A Facile Synthesis of *N*-Boc-Protected Pyrroles by Cyclodehydration of γ-Amino-α,β-enals and -enones

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A novel series of *N*-Boc-substituted and fused pyrroles was prepared by cyclodehydration of readily accessible (*E*)-γ-(*tert*-butoxycarbonylamino)-α,β-enals and -enones. Functionalisation of the pyrrole ring was then explored with 2-borylated pyrroles in the Suzuki–Miyaura coupling.

Introduction

Widely used in material sciences,[1] pyrrole ring systems are also present in many biologically active substances.[2,3] Accordingly, considerable efforts have been devoted to the development of straightforward reactions to build up pyrroles.

Of the numerous pyrrole synthesis reported in the literature,[4,5] some involve cyclisation processes with linear precursors consisting of a nitrogen-containing function (imino,[6−9] amino[10−14] or nitro[15] group) linked to a four-carbon chain bearing a terminal electrophilic carbon centre.

In this context, (*Z*)-γ-amino-α,β-unsaturated aldehydes or ketones such as **1** are assumed to be the key intermediates in a number of reactions affording pyrroles (Figure 1). In reported procedures, *Z* intermediates **1** have been generated and cyclised in situ by different methods including the photolysis of dihydro-1,2-oxazines,[16] the palladium-catalysed allylic benzylamination of α-acetoxy-α-vinylalkanones,[17] rhodium-catalysed hydroformylation,[18] the carbocupration/acylation of γ-aminoacetylenic esters,[19] the ring-opening of 2-oxoalkyl-2-oxazolidinones,[20] the oxidation of *N*-[(*Z*)-4-hydroxybut-2-enyl]alkynamide[21] and more recently the *N*-deprotection of *N*,*N*-disubstituted γ-amino-α,β-enones.[22]

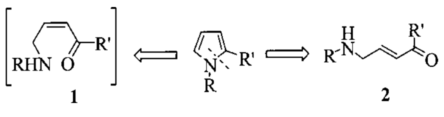

Figure 1. Cyclisation processes

We observed that the isolable (*E*)-γ-(*tert*-butoxycarbonylamino)enals and -enones **2**, initially envisaged for the synthesis of [penta-2,4-dienyl]amines, could easily be cyclised into *N*-Boc-pyrroles under acidic conditions.

To the best of our knowledge, the direct construction of substituted pyrroles possessing a deprotective group such as *tert*-butoxycarbonyl (Boc) on the nitrogen atom has only been reported by Cushman and co-workers, in a tandem aldol reaction/heterocyclisation sequence.[23] However, the Cushman approach suffered from low yields (5−42%). We hence decided to investigate the scope and limitations of this route to pyrroles.

It appeared to be a simple, general and efficient pathway to polysubstituted *N*-Boc pyrroles. An α-lithiation/borylation sequence with monosubstituted pyrroles afforded the corresponding boronic acids, which were used in Suzuki−Miyaura couplings with a variety of aryl halides. Here we present our results on the synthesis of 2-, 2,5- and 2,3,5-substituted pyrroles.

Results and Discussion

γ-(*tert*-Butoxycarbonylamino)enals **4a−d** were prepared by Wittig condensation of (triphenylphosphoranylidene)acetaldehyde with *N*-Boc-α-aminoaldehydes[24−26] **3a−d** (Scheme 1).

^{1}H NMR analysis of the crude Wittig reaction mixtures before any treatment indicated the presence only of *E* enals **4a−d**, together with triphenylphosphane oxide. Nevertheless, purification of the crude products by column chromatography on silica gel resulted in the isolation of compounds **4a−d** contaminated by small amounts of pyrroles **5a−d**, respectively (5−10%). The presence of pyrroles **5a−d** suggested initial isomerisation of (*E*)-enals **4a−d** into their corresponding *Z* isomers, followed by a cyclodehydration reaction during the purification step. In order to clarify this

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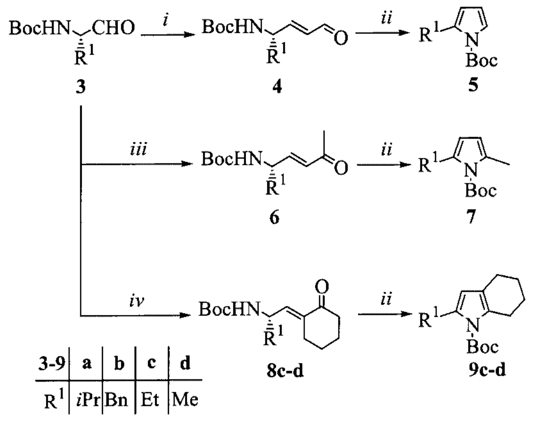


3-9	a	b	c	d
R^1	*i*Pr	Bn	Et	Me

Scheme 1. *i*) $Ph_3P=CH-CHO$, 70 °C, toluene (70−79%); *ii*) 2 M HCl ethereal sol., room temperature, CH_2Cl_2 (73−90%); *iii*) $Ph_3P=CH-COMe$, 70 °C, toluene (70−86%); *iv*) 2-(triphenylphosphoranylidene)cyclohexanone, 70 °C, toluene (53−80%)

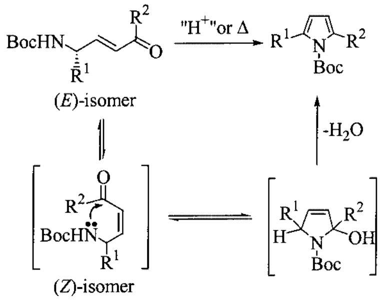
point, *E* enals **4a−d** were separated from Ph_3PO by crystallisation from ether/pentane mixtures and treated with catalytic amounts of *para*-toluenesulfonic acid (PTSA, 0.1 equiv.) in CH_2Cl_2 at room temperature. Under these conditions, complete conversion of *E* enals **4a−d** into 2-substituted *N*-Boc-pyrroles **5a−d** was cleanly achieved within one hour, only 15 minutes being required with a catalytic amount of ethereal HCl (0.1 equiv.). The scope of this cyclisation process was then extended to enones **6** and **8**, obtained analogously from **3a−d** and 1-triphenylphosphoranylidene-2-propanone or **3c−d** and 2-(triphenylphosphoranylidene)cyclohexanone,[27] respectively. The cyclodehydrations of enones **6** and **8** under catalytic acidic conditions (0.1 equiv. PTSA, room temperature) required longer reaction time (about 24 h) than those of the enals. This was circumvented by use of stoichiometric amounts of HCl. In this case, the reactions went to completion within 15 minutes (Scheme 1); results are summarised in Table 1. In the preparations of the enones **8**, it was noteworthy that significant amounts of the corresponding fused pyrroles **9** (10% for **8c**, 20% for **8d**) were detected in the crude Wittig olefination reaction mixtures. We speculated that, prior to the cyclodehydration, the isomerisation of the *E* compounds might also be inducible thermally. After isolation, the pure *E* enone **8c** was accordingly heated under reflux in [D$_6$]benzene and the reaction was monitored by ^1H NMR. Although slow, conversion of **8c** into **9c** occurred under thermal conditions (12% and 32% after 24 h and 48 h, respectively, additional heating for 24 h at 110 °C being necessary for it to go to completion).

Under acidic conditions, monitoring of the reactions of enals or enones by ^1H NMR did not result in the presence either of *Z* isomers or of hydroxy-pyrroline intermediates being detected (Scheme 2). However, the involvement of such a key *Z* intermediate in the pyrrole formation mechanism would agree with the work of Dieter, who observed that traces of HCl were sufficient to effect isomerisation of *N*,*N*-disubstituted γ-amino-enones.[22]

Table 1. Synthesis of *N*-Boc-protected substituted pyrroles **5, 7** and **9**

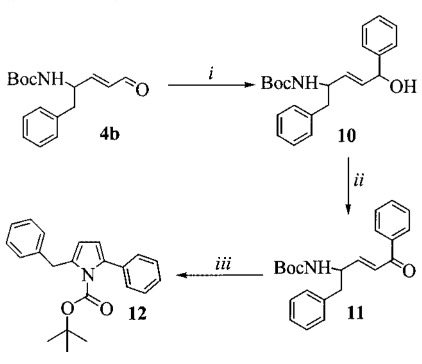
Product	R^1	R^2	Yield (%)[a]
5a	*i*Pr	H	78
5b	Bn	H	80
5c	Et	H	73
5d	Me	H	78
7a	*i*Pr	Me	87
7b	Bn	Me	75
7c	Et	Me	81
7d	Me	Me	90
9c	Me	C_4 fused	90
9d	Et	C_4 fused	87

[a] Isolated pure compounds.



Scheme 2

With an easy synthesis of *N*-Boc-alkylpyrroles in hand, extension to arylpyrroles was envisaged. The synthesis of *N*-Boc-2-arylpyrroles from a linear precursors, enal **4b**, by a 1,2-addition/oxidation sequence was evaluated first. An excess of phenylmagnesium bromide was added to **4b**, and the resulting allylic alcohol **10** (55%) was subsequently oxidised to γ-aminophenone **11** in 86% yield. As expected, cyclodehydration of compound **11** under acidic conditions provided the corresponding *N*-Boc-2-phenyl pyrrole **12** in 80% yield (Scheme 3).

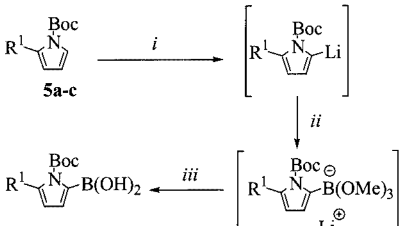


Scheme 3. *i*) PhMgBr (3 equiv.), −78 °C, THF (55%); *ii*) Dess−Martin periodinane, room temp., CH_2Cl_2 (86%); *iii*)2 M HCl ethereal solution, CH_2Cl_2 (80%)

The route depicted in Scheme 3, allowing the introduction of various aryl groups, should be compared with an approach allowing the introduction of the aryl moiety onto the already formed pyrrole unit at the last stage. For this purpose, the Suzuki−Miyaura coupling reaction[28] appeared to be an attractive alternative.

Despite a growing interest in the field of catalysed C-C bond-formation,[29] the use of *N*-Boc-pyrrole-2-boronic acids as potent building blocks has not been widely reported in the literature.[30−33] We turned our attention to the synthetic use of such compounds.

Borylated pyrroles **13** were obtained by means of an α-lithiation/borylation sequence under Schlüter's conditions.[34] An aqueous workup allowed their isolation in 48−86% yields (Scheme 4) as rather unstable solids that had to be promptly engaged in further transformations.[35]



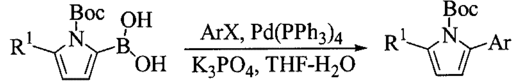
13	R^1
a	*i*Pr, 86%
b	Bn, 78%
c	Et, 48%

Scheme 4. *i*) LiTMP, −78 °C, THF; *ii*) (xs) $B(OMe)_3$, −78 °C; *iii*) sat. aq. NH_4Cl

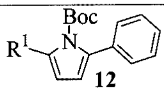
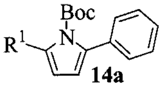
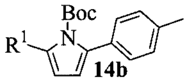
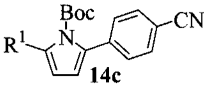
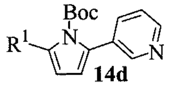
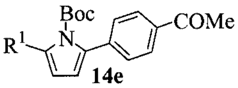
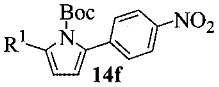
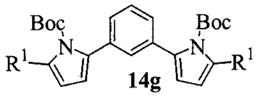
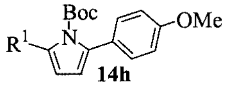
The freshly isolated boronic acids **13a−c** (1.25 equiv.) were each dissolved in a THF/H_2O mixture (3:1) with the aryl halide (1.0 equiv.), potassium phosphate (2.0 equiv.) and $Pd(PPh_3)_4$ (5 mol %), and the solution was warmed to 70 °C for 15−18 h. As shown in Table 2, *N*-Boc-2-aryl-substituted pyrroles **12** and **14a−h** were isolated in moderate to good yields. Best results were obtained with aryl bromides bearing electron-withdrawing groups. Aryl iodides gave moderate yields, while the reaction completely failed with the electron-rich 4-bromoanisole (Table 2, entry 9). These yields could not be improved because of the protodeboronation side-reaction that competed with the coupling under the reaction conditions chosen.[36,37]

Removal of the Boc protecting group was performed with **14g** as a representative example by heating the neat pyrrole[38] at 185 °C (Scheme 5). This decarboxylation afforded the corresponding 1*H*-pyrrole **15** in 79% yield.

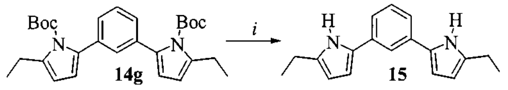
Table 2. Suzuki−Miyaura coupling reactions



13 **12, 14**

Entry	ArX	R^1	Compound	Yield(%)[a]
1	PhI	Bn	 **12**	48
2	PhI	*i*Pr	 **14a**	58
3	4-MeC_6H_4I	*i*Pr	 **14b**	60
4	4-CNC_6H_4Br	*i*Pr	 **14c**	54
5	3-pyridylBr	*i*Pr	 **14d**	70
6	4-AcC_6H_4Br	*i*Pr	 **14e**	85
7	4-$NO_2C_6H_4Br$	*i*Pr	 **14f**	89
8	3-BrC_6H_4I	Et	 **14g**	71[b]
9	4-$MeOC_6H_4Br$	*i*Pr	 **14h**	0[c]

[a] Isolated pure compound. [b] 4 equiv. of base used. [c] **5a** was isolated in 78% yield.



Scheme 5. *i*) neat 185 °C, 30 min (79%)

Conclusion

We describe a clean and high-yielding synthesis of *N*-Boc-pyrroles, based on the cyclodehydration of easily accessible and isolable (*E*)-γ-(*tert*-butoxycarbonyl)amino-α,β-unsaturated aldehydes or ketones. This synthesis, which requires mild acidic or thermal conditions at a late stage, seems to be a flexible and promising route for the construction of elaborated polysubstituted pyrroles and should be of wide interest to heterocyclic chemists. In terms of the synthesis of 2-arylpyrroles, the cyclodehydration of α,β-unsaturated phenones appears to be a valuable approach to complement the Suzuki−Miyaura coupling of borylated pyrroles. Although the couplings were successful, the newly synthesised *N*-Boc-2-pyrrole boronic acids unfortunately suffered from their limited lifetimes, representing a severe restriction for extensive use. Extension of this work is under active investigation in our laboratory.

Experimental Section

General Remarks: All reactions were performed under a positive N_2 pressure unless indicated. All chemicals were obtained from commercial suppliers and used without purification. THF and toluene were distilled from Na/benzophenone prior to use, and CH_2Cl_2 was distilled over CaH_2. Melting points are uncorrected. All NMR spectra were recorded on Bruker instruments at 200 and 300 MHz (^1H), 50 and 75 MHz (^{13}C) and 96 MHz (^{11}B). NMR chemical shifts are expressed in ppm relative to internal TMS (^1H, ^{13}C), and coupling constants were measured in Hz. For ^{11}B NMR, $BF_3{\cdot}Et_2O$ has been used as a reference. $CDCl_3$ was distilled over CaH_2 prior to use. Mass spectra were taken in EI or FAB (*m*NBA: *m*-nitrobenzyl alcohol as matrix) mode. Column chromatography was carried out on silica gel [silica gel 60 (30−40 mesh)]. Thin-layer chromatography (TLC) was performed on silica gel ($60F_{254}$, Merck).

General Procedure for the Wittig Homologation: *N*-(Boc)-α-aminoaldehydes **3a−d** were prepared from commercially available *N*-(Boc)amino alcohols by known procedures[24,26] and used directly in the Wittig homologation step without purification. The ylide [1.0 equiv. of (triphenylphosphoranylidene)acetaldehyde, 1-(triphenylphosphoranylidene)-2-propanone or 2-(triphenylphosphoranylidene)cyclohexanone] was added to a solution of 3 (7.7 mmol) in toluene (80 mL) and the reaction mixture was warmed to 70 °C and stirred at that temperature until TLC indicated the total disappearance of starting material. After removal of the solvent under vacuum, compounds were purified by precipitation of Ph_3PO from a ether/pentane mixture with subsequent filtration, or directly submitted to column chromatography on SiO_2. These compounds were not stored but used directly in the next step.

***tert*-Butyl [(2*E*)-1-Isopropyl-4-oxobut-2-enyl]carbamate (4a):** *N*-(Boc)-valinal **3a** (0.6 g, 7.7 mmol) and (triphenylphosphoranylidene)acetaldehyde (2.34 g, 7.7 mmol) were heated for 4 h according to the general procedure. After removal of Ph_3PO by precipitation, the crude enal was passed through a plug of neutralised SiO_2 (EtOAc/Hept/Et_3N, 25:74:1), to afford 0.45 g (70%) of compound **4a** as a yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.86 (d, *J* = 6.8 Hz, 3 H, $(CH_3)_2CH$), 0.89 (d, *J* = 6.8 Hz, 3 H, $(CH_3)_2CH$), 1.35 (s, 9 H, $[(CH_3)_3]$), 1.83 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 4.21 (br. s, 1 H, CH), 5.06 (br. d, *J* = 8.5 Hz, 1 H, NH), 6.13 (ddd, *J* = 15.7, 7.8, 1.5 Hz, 1 H, HC=C*H*-CHO), 6.72 (dd, *J* = 15.7, 4.9 Hz, 1 H, *H*C=CH-CHO), 9.49 (d, *J* = 7.8 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.4 (CH_3), 19.3 (CH_3), 28.6 $[(CH_3)_3]$, 32.4 (CH), 57.4 (NCH), 80.0 $[C(CH_3)_3]$, 132.4 (=CH), 155.8 (=CH), 157.2 (C_q), 193.6 (C_q) ppm. HR-EIMS calcd. for $C_8H_{13}NO_3$ ($[M - C_4H_8]^{+\cdot}$) 171.0895; found 171.0894.

***tert*-Butyl [(2*E*)-1-Benzyl-4-oxobut-2-enyl]carbamate (4b):** *N*-(Boc)-phenylalaninal **3b** (4.1 g, 16.4 mmol) and (triphenylphosphoranylidene)acetaldehyde (4.99 g, 16.4 mmol) were heated for 5 h according to the general procedure. After removal of Ph_3PO by precipitation, the crude enal was passed through a plug of neutralised SiO_2 (EtOAc/Hept/Et_3N, 25:74:1) to afford 3.2 g (70%) of compound **4b** as a yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, $[(CH_3)_3]$), 2.96 (m, 2 H, CH_2), 4.80 (m, 2 H, NH + CH), 6.17 (ddd, *J* = 15.7, 7.8, 1.4 Hz, 1 H, HC=C*H*-CHO), 6.78 (dd, *J* = 15.6, 4.8 Hz, 1 H, *H*C=CH-CHO), 7.19−7.40 (m, 5 H, H_{ar}), 9.56 (d, *J* = 7.8 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.7 $[(CH_3)_3]$, 40.9 (CH_2), 53.1 (NCH), 80.5 $[C(CH_3)_3]$, 127.5 (CH_{ar}), 129.1 (CH_{ar}), 129.7 (CH_{ar}), 131.9 (=CH), 136.5 ($^{IV}C_{ar}$), 155.4 [CO(Boc)], 157.0 (=CH), 193.6 (CHO) ppm. HR-EIMS calcd. for $C_{16}H_{21}NO_3$ ($[M]^{+\cdot}$) 275.1522; found 275.1519.

***tert*-Butyl [(2*E*)-1-Ethyl-4-oxobut-2-enyl]carbamate (4c):** *N*-(Boc)-ethylglycinal **3c** (5.9 g, 32 mmol) and (triphenylphosphoranylidene)-acetaldehyde (9.74 g, 32.0 mmol) were heated for 4 h according to the general procedure. After removal of Ph_3PO by precipitation, the crude enal was passed through a plug of neutralised SiO_2 (EtOAc/Hept/Et_3N, 25:74:1) to afford 5.0 g (79%) of compound **4c** as a yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.45 (s, 9 H, $[(CH_3)_3]$, 1.51−1.80 (m, 2 H, CH_2), 4.34 (br. s, 1 H, NCH), 4.55 (br. s, 1 H, NH), 6.19 (ddd, *J* = 15.7, 7.8, 1.6 Hz 1 H, HC=C*H*-CHO), 6.75 (dd, *J* = 15.6, 4.8 Hz, 1 H, *H*C=CH-CHO), 9.57 (d, *J* = 7.7 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 10.2 (CH_3), 27.3 (CH_2), 28.3 $[(CH_3)_3]$, 53.0 (NCH), 80.0 $[C(CH_3)_3]$, 131.3 (=CH), 155.3 (C_q), 157.5 (=CH), 193.5 (C_q) ppm. HR-EIMS calcd. for $C_7H_{11}NO_3$ ($[M - C_4H_8]^{+\cdot}$) 157.0739; found 157.0739.

***tert*-Butyl [(2*E*)-1-Methyl-4-oxobut-2-enyl]carbamate (4d):** *N*-(Boc)-alaninal **3d** (3.5 g, 20 mmol) and (triphenylphosphoranylidene)acetaldehyde (6.08 g, 20.0 mmol) were heated for 3 h according to the general procedure. After removal of Ph_3PO by precipitation the crude enal was passed through a plug of neutralised SiO_2 (EtOAc/Hept/Et_3N, 25:74:1) to afford 3.0 g (75%) of compound **7c** as a yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.31 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.42 (s, 9 H, $[(CH_3)_3]$), 4.49 (br. s, 1 H, NCH), 4.60 (br. s, 1 H, NH), 6.15 (ddd, *J* = 15.7, 7.8, 1.6 Hz, 1 H, HC=C*H*-CHO), 6.77 (dd, *J* = 15.6, 4.5 Hz, 1 H, *H*C=CH-CHO), 9.55 (d, *J* = 7.7 Hz, 1 H, CHO) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.3 (CH_3), 28.7 $[(CH_3)_3]$, 48.5 (NCH), 80.5 $[C(CH_3)_3]$, 131.0 (=CH), 155.3 (C_q), 158.8 (=CH), 193.9 (C_q).

***tert*-Butyl [(2*E*)-1-Isopropyl-4-oxopent-2-enyl]carbamate (6a):** *N*-(Boc)-valinal **3a** (162 mg, 0.81 mmol) and 1-triphenylphosphoranylidene-2-propanone (0.26 g, 0.81 mmol) were heated for 4 h according to the general procedure. After purification by column chromatography on SiO_2 (EtOAc/Hept/Et_3N, 25:74:1), **6a** (137 mg, 70%) was isolated as a colourless oil.^1H NMR (200 MHz, $CDCl_3$): δ = 0.85 and 0.88 (d, *J* = 6.7 Hz, 6 H, $(CH_3)_2CH$), 1.37 (s, 9 H, $[(CH_3)_3]$), 1.82 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 2.19 (s, 3 H, $COCH_3$), 4.12 (br. s, 1 H, NCH), 4.69 (br. d, *J* = 8.5 Hz, 1 H, NH), 6.10 (dd, *J* = 16.0, 1.7 Hz, 1 H, HC=C*H*-CO-), 6.72 (dd, *J* = 15.9, 5.6 Hz, 1 H, *H*C=CH-CO-) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.0 (CH_3), 19.0 (CH_3), 27.5 (CH), 28.3 $[(CH_3)_3]$, 32.2 ($COCH_3$), 56.8 (NCH), 79.6 $[C(CH_3)_3]$, 130.4 (=CH), 146.3 (=CH), 155.4 (C_q), 198.1 ($COCH_3$) ppm. HR-EIMS calcd. for $C_{10}H_{16}NO_3$ ($[M - C_3H_7]^{+\cdot}$) 198.1130; found 198.1123.

***tert*-Butyl [(2*E*)-1-Benzyl-4-oxopent-2-enyl]carbamate (6b):** *N*-(Boc)-phenylalaninal **3b** (0.65 g, 2.6 mmol) and 1-triphenylphosphoranylidene-2-propanone (0.83 g, 2.6 mmol) were heated for 2 h according to the general procedure. After purification by column chromatography on SiO_2 (EtOAc/Hept, 1:3), **6b** (0.54 g,71%) was isolated as a pale yellow solid: M.p. 89−91 °C; ^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, $[(CH_3)_3]$), 2.26 (s, 3 H, $COCH_3$), 2.94 (m, 2 H, CH_2), 4.64 (m, 2 H, NH+CH), 6.13 (d, *J* = 16.1 Hz, 1 H, CH=C*H*-CO-), 6.76 (dm, *J* = 16.0 Hz, 1 H, C*H*=CH-CO-), 7.18−7.38 (m, 5 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.8 ($COCH_3$), 28.7 $[(CH_3)_3]$, 41.3 (CH_2), 52.9 (CH), 80.4 $[C(CH_3)_3]$, 127.4 (CH_{ar}), 129.0 (CH_{ar}), 129.8 (CH_{ar}), 130.2 (=CH), 136.8 (C_q), 146.8 (=CH), 155.4 (C_q), 198.4 ($COCH_3$) ppm. HR-EIMS calcd. for $C_{15}H_{20}NO_2$ ($[M - COCH_3]^{+\cdot}$) 246.1494; found 246.1413.

***tert*-Butyl [(2*E*)-1-Ethyl-4-oxopent-2-enyl]carbamate (6c):** *N*-(Boc)-ethylglycinal **3c** (0.50 g, 2.7 mmol) and 1-triphenylphosphoranylidene-2-propanone (0.86 g, 2.7 mmol) were heated for 2 h according to the general procedure. After purification by column chromatography on SiO_2 (EtOAc/Hept, 1:3), **6c** (0.49 g,81%) was isolated as a pale yellow oil: ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (t, *J* =

7.3 Hz, 3 H, CH_3), 1.37 (s, 9 H, $[(CH_3)_3]$), 1.54 (m, 2 H, CH_2), 2.20 (s, 3 H, COC*H*$_3$), 4.17 (br. s, 1 H, NCH), 4.49 (br. s, 1 H, NH), 6.09 (dd, *J* = 15.9, 1.3 Hz 1 H, HC=C*H*-CO-), 6.61 (dd, *J* = 15.9, 5.3 Hz, 1 H, *H*C=CH-CO-) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 10.6 (CH_3), 27.8 (CO*C*H$_3$), 28.0 (CH_2), 28.7 $[(CH_3)_3]$, 53.2 (NCH), 80.2 [*C*$(CH_3)_3$], 130.1 (=CH), 147.6 (=CH), 155.6 (C_q), 198.7 (*C*OCH$_3$) ppm. HR-EIMS calcd. for $C_{10}H_{16}NO_3$ ($[M - C_2H_5^{\cdot}]^+$) 198.1130; found 198.1123.

***tert*-Butyl [(2*E*)-1-Methyl-4-oxopent-2-enyl]carbamate (6d):** *N*-(Boc)-alaninal **3d** (0.76 g, 4.4 mmol) and 1-triphenylphosphoranylidene-2-propanone (1.40 g, 4.4 mmol) were heated for 3 h according to the general procedure. After purification by column chromatography on SiO_2 (EtOAc/Hept, 1:3), **6d** (0.80 g,86%) was isolated as a pale yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.44 (s, 9 H, $[(CH_3)_3]$), 2.26 (s, 3 H, COC*H*$_3$), 4.40 (br. s, 1 H, NCH), 4.73 (br. s, 1 H, NH), 6.13 (dd, *J* = 16.1, 1.5 Hz, 1 H, HC=C*H*-CO-), 6.71 (dd, *J* = 16.1, 5.1 Hz, 1 H, *H*C=CH-CO-) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.6 (CH_3), 27.6 (CO*C*H$_3$), 28.7 $[(CH_3)_3]$, 47.5 (NCH), 80.2 [*C*$(CH_3)_3$], 129.4 (=CH), 148.7 (=CH), 155.3 (C_q), 198.8 ($COCH_3$) ppm. HR-EIMS calcd. for $C_7H_{11}NO_3$ ($[M - C_4H_8]^{+\cdot}$) 157.0739; found 157.0747.

***tert*-Butyl {1-[(*E*)-(2-Oxocyclohexylidene)methyl]propyl}carbamate (8c):** *N*-Boc-ethylglycinal **3c** (500 mg; 2.7 mmol) and 2-(triphenylphosphoranylidene)cyclohexanone[27] (0.97 g, 2.7 mmol) were heated for 18 h according to the general procedure. Purification on SiO_2 (EtOAc/Hept/Et_3N, 25:74:1) afforded 570 mg (80%) of compound **8c** as a white solid: M.p. 110−112 °C. ^{1}H NMR (200 MHz, C_6D_6): δ = 0.75 (t, *J* = 6.1 Hz, 3 H, CH_3), 1.18−1.30 (m, 6 H, CH_2), 1.49 (s, 9 H, $[(CH_3)_3]$), 2.19 [m, 3 H, CH_2 + CH_{2a})], 2.66 (m, 1 H, CH_{2b})], 4.40 (m, 2 H, NH + NCH), 6.46 (d, *J* = 8.8 Hz, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, C_6D_6): δ = 10.5 (CH_3), 23.7 (CH_2), 24.1, 27.7, 28.7 (CH_2), 28.9 $[(CH_3)_3]$, 40.8 (CH_2), 49.8 (NCH), 79.1 [*C*$(CH_3)_3$], 128.7 (C_q), 137.8 (=CH), 155.7 (C_q), 198.8 (C_q) ppm. HR-EIMS calcd. for $C_{13}H_{20}NO_3$ ($[M - C_2H_5]^{+\cdot}$) 238.1443; found 238.1442.

***tert*-Butyl [(2*E*)-1-Methyl-2-(2-oxocyclohexylidene)ethyl]carbamate (8d):** *N*-Boc-alaninal **3d** (513 mg; 2.97 mmol) and 2-(triphenylphosphoranylidene)cyclohexanone[27] (1.06 g, 2.97 mmol) were heated for 24 h according to the general procedure. Purification by column chromatography on SiO_2 (EtOAc/Hept/Et_3N, 25:74:1) afforded 369 mg (53%) of compound **8d** as a colourless oil.^{1}H NMR (200 MHz, C_6D_6): δ = 1.20 (d, *J* = 6.8 Hz, 3 H), 1.54 (m, 4 H, CH_2)], 1.67 (s, 9 H, $[(CH_3)_3]$), 2.40 (m, 3 H, CH_2 + CH_{2a}), 2.76 (m, 1 H, CH_{2b})], 4.78 (m, 1 H, NCH), 5.07 (br. d, 1 H, NH), 6.46 (d, *J* = 9.1 Hz, 1 H, =CH) ppm. ^{13}C NMR (50 MHz, C_6D_6): δ = 14.7 (CH_3), 23.7 (CH_2), 24.0 (CH_2), 27.3 (CH_2), 28.9 $[(CH_3)_3]$, 40.8 (CH_2), 44.4 (NCH), 79.1 [*C*$(CH_3)_3$], 136.5 (C_q), 139.3 (=CH), 155.6 (C_q), 200.0 (C_q) ppm. HR-EIMS calcd. for $C_{10}H_{15}NO_3$ ($[M - C_4H_8]^{+\cdot}$) 197.1052; found 197.1046.

***tert*-Butyl [(2*E*)-1-Benzyl-4-oxo-4-phenylbut-2-enyl]carbamate (11):** A solution of compound **4b** (0.93 mmol) in THF (5 mL) was cooled to −70 °C and a solution of phenylmagnesium bromide (2.80 mmol) in ether (4 mL) was added dropwise. After 10 min the mixture was warmed to 0 °C and neutralised by addition of a saturated NH_4Cl solution (5 mL) and water (5 mL). After extraction, drying and evaporation of the solvent, the crude material was purified by column chromatography (EtOAc/Hept, 1:2) to afford 174 mg (55%) of alcohol **10** as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, $[(CH_3)_3]$), 2.86 (d, *J* = 6.8 Hz, 2 H, CH_2), 3.12 (br. s, 1 H, OH), 4.43 (br. s, 1 H, NCH), 4.69 (br. s, 1 H, NH), 5.20 (br. s, 1 H, C*H*OH), 6.17 (m, 2 H, =CH), 7.16−7.38 (m, 10 H, H_{ar}) ppm. HR-EIMS calcd. for $C_{15}H_{20}NO_3$ ($[M - C_7H_7]^{+\cdot}$) 351.1834; found 351.1829.

Dess−Martin periodinane (1.5 equiv.) was added to a solution of alcohol **10** (133 mg, 0.38 mmol) in CH_2Cl_2 (5 mL) and the mixture was stirred for 30 min before evaporation of the solvent. The residue was then dissolved in a mixture of EtOAc/Hept (1:3, v/v) and filtered over a plug of SiO_2 to afford 108 mg (82%) of enone **11** as a pale yellow solid: M.p. 98−99 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.46 (s, 9 H, $[(CH_3)_3]$), 2.98 (d, *J* = 6.6 Hz, 2 H, CH_2), 4.74 (br. s, 1 H, NCH), 4.53 (br. s, 1 H, NH), 6.96 (m, 2 H, H_{ar}), 7.22−7.58 (m, 8 H, =CH + H_{ar}), 7.89 (d, *J* = 8.5 Hz, 2 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.7 $[(CH_3)_3]$, 41.4 (CH_2), 53.5 (NCH), 80.3 [*C*$(CH_3)_3$], 125.7 (CH), 127.3, 128.9, 129.0 (2CH), 129.9, 133.3 (CH), 137.0 (C_q), 138.0 (C_q), 147.9 (CH), 155.5 (C_q), 190.8 (C_q) ppm. HR-EIMS calcd. for $C_{22}H_{25}NO_3$ ($[M]^{+\cdot}$) 351.1834; found 351.1829.

General Procedure for Cyclisation of Enals and Enones: HCl (0.1 equiv. for **5**, 1.0 equiv. for **6** and **8**, 2 M ethereal solution) was added to a solution of compound **5**, **6** or **8** (1 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred at room temperature until TLC indicated the total disappearance of starting material (completion proceeded within 15 min). After evaporation of the solvent, the crude pyrrole was purified by silica gel chromatography with the eluent specified or by bulb-to-bulb distillation.

***tert*-Butyl 2-Isopropyl-1*H*-pyrrole-1-carboxylate (5a):** Treatment of compound **4a** (1.10 g, 4.8 mmol) according to the general procedure followed by bulb-to-bulb distillation gave the pyrrole (0.78 g, 77%) as a colourless oil: B.p. 60−70 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 6.7 Hz, 6 H, (C*H*$_3$)$_2$CH), 1.47 (s, 9 H, $[(CH_3)_3]$), 3.41 (hept, *J* = 6.7 Hz, 1 H, $(CH_3)_2$C*H*), 5.89 (m, 1 H, 3-H), 5.96 (t, *J* = 3.3 Hz, 1 H, 4-H), 7.07 (dd, *J* = 3.3, 1.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.4 (CH_3), 27.3 (CH), 28.4 $[(CH_3)_3]$, 83.6 [*C*$(CH_3)_3$], 108.7 (CH), 110.2, 121.5 (CH), 143.5 (C_q), 149.9 (C_q) ppm. HR-EIMS calcd. for $C_{12}H_{19}NO_2$ ($[M]^{+\cdot}$) 209.1416; found 209.1413.

***tert*-Butyl 2-Benzyl-1*H*-pyrrole-1-carboxylate (5b):** Treatment of compound **4b** (1.32 g, 4.8 mmol) according to the general procedure followed by bulb-to-bulb distillation gave the pyrrole (0.99 g, 80%) as a colourless oil: B.p. 100−110 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.60 (s, 9 H, $[(CH_3)_3]$), 4.33 (s, 2 H, CH_2), 5.88 (m, 1 H, 3-H), 6.19 (t (dd), *J* = 3.3 Hz, 1 H, 4-H), 7.23−7.45 (m, 6 H, 5-H + H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.4 $[(CH_3)_3]$, 35.5 (CH_2), 83.9 [*C*$(CH_3)_3$], 110.5 (CH), 113.7, 121.8, 126.5, 128.7, 129.2 (CH), 134.7 (C_q), 140.3, 150.0 (C_q) ppm. $C_{16}H_{19}NO_2$: C 74.68, H 7.44, N 5.44; found C 74.69, H 7.42, N 5.32.

***tert*-Butyl 2-Ethyl-1*H*-pyrrole-1-carboxylate (5c):** Treatment of compound **4c** (0.95 g, 4.5 mmol) according to the general procedure followed by bulb-to-bulb distillation gave the pyrrole (0.63 g, 73%) as a colourless oil: B.p. 60−70 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.59 (s, 9 H, $[(CH_3)_3]$), 2.86 (dq, *J* = 7.3, 1.0 Hz, 2 H, CH_2), 6.05 (m, 1 H, 3-H), 6.12 (t (dd), *J* = 3.3 Hz, 1 H, 4-H), 7.21 (dd, *J* = 3.3, 1.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.3 (CH_3), 22.2 (CH_2), 28.0 $[(CH_3)_3]$, 83.2 [*C*$(CH_3)_3$], 109.8 (CH), 109.9, 120.8 (CH), 138.0 (C_q), 149.5 (C_q) ppm. HR-EIMS calcd. for $C_{11}H_{17}NO_2$ ($[M]^{+\cdot}$) 195.1259; found 195.1252.

***tert*-Butyl 2-Methyl-1*H*-pyrrole-1-carboxylate (5d):** Treatment of compound **4d** (0.52 g, 2.6 mmol) according to the general procedure followed by bulb-to-bulb distillation gave the pyrrole (0.37 g, 78%) as a colourless oil: B.p. 50−60 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, $[(CH_3)_3]$), 2.31 (d, *J* = 0.4 Hz, 3 H, CH_3), 5.80 (dm, *J* = 3.3 Hz, 1 H, 3-H), 5.84 (t (dd), *J* = 3.3 Hz, 1 H, 4-H), 7.07 (dd, *J* = 3.3, 1.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.8 (CH_3), 28.4 (CH_3), 83.6 (C_q), 110.3 (CH), 112.2, 120.9 (CH), 131.9 (C_q), 150.1 (C_q) ppm. HR-EIMS calcd. for $C_{10}H_{15}NO_2$ ($[M]^{+\cdot}$) 181.1103; found 181.1101.

***tert*-Butyl 2-Isopropyl-5-methyl-1*H*-pyrrole-1-carboxylate (7a):** Treatment of compound **6a** (172 mg, 0.71 mmol) according to the general procedure followed by bulb-to-bulb distillation gave the pyrrole (139 mg, 87%) as a colourless oil. B.p. 60−65 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$), 1.62 (s, 9 H, $[(CH_3)_3]$), 2.38 (s, 3 H, CH_3), 3.47 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 5.81 (d, *J* = 3.3 Hz, 1 H, 3-H or 4-H), 5.85 (d, *J* = 3.3 Hz, 1 H, 4-H or 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.5 (CH_3), 23.3 (CH_3), 27.3 (CH), 28.4 $[(CH_3)_3]$, 83.4 $[C(CH_3)_3]$, 106.6 (CH), 110.1 (CH), 131.3 (C_q), 142.7, 150.9 (C_q) ppm. HR-EIMS calcd. for $C_{13}H_{21}NO_2$ ($[M]^{+\cdot}$) 223.1572; found 223.1573.

***tert*-Butyl 2-Benzyl-5-methyl-1*H*-pyrrole-1-carboxylate (7b):** Treatment of compound **6b** (190 mg, 0.66 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:6) gave the pyrrole (133 mg, 75%) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.53 (s, 9 H, $[(CH_3)_3]$), 2.48 (s, 3 H, CH_3), 4.26 (s, 2 H, CH_2), 5.76 (d, *J* = 3.2 Hz, 1 H, 3-H or 4-H), 5.93 (d, *J* = 3.1 Hz, 1 H, 4-H or 3-H), 7.20−7.38 (m, 5 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.9 (CH_3), 28.3 $[(CH_3)_3]$, 36.2 (CH_2), 83.9 $[C(CH_3)_3]$, 110.6 (CH), 112.1, 126.4, 128.7, 129.1 (CH), 132.5 (C_q), 134.1, 140.7, 150.6 (C_q) ppm. HR-EIMS calcd. for $C_{17}H_{21}NO_2$ ($[M]^{+\cdot}$) 271.1572; found 271.1571.

***tert*-Butyl 2-Ethyl-5-methyl-1*H*-pyrrole-1-carboxylate (7c):** Treatment of compound **6c** (387 mg, 1.70 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:6) gave the pyrrole (288 mg, 81%) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.51 (s, 9 H, $[(CH_3)_3]$), 2.30 (m, 3 H, CH_3), 2.73 (q, *J* = 7.3 Hz, 2 H, CH_2), 5.73 (s, 2 H, 3-H and 4-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 12.5 (CH_3), 15.5 (CH_3), 21.9 (CH_2), 27.0 $[(CH_3)_3]$, 82.1 $[C(CH_3)_3]$, 107.2 (CH), 109.1 (CH), 130.2 (C_q), 136.7 (C_q), 149.5 (C_q) ppm. HR-EIMS calcd. for $C_{10}H_{13}NO_3$ ($[M]^{+\cdot}$) 209.1416; found 209.1413.

***tert*-Butyl 2,5-Dimethyl-1*H*-pyrrole-1-carboxylate (7d):** Treatment of compound **6d** (177 mg, 0.83 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:6) gave the pyrrole (146 mg, 90%) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.66 (s, 9 H, $[(CH_3)_3]$), 2.45 (s, 6 H, CH_3), 5.85 (s, 2 H, 3-H and 4-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.9 (CH_3), 28.4 $[(CH_3)_3]$, 83.6 (C_q), 110.5 (CH), 131.6 (C_q), 150.9 (C_q). Spectroscopic data were in agreement with literature data.[39]

***tert*-Butyl 2-Ethyl-4,5,6,7-tetrahydro-1*H*-indole-1-carboxylate (9c):** Treatment of compound **8c** (155 mg, 0.58 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:10) gave the tetrahydroindole (126 mg, 87%) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.48 (s, 9 H, $[(CH_3)_3]$), 1.58−1.68 (m, 4 H, $-CH_2-$), 2.31 (m, 2 H, CH_2), 2.72 (m, 4 H, $-CH_2-$), 5.66 (s, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 12.6 (CH_3), 21.7 (CH_2), 21.9 (CH_2), 22.2 (CH_2), 22.8 (CH_2), 24.7 (CH_2), 27.1 $[(CH_3)_3]$, 81.7 $[C(CH_3)_3]$, 108.6 (CH), 119.3 (C_q), 128.2 (C_q), 135.8 (C_q), 149.3 (C_q) ppm. HR-EIMS calcd. for $C_{15}H_{23}NO_2$ ($[M]^{+\cdot}$) 249.1729; found 249.1724.

***tert*-Butyl 2-Methyl-4,5,6,7-tetrahydro-1*H*-indole-1-carboxylate (9d):** Treatment of compound **8d** (130 mg, 0.51 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:10) gave the tetrahydroindole (108 mg, 90%) as a colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.65 (s, 9 H, $[(CH_3)_3]$), 1.58−1.68 (m, 4 H, $-CH_2-$), 2.46 (m, 5 H, CH_3 + CH_2), 2.86 (m, 2 H, CH_2), 5.79 (d, *J* = 0.8 Hz, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.7 (CH_3), 23.3 (CH_2), 23.6 (CH_2), 24.2 (CH_2), 26.2 (CH_2), 28.6 $[(CH_3)_3]$, 83.2 $[C(CH_3)_3]$, 111.9 (CH), 120.8 (C_q), 129.6 (C_q), 130.8 (C_q), 150.8 (C_q) ppm. HR-EIMS calcd. for $C_{14}H_{21}NO_2$ ($[M]^{+\cdot}$) 235.1572; found 275.1572.

***tert*-Butyl 2-Benzyl-5-phenyl-1*H*-pyrrole-1-carboxylate (12):** Treatment of compound **11** (101 mg, 0.29 mmol) according to the general procedure followed by chromatography on SiO_2 (EtOAc/Hept, 1:10) gave the pyrrole (78 mg, 81%) as a colourless solid: M.p. 93−94 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.03 (s, 9 H, $[(CH_3)_3]$), 4.14 (s, 2 H, CH_2), 5.76 (d, *J* = 3.3 Hz, 1 H, 4-H), 6.01 (d, *J* = 3.3 Hz, 1 H, 3-H), 7.08−7.23 (m, 10 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.6 $[(CH_3)_3]$, 35.3 (CH_2), 83.9 $[C(CH_3)_3]$, 111.9 (CH), 112.3, 126.5, 127.1, 128.2, 128.7 (2CH), 129.3 (CH), 135.6 (C_q), 135.8, 136.1, 140.0, 150.3 (C_q) ppm. HR-EIMS calcd. for $C_{22}H_{23}NO_2$ ($[M]^{+\cdot}$) 333.1729; found 333.1736.

Typical Procedure for the Preparation of Boronic Acids 13a−c: Under an argon atmosphere, *n*BuLi (1.6 N in hexane, 4.7 mL, 7.52 mmol) was slowly added at −78 °C to a solution of 2,2,6,6-tetramethylpiperidine (1.15 mL, 6.83 mmol) in THF (25 mL). After stirring for 15 min at that temperature, the mixture was allowed to warm to 0 °C over 30 min. After the mixture had been cooled back to −78 °C, a solution of pyrrole **5** (6.21 mmol) in THF (5 mL) was added at such a rate that the temperature remained below −65 °C. The reaction mixture was stirred for 30 min at −78 °C, prior to the addition of trimethylborate (3.53 mL, 31.08 mmol). The solution was allowed to warm to room temperature overnight. A saturated NH_4Cl solution (20 mL) was then added. The aqueous phase was extracted with Et_2O, and the combined organic phases were washed with aqueous HCl (1 N, 20 mL) and brine. The solution was then slowly concentrated until a solid started to precipitate. The product was filtered off, washed with cold Et_2O and dried under vacuum. The boronic acids **13** were not stored but used directly in the next step.

1-(*tert*-Butoxycarbonyl)-5-isopropyl-1*H*-pyrrol-2-ylboronic Acid (13a): Pyrrole **5a** (1.30 g, 6.21 mmol) was treated according to the general procedure to give the boronic acid (1.35 g, 86%) as a pale yellow solid. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.26 (d, *J* = 6.7 Hz, 6 H, $(CH_3)_2CH$), 1.63 (s, 9 H, $[(CH_3)_3]$), 3.41 (hept, *J* = 6.7 Hz, 1 H, $(CH_3)_2CH$), 6.14 (dd, *J* = 3.5, 0.8 Hz, 1 H, 3-H), 7.04 (d, *J* = 3.5 Hz, 1 H, 4-H), 7.20 (br. s, 2 H, $B(OH)_2$] ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.4 (CH_3), 28.3 $[(CH_3)_3]$, 28.5 (CH), 86.3 $[C(CH_3)_3]$, 110.4 (CH), 127.4 (CH), 149.2 (C_q), 153.7 (C_q) ppm. ^{11}B NMR (96 MHz, $CDCl_3$): δ = 26.1. HR-FABMS calcd. for $[C_{26}H_{30}N_3O_8B+H]^+$ 524.2209; found 524.2223. Observed as the boronic ester resulting from the esterification of **13a** with the matrix (*m*NBA).

1-(*tert*-Butoxycarbonyl)-5-benzyl-1*H*-pyrrol-2-ylboronic Acid (13b): Pyrrole **5b** (0.80 g, 3.10 mmol) was treated according to the general procedure to give the boronic acid (0.73 g, 78%) as a slightly brown solid. Fast deboronation took place in $CDCl_3$ during the recording of the ^{13}C NMR spectrum. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, $[(CH_3)_3]$), 4.27 (br. s, 2 H), 5.96 (dt, *J* = 3.4, 0.7 Hz, 1 H, 3-H), 7.06−7.12 [m, 3 H, 4-H + $B(OH)_2$], 7.26−7.35 (m, 5 H, H_{ar}) ppm. HR-FABMS calcd. for $[C_{30}H_{30}N_3O_8B+H]^+$ 572.2210; found 572.2207.

1-(*tert*-Butoxycarbonyl)-5-ethyl-1*H*-pyrrol-2-ylboronic Acid (13c): Pyrrole **5c** (0.46 g, 2.36 mmol) was treated according to the general procedure to give the boronic acid (0.27 g, 48%) as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.62 (s, 9 H, $[(CH_3)_3]$), 2.81 (q, *J* = 7.4 Hz, 2 H, CH_2), 6.05 (d, *J* = 3.4 Hz, 1 H, 3-H), 7.02 (d, *J* = 3.4 Hz, 1 H, 4-H), 7.35 [br. s, 2 H, $B(OH)_2$] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 24.1 (CH_2), 28.1 $[(CH_3)_3]$, 85.9 $[C(CH_3)_3]$, 111.8 (CH), 127.5 (CH), 144.1 (C_q), 153.4 (C_q) ppm. ^{11}B NMR (96 MHz, $CDCl_3$): δ = 26.2 ppm.

General Procedure for the Suzuki Pyrrol-2-ylboronic Acid Coupling: A THF/H_2O solution (5 ml, 4:1, v/v) containing a mixture of freshly isolated boronic acid **13** (1.25 equiv.), the aryl halide (0.37 mmol), potassium phosphate monohydrate (2.0 equiv.) and $Pd(PPh_3)_4$ (0.05 equiv.) was heated at 70 °C under an argon atmosphere for 15−18 h. After cooling, the solvent was removed under reduced pressure. The residue was extracted with Et_2O. The organic phase was washed with brine and dried over magnesium sulfate, and the solvents were evaporated to dryness. The crude compound was purified by silica gel chromatography with the eluent specified, followed in some cases by bulb-to-bulb distillation.

***tert*-Butyl 2-Benzyl-5-phenyl-1*H*-pyrrole-1-carboxylate (12):** The boronic acid **13b** (361 mg, 1.20 mmol) and iodobenzene (204 mg, 1.00 mmol) were coupled according to the general procedure, without heating. Purification on SiO_2 (CH_2Cl_2/heptane, 1:6) afforded a colourless solid (160 mg, 48%): M.p. 93−94 °C. Spectroscopic data were in agreement with those previously obtained (see above).

***tert*-Butyl 2-Isopropyl-5-phenyl-1*H*-pyrrole-1-carboxylate (14a):** The boronic acid **13a** (108 mg, 0.43 mmol) and iodobenzene (70 mg, 0.34 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:6) followed by bulb-to-bulb distillation afforded a colourless oil (60 mg, 58%) that slowly crystallised: B.p. 90−100 °C (0.01 Torr). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (s, 9 H, $[(CH_3)_3]$), 1.28 (d, *J* = 6.6 Hz, 6 H, $(CH_3)_2CH$), 3.47 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 6.03 (dd, *J* = 3.5, 0.8 Hz, 1 H, 4-H), 6.12 (d, *J* = 3.5 Hz, 1 H, 3-H), 7.28−7.36 (m, 5 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.1 (CH_3), 26.7 (CH), 27.3 $[(CH_3)_3]$, 83.6 (C_q), 106.5 (CH), 111.8, 126.7, 127.9, 128.3 (CH), 134.8 (C_q), 135.5, 144.3, 150.4 (C_q) ppm. HR-EIMS calcd. for $C_{18}H_{23}NO_2$ ($[M]^{+\cdot}$) 285.1729; found 285.1716. $C_{18}H_{23}NO_2$: C 75.76, H 8.12, N 4.91; found C 74.89, H 8.08, N 4.65.

***tert*-Butyl 2-Isopropyl-5-(4-methylphenyl)-1*H*-pyrrole-1-carboxylate (14b):** The boronic acid **13a** (115 mg, 0.45 mmol) and 1-iodo-4-methylbenzene (79 mg, 0.36 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:6) followed by bulb-to-bulb distillation afforded a colourless oil (64 mg, 60%) that slowly crystallised: B.p. 90−100 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (m, 15 H, $[(CH_3)_3]$ + $(CH_3)_2CH$), 2.37 (s, 3 H, CH_3), 3.45 (hept, *J* = 6.6 Hz, 1 H, $(CH_3)_2CH$), 6.01 (dd, *J* = 3.3, 0.8 Hz, 1 H, 4-H), 6.09 (d, *J* = 3.3 Hz, 1 H, 3-H), 7.17- 7.22 (m, 4 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3 (CH_3), 23.3 (CH_3), 26.8 (CH), 27.4 $[(CH_3)_3]$, 83.5 $[C(CH_3)_3]$, 107.0 (CH), 111.5, 128.2, 128.6 (CH), 132.6 (C_q), 134.9, 136.4, 144.0, 150.5 (C_q) ppm. HR-EIMS calcd. for $C_{19}H_{25}NO_2$ ($[M]^{+\cdot}$) 299.1885; found 299.1887. $C_{19}H_{25}NO_2$: C 76.22, H 8.42, N 4.68; found C 76.13, H 8.15, N 4.52.

***tert*-Butyl 2-(4-Cyanophenyl)-5-isopropyl-1*H*-pyrrole-1-carboxylate (14c):** The boronic acid **13a** (173 mg, 0.68 mmol) and 4-bromobenzonitrile (93 mg, 0.51 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:8) afforded a pale yellow oil (86 mg, 54%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$), 1.31 (s, 9 H, $[(CH_3)_3]$), 3.45 (hept, *J* = 6.6 Hz, 1 H, $(CH_3)_2CH$), 6.06 (dd, *J* = 3.5, 0.8 Hz, 1 H, 4-H), 6.21 (d, *J* = 3.5 Hz, 1 H, 3-H), 7.39 (d, *J* = 8.6 Hz, 2 H, H_{ar}), 7.63 (d, *J* = 8.6 Hz, 2 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.1 (CH_3), 26.8 (CH), 27.3 $[(CH_3)_3]$, 84.3 (C_q), 107.2 (CH), 109.7 (*C*-CN), 113.9 (CH), 119.1 (*C*N), 128.7 (CH), 131.7 (CH), 132.9 (C_q), 139.8 (C_q), 145.9 (C_q), 146.1 (C_q) ppm. HR-EIMS calcd. for $C_{19}H_{22}N_2O_2$ ($[M]^{+\cdot}$) 310.1681; found 310.1685.

***tert*-Butyl 2-Isopropyl-5-(pyridin-3-yl)-1*H*-pyrrole-1-carboxylate (14d):** The boronic acid **13a** (160 mg, 0.63 mmol) and 3-bromopyridine (80 mg, 0.51 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:3) followed by bulb-to-bulb distillation afforded a pale yellow oil (102 mg, 70%); B.p. 100−110 °C (0.01 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (s, 9 H, $[(CH_3)_3]$), 1.29 (d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$), 3.50 (hept, *J* = 6.6 Hz, 1 H, $(CH_3)_2CH$), 6.07 (dd, *J* = 3.5, 0.8 Hz, 1 H, 4-H), 6.17 (d, *J* = 3.5 Hz, 1 H, 3-H), 7.27 (ddd, *J* = 7.8, 4.8, 0.8 Hz, 1 H, H_{ar}), 7.60 (dt, *J* = 2.3, *J* = 7.8, 1 H, H_{ar}), 8.51 (dd, *J* = 4.8, 2.3 Hz, 1 H, H_{ar}), 8.56 (dd, *J* = 2.3, 0.8 Hz, 1 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.2 (CH_3), 27.0 (CH), 27.5 $[(CH_3)_3]$, 84.2 $[C(CH_3)_3]$, 107.3 (CH), 113.4 (CH), 122.8 (CH), 131.0 (C_q), 131.7 (C_q), 135.5 (CH), 145.6 (C_q), 146.1 (CH), 147.5 (CH), 149.1 (C_q) ppm. HR-EIMS calcd. for $C_{19}H_{22}N_2O_2$ ($[M]^{+\cdot}$) 310.1681; found 310.1688.

***tert*-Butyl 2-(4-Acetylphenyl)-5-isopropyl-1*H*-pyrrole-1-carboxylate (14e):** The boronic acid **13a** (200 mg, 0.79 mmol) and 4-bromoacetophenone (125 mg, 0.63 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:6) afforded a pale yellow oil (175 mg, 85%). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$), 1.30 (s, 9 H, $[(CH_3)_3]$), 2.62 (s, 3 H, $COCH_3$), 3.45 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 6.05 (dd, *J* = 3.5, 0.8 Hz, 1 H, 4-H), 6.21 (d, *J* = 3.5 Hz, 1 H, 3-H), 7.37 (d, *J* = 8.8 Hz, 2 H, H_{ar}), 7.94 (d, *J* = 8.8 Hz, 2 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.2 (CH_3), 26.7 ($COCH_3$), 26.8 (CH), 27.4 $[(CH_3)_3]$, 84.2 $[C(CH_3)_3]$, 107.0 (CH), 113.4, 127.9, 128.1 (CH), 133.7 (C_q), 135.1, 140.1, 145.7, 150.2, 197.7 (C_q) ppm. HR-EIMS calcd. for $C_{20}H_{25}NO_3$ ($[M]^{+\cdot}$) 327.1834; found 327.1839.

***tert*-Butyl 2-Isopropyl-5-(4-nitrophenyl)-1*H*-pyrrole-1-carboxylate (14f):** The boronic acid **13a** (75 mg, 0.37 mmol) and 1-bromo-4-nitrobenzene (170 mg, 0.74 mmol) were coupled according to the general procedure. Purification on SiO_2 (CH_2Cl_2/heptane, 1:3) afforded a yellow solid (108 mg, 89%): M.p. 118−119 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 6.8 Hz, 6 H, $(CH_3)_2CH$), 1.34 (s, 9 H), 3.46 (hept, *J* = 6.8 Hz, 1 H, $(CH_3)_2CH$), 6.08 (dd, *J* = 3.5, 0.8 Hz, 1 H, 4-H), 6.28 (d, *J* = 3.5 Hz, 1 H, 3-H), 7.43 (d, *J* = 9.1 Hz, 2 H, H_{ar}), 8.22 (d, *J* = 9.1 Hz, 2 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.2 (CH_3), 26.9 (CH), 27.5 $[(CH_3)_3]$, 84.6 $[C(CH_3)_3]$, 107.5 (CH), 114.6, 123.4, 128.2 (CH), 132.6 (C_q), 141.7, 146.1, 146.7, 149.9 (C_q) ppm. HR-EIMS calcd. for $C_{18}H_{22}N_2O_4$ ($[M]^{+\cdot}$) 330.1580; found 330.1571. $C_{18}H_{22}N_2O_4$: C 65.44, H 6.71, N 8.48; found C 64.75, H 6.62, N 8.18.

Di-*tert*-butyl 5,5′-Diethyl-2,2′-(1,3-phenylene)bis(1*H*-pyrrole)-1,1′-dicarboxylate (14g): The boronic acid **13c** (180 mg, 0.75 mmol) and 1-bromo-3-iodobenzene (75 mg, 0.37 mmol) were coupled according to the general procedure, with 4 equiv. of base. Purification on SiO_2 (CH_2Cl_2/heptane, 1:3) afforded a colourless solid (99 mg, 71%): M.p. 105−106 °C. ^{1}H NMR (200 MHz, CD_3CN): δ = 1.27 (t, *J* = 7.6 Hz, 6 H, CH_3), 1.34 (s, 18 H, $[(CH_3)_3]$), 2.85 (qd, *J* = 7.6, 0.9 Hz, 4 H, CH_2), 6.04 (dt, *J* = 3.3, 0.9 Hz, 2 H, 4-H), 6.19 (d, *J* = 3.3 Hz, 2 H, 3-H), 7.20−7.42 (m, 4 H, H_{ar}) ppm. ^{13}C NMR (50 MHz, CD_3CN): δ = 12.6 (CH_3), 21.1 (CH_2), 26.3 $[(CH_3)_3]$, 83.5 $[C(CH_3)_3]$, 108.0 (CH), 111.6, 125.8, 126.8, 127.3 (CH), 134.0 (C_q), 134.3, 138.8, 149.8 (C_q) ppm. HR-EIMS calcd. for $C_{28}H_{36}N_2O_4$ ($[M]^{+\cdot}$) 464.2675; found 464.2676.

5,5′-Diethyl-2,2′-(1,3-phenylene)bis(1*H*-pyrrole) (15): Compound **14g** (51 mg, 0.11 mmol) was placed in a flask and the flask was flushed several time with argon. The flask was then placed in an oil bath (preheated at 185 °C). Decarboxylation took place immediately, as evidenced by the slow bubbling. After 30 min, gas evolution ceased and the flask was cooled to room temperature. The brown residue was then purified by silica gel chromatography (CH_2Cl_2/Hept, 1:6) to afford 23 mg (79%) of bis(pyrrole) **15** as a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.37 (t, J = 7.6 Hz, 6 H, CH_3), 2.76 (q, J = 7.6 Hz, 4 H, CH_2), 6.07 (m, 2 H, 4-H), 6.51 (d, J = 3.3 Hz, 2 H, 3-H), 7.25−7.41 (m, 3 H, H_{ar}), 7.54 (t, J = 1.8 Hz, 1 H, H_{ar}), 8.21 (br. s, 2 H, NH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.4 (CH_2), 106.6 (CH), 106.7, 119.1, 121.3, 129.7 (CH), 131.0 (C_q), 133.9, 136.1 (C_q) ppm. HR-EIMS calcd. for $C_{18}H_{20}N_2$ ($[M]^{+\cdot}$) 264.1626; found 264.1627.

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