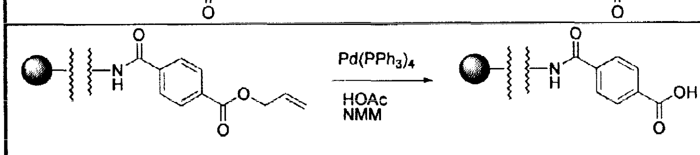
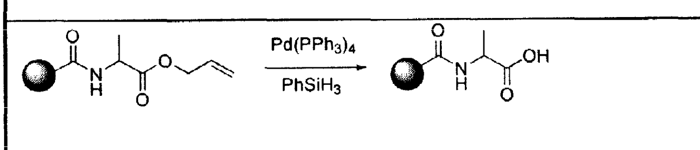
	**[2+2]** MBHA resin 4140 examples overall yield reported	130
	**[3+2]** PS carboxylic acid resin 1 regioisomer formed 6 examples yield: 23-27% over 6 steps	88
	**[3+2]** PS carboxylic acid resin library of 84 compounds	131
	**[3+2]** Rink amide resin 9 examples yield: 45% overall	132
	**[3+2]** Wang or Rink resin monitoring by chloranil test 8 examples yield: 32-75%	132
	**1,3-dipolar** Wang resin Carbene formation monitoring by FTIR 18 examples overall yield reported	48
	**[3+2]** polystyrene resin monitoring by FTIR of nitrile oxide 6 examples overall yield reported	133
	**[3+2]** polystyrene resin monitoring by FTIR 2 examples overall yield reported	133

Type of reaction: Cycloaddition

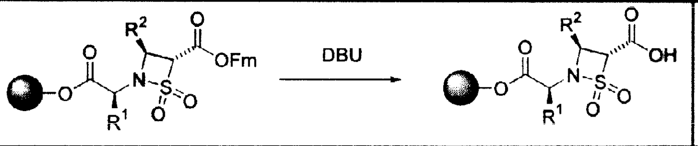
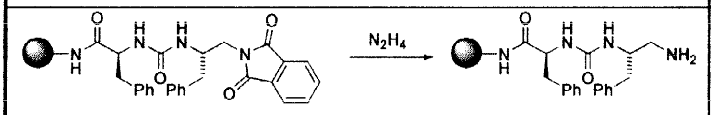
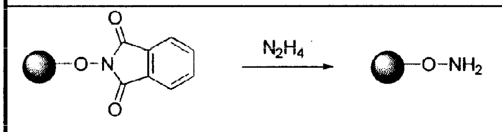
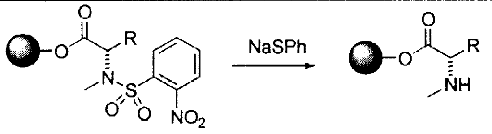
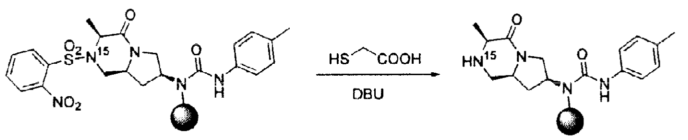
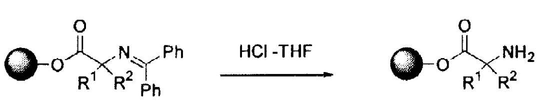
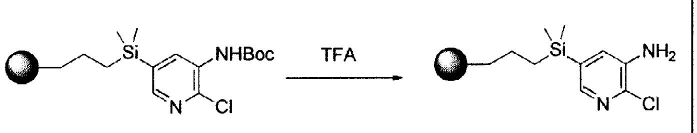
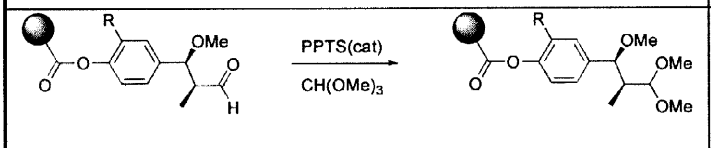
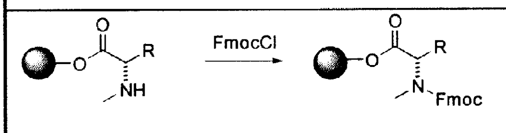
	**[3+2]** **polystyrene resin** **6 examples** **yield: 32-50%**	127
	**[4+2]** **Diels–Alder** Merrifield resin 8 examples + library yield: 37-87% after cleavage	109
	**[4+2]** **Diels–Alder** Merrifield resin 7 examples yield: 31-63% after cleavage	109

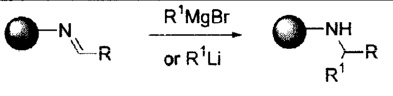
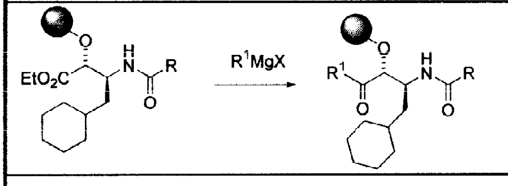
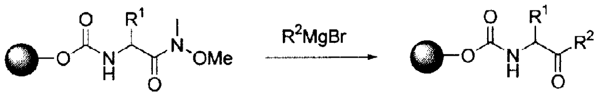
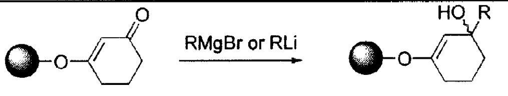
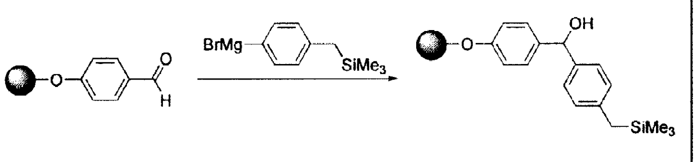
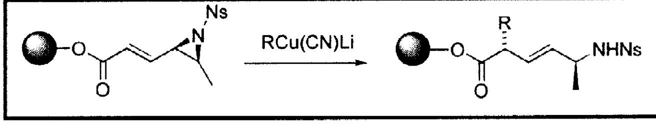
Type of reaction: Deprotection/protection	Comment	Ref
	**Ketone-deprotection** Merrifield resin monitoring by gel-phase ^{13}C NMR and FTIR 1 example overall yield reported	37
	**Alcohol-deprotection** Wang resin monitoring by FTIR 2 examples yield: ~97%	134a
	**Alcohol-deprotection** Merrifield resin radiofrequency tags 3 examples overall yield reported	85
	**Alcohol-deprotection** ArgoGel resin 1 example overall yield reported	31
	**Alcohol-deprotection** amine resin 1 example overall yield reported	110

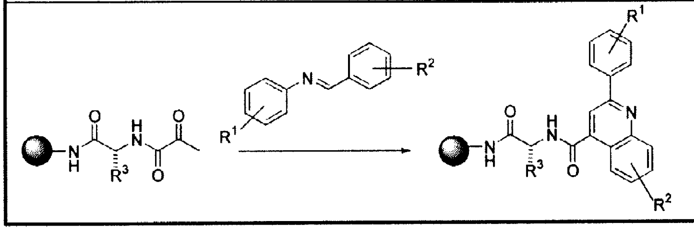
Type of reaction: Deprotection/protection

	**Alcohol-deprotection** MBHA resin 1 example overall yield reported	40
	**Phenol-deprotection** Tentagel S-OH 1 example overall yield reported	62
	**Phenol-deprotection** Hydroxymethylene resin 2 examples overall yield reported	103
	**Phenol-deprotection** Wang resin 2 examples overall yield reported	72
	**Carboxylic acid-deprotection Saponification** Rink amide resin 6 examples	26
	**Carboxylic acid-deprotection Saponification** 2-Chlorotrityl resin 2 examples overall yield reported	134b
	**Carboxylic acid-deprotection** 2-Chlorotrityl resin 1 example overall yield reported	134b
	**Carboxylic acid-deprotection** TentaGel trityl resin library of 6x6x8 compounds	51
	**Carboxylic acid-deprotection** Rink amide resin 4 examples overall yield reported	54
	**Carboxylic acid-deprotection** MBHA resin 3 examples yield: >90%	135

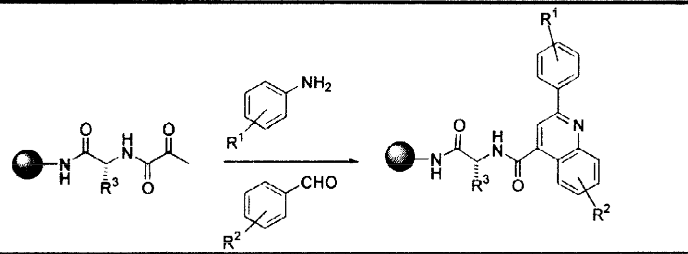
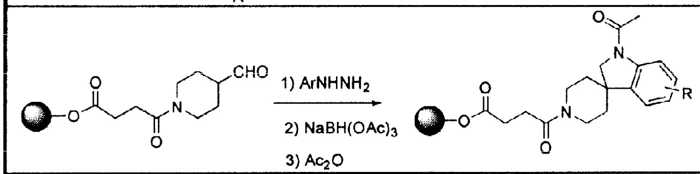
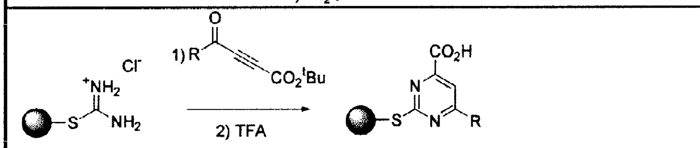
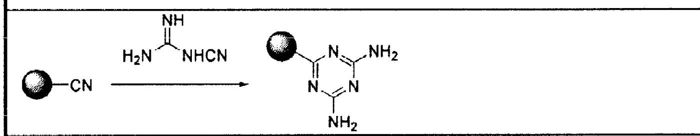
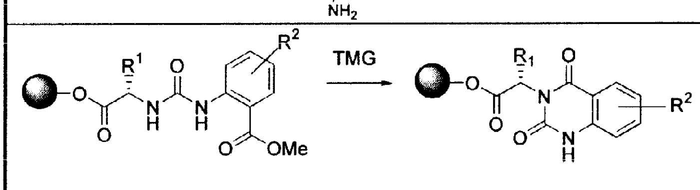
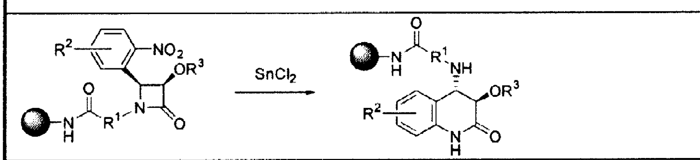
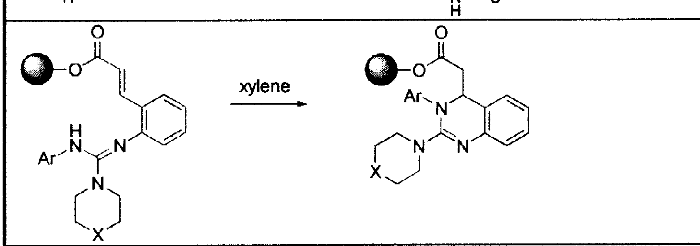
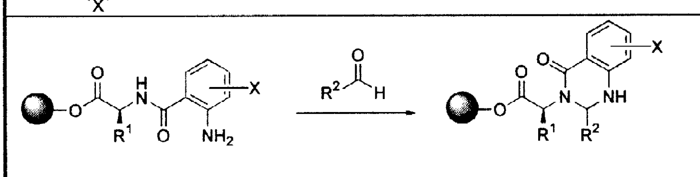
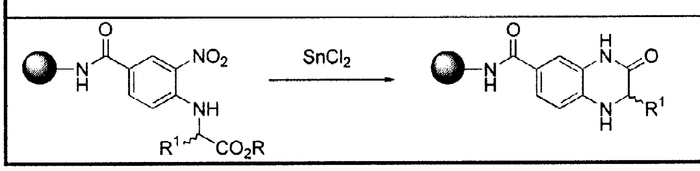
Type of reaction: Deprotection/protection

	**Carboxylic acid-deprotection** TentaGel resin 1 example overall yield reported	129
	**Amine-deprotection** Rink amide resin 160 examples	136a
	**Alkoxyamine-deprotection** Rink, Sasrin and Wang resin 3 examples yield: 95%	115
	**Amine-deprotection** 2-chlorotrityl resin 8 examples yield: 80-100% over 4 steps	136b
	**Amine-deprotection** ArgoGel OH resin 1 example monitoring by ^{15}N gel-phase NMR overall yield reported	31
	**Amine-deprotection** Wang resin conditions optimised 24 examples overall yield reported	137
	**Aniline-deprotection** Polystyrene resin 1 example overall yield reported no cleavage from resin observed	75
	**Thiol-deprotection** BHA resin monitoring by triphenylmethane production 1 example yield: 95%	47b
	**Aldehyde-protection (acetal)** Carboxylated polystyrene resin 4 examples overall yield reported	96
	**Amine-protection** 2-chlorotrityl resin 8 examples yield: 80-100% over 4 steps	136b

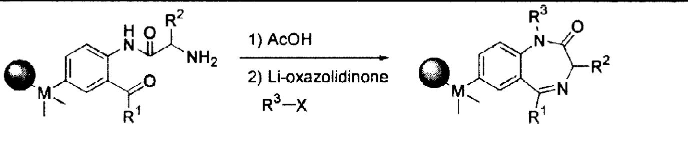
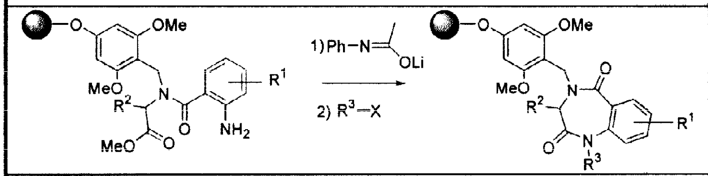
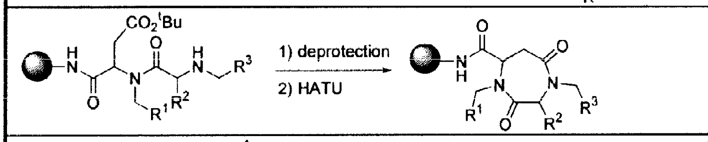
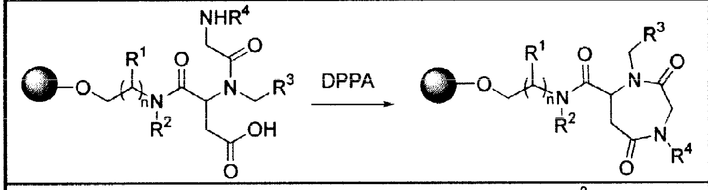
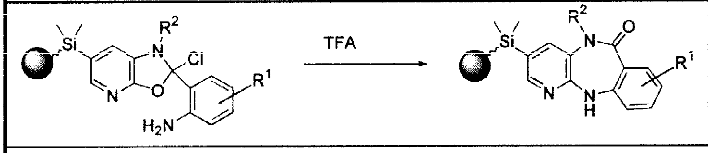
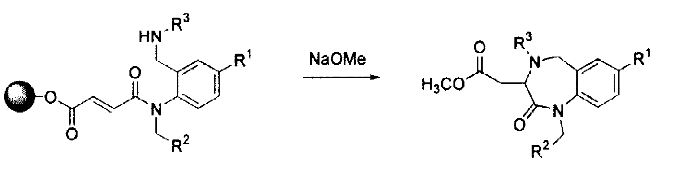
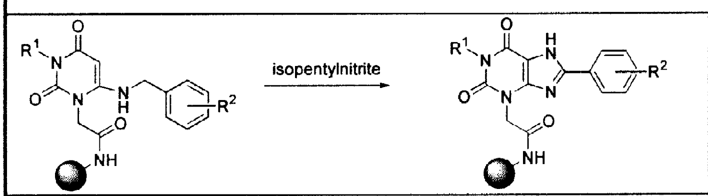
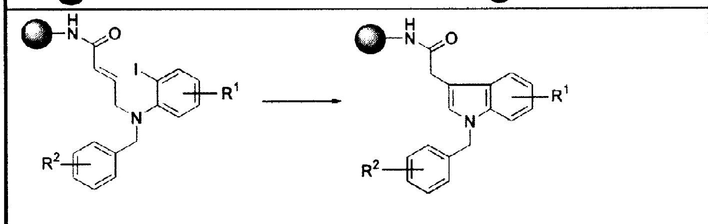
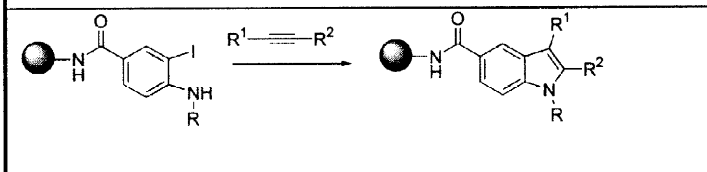
Type of reaction: Grignard and related reactions	Comment	Ref
	**Imine to amine** Rink resin 14 examples overall yield reported	138
	**Ester to ketone** DHP- linked polystyrene 11 examples yield: 13-68%	152
	**Weinreb amide to ketone** ArgoGel Wang resin 12 examples automated synthesis yield: 83-94%	67
	**Ketone to alcohol** Hydroxymethylene polystyrene resin 13 examples yield: 34-86%	69
	**Ketone to alcohol** Merrifield or formyl polystyrene resin 2 examples monitoring by FTIR, ^{13}C gel-phase NMR overall yield reported	38
	**Cuprate** Wang resin 5 examples overall yield reported	139

Type of reaction: Heterocycle formation	Comment	Ref
	**Quinoline** Rink amide resin 5 examples yield: 60-92%	140

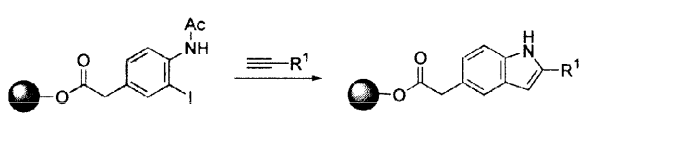
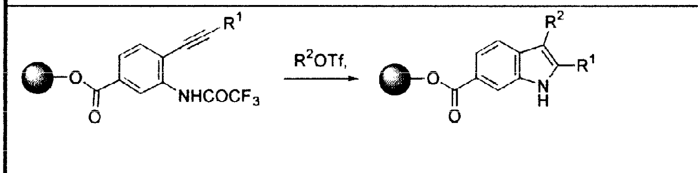
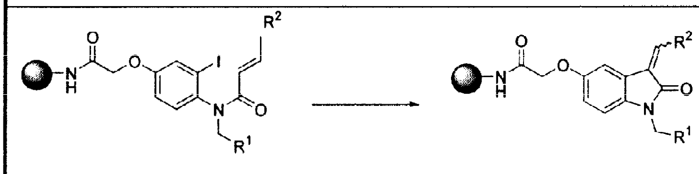
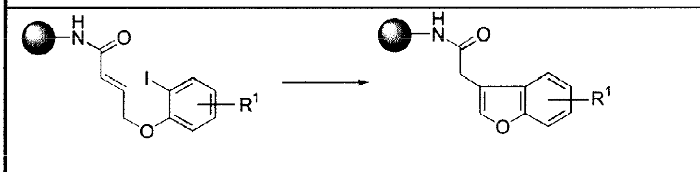
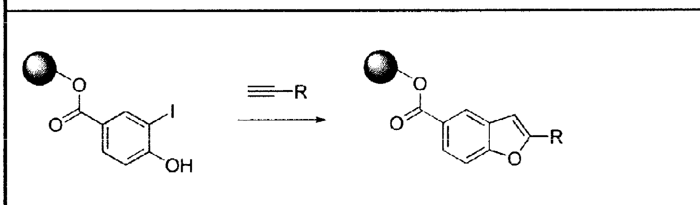
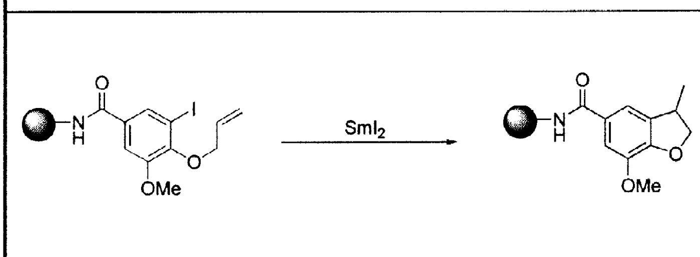
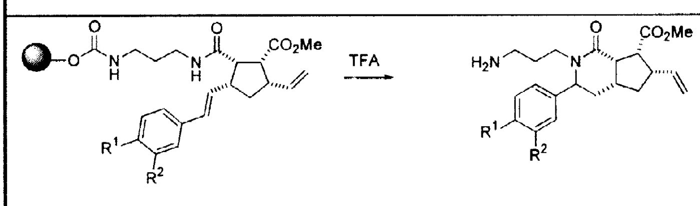
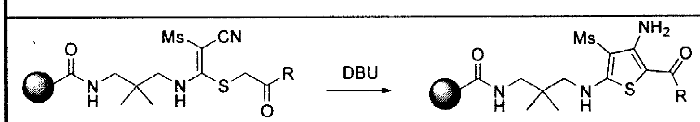
Type of reaction: Heterocycle formation

	**Quinoline** **Multiple component condensation** Rink amide resin 5 examples yield: 60-88%	140
	**Spiroindoline** **Fischer indole** Tentagel S HMB resin 16 examples yield: 83-95%	141
	**Pyrimidine** Merrifield resin monitoring by FTIR 3 examples overall yield reported	119
	**Triazine** Merrifield resin 1 example yield:100%	142
	**Quinazoline-2,4-dione** Sasrin resin monitoring by gel-phase ^{13}C NMR 9 examples yield: >90%	143
	**Dihydroquinolinone** MBHA resin 4140 examples yield: 68-100% overall	130
	**Dihydroquinazoline** Intramolecular Michael addition Wang resin 9 examples yield: 87-100% overall	43
	**Dihydroquinazolinone** Wang resin 2 examples monitoring by ^{13}C gel-phase NMR yield: 55-66%	52
	**Tetrahydro quinoxalin-2-one** Rink amide resin 5 examples overall yield reported	74

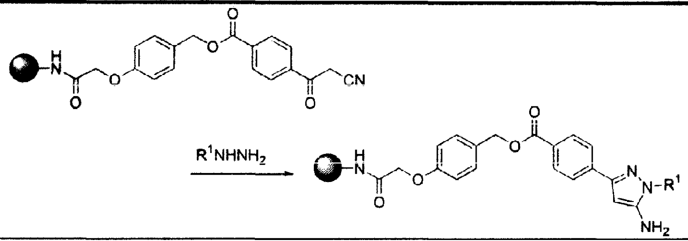
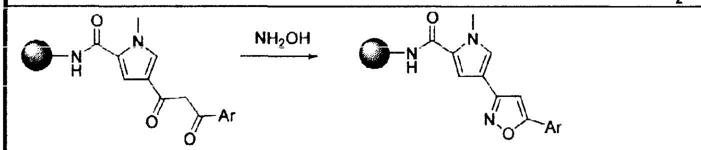
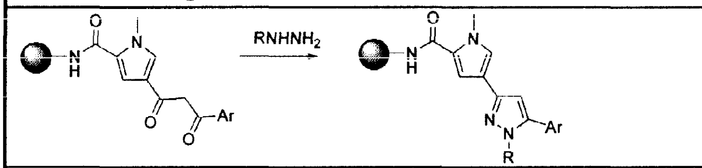
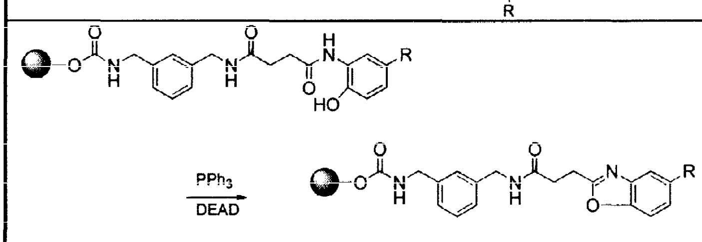
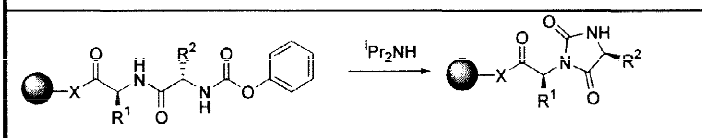
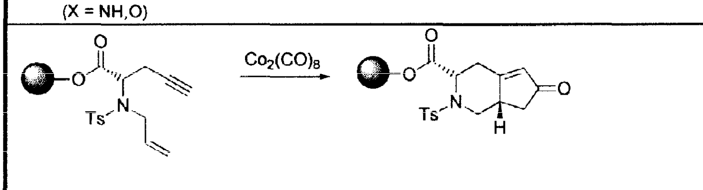
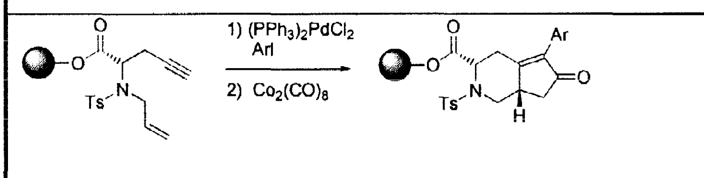
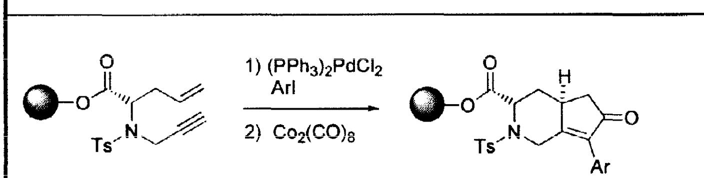
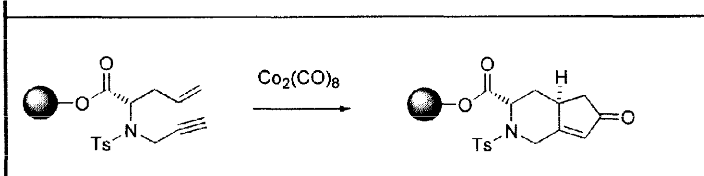
Type of reaction: Heterocycle formation

	**Benzodiazepine-2-one** Aminomethylene polystyrene resin M is Si or Ge 8 examples yield: 47-68%	71
	**Benzodiazepine-2,5-dione** Merrifield resin > 12 examples yield: > 95%	122
	**Diazepine-2,5-dione** MBHA resin 40 examples T-bag method	144
	**Diazepine-2,5-dione** TentaGel trityl resin library: 6x6x8	51
	**Pyridobenzodiazepinone** Polystyrene resin 4 examples overall yield reported	75
	**Dihydrobenzodiazepine-2-one** Methanolysis followed by intramolecular Michael addition Wang resin monitoring by FTIR 120 examples typical yield: 79%	124
	**Xanthine** Rink resin 4 examples monitoring by UV overall yield reported	145
	**Indole** **Heck reaction** Rink amide resin cat: $Pd(PPh_3)_2Cl_2$ 15 examples yield: 67-88%	26
	**Indole** **Heck reaction** Rink amide resin cat. $Pd(OAc)_2$ 14 examples yield: 38-100%	27

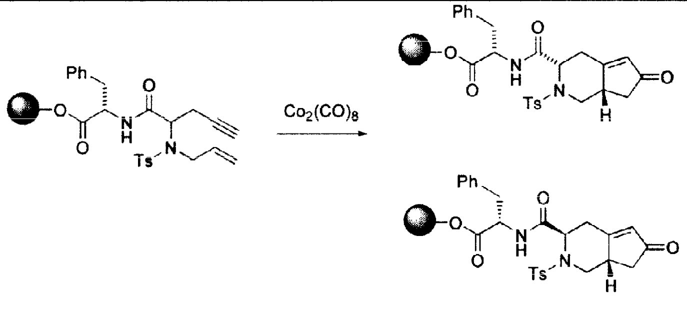
Type of reaction: Heterocycle formation

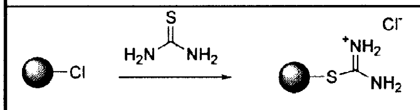
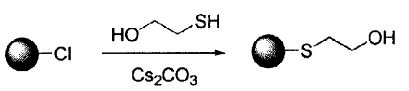
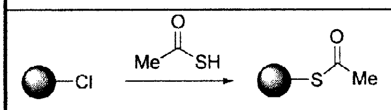
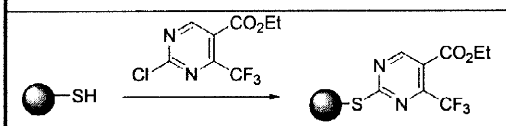
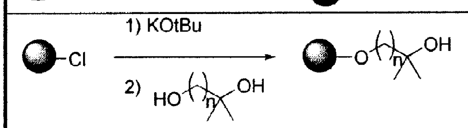
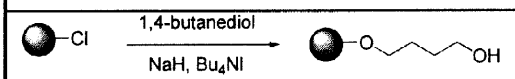
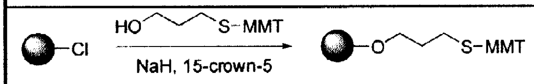
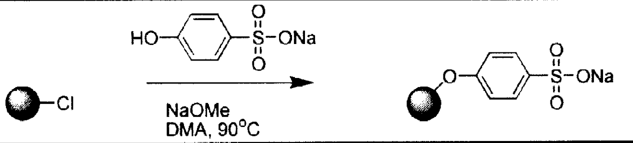
	**Indole** **Heck reaction** Tentagel S-OH resin cat: $Pd(PPh_3)_2Cl_2$ 13 examples yield: 48 - 95%	61
	**Indole** Wang resin cat: $Pd(PPh_3)_4$ R^2 is substituted vinyl 6 examples yield: 33-76 % overall	58
	**2-Oxindole** **Heck reaction** Rink resin cat: $Pd(OAc)_2$ 9 examples yield: 65-92%	60
	**Benzofuran** **Heck reaction** Rink amide resin cat: $Pd(PPh_3)_2Cl_2$ 2 examples yield: 81-83%	26
	**Benzofuran** **Heck reaction** Tentagel S-OH resin cat: $Pd(PPh_3)_2Cl_2$ 10 examples yield: 40-71% after cleavage	62
	**Benzofuran** Radical cyclisation Rink (or PEG grafted) resin monitoring by ^{13}C gel-phase NMR 10 examples yield: 11-63% overall	146
	**Cyclopentapiperidi-none** Cyclisation and cleavage from resin Wang resin 5 examples yield: 53-85%	147
	**Thiophene** Wang resin 9 examples yield: 24-85% overall	57

Type of reaction: Heterocycle formation

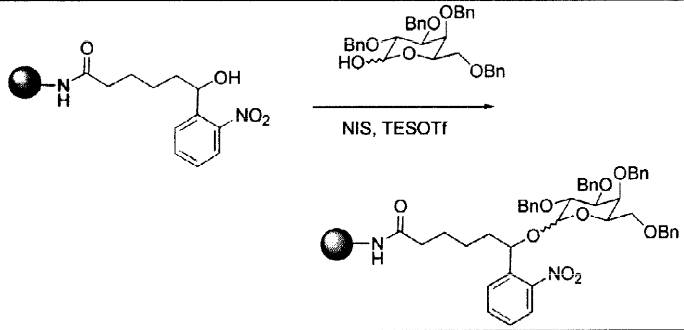
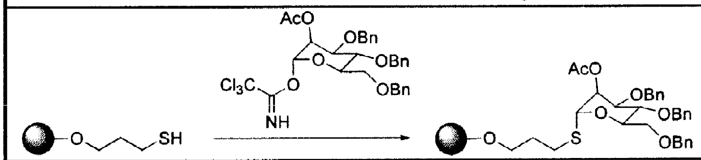
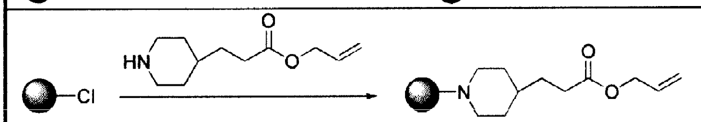
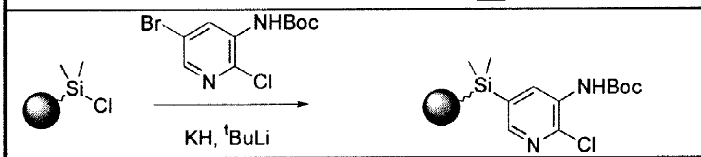
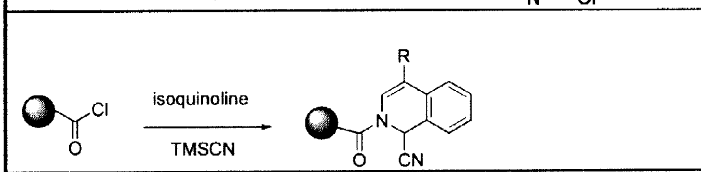
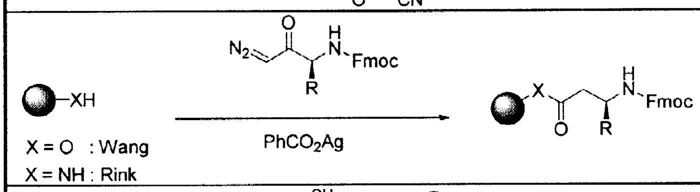
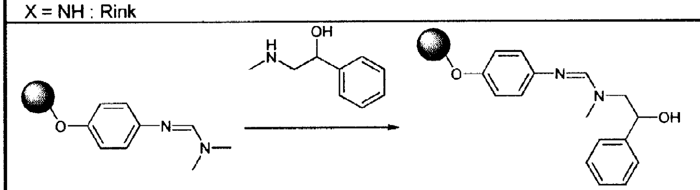
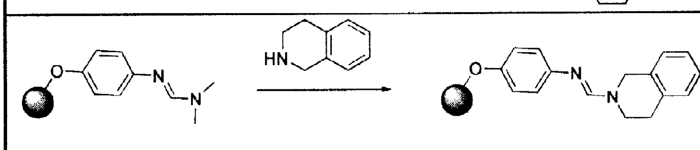
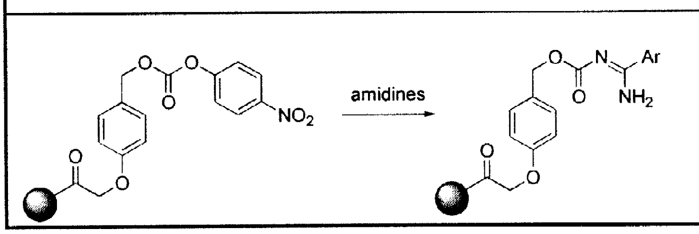
	**Pyrazole** **TentaGel S NH_2 resin** **4 examples** **yield: not reported**	45
	**Isoxazole** Rink amide resin 140 examples split/pool 2 regioisomers formed	128
	**Pyrazole** Rink amide resin 5740 examples split/pool 2 regioisomers formed	128
	**Benzoxazole** **Mitsunobu** Wang resin 7 examples yield: 79-99%	50
 (X = NH,O)	**Hydantoin** TentaGel S AM resin monitoring by UV 6 examples yield: 89-95%	30
	**Tetrahydrocyclopenta -pyridine** **Pauson-Khand** Wang resin 1 example yield: 84% overall	28
	**Tetrahydrocyclopenta -pyridine** **Pauson-Khand** Wang resin 4 examples yield: 38-86% overall	28
	**Tetrahydrocyclopenta -pyridine** **Pauson-Khand** Wang resin 4 examples yield: 46-88% overall	28
	**Tetrahydrocyclopenta -pyridine** **Pauson-Khand** Wang resin 1 example yield: 74% overall	28

Type of reaction: Heterocycle formation

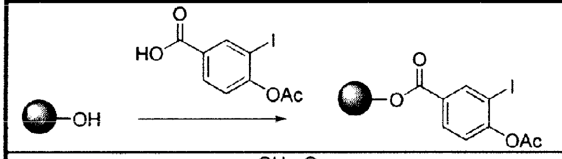
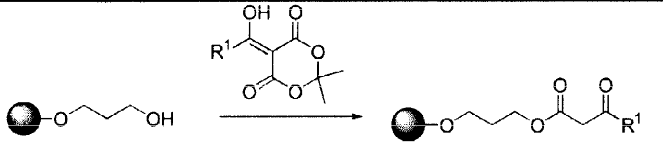
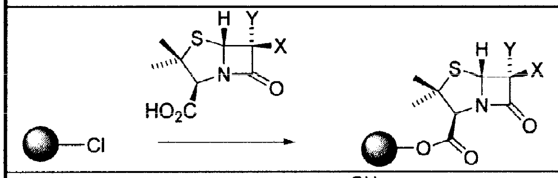
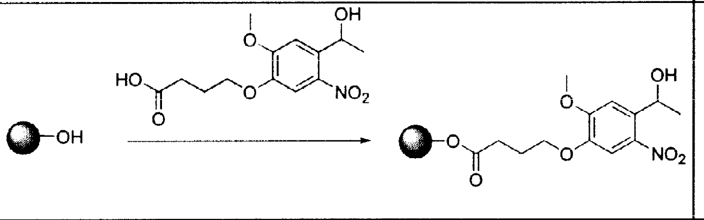
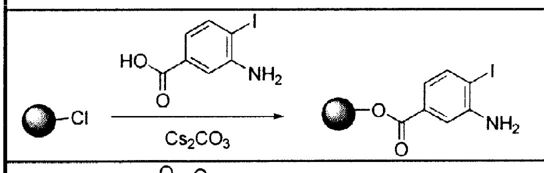
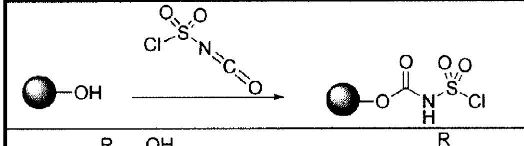
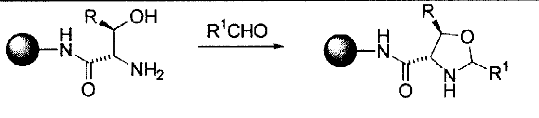
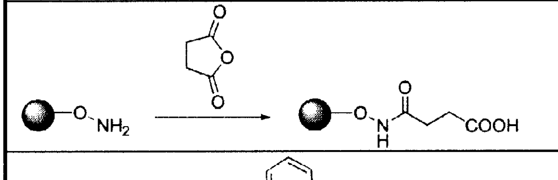
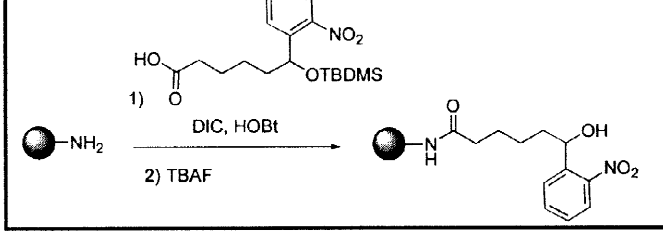
	**Tetrahydrocyclopenta –pyridine** **Pauson–Khand** Wang resin 1 example yield: 68% overall	28

Type of reaction: Immobilisation onto resin	Comment	Ref
	**S-alkylation** Merrifield resin 1 example overall yield reported	119
	**S-alkylation** Merrifield resin monitoring by FTIR, Cl analysis 1 example yield: 90-99%	104
	**S-alkylation** (Chloromethylphenyl) pentyl polystyrene (CMPP) resin 1 example overall yield reported	78
	**S-arylation** TentaGel SH 1 example overall yield reported	120
	**O-alkylation** Merrifield resin monitoring by FTIR 4 examples overall yield reported	39
	**O-alkylation** Merrifield resin 1 example overall yield reported	85
 MMT = monomethoxytrityl	**O-alkylation** Merrifield resin 1 example overall yield reported	112
	**O-alkylation** Merrifield resin 1 example overall yield reported	46

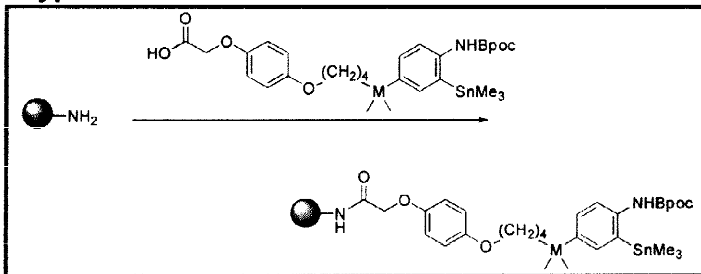
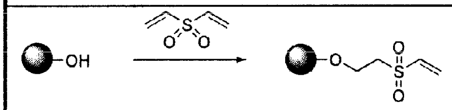
Type of reaction: Immobilisation onto resin

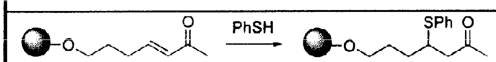
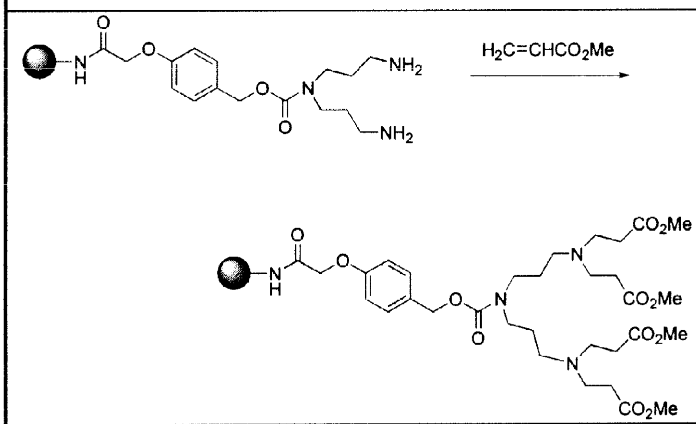
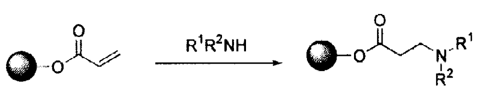
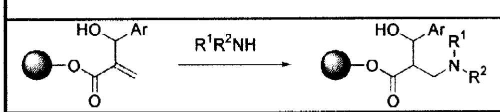
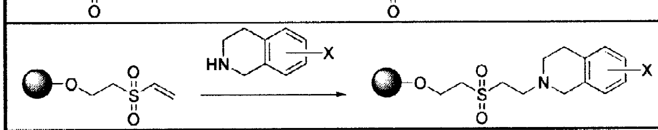
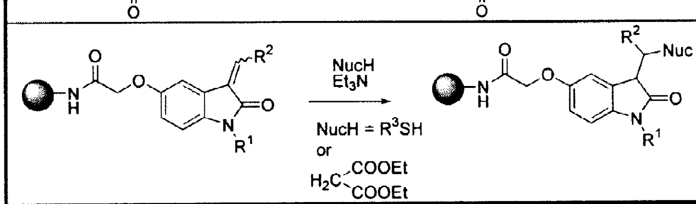
	**Glycosylation** amine resin overall yield reported	110
	**Glycosylation** Merrifield resin overall yield reported	112
	**N-alkylation** 2-chlorotrityl resin 1 example overall yield reported	134b
	**Si-arylation** Polystyrene resin 1 example overall yield reported	75
	**Reissert condensation** PS carboxylic acid resin monitoring by FTIR 3 examples overall yield reported	88
	**Arndt–Eistert** Wang or Rink resin 14 examples yield: 60-80%	148
	**Transamination** Merrifield resin monitoring by gel-phase ^{13}C-NMR, FTIR 1 example overall yield reported	99
	**Transamination** Merrifield resin 3 examples yield: 76-84%	100
	**Amidine** aminomethyl polystyrene monitoring by HPLC, nitrophenol released 5 examples yield: 41-71% (2 steps)	118

Type of reaction: Immobilisation onto resin

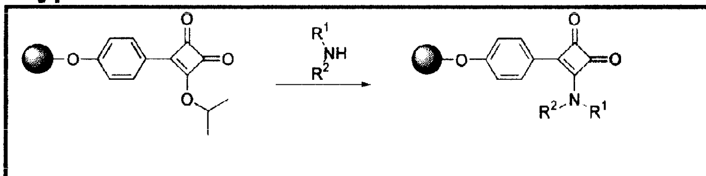
	**Esterification Mitsunobu** Tentagel S-OH 1 example overall yield reported	62
	**Esterification Decarboxylation** Wang resin monitoring by FTIR 5 examples overall yield reported	82
	**Esterification** Merrifield resin 3 examples overall yield reported	114
	**Esterification Photocleavable linker** Wang resin improved synthesis 1 example overall yield reported	149
	**Esterification** Wang resin 1 example overall yield reported	58
	**Sulfonylcarbamation** Wang resin 1 example overall yield reported	44
	**Condensation** Synphase crown (Sasrin linker) "resin-capture" of aldehydes 3 examples overall yield reported	105
	**Acylation** Trityl polystyrene monitoring by FTIR 1 example overall yield reported	33
	**Acylation Photocleavable linker** amine resin 1 example overall yield reported	110

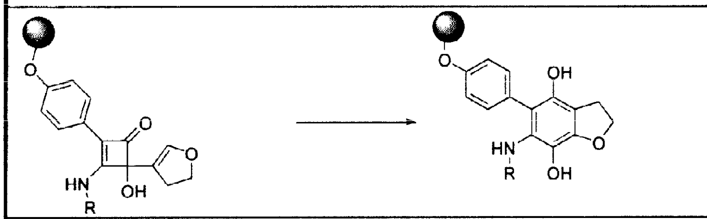
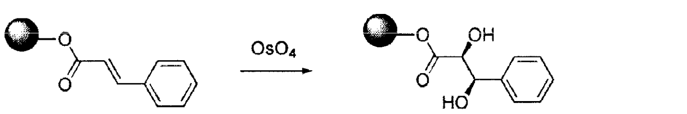
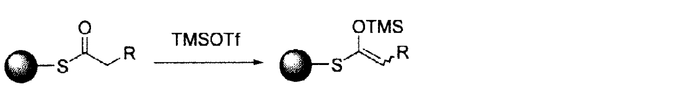
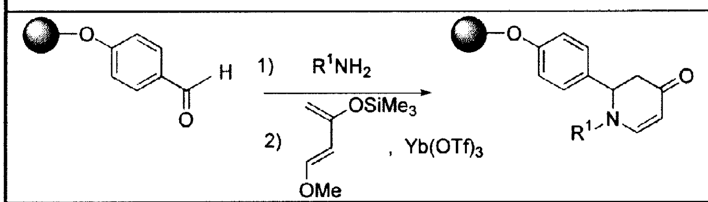
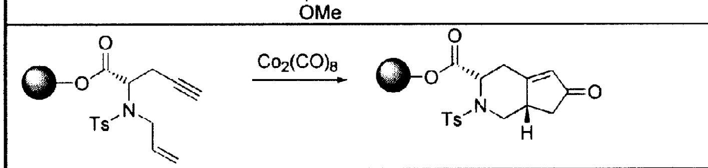
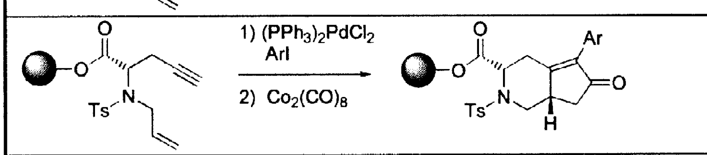
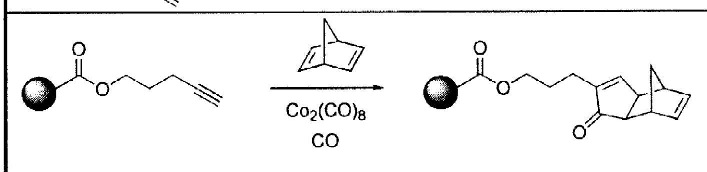
Type of reaction: Immobilisation onto resin

	**Acylation** **Traceless linker** **aminomethylene resin** **yield: quantitative**	71
	**Michael addition** Hydroxymethylene resin 1 example overall yield reported	103

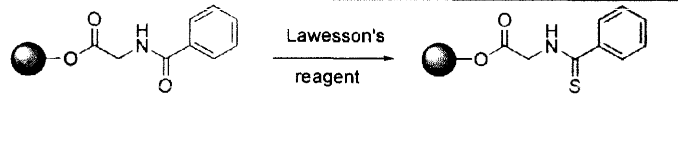
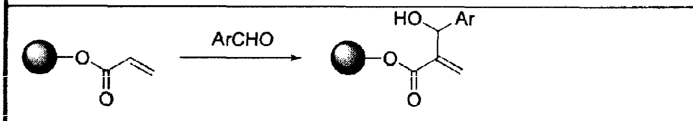
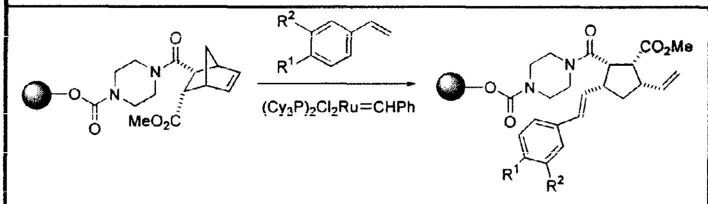
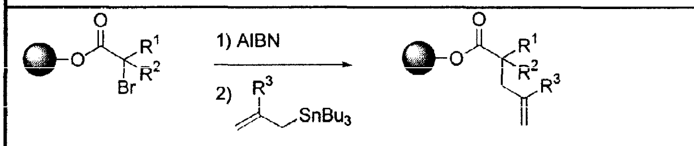
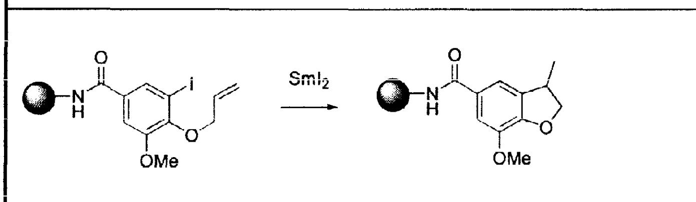
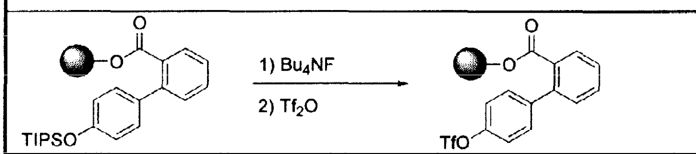
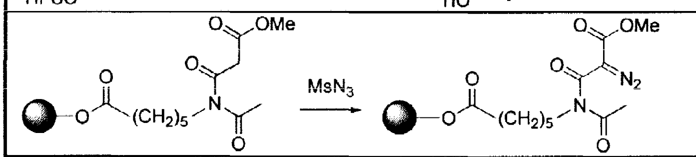
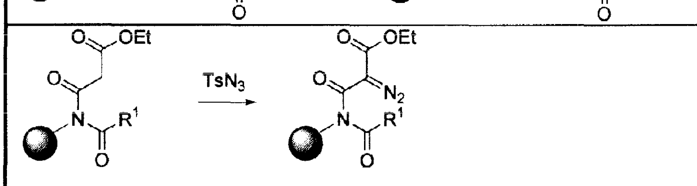
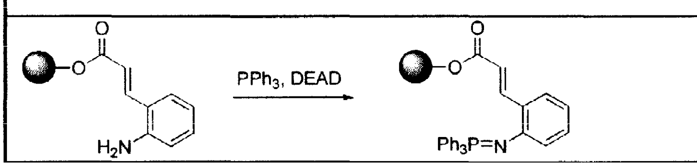
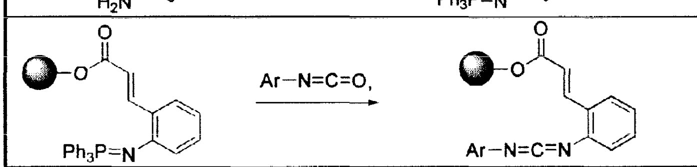
Type of reaction: Michael addition	Comment	Ref
	Trityl resin 3 examples	150
	TentaGel monitoring by ninhydrin, ES-MS 4 examples yield: 94% average high-loading	151
	PS (REM) resin several examples monitoring by FTIR and ^{13}C gel-phase NMR overall yield reported	102
	Hydroxyethylene resin 18 examples overall yield reported	121
	Hydroxymethylene resin 3 examples overall yield reported	103
	Rink resin 3 examples yield: 80-90%	60

Type of reaction: Michael addition

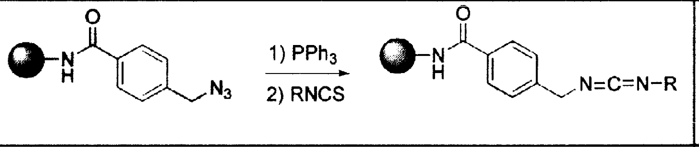
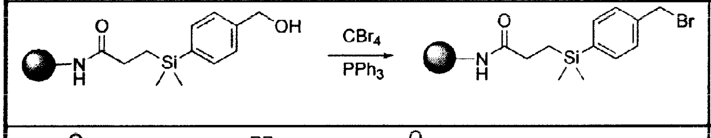
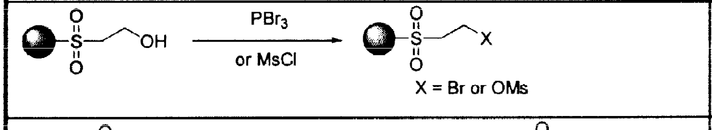
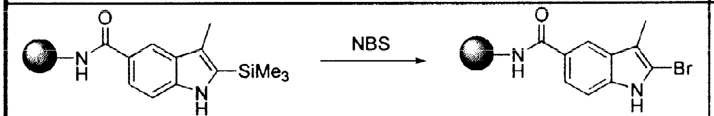
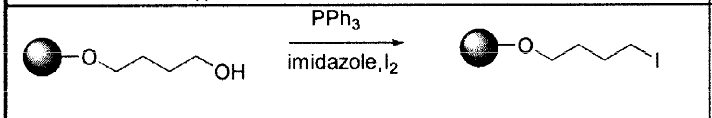
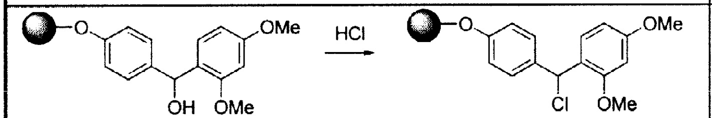
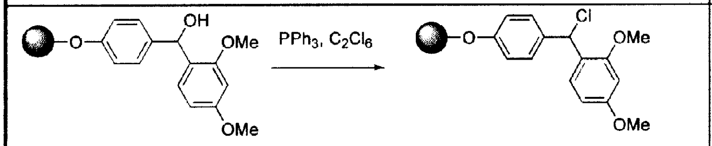
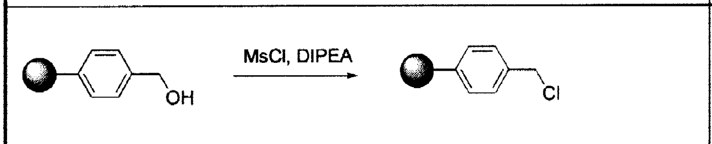
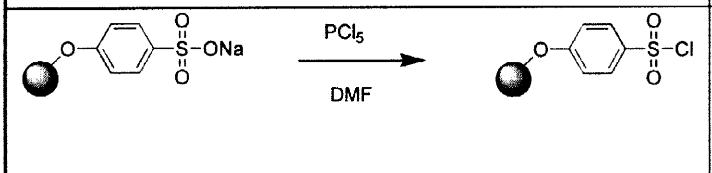
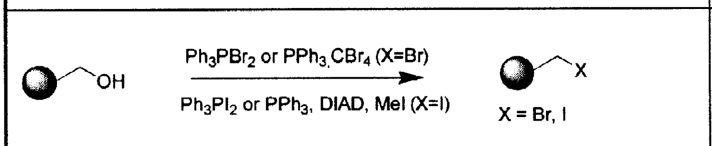
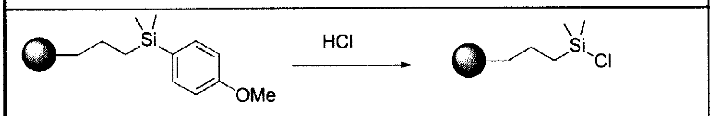
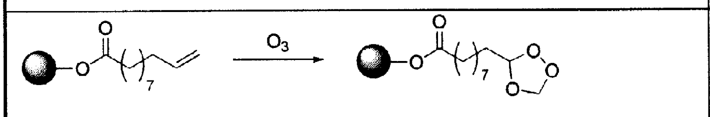
	**Michael addition followed by elimination** Wang resin 6 examples overall yield reported	70

Type of reaction: Miscellaneous	Comment	Ref
	**Rearrangement** Multiple Core Structure Library (MCSL) Wang resin 25 examples overall yield reported	70
	**Dihydroxylation** Asymmetric Merrifield, Wang and TentaGel resin reaction optimisation cat: $(DHQD)_2PHAL$ 10 examples yield: 25-85% ee: 88-99%	123
	**Enolisation** (Chloromethylphenyl) pentyl polystyrene (CMPP) resin 2 examples overall yield reported	78
	**Tandem Mannich–Michael reaction** Wang resin 8 examples yield: 60-90%	153
	**Pauson–Khand** Wang resin 1 example yield: 84% overall	28
	**Pauson–Khand** Wang resin 4 examples yield: 38-86% overall	28
	**Pauson–Khand** PS carboxylic acid or trityl resin monitoring by FTIR 8 examples yield: 0-99%	154

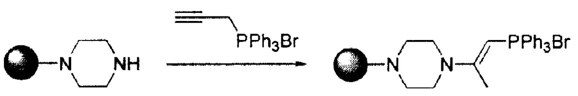
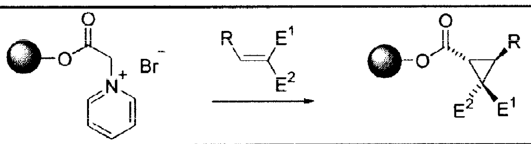
Type of reaction: Miscellaneous

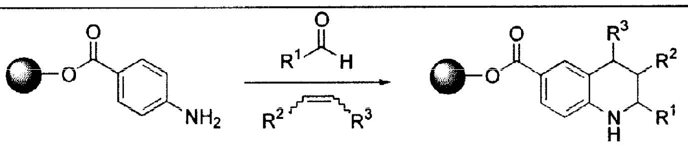
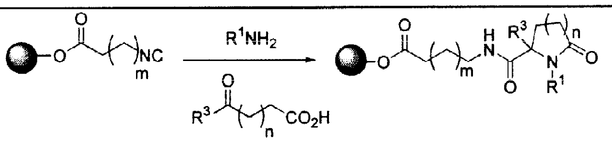
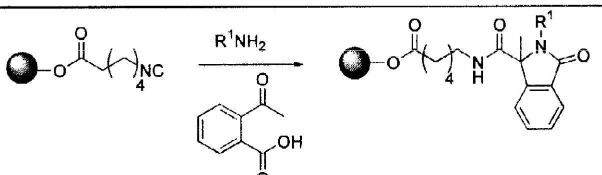
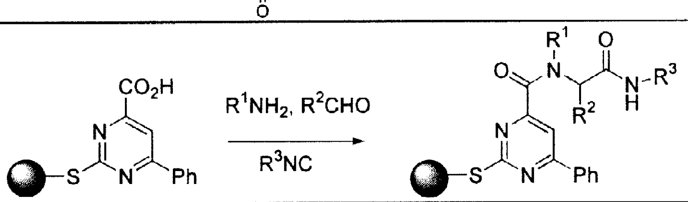
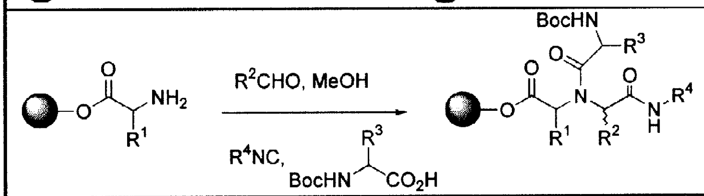
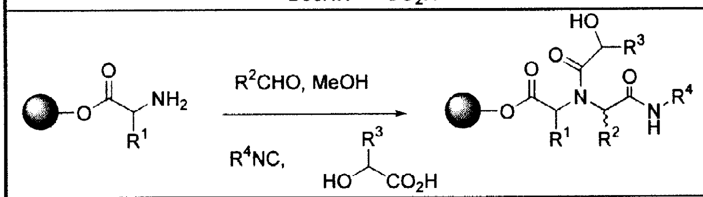
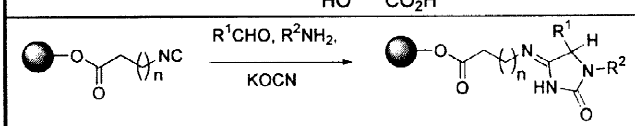
	**Oxygen-sulfur exchange** Polystyrene resin monitoring by FTIR 1 example yield: not reported	155
	**Baylis–Hillman** Hydroxymethylene resin 6 examples overall yield reported	121
	**Ring opening, cross metathesis** Wang resin monitoring by gel phase ^{1}H NMR 9 examples yield: 60-85%	147
	**Radical C-C bond formation** Wang resin 10 examples yield: 58-95%	156
	**Radical cyclisation** Rink (or PEG grafted) resin monitoring by ^{13}C gel-phase NMR 10 examples yield: 11-63% overall	146
	**O-Triflation** Wang resin 2 examples overall yield reported	72
	**Diazo transfer** Wang resin 6 examples overall yield reported	48
	**Diazo transfer** TentaGel NH_2 resin monitoring by ^{13}C gel phase NMR 3 examples overall yield reported	90
	**Iminophosphorane formation** Wang resin several examples yield: >95%	43
	**Aza-Wittig** Wang resin 1 example overall yield reported	43

Type of reaction: Miscellaneous

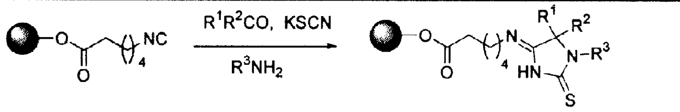
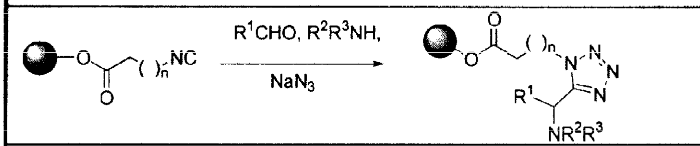
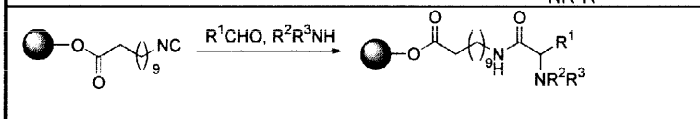
	**Aza-Wittig** Rink resin 2 examples *via* iminophosphorane yield: >95%	42
	**Bromination** BHA resin 1 example overall yield reported	89
	**Bromination** Merrifield resin 1 example overall yield reported	104
	**Bromination** Rink amide resin 2 examples yield:88-91%	27
	**Iodonation** Merrifield 1 example overall yield reported	85
	**Chlorination** Rink acid resin 1 example yield: 70 %	117
	**Chlorination** Rink acid resin 1 example overall yield reported	66
	**Chlorination** Wang, Sasrin or TentaGel resin 4 examples yield: 100%	157
	**Chlorination** Merrifield resin 1 example elemental analysis for Cl overall yield reported	46
	**Halogenation** Wang and TentaGel SAC resin 4 examples overall yield reported	158
	**Si-Cl formation** Polystyrene resin 1 example traceless linker	75
	**Ozonolysis** Merrifield resin 1 example yield: not reported	159

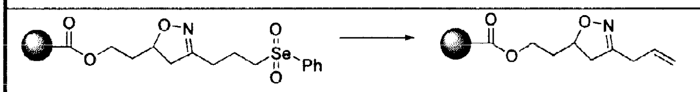
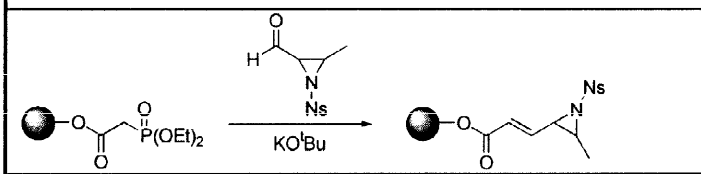
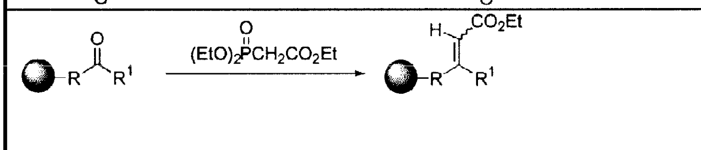
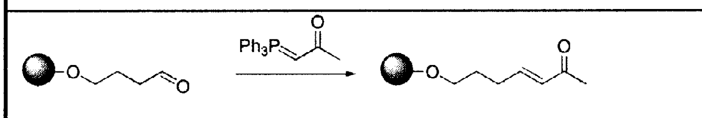
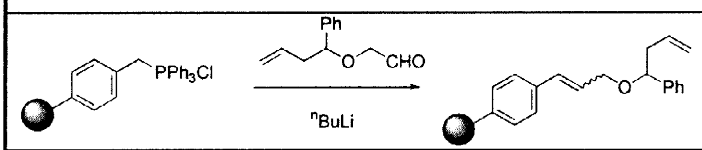
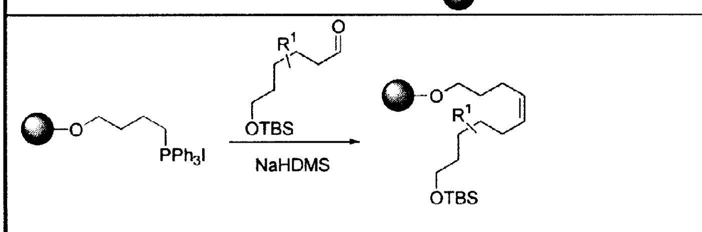
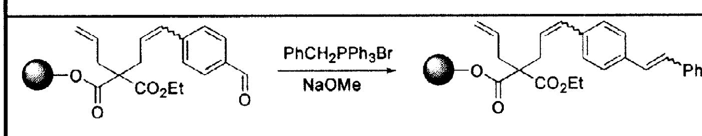
Type of reaction: Miscellaneous

	**β-Enamino phosphonium salt** Merrifield resin monitoring by elemental analysis 1 example yield: 100%	108
	**Cyclopropanation** Wang resin 6 examples yield: 65-68%	160

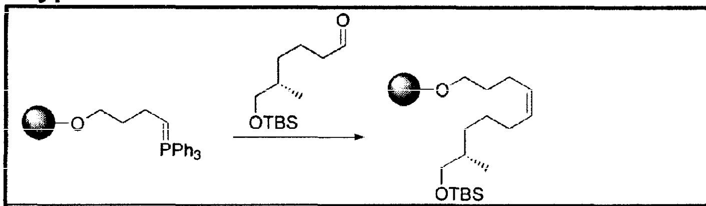
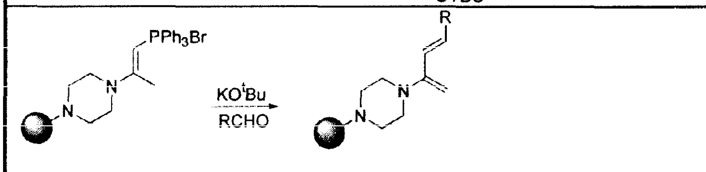
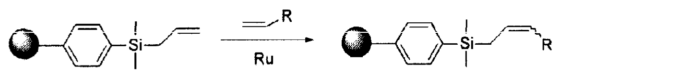
Type of reaction: Multiple Component Condensation	Comment	Ref
	**Grieco** **3CC** Wang resin 40 examples yield: 53-92%	161
	**Ugi** **4CC** Wang resin several examples yield: 47-98%	162, 163
	**Ugi** **4CC** Wang resin 2 examples yield: 35-38% overall	162
	**Ugi** **4CC** Merrifield resin 5 examples overall yield reported	119
	**Ugi** **4CC** Tentagel S-OH resin 12 examples yield: 13-98% overall	80
	**Ugi** **4CC** Tentagel S-OH resin 3 examples yield: 16-56% overall	80
	**4CC** Wang resin 10 examples yield: 36-81% overall	163

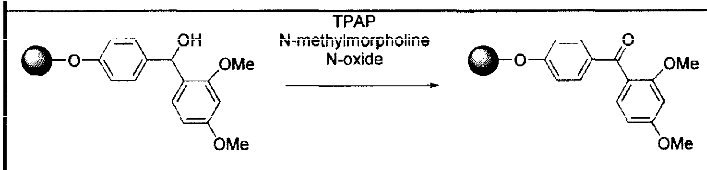
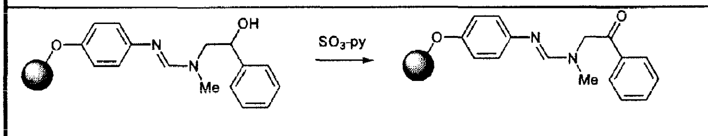
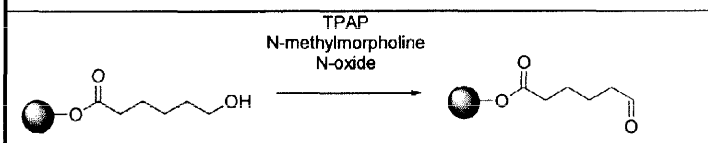
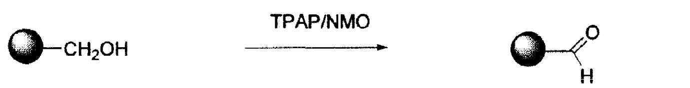
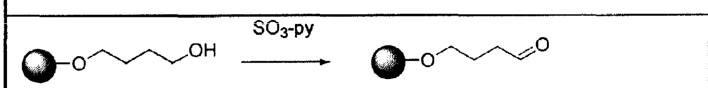
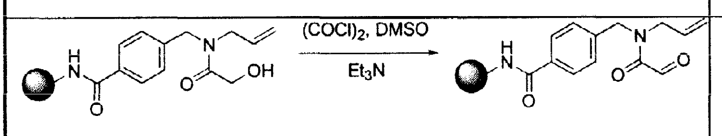
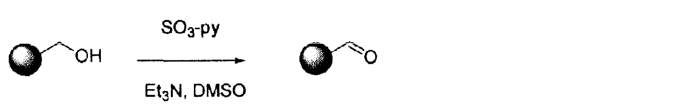
Type of reaction: Multiple Component Condensation

	**4CC** **Wang resin** **2 examples** **yield: 5-11% overall**	163
	**4CC** Wang resin 4 examples yield: 33-52% overall	163
	**4CC** Wang resin 2 examples yield: 52-57% overall	163

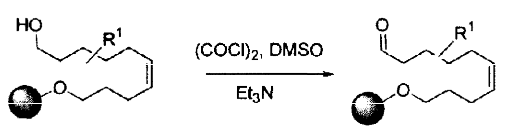
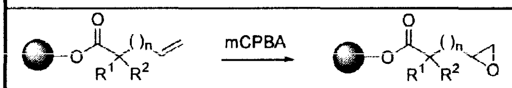
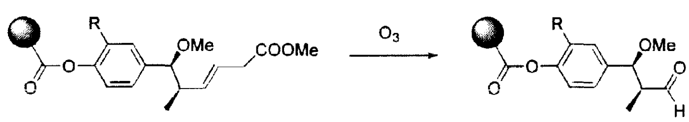
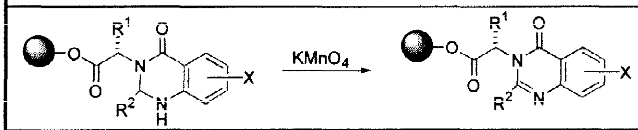
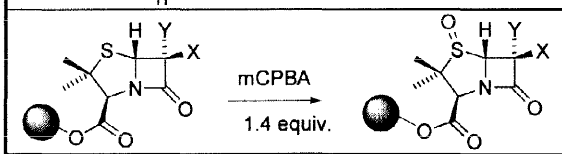
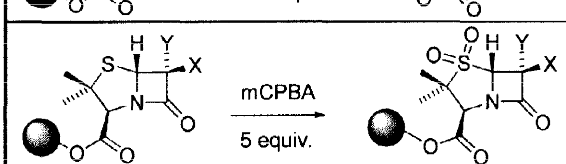
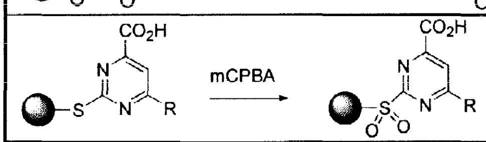
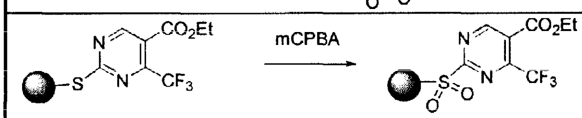
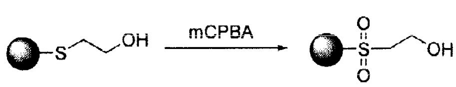
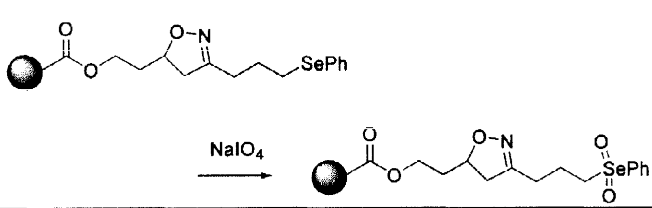
Type of reaction: Olefin formation	Comment	Ref
	**Elimination** PS carboxylic acid resin library of 84 compounds	131
	**Horner–Emmons** Wang resin 5 examples overall yield reported	139
	**Horner–Emmons** TentaGel PAL resin 11 examples 1:1 E:Z isomers yield: not reported	164
	**Wittig** Trityl resin 3 examples yield: not reported	150
	**Wittig** Polystyrene resin 1 example overall yield reported	84
	**Wittig** Merrifield resin monitoring by ozonolysis and recovered aldehyde radiofrequency tags 3 examples yield: 75 %	85
	**Wittig** Merrifield 1 example overall yield reported	86

Type of reaction: Olefin formation

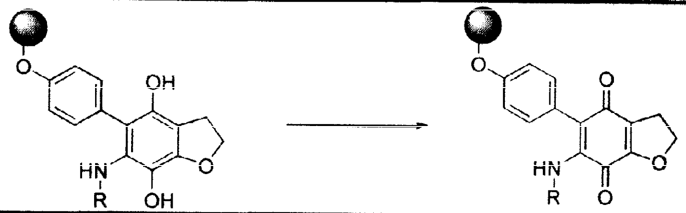
	**Wittig** Merrifield resin 1 example yield: >70% part of total synthesis	56
	**Wittig** monitoring by elemental analysis Merrifield resin 1 example yield: 100%	108
	**Metathesis** Polystyrene resin 8 examples overall yield reported	92

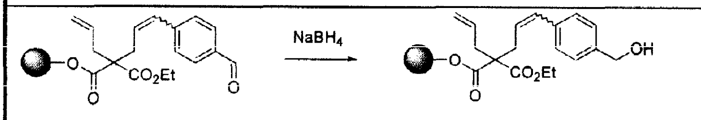
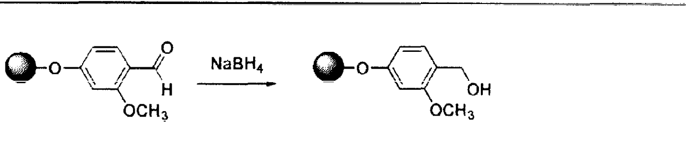
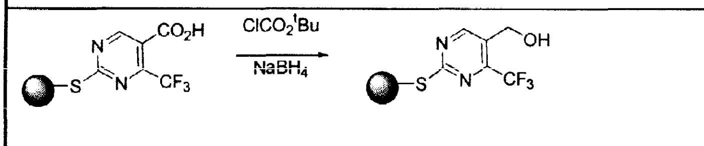
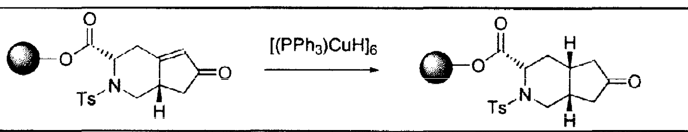
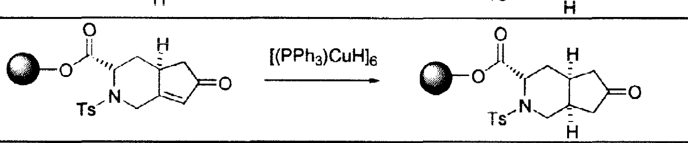
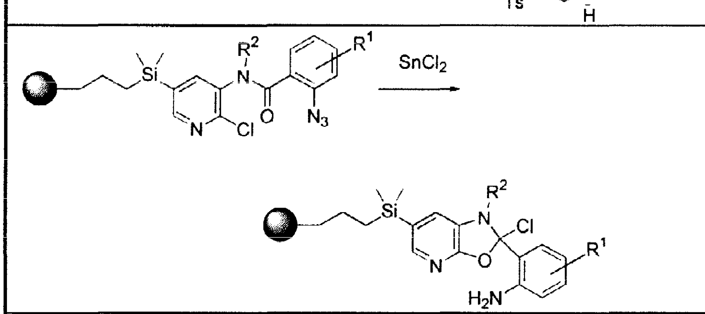
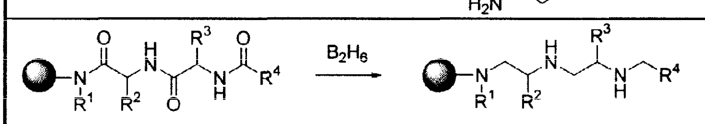
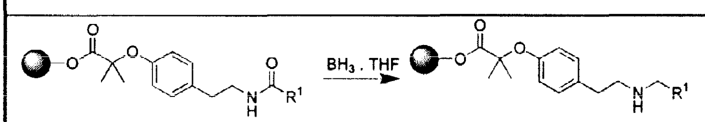
Type of reaction: Oxidation	Comment	Ref
	**Alcohol to ketone** Wang resin monitoring by FTIR 1 example yield: ~97%	134
	**Alcohol to ketone** Merrifield resin monitoring by FTIR 1 example overall yield reported	99
	**Alcohol to aldehyde** Wang resin monitoring by FTIR 1 example yield: not reported	134
	**Alcohol to aldehyde** Wang resin or TentaGel S PHB quantitative UV monitoring by decrease of dansylhydrazine	165a
	**Alcohol to aldehyde** Trityl resin 1 example	150
	**Alcohol to aldehyde** Rink resin 1 example overall yield reported	132
	**Alcohol to aldehyde** Sasrin resin monitoring by NMR AMEBA resin synthesis 1 example overall yield reported	125

Type of reaction: Oxidation

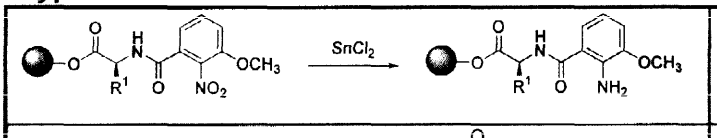
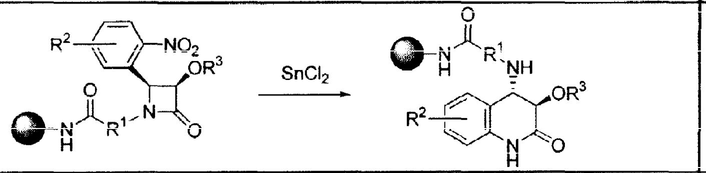
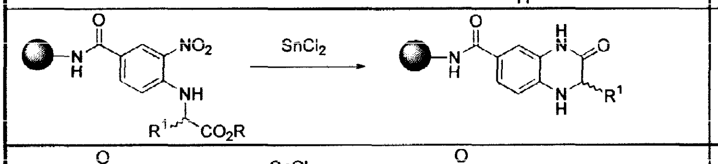
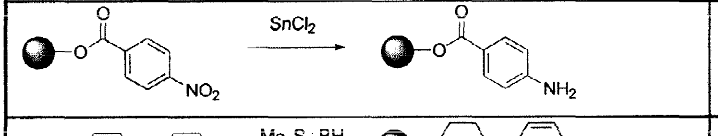
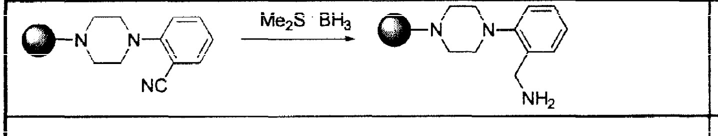
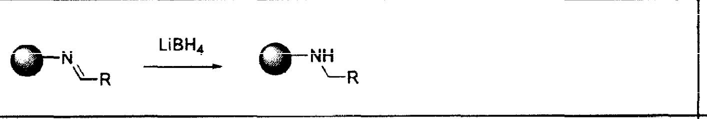
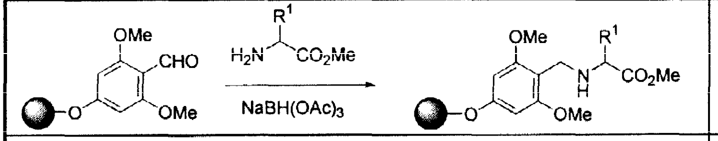
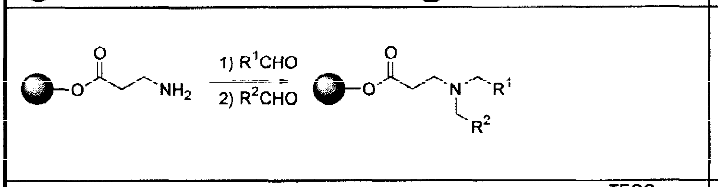
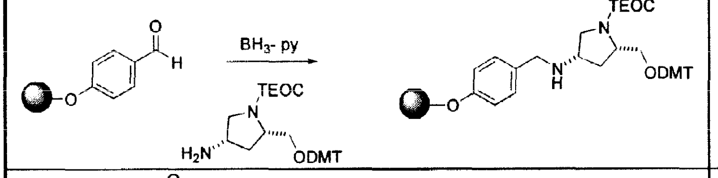
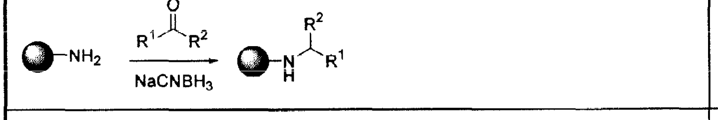
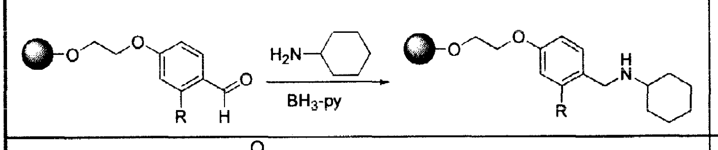
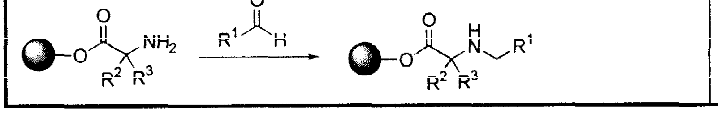
	**Alcohol to aldehyde** Merrifield resin monitoring by FTIR and TLC of products after ozonolysis radiofrequency tags 3 examples yield: > 95% (2 steps)	56, 85
	**Epoxidation** Merrifield resin 4 examples	81
	**Ozonolysis** Carboxylated polystyrene resin 4 examples overall yield reported	96
	**Aminal to amidine** Wang resin 2 examples yield: 80-98%	52
	**Sulfide to sulfoxide** Wang and Merrifield resin 6 examples overall yield reported	114
	**Sulfide to sulfone** Merrifield resin 3 examples overall yield reported	114
	**Sulfide to sulfone** Merrifield resin 3 examples overall yield reported	119
	**Sulfide to sulfone** Tentagel SH 1 example overall yield reported	120
	**Sulfide to sulfone** Merrifield resin monitoring by FTIR 1 example overall yield reported	104
	**Selenide to selenoxide** PS carboxylic acid resin library of 84 compounds	131

Type of reaction: Oxidation

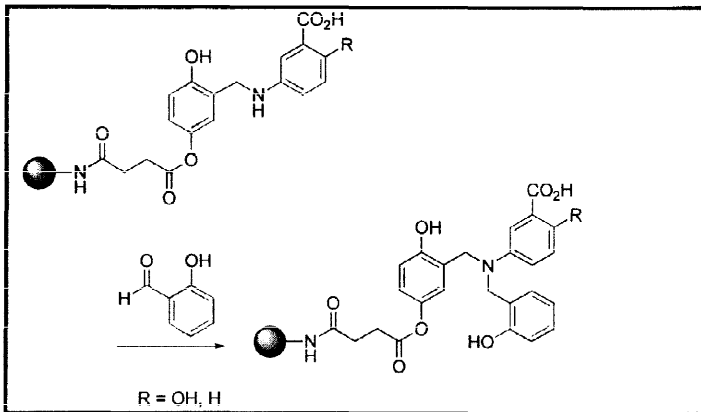
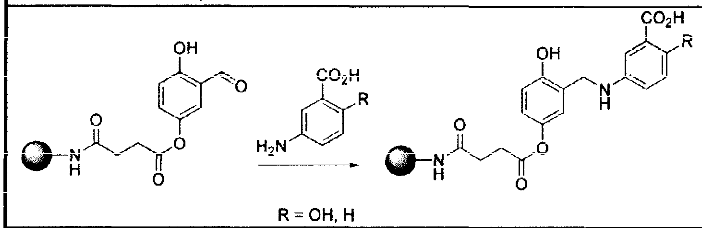
	**1,4-Phenol to 1,4-quinone** Wang resin 25 examples overall yield reported	70

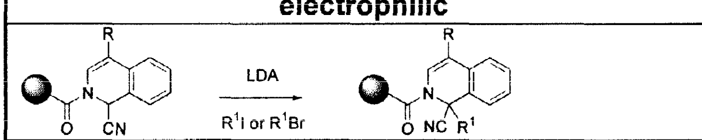
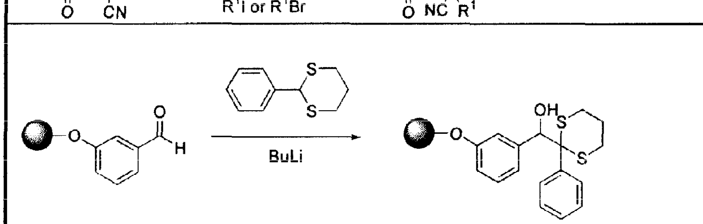
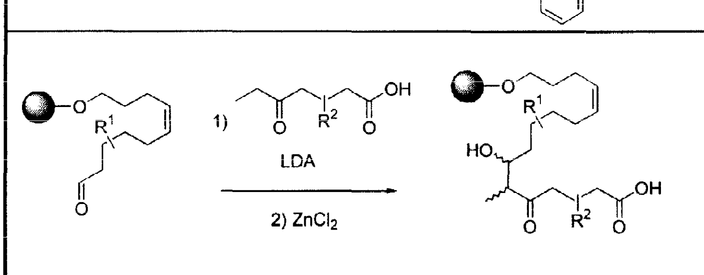
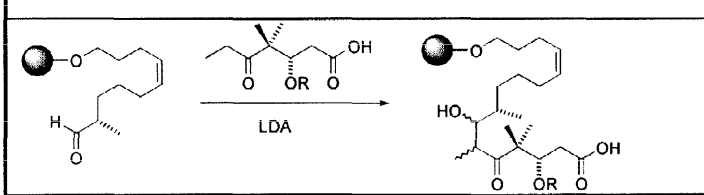
Type of reaction: Reduction	Comment	Ref
	**Aldehyde to alcohol** Merrifield 1 example overall yield reported	86
	**Aldehyde to alcohol** Merrifield resin 1 example monitoring by NMR synthesis of Sasrin overall yield reported	165b
	**Carboxylic acid to alcohol** Tentagel SH 1 example overall yield reported	120
	**Alkene to alkane** Wang resin 1 example yield: 65% overall	28
	**Alkene to alkane** Wang resin 1 example yield: 85% overall	28
	**Azide to amine** Polystyrene resin 4 examples overall yield reported	75
	**Amide to amine** MBHA resin library of 473,600 compounds	34
	**Amide to amine** Sasrin resin 4 examples yield: 54-96%	166

Type of reaction: Reduction

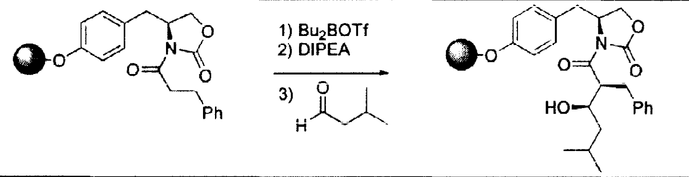
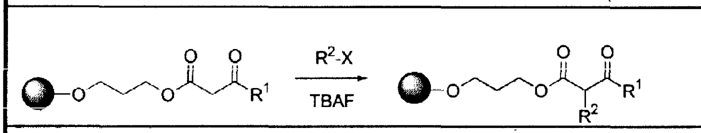
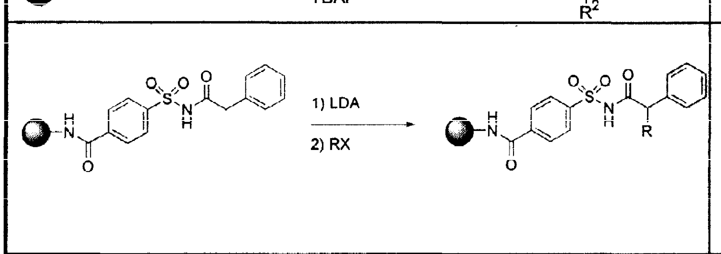
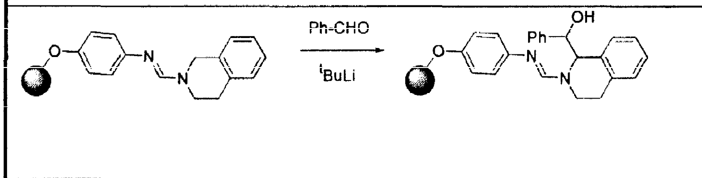
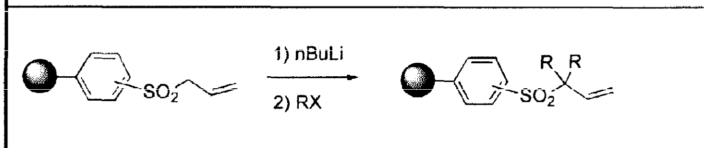
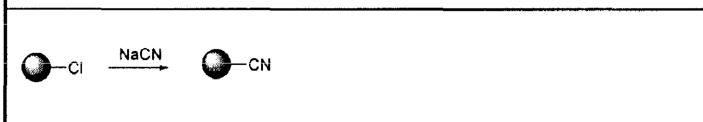
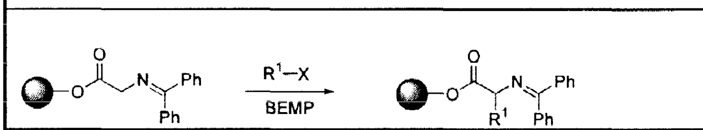
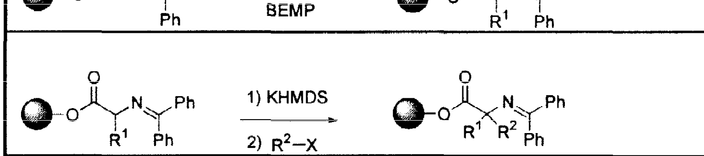
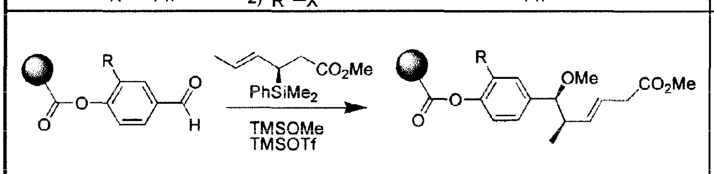
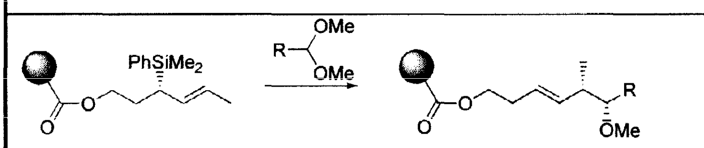
	**Nitro to amine** Wang resin 1 example overall yield reported	52
	**Nitro to amine** MBHA resin 4140 examples yield: 68-100% overall	130
	**Nitro to amine** Rink amide resin 5 examples overall yield reported	74
	**Nitro to amine** Wang resin 1 example yield: 75-86%	161
	**Nitrile to amine** Merrifield resin 1 example yield: >80%	98
	**Imine to amine** Rink resin 2 examples yield: 74-100% overall	138
	**Reductive Amination** Merrifield resin 10 examples overall yield reported	122
	**Reductive amination** PS (REM) resin 1 example monitoring by FTIR and ^{13}C gel-phase NMR yield: 38% overall	102
	**Reductive amination** ArgoGel-OH resin 1 example monitoring by ^{13}C gel-phase NMR overall yield reported	31
	**Reductive amination** Rink amide resin 8 examples yield: 50-99	167
	**Reductive amination** ArgoGel-OH ArgoGel MB-CHO resin 2 examples overall yield reported	168
	**Reductive amination** Wang resin 18 examples overall yield reported	83

Type of reaction: Reduction

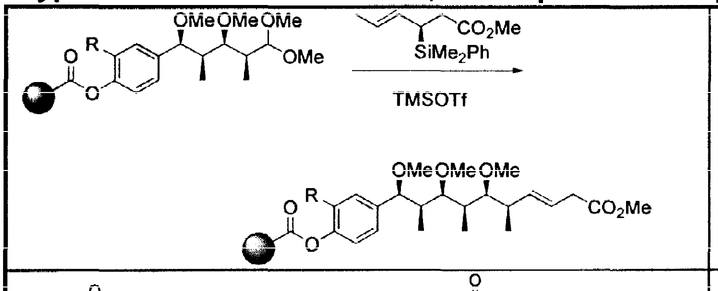
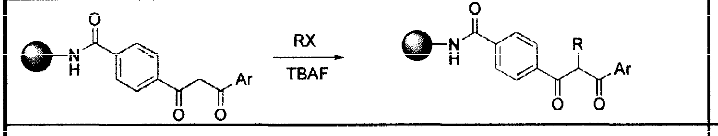
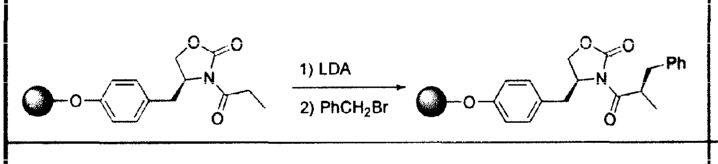
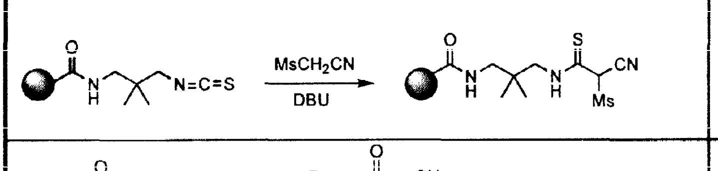
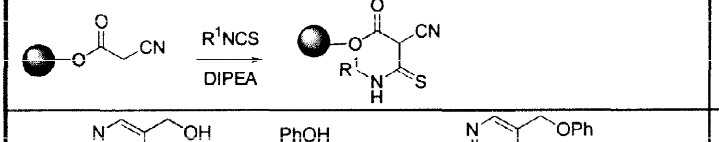
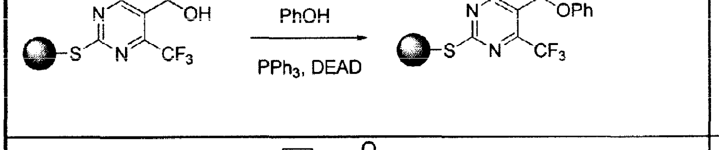
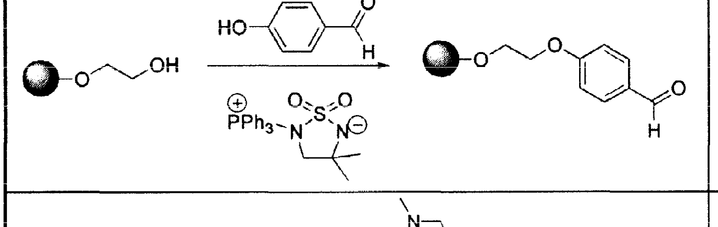
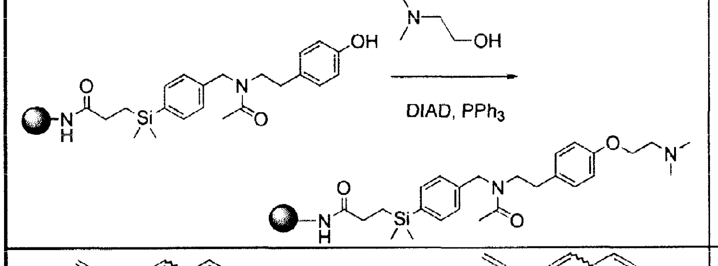
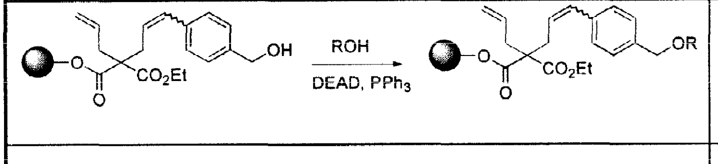
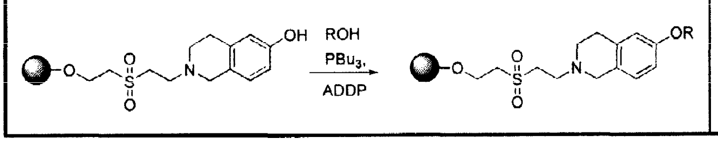
	**Reductive amination** Aminomethylene resin 2 examples yield: 73-77%	169
	**Reductive amination** Aminomethylene resin 2 examples overall yield reported	169

Type of reaction: Substitution, nucleophilic/ electrophilic	Comment	Ref
	**C-alkylation** PS carboxylic acid resin 8 examples yield: 95-100%	88
	**C-alkylation** **Aldol** Merrifield resin monitoring by elemental analysis of sulphur 1 example yield: 91%	37
	**C-alkylation** **Aldol** Merrifield resin monitoring recovered aldehyde after ozonolysis radiofrequency tags 9 examples yield: > 90%	85
	**C-alkylation** **Aldol** Merrifield resin 1 example yield: 90% part of total synthesis	56

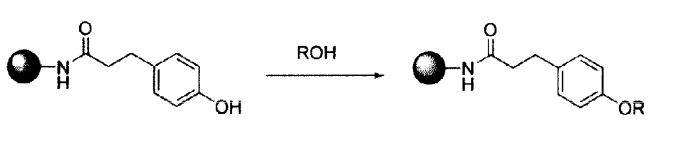
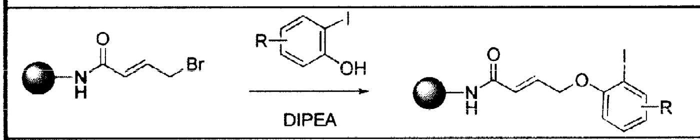
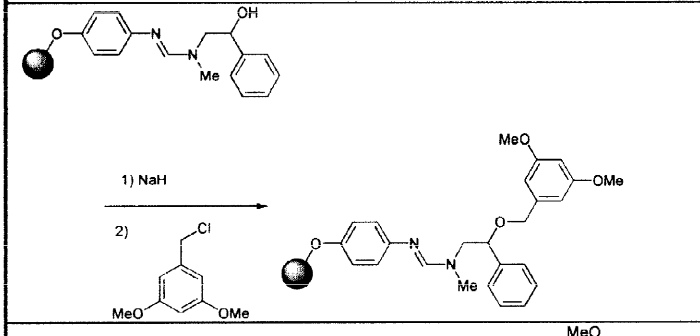
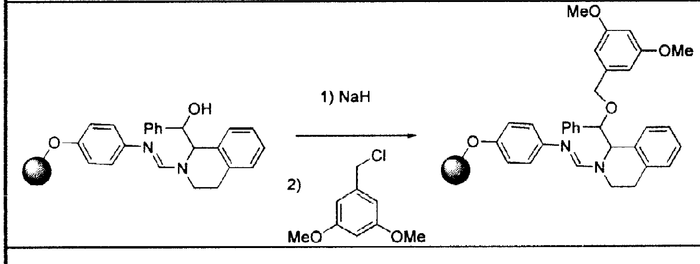
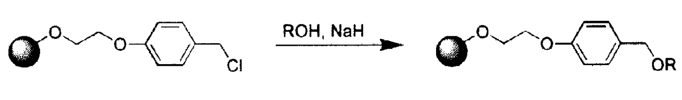
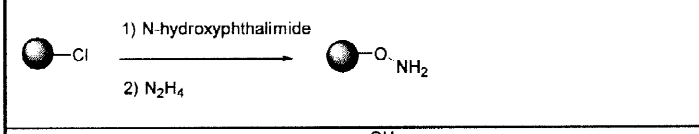
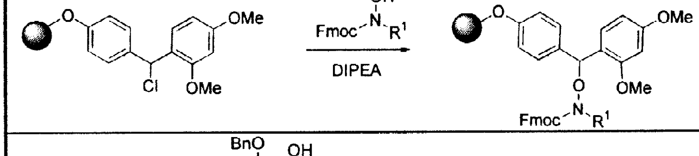
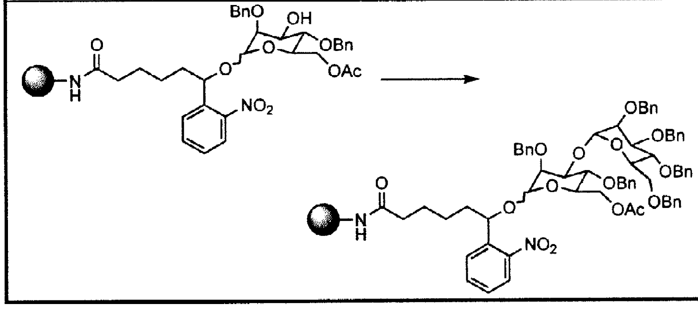
Type of reaction: Substitution, nucleophilic/electrophilic

	**C-alkylation** **Aldol** Chiral linker Wang resin 1 example yield: not reported	49
	**C-alkylation** Wang resin 7 examples overall yield reported	82
	**C-alkylation** Aminomethylene PS safety catch or Argo-X203 safety catch resin 3 examples yield (Argo-X203): 63-71% yield (PS): 18-20%	67
	**C-alkylation** Merrifield resin monitoring by FTIR 2 diastereoisomers 3 examples overall yield reported	100
	**C-alkylation** polystyrene resin monitoring by FTIR 4 examples overall yield reported	93
	**C-cyanation** Merrifield resin 1 example yield: 90%	142
	**C-alkylation** Wang resin several examples overall yield reported	137, 170
	**C-alkylation** Wang resin 24 examples yield: 60-95% overall	137
	**C-alkylation** Carboxylated polystyrene resin 2 examples overall yield reported	96
	**C-alkylation** Carboxylated polystyrene resin 9 examples yield: 70-92%	96

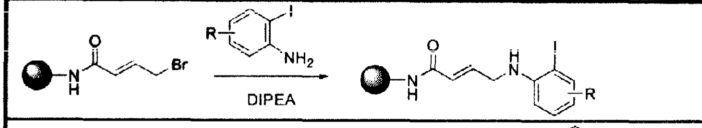
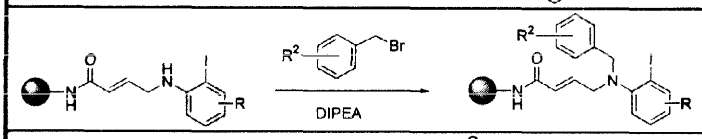
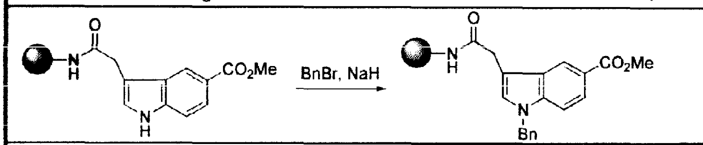
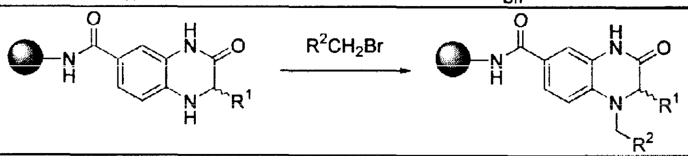
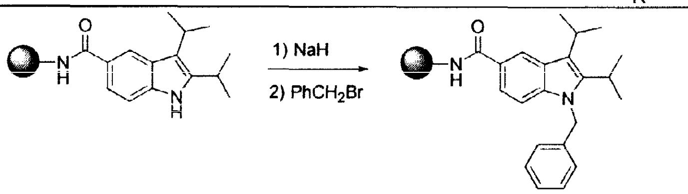
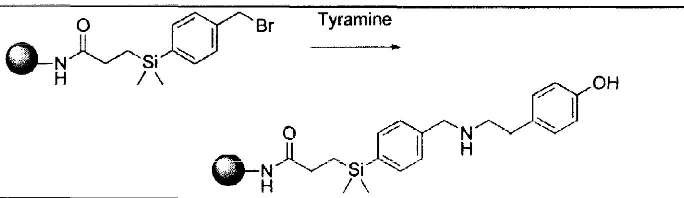
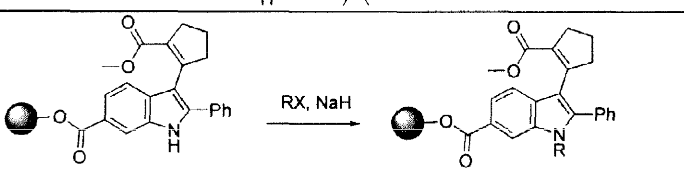
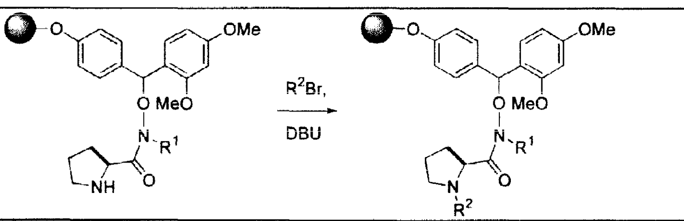
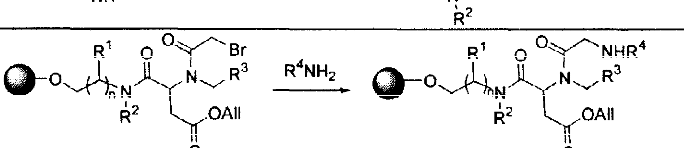
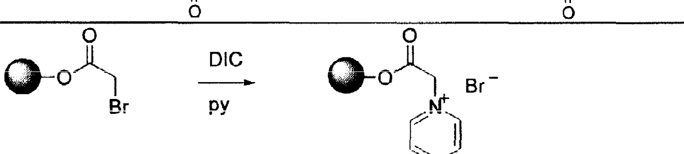
Type of reaction: Substitution, nucleophilic/electrophilic

	**C-alkylation** Carboxylated polystyrene resin several examples yield: 37% overall	96
	**C-alkylation** Rink amide resin 10 examples yield: 0-90%	128
	**C-alkylation** Merrifield, Wang or TentaGel R PHB resin 1 example overall yield reported	95
	**C-acylation** Wang resin Thioamide formation 9 examples overall yield reported	57
	**C-acylation** Wang resin 4 examples overall yield reported	91
	**O-alkylation** **Mitsunobu** TentaGel SH resin 1 example overall yield reported	120
	**O-alkylation** **Mitsunobu** ArgoGel-OH resin 1 example monitoring by ^{13}C gel-phase NMR overall yield reported	168
	**O-alkylation** **Mitsunobu** BHA resin 1 example overall yield reported	89
	**O-alkylation** **Mitsunobu** Merrifield 1 example overall yield reported	86
	**O-alkylation** **Mitsunobu** Hydroxymethylene resin 10 examples overall yield reported	103

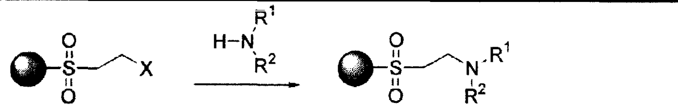
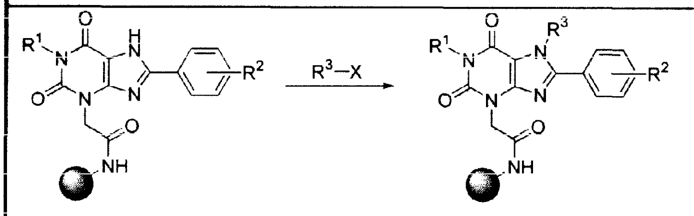
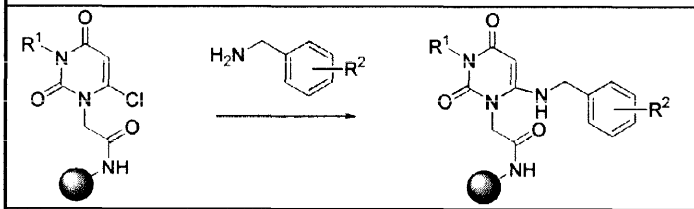
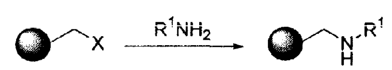
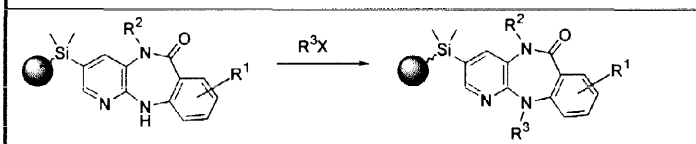
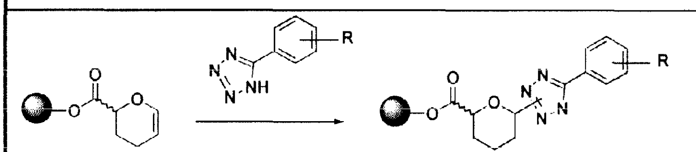
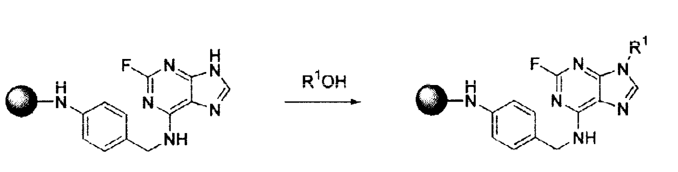
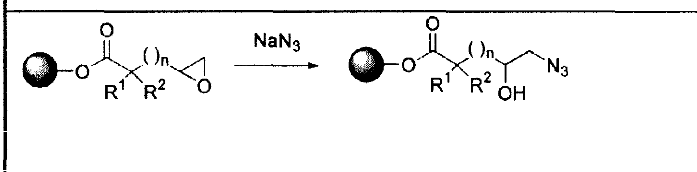
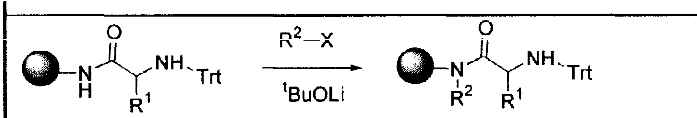
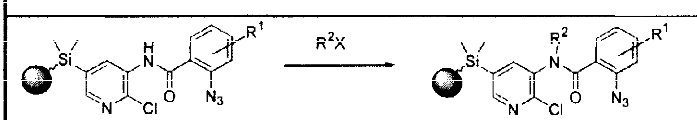
Type of reaction: Substitution, nucleophilic/electrophilic

	**O-alkylation** **Mitsunobu** ArgoGel Rink resin 3 examples yield: 88-97% automated synthesis	67
	**O-alkylation** Rink amide resin 2 examples	26
	**O-alkylation** Merrifield resin monitoring by FTIR 1 example overall yield reported overall yield reported	99
	**O-alkylation** Merrifield resin monitoring by FTIR 3 examples overall yield reported	100
	**O-alkylation** ArgoGel -Wang monitoring by gel-phase ^{13}C NMR, colourometric tests 5 examples overall yield reported	94
	**O-alkylation** Trityl polystyrene monitoring by FTIR 1 example overall yield reported	33
	**O-alkylation** Rink acid resin 12 examples yield: 58-95 %	117
	**O-glycosylation** amine resin 2 examples overall yield reported	110

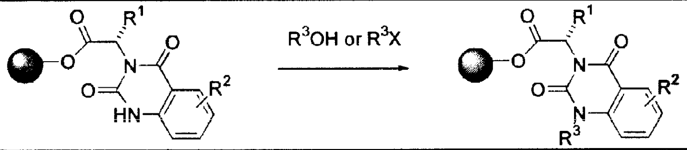
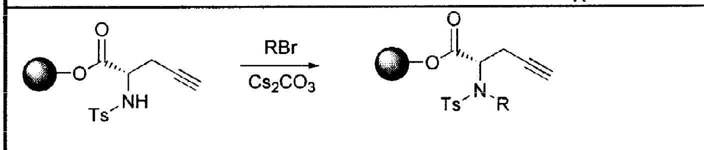
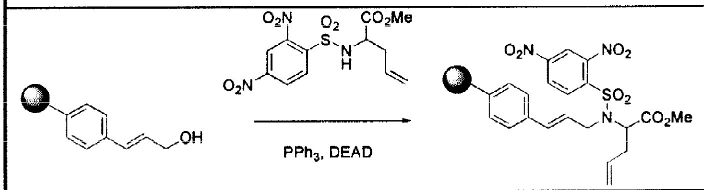
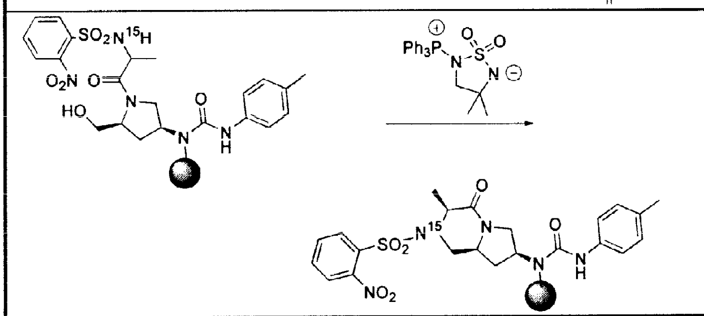
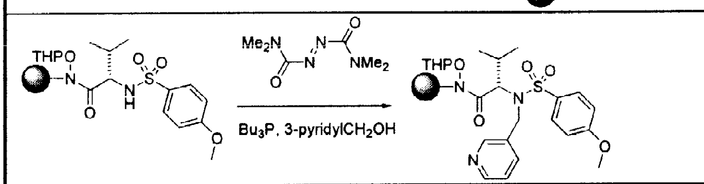
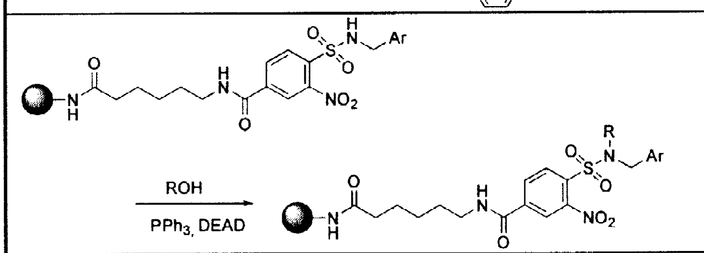
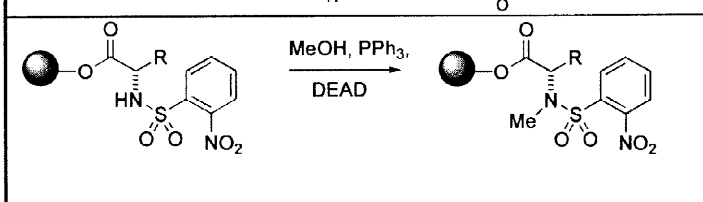
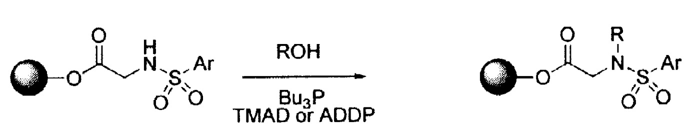
Type of reaction: Substitution, nucleophilic/electrophilic

	**N-alkylation** Rink amide resin 4 examples overall yield reported	26
	**N-alkylation** Rink amide resin 6 examples overall yield reported	26
	**N-alkylation** Rink amide resin 1 example yield: 83%	26
	**N-alkylation** Rink amide resin 2 examples yield: 32-93%	74
	**N-alkylation** Rink amide resin 1 example yield:80%	27
	**N-alkylation** BHA resin 1 example overall yield reported	89
	**N-alkylation** Wang resin 12 examples yield: 33-73 %	58
	**N-alkylation** Rink acid resin 1 example overall yield reported	117
	**N-alkylation** TentaGel trityl resin library: 6x6x8	51
	**N-alkylation** Wang resin 1 example overall yield reported	160

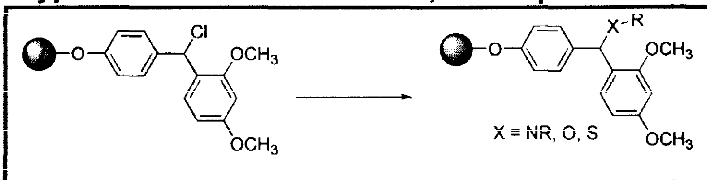
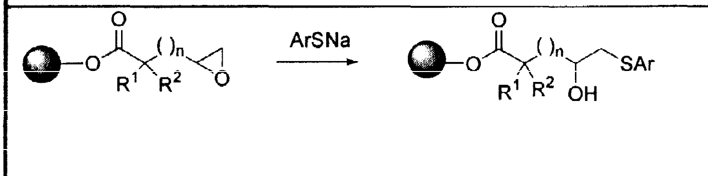
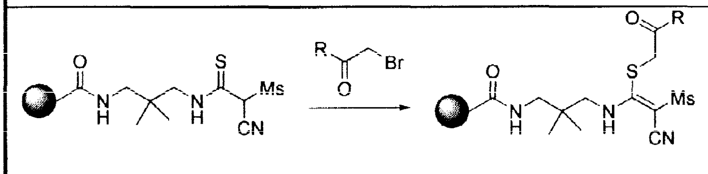
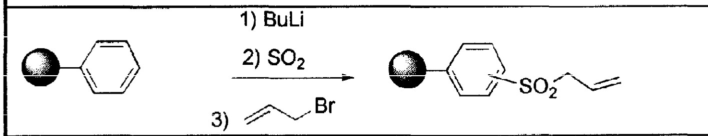
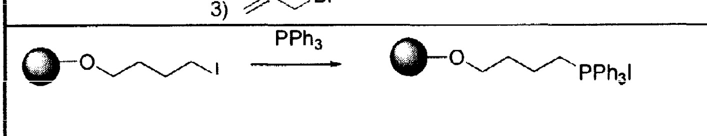
Type of reaction: Substitution, nucleophilic/electrophilic

	**N-alkylation** Merrifield resin few examples overall yield reported	104
	**N-alkylation** Rink resin 3 examples yield 10-32% overall	145
	**N-alkylation** Rink resin 4 examples overall yield reported	145
 X = I, Br, OMs, OTs, ONs	**N-alkylation** Wang and TentaGel SAC resin 42 examples overall yield reported different leaving groups studied	158
	**N-alkylation** Polystyrene resin 3 examples overall yield reported acylation also performed	75
 R = Me, Br	**N-alkylation** Merrifield resin 4 examples yield: 41-58%	64
	**N-alkylation** **Mitsunobu** PAL derivatised MBHA resin selective N-9 alkylation 9 examples yield: 73-88%	76
	**N-alkylation** (epoxide opening) Merrifield resin monitoring by FTIR 4 examples overall yield reported	81
	**N-alkylation (amide)** MBHA resin 2 examples yield: not reported	34
	**N-alkylation (amide)** Polystyrene resin 4 examples overall yield reported	75

Type of reaction: Substitution, nucleophilic/electrophilic

	**N-alkylation (urea)** Sasrin resin 10 examples overall yield reported	143
	**N-alkylation (sulfonamide)** Wang resin 3 examples overall yield reported	28
	**N-alkylation (sulfonamide) Mitsunobu** Polystyrene resin 1 example overall yield reported	84
	**N-alkylation (sulfonamide) Mitsunobu-like** ArgoGel OH resin monitoring by ^{15}N gel-phase NMR 1 example overall yield reported	31
	**N-alkylation Mitsunobu** Tentagel S NH_2 resin 1 example overall yield reported	116
	**N-alkylation (sulfonamide) Mitsunobu** BHA resin 10 examples yield: 0-100%	97
	**N-alkylation (sulfonamide) Mitsunobu** 2-chlorotrityl resin 8 examples yield: 80-100% over 4 steps	136b
	**N-alkylation (sulfonamide) Mitsunobu** ArgoGel (Wang), Wang and Sasrin resin 45 examples yield: 0-100% higher purity observed with ArgoGel (Wang) resin	171

Type of reaction: Substitution, nucleophilic/electrophilic

	**N,O,S-Alkylation** Rink chloride resin monitoring by MAS NMR 12 examples yield: 84-96%	66
	**S-alkylation** (epoxide opening) Merrifield resin monitoring by FTIR 4 examples overall yield reported	81
	**S-alkylation** Wang resin 9 examples overall yield reported	57
	**S-alkylation** polystyrene resin monitoring by FTIR overall yield reported	93
	**P-alkylation** Merrifield 1 example overall yield reported	85

Internet Footnote

Whilst compiling this review, we have noticed a number of websites with relevent information, *e.g.* www.combinatorial.com and www.5z.com.

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References

1. Hermkens, P.H.H.; Ottenheijm, H.C.J.; Rees, D.C. *Tetrahedron* **1996,** *52*, 4527-4554.
2. Hermkens, P.H.H.; Ottenheijm, H.C.J.; Rees, D.C. *Tetrahedron* **1997,** *53*, 5643-5678.
3. Nuss, J.M.; Desai, M.C.; Zuckermann, R.N.; Singh, R.; Renhowe, P.A.; Goff, D.A.; Chinn, J.P.; Wang, L.; Dorr, H.; Brown, E.G.; Subramanian, S. *Pure & Applied Chemistry* **1997,** *69*, 447-452.
4. Kantorowski, E.J.; Kurth, M.J. *Molecular Diversity* **1996**, *2*, 207-216.
5. *Chemical Reviews*, **1997**, *97*, 349-509
6. Hodge, P. *Chemical Society Reviews* **1997**, *26*, 417-424

7. Brown, R. *Contemporary Organic Synthesis* **1997**, 216-237.
8. Choong, I. C.; Ellman, J.A. *Annual Reports in Medicinal Chemistry* **1997**, *31*, 309-318.
9. Backes, B.J.; Ellman, J.A. *Curr. Opin. Chem. Biol.* **1997**, *1*, 86-93
10. Novabiochem, The Combinatorial Chemistry Catalog, March **1998**, Solid Phase Organic synthesis notes, page S1-S54.
11. Lemmo, A.V.; Fisher, J.T.; Geysen, H.M.; Rose D.K. *Anal.Chem.* **1997**, *69*, 543-551.
12. Cargill, J.F.; Lebl, M. *Curr. Opin. Chem. Biol.* **1997**, *1*, 67-71.
13. Egner, B.J.; Bradley, M. *Drug Discovery Today* **1997**, *2*, 102-109.
14. Pivonka, D.E.; Russell, K.; Gero, T. *Applied Spectroscopy* **1997**, *50*, 1471-1478.
15. Loo, J.A.; DeJohn, D.E.; Ogorzalek Loo, R.R.; Andrews, P.C. *Annual Reports in Medicinal Chemistry* **1997**, *31*, 319-325.
16. Shuttleworth, S.J.; Allin, S.M.; Sharma, P.K. *Synthesis* **1997**, 1217-1239.
17. Kaldor, S.W.; Siegel, M.G. *Curr. Opin. Chem. Biol.* **1997**, 1, 101-106.
18. Maehr, H. *Bioorg. Med. Chem.* **1997**, *5*, 473-491.
19. Dolle, R.E. *Molecular Diversity* **1996**, *2*, 223-236.
20. Myers, P.L. *Curr. Opin. Biotech.* **1997**, *8*, 701-707.
21. Cowley, P.M.; Rees D.C. *Curr. Med. Chem.* **1997**, *4*, 211-227.
22. Plunkett, M.J.; Ellman, J.A. *Scientific American* **1997**, 55-59.
23. Brown D. *Molecular Diversity* **1997**, *2*, 217-222.
24. Hall S.E. *Pharmaceutical Research* **1997**, *14*, 1104-1105.
25. a) *Annual Reports in Combinatorial Chemistry and Molecular Diversity*, Volume 1, Eds. Moos, W.H.; Pavia, M.R.; Kay, B.K.; Ellington, A.D., ESCOM, Leiden, 1997.
b) Patent issues see, Newton, C.G. *Exp. Opin. Ther. Patents* **1996**, *6*, 827-835 and Newton, C.G. *ibid* **1997**, *7*, 1183-1194.
26. Zhang, H. C.; Maryanoff, B. E. *J. Org. Chem.* **1997**, *62*, 1804-1809.
27. Zhang, H. C.; Brumfield, K. K.; Maryanoff, B. E. *Tetrahedron Lett.* **1997**, *38*, 2439-2442.
28. Bolton, G. L.; Hodges, J. C.; Rubin, J. R. *Tetrahedron* **1997**, *53*, 6611-6634.
29. Wang, G. T.; Chen, Y.; Wang, S.; Sciotti, R.; Sowin, T. *Tetrahedron Lett.* **1997**, *38*, 1895-1898.
30. Xiao, X.; Ngu, K.; Chao, C.; Patel, D. V. *J. Org. Chem.* **1997**, *62*, 6968-6973.
31. Swayze, E. E. *Tetrahedron Lett.* **1997**, *38*, 8643-8646.
32. Corbett, J. W.; Graciani, N. R.; Mousa, S. A.; Degrado, W. F. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1371-1376.
33. Bauer, U.; Ho, W. B.; Koskinen, A. M. P. *Tetrahedron Lett.* **1997**, *38*, 7233-7236.
34. Nefzi, A.; Ostresh, J. M.; Meyer, J. P.; Houghten, R. A. *Tetrahedron Lett.* **1997**, *38*, 931-934.
35. Matthews, J.; Rivero, R. A. *J. Org. Chem.* **1997**, *62*, 6090-6092.
36. Smith, J.; Liras, J. L.; Schneider, S. E.; Anslyn, E. V. *J. Org. Chem.* **1996**, *61*, 8811-8818.
37. Routledge, A.; Abell, C.; Balasubramanian, S. *Tetrahedron Lett.* **1997**, *38*, 1227-1230.
38. Routledge, A.; Stock, H. T.; Flitsch, S. L.; Turner, N. J. *Tetrahedron Lett.* **1997**, *38*, 8287-8290.
39. Hernandez, A. S.; Hodges, J. C. *J. Org. Chem.* **1997**, *62*, 3153-3157.
40. García-Echeverría, C. *Tetrahedron Lett.* **1997**, *38*, 8933-8934.
41. Robinson, S.; Roskamp, E. J. *Tetrahedron* **1997**, *53*, 6697-6705.
42. Drewry, D. H.; Gerritz, S. W.; Linn, J. A. *Tetrahedron Lett.* **1997**, *38*, 3377-3380.
43. Wang, F. J.; Hauske, J. R. *Tetrahedron Lett.* **1997**, *38*, 8651-8654.
44. Fitzpatrick, L. J.; Rivero, R. A. *Tetrahedron Lett.* **1997**, *38*, 7479-7482.
45. Watson, S. P.; Wilson, R. D.; Judd, D. B.; Richards, S. A. *Tetrahedron Lett.* **1997**, *38*, 9065-9068.
46. Zhong, H.M.; Greco, M.N.; Maryanoff, B.E. *J. Org. Chem.* **1997**, *62*, 9326-9330.

47. a) Raju, B.; Kogan, T. P. *Tetrahedron Lett.* **1997**, *38*, 3373-3376. b) Vlattas, I.; Dellureficio, J.; Dunn, R.; Sytwu, I. I.; Stanton, J. *Tetrahedron Lett.* **1997**, *38*, 7321-7324.
48. Whitehouse, D. L.; Nelson, K. H.; Savinov, S. N.; Austin, D. J. *Tetrahedron Lett.* **1997**, *38*, 7139-7142.
49. Purandare, A. V.; Natarajan, S. *Tetrahedron Lett.* **1997**, *38*, 8777-8780.
50. Wang, F. J.; Hauske, J. R. *Tetrahedron Lett.* **1997**, *38*, 6529-6532.
51. Krchnák, V.; Weichsel, A. S. *Tetrahedron Lett.* **1997**, *38*, 7299-7302.
52. Mayer, J. P.; Lewis, G. S.; Curtis, M. J.; Zhang, J. W. *Tetrahedron Lett.* **1997**, *38*, 8445-8448.
53. Marti, R. E.; Yan, B.; Jarosinski, M. A. *J. Org. Chem.* **1997**, *62*, 5615-5618.
54. Nielsen, J.; Jensen, F. R. *Tetrahedron Lett.* **1997**, *38*, 2011-2014.
55. Xiao, X. Y.; Parandoosh, Z.; Nova, M. P. *J. Org. Chem.* **1997**, *62*, 6029-6033.
56. Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E. *Nature* **1997**, *387*, 268-272.
57. Stephensen, H.; Zaragoza, F. *J. Org. Chem.* **1997**, *62*, 6096-6097.
58. Collini, M. D.; Ellingboe, J. W. *Tetrahedron Lett.* **1997**, *38*, 7963-7966.
59. Ruhland, B.; Bombrun, A.; Gallop, M. A. *J. Org. Chem.* **1997**, *62*, 7820-7826.
60. Arumugam, V.; Routledge, A.; Abell, C.; Balasubramanian, S. *Tetrahedron Lett.* **1997**, *38*, 6473-6476.
61. Fagnola, M. C.; Candiani, I.; Visentin, G.; Cabri, W.; Zarini, F.; Mongelli, N.; Bedeschi, A. *Tetrahedron Lett.* **1997**, *38*, 2307-2310.
62. Fancelli, D.; Fagnola, M. C.; Severino, D.; Bedeschi, A. *Tetrahedron Lett.* **1997**, *38*, 2311-2314.
63. Akaji, K.; Kiso, Y. *Tetrahedron Lett.* **1997**, *38*, 5185-5188.
64. Yoo, S.; Seo, J.; Yi, K.; Gong, Y. *Tetrahedron Lett.* **1997**, *38*, 1203-1206.
65. Brown, S. D.; Armstrong, R. W. *J. Org. Chem.* **1997**, *62*, 7076-7077.
66. Garigipati, R. S. *Tetrahedron Lett.* **1997**, *38*, 6807-6810.
67. Porco, J. A.; Deegan, T.; Devonport, W.; Gooding, O. W.; Heisler, K.; Labadie, J. W.; Newcomb, B.; Nguyen, C.; v. Eikeren, P.; Wong, J.; Wright, P. *Molecular Diversity* **1996**, *2*, 197-206.
68. Piettre, S. R.; Baltzer, S. *Tetrahedron Lett.* **1997**, *38*, 1197-1200.
69. Fraley, M. E.; Rubino, R. S. *Tetrahedron Lett.* **1997**, *38*, 3365-3368.
70. Tempest, P. A.; Armstrong, R. W. *J. Am. Chem. Soc.* **1997**, *119*, 7607-7608.
71. Plunkett, M. J.; Ellman, J. A. *J. Org. Chem.* **1997**, *62*, 2885-2893.
72. Rottländer, M.; Knochel, P. *Synlett* **1997**, 1084-1086.
73. Burgess, K.; Lim, D.; Bois-Choussy, M.; Zhu, J. *Tetrahedron Lett.* **1997**, *38*, 3345-3348.
74. Lee, J.; Murray, W. V.; Rivero, R. A. *J. Org. Chem.* **1997**, *62*, 3874-3879.
75. Woolard, F. X.; Paetsch, J.; Ellman, J. A. *J. Org. Chem.* **1997**, *62*, 6102-6103.
76. Gray, N. S.; Kwon, S.; Schultz, P. G. *Tetrahedron Lett.* **1997**, *38*, 1161-1164.
77. Nugiel, D. A.; Cornelius, L. A. M.; Corbett, J. W. *J. Org. Chem.* **1997**, *62*, 201-203.
78. Kobayashi, S.; Moriwaki, M. *Tetrahedron Lett.* **1997**, *38*, 4251-4254.
79. Park, B. D.; Lee, H. I.; Ryoo, S. J.; Lee, Y. S. *Tetrahedron Lett.* **1997**, *38*, 591-594.
80. Szardenings, A. K.; Burkoth, T. S.; Lu, H. H.; Tien, D. W.; Campbell, D. A. *Tetrahedron* **1997**, *53*, 6573-6593.
81. Le Hetet, C.; David, M.; Carreaux, F.; Carboni, B.; Sauleau, A. *Tetrahedron Lett.* **1997**, *38*, 5153-5156.
82. Tietze, L. F.; Steinmetz, A.; Balkenhohl, F. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1303-1306.
83. Kim, S. W.; Ahn, S. Y.; Koh, J. S.; Lee, J. H.; Ro, S.; Cho, H. Y. *Tetrahedron Lett.* **1997**, *38*, 4603-4606.
84. Piscopio, A. D.; Miller, J. F.; Koch, K. *Tetrahedron Lett.* **1997**, *38*, 7143-7146.

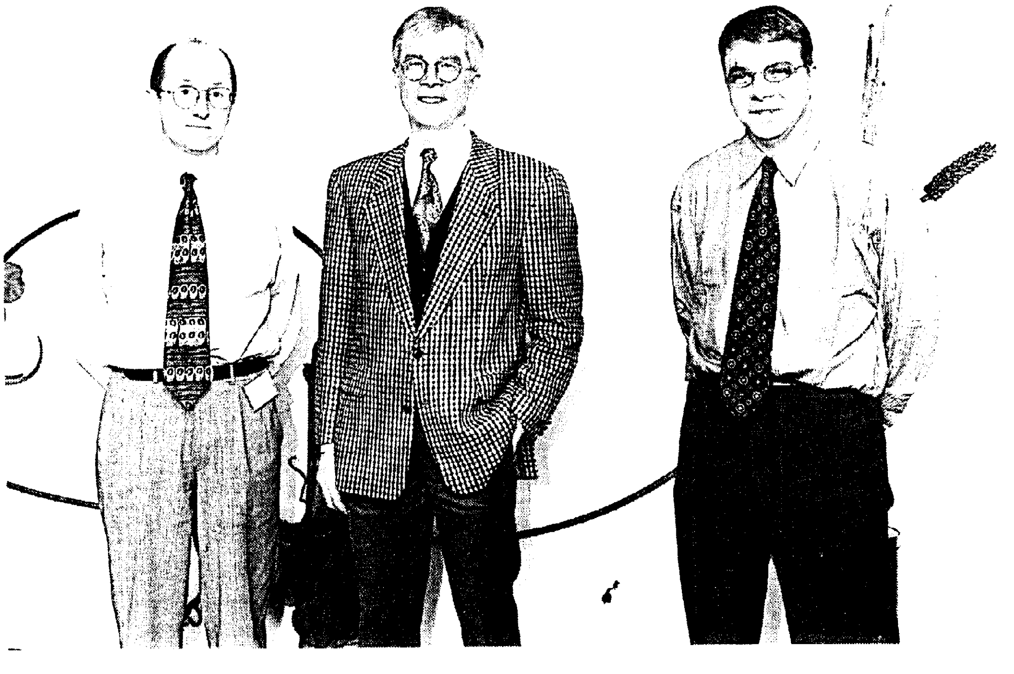
85. Nicolaou, K. C.; Vourloumis, D.; Li, T.; Pastor, J.; Winssinger, N.; He, Y.; Ninkovic, S.; Sarabia, F.; Vallberg, H.; Roschangar, F.; King, N. P.; Finlay, M. R. V.; Giannakakou, P.; Verdier-Pinard, P.; Hamel, E. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2097-2103.
86. Peters, J. U.; Blechert, S. *Synlett* **1997**, 348-350.
87. Pernerstorfer, J.; Schuster, M.; Blechert, S. *Chem. Commun.* **1997**, 1949-1950.
88. Lorsbach, B. A.; Miller, R. B.; Kurth, M. J. *J. Org. Chem.* **1996**, *61*, 8716-8717.
89. Newlander, K. A.; Chenera, B.; Veber, D. F.; Yim, N. C. F.; Moore, M. L. *J. Org. Chem.* **1997**, *62*, 6726-6732.
90. Gowravaram, M. R.; Gallop, M. A. *Tetrahedron Lett.* **1997**, *38*, 6973-6976.
91. Zaragoza, F. *Tetrahedron Lett.* **1997**, *38*, 7291-7294.
92. Schuster, M.; Lucas, N.; Blechert, S. *Chem. Commun.* **1997**, 823-824.
93. Halm, C.; Evarts, J.; Kurth, M. J. *Tetrahedron Lett.* **1997**, *38*, 7709-7712.
94. Deegan, T. L.; Gooding, O. W.; Baudart, S.; Porco, J. A. *Tetrahedron Lett.* **1997**, *38*, 4973-4976.
95. Burgess, K.; Lim, D. *Chem. Commun.* **1997**, 785-786.
96. Panek, J. S.; Zhu, B. *J. Am. Chem. Soc.* **1997**, *119*, 12022-12023.
97. Kay, C.; Murray, P. J.; Sandow, L.; Holmes, A. B. *Tetrahedron Lett.* **1997**, *38*, 6941-6944.
98. Conti, P.; Demont, D.; Cals, J.; Ottenheijm, H. C. J.; Leysen, D. *Tetrahedron Lett.* **1997**, *38*, 2915-2918.
99. Furth, P. S.; Reitman, M. S.; Cook, A. F. *Tetrahedron Lett.* **1997**, *38*, 5403-5406.
100. Furth, P. S.; Reitman, M. S.; Gentles, R.; Cook, A. F. *Tetrahedron Lett.* **1997**, *38*, 6643-6646.
101. Ho, C. Y.; Kukla, M. J. *Tetrahedron Lett.* **1997**, *38*, 2799-2802.
102. Brown, A. R.; Rees, D. C.; Rankovic, Z.; Morphy, J. R. *J. Am. Chem. Soc.* **1997**, *119*, 3288-3295.
103. Heinonen, P.; Lönnberg, H. *Tetrahedron Lett.* **1997**, *38*, 8569-8572.
104. Kroll, F. E. K.; Morphy, R.; Rees, D.; Gani, D. *Tetrahedron Lett.* **1997**, *38*, 8573-8576.
105. Ede, N. J.; Bray, A. M. *Tetrahedron Lett.* **1997**, *38*, 7119-7122.
106. Pothion, C.; Paris, M.; Heitz, A.; Rocheblave, L.; Rouch, F.; Fehrentz, J. A.; Martinez, J. *Tetrahedron Lett.* **1997**, *38*, 7749-7752.
107. Fehrentz, J. A.; Paris, M.; Heitz, A.; Velek, J.; Winternitz, F.; Martinez, J. *J. Org. Chem.* **1997**, *62*, 6792-6796.
108. Hird, N. W.; Irie, K.; Nagai, K. *Tetrahedron Lett.* **1997**, *38*, 7111-7114.
109. Crawshaw, M.; Hird, N. W.; Irie, K.; Nagai, K. *Tetrahedron Lett.* **1997**, *38*, 7115-7118.
110. Rodebaugh, R.; Fraser-Reid, B.; Geysen, H. M. *Tetrahedron Lett.* **1997**, *38*, 7653-7656.
111. Fukase, K.; Egusa, K.; Nakai, Y.; Kusumoto, S. *Molecular Diversity* **1997**, *2*, 182-188.
112. Rademann, J.; Schmidt, R. R. *J. Org. Chem.* **1997**, *62*, 3650-3653.
113. Atrash, B.; Bradley, M. *Chem. Commun.* **1997**, 1397-1398.
114. Mata, E. G. *Tetrahedron Lett.* **1997**, *38*, 6335-6338.
115. Richter, L. S.; Desai, M. C. *Tetrahedron Lett.* **1997**, *38*, 321-322.
116. Ngu, K.; Patel, D. V. *J. Org. Chem.* **1997**, *62*, 7088-7089.
117. Mellor, S. L.; Chan, W. C. *Chem. Commun.* **1997**, 2005-2006.
118. Roussel, P.; Bradley, M.; Matthews, I.; Kane, P. *Tetrahedron Lett.* **1997**, *38*, 4861-4864.
119. Obrecht, D.; Abrecht, C.; Grieder, A.; Villalgordo, J. M. *Helvetica Chimica Acta* **1997**, *80*, 65-72.
120. Gayo, L. M.; Suto, M. J. *Tetrahedron Lett.* **1997**, *38*, 211-214.
121. Prien, O.; Rölfing, K.; Thiel, M.; Künzer, H. *Synlett* **1997**, 325-326.
122. Boojamra, C. G.; Burow, K. M.; Thompson, L. A.; Ellman, J. A. *J. Org. Chem.* **1997**, *62*, 1240-1256.
123. Han, H.; Janda, K. D. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1731-1733.

124. Bhalay, G.; Blaney, P.; Palmer, V. H.; Baxter, A. D. *Tetrahedron Lett.* **1997**, *38*, 8375-8378.
125. Fivush, A. M.; Willson, T. M. *Tetrahedron Lett.* **1997**, *38*, 7151-7154.
126. Youngman, M. A.; Dax, S. L. *Tetrahedron Lett.* **1997**, *38*, 6347-6350.
127. Pearson, W. H.; Clark, R. B. *Tetrahedron Lett.* **1997**, *38*, 7669-7672.
128. Marzinzik, A. L.; Felder, E. R. *Molecules* **1997**, *2*, 17-30.
129. Gordeev, M. F.; Gordon, E. M.; Patel, D. V. *J. Org. Chem.* **1997**, *62*, 8177-8181.
130. Pei, Y. Z.; Houghten, R. A.; Kiely, J. S. *Tetrahedron Lett.* **1997**, *38*, 3349-3352.
131. Kurth, M. J.; Randall, L. A. A.; Takenouchi, K. *J. Org. Chem.* **1996**, *61*, 8755-8761.
132. Marx, M. A.; Grillot, A. L.; Louer, C. T.; Beaver, K. A.; Bartlett, P. A. *J. Am. Chem. Soc.* **1997**, *119*, 6153-6167.
133. Kantorowski, E. J.; Kurth, M. J. *J. Org. Chem.* **1997**, *62*, 6797-6803.
134. a) Yan, B.; Sun, Q.; Wareing, J. R.; Jewell, C. F. *J. Org. Chem.* **1996**, *61*, 8765-8770. b) Hoekstra, W.J.; Greco, M.N.; Yabut, S.C.; Hulshizer, B.L.; Maryanoff, B.E. *Tetrahedron Lett.* **1997**, *38*, 2629-2632.
135. Thieriet, N.; Alsina, J.; Giralt, E.; Guibe, F.; Albericio, F. *Tetrahedron Lett.* **1997**, *38*, 7275-7278.
136. a) Burgess, K.; Ibarzo, J.; Linthicum, D. S.; Russell, D. H.; Shin, H.; Shitangkoon, A.; Totani, R.; Zhang, A. J. *J. Am. Chem. Soc.* **1997**, *119*, 1556-1564. b) Yang, L.; Chiu, K. *Tetrahedron Lett.* **1997**, *38*, 7307-7310.
137. Griffith, D. L.; Odonnell, M. J.; Pottorf, R. S.; Scott, W. L.; Porco, J. A. *Tetrahedron Lett.* **1997**, *38*, 8821-8824.
138. Katritzky, A. R.; Xie, L. H.; Zhang, G. F.; Griffith, M.; Watson, K.; Kiely, J. S. *Tetrahedron Lett.* **1997**, *38*, 7011-7014.
139. Wipf, P.; Henninger, T. C. *J. Org. Chem.* **1997**, *62*, 1586-1587.
140. Gopalsamy, A.; Pallai, P. V. *Tetrahedron Lett.* **1997**, *38*, 907-910.
141. Cheng, Y.; Chapman, K. T. *Tetrahedron Lett.* **1997**, *38*, 1497-1500.
142. Deans, R.; Rotello, V. M. *J. Org. Chem.* **1997**, *62*, 4528-4529.
143. Gordeev, M. F.; Hui, H. C.; Gordon, E. M.; Patel, D. V. *Tetrahedron Lett.* **1997**, *38*, 1729-1732.
144. Nefzi, A.; Ostresh, J. M.; Houghten, R. A. *Tetrahedron Lett.* **1997**, *38*, 4943-4946.
145. Heizmann, G.; Eberle, A. N. *Molecular Diversity* **1997**, *2*, 171-174.
146. Du, X. H.; Armstrong, R. W. *J. Org. Chem.* **1997**, *62*, 5678-5679.
147. Cuny, G. D.; Cao, J. R.; Hauske, J. R. *Tetrahedron Lett.* **1997**, *38*, 5237-5240.
148. Marti, R. E.; Bleicher, K. H.; Bair, K. W. *Tetrahedron Lett.* **1997**, *38*, 6145-6148.
149. Whitehouse, D. L.; Savinov, S. N.; Austin, D. J. *Tetrahedron Lett.* **1997**, *38*, 7851-7852.
150. Chen, C. X.; Randall, L. A. A.; Miller, R. B.; Jones, A. D.; Kurth, M. J. *Tetrahedron* **1997**, *53*, 6595-6609.
151. Swali, V.; Wells, N. J.; Langley, G. J.; Bradley, M. *J. Org. Chem.* **1997**, *62*, 4902-4903.
152. Wallace, O. B. *Tetrahedron Lett.* **1997**, *38*, 4939-4942.
153. Wang, Y. H.; Wilson, S. R. *Tetrahedron Lett.* **1997**, *38*, 4021-4024.
154. Spitzer, J. L.; Kurth, M. J.; Schore, N. E.; Najdis, D. *Tetrahedron* **1997**, *53*, 6791-6808.
155. Deben, I. E. A.; van Wijk, T. H. M.; van Doornum, E. M.; Hermkens, P. H. H.; Kellenbach, E. R. *Mikrochimica Acta* **1997**, 245-246.
156. Sibi, M. P.; Chandramouli, S. V. *Tetrahedron Lett.* **1997**, *38*, 8929-8932.
157. Nugiel, D. A.; Wacker, D. A.; Nemeth, G. A. *Tetrahedron Lett.* **1997**, *38*, 5789-5790.
158. Ngu, K.; Patel, D.V. *Tetrahedron Lett.* **1997**, *38*, 973-976.
159. Sylvain, C.; Wagner, A.; Mioskowski, C. *Tetrahedron Lett.* **1997**, *38*, 1043-1044.
160. Vo, N. H.; Eyermann, C. J.; Hodge, C. N. *Tetrahedron Lett.* **1997**, *38*, 7951-7954.
161. Kiselyov, A. S.; Armstrong, R. W. *Tetrahedron Lett.* **1997**, *38*, 6163-6166.

162. Short, K. M.; Mjalli, A. M. M. *Tetrahedron Lett.* **1997**, *38*, 359-362.
163. Short, K. M.; Ching, B. W.; Mjalli, A. M. M. *Tetrahedron* **1997**, *53*, 6653-6679.
164. Vagner, J.; Krchnak, V.; Lebl, M.; Barany, G *Collection of Czechoslovak Chemical Communications* **1996**, *61*, 1697-1702.
165. a) Yan, B.; Li, W. *J. Org. Chem.* **1997**, *62*, 9354-9357. b) Katritzky, A. R.; Toader, D.; Watson, K.; Kiely, J. S. *Tetrahedron Lett.* **1997**, *38*, 7849-7850.
166. Brown, P. J.; Hurley, K. P.; Stuart, L. W.; Willson, T. M. *Synthesis* **1997**, 778-782.
167. Brown, E. G.; Nuss, J. M. *Tetrahedron Lett.* **1997**, *38*, 8457-8460.
168. Swayze, E. E. *Tetrahedron Lett.* **1997**, *38*, 8465-8468.
169. Devraj, R.; Cushman, M. *J. Org. Chem.* **1996**, *61*, 9368-9373.
170. O'Donnell, M. J.; Lugar, C. W.; Pottorf, R. S.; Zhou, C. Y.; Scott, W. L.; Cwi, C. L. *Tetrahedron Lett.* **1997**, *38*, 7163-7166.
171. Dankwardt, S. M.; Smith, D. B.; Porco, J. A.; Nguyen, C. H. *Synlett* **1997**, 854-855.
172. Gravert, D. J.; Janda, K. D. *Chemical Reviews* **1997**, *97*, 489-509.
173. Dreef-Tromp, C. M.; Willems, H. A. M.; Westerduin, P.; van Veelen, P.; van Boeckel, C. A. A. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1175-1180.
174. Chen, S. Q.; Janda, K. D. *J. Am. Chem. Soc.* **1997**, *119*, 8724-8725.
175. Studer, A.; Hadida, S.; Ferritto, R.; Kim, S. Y.; Jeger, P.; Wipf, P.; Curran, D. P. *Science* **1997**, *275*, 823-826.
176. Studer, A.; Curran, D. P. *Tetrahedron* **1997**, *53*, 6681-6696.
177. Studer, A.; Jeger, P.; Wipf, P.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 2917-2924.
178. Hoshino, M.; Degenkolb, P.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 8341-8349.
179. Betzemeier, B.; Knochel, P. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2623-2624.
180. Bhattacharyya, P.; Gudmunsen, D.; Hope, E. G.; Kemmitt, R. D. W.; Paige, D. R.; Stuart; A. M. *J. Chem. Soc. Perkin Transactions I*, **1997**, 3609-3612.
181. Borman, S. *C&EN* **1998**, *April 6*, 47-67.
182. Brown, A.R.; Hermkens, P.H.H.; Ottenheijm, H.C.J.; Rees, D.C. *Synlett*, **1998**, 817-827.

Biographical sketch

Susan E. Booth



David C. Rees, Harry C. J. Ottenheijm and Pedro H. H. Hermkens

Susan E. Booth, received her PhD in organic synthesis from Leicester University in 1992. Subsequently she worked as a post-doctoral fellow with Prof. K. Undheim at Oslo University, Norway and J.D. Kilburn at Southampton University. In 1996 she joined Organon Laboratories Scotland, and is doing combinatorial chemistry in the Lead Discovery Unit.

David C. Rees, received his Ph.D. in organic synthesis from Cambridge University in 1982 and then worked as a postdoctoral fellow with E.J. Corey at Harvard University. In 1984 he returned to the UK to the Parke-Davis Neuroscience Research Centre to work on drug discovery based on neuropeptides. Almost 4 years ago he was fortunate enough to move to Scotland where he is responsible for medicinal chemistry at Organon Laboratories.

Harry C.J. Ottenheijm, graduated from the University of Groningen and received (1968) his Ph.D. degree in organic synthesis from the University of Frankfurt/am Main. Subsequently, he spent 3¼ years as post-doctoral fellow in three laboratories (M. Calvin, J. Meinwald, B. Witkop) in the United States after which he started an academic career at the University of Nijmegen.
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Pedro H.H. Hermkens, received his Ph.D.-in organic synthesis from the University of Nijmegen in 1990 for his research on the syntheses, applications, and biological activities of N-hydroxy-β-carbolines. Since 1989 he has been working in the department of medicinal chemistry of NV Organon and was involved in research aiming at psychotropic drugs. His research interest involve peptidomimetics, heterocyclic chemistry, solid phase organic chemistry, combinatorial chemistry and automated chemistry. Currently he is head of the CombiChem group Oss in the Lead Discovery Unit.