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Stereoselective synthesis of *N*-protected pyrrolidines via Pd-catalyzed reactions of γ-(*N*-acylamino) alkenes and γ-(*N*-Boc-amino) alkenes with aryl bromides

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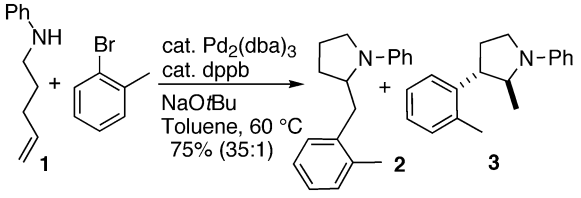
Abstract—The stereoselective synthesis of *N*-acyl- and *N*-Boc-protected pyrrolidines via Pd-catalyzed reactions of γ-(*N*-acylamino) alkenes and γ-(*N*-Boc-amino) alkenes with aryl bromides is described. These reactions effect formation of two bonds in a single operation and proceed with generally high levels of diastereoselectivity. In contrast to previously described reactions of γ-(*N*-arylamino) alkenes, these transformations proceed in high yield and high regioselectivity with both electron-rich and electron-deficient aryl bromides as well as vinyl bromide substrates.

1. Introduction

A diverse array of biologically active molecules contain substituted pyrrolidine cores.[1] Many strategies for the synthesis of substituted pyrrolidines employ intramolecular C–N bond-forming reactions for the construction of the heterocyclic ring.[2] However, very few methods allow for simultaneous intramolecular C–N bond formation and intermolecular formation of a C1′ carbon–carbon bond;[3] existing methods are limited in scope and/or require harsh reaction conditions or toxic reagents.

We recently described a new method for the stereoselective synthesis of *N*-aryl pyrrolidines via Pd-catalyzed reactions of γ-(*N*-arylamino) alkenes with aryl bromides (Eq. 1).[4,5] This transformation effects the formation of two bonds (one C–C bond and one C–N bond) along with upto two stereocenters in a single step. This method is effective for the preparation of a number of *N*-aryl pyrrolidine derivatives (e.g., **2**), and substrates bearing substituents at C-1 or C-3 are converted to the corresponding *cis*-2,5-disubstituted- or *trans*-2,3-disubstituted pyrrolidines in good yield with excellent (>20:1) diastereoselectivity. In most reactions small amounts of regioisomeric products **3** are formed in addition to the desired product **2**, although ratios of **2**:**3** are typically ≥10:1.



(1)

Despite the utility of this transformation for the synthesis of *N*-aryl pyrrolidines, these products cannot be easily transformed into other *N*-substituted (or unsubstituted) pyrrolidine derivatives, as cleavage of the aryl C–N bond is not readily accomplished.[6] In addition, reactions of **1** or related γ-*N*-(*p*-methoxyphenyl) aminoalkenes provide only moderate yields of the desired product when vinyl bromides or electron-deficient aryl bromides are used as coupling partners due to competing *N*-arylation or *N*-vinylation of the relatively electron-rich nitrogen.

To address the limitations described above, we have developed conditions to effect the conversion of *N*-acyl and *N*-Boc protected γ-aminoalkenes into the corresponding pyrrolidines. The Boc and acyl protecting groups can be readily cleaved under relatively mild conditions,[7] and also serve to minimize competing *N*-arylation side reactions by decreasing the nucleophilicity of the nitrogen atom. Our preliminary studies on the scope and limitations of these transformations are described herein.

Keywords: Stereoselective synthesis; Pyrrolidines; Diastereoselectivity; Palladium; Arylhalide.
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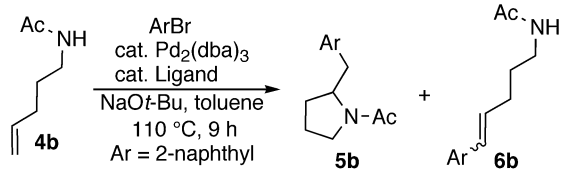
2. Results and discussion

2.1. Optimization studies

In order to develop a new route to *N*-protected pyrrolidines, we initially examined Pd-catalyzed reactions of 2-bromonaphthalene with *N*-4-pentenylacetamide (**4b**). Our previous studies on Pd/phosphine-catalyzed reactions of γ-(*N*-arylamino) alkenes with aryl bromides showed that the nature of the phosphine ligand had a pronounced effect on the yield of the desired pyrrolidine product.[4] Thus, **4b** was treated with 2-bromonaphthalene and NaO*t*Bu in the presence of a catalytic amount of $Pd_2(dba)_3$ and various phosphine ligands. The reactions were heated at 110 °C for 9 h, quenched, and assayed by GC. As shown in Table 1, dpe-phos[8] gave the highest yield in the conversion of **4b** to **5b**. The use of rigid bidentate phosphine ligands generally provides higher yields than monodentate ligands. However, subsequent studies on the scope of these reactions revealed that the optimal bidentate ligand for a given transformation is somewhat dependent on substrate structure. The use of dppe,[8] dppb,[8] or nixantphos[8] provides the highest yields in some reactions (see below), and in some cases $Pd(OAc)_2$ was found to provide slightly better results than $Pd_2(dba)_3$.

Table 1. Ligand effects



Ligand	% Conversion	GC ratio		
		5b	**6b**	Other[a]
PPh_3	59	34	6	19
P(*o*-tol)$_3$[b]	35		23	3
Dppb	61	53	8	—
Dppf	91	76	10	5
Xantphos	95	84	7	4
Dpe-phos	96	85	5	6

[a] Small amounts of other side products including regioisomers of **6b** and *N*-arylated compounds were also formed.
[b] The reaction was conducted for 20 h.

The effect of *N*-protecting groups on the efficiency of these transformations was probed by conducting reactions of 2-bromonaphthalene with various *N*-protected 5-amino-1-pentene derivatives in the presence of NaO*t*Bu and a catalytic amount of $Pd_2(dba)_3$/dpe-phos (Table 2). These transformations afford the desired pyrrolidine **5** along with Heck-type[9] side product **6** and/or *N*-arylated[10] side product **7**. As expected, the nature of the *N*-protecting group has a large impact on the ratio of **5**:**6**:**7**. In most cases, as the electron-withdrawing ability of the protecting group increased, the amount of *N*-arylation decreased but the amount of Heck olefination increased. For example, the reaction of a substrate bearing an *N*-phenyl substituent (**1**) afforded a 75:25 ratio of **5**:**7**, whereas the analogous transformation of a *N*-benzoyl substituted amine (**4e**) provided a 58:42 ratio of **5**:**6**; the formation of **7** was not observed. The best results were obtained in reactions of *N*-acyl and *N*-Boc substituted substrates **4b** and **4c**, which were converted to the desired pyrrolidines in good yield with high regioselectivity. In contrast, the Pd-catalyzed reactions of 2-bromonaphthalene with *N*-benzyl substituted substrate **4a** and *N*-(*p*-trifluoromethylbenzoyl) substituted derivative **4f** failed to provide detectable amounts of pyrrolidine products.[11]

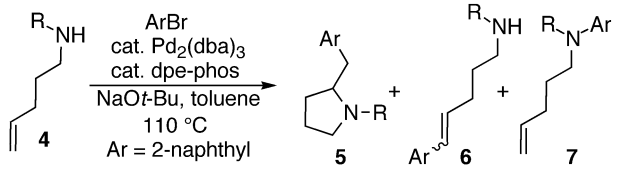
The effect of other parameters such as solvent and base was also examined in several different reactions. In general, weak bases such as K_2CO_3 or Cs_2CO_3 were less effective than NaO*t*Bu; their use resulted in the formation of large amounts of Heck-type products. Toluene was found to be the optimal solvent although ethereal solvents such as DME and dioxane provided satisfactory results in many instances. Use of THF as solvent in reactions of Boc-protected substrates led to diminished product yields due to base-induced cleavage of the boc-group from the substrate.[12,13]

2.2. Scope and limitations

Following our initial optimization studies we examined reactions of *N*-acyl-protected substrate **4b** and *N*-Boc-protected substrate **4c** with a variety of different aryl and vinyl bromides. As shown in Table 3, the transformations proceed in good yield with electron-neutral (entries 1, 2, and 5) and electron-poor (entries 3 and 6) aryl bromides. Use of an electron-rich aryl bromide afforded a moderate yield of the desired product, although partial oxidation of the *N*-acyl pyrrolidine product to the corresponding 2,3-dihydropyrrole occurred under the reaction conditions (entry 7).[14] In all cases examined a single product regioisomer was formed. The major side products observed in reactions of **4b** and **4c** derive from competing Heck arylation or *N*-arylation of the substrate. The competing Heck arylation is more problematic in reactions of acetate protected substrate **4b**.

Most transformations are efficiently catalyzed by mixtures of $Pd_2(dba)_3$ and dpe-phos. However, use of dppe as ligand provided higher yields for some substrate combinations

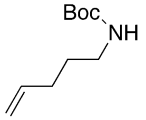
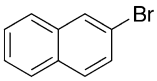
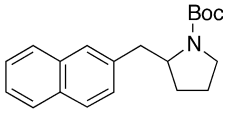
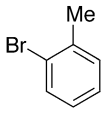
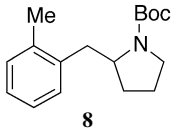
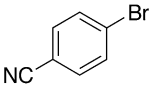
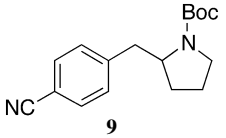
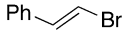
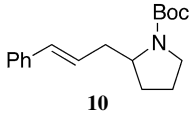
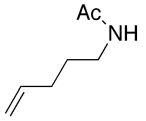
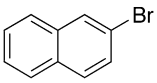
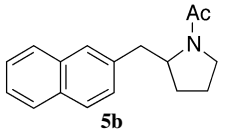
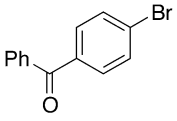
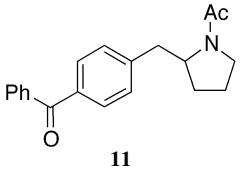
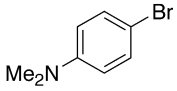
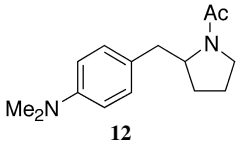
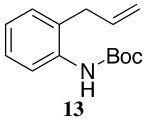
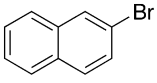
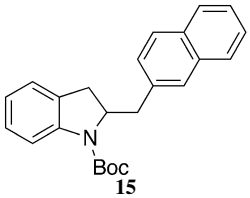
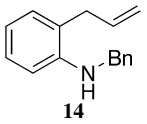
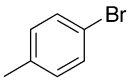
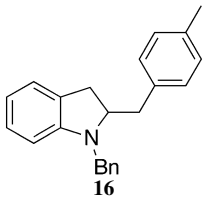
Table 2. *N*-Substitutent effects



N-Substituent	GC ratio (isolated yield)		
	5	**6**	**7**
R=Bn[a] (**4a**)	—	40[b]	34
R=Ph (**1**)	75 (63%)[c–e]	—	25
R=Ac[a] (**4b**)	88 (72%)	12	—
R=Boc[a] (**4c**)	82 (77%)	4[b]	—
R=4-MeO-Bz (**4d**)	77 (63%)	23	—
R=Bz (**4e**)	58 (48%)	42	—
R=4-F_3C-Bz[a] (**4f**)	—	89[b]	—

[a] Other minor, unidentified side products were also observed.
[b] Mixtures of alkene regioisomers were obtained.
[c] GC yield.
[d] This product was obtained as a 15:1 mixture of regioisomers.
[e] Use of 1,4-bis(diphenylphosphino) butane (dppb) as ligand provided a 94% isolated yield of **5** as a 25:1 mixture of regioisomers. See Ref. 4.

Table 3. Synthesis of *N*-protected pyrrolidines and indolines[a]

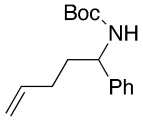
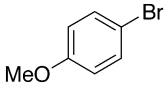
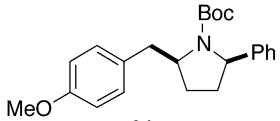
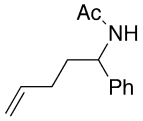
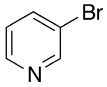
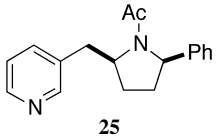
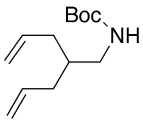
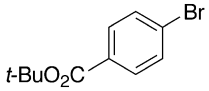
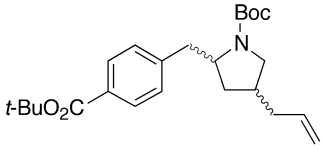
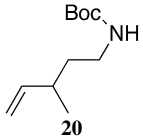
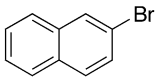
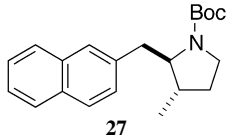
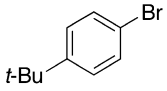
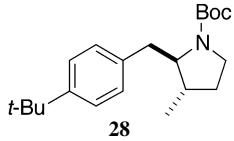
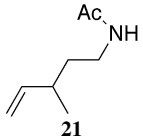
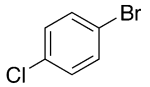
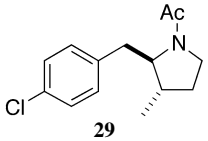
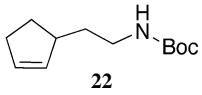
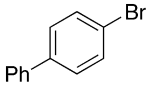
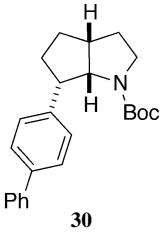
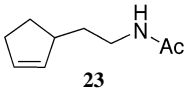
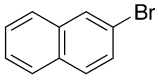
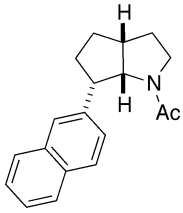
Entry	Amine	Aryl bromide	Catalyst	Product	Yield
1	 **4c**		$Pd(OAc)_2$/dpe-phos	 **5c**	77[b]
2			$Pd_2(dba)_3$/dpe-phos	 **8**	81
3			$Pd_2(dba)_3$/dppb	 **9**	71
4			$Pd(OAc)_2$/dppe	 **10**	75[b]
5	 **4b**		$Pd_2(dba)_3$/dpe-phos	 **5b**	72
6			$Pd_2(dba)_3$/dppe	 **11**	78
7			$Pd_2(dba)_3$/xantphos	 **12**	67[c]
8	 **13**		$Pd_2(dba)_3$/dpe-phos	 **15**	50
9	 **14**		$Pd_2(dba)_3$/nixantphos	 **16**	48

[a] Conditions: 1.0 equiv substrate, 1.1–1.2 equiv ArBr, 1.2–2.0 equiv NaO*t*Bu, 2 mol% Pd (1 mol% $Pd_2(dba)_3$ or 2 mol% $Pd(OAc)_2$), 2–4 mol% ligand, toluene (0.25 M), 105 °C.
[b] The reaction was conducted at 65 °C.
[c] This material contained ca 15% of the corresponding 2,3-dihydropyrrole (1-[5-(4-dimethylaminobenzyl)-2,3-dihydropyrrol-1-yl]ethanone).

by minimizing competing *N*-arylation or *N*-vinylation processes (Table 3, entries 4 and 6).[10] The reaction of the electron-rich *N*,*N*-dimethyl-4-bromoaniline was most efficiently catalyzed by a mixture of $Pd_2(dba)_3$ and xantphos (entry 7).

The results obtained in the reactions of **4b** and **4c** described above contrast with related transformations of *N*-phenyl substituted substrate **1**. For example, the Pd-catalyzed reaction of **4b** with 4-bromobenzophenone proceeded in 78% isolated yield (entry 6), whereas the analogous reaction of **1** provided only a modest 45% yield.[4] Additionally, the reaction of **1** with β-bromostyrene proceeds in low yield due to competing *N*-vinylation,[15,16] but the reaction of **4c** with this vinyl bromide affords the desired product in 75% isolated yield (entry 4).

Table 4. Stereoselective synthesis of *N*-protected pyrrolidines[a]

Entry	Amine	Aryl bromide	Catalyst	Product	dr[b]	Yield
1	 **17**		$Pd_2(dba)_3$/dppb	 **24**	>20:1	60
2	 **18**		$Pd_2(dba)_3$/dppb	 **25**	>20:1	82
3	 **19**		$Pd_2(dba)_3$/dpe-phos	 **26**	3:1	72
4	 **20**		$Pd(OAc)_2$/dpe-phos	 **27**	>20:1	66[c,d]
5			$Pd(OAc)_2$/dpe-phos	 **28**	>20:1	59[c,d]
6	 **21**		$Pd_2(dba)_3$/dpe-phos	 **29**	>20:1	61[c]
7	 **22**		$Pd(OAc)_2$/xantphos	 **30**	>20:1	53[d]
8	 **23**		$Pd_2(dba)_3$/nixantphos	 **31**	>20:1	61[e,f]

[a] Conditions: 1.0 equiv substrate, 1.1–1.2 equiv ArBr, 1.2–2.0 equiv NaO*t*Bu, 2 mol% Pd (1 mol% $Pd_2(dba)_3$ or 2 mol% $Pd(OAc)_2$), 2–4 mol% ligand, toluene (0.25 M), 105 °C.
[b] Diastereomeric ratios described in Table 4 represent ratios of diastereomers for the isolated material upon which the yield is based. These ratios may differ from diastereomeric ratios observed in crude reaction mixtures as noted below.
[c] A 10:1 ratio of diastereomers was observed in the crude reaction mixture.
[d] The reaction was conducted at 65 °C.
[e] The reaction was conducted using 2.5 mol% $Pd_2(dba)_3$.
[f] The reaction was stopped at 77% conversion after two days at 110 °C.

The synthesis of *N*-protected indolines from *N*-allylaniline derivatives was also briefly examined (Table 3, entries 8 and 9). Treatment of *N*-Boc-2-allylaniline (**13**) with 2-bromonaphthalene under our optimized reaction conditions afforded a 50% yield of the desired indoline product **15**. The moderate yield in this transformation was mainly due to competing base-induced cleavage of the Boc-group from the substrate[12] and/or base-induced olefin isomerization of the substrate.[17] In contrast to the reactions of *N*-benzyl protected aliphatic amine substrates, *N*-benzyl-2-allylaniline (**14**) was converted to the *N*-benzyl-2-benzylindoline **16** in 48% yield. The major side product obtained

in this reaction was *N*-benzyl-2-methylindole, which presumably derives from Pd-catalyzed oxidative amination of the substrate.[18] Attempts to transform *N*-acyl-2-allylaniline to the corresponding indoline were unsuccessful; competing Heck arylation was observed.

The stereoselective synthesis of disubstituted pyrrolidines bearing *N*-Boc or *N*-acyl groups was achieved via Pd-catalyzed carboamination of substrates **17–21** bearing substituents on the tether between the alkene and the nitrogen (Table 4). Comparable diastereoselectivities were obtained with both *N*-acyl and *N*-Boc protected substrates, and the nature of the aryl bromide did not have a large effect on diastereoselectivity in the transformations examined. The synthesis of *trans*-2,3-disubstituted pyrrolidines (entries 4–6) and *cis*-2,5-disubstituted pyrrolidines (entries 1 and 2) was effected in good yield with good levels of diastereoselectivity.[19,20] In contrast, the reaction of **19** with *tert*-butyl-(4-bromo)benzoate afforded a 2,4-disubstituted pyrrolidine product in 72% yield, but with only modest (ca 3:1) diastereoselectivity (entry 3). The reactions of **17–21** proceed with similar diastereoselectivities and significantly higher regioselectivities than transformations of the analogous *N*-aryl substituted substrates.[4]

The yields obtained in reactions of substrates **17–18** bearing substituents at the 1- or 3-position were slightly lower than yields obtained in reactions of unsubstituted substrates **4b–c**. The diminished yields are due in part to competing base-induced cleavage of the Boc group from the more hindered substrates.[12] The rate of Boc cleavage is relatively rapid in THF at 65 °C and toluene at 110 °C, whereas little or no cleavage occurs in toluene at 65 °C. Competing Heck arylation also becomes more problematic as steric hindrance at C-1 or C-3 increases. The Heck side products formed in reactions of *N*-acylated substrates were more difficult to separate from the desired product than the side products obtained in analogous reactions of Boc-protected substrates, which also led to slightly diminished yields.

The transformations of substrates **22–23** bearing internal cyclic alkenes proceeded in moderate yield with excellent regioselectivity and diastereoselectivity (>20:1) to afford products **30** and **31** (entries 7 and 8).[21] In both reactions the observed diastereomer derives from *syn* addition of the nitrogen and the aryl group across the double bond.[20] The yields and regioselectivities in these transformations sharply contrast with those obtained in the reaction of the analogous *N*-(4-methoxyphenyl) substituted substrate, which afforded a mixture of two regioisomeric products along with an *N*-arylated side product and a side product derived from oxidative amination of the substrate.[4]

2.3. Proposed catalytic cycle and mechanism

A proposed catalytic cycle for this transformation is shown (Fig. 1). The catalytic cycle presumably commences with oxidative addition of the aryl bromide to the Pd(0) catalyst to afford Pd(Ar)(Br) complex **32**. Reaction of this complex with the γ-aminoalkene substrate in the presence of NaO*t*Bu likely results in the formation of palladium aryl(amido) complex **33**,[10] which undergoes insertion of the alkene into the Pd–N bond[4,22] followed by C–C bond-forming reductive elimination[23] of the resulting intermediate **34** to afford the observed pyrrolidine with concomitant regeneration of the Pd(0) catalyst.

This mechanism described above is analogous to that previously proposed for reactions of γ-(*N*-arylamino) alkene substrates.[4] The formation of products that result from *syn* addition of the aryl group and the nitrogen across the C–C double bond (Table 4, entries 7 and 8) is consistent with this mechanistic proposal.[24] This mechanism also accounts for the formation of *N*-benzyl-2-methylindole as a side product in the reaction of *N*-benzyl-2-allylaniline (Table 3, entry 9). The *N*-benzyl-2-methylindole likely derives from competing β-hydride elimination of intermediate **34** followed by double bond isomerization.[18a]

The regioisomeric products **3** observed in reactions of *N*-aryl substituted substrates[4] (e.g., **1**) are believed to derive from reversible β-hydride elimination/reinsertion processes as shown in Scheme 1. The absence of these side products in reactions of *N*-Boc and *N*-acyl protected substrates may result from a decrease in the rate of β-hydride elimination of intermediate **34**. This may be due to stabilization of **34** through chelation of the metal to the carbonyl of the amide or carbamate,[25] or due to electronic effects induced by the less electron-donating nature of the protected nitrogen.[26,27] The increased yields obtained in reactions of *N*-Boc and *N*-acyl protected amines with electron-deficient aryl bromides and vinyl bromides is likely due to the fact that C–N bond-forming reductive elimination of intermediate **33**

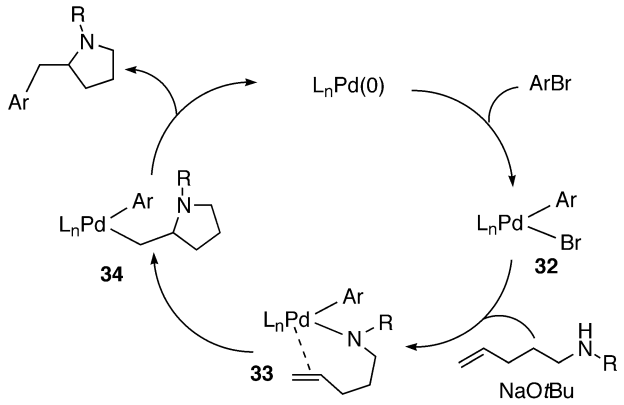
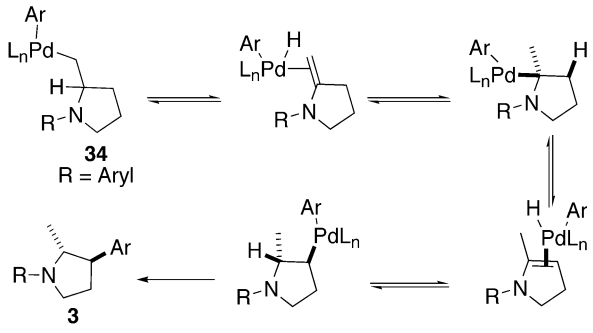


Figure 1. Proposed catalytic cycle.



Scheme 1.

slows as the nucleophilicity of the amine, amide, or carbamate decreases.[28]

3. Summary and conclusion

In conclusion, the synthesis of *N*-Boc and *N*-acyl pyrrolidine derivatives via reactions of *N*-protected γ-aminoalkenes is achieved in good yield with excellent regioselectivity and diastereoselectivities of up to >20:1. In contrast to related transformations of γ-(*N*-arylamino) alkenes, reactions of *N*-Boc or *N*-acyl protected substrates with vinyl bromides or electron-deficient aryl bromides proceed in good yield with minimal competing *N*-arylation/vinylation. The *N*-Boc and *N*-acyl substituents can be readily cleaved from the products, which allows for potential access to a broad variety of pyrrolidine derivatives.

4. Experimental

4.1. General

All reactions were carried out under an argon or nitrogen atmosphere in oven or flame dried glassware. Palladium acetate, tris(dibenzylideneacetone)dipalladium(0), and all phosphine ligands were purchased from Strem Chemical Co. and used without further purification. Acetic anhydride, di-*tert*-butyldicarbonate, cyclopent-2-enyl-acetic acid, and all aryl bromides were obtained from commercial sources (Aldrich Chemical Co. or Acros Chemical Co.) and were used as without purification. Pent-4-enylphenylamine (**1**),[4] *N*-benzyl-4-pentenylamine (**4a**),[29] *N*-(pent-4-enyl-benzamide) (**4e**),[30] and 2-allylaniline[31] were prepared according to published procedures. *N*-Benzyl-2-allylaniline (**14**)[32] was prepared by *N*-benzylation[33] of 2-allylaniline. Toluene and THF were purified using a GlassContour solvent purification system. Product regiochemistry was assigned on the basis of ^{1}H NMR 2-D COSY experiments; stereochemistry was assigned on the basis of ^{1}H NMR NOE experiments. Ratios of regioisomers and/or diastereomers were determined by either ^{1}H NMR or capillary GC analysis of crude reaction mixtures. Yields refer to isolated yields of compounds estimated to be ≥95% pure as determined by ^{1}H NMR, and either capillary GC (known compounds) or combustion analysis (new compounds). The yields reported in Section 4 describe the result of a single experiment, whereas the yields reported in Tables 2–4 are average yields of two or more experiments. Thus, the yields reported in the Section 4 may differ from those shown in Tables 2–4.

4.2. Synthesis of *N*-protected γ-aminoalkenes

4.2.1. *N*-Pent-4-enyl-acetamide (4b).[34] A flame-dried flask was cooled under a stream of nitrogen and charged with 4-pentenoic acid (5.7 mL, 49.8 mmol). The flask was purged with nitrogen, benzene (100 mL) was added and the resulting solution was cooled to ca 10 °C using an ice water bath. Oxalyl chloride (8.7 mL, 100 mmol) was added dropwise via syringe to the solution and the resulting mixture was warmed to rt, stirred for 1 h, and then concentrated in vacuo. The crude 4-pentenoyl chloride was dissolved in THF (100 mL), and slowly added to a separate flask containing aqueous ammonium hydroxide (100 mL) at 0 °C. The resulting mixture was stirred for 6 h and then concentrated in vacuo. The mixture was diluted with H_2O (50 mL) and ethyl acetate (100 mL), the layers were separated and the aqueous layer was extracted with ethyl acetate (2×100 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to afford 3.86 g (77%) of 4-pentenamide[35] as a white solid; mp 104–106 °C (lit. mp 106 °C)[35] that was used without further purification.

A flame-dried round-bottom flask was cooled under a stream of nitrogen and charged with 4-pentenamide (3.30 g, 33.3 mmol). The flask was purged with nitrogen, THF (100 mL) was added via syringe and the resulting solution was cooled to 0 °C. A solution of $LiAlH_4$ in THF (100 mL, 100 mmol, 1.0 M) was added dropwise via syringe. The reaction mixture was warmed to rt, and stirred for 36 h, then was cooled to 0 °C, quenched with H_2O (16 mL), and diluted with ether (200 mL). An aqueous solution of NaOH (30 mL, 10 M) was added and an insoluble white material precipitated. The organic supernatant was decanted to a clean Erlenmeyer flask and the precipitate was washed with ether (100 mL). The combined organic extracts were dried over anhydrous sodium sulfate and filtered to afford a solution of 4-pentenylamine[36] in diethyl ether (ca 0.1 M), which was used without further purification.

A flame-dried round-bottom flask was cooled under a stream of nitrogen and charged with a solution of 4-pentenylamine in diethyl ether (165 mL, 16.5 mmol, 0.1 M). The solution was cooled to 0 °C and acetic anhydride (4.7 mL, 5.10 g, 50 mmol) was added via syringe. The resulting mixture was stirred for 5 h and then aqueous NaOH (100 mL, 1.0 M) was added. The biphasic mixture was vigorously stirred for 12 h and then the layers were separated. The aqueous layer was extracted with ethyl acetate (3×75 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel to afford 1.36 g (65%) of the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86–5.57 (m, 2H), 5.07–4.93 (m, 2H), 3.25 (q, J=6.0 Hz, 2H), 2.12–2.02 (m, J=5.8 Hz, 2H), 1.95 (s, 3H), 1.59 (p, J=7.7 Hz, 2H).

4.2.2. Pent-4-enyl-carbamic acid *tert*-butyl ester (4c).[37] A flame-dried round bottom flask was cooled under a stream of nitrogen and charged with a solution of 4-pentenylamine (165 mL, 16.5 mmol, 0.1 M). Di-*tert*-butyl dicarbonate (5.4 g, 25 mmol) was added to the solution and the resulting mixture was stirred for 4 h and then aqueous NaOH (100 mL, 1.0 M) was added. The biphasic mixture was vigorously stirred for 12 h and then the layers were separated. The aqueous layer was extracted with ethyl acetate (3×75 mL). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel to afford 2.05 g (67%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80–5.70 (m, 1H), 5.01–4.90 (m, 2H), 4.54 (s, br, 1H), 3.13–2.98 (m, 2H), 2.03 (q, J=6.6 Hz, 2H), 1.52 (p, J=6.6 Hz, 2H), 1.39 (s, 9H).

4.2.3. *N*-(Pent-4-enyl)-4-methoxybenzamide (4d).[30] An oven-dried round-bottom flask was charged with 1,1′-carbonyldiimidazole (486 mg, 3.0 mmol) and then purged with argon. THF (15 mL) and 4-methoxybenzoic acid (456 mg, 3.0 mmol) were added to the flask, and the resulting mixture was stirred at rt for 1 h. A solution of 4-pentenylamine in ether (30 mL, 3.0 mmol, 0.1 M) was then added via syringe and the mixture was stirred at rt for 4 h. The reaction mixture was then diluted with ethyl acetate (15 mL) and H_2O (15 mL), the layers were separated, and the aqueous layer was extracted with ethyl acetate (3× 40 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to afford 438 mg (67%) of the title compound as a white solid; mp 42–44 °C (lit. mp not reported). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J=8.8 Hz, 2H), 6.87 (d, J=8.8 Hz, 2H), 6.10 (br s, 1H), 5.85–5.75 (m, 1H), 5.05–4.95 (m, 2H), 3.80 (s, 3H), 3.41 (q, J=7.0 Hz, 2H), 2.11 (q, J=7.0 Hz, 2H), 1.68 (p, J=7.7 Hz, 2H).

4.2.4. *N*-Pent-4-enyl-4-trifluoromethyl benzamide (4f). Treatment of 570 mg (3.0 mmol) of 4-(trifluoromethyl) benzoic acid with a solution of 4-pentenylamine in ether (30 mL, 3.0 mmol) using a procedure analogous to that described above in the synthesis of **4d** afforded 475 mg (63%) of the title compound as a white solid; mp 69–71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J=8.1 Hz, 2H), 7.60 (d, J=8.1 Hz, 2H), 6.60 (s, br, 1H), 5.83–5.70 (m, 1H), 5.05–4.90 (m, 2H), 3.45–3.36 (m, 2H), 2.15–2.05 (m, 2H), 1.73–1.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 138.2, 137.8, 133.2 (q, J=41 Hz), 127.5, 125.7, 123.8 (q, J=340 Hz), 115.6, 40.0, 31.4, 28.8; IR (film) 3309, 2930, 1638, 1550 cm^{-1}. Anal. Calcd for $C_{13}H_{14}F_3NO_2$: C, 60.70; H, 5.49; N, 5.44. Found: C, 60.97; H, 5.46; N, 5.40.

4.2.5. (2-Allylphenyl) carbamic acid *tert*-butyl ester (13).[38] Treatment of 904 mg (6.8 mmol) of 2-allylaniline[31] with 2.2 g (10.2 mmol) of di-*tert*-butyldicarbonate using a procedure analogous to that described above in the synthesis of **4c** (with THF used in place of diethyl ether as solvent) afforded 1.11 g (70%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J=7.7 Hz, 1H), 7.20 (t, J=8.4 Hz, 1H), 7.11 (d, J=7.7 Hz, 1H), 7.02 (t, J=7.3 Hz, 1H), 6.41 (s, br, 1H), 5.97–5.88 (m, 1H), 5.14–5.00 (m, 2H), 3.33 (d, J=6.2 Hz, 2H), 1.47 (s, 9H).

4.2.6. (1-Phenylpent-4-enyl) carbamic acid *tert*-butyl ester (17). A flame-dried round bottom flask was cooled under a stream of argon and charged with 1-phenylpent-4-en-1-one[39] (11.0 g, 69.0 mmol), activated 3 Å molecular sieves (10.0 g), and methanol (200 mL). The mixture was stirred at rt for 5 min and then ammonium acetate (53 g, 690 mmol) and sodium cyanoborohydride (4.3 g, 69 mmol) were added. The flask was purged with argon and then stirred at rt for 19 h. Ether (500 mL) was added, the mixture was decanted, and the organic phase was washed with 200 mL of aqueous $NaHCO_3$. The layers were separated, the aqueous phase was extracted with ether (1×100 mL), and the combined organic layers were extracted with 1 M HCl (3×100 mL). The organic phase was discarded and the combined acidic aqueous extracts were basicified to pH 10 with 10 M NaOH and extracted with ether (3×100 mL). The combined organic extracts were diluted with hexanes (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel to afford 2.1 g (19%) of 1-phenyl-pent-4-enylamine[40] as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.36–7.29 (m, 4H), 7.27–7.21 (m, 1H), 5.87–5.76 (m, 1H), 5.05–4.94 (m, 2H), 3.92–3.87 (m, 1H), 2.14–1.96 (m, 2H), 1.84–1.70 (m, 2H), 1.52 (s, 2H).

Treatment of 1.51 g (9.4 mmol) of 1-phenylpent-4-enylamine with 2.62 g (12.0 mmol) of di-*tert*-butyl dicarbonate using a procedure analogous to that described above in the synthesis of **4c** provided 2.26 g (92%) of the title compound as a white solid; mp 76–78 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.16 (m, 5H), 5.83–5.70 (m, 1H), 5.02–4.91 (m, 2H), 4.88–4.74 (s, br, 1H), 4.67–4.52 (s, br, 1H), 2.10–1.92 (m, 2H), 1.90–1.71 (m, 2H), 1.38 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 143.0, 137.8, 128.8, 127.4, 126.6, 115.4, 79.6, 54.7, 36.2, 30.6, 28.6; IR (film) 3370, 2978, 1687, 1519 cm^{-1}. Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.41; H, 8.78; N, 5.32.

4.2.7. *N*-(1-Phenylpent-4-enyl)-acetamide (18). Treatment of 517 mg (3.21 mmol) of 4-pentenylamine with 0.8 mL (8.03 mmol) of acetic anhydride using a procedure analogous to that described above in the synthesis of **4b** provided 530 mg (81%) of the title compound as a white solid; mp 44–46 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.16 (m, 5H), 6.25 (d, J=8.1 Hz, 1H), 5.80–5.70 (m, 1H), 4.97–4.90 (m, 3H), 2.09–1.92 (m, 2H), 1.90 (s, 3H), 1.88–1.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 142.4, 137.8, 128.8, 127.5, 126.8, 115.4, 53.3, 35.5, 30.6, 23.5; IR (film) 3279, 2934, 1646, 1549 cm^{-1}. MS (ESI) 226.1206 (226.1208 calcd for $C_{13}H_{17}NO$, M+Na$^+$).

4.2.8. 1-Allylbut-3-enyl-carbamic acid *tert*-butyl ester (19). A flame-dried round bottom flask was cooled under a stream of nitrogen and charged with diisopropylamine (8.4 mL, 60 mmol) and THF (100 mL). The flask was cooled to −78 °C and a solution of *n*-butyllithium in hexanes (22 mL, 55 mmol, 2.5 M) was added dropwise. The mixture was stirred at −78 °C for 1 h and then acetonitrile (2.6 mL, 50 mmol) was added dropwise. The mixture was warmed to rt and stirred for 3 h, then allyl bromide (4.8 mL, 55 mmol) was added dropwise. The mixture was stirred for 1 h, then a solution of saturated aqueous ammonium chloride (50 mL) was added. The mixture was extracted with ether (3×150 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo to afford a mixture of 4-cyano-1-butene, 4-cyano-4-allyl-1-butene, and 4-cyano-4,4-diallyl-1-butene (ca 50 mmol) that was used without further purification.

A flame-dried round-bottom flask was cooled under a stream of nitrogen and charged with a mixture of 4-cyano-1-butene, 4-cyano-4-allyl-1-butene, and 4-cyano-4,4-diallyl-1-butene (ca 50 mmol). The flask was purged with nitrogen, ether (200 mL) was added via syringe and the resulting solution was cooled to 0 °C. A solution of $LiAlH_4$ in ether (150 mL, 150 mmol, 1.0 M) was added dropwise via syringe. The reaction mixture was warmed to rt and stirred for 12 h, then was cooled to 0 °C, quenched with H_2O (30 mL), and diluted with ether (150 mL). An aqueous

solution of NaOH (80 mL, 10 M) was added and an insoluble white material precipitated. The organic supernatant was decanted to a clean Erlenmeyer flask and the solution was dried over anhydrous sodium sulfate and filtered to afford a mixture of 4-pentenylamine, 3-allyl-4-pentenylamine, and 3,3-diallyl-4-pentenylamine as a solution in diethyl ether (550 mL, ca 0.1 M). This mixture was used without further purification.

A solution containing a mixture of 4-pentenylamine, 3-allyl-4-pentenylamine, and 3,3-diallyl-4-pentenylamine in ether (100 mL, 10 mmol, 0.1 M) was treated with 2.62 g (12 mmol) of di-*tert*-butyl dicarbonate using a procedure analogous to that described above in the synthesis of **4c**. The three products were separated by flash chromatography on silica gel to afford 675 mg (30%) of **19** as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80–5.67 (m, 2H), 5.04–4.96 (m, 4H), 4.52 (s, br, 1H), 3.03 (t, $J=6.2$ Hz, 2H), 2.08–1.94 (m, 4H), 1.72–1.57 (m, 1H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 136.5, 116.8, 79.9, 43.7, 38.3, 36.2, 28.6; IR (film) 3351; 2978, 1694, 1515 cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_2$: C, 69.29; H, 10.29; N, 6.22. Found: C, 69.27; H, 10.26; N, 6.22.

4.2.9. (3-Methylpent-4-enyl)-carbamic acid *tert*-butyl ester (20). 3-Methyl-pent-4-enoic acid[41] (3.33 g, 29.2 mmol) was converted to 3.0 g (52%) of the title compound using a four-step procedure analogous to that described above for the conversion of 4-pentenoic acid to **4c**. The product was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62–5.53 (m, 1H), 4.90–4.82 (m, 2H), 4.59 (s, br, 1H), 3.09–2.91 (m, 2H), 2.15–2.02 (m, 1H), 1.44–1.27 (m, 11H), 0.91 (d, $J=6.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 143.9, 113.4, 79.0, 38.9, 36.7, 35.8, 28.5, 20.3; IR (film) 3351, 2977, 1694, 1526 cm^{-1}. Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.04; H, 10.60; N, 6.97.

4.2.10. *N*-(3-Methylpent-4-enyl) acetamide (21). Treatment of a solution of 3-methyl-4-pentenylamine in ether (100 mL, 10 mmol, 0.1 M) with 3 mL (30 mmol) of acetic anhydride using a procedure analogous to that described above in the synthesis of **4b** provided 720 mg (51%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (s, br, 1H), 5.61–5.52 (m, 1H), 4.90–4.82 (m, 2H), 3.15–3.07 (m, 2H), 2.13–2.03 (m, 1H), 1.85 (s, 3H), 1.46–1.32 (m, 2H); 0.90 (d, $J=7.0$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 143.8, 113.5, 38.0, 36.2, 35.9, 23.3, 20.4; IR (film) 3290, 2964, 1649, 1558 cm^{-1}. MS (ESI) 142.1228 (142.1232 calcd for $C_8H_{16}NO$, $M+H^+$).

4.2.11. (2-Cyclopent-2-enylethyl) carbamic acid *tert*-butyl ester (22). Cyclopent-2-enyl-acetic acid (3.0 g, 23.8 mmol) was converted to 2.41 g (48%) of the title compound using a four-step procedure analogous to that described above the conversion of 4-pentenoic acid to **4c**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69–5.65 (m, 1H), 5.62–5.57 (m, 1H), 4.52 (s, br, 1H), 3.16–2.99 (m, 2H), 2.67–2.56 (m, 1H), 2.34–2.15 (m, 2H), 2.06–1.94 (m, 1H), 1.59–1.48 (m, 1H), 1.45–1.31 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 134.5, 131.0, 79.2, 43.2, 39.5, 36.4, 32.1, 29.9, 28.6; IR (film) 3351, 2977, 1692, 1524 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 67.99; H, 10.06; N, 6.63.

4.2.12. *N*-(2-Cyclopent-2-enylethyl) acetamide (23). Cyclopent-2-enyl-acetic acid (2.0 g, 15.9 mmol) was converted to 1.27 g (52%) of the title compound using a four-step procedure analogous to that described above the conversion of 4-pentenoic acid to **4b**. The product was obtained as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.99 (s, br, 1H), 5.68–5.63 (m, 1H), 5.59–5.55 (m, 1H), 3.18 (q, $J=7.3$ Hz, 2H), 2.65–2.55 (m, 1H), 2.33–2.14 (m, 2H), 2.03–1.93 (m, 1H), 1.89 (s, 3H), 1.59–1.49 (m, 1H), 1.45–1.28 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 134.3, 131.1, 43.3, 38.5, 35.8, 32.1, 29.8, 23.4; IR (film) 3289, 2932, 1653, 1559 cm^{-1}. MS (ESI) 153.1154 (153.1153 calcd for $C_9H_{15}NO$).

4.3. General procedures for the Pd-catalyzed synthesis of pyrrolidines

General procedure A: Palladium-catalyzed synthesis of pyrrolidines and indolines using Pd(OAc)$_2$. A flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with $Pd(OAc)_2$ (2 mol%) and a bidentate phosphine ligand (4 mol%). The tube was purged with nitrogen and toluene was added (2 mL/mmol amine). The mixture was stirred at rt for ~2 min then the aryl bromide (1.2 equiv) was added followed by a solution of the amine (1 equiv) in toluene (2 mL/mmol amine). The mixture was allowed to stir ~1 min before the addition of NaO*t*Bu (2.0 equiv). The tube was purged with nitrogen and the sides of the flask were rinsed with toluene (2 mL/mmol amine; final concentration = 0.17 M). The mixture was heated to 65 °C with stirring until the starting material had been consumed as judged by GC or ^{1}H NMR analysis. The reaction mixture was cooled to rt, quenched with saturated aqueous NH_4Cl and diluted with ethyl acetate. The layers were separated, the aqueous layer was extracted with ethyl acetate, and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

General procedure B: Palladium-catalyzed synthesis of pyrrolidines and indolines using Pd$_2$(dba)$_3$. A flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with $Pd_2(dba)_3$ (1 mol% complex, 2 mol% Pd), a bidentate phosphine ligand (2 mol%), NaO*t*Bu (1.2 equiv), and the aryl bromide (1.1 equiv). The tube was purged with nitrogen and a solution of the amine substrate (1.0 equiv) in toluene (4 mL/mmol amine) was added. The mixture was heated to 105 °C with stirring until the starting material had been consumed as judged by GC or ^{1}H NMR analysis. The reaction mixture was cooled to rt, quenched with saturated aqueous NH_4Cl and diluted with ethyl acetate. The layers were separated, the aqueous layer was extracted with ethyl acetate, and the combined organic extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel.

4.3.1. (4-Methoxyphenyl)-(2-naphthalen-2-ylmethyl-pyrrolidin-1-yl) methanone (5d). Reaction of 52 mg

(0.25 mmol) of **4d** with 2-bromonaphthalene (57 mg, 0.28 mmol), dpe-phos (2.7 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following general procedure B afforded 54.3 mg (63%) of the title compound as a pale yellow oil that was contaminated with ca 5% of Heck-type side product **6d**. The title compound was found to exist as a ca 9:1 mixture of rotamers as judged by ^{1}H NMR analysis. Data are for the major rotamer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.58 (m, 4H), 7.57–7.30 (m, 5H), 6.88 (d, $J=8.8$ Hz, 2H), 4.62–4.49 (m, 1H), 3.80 (s, 3H), 3.45–3.30 (m, 2H), 3.26–3.14 (m, 1H), 3.13–3.00 (m, 1H), 2.01–1.83 (m, 1H), 1.82–1.51 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 161.2, 136.4, 133.7, 132.4, 129.6, 128.7, 128.4, 127.9, 127.8, 127.7, 126.1, 125.5, 113.7, 58.7, 55.5, 51.1, 39.0, 29.6, 25.3 (two aromatic signals are incidentally equivalent); IR (film) 2967, 1608, 1420 cm^{-1}. MS (ESI) 368.1625 (368.1626 calcd for $C_{23}H_{23}NO_2$, M+Na$^+$).

4.3.2. (2-Naphthalen-2-ylmethylpyrrolidin-1-yl) phenylmethanone (5e). Reaction of 48 mg (0.25 mmol) of **4e** with 2-bromonaphthalene (57 mg, 0.28 mmol), dpe-phos (2.7 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following general procedure B afforded 38 mg (48%) of the title compound as a pale yellow oil. This compound was found to exist as a 4:1 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.78 (m, 3H), 7.78–7.74 (m, 0.2H), 7.72 (s, 0.8H), 7.70–7.60 (m, 0.8H), 7.56–7.42 (m, 1.4H), 7.50–7.38 (m, 5.8H), 7.19 (s, 0.2H), 6.74–6.68 (m, 0.2H), 4.62–4.52 (m, 1H), 4.20–4.11 (m, 0.2H), 3.78–3.67 (m, 0.4H), 3.43–3.29 (m, 1.6H), 3.22–3.13 (m, 0.8H), 3.12–3.03 (m, 0.8H), 2.77–2.18 (m, 0.2H), 2.61–2.50 (m, 0.2H), 2.04–1.88 (m, 1H), 1.87–1.73 (m, 1H), 1.72–1.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 137.6, 136.4, 135.8, 133.7, 132.4, 130.2, 129.6, 128.7, 128.5, 128.3, 128.0, 127.8, 127.7, 127.5, 127.3, 126.7, 126.2, 126.1, 125.7, 125.5, 60.9, 58.7, 50.9, 46.0, 41.2, 39.0, 29.9, 29.5, 25.1, 22.1 (three sets of carbons are incidentally equivalent); IR (film) 2968, 1625, 1412 cm^{-1}. MS (ESI) 338.1519 (338.1521 calcd for $C_{22}H_{21}NO$, M+Na$^+$).

4.3.3. 2-Napthalen-2-ylmethylpyrrolidine-1-carboxylic acid *tert*-butyl ester (5c). Reaction of 93 mg (0.50 mmol) of **4c** with 2-bromonaphthalene (124 mg, 0.60 mmol), dpe-phos (11 mg, 0.02 mmol 4 mol%) and NaO*t*Bu (96 mg, 1.0 mmol) following general procedure A afforded 120 mg (77%) of the title compound as a pale yellow oil. This compound was found to exist as a 1:1 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.74 (m, 3H), 7.78–7.58 (m, 1H), 7.51–7.30 (m, 3H), 4.21–4.02 (m, 1H), 3.46–3.18 (m, 3H), 2.78–2.63 (m, 1H), 1.73 (m, 4H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 137.0, 133.8, 132.3, 128.5, 128.2, 128.0, 127.8, 127.7, 126.2, 126.1, 125.6 125.5, 79.5, 79.3, 59.0, 47.1, 46.5, 41.0, 39.9, 29.9, 29.1, 28.8, 23.7, 22.9 (nine sets of carbons are incidentally equivalent); IR (film) 3052, 2973, 1692, 1395 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; N, 4.50. Found: C, 76.78; H, 8.24; N, 4.57.

4.3.4. 2-(2-Methylbenzyl) pyrrolidine-1-carboxylic acid *tert*-butyl ester (8). Reaction of 93 mg (0.5 mmol) of **4c** with 2-bromotoluene (66 μL, 94 mg, 0.55 mmol), dpe-phos (5.4 mg, 0.01 mmol, 2 mol%) and NaO*t*Bu (58 mg, 0.6 mmol) following general procedure B afforded 112 mg (81%) of the title compound as a pale yellow oil. This compound was found to exist as a 2:1 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.08 (m, 4H), 4.02 (s, br, 1H), 3.42–3.02 (m, 3H), 2.50–2.29 (m, 4H), 1.92–1.59 (m, 4H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8; 154.2, 137.9, 137.2, 130.7, 130.5, 126.9, 126.6, 126.1, 79.7, 79.6, 57.5, 46.9. 46.4, 38.5, 37.7, 37.0, 29.7, 29.2, 28.8, 28.7, 23.7, 22.8, 20.0, 19.9 (three sets of signals are incidentally equivalent); IR (film) 2973, 1693, 1394 cm^{-1}. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.84; H, 9.16; N, 5.10.

4.3.5. 2-(4-Cyanobenzyl)pyrrolidine-1-carboxylic acid *tert*-butyl ester (9). Reaction of 185 mg (1.00 mmol) of **4c** with 4-bromobenzonitrile (200 mg, 1.10 mmol), dppb (8.8 mg, 0.02 mmol, 2 mol%) and NaO*t*Bu (116 mg, 1.20 mmol) following general procedure B afforded 203 mg (71%) of the title compound as a pale yellow oil. This compound was found to exist as a 1:1 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.46 (m, 2H), 7.26–7.22 (m, 2H), 3.80–3.97 (m, 1H), 3.35–2.95 (m, 4H), 2.62–2.55 (m, 1H), 1.81–1.52 (m, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 145.1, 132.6, 132.2, 130.4, 128.2, 119.0, 110.3, 79.5, 58.4, 46.81, 46.79, 41.0, 40.1, 30.1, 28.9, 28.7, 23.6, 22.9 (five sets of signals are incidentally equivalent); IR (film) 2974, 2228, 1690, 1395 cm^{-1}. Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.15; H, 7.82; N, 9.69.

4.3.6. 2-(3-Phenylallyl)pyrrolidine-1-carboxylic acid *tert*-butyl ester (10). Reaction of 93 mg (0.50 mmol) of **4c** with β-bromostyrene (80 μL, 110 mg, 0.60 mmol), dppe (8 mg, 0.02 mmol, 4 mol%) and NaO*t*Bu (96 mg, 1.00 mmol) following general procedure A afforded 108 mg (79%) of the title compound as a pale yellow oil. This compound was found to exist as a 1:1 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.10 (m, 5H), 6.38 (d, $J=16.0$ Hz, 1H), 6.20–6.05 (m, 1H), 3.90–3.78 (m, 1H), 3.42–3.32 (m, 2H), 2.71–2.52 (m, 1H), 2.32–2.23 (m, 1H), 1.95–1.73 (m, 4H); 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 138.0, 137.7, 132.4, 128.7, 127.2, 126.2, 79.39, 79.36, 57.4, 46.9, 46.6, 38.4, 37.6, 30.5, 29.6, 28.8, 23.9, 23.2 (nine sets of signals are incidentally equivalent); IR (film) 2972, 1693, 1394 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.24; H, 8.59; N, 4.81.

4.3.7. 1-(2-Naphthalen-2-ylmethylpyrrolidin-1-yl) ethanone (5b). Reaction of 32 mg (0.25 mmol) of **4b** with 2-bromonaphthalene (57 mg, 0.28 mmol), dpe-phos (2.7 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following general procedure B afforded 44 mg (70%) of the title compound as a pale yellow oil. This compound was found to exist as a 7:3 mixture of rotamers as judged by ^{1}H NMR analysis; data are for the mixture. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83–7.78 (m, 3H), 7.66 (s, 0.3H), 7.60 (s, 0.3H), 7.51–7.40 (m, 3H), 4.45–4.38 (m, 0.7H), 4.15–4.08 (m, 0.3H), 3.63–3.48 (m, 0.7H), 3.43–3.31

(m, 2H), 3.07–3.00 (m, 0.3H), 2.84–2.70 (m, 1H), 2.14–2.03 (m, 3H), 1.96–1.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 169.4, 137.0, 135.7, 135.7, 133.8, 132.5, 132.4, 128.7, 128.4, 128.15, 128.05, 128.03, 127.94, 127.87, 127.76, 127.72, 126.5, 126.2, 126.0, 125.6, 60.3, 58.6, 48.2, 45.8, 41.2, 39.1, 30.3, 28.7, 24.0, 23.4, 22.4, 22.1 (one set of carbons are incidentally equivalent); IR (film) 2968, 1637, 1417 cm^{-1}. MS (ESI) 276.1359 (276.1364 calcd for $C_{17}H_{19}NO$, M+Na$^+$).

4.3.8. 1-[2-(4-Benzoylbenzyl)pyrrolidin-1-yl]ethanone (11). Reaction of 32 mg (0.25 mmol) of **4b** with 4-bromobenzophenone (72 mg, 0.28 mmol), dppe (2.0 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following the general procedure B afforded 61 mg (80%) of the title compound as a pale yellow oil. This compound was found to exist as a 3:1 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.64 (m, 4H), 7.58–7.51 (m, 1H), 7.47–7.40 (m, 2H), 7.32–7.22 (m, 2H), 4.34–4.26 (m, 0.75H), 4.08–4.00 (m, 0.25H), 3.60–3.32 (m, 2H), 3.24 (dd, J=3.3, 12.8 Hz, 0.75H), 2.92 (dd, J=5.1, 13.6 Hz, 0.25H), 2.72 (m, 0.25H), 2.67–2.60 (m, 0.75H), 2.20–2.05 (m, 0.75H), 2.06–1.98 (m, 3H), 1.90–1.74 (m, 3.25H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.7, 196.6, 169.6, 169.5, 144.5, 143.0, 138.3, 138.0, 136.2, 135.8, 132.7, 132.5, 130.8, 130.5, 130.2, 129.6, 129.4, 128.5, 128.4, 60.0, 58.4, 48.2, 45.7, 41.1, 39.0, 30.3, 28.7, 24.0, 23.2, 22.3, 22.0 (one set of carbons are incidentally equivalent); IR (film) 2960, 1638, 1414 cm^{-1}. MS (ESI) 330.1466 (330.1470 calcd for $C_{20}H_{21}NO_2$, M+Na$^+$).

4.3.9. 1-[2-(4-Dimethylaminobenzyl)pyrrolidin-1-yl]-ethanone (12). Reaction of 32 mg (0.25 mmol) of **4b** with *N*,*N*-dimethyl-4-bromoaniline (55 mg, 0.28 mmol), xantphos (2.9 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following general procedure B afforded 42 mg (67%) of the title compound as a pale yellow oil. This compound was found to exist as a 3:2 mixture of rotamers as judged by ^{1}H NMR analysis. This material contained ca 15% of the corresponding 2,3-dihydropyrrole (1-[5-(4-dimethylaminobenzyl)-2,3-dihydropyrrol-1-yl]ethanone), which could not be separated by chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–6.95 (m, 2H), 6.72–6.57 (m, 2H), 4.32–4.20 (m, 0.6H), 4.01–3.88 (m, 0.4H), 3.57–3.39 (m, 0.8H), 3.38–3.29 (m, 1.2H), 3.06–2.98 (m, 0.6H), 2.93–2.85 (m, 6H), 2.77–2.70 (m, 0.4H), 2.57–2.43 (m, 1H), 2.07–1.95 (m, 3H), 1.89–1.67 (m, 4H); ^{13}C NMR (125 MHz, CD_3OH) δ 170.9, 170.6, 150.1, 149.8, 129.9, 129.8, 113.4 113.3, 112.6, 112.4, 60.9, 59.0, 45.3, 40.1, 40.0, 39.9, 39.8, 39.1, 38.9, 36.9, 23.1, 21.5, 21.33, 21.28, 20.6; IR (film) 2930, 1638, 1417 cm^{-1}. MS (ESI) 269.1361 (269.1630 calcd for $C_{15}H_{22}N_2O$, M+Na$^+$).

4.3.10. 2-Naphthalen-2-ylmethyl-2,3-dihydroindole-1-carboxylic acid *tert*-butyl ester (15). Reaction of 59 mg (0.25 mmol) of **13** with 2-bromonaphthalene (57 mg, 0.28 mmol), dpe-phos (2.7 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.30 mmol) following general procedure B afforded 44 mg (50%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.76 (m, 3H), 7.63 (s, 1H), 7.48–7.34 (m, 4H), 7.22–7.30 (m, 2H), 6.94 (t, J=7.3 Hz, 1H), 4.71 (s, br, 1H), 3.41 (s, br, 1H) 3.21–3.00 (m, 1H), 2.81–2.67 (m, 2H), 1.59 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5, 142.2, 135.7, 133.8, 132.5, 130.2, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 126.2, 125.7, 125.3, 122.7, 115.6, 81.1, 60.8, 40.6, 31.7, 28.7; IR (film) 2974, 1702, 1483, 1392 cm^{-1}. MS (ESI) 382.1787 (382.1783 calcd for $C_{24}H_{25}NO_2$, M+Na$^+$).

4.3.11. 1-Benzyl-2-(4-methylbenzyl)-2,3-dihydro-1*H*-indole (16). Reaction of 65 mg (0.29 mmol) of **14** with 4-bromotoluene (40 μL, 55 mg, 0.32 mmol), nixantphos (3.2 mg, 0.0058 mmol, 2 mol%) and NaO*t*Bu (34 mg, 0.30 mmol) following general procedure B afforded 44 mg (48%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 7.07–6.94 (m, 6H), 6.59 (t, J=7.0 Hz, 1H), 6.33 (d, J=7.7 Hz, 1H), 4.46 (d, J=16.1 Hz, 1H), 4.24 (d, J=16.1 Hz, 1H), 3.86–3.78 (m, 1H), 3.12 (dd, J=4.0, 13.2 Hz, 1H), 2.96–2.89 (m, 1H), 2.78–2.62 (m, 2H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 139.2, 136.0, 135.6, 129.33 129.29, 128.69, 128.67 127.56, 127.54, 127.2, 124.4, 117.7, 107.1, 66.7, 51.8, 40.1, 35.1, 21.2; IR (film) 2921, 2360, 1484 cm^{-1}. MS (ESI) 314.1901 (314.1909 calcd for $C_{23}H_{23}N$, M+H$^+$).

4.3.12. (±)-(2*S*,5*R*)-2-(4-Methoxybenzyl)-5-phenylpyrrolidine-1-carboxylic acid *tert*-butyl ester (24). Reaction of 261 mg (1.00 mmol) of **17** with 4-bromoanisole (140 μL, 206 mg, 1.1 mmol), dppb (8.0 mg, 0.02 mmol, 2 mol%) and NaO*t*Bu (116 mg, 1.20 mmol) following general procedure B afforded 219 mg (60%) of the title compound as a pale yellow oil. This compound was found to exist as a 7:3 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.05 (m, 7H), 6.82 (d, J=8.4 Hz, 2H), 4.97–4.61 (m, 1H), 4.22–3.98 (m, 1H), 3.76 (s, 3H), 3.56–3.29 (m, 1H), 2.59 (t, J=11.4 Hz, 1H), 2.22 (sx, J=6.6 Hz, 1H), 1.97–1.81 (m, 1H), 1.82–1.66 (m, 2H), 1.62–1.04 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 155.1, 131.6, 130.5, 128.5, 128.3, 126.6, 125.8, 114.1, 79.5, 63.3, 61.3, 55.4, 40.6, 34.4, 28.5 (nine sets of carbons are incidentally equivalent); IR (film) 2974, 1686, 1454 cm^{-1}. MS (ESI) 390.2038 (390.2045 calcd for $C_{23}H_{29}NO_3$, M+Na$^+$).

4.3.13. (±)-(2*S*,5*R*)-1-(2-Phenyl-5-pyridin-3-ylmethyl-pyrrolidin-1-yl) ethanone (25). Reaction of 51 mg (0.25 mmol) of **18** with 3-bromopyridine (27 μL, 43.5 mg, 0.28 mmol), dppb (2.2 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.3 mmol) following general procedure B afforded 57.2 mg (82%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49–8.41 (m, 2H), 7.67–7.62 (m, 1H), 7.38–7.18 (m, 6H), 4.85 (t, J=7.3 Hz, 1H), 4.41–4.34 (m, 1H), 3.62 (dd, J=7.3, 12.8 Hz, 1H), 2.59 (dd, J=10.6, 12.8 Hz, 1H), 2.34 (sx, J=7.6 Hz, 1H), 2.03–1.94 (m, 1H), 1.80–1.72 (m, 4H), 1.66–1.58 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 150.6, 148.1, 143.2, 137.0, 134.8, 129.2, 127.6, 125.7, 123.7, 64.1, 60.6, 37.6, 35.5, 28.2, 23.4; IR (film) 2968, 1643, 1404 cm^{-1}. MS (ESI) 281.1653 (281.1654 calcd for $C_{18}H_{20}N_2O$, M+H$^+$).

4.3.14. 4-Allyl-2-(4-*tert*-butoxycarbonyl-benzyl) pyrrolidine-1-carboxylic acid *tert*-butyl ester (26). Reaction of 57 mg (0.25 mmol) of **19** with 4-bromo-*tert*-butyl benzoate (71 mg, 0.28 mmol), dpe-phos (2.7 mg, 0.005 mmol, 2 mol%) and NaO*t*Bu (29 mg, 0.3 mmol) following general procedure B afforded 80 mg (70%) of the title compound as

a pale yellow oil. This product was isolated as a ca 3:1 mixture of diastereomers. Data are for the mixture. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.79 (m, 2H), 7.17 (s, br, 2H), 5.72–5.57 (m, 1H), 4.99–4.86 (m, 2H), 4.06–2.83 (m, br, 3H), 2.76–2.48 (m, 2H), 2.07–1.88 (m, 4H), 1.57–1.40 (m, 18H), 1.27–1.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 157.5, 154.7, 149.5, 146.2, 143.8, 136.4, 130.2, 129.7, 116.3, 116.2, 81.0, 79.4, 77.6, 77.2, 76.9, 58.7, 52.7, 52.1, 51.7, 41.8, 41.0, 40.1, 37.9, 37.7, 37.3, 37.0, 36.3, 35.6, 34.9, 28.8, 28.4; IR (film) 2976, 1712, 1694, 1395 cm^{-1}. Anal. Calcd for $C_{24}H_{35}NO_4$: C, 71.79; H, 8.79; N, 3.49. Found: C, 71.60; H, 8.75; N, 3.45.

4.3.15. (±)-(2*R*,3*S*)-3-Methyl-2-naphthalen-2-ylmethyl-pyrrolidine-1-carboxylic acid *tert*-butyl ester (27). The reaction of 100 mg (0.5 mmol) of **20** with 2-bromonaphthalene (124 mg, 0.60 mmol), dpe-phos (10.8 mg, 0.02 mmol, 4 mol%) and NaO*t*Bu (96 mg, 1.00 mmol) was conducted following general procedure A. ^{1}H NMR analysis of the crude product showed the formation of the desired product as a 10:1 mixture of diastereomers. The minor diastereomer was separated upon chromatographic purification to afford 106 mg (65%) of the title compound as a white solid with >20:1 dr; mp 107 °C. Data are for the major diastereomer, which was found to exist as a 1:1 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85–7.73 (m, 3H), 7.62 (d, J=16.3 Hz, 1H), 7.50–7.28 (m, 3H), 3.78–3.60 (m, 1H), 3.61–3.38 (m, 1H), 3.33–3.08 (m, 2H), 2.96–2.73 (m, 1H), 2.15–2.09 (m, 1H), 1.98–1.80 (m, 1H), 1.53 (s, 9H), 1.49–1.34 (m, 1H), 0.84 (s, br, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 136.8, 133.7, 132.3, 128.6, 128.2, 128.0, 127.8, 127.7, 126.2, 126.0, 125.5, 125.4, 79.6, 79.5, 66.0, 65.7, 45.7, 45.0, 40.6, 39.1, 37.0, 36.1, 31.3, 30.4, 28.8, 19.6, 19.4 (seven sets of carbons are incidentally equivalent); IR (film) 2964, 1692, 1396 cm^{-1}. MS (ESI) 348.1943 (348.1939 calcd for $C_{21}H_{27}NO_2$, M+Na^+).

4.3.16. (±)-(2*R*,3*S*)-2-(4-*tert*-Butylbenzyl)-3-methyl-pyrrolidine-1-carboxylic acid *tert*-butyl ester (28). The reaction of 100 mg (0.5 mmol) of **20** with 4-bromo-*tert*-butylbenzene (105 μL, 128 mg, 0.60 mmol), dpe-phos (10.8 mg, 0.02 mmol, 4 mol%) and NaO*t*Bu (96 mg, 1.00 mmol) was conducted following general procedure A. ^{1}H NMR analysis of the crude product showed the formation of the desired product as a 10:1 mixture of diastereomers. The minor diastereomer was separated upon chromatographic purification to afford 97.4 mg (59%) of the title compound as a pale yellow oil with >20:1 dr. Data are for the major diastereomer, which was found to exist as a 3:2 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.25 (m, 2H), 7.16–7.06 (m, 2H), 3.69–3.37 (m, 2H), 3.31–2.92 (m, 2H), 2.76–2.56 (m, 1H), 2.05 (s, br, 1H), 1.97–1.79 (m, 1H), 1.51 (s, 9H), 1.45–1.35 (m, 1H), 1.32 (s, 9H), 0.88 (d, J=6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 149.2, 149.0, 136.1, 129.5, 129.3, 125.5, 125.3, 79.4, 79.1, 66.1, 65.6, 45.6, 45.0, 39.9, 38.5, 37.1, 36.0, 34.6, 31.6, 31.2, 30.4, 28.8, 19.7, 19.5 (five sets of carbons are incidentally equivalent); IR (film) 2963, 1696, 1395 cm^{-1}. MS (ESI) 354.2402 (354.2409 calcd for $C_{21}H_{33}NO_2$, M+Na^+).

4.3.17. (±)-(2*R*,3*S*)-1-[2-(4-Chlorobenzyl)-3-methyl pyrrolidin-1-yl]ethanone (29). The reaction of 72 mg (0.5 mmol) of **21** with 4-bromochlorobenzene (106 mg, 0.55 mmol), dpe-phos (10.8 mg, 0.02 mmol, 4 mol%) and NaO*t*Bu (58 mg, 1.00 mmol) was conducted following general procedure B. ^{1}H NMR analysis of the crude product showed the formation of the desired product as a 10:1 mixture of diastereomers. The minor diastereomer was separated upon chromatographic purification to afford 69.4 mg (61%) of the title compound as a pale yellow oil with >20:1 dr. Data are for the major diastereomer, which was found to exist as a 7:3 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.16 (m, 2H), 7.12–7.00 (m, 2H), 3.86–3.78 (m, 0.7H), 3.71–3.60 (m, 0.3H), 3.55–3.48 (m, 0.3H), 3.47–3.29 (m, 1H), 3.26–3.16 (m, 0.7H), 3.08–2.98 (m, 0.7H), 2.81–2.73 (m, 0.3H), 2.72–2.57 (m, 1H), 2.14–2.08 (m, 0.3H), 2.07–1.95 (m, 3.1H), 1.92–1.84 (m, 1.6H), 1.52–1.38 (m, 1H), 0.89–0.80 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 169.7, 137.5, 136.5, 132.8, 132.1, 131.1, 130.7, 129.1, 128.6, 67.4, 65.3, 46.9, 44.1, 40.6, 37.7, 37.2, 35.6, 31.4, 29.1, 23.2, 22.2, 19.8, 19.3; IR (film) 2961, 1641, 1417 cm^{-1}. MS (ESI) 274.0969 (274.0975 calcd for $C_{14}H_{18}ClNO$, M+Na^+).

4.3.18. (±)-(3a*R*,6*S*,6a*S*)-6-Biphenyl-4-yl-hexahydro-cyclopenta[*b*]pyrrole-1-carboxylic acid *tert*-butyl ester (30). Reaction of 53 mg (0.25 mmol) of **22** with 4-bromobiphenyl (64 mg, 0.28 mmol), xantphos (5.8 mg, 0.01 mmol, 4 mol%) and NaO*t*Bu (36 mg, 0.38 mmol) following general procedure A afforded 42.8 mg (47%) of the title compound as a white solid; mp 128 °C. This compound was found to exist as a 3:2 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.34 (m, 6H), 7.32–7.16 (m, 3H), 4.54–4.30 (m, 1H), 3.83–3.71 (m, 0.6H), 3.55–3.17 (m, 1.4H), 3.10–2.78 (m, 2H), 2.12–1.98 (m, 1H), 1.97–1.60 (m, 5H), 1.21–0.89 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 141.6, 141.2, 139.4, 129.6, 128.9, 127.2, 127.1, 127.0, 126.6, 94.6, 79.0, 65.4, 52.3, 51.2, 47.8, 43.5, 42.5, 34.2, 33.7, 32.4, 32.2, 31.8, 28.4, 27.9 (thirteen sets of carbons are incidentally equivalent); IR (film) 2952, 1689, 1392 cm^{-1}. MS (ESI) 386.2105 (386.2096 calcd for $C_{24}H_{29}NO_2$, M+Na^+).

4.3.19. (±)-(3a*R*,6*S*,6a*S*)-1-(6-Naphthalen-2-yl-hexa-hydrocyclopenta[*b*]pyrrol-1-yl) ethanone (31). Reaction of 78 mg (0.25 mmol) of **23** with 2-bromonaphthalene (114 mg, 0.55 mmol), nixantphos (13.8 mg, 0.025 mmol, 5 mol%), $Pd_2(dba)_3$ (11.4 mg, 0.0125 mmol, 2.5 mol%) and NaO*t*Bu (58 mg, 0.60 mmol) following general procedure B afforded 85 mg (61%) of the title compound as a pale yellow oil. This compound was found to exist as a 7:3 mixture of rotamers as judged by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.69 (m, 3H), 7.57 (s, 1H), 7.48–7.34 (m, 2H), 7.28–7.24 (m, 1H), 4.90 (t, J=8.6 Hz, 0.3H), 4.43 (t, J=7.0 Hz, 0.7H), 4.14–4.06 (m, 0.70H), 3.54 (q, J=8.1 Hz, 0.3H), 3.48–3.20 (m, 2H), 3.13–3.04 (m, 0.7H), 2.92–2.82 (m, 0.3H), 2.17–1.92 (m, 4H), 1.85–1.72 (m, 2H), 1.64 (s, 0.6H), 1.11 (s, 2.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 168.8, 139.2, 138.2, 133.6, 133.5, 132.7, 132.4, 128.31, 128.29, 128.1, 127.91, 127.90, 129.86, 127.81, 127.2, 127.0, 126.6, 126.4, 125.9, 125.8, 125.3, 67.0, 65.2, 53.4, 49.9, 49.1, 47.4, 44.0, 42.3, 33.7, 32.6, 32.4, 32.3, 32.2, 31.4, 22.5, 21.8; IR (film) 2950, 1638,

1413 cm^{-1}. MS (ESI) 302.1523 (302.1521 calcd for $C_{19}H_{21}NO$, $M+Na^+$).

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20. The relative stereochemistry of the pyrrolidine products was assigned on the basis of ^1H NMR NOE experiments. Diastereomeric ratios were determined by GC and/or ^1H NMR analysis.
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