Solid-phase synthesis of 4-methylene pyrrolidines and allylic amines using palladium-activated allylic linkers

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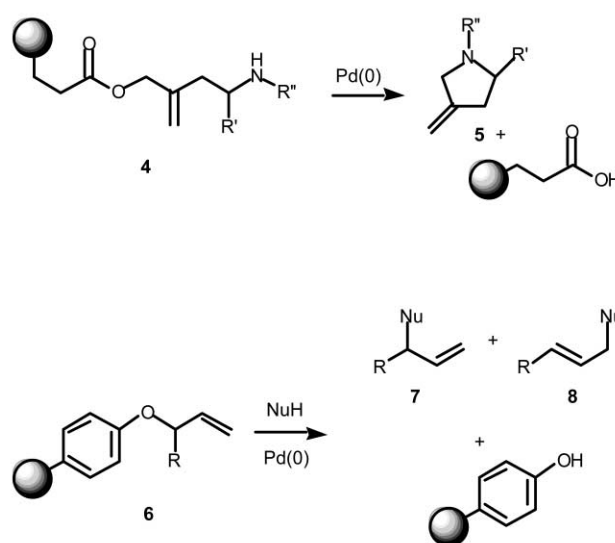E-mail: rcb1@soton.ac.uk; Fax: 023 8059 6805; Tel: 023 80594108*

The solid-phase synthesis of 4-methylene pyrrolidines and allylic amines has been achieved using palladium-catalysed nucleophilic cleavage of allylic linkages. Six pyrrolidines were synthesised in five steps from a carboxyethyl resin **20**, where the key transformations included a Lewis-acid promoted imino-Sakurai type reaction and reductive alkylation prior to the final palladium-catalysed cyclisation cleavage of the allylic carboxylate linkage. Allylic carboxylate resin **22** was also shown to undergo "traceless" cleavage using various hydride sources in the presence of catalytic palladium. A more robust allylic ether linkage was also investigated. Starting from a phenol resin **36**, a number of 3-aryl-allylamines were prepared using a palladium-catalysed nucleophilic cleavage reaction.

Introduction

The increasing throughput of modern screening methods, combined with the growing number and diversity of potential therapeutic targets, has led to a huge demand for small molecules for biological evaluation.[1] To address this need for large numbers of compounds, there has been considerable interest in the use of solid-phase synthesis to produce combinatorial libraries,[2] and as a consequence substantial research effort has been focused on the development of new solid-phase methodology,[3] and linkers.[4]

We have been interested in the development of new linkers and cleavage strategies for some time, and our attention has focused on nucleophile-cleavable linkers and so-called cyclisation–cleavage strategies.[5,6] The appeal being that either an additional element of diversity or a key structural feature is introduced in the cleavage step. In addition, the cyclisation-cleavage approach is often associated with products of higher purity than might be expected if the cleavage step was independent of cyclisation.

Successful linkers are required to cleave under mild conditions, whilst being inert to a wide variety of reaction conditions needed to introduce structural diversity into the target molecules. Allylic carboxylate linkers partially satisfy the above criteria, providing reasonable stability to nucleophiles, good acid stability and are cleaved under mild conditions in the presence of catalytic palladium (Scheme 1).[7,8] Allylic linkers were first reported for the release of glycopeptides and peptides from the solid-phase, where cleavage produced a carboxylate functionality (Scheme 1).[7a] Subsequently, the method was extended to allow the release of amines.[7c] It occurred to us, that by reversing the allylic carboxylate linkage, palladium-catalysed activation in the presence of nucleophiles would result in cleavage proceeding with the incorporation of the nucleophile into the product (Scheme 2).[9–12] In the case of an internal nucleophile,

Scheme 1 Conventional allylic linker.

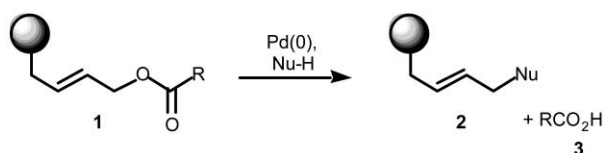† *Present address:* Evotec OAI Ltd., Milton Park, Abingdon, Oxon, UK OX14 4SD.

Scheme 2 Reversed allylic linkage.

the result would be the release of cyclic products from the solid-phase. We also imagined that resin-bound allyl phenyl ethers would be suitable substrates for palladium-catalysed nucleophilic cleavage, and in the absence of the catalyst, would display excellent stability to basic and nucleophilic conditions.[13] Phenolic ethers have the added attraction that they are readily prepared under Mitsunobu conditions and were therefore also chosen as potential candidates for novel linkers.[14,15] Here we provide a full account of the development of two new palladium-catalysed nucleophilic cleavage strategies based on allylic linkers, and their application to the synthesis of cyclic and acyclic allylic amines.[9,10]
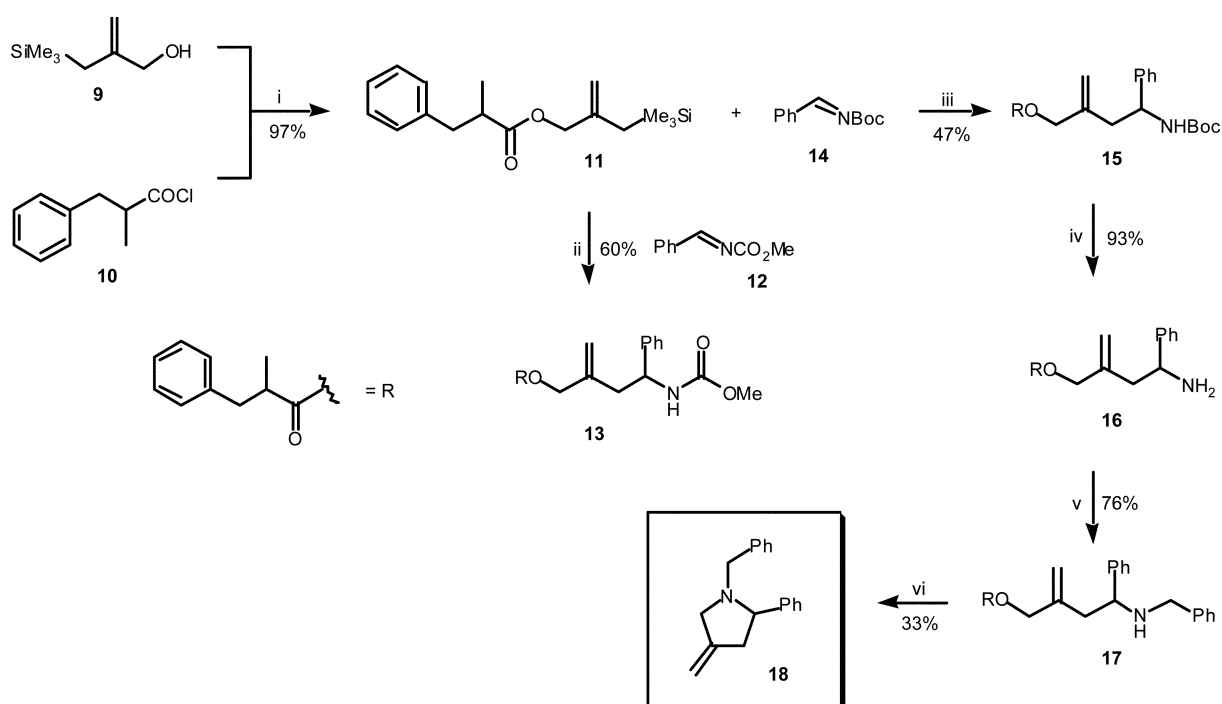
Results and discussion

(i) Synthesis of 4-methylene pyrrolidines

Initial investigation into the potential utility of allylic carboxylate linkers focused on the solid-phase synthesis of methylene pyrrolidines by adaptation of methodology described by Trost *et al.*[16,17] Prior to any solid-phase chemistry the general strategy was validated using a solution model (Scheme 3), substituting the carboxylate support with the 2-methyl-3-phenylpropionyl group. The solution model incorporated a
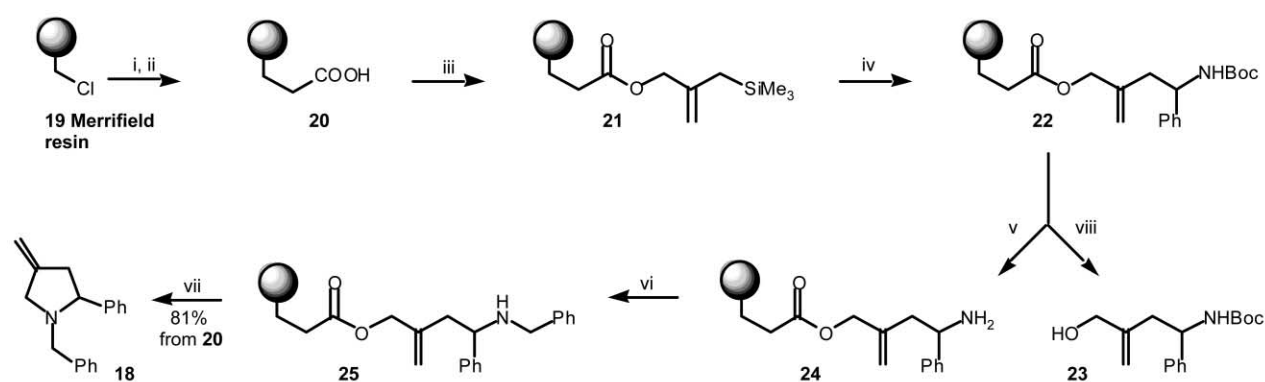
Scheme 3 *Reagents and conditions*: i) Pyridine, CH₂Cl₂; ii) **12**, BF₃·OEt₂, CH₂Cl₂; iii) **14**, BF₃·OEt₂, CH₂Cl₂; iv) TFA, CH₂Cl₂; v) PhCHO, AcOH, Me₄NB(OAc)₃H, CH₂ClCH₂Cl; vi) Pd(acac)₂, dppe, THF.

Scheme 4 *Reagents and conditions*: i) Diethyl malonate, NaH, DMF; ii) KOH, THF, H₂O then H₂SO₄; iii) **9**, DIC, DMAP, CH₂Cl₂; iv) **14**, BF₃·OEt₂, CH₂Cl₂; v) TFA, CH₂Cl₂; vi) PhCHO, AcOH, Me₄NB(OAc)₃H, CH₂ClCH₂Cl; vii) Pd(acac)₂, dppe, THF; viii) LiBH₄, THF.

more sterically demanding carboxylate ester in the hope that stability towards nucleophilic attack would be improved, and that cross-linking due to dialkylation of the malonic diester would be avoided during the synthesis of the linker on the solid-phase (see Scheme 4 for solid-phase synthesis).

The solution model study began by the conversion of diethyl methylmalonate to the acid chloride **10** using standard chemistry.[18–20] Acid chloride **10** was then coupled with the alcohol **9**,[21] providing the allylic silane **11** in excellent yield. Imino–Sakurai reaction with an *in situ*-generated *N*–methoxycarbonyl imine **12** gave the carbamate **13** (60%),[22,23] which failed to undergo cyclisation in the presence of either Pd(acac)₂ and dppe or Pd(PPh₃)₄ with or without base. This result is perhaps surprising in light of the related [3 + 2] cycloaddition reactions of sulfonylimines with 2-[(trimethylsilyl)methyl]allyl esters described by Trost and Marrs.[17]

In order to gain access to a more nucleophilic free amine containing substrate, the sequence was repeated with Boc protection of the nitrogen, to provide the analogous *tert*-butyl carbamate **15** in a modest but unoptimised 47% yield. Carbamate **15** was subsequently deprotected to yield the primary amine **16**, which afforded complex mixtures of products when subjected to various palladium–ligand combinations. One potential problem was dialkylation of **16** by the π-allyl palladium species, and as secondary amines had previously been shown to undergo efficient

palladium-catalysed cyclisation, primary amine **16** was converted to **17** by reductive alkylation. Carrying out the reaction in 1% acetic acid in DCE using 1.0 equivalent of benzaldehyde and 4.0 equivalents of Me₄NB(OAc)₃H gave **17** in good yield with no evidence of dialkylation.[24] As expected, the secondary amine **17** cyclised upon refluxing in the presence of 10 mol% Pd(acac)₂ and 15 mol% dppe in THF, to give the desired methylenepyrrolidine **18** in 33% yield. Although some of the yields in the solution pyrrolidine synthesis were rather low, we chose not to conduct any optimisation at this point, postponing efforts for the solid-phase chemistry.

The solid-phase synthesis of pyrrolidines required a carboxylate resin, and the original synthetic approach mirrored the solution route exactly. Alkylation of Merrifield resin with diethyl methylmalonate proceeded efficiently according to the on-bead IR spectra. However, the subsequent hydrolysis using aqueous sodium hydroxide in THF proved troublesome and we were unable to drive the reaction to completion. As an alternative, Merrifield resin was alkylated with the sodium salt of diethyl malonate, and in this case the subsequent hydrolysis and decarboxylation of the less hindered diester proceeded smoothly to afford the desired carboxyethyl polystyrene (**20**) (Scheme 4). The loading of the resin **20** was determined by coupling with *N*-ε–Fmoc-ʟ-lysine methylester followed by deprotection to remove the Fmoc group and UV quantification

Table 1 Optimisation of the solid-phase imino–Sakurai reaction (step iv, Scheme 4)

Entry	Molar ratio of N-acylimine[a]	Molar ratio of $BF_3 \cdot OEt_2$[a]	Time/h	Yield (%)
1	8	12	12	16
2	8	4	12	25
3	15	8	12	61
4	15	8	28	49
5	23	8	12	70
6	23	8	3	70
7	23	4	3	70

[a] The yield represents the amount of purified isolated alcohol **23** cleaved from resin **22**, and is calculated from the loading of the carboxylated resin **20**. Molar ratios are also based upon the loading of resin **20**.

of the Fmoc adduct.[25] A typical batch loading for the carboxyethyl polystyrene (**20**) was approximately 0.6 mmol g^{-1} using this method of quantification.

The allylic alcohol **9** was coupled to the resin using standard carbodiimide conditions, however excess DMAP was necessary to prevent formation of an acylisourea byproduct formed by the well known rearrangement of the DIC–acid adduct.[26,27] The imino–Sakurai reaction required some optimisation, and the success of altering the various reaction parameters was assessed by reductive cleavage of allylic alcohol **23** from resin **22** using LiBH$_4$ (Table 1). The results indicated that a large excess of the N-acylimine **14** was required to obtain a good conversion of the allylic silane, and that excess Lewis-acid and prolonged reaction times were not helpful, probably causing some product decomposition–Boc deprotection. The most efficient conditions identified employed a large excess of preformed N-acylimine **14** (23 eq.) and 4 eq. of $BF_3 \cdot Et_2O$ (entry 7, Table 1). Subsequently, the synthesis of resin **21** was scaled up and on the new batch of resin the same conditions provided a 90% yield of the alcohol after reductive cleavage with LiBH$_4$.

Removal of the Boc protecting group from **22** under standard conditions provided primary amine **24**, which underwent reductive alkylation to give secondary amine **25**, allowing the key cyclisation cleavage step to be examined. When resin **25** was subjected to the conditions used in the solution model, refluxing resin **25** in THF with Pd(acac)$_2$ and dppe (1.5 eq. with respect to Pd), the desired pyrrolidine **18** was obtained in poor yields (5–18%, using Pd 5–50 mol%). However, when the amount of ligand was increased to 3.0 equivalents very efficient release of pyrrolidine **18** (81%) occurred using 10 mol% Pd(acac)$_2$. The yield decreased with lower catalyst loadings (40% yield using 5 mol% Pd), although it was gratifying to note that, even using 10 mol% Pd, the crude material obtained from the resin contained relatively little catalyst residue and other impurities by ^{1}H NMR.

To further examine the palladium-catalysed cyclisation strategy we undertook the synthesis of a small number of 2-substituted-4-methylene pyrrolidines (Scheme 5), introducing different substituents in both the imino–Sakurai and reductive alkylation steps. Reductive alkylation of amine **24**, using various aldehydes gave pyrrolidines **30a** (30%), **30b** (70%) and **30c** (15%) after submission to the cyclisation–cleavage conditions. The lower yields of **30a** and **30c** were due to the inefficiency of the reductive alkylation step rather then the cyclisation–cleavage step, which was evident from comparison of the ^{1}H NMR spectra of the crude cyclic (pyrrolidines) and acyclic products (released from the resins **29a** and **29c** by reduction using lithium borohydride). In each case the spectra of the crude pyrrolidines were cleaner than that of their reduced acyclic precursors.

Variation of the substituent R^1, which is introduced during the imino–Sakurai reaction was also examined. Reaction with 4-chlorobenzaldehyde provided two further examples of 4-methylene pyrrolidines **30d** and **30e** in yields of 70% and 31% respectively. However, pivaldehyde failed to react in the imino–Sakurai reaction and in this case the starting allylic silane resin **21** was recovered.

The observation that 4-methylene pyrrolidines were typically cleaner than the corresponding acyclic alcohols obtained from LiBH$_4$ cleavage of the same resin suggested that some of the by-products were not released under the cyclisation cleavage conditions. To test this theory further some of the immobilised intermediates (**22** and **24**) and potential by-products (the tertiary amine resin **31**, see Scheme 6) were subjected to the palladium-catalysed cleavage conditions. Interestingly, none of the cleavage reactions afforded significant amounts of cleaved material suggesting that incomplete Boc deprotection, incomplete reductive alkylation or over alkylation would not have a dramatic effect on the purity of the final 4-methylene pyrrolidines released from the resin. In order to establish whether the resin-bound material had been affected under the reaction conditions, the resin recovered after treatment of **22** with Pd(acac)$_2$–dppe was subjected to the LiBH$_4$ cleavage conditions and the crude filtrate examined by NMR (Scheme 7). Surprisingly, it was found that the major product **32** was due to reduction at the allylic position, effectively providing a traceless cleavage from the support.

It is not clear whether a stable, resin-bound π-allylpalladium intermediate had been formed during the attempted cyclisation cleavage of resin, and it was this that had undergone reduction, or whether some palladium had simply remained in the resin. Regardless of the exact reaction pathway, we felt that the palladium-catalysed reduction might provide a useful means of traceless release of propenyl-substituted compounds. Accordingly, resin **22** was treated with Pd(acac)$_2$ (20 mol%) and dppe (60 mol%) in the presence of various hydride sources. LiBH$_4$ gave inconsistent results, affording mixtures of alcohol **23** and propene derivative **32**, whereas formic acid or ammonium formate returned complex mixtures including Boc deprotected compounds. The use of Et$_3$SiH (10 eq.) did provide the propene derivative cleanly, but in poor yield (27%). The highest yield was obtained using Me$_4$NB(OAc)$_3$H as the source of hydride, affording **32** in 69%. No further effort was made to optimise the palladium-catalysed reductive cleavage reactions, although it should be noted that Schürer and Blechert have also recently reported the reductive release of propenyl derivatives from immobilised allylic carboxylate resins using triethylammonium formate in the presence of Pd(PPh$_3$)$_4$.[11]

The potential utility of allylic ester linkages had been demonstrated by the synthesis of a number of 4-methylene pyrrolidines, and the linkage had displayed good stability to acidic and Lewis-acidic conditions. However, the allylic ester underwent facile cleavage in the presence of nucleophilic reagents such as LiBH$_4$. To extend the utility of the methodology we desired a complementary strategy in which the linkage would be compatible with nucleophilic conditions leading us to consider the use of allyl phenyl ether linkers.

(ii) Synthesis of allylic amines

Allylic phenyl ethers display excellent resistance to nucleophilic cleavage, but are readily cleaved by various nucleophiles in the presence of catalytic palladium.[13,28,29] Therefore, allylic phenyl
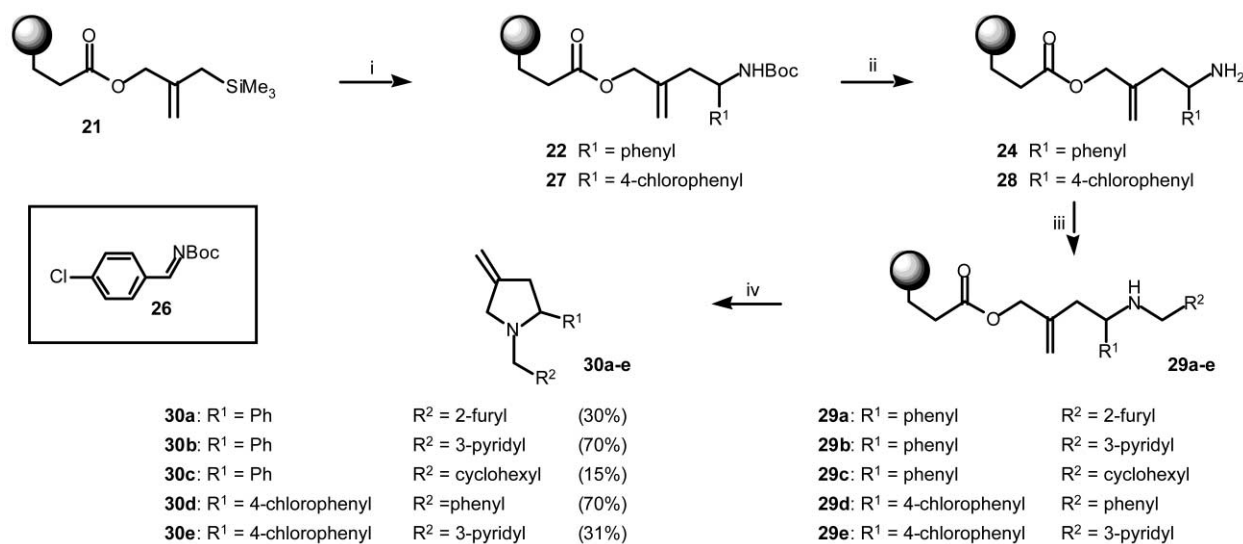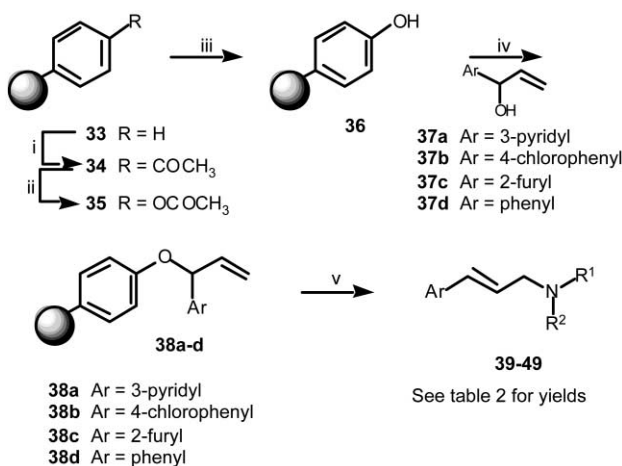
Scheme 5 *Reagents and conditions:* i) **14** or **26**, BF$_3$·OEt$_2$, CH$_2$Cl$_2$; ii) TFA, CH$_2$Cl$_2$; iii) R^{2}CHO, AcOH, Me$_4$NB(OAc)$_3$H, CH$_2$ClCH$_2$Cl; iv) Pd(acac)$_2$, dppe, THF.
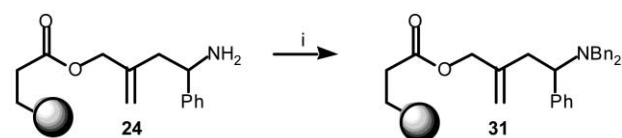
Scheme 6 *Reagents and conditions:* i) PhCHO, AcOH, Me$_4$NB-(OAc)$_3$H, CH$_2$ClCH$_2$Cl, 24 h.
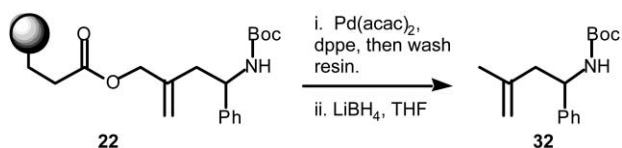
Scheme 7 Failed cyclisation cleavage of resin **22** and LiBH$_4$ treatment of recovered resin.

Scheme 8 *Reagents and conditions*: i) AcCl, AlCl$_3$, CS$_2$; ii) *m*-CPBA, CH$_2$Cl$_2$; iii) TMSOK, MeOH, CH$_2$Cl$_2$; iv) PPh$_3$, DEAD, alcohols **37a**–**d**; v) Pd(acac)$_2$ (5 mol%), dppe (10 mol%), amine, THF or Pd(PPh$_3$)$_4$ (10 mol%), amine, THF.

ether linker **38** would provide a mild means of generating electrophilic π-allyl palladium species that could be trapped with heteroatom or carbon nucleophiles. To demonstrate the principle we chose to investigate the palladium-catalysed release of allylic amines from hydroxypolystyrene resin (**36**, Scheme 8).

The synthesis of the starting resin began by acylation of polystyrene (**33**) under standard Friedel–Crafts conditions to give a resin-bound acetophenone **34**.[30,31] Treatment with

m-CPBA then afforded acetoxypolystyrene (**35**), which underwent clean conversion to hydroxypolystyrene (**36**) upon transesterification with potassium trimethylsilanolate and methanol.[32,33] The progress of the reactions was conveniently monitored using on-bead IR and no evidence was found to support the presence of the regioisomeric methylbenzoate resin. The loading of the resin **36** was estimated to be 1.8 mmol g^{-1} by the Fmoc method, after coupling with Fmoc-Ala–OH.[25]

Allylic alcohols, prepared by reaction of the corresponding aldehydes with vinyl Grignard,[34–36] were coupled to the hydroxypolystyrene (**36**) under Mitsunobu conditions to afford resins **38a**–**d**.[14,37,38] The presence of the secondary allylic ether **38d**, rather than the S$_N$2′ product, was supported by signals at 138.4 (CH), 116.4 (CH$_2$) and 81.1 (CH) ppm in the gel-phase ^{13}C NMR spectrum. Nucleophilic cleavage of allyl ether **38d** was first investigated with piperidine in the presence of Pd(acac)$_2$ and dppe (Scheme 8), and we were pleased to observe the desired allylic amine **39** with only a trace amount of the regioisomeric secondary amine (from integration of the crude ^{1}H NMR spectrum).

In order to optimise the cleavage conditions we investigated the effect of changing reaction parameters, including amount of catalyst, reaction time, amount of ligand, and amount of piperidine. Monitoring the release of product **39** over time by GC showed that the palladium-catalysed nucleophilic cleavage reaction was quite fast in refluxing THF, but that the product underwent a slower degradation under prolonged heating (3 to 8 hours). In addition, all attempted reactions at room temperature failed to afford any cleaved material and as expected, there was no reaction in the absence of Pd(acac)$_2$ and dppe. The intermolecular cleavage reaction of allyl phenyl ethers was less sensitive to Pd–ligand stoichiometry than the cyclisation reactions described above, with ratios of Pd–dppe between 1 : 1 and 1 : 3 providing comparable yields (using 5 eq. piperidine and 5 mol% Pd with the following Pd–dppe ratios: 1 : 1, 65%; 1 : 2, 70%; 1 : 3, 71% by GC). Further increase in the ratio of ligand to palladium (5 eq. of dppe relative to Pd) caused a dramatic decrease in the rate of the reaction as expected. The best conditions found gave a maximum yield (70% by GC, 52% isolated after flash chromatography) after 1 to 2 hours at reflux with 5 mol% Pd(acac)$_2$ and 10 mol% dppe using 1 to 5 equivalents of piperidine. No further product could be obtained by resubmitting the recovered resin to the cleavage conditions.

To investigate the scope of the palladium-catalysed nucleophilic cleavage process, reactions of four different primary and secondary amines with four resin-bound allylic ethers **38a**–**d** were investigated. The reactions of three of the substrates **38a**,

Table 2 Palladium-catalysed release of allylic amines (see Scheme 8)

| Entry	Resin–Ar	Amine	Catalyst[a]	Product	Yield (%)[b]
1	**38d**–Ph	Piperidine	a	**39**	53
2	**38d**–Ph	BnNH$_2$[d]	b	**40**	82
3	**38d**–Ph	BnEtNH	a	**41**	51
4	**38b**–p-Cl(C$_6$H$_4$)	BnNH$_2$[d]	b	**42**	79
5	**38b**–p-Cl(C$_6$H$_4$)	Piperidine	b	**43**	79
6	**38b**–p-Cl(C$_6$H$_4$)	BnEtNH	a	**44**	70
7	**38b**–p-Cl(C$_6$H$_4$)	NBS-pip[c]	a	**45**	52
8	**38a**–3-pyridyl	BnNH$_2$[d]	b	**46**	30
9	**38a**–3-pyridyl	Piperidine	a	**47**	53
10	**38a**–3-pyridyl	BnEtNH	a	**48**	51
11	**38a**–3-pyridyl	NBS-pip[c]	a	**49**	61

[a] Catalyst a = Pd(acac)$_2$–dppe; b = Pd(PPh$_3$)$_4$. [b] Yield based on the loading of the hydroxypolystyrene resin **36**, assuming quantitative conversion for solid-phase reactions. [c] NBS–pip = 1-(2-nitrobenzenesulfonyl)piperazine. [d] Crude products from the reactions using BnNH$_2$ contained 5 to 8% of the corresponding branched isomer (ratio by ^{1}H NMR).

38b and **38d** all afforded the desired products in acceptable yields under the optimised conditions (Table 2). However, nucleophilic cleavage of the furyl derivative **38c** gave only traces of the desired allylic amines, possibly due to failure of the prior Mitsunobu reaction of the more electron rich alcohol **37c**. When Pd(acac)$_2$ was used as the palladium source some of the crude cleavage reaction mixtures contained a by-product **50** (Fig. 1), arising from the attack by the acetylacetonate ligand, in varying quantities (0–10% depending on the nucleophilicity of the amine). Fortunately, the side reaction was easily avoided by using Pd(PPh$_3$)$_4$, which typically provided the allylic amines in superior yields. The cleavage reactions using a single equivalent of primary amines produced a significant amount of diallylated product **51**, whereas four equivalents of the primary amine gave predominantly the desired allylic amines. The reactions using BnNH$_2$ also gave small amounts of the branched isomer (5 to 8% by NMR), which was separated from the major isomers by chromatography.
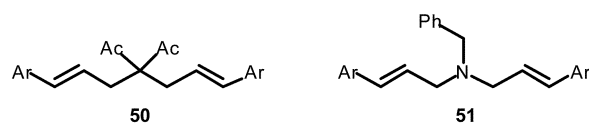
Fig. 1 By-products **50** and **51** from Pd(acac)$_2$ and BnNH$_2$ reactions respectively.

One of the problems often associated with nucleophilic cleavage strategies is separation of the product from any un-reacted nucleophile, and this was observed for products **39** to **49**, particularly when an excess of the primary amine was employed. In this case the use of scavenger resins greatly facilitated the work-up and purification (Fig. 2).[39] Selective scavenging of primary amines from secondary amine products was achieved using acetoacetoxy methacrylate (AAEM) resin **52**,[40,41] and secondary amines were removed from the reaction mixtures containing tertiary amine products using isocyanate resin **53**.[39] Once excess starting amines had been removed, a relatively simple column chromatography provided the pure allylic amines, although one could imagine using SPE methods to separate the basic products from residual ligand and catalyst impurities if higher throughput was required.
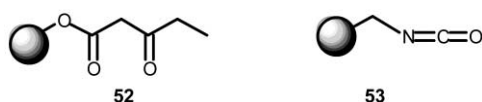
Fig. 2 AAEM and isocyanate scavenger resins.

Conclusions

The viability of a palladium-catalysed cyclisation–cleavage reaction has been demonstrated by the solid-phase synthesis of several pyrrolidines using an allylic carboxylate linker. During the synthesis of the cyclisation precursors **25** and **29a**–**e**, the imino–Sakurai reaction was used as the key C–C bond-forming step illustrating the compatibility of the linkage with Lewis-acidic conditions. It was also demonstrated that various intermediates and potential by-products along the route to the cyclisation precursor **25** were not cleaved efficiently under the cyclisation conditions, remaining attached to the resin. A facile synthesis of immobilised allylic phenyl ethers has also been described, providing a robust linkage that resists nucleophilic cleavage until catalytic palladium is added. The immobilised allylic phenyl ethers were used as precursors for the synthesis of a variety of secondary and tertiary allylic amines. Although pyrrolidines and allylic amines are important targets in their own right,[42] the cleavage strategies described here should be of more general utility in solid-phase synthesis given the vast scope of π-allyl palladium chemistry.[8]

Experimental

2-Methyl-3-phenylpropionic acid 2-trimethylsilanylmethylallyl ester (11)

Alcohol **9**[21] (1.44 g, 10.0 mmol) was dissolved in CH$_2$Cl$_2$ (25 mL) and cooled to 4 °C. Pyridine (890 μL, 11.0 mmol) was added followed by 2-methyl-3-phenylpropanoyl chloride (**10**)[18] (1.83 g, 10.0 mmol) in CH$_2$Cl$_2$ (10 mL). The reaction was stirred at rt for 35 min, during which time a fine white precipitate formed. The suspension was washed with aq. KHSO$_4$ (0.1 M, 2 × 15 mL), saturated aqueous NaHCO$_3$ (15 mL), brine (15 mL), dried (MgSO$_4$) and the solvents removed *in vacuo*. Purification by flash chromatography (4.0 × 10.0 cm silica) eluting with Et$_2$O : hexane (3 : 97) afforded the title compound as a colourless liquid (2.84 g, 9.8 mmol, 97%). v_{max} (film)/cm^{-1} 3063m, 2952s, 1734s, 1639m, 1604w, 1496m, 1248s, 1163s, 852s, 699s; ^{1}H NMR (300 MHz, CDCl$_3$) 7.32–7.16 (5H, m), 4.81 (1H, q, J = 1.5 Hz), 4.69 (1H, s), 4.42 (2H, s), 3.07 (1H, dd, J = 6.6, 13.2 Hz), 2.81 (1H, sextet, J = 7.3 Hz), 2.70 (1H, dd, J = 7.3, 13.2), 1.48 (2H, s), 1.20 (3H, d, J = 6.6 Hz), 0.05 (9H, s); ^{13}C NMR (75 MHz, CDCl$_3$) 175.91, 141.81, 139.47, 129.15, 128.53, 126.48, 109.61, 67.82, 41.70, 39.88, 23.56, 17.03, −1.30; m/z (CI) (rel. intensity) 290 (4[M]$^+$), 221 (9), 143 (19), 119 (21), 91 (63), 73 (100).

2-Methyl-3-phenylpropionic acid 2-(2-methoxycarbonylamino-2-phenylethyl)allyl ester (13)

A solution of methylcarbamate (87 mg, 1.15 mmol) and benzaldehyde dimethyl acetal (170 μL, 1.15 mmol) in CH$_2$Cl$_2$ (5 mL) was cooled to −78 °C. BF$_3$·OEt$_2$ (285 μL, 2.32 mmol) was added and the solution allowed to warm to rt. Stirring for 20 min afforded a yellow solution, which was cooled to −78 °C and a solution of allylic silane **11** (300 mg, 1.03 mmol) in

CH$_2$Cl$_2$ (1.0 mL) was added dropwise over 10 min. The reaction was stirred at −20 °C for 1 h and then allowed to warm to rt over 2 h. Saturated aqueous NaHCO$_3$ (10 mL) was added and the mixture extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (10 mL), dried (MgSO$_4$) and the solvents removed *in vacuo*. Purification by flash chromatography (4.0 × 7.0 cm silica) eluting with EtOAc : hexanes (20 : 80) afforded the title compound as a colourless gum (230 mg, 0.6 mmol, 60%). ν_{max} (film)/cm^{-1} 3331br, 2931s, 1731s, 1698s, 1656w, 1603w; ^{1}H NMR (300 MHz, CDCl$_3$) 7.42–7.15 (10H, m), 5.08 (1H, s), 4.96 (1H, s), 4.84 (1H, s), 4.46 (2H, s), 3.62 (3H, s), 3.05 (1H, dd, J = 6.6, 13.2 Hz), 2.82 (1H, sextet, J = 6.6 Hz), 2.70 (1H, dd, J = 7.3, 13.2 Hz), 2.51–2.33 (2H, m), 1.20 (3H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 175.87, 156.44, 142.36, 140.11, 139.39, 129.13, 128.80, 128.55, 127.63, 126.53, 126.30, 116.61, 66.73, 53.75, 52.34, 41.68, 40.63, 39.87, 17.09; m/z (ES) (rel. intensity) 404.5 (74[M + Na]$^+$), 382.5 (100[M + H]$^+$), 307.4 (27); HRMS (ES) m/z 404.1836 C$_{23}$H$_{27}$NO$_4$Na ([M + Na]$^+$) requires 404.1832.

2-Methyl-3-phenylpropionic acid 2-(2-*tert*-butoxycarbonyl-amino-2-phenylethyl)allyl ester (15)

A solution of *tert*-butylcarbamate (260 mg, 2.22 mmol) and benzaldehyde dimethyl acetal (333 μL, 2.22 mmol) in CH$_2$Cl$_2$ (6 mL) was cooled to −78 °C. BF$_3$·OEt$_2$ (550 μL, 4.48 mmol) was added and the solution allowed to warm to rt. Stirring for 20 min afforded a yellow solution, which was cooled to −78 °C whereupon a solution of the allylic silane 11 (560 mg, 1.93 mmol) in CH$_2$Cl$_2$ (3 mL) was added dropwise over 10 min. The reaction was stirred at −20 °C for 1 h and then allowed to warm to rt over 2 h. Saturated aqueous NaHCO$_3$ (7 mL) was added and the mixture extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (10 mL) and dried (MgSO$_4$) and the solvents removed *in vacuo*. Purification by flash chromatography (4.5 × 6.0 cm silica) eluting with EtOAc : hexane (10 : 90) afforded a cream solid (380 mg, 0.90 mmol, 47%). Mp 101–103 °C; ν_{max} (soln)/cm^{-1} 3059m, 2976m, 1727s, 1701s; ^{1}H NMR (300 MHz, CDCl$_3$) 7.37–7.16 (10H, m), 5.06 (1H, s), 4.86 (1H, br), 4.50–4.39 (2H, m), 3.05 (1H, dd, J = 6.6, 12.9 Hz), 2.80 (1H, sextet, J= 6.6 Hz), 2.69 (1H, dd, J= 6.6, 13.2 Hz), 2.49–2.32 (2H, m), 1.41 (9H, br s), 1.20 (3H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 175.79, 155.29, 142.87, 140.24, 139.41, 129.13, 128.73, 128.54, 127.45, 126.51, 126.30, 116.28, 79.84, 66.73, 53.34, 41.68, 40.89, 39.88, 28.48, 17.07; m/z (ES) (rel. intensity) 462.2 (21[M + K]$^+$), 446.3 (89[M + Na]$^+$), 424.3 (100[M + H]$^+$), 368.2 (94), 324.1 (17); anal. calcd. for C$_{26}$H$_{33}$NO$_4$ C, 73.73; H, 7.85; N, 3.31; Found C, 73.62; H, 7.85; N, 3.32%.

2-Methyl-3-phenylpropionic acid 2-(2-amino-2-phenylethyl)allyl ester (16)

TFA (700 μL) was added to a solution of Boc-protected amine 15 (308 mg, 0.73 mmol) in CH$_2$Cl$_2$ (7 mL). The resulting orange solution was stirred at rt for 2.5 h. Saturated aqueous NaHCO$_3$ (20 mL) was added and the mixture extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (MgSO$_4$) and the solvent removed *in vacuo* to afford a yellow oil (220 mg, 0.68 mmol, 93%). ν_{max} (film)/cm^{-1} 3370m, 3212w, 3027s, 2934s, 1730s, 1653m, 1603m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.38–7.17 (10H, m), 5.06 (1H, s), 5.01 (1H, s), 4.51 (2H, s), 4.07 (1H, dd, J = 9.6, 5.0 Hz), 3.06 (1H, dd, J = 6.6, 12.5 Hz), 2.81 (1H, sextet, J = 7.4 Hz), 2.70 (1H, dd, J = 7.4, 12.5 Hz), 2.39 (1H, dd, J = 5.2, 14.0 Hz), 2.29 (1H, dd, J = 8.8, 14.0 Hz), 1.20 (3H, d, J = 7.4 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 175.89, 145.81, 141.20, 139.41, 129.14, 128.66, 128.56, 127.32, 126.54, 126.45, 115.63, 66.56, 53.98, 44.11, 41.74, 39.90, 17.13; m/z (ES) (rel. intensity) 324.2 (100[M + H]$^+$); HRMS (ES) m/z 346.1777 C$_{21}$H$_{25}$NO$_2$Na ([M + Na]$^+$) requires 346.1778.

2-Methyl-3-phenylpropionic acid 2-(2-benzylamino-2-phenylethyl)allyl ester (17)

AcOH (30 μL) in DCE (1.0 mL), followed by Me$_4$N$^+$(AcO)$_3$BH$^-$ (79 mg, 0.3 mmol), was added to a solution of amine 16 (50 mg, 0.15 mmol) and benzaldehyde (15 μL, 0.15 mmol) in DCE (2.0 mL). The solution was stirred at rt for 17 h. Additional quantities of Me$_4$N$^+$(AcO)$_3$BH$^-$ (79 mg, 0.3 mmol) and AcOH (30 μL) were added and the reaction stirred for a further 3 days. Saturated aqueous NaHCO$_3$ (7 mL) was added and the mixture extracted with CH$_2$Cl$_2$ (4 × 10 mL). The combined organic layers were washed with brine (7 mL), dried (MgSO$_4$) and the solvent removed *in vacuo*. Purification by flash chromatography (3.2 × 4.5 cm silica) eluting with Et$_2$O : hexane (1 : 4) afforded a colourless oil (47 mg, 0.11 mmol, 76%). ν_{max} (film)/cm^{-1} 3438br, 3060m, 3025m, 2931m, 1731s, 1650m, 1602m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.38–7.16 (15H, m), 5.02 (1H, d, J = 5.1 Hz), 4.94 (1H, s), 4.43 (2H, s), 3.78 (1H, dd, J = 5.9, 8.1 Hz), 3.68 (1H, d, J = 13.2 Hz), 3.50 (1H, d, J = 13.2 Hz), 3.05 (1H, dd, J = 6.6, 12.5 Hz), 2.78 (1H, sextet, J = 7.3 Hz), 2.69 (1H, dd, J = 7.4, 12.5 Hz), 2.42–2.35 (2H, m), 1.19 (3H, d, J = 7.3 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 175.82, 145.85, 141.03, 140.60. 139.40, 129.13, 128.64, 128.54, 128.29, 127.39, 127.07, 126.53, 115.52, 66.46, 60.11, 51.68, 43.00, 41.69, 39.85, 17.09; m/z (ES) (rel. intensity) 414.6 (100[M + H]$^+$); HRMS m/z (ES) 414.2420 C$_{28}$H$_{32}$NO$_2$ ([M + H]$^+$) requires 414.2428.

1-Benzyl-4-methylene-2-phenylpyrrolidine (18)

18 From 2-methyl-3-phenylpropionic acid 2-(2-benzylamino-2-phenylethyl)allyl ester (17). Pd(acac)$_2$ (5.9 mg, 19.4 μmol, 10 mol%) and dppe (11.6 mg, 29.1 μmol, 15 mol%) were added to a solution of 17 (80 mg, 0.19 mmol) in THF (4 mL). The yellow solution was stirred, under nitrogen, at reflux for 13 h after which additional quantities of Pd(acac)$_2$ (5.9 mg, 19.4 μmol, 10 mol%) and dppe (11.6 mg, 29.1 μmol, 15 mol%) were added and the reaction heated at reflux for a further 12 h. The reaction was allowed to cool to rt and saturated aqueous NaHCO$_3$ (4 mL) added. The mixture was extracted with CH$_2$Cl$_2$ (5 × 8 mL) and the combined organic layers were washed with brine (5 mL), dried (MgSO$_4$) and the solvent removed *in vacuo*. Purification by flash chromatography (2.0 cm × 3.0 cm), eluting with an Et$_2$O : hexane (2 : 98) mixture, afforded a colourless oil (15 mg, 60.2 μmol, 33%). ν_{max} (film)/cm^{-1} 3060m, 3026m, 2923m, 2787s, 1662m, 1601m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.53–7.24 (10H), 4.86 (2H, s), 3.88 (1H, d, J = 13.1 Hz), 3.66 (1H, d, J = 13.4 Hz), 3.57 (1H, dd, J = 6.6, 10.2 Hz), 3.04 (1H, d, J = 13.1 Hz), 2.93 (1H, dddd, J = 1.1, 2.7, 5.3, 13.5 Hz), 2.85 (1H, dddd, J = 1.5, 1.5, 6.6, 15.9 Hz), 2.51 (1H, ddq, J = 4.1, 10.2, 15.9 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 147.13, 142.74, 139.45, 128.70, 128.32, 127.74, 127.54, 126.98, 104.84, 69.82, 58.86, 58.19, 42.98; m/z (ES) (rel. intensity): 250.3 (100[M + H]$^+$); HRMS m/z (ES) 250.1592 C$_{18}$H$_{20}$N ([M + H]$^+$) requires 250.1596.

18 From 3-polystyrylpropionic acid 2-(2-benzylamino-2-phenylethyl)allyl ester (25). Pd(acac)$_2$ (2.7 mg, 8.9 μmol), dppe (10.6 mg, 26.6 μmol) and resin 25 (200 mg, 104 μmol based on loading of 20) in THF (4 mL) was heated at reflux, under nitrogen, for 12 hours. The resin was collected by filtration and washed with CH$_2$Cl$_2$ (30 mL) and the filtrate solvent was removed *in vacuo*. Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with an Et$_2$O : hexane mixture (2 : 98), afforded a colourless oil (21 mg, 84 μmol, 81%). Spectroscopic data were identical with that reported above.

3-Polystyrylpropionic acid (20)

Diethyl malonate (5.0 mL, 33.0 mmol) was added dropwise, over 20 min, to a suspension of NaH (1.33 g of a 60% dispersion in mineral oil, 33.0 mmol) in DMF (35 mL). After

hydrogen evolution ceased Merrifield resin (1 mol equivalents of Cl g^{-1}, 2% cross-linked with DVB, 5.0 g) was added and the reaction heated at 60 °C for 14 h. The reaction was cooled to rt and the resin collected by filtration, washed with CH_2Cl_2, MeOH, H_2O, MeOH and CH_2Cl_2 (2 × 20 mL each) and dried *in vacuo* for 2 h (50 °C). This afforded diethyl 2-polystyryl-methylmalonate as a white solid (5.04 g). v_{max} (on-bead)/cm^{-1} 3025w, 2979w, 2920m, 1726s, 1601w; ^{1}H-MAS NMR 4.10 (br, –$CO_2CH_2CH_3$), 3.60 (br, –CH), 1.17 (br, –$CO_2CH_2CH_3$). A suspension of the functionalised polystyrene **20** (1.0 g, 1.0 mmol theoretical) in THF (20 mL) and aq. KOH (2 M, 2.0 mL) was heated at reflux for 15 h. The reaction was allowed to cool to rt and the resin was collected by filtration washing with H_2O, MeOH, Et_2O and CH_2Cl_2 (2 × 20 mL each). The resin was suspended in THF (20 mL) and aq. HCl (2 M, 2.0 mL) was added. The reaction was heated at reflux for 2.5 h. After cooling to rt the resin was collected by filtration, washing with H_2O, MeOH, Et_2O and CH_2Cl_2 (2 × 20 mL each) and dried *in vacuo* for 2 h (50 °C). This afforded a white solid (0.95 g) with an estimated loading of 0.6 mmol g^{-1}.[25] v_{max} (on-bead)/cm^{-1} 3023w, 2919m, 1708s, 1600m.

3-Polystyrylpropionic acid 2-trimethylsilanylmethylallyl ester (21)

The acid resin **20** (1.0 g, 0.6 mmol) was suspended in CH_2Cl_2 (12 mL) and stirred for 5 min before DMAP (488 mg, 4.0 mmol), DIC (628 μL, 4.0 mmol) and alcohol **9**[21] (576 mg, 4.0 mmol) were added. After 17 h at rt the resin was collected by filtration, washed with CH_2Cl_2 and MeOH (100 mL each) and dried *in vacuo* for 2 h (50 °C). This afforded a white solid (0.95 g). v_{max} (on-bead)/cm^{-1} 3027m, 2922s, 1734s, 1601m; ^{1}H-MAS NMR 4.89 (br), 4.75 (br), 4.45 (br), 1.50 (br s), 0.00 (br s); ^{13}C NMR (Gel-phase, 75 MHz, $CDCl_3$) 172.55, 141.78, 109.63, 67.77, 23.70, −1.28.

3-Polystyrylpropionic acid 2-(2-*tert*-butoxycarbonylamino-2-phenylethyl)allyl ester (22)

A solution of *tert*-butylcarbamate (5.6 g, 48.0 mmol) and benzaldehyde dimethylacetal (7.2 mL, 48.0 mmol) in CH_2Cl_2 (50 mL) was cooled to −78 °C, then BF_3·OEt_2 (960 μL, 8.0 mmol) was added and the solution allowed to warm to rt. After 30 min the resulting yellow solution was transferred, *via* a cannula, to a suspension of the resin **21** (4.0 g) in CH_2Cl_2 (20 mL) at 0 °C, and the resulting mixture was allowed to warm to rt and stirred for 4.5 h. The resin was collected by filtration, washed with CH_2Cl_2 and MeOH (200 mL each) and dried *in vacuo* for 2 h (50 °C) to afford a white solid (4.35 g). v_{max} (on-bead)/cm^{-1} 3061w, 3025m, 2919s, 2848w, 1731s, 1705s, 1651w, 1601m; ^{1}H-MAS NMR (selected signals) 5.08 (br), 4.92 (br), 4.85 (br), 4.50 (br), 2.45 (br), 1.35 (br s).

2-(2-*tert*-Butoxycarbonylamino-2-phenylethyl)propen-1-ol (23)

To an ice-cooled pre-swollen suspension of resin **22** (200 mg, 104 μmol based on loading of **20**) in THF (3.0 mL) was added $LiBH_4$ (1.0 mL of a 2 M solution in THF, 2.0 mmol) followed by MeOH (80 μL, 2.0 mmol).The ice bath was removed and the reaction stirred at rt overnight. The resin was collected by filtration and washed with CH_2Cl_2 (30 mL) and MeOH (30 mL). Removal of the filtrate solvent *in vacuo* afforded a white solid, which was dissolved in a mixture of saturated aqueous $NaHCO_3$ solution (5 mL) and CH_2Cl_2 (10 mL). The organic layer was separated, re-extracting the aqueous layer with CH_2Cl_2 (5 × 10 mL) and the combined organic layers were washed with brine (10 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude product purified by flash chromatography (1.5 × 6.0 cm silica), eluting with Et_2O : hexane (40 : 60), to afford the title compound as white solid (26 mg, 94 μmol, 90% based on loading of resin **20**). Mp 132–

134 °C; v_{max} (soln)/cm^{-1} 3604w, 3435m, 2931m, 1709s, 1604w; ^{1}H NMR (300 MHz, $CDCl_3$) 7.32–7.18 (5H, m), 5.06 (1H, s), 4.99–4.80 (2H, br m), 4.88 (1H, s), 4.03 (2H, s), 2.54 (1H, dd, J = 14.6, 5.9 Hz), 2.43 (1H, dd, J = 14.6, 8.8 Hz), 2.23 (1H, br s), 1.36 (9H, s); ^{13}C NMR (100 MHz, $CDCl_3$) 155.89, 145.34, 142.51, 128.78, 127.50, 126.41, 114.38, 79.90, 66.45, 53.78, 41.95, 28.50; *m/z* (ES) (rel. intensity): 278.3 (77[M + H]$^+$), 223.3 (13), 222.1 (100); anal. calcd. for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.32; H, 8.40; N, 5.02%.

3-Polystyrylpropionic acid 2-(2-amino-2-phenylethyl)allyl ester (24)

TFA (2 mL) was added to a suspension of resin **22** (200 mg) in CH_2Cl_2 (2 mL). After 20 min the resin was collected by filtration and then suspended in a solution of *N*,*N*-diisopropyl-amine (500 μL) in CH_2Cl_2 (5 mL). After 10 min the resin was collected by filtration, washed with CH_2Cl_2 (50 mL) and dried *in vacuo* for 2 h (50 °C) affording the title resin as a white solid (192 mg). v_{max} (on-bead)/cm^{-1} 3027m, 2917m, 2847w, 1726s, 1651w; ^{1}H-MAS NMR (selected signals) 5.10 (br), 5.03 (br), 4.55 (br s), 4.10 (br), 2.50–2.28 (br m).

3-Polystyryl-propionic acid 2-(2-benzylamino-2-phenyl-ethyl)-allyl ester (25)

Benzaldehyde (2.3 mL, 21.5 mmol) and AcOH (1.0 mL) were added to a suspension of the resin **24** (2.15 g) in DCE (50 mL). After stirring at rt overnight the resin was collected by filtration, then suspended in a solution of $Me_4NB(AcO)_3H$ (4.5 g, 17.2 mmol) in AcOH (1.0 mL) and DCE (50 mL). The suspension was stirred at rt for 24 h and then the resin was collected by filtration. After washing with CH_2Cl_2 (250 mL) and MeOH (100 mL) the resin was dried *in vacuo* for 2 h (50 °C) affording a white solid (2.28 g). v_{max} (on-bead)/cm^{-1} 3027m, 2917s, 1731s, 1595m; ^{1}H-MAS NMR (selected signals) 5.02 (br s), 4.91 (br s), 4.86 (br s), 3.80 (br), 3.68 (br), 3.50 (br), 2.40 (br).

3-Polystyryl-propionic acid 2-[2-*tert*-butoxycarbonylamino-2-(4-chlorophenyl)-ethyl]-allyl ester (27)

To a solution of *tert*-butylcarbamate (1.4 g, 12.0 mmol) and 4-chlorobenzaldehyde (1.69 g, 12.0 mmol) in CH_2Cl_2 (15 mL) at −78 °C was added BF_3·OEt_2 (240 μL, 2.0 mmol) and the resulting solution allowed to warm to rt. After 30 min the resulting yellow solution was transferred, *via* a cannula, to a suspension of the resin **21** (1.0 g) in CH_2Cl_2 (5 mL) at 0 °C. The mixture was allowed to warm to rt and stirred for 6 h. The resin was collected by filtration, washed with CH_2Cl_2 and MeOH (100 mL each) and dried *in vacuo* for 2 h (50 °C) to afford a white solid (1.06 g). v_{max} (on-bead)/cm^{-1} 3024m, 2921m, 1715s, 1602m.

3-Polystyrylpropionic acid 2-[2-amino-2-(4-chlorophenyl)-ethyl]allyl ester (28)

A suspension of resin **27** (850 mg) in TFA (8 mL) and CH_2Cl_2 (8 mL) was stirred at rt for 30 min, then the resin was collected by filtration and washed with a solution of *N*,*N*-diisopropyl-amine (10 mL) in CH_2Cl_2 (80 mL) followed by CH_2Cl_2 (200 mL). The resin was dried *in vacuo* for 2 h (50 °C) affording a white solid (807 mg). v_{max} (on-bead)/cm^{-1} 3027m, 2922m, 2852w, 1730s, 1600m.

3-Polystyrylpropionic acid 2-[2-(2-furylmethyl)amino-2-phenyl-ethyl]allyl ester (29a)

Using the procedure described for **25** using the following amounts: 2-furaldehyde (360 μL, 4.3 mmol), resin **24** (600 mg) in DCE (10 mL), $Me_4NB(AcO)_3H$ (1.63 g, 6.2 mmol) in AcOH (200 μL) and DCE (10 mL) afforded a white solid (634 mg). v_{max} (on-bead)/cm^{-1} 3026m, 2926m, 2851w, 1729s, 1599m.

3-Polystyrylpropionic acid 2-[2-(3-pyridylmethyl)amino-2-phenylethyl]allyl ester (29b)

Using the procedure described for **25** using the following amounts: 3-pyridinecarboxaldehyde (410 µL, 4.3 mmol), AcOH (200 µL), resin **24** (600 mg) in DCE (10 mL), Me$_4$NB(AcO)$_3$H (1.63 g, 6.2 mmol) in AcOH (200 µL) and DCE (10 mL) afforded a white solid (629 mg). v_{max} (on-bead)/cm^{-1} 3027m, 2922m, 2852w, 1731s, 1595s.

3-Polystyrylpropionic acid 2-[2-(cyclohexylmethyl)-2-phenylethyl]allyl ester (29c)

Using the procedure described for **25** using the following amounts: cyclohexane carboxaldehyde (360 µL, 3.0 mmol), AcOH (100 µL), resin **24** (600 mg), Me$_4$NB(AcO)$_3$H (0.8 g, 3.0 mmol) in DCE (10 mL) afforded a white solid (641 mg). v_{max} (on-bead)/cm^{-1}3031m, 2916s, 2846m, 1729s, 1604m.

3-Polystyryl-propionic acid 2-[2-benzylamino-2-(4-chlorophenyl)-ethyl]-allyl ester (29d)

Using the procedure described for **25** using the following amounts: benzaldehyde (380 µL, 3.5 mmol), AcOH (160 µL), resin **28** (350 mg) in DCE (8 mL), Me$_4$NB(AcO)$_3$H (730 mg, 2.8 mmol) in AcOH (160 µL) and DCE (8 mL) afforded a white solid (359 mg). v_{max} (on-bead)/cm^{-1} 3027m, 2917m, 1730s (C=O), 1600m.

3-Polystyrylpropionic acid 2-[2-(3-pyridylmethyl)amino-2-(4-chlorophenyl)ethyl]allyl ester (29e)

Using the procedure described for **25** using the following amounts: 3-pyridinecarboxaldehyde (240 µL, 2.5 mmol), AcOH (160 µL), resin **28** (350 mg) in DCE (8 mL), Me$_4$NB(AcO)$_3$H (950 mg, 3.6 mmol) in AcOH (160 µL) and DCE (8 mL) afforded a white solid (371 mg). v_{max} (on-bead)/cm^{-1}3027m, 2922s, 1725s, 1595m.

General procedure for pyrrolidines 30a–e.

A mixture of Pd(acac)$_2$ (5.5 mg, 18.0 µmol), dppe (21.3 mg, 53.5 µmol) and resin **29a–e** (500 mg, 0.26 mmol based on loading of resin **20**) in THF (10 mL) was heated at reflux for 12 h. The resin was collected by filtration and washed with CH$_2$Cl$_2$ (50 mL). The filtrate solvent was removed *in vacuo* to afford the crude product.

1-(2-Furylmethyl)-4-methylene-2-phenylpyrrolidine (30a).

Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with CH$_2$Cl$_2$, afforded a colourless oil (19 mg, 79 µmol, 30% from **20**). v_{max} (film)/cm^{-1}3054m, 1644m, 1597m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.48–7.25 (6H, m), 6.31 (1H, dd, $J = 1.7, 3.2$ Hz), 6.13 (1H, d, $J = 3.2$ Hz), 4.91 (1H, br s), 4.88 (1H, br s), 3.76 (2H, d, $J = 14.4$ Hz), 3.56 (1H, dd, $J = 6.7, 10.3$ Hz), 3.27 (1H, d, $J = 14.4$ Hz), 3.13 (1H, br d, $J = 14.0$ Hz), 2.81 (1H, br dd, $J = 6.7, 16.2$ Hz), 2.51 (1H, m); ^{13}C NMR (100 MHz, CDCl$_3$) 152.84, 146.73, 142.34, 128.98, 128.05, 127.90, 110.45, 108.53, 105.37, 69.08, 58.83, 49.37, 43.02; m/z (ES) (rel. intensity) 240.3 (100[M + H]$^+$); HRMS m/z (ES) 240.1389 C$_{16}$H$_{18}$NO ([M + H]$^+$) requires 240.1388.

1-(3-pyridylmethyl)-4-methylene-2-phenylpyrrolidine (30b).

From resin **29b** (175 mg, 91 µmol). Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with an Et$_2$O : hexane mixture (60 : 40), afforded a colourless oil (16 mg, 64 µmol, 70% from **20**). v_{max} (film)/cm^{-1} 3023m, 1652w, 1605m; ^{1}H NMR (300 MHz, CDCl$_3$) 8.51 (2H, br s), 7.65 (1H, d, $J = 8.1$ Hz), 7.50 (2H, d, $J = 7.3$ Hz), 7.43–7.28 (3H, m), 7.24 (1H, dd, $J = 4.1, 7.0$ Hz), 4.89 (2H, s), 3.84 (1H, d, $J = 13.2$ Hz), 3.64 (1H, d, $J = 13.3$ Hz), 3.62 (1H, dd, $J = 6.6, 10.0$ Hz), 3.11 (1H, d, $J = 13.4$ Hz), 2.95 (1H, dd, $J = 2.0, 13.2$ Hz), 2.86 (1H,

dd, $J = 6.5, 15.9$ Hz), 2.53 (1H, ddq, $J = 10.3, 16.2, 2.2$ Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 150.03, 148.57, 146.24, 142.13, 136.48, 134.76, 128.81, 127.77, 123.48, 105.32, 69.93, 58.74, 55.41, 42.79; m/z (ES) (rel. intensity) 251.2 (100[M + H]$^+$); HRMS m/z (ES) 251.1543 C$_{17}$H$_{19}$N$_2$ ([M+H]$^+$) requires 251.1543.

1-(Cyclohexylmethyl)-4-methylene-2-phenylpyrrolidine (30c).

From resin **29c** (500 mg, 260 µmol). Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with Et$_2$O : hexane (3 : 97), afforded a colourless oil (10 mg, 39 µmol, 15% from **20**). v_{max} (film)/cm^{-1} 3012w, 2934m, 2840m, 1648w, 1602m; ^{1}H NMR (400 MHz, CDCl$_3$) 7.43–7.21 (5H, m), 4.92 (1H, s), 4.87 (1H, s), 3.90 (1H, d, $J = 13.9$ Hz), 3.36 (1H, dd, $J = 6.5, 10.5$ Hz), 2.85 (1H, br d, $J = 13.9$ Hz), 2.76 (1H, dd, $J = 6.5, 16.4$ Hz), 2.43–2.33 (1H, m), 2.27 (1H, t, $J = 11.4$ Hz), 2.07 (1H, br d, $J = 13.4$ Hz), 1.88 (1H, dd, $J = 3.5, 11.4$ Hz), 1.73–1.59 (3H, m), 1.53 (1H, br d, $J = 12.4$ Hz), 1.48–1.33 (1H, m), 1.29–1.02 (3H, m), 0.85–0.64 (2H, m); ^{13}C NMR (100 MHz, CDCl$_3$) 147.99, 143.72, 128.70, 127.95, 127.45, 104.68, 70.82, 61.84, 59.58, 43.45, 37.20, 32.42, 31.64, 27.25, 26.66, 26.45; m/z (ES) (rel. intensity) 256.2 (100[M + H]$^+$); HRMS (ES) m/z 256.2069 C$_{18}$H$_{26}$N ([M + H]$^+$) requires 256.2065.

1-Benzyl-2-(4-chlorophenyl)-4-methylenepyrrolidine (30d).

From resin **29d** (200 mg, 102 µmol). Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with Et$_2$O : hexane (2 : 98), afforded a colourless oil (20 mg, 70 µmol, 70% from **20**). v_{max} (film)/cm^{-1} 2987m, 1638m, 1605m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.51–7.40 (1H, m), 7.39–7.15 (8H, m), 4.87 (2H, s), 3.83 (1H, d, $J = 13.4$ Hz), 3.64 (1H, d, $J = 13.9$ Hz), 3.55 (1H, dd, $J = 6.5, 9.9$ Hz), 3.03 (1H, d, $J = 13.4$ Hz), 2.94 (1H, d, $J = 13.9$ Hz), 2.83 (1H, dd, $J = 6.5, 16.4$ Hz), 2.55–2.40 (1H, m); ^{13}C NMR (75 MHz, CDCl$_3$) 146.54, 141.40, 139.15, 133.08, 129.07, 128.88, 128.68, 128.39, 127.10, 105.08, 69.07, 58.76, 58.13, 42.95; m/z (ES) (rel. intensity) 284.2 (100[M + H]$^+$); HRMS m/z (ES) 284.1203 C$_{18}$H$_{19}$ClN ([M + H]$^+$) requires 284.1206.

1-(3-Pyridylmethyl)-4-methylene-2-(4-chlorophenyl)-pyrrolidine (30e).

From resin **29e** (200 mg, 102 µmol). Purification by flash chromatography (1.5 × 5.0 cm silica), eluting with Et$_2$O : hexane (60 : 40), afforded a colourless oil (9 mg, 32 µmol, 31% from **20**). v_{max} (film)/cm^{-1} 3029m, 1621m, 1597m; ^{1}H NMR (300 MHz, CDCl$_3$) 8.53 (2H, br s), 7.66 (1H, d, $J = 8.1$ Hz), 7.44 (2H, d, $J = 6.8$ Hz), 7.34 (2H, d, $J = 6.8$ Hz), 7.24 (1H, dd, $J = 4.4, 7.4$ Hz), 4.90 (2H, s), 3.81 (1H, d, $J = 14.0$ Hz), 3.62 (1H, d, $J = 14.0$ Hz), 3.57 (1H, dd, $J = 6.6, 10.3$ Hz), 3.10 (1H, d, $J = 14.0$ Hz), 2.94 (1H, br dd, $J = 2.2, 14.0$ Hz), 2.86 (1H, br dd, $J = 6.6, 16.2$ Hz), 2.45 (1H, ddq, $J = 10.3, 16.2, 3.0$ Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 150.30, 148.82, 146.58, 142.50, 136.73, 135.03, 129.73, 128.01, 123.73, 105.54, 70.19, 59.04, 55.70, 43.10; m/z (ES) (rel. intensity) 285.1 (100[M + H]$^+$); HRMS (ES) m/z 285.1160 C$_{17}$H$_{18}$ClN$_2$ ([M + H]$^+$) requires 285.1159.

tert-Butyl 3-methyl-1-phenylbut-3-enylcarbamate (32)

Pd(acac)$_2$ (1.5 mg, 4.9 µmol, 20 mol%), dppe (5.8 mg, 14.6 µmol, 60 mol%) and Me$_4$NB(AcO)$_3$H (63 mg, 240 µmol) were added to a solution of **22** (50 mg, 26 µmol) in THF (2 mL). The yellow solution was stirred, under nitrogen, at room temperature for 18 h. The resin was collected by filtration and washed with CH$_2$Cl$_2$ (70 mL) and CH$_3$OH (30 mL) and the filtrate solvent removed *in vacuo*. Purification by flash chromatography (1.5 × 5.0 cm silica), using a CH$_2$Cl$_2$: hexane (1 : 1) eluent system, afforded a white solid (4.8 mg, 18.0 µmol, 69%). Mp 106-109 °C; v_{max} (soln)/cm^{-1} 3386m, 2975m, 2930m, 1681s, 1518s, 1251m, 1173s, 1018m; ^{1}H NMR (300 MHz, CDCl$_3$) 7.28–7.14 (5H, m), 4.76–4.68 (3H, m), 4.66 (1H, s), 2.42–2.27 (2H, m), 1.65 (3H, s), 1.21 (9H, s); ^{13}C NMR (100 MHz, CDCl$_3$) 154.24, 140.90, 127.46, 126.06, 125.09, 112.77, 78.43,

51.85, 44.81, 27.31, 20.97; m/z (ES) (rel. intensity): 262.2 (100[M + H]$^+$); HRMS m/z (ES) 284.1622 $C_{16}H_{23}NO_2$ ([MNa]$^+$) requires 284.1621.

Polystyryl acetone (34)

Following the method described by Fréchet and Nuyens,[31] acetyl chloride (11.5 mL, 12.6 g, 160 mmol) was added drop-wise to a suspension of polystyrene resin (33, 1% DVB cross-linked, 20.6 g) and finely ground $AlCl_3$ (21.5 g, 160 mmol) in carbon disulfide (200 mL) at 0 °C under nitrogen. The suspension was heated at reflux for 5.5 h. The resin was allowed to cool to rt, collected by filtration and washed with CH_2Cl_2, H_2O (**CAUTION!** Vigourous reaction with the residual $AlCl_3$), aq. HCl (2 M), H_2O, DMF, MeOH and CH_2Cl_2 (500 mL of each). Drying the resin *in vacuo* (50 °C) for 2 h afforded a yellow solid (21.78 g). v_{max} (on-bead)/cm^{-1} 1679s (C=O), 1605m; ^{1}H-MAS NMR 2.55 (br s, –COCH$_3$).

Polystyryl acetate (35)

m-CPBA (70.0 g, ~0.22 mol) was added to a suspension of resin **34** (21.18 g) in CH_2Cl_2 (200 mL) at rt and stirred for 1 day. The resin was collected by filtration, washed with CH_2Cl_2, MeOH, H_2O, MeOH, CH_2Cl_2 (200 mL of each) and dried *in vacuo* (50 °C) for 2 h to give a pale yellow solid (21.77 g). v_{max} (on-bead)/cm^{-1} 1759s (C=O), 1505m, 1368m, 1194s, 1166s; ^{1}H-MAS NMR 2.28 (br s, –O$_2$CCH$_3$).

Hydroxypolystyrene resin (36)

CH_2Cl_2 (160 mL) and MeOH (60 mL) were added to a mixture of the resin-bound acetate **35** (18.0 g) and TMSOK (13.2 g, 0.10 mol) at rt under nitrogen. The suspension turned brown and was stirred overnight. The resin was collected by filtration, washed with CH_2Cl_2, MeOH, H_2O, aq. HCl (2 M), H_2O, MeOH, CH_2Cl_2 (200 mL of each) and dried *in vacuo* (50 °C) for 2 h. This afforded a beige solid (15.48 g) with an estimated loading of 1.5 mmol g^{-1}.[25] v_{max} (on-bead)/cm^{-1} 1600m, 1511s, 1455m, 1238s, 1171m, 830s.

1-(3-Pyridyl)allyl polystyryl ether (38a)

1-(Pyridin-3-yl)allylalcohol **37a**[34] (3.05 g, 22.6 mmol) and tri-phenylphosphine (5.92 g, 22.6 mmol) were added to a suspension of hydroxypolystyrene (**36**, 2.04 g, 3.06 mmol) in THF (30 mL) under nitrogen. The suspension was cooled to 0 °C and after 10 min DEAD (3.60 mL, 3.98 g, 22.9 mmol) was added dropwise. The ice-bath was removed and the resulting orange suspension was stirred at rt overnight. The resin was collected by filtration, washed with CH_2Cl_2, DMF, MeOH and CH_2Cl_2 (150 mL of each) and dried *in vacuo* (50 °C) for 2 h to afford the title product as a brown solid (2.61 g). v_{max} (on-bead)/cm^{-1} 3191m, 1662m, 1612m, 1511s.

1-(4-Chlorophenyl)allyl polystyryl ether (38b)

The procedure as described for **38a** using following amounts: 1-(4-chlorophenyl)allylalcohol **37b**[36] (4.21 g, 25.0 mmol), tri-phenylphosphine (7.52 g, 28.7 mmol), hydroxypolystyrene (**36**, 2.50 g, 3.75 mmol) and DEAD (4.5 mL, 4.98 g, 28.6 mmol) afforded a beige solid (3.55 g). v_{max} (on-bead)/cm^{-1} 3193w, 1665m, 1610m, 1511s.

1-Phenylallyl polystyryl ether (38d)

The procedure as described for **38a** using the following amounts: 1-phenyl-allylalcohol **37d**[36] (3.83 g, 28.5 mmol), tri-phenylphosphine (7.46 g, 28.4 mmol), hydroxypolystyrene **36** (2.52 g, 3.75 mmol) and DEAD (4.50 mL, 4.98 g, 28.6 mmol) afforded a beige solid (3.16 g). v_{max} (on-bead)/cm^{-1} 3373m, 3234w, 1667m, 1610m, 1511s; ^{13}C NMR (Gel-phase, 75 MHz, CDCl$_3$) 138.4 (PhCH-), 116.4 (CH$_2$), 81.1 (–CH=CH$_2$).

General method for amines 39, 41, 44, 45, 47 and 48

Pd(acac)$_2$ (3.1 mg, 10.2 µmol), dppe (8.1 mg, 20.3 µmol) were added to a suspension of resin **38a–d** (150 mg, 180–195 µmol) in THF (3 mL). The amine (200 µmol) was added and the reaction heated at reflux, under nitrogen, for 1.5 h. The resin was collected by filtration, washed with CH_2Cl_2 (50 mL) and the filtrate concentrated *in vacuo*.

1-(3-Phenylallyl)piperidine (39)

From resin **38d**. Purification by column chromatography (9.0 × 1.5 cm silica), using an Et$_2$O : hexane (1 : 1) eluent system, afforded a yellow oil (21 mg, 104 µmol, 53%). The spectroscopic details were consistent with those reported in the literature.[43]

Benzylethyl-(3-phenylallyl)amine (41)

From resin **38d**. Purification by column chromatography (9.0 × 1.5 cm silica), using an CH_2Cl_2 : hexane (3 : 1) eluent system, afforded a yellow oil (25 mg, 99 µmol, 51%). ^{1}H NMR (300 MHz, CDCl$_3$) 7.40–7.24 (10H, m), 6.55 (1H, d, $J = 15.4$ Hz), 6.32 (1H, dt, $J = 15.9$, 6.5 Hz), 3.66 (2H, s), 3.27 (2H, d, $J = 6.5$ Hz), 2.61 (2H, q, $J = 7.4$ Hz), 1.12 (3H, t, $J = 7.4$ Hz); ^{13}C NMR (100 MHz, CDCl$_3$) 139.87, 137.64, 132.77, 129.41, 128.94, 128.61, 128.13, 127.71, 127.26, 126.68, 58.12, 56.11, 47.64, 12.28; m/z (ES) (rel. intensity): 252.1 (100[M + H]$^+$).

Benzyl-[3-(4-chlorophenyl)allyl]ethyl amine (44)

From resin **38b**. Purification by column chromatography (8.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (3 : 97) eluent system, afforded a yellow oil (36 mg, 126 µmol, 70%). v_{max} (film)/cm^{-1} 2962m, 1629m, 1599m, 1579m, 1506s, 1056s, 847s; ^{1}H NMR (400 MHz, CDCl$_3$) 7.38–7.24 (9H, m), 6.49 (1H, d, $J = 15.9$ Hz), 6.27 (1H, dt, $J = 15.9$, 6.5 Hz), 3.64 (2H, s), 3.25 (2H, dd, $J = 6.5$ Hz, 1.0 Hz), 2.59 (2H, q, $J = 7.0$ Hz), 1.11 (3H, t, $J = 7.0$ Hz); ^{13}C NMR (100 MHz, CDCl$_3$) 139.65, 135.91, 133.05, 131.13, 129.12, 128.84, 128.40. 127.63, 127.05, 58.00, 55.86, 47.55, 12.08; m/z (ES) (rel. intensity) 287.9 (35), 286.0 (100[M + H]$^+$); HRMS m/z (ES) 286.1369 $C_{18}H_{21}ClN$ ([M + H]$^+$) requires 286.1363.

1-[3-(4-Chlorophenyl)allyl]-4-(2-nitrobenzenesulfonyl) piperazine (45)

From resin **38b**. Purification by column chromatography (9.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (4 : 96) eluent system, afforded a yellow oil (39 mg, 93 µmol, 52%). v_{max} (film)/cm^{-1} 2956m, 1605m, 1589s, 1520s, 1362s, 1347s, 1165s, 861s, 769s; ^{1}H NMR (400 MHz, CDCl$_3$): 7.96–7.93 (1H, m), 7.80–7.60 (3H, m), 7.28–7.25 (4H, m), 6.47 (1H, d, $J= 15.9$ Hz), 6.15 (1H, dt, $J= 15.9$ Hz, 6.5 Hz), 3.27–3.24 (4H, m), 3.15 (2H, d, $J = 6.5$ Hz), 2.58–2.55 (4H, m); ^{13}C NMR (100 MHz, CDCl$_3$) 148.71, 135.29, 133.91, 133.50, 132.61, 131.60, 131.09, 128.92, 127.72, 126.47, 124.25, 60.62, 52.55, 46.13; m/z (ES) (rel. intensity) 421.9 (100[M + H]$^+$); HRMS m/z (ES) 422.0936; $C_{19}H_{21}$-ClN_3O_4S ([M + H]$^+$) requires 422.0941.

3-(3-Piperidin-1-yl-propenyl)pyridine (47)

From resin **38a**. Purification by column chromatography (7.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (5 : 95) eluent system, afforded an orange oil (21 mg, 104 µmol, 53%). v_{max} (film)/cm^{-1} 2890w, 1625w, 1608m, 1585m, 1498m, 1374m, 817s; ^{1}H NMR (400 MHz, CDCl$_3$) 8.56 (1H, br s), 8.43 (1H, br s), 7.68 (1H, dt, $J = 8.0$, 1.5 Hz), 7.21 (1H, dd, $J = 7.9$, 5.0 Hz), 6.48 (1H, d, $J = 15.9$ Hz), 6.36 (1H, dt, $J = 15.9$, 6.5 Hz), 3.13 (2H, dd, $J = 6.5$, 1.0 Hz), 2.43 (4H, br s), 1.64–1.56 (4H, m), 1.47–1.42 (2H, m); ^{13}C NMR (100 MHz, CDCl$_3$) 148.48, 148.32, 132.64, 129.75, 129.00, 123.43, 61.70, 54.67, 25.93, 24.25; m/z (ES) (rel. intensity) 203.0 (100[M + H]$^+$); HRMS m/z (ES) 203.1547 $C_{13}H_{18}N_2$ ([M + H]$^+$) requires 203.1548.

Benzyl-ethyl-(3-pyridin-3-yl-allyl)amine (48)

From resin **38a**. Purification by column chromatography (9.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (2 : 98) eluent system, afforded a yellow oil (25 mg, 100 µmol, 51%). v_{max} (film)/cm^{-1} 2987m, 1612w, 1599m, 1584m, 1501s, 1038s, 873s, 765s; ^{1}H NMR (400 MHz, CDCl$_3$) 8.58 (1H, d, J = 1.0 Hz), 8.45 (1H, dd, J = 4.5, 1.0 Hz), 7.68 (1H, dt, J = 7.9, 2.0 Hz), 7.39–7.21 (6H, m), 6.52 (1H, d, J = 16.2 Hz), 6.36 (1H, dt, J = 16.2, 6.2 Hz), 3.64 (2H, s), 3.97 (2H, dd, J = 6.2, 1.0 Hz), 2.59 (2H, q, J= 7.0 Hz), 1.11 (3H, t, J = 7.0 Hz); ^{13}C NMR (100 MHz, CDCl$_3$) 148.37, 148.26, 139.50, 132.81, 132.65, 130.68, 128.90, 128.45, 128.24, 126.90, 123.39, 57.91, 55.76, 47.50, 11.94; m/z (ES) (rel. intensity): 252.1 (100[M + H]$^+$); HRMS m/z (ES) 253.1706 $C_{17}H_{21}N_2$ ([M + H]$^+$) requires 253.1705.

1-(2-Nitrobenzenesulfonyl)-4-(3-pyridin-3-yl-allyl)piperazine (49)

Pd(acac)$_2$ (3.0 mg, 9.8 µmol), dppe (7.7 mg, 19.3 µmol) were added to a suspension of resin **38a** (152 mg, 197 µmol based on loading of resin **36**) in THF (3 mL). 1-(2-Nitrobenzene-sulfonyl)piperazine (103 mg, 380 µmol) was added and the reaction heated at reflux, under nitrogen, for 3 h. The resin was collected by filtration, washed with CH_2Cl_2 (60 mL) and the filtrate solvent removed *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (7 mL) and isocyanate resin **53** (230 mg, 0.25 mmol) was added. The suspension was stirred at rt for 1 h, a further quantity of isocyanate resin **53** (80 mg, 0.09 mmol) was added and stirring continued for another 2 h. The resin was collected by filtration, washed with CH_2Cl_2 (80 mL) and the filtrate solvent removed *in vacuo*. Purification by column chromatography (7.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (3 : 97) eluent system, afforded a yellow oil (47 mg, 121 µmol, 61%). v_{max} (film)/cm^{-1} 2947m, 1602m, 1584s, 1525s, 1356s, 1347s, 1159s, 833s, 762s; ^{1}H NMR (400 MHz, CDCl$_3$) 8.56 (1H, br s), 8.44 (1H, d, J = 3.5 Hz), 7.94 (1H, dd, J = 7.0, 2.0 Hz), 7.71–7.42 (4H, m), 7.23 (1H, dd, J = 7.9, 4.4 Hz), 6.50 (1H, d, J = 15.9 Hz), 6.24 (1H, dt, J = 15.9, 6.5 Hz), 3.34–3.31 (4H, m), 3.18 (2H, d, J = 6.5 Hz), 2.58–2.55 (4H, m); ^{13}C NMR (100 MHz, CDCl$_3$) 149.07, 148.55, 134.16, 133.35, 132.64, 131.86, 131.35, 130.57, 128.37, 124.53, 123.93, 60.80, 52.80, 46.27; m/z (ES) (rel. intensity) 389.1 (98 [M + H]$^+$), 215.1 (41), 213.1 (100); HRMS m/z (ES) 389.1287; $C_{18}H_{21}N_4O_4S$ ([M + H]$^+$) requires 389.1284.

Benzyl-(3-phenyl-allyl)amine (40)

Pd(PPh$_3$)$_4$ (12.1 mg, 10.5 µmol) and benzylamine (107 mg, 0.84 mmol) were added to a suspension of resin **38d** (150 mg, 195 µmol based on the loading of resin **36**) in THF (3 mL). The reaction was heated at reflux under nitrogen for 2 h. The resin was collected by filtration, washed with CH_2Cl_2 (60 mL) and the filtrate solvent removed *in vacuo*. Purification by column chromatography (6.0 × 1.5 cm silica) eluting with MeOH : CH_2Cl_2 (1 : 99) afforded a yellow oil (36 mg, 161 µmol, 82%), which contained the title compound **40** and the branched isomer in a ratio of 12 : 1 (NMR). The spectroscopic data for both compounds were consistent with those reported in the literature.[44,45]

Benzyl-[3-(4-Chlorophenyl)allyl]amine (42)

The procedure as described for **40** using following amounts: Pd(PPh$_3$)$_4$ (11.0 mg, 9.5 µmol), benzylamine (81 mg, 760 µmol) and resin **38b** (151 mg, 181 µmol). Purification by column chromatography (6.0 × 1.5 cm silica), using an Et$_2$O : hexane (40 : 60) eluent system, afforded a yellow oil (37 mg, 144 µmol, 79%). IR and ^{1}H NMR data were consistent with those reported in the literature.[45] ^{13}C NMR (100 MHz, CDCl$_3$) 140.09, 135.64, 132.95, 130.15, 129.13, 128.69, 128.47, 128.20, 127.46, 127.06, 53.39, 51.07; m/z (ES) (rel. intensity) 299.1

(39[M + K]$^+$), 260.1 (35), 258.1 (100[M + H]$^+$); HRMS m/z (ES) 258.1047; $C_{16}H_{17}ClN$ ([M+H]$^+$) requires 258.1050.

1-[3-(4-Chlorophenyl)allyl)]piperidine (43)

The procedure as described for **40** using following amounts : Pd(PPh$_3$)$_4$ (11.0 mg, 9.5 µmol), piperidine (15.8 mg, 190 µmol) and resin **38b** (151 mg, 181 µmol). Purification by column chromatography (6.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (5 : 95) eluent system, afforded a yellow oil (34 mg, 144 µmol, 79%). The spectroscopic details have been reported previously.[9]

Benzyl-(3-pyridin-3-yl-allyl)amine (46)

Pd(PPh$_3$)$_4$ (11.3 mg, 9.8 µmol) and benzylamine (84 mg, 0.78 mmol) were added to a suspension of resin **38a** (150 mg, 195 µmol) in THF (3 mL). The reaction was heated at reflux, under nitrogen, for 2 h. The resin was collected by filtration, washed with CH_2Cl_2 (60 mL) and the filtrate solvent removed *in vacuo* to afford an orange oil, which was dissolved in CH_2Cl_2 (5 mL) and AAEM resin **52** (195 mg, 0.59 mmol) was added. The suspension was stirred at rt for 2 h. The resin was collected by filtration, washed with CH_2Cl_2 (80 mL) and the filtrate solvent removed *in vacuo*. Purification by column chromatography (6.0 × 1.5 cm silica), using a MeOH : CH_2Cl_2 (2 : 98) eluent system, afforded a yellow oil (13 mg, 58 µmol, 30%). v_{max} (film)/cm^{-1} 3427w, 2964m, 1614w, 1586m, 1498s, 1052s, 864s, 774s; ^{1}H NMR (400 MHz, CDCl$_3$) 8.59 (1H, br s), 8.47 (1H, d, J = 3.5 Hz), 7.69 (1H, dt, J = 7.9, 1.5 Hz), 7.37–7.24 (6H, m), 6.55 (1H, d, J = 16.2 Hz), 6.40 (1H, dt, J= 16.2, 5.8 Hz), 3.84 (2H, s), 3.45 (2H, d, J = 5.8 Hz); ^{13}C NMR (75 MHz, CDCl$_3$) 132.93, 132.85, 130.36, 129.16, 129.07, 128.76, 128.60, 128.55, 127.55, 127.31, 58.53, 56.38; m/z (ES) (rel. intensity) 225.1 (100[M + H]$^+$); HRMS m/z (ES) 225.1390 $C_{15}H_{16}N_2$ ([M + H]$^+$) requires 225.1392.

Acknowledgements

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