### Microwave-Assisted Paal–Knorr Reaction – Three-Step Regiocontrolled Synthesis of Polysubstituted Furans, Pyrroles and Thiophenes

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An efficient and highly versatile synthesis of furans, pyrroles and thiophenes is described. Starting from commercially available or easily prepared  $\beta$ -keto esters, functional homologation provides differently substituted 1,4-diketones that can be transformed, through a microwave-assisted Paal–Knorr condensation, into the corresponding methoxycarbonyl heterocycles. The methoxycarbonyl moiety can be directly transformed into an NH<sub>2</sub> group by hydrolysis to carboxylic acid and Curtius rearrangement or into an amide by reaction

with a primary amine in the presence of  $Me_3Al$ . The method is compatible with the presence of a CbzNH group so that the final heterocycle can be inserted into a peptide sequence as a turn inducer. By using this procedure, a collection of more than 60 different tetrasubstitued pyrroles or trisubstituted thiophenes has been prepared.

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Heterocyclic chemistry is currently experiencing a renaissance because of the interest in heterocyclic scaffolds as templates for combinatorial chemistry.<sup>[1]</sup> As heteroaromatic compounds are present in many natural products<sup>[2]</sup> and are the constituents of numerous therapeutic agents.<sup>[3]</sup> they represent ideal druglike structures for the elaboration of and increase in molecular diversity. Thus, the availability of simple synthetic procedures that enable the preparation of different heterocycles with functionalisable groups as substituents is an important task for organic and medicinal chemists. The Paal-Knorr cyclocondensation of 1,4-diketones with amines and other nitrogen derivatives is a well-established and valuable tool for the preparation of pyrroles and related heterocycles.<sup>[4]</sup> The 1,4-dicarbonyl compound provides four atoms (with the substituents) and the amine group provides the nitrogen atom with the substituent. The drawbacks of this reaction are the harsh conditions required for the cyclisation and some synthetic problems related to the availability of differently substituted 1,4-diketones.[5]

We recently communicated a possible solution to this problem that is based on the functional homologation of commercially available  $\beta$ -keto esters with Et<sub>2</sub>Zn/CH<sub>2</sub>I<sub>2</sub> and aldehydes followed by pyridinium chlorochromate (PCC) oxidation, which provides polysubstituted 1,4-dicarbonyl compounds in two steps. Further microwave-assisted Paal–Knorr cyclisation afforded pyrroles in good yields.<sup>[6]</sup>

With the aim of using this procedure for the preparation of different scaffolds for parallel synthesis of arrays of polyfunctionalised heterocycles, we began to investigate the potentials and the limitations of this synthetic procedure. We report now that, with this synthetic strategy, it is possible to prepare template structures that contain furan, pyrrole and thiophene rings with a high level of diversity and with different functional groups that can be used for further decoration of the scaffold.

Since the common intermediate for the synthesis of these families of heterocycles is the keto ester with the general formula 2 (Scheme 1), we started to look for the best reaction conditions that are compatible with the presence of different functional groups for  $R^1$  and  $R^2$ .



Scheme 1. Retrosynthetic analysis of five-membered heterocycles.

Compound **2** was obtained from the reaction of a  $\beta$ -keto ester with Et<sub>2</sub>Zn/CH<sub>2</sub>I<sub>2</sub>. The cyclopropyl intermediate rearranges to the carbanion, which is quenched by an electrophile.<sup>[7]</sup> When an aldehyde is used, the alcohol **4** is obtained, which requires an additional oxidative step to obtain the diketone **2**.

In order to avoid the last step, we tried different C=O electrophiles to directly introduce the required functionality into the molecule by using the  $\beta$ -keto ester with R<sup>1</sup> = *t*Bu

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as the model compound. Acyl chlorides, and other kinds of activated carbonyl compounds such as RCOOCOEt, RCOOBt (Bt = benzotriazol-1-yl), RCOOC<sub>6</sub> $F_5$  or nitriles RCN did not react. When thioesters RCOSEt were used, the formation of the expected ketones in acceptable yields was observed.<sup>[8]</sup> However, different amounts of the products from the simple homologation were obtained (3; E = H inScheme 2), and thus required a chromatographic purification step. The reported yields of the products obtained with this procedure compared with those of the products obtained by addition of the aldehyde and PCC oxidation of the crude are reported in Table 1. When the  $R^1$  and  $R^2$ groups are structurally not complex, the use of thioester as the electrophile may be more convenient, whereas with more complex substrates, the two-step procedure with the aldehyde is recommended. With regard to the oxidation of alcohol 4 to ketone 5, 1-2 equiv. of PCC is generally required for a quantitative conversion. In this case the yields were unsatisfactory, and the reaction could be driven to completion by further addition of PCC until the starting material disappeared. It is worth mentioning that this result was not obtained when starting with a large excess of PCC. Purification of products 6-25 (obtained from the last method) was carried out by passing the crude through a plug of silica and eluting with Et<sub>2</sub>O. This process generally gave a product that was sufficiently pure for further cyclocondensation.

When an acid proton was present, as in the case of *N*-Cbz  $\alpha$ - or  $\beta$ -amino aldehydes, the simple homologated  $\gamma$ -keto ester was exclusively generated by quenching of the Zn intermediate (**3**; E = H in Scheme 2).<sup>[9]</sup> A possible solution to this problem is the use of aldehydes that carry a doubly protected nitrogen atom such as NCBz<sub>2</sub> or NBn<sub>2</sub>. However, the increase in the hindrance around the nitrogen atom de-

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Scheme 2. Mechanism for the transformation of a  $\beta$ -keto ester into a 1,4-dicarbonyl ester.

creased the reactivity of the aldehyde and reduced the yields in the further cyclisation reaction.

It was more convenient to remove the proton from the NHCbz group by using an additional equivalent of  $Et_2Zn$ . Thus, when a solution of the  $\alpha$ - or  $\beta$ -amino aldehydes **29–30** was treated with  $Et_2Zn$  and then added to the reaction mixture containing the  $\beta$ -keto ester,  $Et_2Zn$  and  $CH_2I_2$ , the expected alcohols were obtained. Further oxidation with PCC gave compounds **21–27** in acceptable yields (see Scheme 3 and Table 1).

The Paal–Knorr reaction is a powerful method for the construction of cyclic structures and has been widely applied to the synthesis of heterocycles.<sup>[4d]</sup> Recently, microwaves have been applied to increase the yields, reduce the reaction time and provide milder reaction conditions.<sup>[10]</sup> Previously prepared diketones were subjected to microwave-assisted reactions in AcOH in the presence of different amines to give the corresponding pyrroles. The best results were obtained in an open vessel at 120–150 °C for 2–10 min, depending on the nature of the substrates em-

COOMe

0

	$R^1$ OMe $R^1$ $R^2$									
					6-23 Ö					
<b>R</b> <sup>1</sup>	<b>R</b> <sup>2</sup>	Meth- od <sup>[a]</sup>	Compound: yield [%] <sup>[b]</sup>	$\mathbb{R}^1$	$\mathbb{R}^2$	Method <sup>[a]</sup>	Compound: yield [%]			
tBu	C <sub>6</sub> H <sub>5</sub>	А	<b>6</b> : 75	C <sub>6</sub> H <sub>5</sub>	p-Cl-C <sub>6</sub> H <sub>4</sub>	В	<b>16</b> : 70			
tBu	$C_6H_5$	В	<b>6</b> : 90	$C_6H_5$	$C_3H_7$	В	<b>17</b> : 74			
tBu	$p-Cl-C_6H_4$	А	<b>7</b> : 70	$C_6H_5$	$C_6H_5CH_2$	В	<b>18</b> : 76			
tBu	p-Cl-C <sub>6</sub> H <sub>4</sub>	В	<b>7</b> : 76	Me	$C_6H_5$	В	<b>19</b> : 68 <sup>[c]</sup>			
tBu	o-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	А	<b>8</b> : 20	Me	$C_3H_7$	В	<b>20</b> : 83			
tBu	o-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	В	<b>8</b> : 70	Et	CbzNHCH <sub>2</sub> CH <sub>2</sub>	С	<b>21</b> : 76			
tBu	$C_6H_5CH_2$	А	<b>9</b> : 61	tBu	CbzNHCH <sub>2</sub> CH <sub>2</sub>	С	<b>22</b> : 54 <sup>[c]</sup>			
tBu	$C_{6}H_{5}(CH_{2})_{2}$	В	<b>10</b> : 88	tBu	PhCH <sub>2</sub> CH(NHCbz)CH <sub>2</sub>	С	<b>23</b> : 51			
tBu	$C_3H_7$	В	<b>11</b> : 76	$C_6H_5$	CbzNHCH <sub>2</sub> CH <sub>2</sub>	С	<b>24</b> : 70			
Et	$C_6H_5$	В	<b>12</b> : 77	Me	PhCH <sub>2</sub> CH(NHCbz)CH <sub>2</sub>	С	<b>25</b> : 66 <sup>[c]</sup>			
Et	$p-Cl-C_6H_4$	В	<b>13</b> : 88	Me	CbzNHCH <sub>2</sub> CH <sub>2</sub>	С	<b>26</b> : 65 <sup>[c]</sup>			
Et	$C_6H_5$	С	<b>14</b> : 67 <sup>[c]</sup>	tBu	PhCH <sub>2</sub> CH(NHCbz)	С	<b>27</b> : 63 <sup>[c]</sup>			
Et	СН	D	15.86							

method A B or C

Table 1. Preparation of 1,4-dicarbonyl compounds.

[a] Method A: Et<sub>2</sub>Zn, CH<sub>2</sub>I<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, R<sup>2</sup>COSEt. Method B: a) Et<sub>2</sub>Zn, CH<sub>2</sub>I<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, R<sup>2</sup>CHO; b) PCC, CH<sub>2</sub>Cl<sub>2</sub>, SiO<sub>2</sub>. Method C a) Et<sub>2</sub>Zn, CH<sub>2</sub>I<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub> followed by Et<sub>2</sub>Zn, R<sup>2</sup>CHO in CH<sub>2</sub>Cl<sub>2</sub>; b) PCC, CH<sub>2</sub>Cl<sub>2</sub>, SiO<sub>2</sub>. [b] Yields of crude products with purities higher than 90% (<sup>1</sup>H NMR spectroscopic analysis). [c] Yields of isolated and fully characterised products.



Scheme 3. Use of *N*-Cbz amino aldehydes in the functional homologation.

ployed.<sup>[11]</sup> Finally, an aqueous workup removed the AcOH, and the pyrroles were isolated by column chromatography on silica gel. Starting from diketones 6–26 and by using different amines, pyrroles 31–60 were obtained in good yields (see Table 2). Remarkably, compound 27 did not cyclise, even with nonhindered amines. On the other hand, it is worth noting that the presence of an NHCBz group is compatible with the reaction conditions, since compounds 20–26 gave good yields from the Paal–Knorr reaction. The same trend was also observed in the case of the amine employed in the cyclisation. Esters derived from  $\alpha$ -amino acids did not cyclise properly, whereas 1,2-diamines 61–63 (Scheme 4) (obtained from the corresponding amino acids)

Table 2. Preparation of pyrroles.

<sup>[12]</sup> cyclised to pyrroles **64–70** in good yields. This behaviour suggests that the reaction may be successfully carried out when at least two  $CH_2$  groups are close to the reactive centres of the partner.



Scheme 4.

Furans 71–73 were easily obtained by heating diketones 6, 10 and 19 under microwave irradiation (sealed vessel, 100 °C, 13.6 atm max. internal pressure) in acid solution (see Table 3).<sup>[13]</sup> Analogously, thiophenes 74–78 were obtained from diketones by a microwave-assisted reaction using Lawesson's reagent for the introduction of the sulfur atom.<sup>[14]</sup> The reaction was carried out in toluene at 110 °C, and the presence of Lawesson's reagent in solution allowed this temperature to be reached even when using a solvent with a low value of tan  $\delta$  (as is the case for toluene).<sup>[15]</sup> Thiophenes 74–78 were always obtained together with different amounts (from 10 to 25%) of the corresponding fu-

COOMe

				NH <sub>2</sub>			
		R <sup>1</sup>	.K <sup>2</sup>			52	
		ö	IVI V	, ACOH	. N. г	1	
$\mathbf{R}^1$	R <sup>2</sup>	R <sup>3</sup>	Pyrrole Yield (%) <sup>[a]</sup>	$\mathbf{R}^1$	R <sup>2</sup>	R <sup>3</sup>	Pyrrole Yield (%) <sup>[a]</sup>
<i>t</i> Bu	C <sub>6</sub> H <sub>5</sub>	$C_6H_5CH_2$	31: 88	Et	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	p-MeOC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CH <sub>2</sub>	46: 72
<i>t</i> Bu	p-ClC <sub>6</sub> H <sub>4</sub>	$C_4H_9$	<b>32</b> : 82	Et	$C_3H_7$	0N	<b>47</b> : 88
<i>t</i> Bu	o-CF3C6H4	Me <sub>2</sub> CHCH <sub>2</sub>	<b>33</b> : 80	C <sub>6</sub> H <sub>5</sub>	$C_3H_7$	Me <sub>2</sub> CHCH <sub>2</sub>	<b>48</b> : 80
tBu	p-ClC <sub>6</sub> H <sub>4</sub>	$C_6H_5CH_2$	<b>34</b> : 82	$C_6H_5$	$C_6H_5CH_2$	C <sub>6</sub> H <sub>5</sub>	<b>49</b> : 81
<i>t</i> Bu	$C_6H_5(CH_2)_2$	$C_6H_5CH_2$	<b>35</b> : 78	$C_6H_5$	$C_3H_7$	ó N−_	<b>50</b> : 79
<i>t</i> Bu	C <sub>6</sub> H <sub>5</sub>	Me <sub>2</sub> CHCH <sub>2</sub>	<b>36</b> : 65	C <sub>6</sub> H <sub>5</sub>	p-ClC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	<b>51</b> : 79
<i>t</i> Bu	C <sub>6</sub> H <sub>5</sub>	0N	37: 89	C <sub>6</sub> H <sub>5</sub>	$C_6H_5CH_2$	MeO MeO	<b>52</b> : 79
<i>t</i> Bu	$C_3H_7$	N N	<b>38</b> : 88	$C_6H_5$	CbzNHCH <sub>2</sub> CH <sub>2</sub>	Me <sub>2</sub> CHCH <sub>2</sub>	<b>53</b> : 79
<i>t</i> Bu	$C_6H_5CH_2$	N	<b>39</b> : 82	Me	$C_3H_7$	N.	<b>54</b> : 79
<i>t</i> Bu	CbzNHCH <sub>2</sub> CH <sub>2</sub>	Me <sub>2</sub> CHCH <sub>2</sub>	<b>40</b> : 69	Me	$C_3H_7$	Me <sub>2</sub> CHCH <sub>2</sub>	<b>55</b> : 79
<i>t</i> Bu	$CbzNHCH_2CH_2\\$	$C_6H_5CH_2$	<b>41</b> : 78	Me	$C_6H_5$	$C_6H_5CH_2$	<b>56</b> : 74
<i>t</i> Bu	Ph NHCbz	Me <sub>2</sub> CHCH <sub>2</sub>	<b>42</b> : 76	Me	$C_3H_7$	C <sub>6</sub> H <sub>5</sub> (CH <sub>2</sub> ) <sub>2</sub>	<b>57</b> : 88
<i>t</i> Bu	Ph NHCbz	$C_6H_5CH_2$	<b>43</b> : 77	Me	Ph NHCbz	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	<b>58</b> : 79
Et	$C_6H_5$	$C_6H_5CH_2$	<b>44</b> : 72	Me	CbzNHCH <sub>2</sub> CH <sub>2</sub>	$C_6H_5CH_2$	<b>59</b> : 79
Et	$C_3H_7$	Me <sub>2</sub> CHCH <sub>2</sub>	<b>45</b> : 69	Me	CbzNHCH <sub>2</sub> CH <sub>2</sub>	Me <sub>2</sub> CHCH <sub>2</sub>	<b>60</b> : 79

**B**<sup>3</sup>

[a] Yields of isolated and fully characterised products.

#### Table 3. Preparation of furans and thiophenes.

$R^1 \xrightarrow{O} COOMe$ $R^2 \xrightarrow{Method A} R^2 \xrightarrow{R^2} R^2$							
$\mathbb{R}^1$	<b>R</b> <sup>2</sup>	Method <sup>[a]</sup>	Compound: yield [%] <sup>[a]</sup>	$\mathbb{R}^1$	<b>R</b> <sup>2</sup>	Method <sup>[a]</sup>	Compound: yield [%] <sup>[b]</sup>
<i>t</i> Bu	C <sub>6</sub> H <sub>5</sub>	A	X = O 71 76	<i>t</i> Bu	$C_6H_5(CH_2)_2$	В	X = S 75 71
tBu	$C_6H_5(CH_2)_2$	A	X = 0.7280	tBu	$C_3H_7$	В	X = S 76 80
Me	$C_3H_7$	А	X = O <b>73</b> 84	Me	$C_3H_7$	В	X = S 77 80
tBu	$C_6H_5$	В	X = S 74 70	$C_6H_5$	$C_3H_7$	В	X = S 78 50

[a] Method A: EtOH/HCl, microwaves, 100 °C, 4 min. Method B: Lawesson's reagent, toluene, microwaves, 120 °C, 6-8 min. [b] Yields of isolated and fully characterised products.

rans and they had to be separated by column chromatography on silica gel. When a large excess of Lawesson's reagent was employed in order to prevent the formation of the furan, the corresponding methyl thiophene-3-thiocarboxylate was obtained.

Thus, starting from a common  $\beta$ -keto ester structure, different heterocycles with a high level of diversity were obtained with a simple three-step (or in some cases two-step) procedure. In order to improve the molecular diversity of our system, we investigated the possibility of additional functionalisations of the heterocyclic substituents. The CO-OMe group in the 3-position of pyrroles **30**, **35**, **46** and **48** and thiophenes **74** and **76** was hydrolysed (NaOH, MeOH,

Table 4. Functionalisation at position 3 of pyrroles and thiophenes.



[a] Yields of crude products with purities higher than 90% (<sup>1</sup>H NMR spectroscopic analysis).

H<sub>2</sub>O) to give acids 79-84 in almost quantitative yields. Acid 80 reacted further with DPPA/H<sub>2</sub>O to give amine 85 through a Curtius rearrangement. These acids or amines could be further functionalised by standard coupling techniques. The COOMe group in the 3-position was also transformed into the corresponding amide by reaction with different amines and AlMe<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub>.<sup>[16]</sup> The reaction was carried out in a parallel mode, working up the crude with stoichiometric amounts of HCl (10% in H<sub>2</sub>O), passing the mixture through a short pad of silica, washing with CH<sub>2</sub>Cl<sub>2</sub> and evaporating the solvent. Pyrrole and thiophene amides 86-96 were obtained in very good yields (see Table 4). Compound 58 was finally employed to introduce the polysubstituted pyrrole moiety into a peptide frame as a possible turn inducer.<sup>[17]</sup> Thus, hydrolysis of the methyl ester of 58 was carried out as described previously, and the resulting acid was coupled with H-Ala-OMe [DMTMM,<sup>[18]</sup> THF, Nmethylmorpholine (NMM), 80%] to give 97. The Cbz group was removed by microwave-assisted transfer hydrogenolysis,<sup>[19]</sup> and the amine was coupled with Boc-Phe-OH in 88% yield. Hydrolysis of the methyl ester provided the acid 98 that could be coupled with other amino acids or peptides through a solution or solid-phase synthesis protocol. Products 97 and 98 (Scheme 5) were obtained as single diastereoisomers (<sup>1</sup>HNMR, 600 MHz analysis), which shows that racemisation did not occur during the synthetic sequence.



Scheme 5. Preparation of pyrrole-containing peptidomimetics.

In summary, we have explored the possibility of using the Paal–Knorr reaction to prepare differently functionalised

pyrroles, furans and thiophenes. These scaffolds can show a high level of diversity with variations in positions 1, 2 and 5 around the pyrrole ring through the original synthetic scheme, and one additional level of diversification at positions 1, 2 and 3 through traditional combinatorial peptide chemistry. The synthesis of new cyclic peptides that incorporate these heterocyclic building blocks and the corresponding structural studies are currently under investigation.

#### **Experimental Section**

**General:** All reagents were purchased from Sigma-Aldrich Italia (Milan, Italy) in the highest available purity and were used as such. All solvents were purchased from Riedel-de Haën and were used without further purification except when differently stated. LC-MS data were recorded with a Waters ZQ electronspray mass spectrometer equipped with an Alliance HT Waters 2790 separation module and a Waters 996 Photodiode array detector using a Luna C18 column (4.6×50 mm, 3 m), eluent: 95% water, 5% acetonitrile, 0.1% formic acid. Proton NMR spectra were recorded with a Bruker ARX 300 MHz instrument using TMS as internal standard. The irradiation with microwaves was carried out in the cavity of a Discover system from CEM.

2-(Methoxycarbonyl)-5,5-dimethyl-1-phenyl-1,4-hexanedione (6): Diethylzinc (30 mL of a 1.0 M solution in hexane, 30 mmol) was dissolved in dry dichloromethane (60 mL) under nitrogen, and the mixture was cooled to 0 °C. Diiodomethane (2.4 mL, 30 mmol) was slowly added, and the mixture was stirred for 10 min. After the formation of a white precipitate, methyl 4,4-dimethyl-3-oxopentanoate (1.2 mL, 7.3 mmol) was added, and the reaction mixture was stirred for 30 min. Benzaldehyde (previously distilled under vacuum and collected over molecular sieves) (0.78 mL, 7.68 mmol) was added, and the mixture was stirred at 0 °C for 1 h. Silica gel (20.0 g) was added, and the mixture was stirred at room temperature for an additional 30 min. The mixture was filtered under vacuum, and the solvent was evaporated. The crude (2.26 g) was dissolved in dry dichloromethane, PCC (3.3 g, 15.3 mmol) was added, and the mixture was stirred at room temperature until TLC analysis (eluent hexane/AcOEt, 5:1) showed the disappearance of the starting material. Eventually, additional PCC (1.65 g, 7.51 mmol) was added. The mixture was passed through a short path of silica gel and eluted with dichloromethane. The eluent was collected, and the solvent was evaporated under vacuum to give product 6 (1.9 g, 90% yield), which was identified by comparison with reported data.<sup>[20]</sup> An analytical sample was purified by column chromatography on silica gel (eluent hexane/AcOEt, 3:1). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.10$  (s, 9 H, tBu), 3.10 (m, 2 H, CH<sub>2</sub>), 3.51 (s, 3 H, COOMe), 4.86 (t, J = 7 Hz, 1 H, CH), 7.30–7.50 (m, 3 H, Ar), 7.91 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.9, 32.5, 44.7, 51.9, 128.3, 129.7 133.3, 138.3, 170.2, 194.7, 213.7 ppm. C<sub>16</sub>H<sub>20</sub>O<sub>4</sub>: calcd. C 69.54, H 7.30; found C 69.10, H 7.20.

**1-(***p***-Chlorophenyl)-2-(methoxycarbonyl)-5,5-dimethyl-1,4-hexanedione (7):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.14 (s, 9 H, *t*Bu), 3.15 and 3.34 (AB part of an ABX system, 2 H, CH<sub>2</sub>), 3.62 (s, 3 H, COOMe), 4.83 (X part of an ABX system, 1 H, CH), 7.41 (m, 2 H, Ar), 7.93 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$ = 29.9, 32.0, 42.7, 50.1, 128.5, 129.8, 133.3, 138.6, 171.2, 196.0, 210.7 ppm. C<sub>16</sub>H<sub>19</sub>ClO<sub>4</sub>: calcd. C 61.84, H 6.16; found C 61.40, H 6.21. **1-**[*o*-(**Trifluoromethyl**)**phenyl**]-**2**-(**methoxycarbonyl**)-**5**,**5**-dimethyl**1**,**4**-hexanedione (8): <sup>1</sup>H NMR  $\delta$  = 1.14 (s, 9 H, *t*Bu), 3.05 and 3.24 (AB part of an ABX system, 2 H, CH<sub>2</sub>), 3.60 (s, 3 H, COOMe), 4.70 (X part of an ABX system, 1 H, CH), 7.40 (m, 2 H, Ar), 7.88 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.4 32.8, 41.7, 50.6, 124.3, 125.5, 127.8, 135.3, 139.9, 171.8, 198.2, 212.6 ppm. C<sub>17</sub>H<sub>19</sub>F<sub>3</sub>O<sub>4</sub>: calcd. C 59.30' H 5.56; found C 59.55, H 5.60.

**3-(Methoxycarbonyl)-6,6-dimethyl-1-phenyl-2,5-heptanedione (9):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.12 (s, 9 H, *t*Bu), 2.91 and 3.09 (AB part of an ABX system, 2 H, CH<sub>2</sub>), 3.52 (s, 3 H, COOMe), 3.86 (AB system, 2 H, CH<sub>2</sub>Ar), 4.10 (X part of an ABX system, 1 H, CH), 7.2 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 26.4, 31.4, 43.7, 48.6, 50.4, 51.4, 126.0, 126.9, 127.0, 134.3, 171.9, 201.2, 210.7 ppm. C<sub>17</sub>H<sub>22</sub>O<sub>4</sub>: calcd. C 70.32, H 7.64; found C 70.50, H 7.59.

**4-(Methoxycarbonyl)-7,7-dimethyl-1-phenyl-3,6-octanedione (10):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.10$  (s, 9 H, *t*Bu), 2.96 and 3.19 (AB part of an ABX system, 2 H, CH<sub>2</sub>), 3.40 (t-like, 2 H, COCH<sub>2</sub>), 3.50 (s, 3 H, COOMe), 3.88 (AB system, 2 H, CH<sub>2</sub>Ar), 4.15 (X part of an ABX system, 1 H, CH), 7.2 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 26.0$ , 31.4, 33.6, 41.7, 48.8, 50.4, 52.7, 126.1, 126.9, 127.0, 134.8, 173.0, 201.9, 214.8 ppm. C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>: calcd. C 71.03, H 7.95; found C 70.99, H 7.99.

**5-(Methoxycarbonyl)-2,2-dimethyl-3,6-nonanedione (11):** Identified by comparison with reported data.<sup>[21]</sup>

**2-(Methoxycarbonyl)-1-phenyl-1,4-hexanedione (12):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.07 (t, *J* = 7 Hz, 3 H, Me), 3.10–3.30 (m, 4 H, CH<sub>2</sub>), 3.50 (s, 3 H, COOMe), 4.86 (m, 1 H, CH), 7.30–7.50 (m, 3 H, Ar), 7.91 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.8, 31.4, 32.5, 49.7, 51.9, 128.3, 129.7, 133.3, 138.3, 171.2, 196.7, 210.7 ppm. C<sub>14</sub>H<sub>16</sub>O<sub>4</sub>: calcd. C 67.73, H 6.50; found C 67.59, H 6.46.

**1-(***p***-Chlorophenyl)-2-(methoxycarbonyl)-1,4-hexanedione (13):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.09 (t, *J* = 7 Hz, 3 H, Me), 3.10–3.30 (m, 4 H, CH<sub>2</sub>), 3.55 (s, 3 H, COOMe), 4.85 (m, 1 H, CH), 7.30–7.60 (m, 4 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.6, 32.4, 33.5, 49.7, 51.0, 126.3, 129.2, 134.3, 139.3, 171.2, 198.7, 211.7 ppm. C<sub>14</sub>H<sub>15</sub>ClO<sub>4</sub>: calcd. C 59.48, H 5.35; found C 59.58, H 5.30.

**3-(Methoxycarbonyl)-1-phenyl-2,5-heptanedione (14):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.00 (t, *J* = 7 Hz, 3 H, Me), 3.00–3.25 (m, 4 H, CH<sub>2</sub>), 3.50 (s, 3 H, COOMe), 4.00 (m, 2 H, CH<sub>2</sub>Ar), 4.85 (m, 1 H, CH), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.8, 32.8, 34.5, 40.8, 49.0, 51.2, 126.0, 127.3, 128.2, 134.3, 171.2, 199.9, 212.7 ppm. C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>: C 68.68, H 6.92; found C 68.55; H 6.89.

**5-(Methoxycarbonyl)-3,6-nonanedione (15):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.00–1.11 (2 t, *J* = 7 Hz, 6 H, 2 Me), 1.89 (m, 2 H, CH<sub>2</sub>), 3.10–3.30 (m, 6 H, 3 CH<sub>2</sub>CO), 3.50 (s, 3 H, COOMe), 4.85 (m, 1 H, CH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 12.9, 14.8, 16.8, 32.8, 34.5, 33.7, 49.8, 51.7, 171.8, 201.6, 206.7 ppm. C<sub>11</sub>H<sub>18</sub>O<sub>4</sub>: calcd. C 61.66, H 8.47; found C 61.40, H 8.40.

**1-(***p***-Chlorophenyl)-2-(methoxycarbonyl)-4-phenyl-1,4-butanedione** (16): Identified by comparison with reported data.<sup>[22]</sup>

**3-(Methoxycarbonyl)-1-phenyl-1,4-heptanedione (17):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.00 (t, *J* = 7 Hz, 3 H, Me), 1.87 (m, 2 H), 3.10–3.35 (m, 4 H, CH<sub>2</sub>), 3.48 (s, 3 H, COOMe), 4.80 (m, 1 H, CH), 7.30–7.50 (m, 3 H, Ar), 7.91 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.8, 17.7, 32.4, 33.5, 49.0, 51.0, 128.0,

129.3, 133.3, 138.5, 174.2, 197.7, 210.7 ppm.  $C_{15}H_{18}O_4{:}$  calcd. C 68.68, H 6.92; found C 68.59, H 6.96.

**3-(Methoxycarbonyl)-1,5-diphenyl-1,4-pentanedione (18):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.35 (m, 2 H, CH<sub>2</sub>), 3.55 (s, 3 H, COOMe), 4.02 (AB system, 2 H, CH<sub>2</sub>Ar), 4.66 (m, 1 H, CH), 7.23–7.60 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 33.5, 41.4, 49.0, 52.0, 126.0, 126.3, 126.9, 127, 8, 129.2, 134.3, 170.5, 199.0, 199.9 ppm. C<sub>19</sub>H<sub>18</sub>O<sub>4</sub>: calcd. C 73.53, H 5.85; found C 73.42, H 5.88.

**2-(Methoxycarbonyl)-1-phenyl-1,4-pentanedione (19):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.78 (s, 3 H, Me), 3.05 (m, 2 H, CH<sub>2</sub>), 3.56 (s, 3 H, COOMe), 4.60 (m, 1 H, CH), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 30.5, 40.4, 52.0, 60.3, 126.0, 126.3, 126.9, 134.3, 170.5, 199.0, 199.9 ppm. C<sub>13</sub>H<sub>14</sub>O<sub>4</sub>: calcd. C 66.66, H 6.02; found C 66.48, H 6.00.

**4-(Methoxycarbonyl)-2,5-octanedione (20):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.11 (t, J = 7 Hz, 3 H, Me), 1.46 (s, 3 H, Me), 2.01 (m, 2 H), 3.00–3.30 (m, 4 H, 2 CH<sub>2</sub>CO), 3.55 (s, 3 H, COOMe), 4.65 (m, 1 H, CH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 12.9, 16.8, 22.7, 24.9, 32.8, 34.5, 49.8, 51.7, 172.8, 201.6, 208.7. C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>: calcd. C 59.98, H 8.05; found C 59.88, H 8.00.

1-[(Benzyloxycarbonyl)amino]-4-(methoxycarbonyl)-3,6-octanedione (21): Diethylzinc (30 mL of a 1.0 M solution in hexane, 30 mmol) was dissolved in dry dichloromethane (60 mL) under nitrogen, and the mixture was cooled to 0 °C. Diiodomethane (2,4 mL, 30 mmol) was slowly added, and the mixture was stirred for 10 min. After the formation of a white precipitate, methyl 3-oxopentanoate (1.3 mL, 7.3 mmol) was added, and the reaction mixture was stirred for 30 min. A solution of 3-Cbz-aminopropanal (1.51 g, 7.3 mmol) in dichloromethane (8 mL) containing diethylzinc (8 mL of a 1.0 M solution in hexane, 8 mmol) was slowly added, and the mixture stirred at 0 °C for 1 h. Silica gel (20.0 g) was added, and the mixture was stirred at room temperature for an additional 30 min. The mixture was filtered under vacuum, and the solvent was evaporated. The crude (2.16 g) was dissolved in dry dichloromethane, PCC (3.3 g, 15.3 mmol) was added, and the mixture was stirred at room temperature until TLC analysis (eluent hexane/AcOEt, 1:1) showed the disappearance of the starting material. Eventually, additional PCC (1.65 g, 7.51 mmol) was added. The mixture was passed through a short path of silica gel and eluted with dichloromethane. The eluent was collected, and the solvent was evaporated under vacuum to give product 21 (1.9 g, 76% yield). An analytical sample was purified by column chromatography on silica gel (eluent hexane/AcOEt, 1:1). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.11 (t, J = 7 Hz, 3 H, Me), 3.00-3.10 (m, 4 H, 2CH<sub>2</sub>CO), 3.36 (t-like, 2 H, COCH<sub>2</sub>), 3.55 (s, 3 H, COOMe), 3.99 (t-like, 2 H, CH<sub>2</sub>N), 4.44 (m, 1 H, CH), 5.10 (s, 2 H, Cbz), 6.00 (s, 1 H, NH), 7.28 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 10.8, 32.4, 33.5, 38.5, 44.9, 49.0, 51.0, 56.8, 126.5, 128.0, 129.3, 138.5, 165.8, 171.2, 202.5, 211.7 ppm. C<sub>18</sub>H<sub>23</sub>NO<sub>6</sub>: calcd. C 61.88, H 6.64; found C 61.59, H 6.66.

**1-[(Benzyloxycarbonyl)amino]-4-(methoxycarbonyl)-7,7-dimethyl-3,6-octanedione (22):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.15 (s, 9 H, *t*Bu), 3.10 (AB part of an ABX system, 2 H, CH<sub>2</sub>CO), 3.38 (t-like, 2 H, COCH<sub>2</sub>), 3.53 (s, 3 H, COOMe), 3.89 (t-like, 2 H, CH<sub>2</sub>N), 4.40 (X part of an ABX system, 1 H, CH), 5.10 (s, 2 H, Cbz), 6.11 (s, 1 H, NH), 7.28 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.8, 32.4, 33.5, 38.5, 41.7, 44.9, 49.0, 51.3, 56.9, 126.5, 128.0, 129.3, 138.5, 165.8, 171.2, 201.5, 215.7 ppm. C<sub>20</sub>H<sub>27</sub>NO<sub>6</sub>: calcd. C 63.64, H 7.21; found C 63.76, H 7.23.

2-[(Benzyloxycarbonyl)amino]-5-(methoxycarbonyl)-8,8-dimethyl-1phenyl-4,7-nonanedione (23): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.15 (s, 9 H, *t*Bu), 3.10 (AB part of an ABX system, 2 H, CH<sub>2</sub>CO), 3.22 (m, 2 H, CH<sub>2</sub>Ph), 3.38 (m, 2 H, COCH<sub>2</sub>), 3.53 (s, 3 H, COOMe), 4.18 (m, 1 H, CH<sub>2</sub>N), 4.40 (m, 1 H, CH), 5.12 (s, 2 H, Cbz), 6.10 (s, 1 H, NH), 7.20–7.35 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.8 (3C), 32.4, 33.5, 38.5, 41.7, 47.9, 49.0, 51.0, 56.9, 126.5, 128.0, 129.3, 138.5, 164.8, 174.2, 203.5, 210.7 ppm. C<sub>27</sub>H<sub>33</sub>NO<sub>6</sub>: calcd. C 69.36, H 7.11; found C 69.56, H 7.13.

**6-[(Benzyloxycarbonyl)amino]-3-(methoxycarbonyl)-1-phenyl-1,4-hexanedione (24):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.10 (m, 2 H, CH<sub>2</sub>CO), 3.38 (t-like, 2 H, COCH<sub>2</sub>), 3.59 (s, 3 H, COOMe), 4.01 (t-like, 2 H, CH<sub>2</sub>N), 4.48 (m, 1 H, CH), 5.16(s, 2 H, Cbz), 6.20 (s, 1 H, NH), 7.20–7.40 (m, 8 H, Ar), 7.89 (m, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 32.4, 33.5, 40.9, 49.0, 51.0, 56.8, 126.5, 126.9, 128.0, 128.8, 129.3, 134.8, 138.5, 169.8, 173.2, 198.5, 210.7 ppm. C<sub>22</sub>H<sub>23</sub>NO<sub>6</sub>: calcd. C 66.49, H 5.83; found C 66.59, H 5.86.

**2-[(Benzyloxycarbonyl)amino]-5-(methoxycarbonyl)-1-phenyl-4,7-octanedione (25):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.98 (s, 3 H, Me), 3.11 (AB part of an ABX system, 2 H, CH<sub>2</sub>CO), 3.22 (m, 2 H, CH<sub>2</sub>Ph), 3.50 (s, 3 H, COOMe), 3.59 (m, 2 H, CH<sub>2</sub>CO), 4.35 (m, 1 H, CH), 4.45 (m, 1 H, CHN), 5.12 (s, 2 H, Cbz), 6.15 (s, 1 H, NH), 7.30 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 30.8, 36.4, 39.5, 42.7, 48.9, 50.0, 57.0, 59.9, 126.5, 128.0 129.3, 138.5, 164.8, 174.2, 203.5, 210.7 ppm. C<sub>24</sub>H<sub>27</sub>NO<sub>6</sub>: C 67.75, H 6.40, N 3.29; found C 67.60, H 6.41, N 3.31.

**1-[(Benzyloxycarbonyl)amino]-4-(methoxycarbonyl)-3,6-heptane dione (26):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.18 (t, *J* = 7 Hz, 3 H, Me), 3.16 (m, 2 H, CH<sub>2</sub>CO), 3.38 (t-like, 2 H, COCH<sub>2</sub>), 3.54 (s, 3 H, COOMe), 3.90 (t-like, 2 H, CH<sub>2</sub>N), 4.46 (m, 1 H, CH), 5.12 (s, 2 H, Cbz), 5.98 (s, 1 H, NH), 7.28 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 16.8, 32.4, 33.5, 44.9, 49.0, 51.0, 56.8, 126.5, 128.0, 129.3, 138.5, 166.8, 170.2, 203.5, 210.7 ppm. C<sub>17</sub>H<sub>21</sub>NO<sub>6</sub>: calcd. C 60.89, H 6.31; found C 60.67, H 6.33.

**2-[(Benzyloxycarbonyl)amino]-4-(methoxycarbonyl)-7,7-dimethyl-1-phenyl-3,6-octanedione (27):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.15 (s, 9 H, *t*Bu), 3.11 (AB part of an ABX system, 2 H, CH<sub>2</sub>CO), 3.22 (m, 2 H, CH<sub>2</sub>Ph), 3.50 (s, 3 H, COOMe), 4.19 (m, 1 H, CH<sub>2</sub>N), 4.45 (m, 1 H, CH), 5.12 (s, 2 H, Cbz), 6.15 (s, 1 H, NH), 7.20–7.35 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.8, 32.4, 33.5, 41.7, 47.9, 49.0, 51.0, 56.9, 126.5, 128.0, 129.3, 138.5, 164.8, 174.2, 203.5, 210.7 ppm. C<sub>26</sub>H<sub>31</sub>NO<sub>6</sub>: C 68.86, H 6.89; found C 68.66, H 6.91.

1-Benzyl-5-tert-butyl-3-(methoxycarbonyl)-2-phenylpyrrole (31): Product 6 (1.0 g, 3,44 mmol) was dissolved in acetic acid (3 mL) in a 50-mL round-bottomed flask, equipped with a stirrer bar and a reflux condenser. Benzylamine (1.84 g, 17.2 mmol) was added, and the flask was inserted into the cavity of a Discovery Microwave System apparatus (from CEM) and heated at 150 W for 12 min (internal temperature 170 °C). The mixture was diluted with Ac-OEt, and the solution was washed several times with a saturated solution of NaHCO<sub>3</sub>. The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, and the solvent was evaporated. The <sup>1</sup>H NMR spectrum of the crude showed the presence of compound 31 together with benzylammonium acetate. The required pyrrole was purified by flash chromatography (eluent hexane/AcOEt, 8:1;  $R_{\rm f} = 0.37$ ) to give product 31 as a solid (0.87 g, 70% yield). M.p. 87-89 °C. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.14 (s, 9 H, *t*Bu), 3.59 (s, 3 H, COOMe), 5.16 (s, 2 H, CH<sub>2</sub>), 6.56 (s, 1 H, 4-H), 7.10-7.30 (m, 10 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.7, 32.2, 49.3, 50.6, 107.1, 112.4, 125.4, 126.8, 127.5, 127.9, 128.2, 130.5, 132.1, 138.9, 140.6, 142.3, 166.7 ppm. ES/MS:  $m/z = 348 [M + 1]^+$ . C<sub>23</sub>H<sub>25</sub>NO<sub>2</sub>: calcd. C 79.51, H 7.25, N 4.03; found C 68.66, H 6.91, N 4.00.

**1-Butyl-5**-*tert*-**butyl-2**-(*p*-**chlorophenyl**)-**3**-(**methoxycarbonyl**)**pyrrole** (**32**): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.67$  (t, J = 7 Hz, 3 H, Me), 0.96–1.17 (m, 2 H, CH<sub>2</sub>), 1.30–1.35 (m, 2 H, CH<sub>2</sub>), 1.38 (s, 9 H, *t*Bu), 3.57 (s, 3 H, COOMe), 3.89 (t, 2 H, J = 8 Hz, N–CH<sub>2</sub>), 6.42 (s, 1 H, 4-H), 7.27 (d-like, 2 H, Ar), 7.36 (d-like, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.7$ , 19.2, 29.5, 30.2, 31.7, 32.5, 45.0, 49.7, 106.4, 110.8, 127.6, 128.7, 131.6, 133.6, 137.4, 140.9, 162.4 ppm. ES/MS: *m*/*z* = 348–350 [M + 1]<sup>+</sup>. C<sub>20</sub>H<sub>26</sub>CINO<sub>2</sub>: calcd. C 69.05, H 7.53, N 4.03; found C 68.97, H 7.60, N 4.01.

**5**-*tert*-**Butyl-2**-*[o*-(trifluoromethyl)phenyl]-3-(methoxycarbonyl)-1-(2methylpropyl)pyrole (33): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.51$ and 0.57 (2 d, J = 7 Hz, 6 H, Me), 1.35 (s, 9 H, *t*Bu), 1.65 (m, 1 H, CH), 3.55 (s, 3 H, COOMe), 3.75 (d, J = 8 Hz, 2 H, N–CH<sub>2</sub>), 6.42 (s, 1 H, 4-H), 7.27–7.56 (m, 4 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.7$ , 16.2, 28.5, 30.0, 32.7, 32.4, 45.6, 48.7, 103.4, 111.8, 127.6, 128.7, 131.6, 133.6, 137.4, 139.7, 140.9, 162.4 ppm. ES/MS: m/z = 382 [M + 1]<sup>+</sup>. C<sub>21</sub>H<sub>26</sub>F<sub>3</sub>NO<sub>2</sub>: calcd. C 66.13, H 6.87, N 3.67; found C 66.07, H 6.80, N 3.71.

**1-Benzyl-5-***tert***-butyl-2-**(*p***-chlorophenyl)-3-**(**methoxycarbonyl)pyrrole (34):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.29 (s, 9 H, *t*Bu), 3.35 (s, 3 H, COOMe), 5.19 (s, 2 H, CH<sub>2</sub>), 6.53 (s, 1 H, 4-H), 7.06–7.30 (m, 9 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 30.5, 31.7, 45.9, 49.9, 104.4, 112.8, 126.5, 126.6, 128.6, 128.7, 129.3, 131.6, 133.6, 137.4, 139.7, 165.4 ppm. ES/MS: *m*/*z* = 383–385 [M + 1]<sup>+</sup>. C<sub>23</sub>H<sub>24</sub>CINO<sub>2</sub>: calcd. C 72.34, H 6.33, N 3.67; found C 72.17, H 6.30, N 3.65.

**1-Benzyl-5-***tert***-butyl-3-(methoxycarbonyl)-2-(2-phenylethyl)pyrrole** (35): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.24 (s, 9 H, *t*Bu), 2.69 (t, 2 H, *J* = 8 Hz, CH<sub>2</sub>), 3.24 (t, 2 H, *J* = 8 Hz, CH<sub>2</sub>), 3.73 (s, 3 H, COOMe), 4.89 (s, 2 H, CH<sub>2</sub>N), 6.45 (s, 1 H, 4-H), 7.25–7.45 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 30.5, 31.7, 37.8, 41.6, 45.9, 49.9, 104.4, 112.8, 126.9, 126.6, 128.6, 128.7, 129.3, 131.6, 133.6, 137.4, 165.4 ppm. ES/MS: *m*/*z* = 376 [M + 1]<sup>+</sup>. C<sub>25</sub>H<sub>29</sub>NO<sub>2</sub>: calcd. C 79.96, H 7.78, N 3.73; found C 79.84, H 7.74, N 3.69.

**5**-*tert*-**Butyl-3**-(**methoxycarbonyl**)-**1**-(**2**-**methylpropyl**)-**2**-**phenylpyrrole (36):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.50$  and 0.59 (2 d, J = 7 Hz, 6 H, Me), 1.35 (s, 9 H, *t*Bu), 1.66 (m, 1 H, CH), 3.58 (s, 3 H, COOMe), 3.75 (d, J = 8 Hz, 2H N–CH<sub>2</sub>), 6.45 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.9$ , 16.0, 29.5, 31.0, 31.7, 32.4, 44.6, 49.7, 103.4, 111.8, 127.6, 128.7, 131.6, 133.6, 137.4, 138.7, 164.4 ppm. ES/MS: m/z = 314 [M + 1]<sup>+</sup>. C<sub>20</sub>H<sub>27</sub>NO<sub>2</sub>: calcd. C 76.64, H 8.68, N 4.47; found C 76.47, H 8.70, N 4.43.

**5**-*tert*-**Butyl-3**-(**methoxycarbonyl)**-1-(2-morpholinoethyl)-2-phenylpyrrole (37): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.39$  (s, 9 H, *t*Bu), 2.03 (t-like, 4 H, CH<sub>2</sub>N), 2.26 (t, J = 7 Hz, 2 H, CH<sub>2</sub>N), 3.48 (tlike, 4 H, CH<sub>2</sub>O), 3.68 (s, 3 H, COOMe), 4.06 (t, J = 7 Hz, 2 H, CH<sub>2</sub>N-pyrrole), 6.40 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 31.2$ , 32.0, 32.4, 49.7, 51,4, 55.4, 66.8, 103.4, 111.8, 126.6, 127.7, 128.0, 130.6, 134.4, 136.7, 165.4 ppm. ES/MS: m/z = 314 [M + 1]<sup>+</sup>. C<sub>22</sub>H<sub>30</sub>N<sub>2</sub>O<sub>3</sub>: C 71.32, H 8.16, N 7.56; found C 71.44, H 8.12 N 7.53.

**5**-*tert*-**Butyl-3**-(methoxycarbonyl)-1-(2-picolyl)-2-propylpyrrole (38): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.74$  (t, J = 7 Hz, 3 H, Me), 1.11 (s, 9 H, *t*Bu), 1.30 (m, 2 H, CH<sub>2</sub>), 2.57 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.65 (s, 3 H, COOMe), 5.28 (s, 2 H, CH<sub>2</sub>), 6.18 (s, 1 H, 4-H), 7.01 (m, 1 H, Ar), 7.41 (m, 2 H, Ar), 8.42 (m, 1 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 14.2$ , 23.4, 27.4, 30.8, 32.1, 50.8, 71.2, 106.9, 110.8, 120.3, 122.4, 137.3, 141.1, 142.3, 149.4, 158.2, 165.9 ppm. C<sub>19</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>: calcd. C 72.58, H 8.33, N 8.91; found C 72.40, H 8.32, N 8.93. **2-Benzyl-5**-*tert*-**butyl-3**-(**methoxycarbonyl**)-1-(2-picolyl)pyrrole (39): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.07$  (s, 9 H, *t*Bu), 3.62 (s, 3 H, COOMe), 4.08 (s, 2 H, CH<sub>2</sub>Ar), 5.15 (s, 2 H, CH<sub>2</sub>N), 6.12 (d, 1 H, 4-H), 6.90–7.20 (m, 8 H, Ar), 8.34 (d-like, 1 H, CH-pyridine) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 23.8$ , 31.0, 50.9, 51.0, 107.1, 112.2, 120.2, 122.3, 126.3, 128.3, 137.2, 138.6, 139.1, 141.9, 149.3, 158.3, 166.1 ppm. C<sub>23</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub>: calcd. C 76.21, H 7.23, N 8.83; found C 76.41, H 7.22, N 8.90.

**2-[2-(Benzyloxycarbonylamino)ethyl]-5**-*tert*-butyl-3-(methoxycarbonyl)-1-(2-methylpropyl)pyrrole (40): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.60$  and 0.65 (2 s, 6 H, Me<sub>2</sub>), 1.10 (s, 9 H, *t*Bu), 1.70 (m, 1 H, CH), 3.03 (t, J = 8 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, COOMe), 4.06 (d, J = 8 Hz, 2 H, CH<sub>2</sub>-N), 4.30 (t, J = 8 Hz, 2 H, CH<sub>2</sub>NHCbz), 5.16 (s, 2 H, OCH<sub>2</sub>Ph), 6.10 (br. s, 1 H, NH), 6.22 (d, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.0, 15.3, 29.5, 31.2$  (3 C), 31.9, 33.4, 44.6, 49.6, 51.7, 70.3, 103.4, 111.8, 127.6, 128.7, 131.6, 133.6, 137.4, 138.7, 156.7, 164.4 ppm. ES/MS: m/z = 415 [M + 1]<sup>+</sup>. C<sub>24</sub>H<sub>34</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 69.54, H 8.27, N 6.76; found C 69.47, H 8.30, N 6.73.

**1-Benzyl-2-[2-(benzyloxycarbonylamino)ethyl]-5***-tert***-butyl-3-(methoxycarbonyl)pyrrole (41):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.10 (s, 9 H, *t*Bu), 3.13 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, CO-OMe), 4.30 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>NRCbz) 4.86 (s, 2 H, CH<sub>2</sub>-N), 5.16 (s, 2 H, OCH<sub>2</sub>Ph), 6.11 (br. s, 1 H, NH), 6.32 (d, 1 H, 4-H), 7.30 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.2, 15.3, 29.5, 31.2, 31.9, 33.4, 40.7, 44.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.4, 127.6, 128.6, 128.7, 131.6, 133.6, 134.6, 137.4, 138.7, 155.7, 165.4 ppm. ES/MS: *m/z* = 449 [M + 1]<sup>+</sup>. C<sub>27</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 72.30, H 7.19, N 6.25; found C 72.20, H 7.12, N 6.29.

**2-[2-(Benzyloxycarbonylamino)-3-phenylpropyl]-5-***tert***-butyl-3-**(methoxycarbonyl)-1-(2-methylpropyl)pyrrole (42): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.61 and 0.63 (2 s, 6 H, Me<sub>2</sub>), 1.10 (s, 9 H, *t*Bu), 1.70 (m, 1 H, CH), 3.00 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar), 3.40 (AB part of an ABX system, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, COOMe), 4.16 (d, *J* = 8 Hz, 2 H, CH<sub>2</sub>-N), 4.50 (m, 1 H, CHNHCbz), 5.16 (s, 2 H, OCH<sub>2</sub>Ph), 6.11 (br. s, 1 H, NH), 6.54 (s, 1 H, 4-H), 7.30 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.2, 15.3, 29.5, 31.2, 31.9, 33.4, 40.7, 44.6, 49.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.4, 127.6, 128.6, 128.7, 131.6, 133.6, 134.6, 137.4, 138.7, 155.7, 165.4 ppm. ES/MS: *m/z* = 506 [M + 1]<sup>+</sup>. C<sub>31</sub>H<sub>40</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 73.78, H 7.99, N 5.55; found C 73.20, H 8.01, N 5.60.

**1-Benzyl-2-[2-(benzyloxycarbonylamino)-3-phenylpropyl]-5-***tert***-butyl-3-(methoxycarbonyl)pyrrole (43):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.12 (s, 9 H, *t*Bu), 3.02 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar), 3.43 (AB part of an ABX system, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, COOMe), 4.50 (m, 1 H, CHNHCbz), 4,87 (s, 2 H, CH<sub>2</sub>–N), 5.10 (s, 2 H, OCH<sub>2</sub>Ph), 6.11 (br. s, 1 H, NH), 6.45 (s, 1 H, 4-H), 7.30 (m, 15 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.7, 15.2, 28.5, 31.2, 32.0, 33.4, 41.7, 44.6, 49.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.4, 127.6, 128.6, 128.7, 128.9, 131.6, 133.6, 135.7, 134.6, 137.4, 138.7, 155.7, 165.4 ppm. ES/MS: *m/z* = 506 [M + 1]<sup>+</sup>. C<sub>34</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 75.81, H 7.11, N 5.20; found C 75.60, H 7.10, N 5.10.

**1-Benzyl-5-ethyl-3-(methoxycarbonyl)-2-phenylpyrrole (44):** Identified by comparison with reported data.<sup>[20]</sup>

**5-Ethyl-3-(methoxycarbonyl)-1-(2-methylpropyl)-2-propylpyrrole** (45): Identified by comparison with reported data.<sup>[20]</sup>

**2-Benzyl-5-ethyl-3-(methoxycarbonyl)-1-[2-(***p***-methoxyphenyl)ethyl]pyrrole (46):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.30$  (t, J = 7 Hz, 3 H, Me), 2.42–2.61 (m, 6 H, CH<sub>2</sub>), 3.66 (s, 3 H, COOMe), 3.86 (s,

3 H, OMe), 4.38 (s, 2 H, CH<sub>2</sub>Ar), 6.44 (s, 1 H, 4-H), 6.81 (d-like, 2 H, Ar), 6.88 (d-like, 2 H, Ar), 7.20 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 12.2, 19.3, 30.8, 36.0, 45.5, 50.6, 55.2, 106.2, 11.18, 114.0, 126.5, 128.1, 128.5, 129.6, 129.8, 134.5, 136.6, 139.2, 158.5, 166.9 ppm. ES/MS: *m*/*z* = 378 [M + 1]<sup>+</sup>. C<sub>24</sub>H<sub>27</sub>NO<sub>3</sub>: calcd. C 76.36, H 7.21, N 3.71; found C 76.21, H 7.18, N 3.72.

**5-Ethyl-3-(methoxycarbonyl)-1-(2-morpholinoethyl)-2-propylpyrrole** (47): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.93$  (t, J = 7 Hz, 3 H, Me), 1.21–1.58 (m, 5 H, CH<sub>2</sub>), 2.41–2.64 (m, 8 H, CH<sub>2</sub>), 2.85 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.65 (s, 3 H, COOMe), 3.87 (t, J = 7 Hz, 6 H, CH<sub>2</sub>), 6.21 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.2$ , 19.3, 30.8, 36.0, 45.5, 51,4, 55.4, 66.8, 103.4, 111.8, 126.6 136.7, 166.4 ppm. ES/MS: m/z = 309 [M + 1]<sup>+</sup>. C<sub>17</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub>: calcd. C 66.20, H 9.15, N 9.08; found C 66.44, H 9.12, N 9.04.

**3-(Methoxycarbonyl)-5-phenyl-1-(2-phenylpropyl)-2-propylpyrrole** (48): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.04$  (t, J = 7 Hz, 3 H, Me), 1.59 (m, 2 H, CH<sub>2</sub>), 2.69 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 2.97 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.65 (s, 3 H, COOMe), 4.19 (t, J = 7 Hz, 2 H, CH<sub>2</sub>N), 6.61 (s, 1 H, 4-H), 6–80–7.50 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.7$ , 19.6, 30.8, 36.8, 41.2, 46.9, 106.8, 116.3, 125.6, 126.2, 126.8, 128.7, 128.9, 128.9, 129.9, 134.4, 134.8, 137.3, 167.2 ppm. ES/MS: m/z = 347 [M + 1]<sup>+</sup>. C<sub>23</sub>H<sub>25</sub>NO<sub>2</sub>: calcd. C 79.51, H 7.25, N 4.03; found C 79.67, H 7.21, N 4.04.

**2-Benzyl-3-(methoxycarbonyl)-1,5-diphenylpyrrole (49):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.60 (s, 3 H, COOMe), 3.99 (s, 2 H, CH<sub>2</sub>), 6.62 (s, 1 H, 4-H), 7.00–7.40 (m, 15 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 36.0, 46.9, 107.8, 112.3, 124.6, 126.2, 126.4, 126.8 (4 C), 127.3, 127.8, 128.0, 128.7, 128.9, 128.9, 129.9, 134.4, 134.8, 137.3, 166.2 ppm. ES/MS: *m*/*z* = 368 [M + 1]<sup>+</sup>. C<sub>25</sub>H<sub>21</sub>NO<sub>2</sub>: calcd. C 81.72, H 5.76, N 3.81; found C 81.75, H 5.79, N 3.79.

**3-(Methoxycarbonyl)-1-(2-morpholinoethyl)-5-phenyl-2-propylpyrrole (50):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.95$  (t, J = 7 Hz, 3 H, Me), 1.69 (m, 2 H, CH<sub>2</sub>), 2.13 (t-like, 4 H, CH<sub>2</sub>N), 2.28 (t, J = 7 Hz, 2 H, CH<sub>2</sub>N), 2.93 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.48 (t-like, 4 H, CH<sub>2</sub>O), 3.67 (s, 3 H, COOMe), 3.95 (t, J = 7 Hz, 2 H, NCH<sub>2</sub>), 6.48 (s, 1 H, 4-H), 7.25 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 14.4$ , 23.8, 27.8, 41.7, 53.9, 56.1, 59.5, 66.0, 110.5, 112.1, 127.8, 128.7, 129.7, 133.4, 133.6, 141.3, 165.4 ppm. ES/MS: m/z = 357 [M + 1]<sup>+</sup>. C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>3</sub>: calcd. C 70.76, H 7.92, N 7.86; found C 70.85, H 7.90, N 7.82.

**1-Benzyl-2-(***p***-chlorophenyl)-3-(methoxycarbonyl)-5-phenylpyrrole** (51): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.61 (s, 3 H, COOMe), 3.90 (s, 2 H, CH<sub>2</sub>), 6.64 (s, 1 H, 4-H), 7.00–7.50 (m, 14 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 35.7, 48.2, 107.8, 112.0, 124.7, 126.6, 126.5, 126.7, 126.8, 127.0, 127.3, 127.8, 128.4, 128.6, 128.7, 129.0, 129.5, 134.7, 135.2, 138.3, 166.2 ppm. ES/MS: *m/z* = 402 and 404 [M + 1]<sup>+</sup>. C<sub>25</sub>H<sub>20</sub>ClNO<sub>2</sub>: calcd. C 74.71, H 5.02, N 3.49; found C 74.65, H 5.09 N 3.51.

**2-Benzyl-1-[2-(3,4-dimethoxyphenyl)ethyl]-3-(methoxycarbonyl)-5phenylpyrrole (52):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.48 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>-Ar), 2.55 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>-Ar), 3.01 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.66 (s, 3 H, COOMe), 3.70 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 4.02 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>-N), 6.59 (s, 1 H, 4-H), 6.80 (m, 3 H, Ar), 7.10–7.30 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 26.4, 38.9, 41.5, 45.6, 50.3, 56.9, 58.7, 106.7, 112.0, 112.6, 113.6, 121.0, 124.6, 126.0, 126.5, 127.3, 127.6, 128.3, 128.9, 134.6, 134.6, 135.0, 145.6, 147.6, 166.7 ppm. ES/MS: *m*/*z* = 470 [M + 1]<sup>+</sup>. C<sub>30</sub>H<sub>31</sub>NO<sub>4</sub>: calcd. C 76.73, H 6.65, N 2.98, found C 76.66, H 6.63, N 2.97.

2-[2-(Benzyloxycarbonylamino)ethyl]-3-(methoxycarbonyl)-1-(2-methylpropyl)-5-phenylpyrrole (53): <sup>1</sup>H NMR (200 MHz,  $CDCl_3$ ):  $\delta$ 

= 0.61 and 0.66 (2 s, 6 H, 2 Me), 1.73 (m, 1 H, CH), 3.06 (t, J = 8 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.63 (s, 3 H, COOMe), 4.00 (d, J = 8 Hz, 2 H, CH<sub>2</sub>-N), 4.35 (t, J = 8 Hz, 2 H, CH<sub>2</sub>NHCbz), 5.16 (s, 2 H, OCH<sub>2</sub>Ph), 6.10 (br. s, 1 H, NH), 7.20–7.40 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.0$ , 15.3, 31.9, 33.7, 45.6, 48.6, 51.9, 71.3, 103.6, 111.9, 126.7, 127.0, 127.5, 127.6, 128.0, 128.7, 131.5, 131.6, 133.6, 137.4, 138.7, 156.7, 164.4 ppm. ES/MS: m/z = 415 [M + 1]<sup>+</sup>. C<sub>26</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 71.87, H 6.96, N 6.45; found C 71.69, H 6.93, N 6.43.

**3-(Methoxycarbonyl)-5-methyl-1-(2-picolyl)-2-propylpyrrole (54):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.92$  (t, J = 7 Hz, 3 H, Me), 1.70 (m, 2 H, CH<sub>2</sub>), 2.11 (s, 3 H, Me), 2.76 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.66 (s, 3 H, COOMe), 5.10 (s, 2 H, CH<sub>2</sub>N), 6.45 (d, 1 H, 4-H), 7.40 (m, 2 H, Ar), 7.86 (m, 1 H, Ar), 8.34 (d-like, 1 H, CH-pyridine) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.4$ , 22.5, 34.6, 37.8, 45.6, 56.7, 106.6, 112.3, 120.5, 126.5, 127.9, 129.8, 135.6, 148.6, 151.2 ppm. C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>: calcd. C 70.56, H 7.40, N 10.29; found C 70.48, H 7.37, N 10.25.

**3-(Methoxycarbonyl)-5-methyl-1-(2-methylpropyl)-2-propylpyrrole** (55): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.60 and 0.64 (d, J = 7 Hz, 6 H, 2 Me), 0.89 (t, J = 7 Hz, 3 H, Me), 1.68 (m, 3 H, CH and CH<sub>2</sub>), 2.02 (s, 3 H, Me), 3.01, (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.65 (s, 3 H, COOMe), 4.01 (d, J = 8 Hz, 2 H, CH<sub>2</sub>N), 6.65 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.4, 11.4, 12.8, 22.5, 26.4, 33.6, 37.8, 46.7, 50.7, 106.6, 112.3, 120.5, 126.5, 166.2 ppm. ES/ MS: m/z = 238 [M + 1]<sup>+</sup>. C<sub>14</sub>H<sub>23</sub>NO<sub>2</sub>: calcd. C 70.85, H 9.77, N 5.90; found C 70.88, H 9.76, N 5.90.

**2-Benzyl-3-(methoxycarbonyl)-5-methyl-1-phenylpyrrole (56):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) 2.02 (s, 3 H, Me), 3.67 (s, 3 H, COOMe), 6.35 (s, 1 H, 4-H), 7.20–7.40 (m, 10 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 26.4, 46.7, 106.6, 112.3, 120.5, 126.5, 126.4, 127.0, 127.8, 128.3, 128.6, 128.9, 134.4, 135.6, 166.2 ppm. ES/MS: *m*/*z* = 292 [M + 1]<sup>+</sup>. C<sub>19</sub>H<sub>17</sub>NO<sub>2</sub>: calcd. C 78.33, H 5.88, N 4.81; found C 78.40, H 5.90, N 4.79.

**3-(Methoxycarbonyl)-5-methyl-1-(2-phenylethyl)-2-propylpyrrole** (57): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.80$  (t, J = 7 Hz, 3 H, Me), 1.67 (m, 2 H, CH<sub>2</sub>), 2.10 (s, 3 H, Me), 2.90 (t, J = 8 Hz, 2 H, CH<sub>2</sub>-Ar), 3.01 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.65 (s, 3 H, COOMe), 3.97 (t, J = 8 Hz, 2 H, CH<sub>2</sub>N), 6.46 (s, 1 H, 4-H), 7.25 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.4$ , 20.7, 26.4, 46.7, 50.4, 56.9, 106.6, 112.3, 120.5, 126.5, 127.0, 128.3, 128.9, 134.4, 166.2 ppm. ES/MS: m/z = 286 [M + 1]<sup>+</sup>. C<sub>18</sub>H<sub>23</sub>NO<sub>2</sub>: calcd. C 75.76, H 8.12, N 4.91; found C 75.60, H 8.11, N 4.89.

**1-Benzyl-2-[2-(benzyloxycarbonylamino)-3-phenylpropyl]-3-(methoxycarbonyl)-5-methylpyrole (58):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.05 (s, 3 H, Me), 3.04 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar), 3.33 (AB part of an ABX system, 2 H, CH<sub>2</sub>-pyrrole), 3.65 (s, 3 H, COOMe), 4.51 (m, 1 H, CHNHCbz), 4,88 (s, 2 H, CH<sub>2</sub>-N), 5.12 (s, 2 H, OCH<sub>2</sub>Ph), 6.21 (br. s, 1 H, NH), 6.45 (s, 1 H, 4-H), 7.30 (m, 15 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.7, 15.2, 24.3, 28.5, 33.4, 41.7, 44.6, 49.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.4 (2 C), 127.6 (2 C), 128.6, 128.7, 128.9, 131.6, 133.6, 135.7, 134.6, 137.4, 138.7, 155.7, 165.4 ppm. ES/MS: *m/z* = 497 [M + 1]<sup>+</sup>. C<sub>31</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 74.98, H 6.50, N 5.64; found C 74.89, H 6.47, N 5.60.

**1-Benzyl-2-[2-(benzyloxycarbonylamino)ethyl]-3-(methoxycarbonyl)-5-methylpyrrole (59):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.10 (s, 3 H, Me), 3.13 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.65 (s, 3 H, CO-OMe), 4.33 (t, J = 8 Hz, 2 H, CH<sub>2</sub>NHCbz), 4.71 (s, 2 H, CH<sub>2</sub>–N), 5.11 (s, 2 H, OCH<sub>2</sub>Ph), 6.11 (br. s, 1 H, NH), 6.60 (s, 1 H, 4-H), 7.30 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.2, 15.3, 26.5, 30.9, 33.4, 40.7, 44.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.4, 127.6, 128.6, 128.7, 131.6, 133.6, 134.6, 137.4, 138.7, 155.7, 165.4 ppm. ES/MS:  $m/z = 407 \ [M + 1]^+$ .  $C_{24}H_{26}N_2O_4$ : calcd. C 70.92, H 6.45, N 6.89; found C 70.80, H 6.41, N 6.88.

**2-[2-(Benzyloxycarbonylamino)ethyl]-3-(methoxycarbonyl)-5-methyl-1-(2-methylpropyl)pyrrole (60):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.60 and 0.71 (d, J = 7 Hz, 6 H, Me<sub>2</sub>), 1.78 (m, 1 H, CHMe<sub>2</sub>), 2.10 (s, 3 H, Me), 3.18 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.65 (s, 3 H, COOMe), 4.33 (d, J = 7 Hz, 2 H, CH<sub>2</sub>NHCbz) 4.51 (d, J = 7 Hz, 2 H, CH<sub>2</sub>-N), 5.11 (s, 2 H, OCH<sub>2</sub>Ph), 6.11 (br. s, 1 H, NH), 6.60 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.2, 15.3, 26.5, 30.9, 33.4, 40.7, 44.6, 52.7, 70.9, 103.4, 111.8, 126.3, 127.6, 128.6, 131.6, 133.6, 134.5, 165.4 ppm. ES/MS: m/z = 373 [M + 1]<sup>+</sup>. C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 67.72, H 7.58, N 7.52; found C 67.79, H 7.54, N 7.56.

**1-[2-(Benzyloxycarbonylamino)ethyl]-5-***tert*-**butyl-3-(methoxycarbonyl)-2-phenylpyrrole (64):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.36 (s, 9 H, *t*Bu), 3.65 (s, 3 H, COOMe), 4.01 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 4.37 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 5.12 (s, 2 H, OCH<sub>2</sub>), 6.10 (br. s, 1 H, NH), 6.48 (s, 1 H, 4-H), 7.20–7.35 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.5, 30.9, 46.7, 54.6, 58.7, 70.9, 103.4, 111.8, 126.3, 126.8, 127.4, 128.3, 134.2, 136.3, 158.7, 165.8 ppm. ES/MS: *m/z* = 435 [M + 1]<sup>+</sup>. C<sub>26</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 71.87, H 6.96, N 6.45; found C 71.49, H 6.99, N 6.46.

**1-[2-(Benzyloxycarbonylamino)-3-phenylpropyl]-5**-*tert*-butyl-3-(methoxycarbonyl)-2-phenylpyrrole (65): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.30 (s, 9 H, *t*Bu), 2.96 (m, 2 H, ArCH<sub>2</sub>), 3.66 (s, 3 H, COOMe), 4.11 (m, 2 H, CH<sub>2</sub>N), 4.47 (m, 1 H, CHN), 5.11 (s, 2 H, OCH<sub>2</sub>), 6.11 (br. s, 1 H, NH), 6.55 (s, 1 H, 4-H), 7.20–7.50 (m, 15 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.5, 30.9, 32.6, 46.0, 54.6, 59.7, 70.9, 103.5, 111.0, 126.4, 126.8, 126.9, 127.4, 127.6, 128.3, 128.4, 134.2, 134.8, 136.0, 158.4, 167.2 ppm. ES/MS: *m/z* = 525 [M + 1]<sup>+</sup>. C<sub>33</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 75.55, H 6.92, N 5.34; found C 75.59, H 6.99, N 5.37.

**1-[2-(Benzyloxycarbonylamino)propyl]-5***tert*-butyl-3-(methoxycarbonyl)-2-phenylpyrrole (66): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.93$  (d, J = 7 Hz, 3 H, Me), 1.30 (s, 9 H, *t*Bu), 3.56 (s, 3 H, COOMe), 4.01 (m, 2 H, CH<sub>2</sub>N), 4.33 (m, 1 H, CHN), 5.15 (s, 2 H, OCH<sub>2</sub>), 6.11 (br. s, 1 H, NH), 6.50 (s, 1 H, 4-H), 7.20 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 13.6$ , 29.5, 30.9, 31.6, 55.6, 58.7, 70.3, 103.5, 111.9, 126.4, 126.8, 127.6, 128.3, 134.2, 135.0, 158.4, 165.2 ppm. ES/MS: m/z = 449 [M + 1]<sup>+</sup>. C<sub>27</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 72.30, H 7.19, N 6.25; found C 72.59, H 7.18, N 6.27.

**1-[2-(Benzyloxycarbonylamino)ethyl]-5-***tert*-**butyl-3-(methoxycarbonyl)-2-propylpyrrole (67):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.86 (t, *J* = 8 Hz, 3 H, Me), 1.36 (s, 9 H, *t*Bu), 1.79 (m, 2 H, CH<sub>2</sub>), 3.07 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, COOMe), 4.08 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 4.37 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 5.10 (s, 2 H, OCH<sub>2</sub>), 6.19 (br. s, 1 H, NH), 6.58 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.5, 28.4, 29.5, 31.4, 43.6, 44.7, 54.6, 58.9, 70.4, 104.4, 110.6, 126.3, 126.8, 127.4, 128.3, 134.2, 136.3, 155.8, 167.8 ppm. ES/MS: *m/z* = 401 [M + 1]<sup>+</sup>. C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 68.97, H 8.05, N 6.99; found C 70.04, H 8.09, N 7.00.

**1-[2-(Benzyloxycarbonylamino)-3-phenylpropyl]-5**-*tert*-butyl-3-(methoxycarbonyl)-2-propylpyrrole (68): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.90$  (t, J = 7 Hz, 3 H, Me), 1.30 (s, 9 H, *t*Bu), 1.80 (m, 2 H, CH<sub>2</sub>), 2.90 (m, 2 H, ArCH<sub>2</sub>), 3.03 (t, J = 8 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.65 (s, 3 H, COOMe), 4.11 (m, 2 H, CH<sub>2</sub>N), 4.47 (m, 1 H, CHN), 5.11 (s, 2 H, OCH<sub>2</sub>), 6.11 (br. s, 1 H, NH), 6.55 (s, 1 H, 4-H), 7.20–7.50 (m, 10 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.4, 17.9, 29.5, 30.9, 32.6, 36.4, 46.0, 54.6, 59.7, 70.9, 103.5,$  111.0, 126.4, 126.8, 126.9, 127.4, 127.6, 128.3, 128.4, 134.2, 134.8, 136.0, 158.4, 167.2 ppm. ES/MS:  $m/z = 490 \text{ [M + 1]}^+$ . C<sub>30</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 73.44, H 7.81, N 5.71; found C 73.51, H 7.84, N 5.73.

**1-[2-(Benzyloxycarbonylamino)propyl]-5**-*tert*-butyl-3-(methoxycarbonyl)-2-propylpyrole (69): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.87 (t, J = 7 Hz, 3 H, Me), 0.91 (d, J = 7 Hz, 3 H, Me), 1.30 (s, 9 H, *t*Bu), 1.87 (m, 2 H, CH<sub>2</sub>), 3.06 (t, J 0 = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.58 (s, 3 H, COOMe), 4.11 (m, 2 H, CH<sub>2</sub>N), 4.37 (m, 1 H, CHN), 5.20 (s, 2 H, OCH<sub>2</sub>), 6.18 (br. s, 1 H, NH), 6.43 (s, 1 H, 4-H), 7.25 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.4, 13.6, 21.6, 29.5, 30.9, 31.6, 34.7, 55.6, 58.7, 70.3, 103.5, 111.9, 126.4, 126.8, 127.6, 128.3, 134.2, 135.0, 158.4, 165.2 ppm. ES/MS: *m/z* = 415 [M + 1]<sup>+</sup>. C<sub>24</sub>H<sub>34</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 69.54, H 8.27, N 6.76; found C 69.59, H 8.28, N 6.77.

**1-[2-(Benzyloxycarbonylamino)ethyl]-5-ethyl-3-(methoxycarbonyl)-2-propylpyrrole (70):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.88$  (t, J = 8 Hz, 3 H, Me), 0.91 (t, J = 8 Hz, 3 H, Me), 1.65 (m, 2 H, CH<sub>2</sub>), 2.78 (q, J = 8 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.07 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.60 (s, 3 H, COOMe), 4.18 (t, J = 8 Hz, 2 H, CH<sub>2</sub>N), 4.30 (t, J = 8 Hz, 2 H, CH<sub>2</sub>N), 5.19 (s, 2 H, OCH<sub>2</sub>), 6.00 (br. s, 1 H, NH), 6.27 (s, 1 H, 4-H), 7.32 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.1$ , 14.5, 28.4, 30.4, 43.6, 44.7, 54.6, 58.9, 70.4, 104.4, 110.6, 126.3, 126.8, 127.4, 128.3, 134.2, 136.3, 155.8, 167.8 ppm. ES/MS: m/z = 372 [M + 1]<sup>+</sup>. C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>: calcd. C 67.72, H 7.58, N 7.52; found C 67.66, H 7.56, N 7.51.

**5-***tert***-Butyl-3-(methoxycarbonyl)-2-phenylfuran (71):** Product **6** (0.5 g, 1,64 mmol) was dissolved in EtOH (2 mL) in a 50-mL round-bottomed flask, equipped with a stirrer bar and a reflux condenser. HCl (0.1 mL of a 37% solution) was added, and the flask was inserted into the cavity of a Discovery Microwave System apparatus (from CEM) and heated at 150 W for 4 min (internal temperature 100 °C). The mixture was diluted with AcOEt, and the solution was washed several times with a saturated solution of NaHCO<sub>3</sub>. The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, and the solvent was evaporated. The <sup>1</sup>H NMR spectrum of the crude showed the presence of pure furan **71** that could eventually be further purified by flash chromatography (eluent hexane/AcOEt, 8:1;  $R_f = 0.75$ ) to give the product (0.49 g, 95% yield). It was identified by comparison with reported data.<sup>[23]</sup>

**5**-*tert*-**Butyl-3**-(**methoxycarbonyl**)-**2**-(**2**-**phenylethyl**)**furan** (72): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.10 (s, 9 H, *t*Bu), 2.8 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>Ar), 3.18 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.60 (s, 3 H, COOMe), 6.98 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.6, 30.3, 34.5, 38.4, 57.8, 106.8, 118.2, 120.5, 126.6, 127.6, 127.8, 130.8, 134.7, 166.6 ppm. ES/MS: *m/z* = 287 [M + 1]<sup>+</sup>. C<sub>18</sub>H<sub>22</sub>O<sub>3</sub>: C 75.50, H 7.74; found C 75.30, H 7.74.

**3-(Methoxycarbonyl)-5-methyl-2-propylfuran (73):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.87 (t, J = 7 Hz, 3 H, Me), 1.19 (m, 2 H, CH<sub>2</sub>), 2.67 (s, 3 H, Me), 3.00 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.56 (s, 3 H, COOMe), 7.00 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.3, 28.9, 30.7, 39.7, 108.8, 119.2, 121.5, 135.7, 165.6 ppm. ES/MS: m/z = 183 [M + 1]<sup>+</sup>. C<sub>10</sub>H<sub>14</sub>O<sub>3</sub>: calcd. C 65.91, H 7.74; found C 65.80, H 7.73.

**5-***tert***-Butyl-3-(methoxycarbonyl)-2-phenylthiophene (74):** Lawesson's reagent (4.0 g) was added to a solution of compound **6** (1.0 g, 3.62 mmol) in toluene (10 mL), and the mixture was heated under microwave irradiation at 150 W (open vessel in the cavity of a Discover apparatus) for 6 min. After cooling, the mixture was filtered through Celite, the solvent was evaporated, and the product was isolated by column chromatography on silica gel (eluent hexane/AcOEt, 3:1) to give the product (0.82 g, 70% yield). <sup>1</sup>H NMR

(200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.13 (s, 9 H, *t*Bu), 3.52 (s, 3 H, COOMe), 7.30 (m, 6 H, Ar + 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.4, 31.3, 53.8, 108.8, 120.2, 123.3, 126.6, 127.6, 127.8, 130.8, 135.7, 167.5 ppm. ES/MS: *m*/*z* = 275 [M + 1]<sup>+</sup>. C<sub>16</sub>H<sub>18</sub>O<sub>2</sub>S: calcd. C 70.04, H 6.61; found C 70.08, H 6.63.

**5**-*tert*-**Butyl-3**-(**methoxycarbonyl)**-**2**-(**2**-**phenylethyl**)**thiophene** (75): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.11 (s, 9 H, *t*Bu), 2.87 (t, *J* = <sup>7</sup> Hz, 2 H, CH<sub>2</sub>Ar), 3.22 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.65 (s, 3 H, COOMe), 7.13 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.6, 31.3, 36.5, 39.4, 57.8, 116.8, 120.2, 121.5, 126.6, 127.6, 127.8, 130.8, 135.7, 164.9 ppm. ES/MS: *m/z* = 287 [M + 1]<sup>+</sup>. C<sub>18</sub>H<sub>22</sub>O<sub>2</sub>S: calcd. C 71.48, H 7.33; found C 71.29, H 7.34.

**5**-*tert*-**Butyl-3**-(methoxycarbonyl)-2-propylthiophene (76): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.76$  (t, J = 7 Hz, 3 H, Me), 1.10 (s, 9 H, *t*Bu), 1.67 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.32 (t, J = 7 Hz, 2 H, CH<sub>2</sub>), 3.55 (s, 3 H, COOMe), 7.10 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 20.5$ , 28.6, 29.9, 31.3, 37.5, 57.8, 107,3, 120.2, 121.5, 135.7, 164.9 ppm. ES/MS: m/z = 241 [M + 1]<sup>+</sup>. C<sub>13</sub>H<sub>20</sub>O<sub>2</sub>S: C 64.96, H 8.39, found C 64.88, H 8.34.

**3-(Methoxycarbonyl)-5-methyl-2-propylthiophene (77):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.89$  (t, J = 7 Hz, 3 H, Me), 1.25 (m, 2 H, CH<sub>2</sub>), 2.33 (s, 3 H, Me), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.50 (s, 3 H, COOMe), 7.23 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 21.3$ , 29.6, 30.7, 38.1, 56.7, 109.8, 120.2, 121.9, 135.7, 165.6 ppm. ES/MS: m/z = 199 [M + 1]<sup>+</sup>. C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>S: calcd. C 60.57, H 7.12;, found C 60.39, H 7.13.

**3-(Methoxycarbonyl)-5-phenyl-2-propylthiophene (78):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.80 (t, *J* = 7 Hz, 3 H, Me), 1.22 (m, 2 H, CH<sub>2</sub>), 3.00 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.50 (s, 3 H, COOMe), 7.30 (s, 6 H, Ar, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 19.3, 28.6, 34.1, 56.7, 109.8, 120.2, 121.9, 126.2, 127.7, 128.9, 134.3, 135.7, 165.6 ppm. ES/MS: *m*/*z* = 261 [M + 1]<sup>+</sup>. C<sub>15</sub>H<sub>16</sub>O<sub>2</sub>S: calcd. C 69.20, H 6.19, found C 69.10, H 6.13.

1-Butyl-5-tert-butyl-2-(p-chlorophenyl)pyrrole-3-carboxylic Acid (79). General Procedure for Acids: Pyrrole 32 (0.1 g, 0.28 mmol) was dissolved in a solution of EtOH (5 mL) that contained NaOH (50 mg, 1.25 mmol). The mixture was stirred at room temperature for 12 h. The solvent was evaporated, and HCl (5% in H<sub>2</sub>O, 2 mL) was added. The aqueous layer was extracted three times with EtOAc, the fractions were collected, and the solvent was evaporated to give product 79, which was practically pure (89 mg, 96%) vield). An analytical sample was isolated by column chromatography on silica gel (eluent EtOAc/hexane, 3:1). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.67$  (t, J = 7 Hz, 3 H, Me), 0.96–1.17 (m, 2 H, CH<sub>2</sub>), 1.25–1.30 (m, 2 H, CH<sub>2</sub>), 1.36 (s, 9 H, tBu), 3.89 (t, J = 8 Hz, 2 H, N-CH<sub>2</sub>), 6.42 (s, 1 H, 4-H), 7.20 (d-like, 2 H, Ar), 7.36 (d-like, 2 H, Ar), 10.2 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): *δ* = 12.7, 19.2, 29.5, 30.2, 31.7, 32.5, 45.0, 106.4, 110.8, 127.6, 128.7, 131.6, 133.6, 137.4, 140.9, 162.4 ppm. ES/MS:  $m/z = 333-335 [M + 1]^+$ . C<sub>19</sub>H<sub>24</sub>ClNO<sub>2</sub>: calcd. C 68.35, H 7.25, N 4.20; found C 68.27, H 7.21, N 4.21.

**1-Benzyl-5**-*tert*-**butyl-2**-(**2**-phenylethyl)pyrrole-3-carboxylic Acid (80): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.23 (s, 9 H, *t*Bu), 2.71 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>), 3.20 (t, *J* = 8 Hz, 2 H,CH<sub>2</sub>), 4.90 (s, 2 H, CH<sub>2</sub>N), 6.41 (s, 1 H, 4-H), 7.20–7.35 (m, 10 H, Ar), 10.3 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 30.5, 31.7, 37.8, 41.6, 45.9, 104.4, 112.8, 126.9, 126.6, 128.6, 128.7, 129.3, 131.6, 133.6, 137.4, 165.4 ppm. ES/MS: *m*/*z* = 366 [M – 1]<sup>+</sup>. C<sub>24</sub>H<sub>27</sub>NO<sub>2</sub>: calcd. C 79.74, H 7.53, N 3.87; found C 79.80, H 7.54, N 3.89.

**5-***tert***-Butyl-1-(2-methylpropyl)-2-phenylpyrrole-3-carboxylic Acid** (81): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.60 and 0.69 (2 d, J = 7 Hz, 6 H, Me), 1.25 (s, 9 H, *t*Bu), 1.72 (m, 1 H, CH), 3.75 (d, J = 8 Hz, 2 H, N–CH<sub>2</sub>), 6.51 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar), 10.4 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.9$ , 16.0, 29.5, 31.0, 31.7, 32.4, 44.6, 103.4, 111.8, 127.6, 128.7, 131.6, 133.6, 137.4, 138.7, 164.4 ppm. ES/MS: m/z = 298 [M – 1]<sup>+</sup>. C<sub>19</sub>H<sub>25</sub>NO<sub>2</sub>: C 76.22, H 8.42, N 4.68; found C 76.37, H 8.40, N 4.63.

**1-(2-Methylpropyl)-5-phenyl-2-propylpyrrole-3-carboxylic Acid (82):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.98 and 1.04 (2 d, *J* = 6 Hz, 6 H, 2 Me), 1.11 (t, *J* = 7 Hz, 3 H, Me), 1.59 (m, 2 H, CH<sub>2</sub>), 2.69 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>), 2.97 (t *J* = 7 Hz, 2 H, CH<sub>2</sub>), 4.19 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>N), 6.61 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar), 10.3 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 12.7, 19.6, 30.8, 36.8, 41.2, 106.8, 116.3, 125.6, 126.2, 126.8, 128.7, 128.9, 128.9, 129.9, 134.4, 134.8, 137.3, 167.2 ppm. ES/MS: *m/z* = 284 [M - 1]<sup>+</sup>. C<sub>18</sub>H<sub>23</sub>NO<sub>2</sub>: calcd. C 79.76, H 8.12, N 4.91; found C 79.69, H 8.11, N 4.94.

**5**-*tert*-**Butyl-2**-phenylthiophene-3-carboxylic Acid (83): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.13 (s, 9 H, *t*Bu), 7.30 (m, 6 H, Ar + 4-H) 11.0 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.4, 31.3, 108.8, 120.2, 123.3, 126.6, 127.6, 127.8, 130.8, 135.7, 167.5 ppm. ES/MS: m/z = 259 [M – 1]<sup>+</sup>. C<sub>15</sub>H<sub>16</sub>O<sub>2</sub>S: calcd. C 69.20, H 6.19; found C 69.18, H 6.16.

**5-Methyl-2-propylthiophene-3-carboxylic Acid (84):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.90$  (t, J = 7 Hz, 3 H, Me), 1.28 (m, 2 H, CH<sub>2</sub>), 2.33 (s, 3 H, Me), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-furan), 7.23 (s, 1 H, 4-H), 9.98 (br. s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 21.3$ , 29.6, 30.7, 38.1, 109.8, 120.2, 121.9, 135.7, 165.6 ppm. ES/MS: m/z = 183 [M – 1]<sup>+</sup>. C<sub>9</sub>H<sub>12</sub>O<sub>2</sub>S: calcd. C 58.67, H 6.56; found C 58.50, H 6.53.

**3-Amino-1-butyl-5***-tert*-**butyl-2**-(*p*-chlorophenyl)pyrrole (85): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.67$  (t, J = 7 Hz, 3 H, Me), 0.96–1.19 (m, 2 H, CH<sub>2</sub>), 1.25–1.33 (m, 2 H, CH<sub>2</sub>), 1.36 (s, 9 H, *t*Bu), 3.80 (t, J = 8 Hz, 2 H, N–CH<sub>2</sub>),3.77 (br. s, 2 H, NH<sub>2</sub>) 6.22 (s, 1 H, 4-H), 7.20 (d-like, 2 H, Ar), 7.36 (d-like, 2 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.7$ , 19.2, 29.5, 30.2, 31.7, 32.5, 45.0, 106.4, 110.8, 127.6, 128.7, 131.6, 133.6, 137.4, 140.9, 162.4 ppm. ES/MS: m/z = 305-307 [M + 1]<sup>+</sup>. C<sub>18</sub>H<sub>25</sub>ClN<sub>2</sub>: calcd. C 70.92, H 8.27, N 9.19; found C 70.83, H 8.21, N 9.21.

*N*,1-Dibenzyl-5-*tert*-butyl-2-phenylpyrrole-3-carboxamide (86): Compound **79** (0.15 g, 0.45 mmol) was dissolved in dry toluene (2 mL) under nitrogen, and DPPA (0.34 g, 1.24 mmol) was added to this solution followed by Et<sub>3</sub>N (0.26 mL). The mixture was heated to reflux for 2 h, then cooled, and H<sub>2</sub>O (1.3 mL) was added. The mixture was heated further to reflux for 2 h, and the solvent was evaporated under vacuum. Column chromatography on silica gel (eluent EtOAc/hexane, 3:1) gave product **86** (0.91 g, 67% yield). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.14 (s, 9 H, *t*Bu), 4.56 (s, 2 H, CH<sub>2</sub>), 5.16 (s, 2 H, CH<sub>2</sub>), 6.56 (s, 1 H, 4-H), 7.10–7.50 (m, 16 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.7, 32.2, 49.3, 55.6, 107.1, 112.4, 125.4, 126.8, 127.5, 127.9, 128.2, 130.5, 132.1, 138.9, 140.6, 142.3, 166.7 ppm. ES/MS: *m/z* = 423 [M + 1]<sup>+</sup>. C<sub>29</sub>H<sub>30</sub>N<sub>2</sub>O: calcd. C 82.43, H 7.16, N 6.63; found C 82.46, H 7.12, N 6.60.

**1-Benzyl-5**-*tert*-**butyl-***N*-**[2**-(*p*-methoxyphenyl)ethyl]-2-phenylpyrrole-**3-carboxamide (87):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 1.16$  (s, 9 H, *t*Bu), 2,09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>Ar), 3.66 (s, 3 H, OMe), 4.06 (t, J = 7 Hz, 2 H), 5.16 (s, 2 H, CH<sub>2</sub>), 6.56 (s, 1 H, 4-H), 7.10–7.50 (m, 15 H, Ar and NH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 28.7$ , 32.2, 49.3, 51.4, 56.6, 60.6, 107.1, 112.4, 125.4, 126.8, 127.5, 127.9, 128.2, 130.5, 132.1, 138.9, 140.6, 142.3, 166.7 ppm. ES/MS: m/z = 467 [M + 1]<sup>+</sup>. C<sub>31</sub>H<sub>34</sub>N<sub>2</sub>O: calcd. C 79.79, H 7.34, N 6.00; found C 79.69, H 7.32, N 6.58. **1-Benzyl-5***-tert*-butyl-*N*-(2-morpholinoethyl)-2-phenylpyrrole-3-carboxamide (88): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.16 (s, 9 H, *t*Bu), 2,29 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>N), 2.67 (m, 4 H, CH<sub>2</sub>N), 3.60 (m, 4 H, CH<sub>2</sub>O), 4.00 (t, *J* = 7 Hz, 2 H, CH<sub>2</sub>), 5.16 (s, 2 H, CH<sub>2</sub>), 6.56 (s, 1 H, 4-H), 7.10–7.50 (m, 11 H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.7, 32.2, 36.8, 44.8, 49.3, 51.4, 60.6, 107.1, 112.4, 125.4, 126.8, 127.5, 127.9, 128.2, 130.5, 132.1, 138.9, 140.6, 142.3, 166.7 ppm. ES/MS: *m*/*z* = 446 [M + 1]<sup>+</sup>. C<sub>28</sub>H<sub>35</sub>N<sub>2</sub>O<sub>3</sub>: C 75.47, H 7.92, N 9.43; found C 75.39, H 7.90, N 9.40.

**5**-*tert*-**Butyl-1-(2-methylpropyl)-3-(morpholinocarbonyl)-2-phenylpyrrole (89):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.60 and 0.69 (2 d, J = 7 Hz, 6 H, Me), 1.25 (s, 9 H, *t*Bu), 1.72 (m, 1 H, CH), 3.60 (m, 4 H, CH<sub>2</sub>O), 3.75 (d, J = 8 Hz, 2 H, N–CH<sub>2</sub>), 4.01 (m, 4 H, CH<sub>2</sub>N), 6.59 (s, 1 H, 4-H), 7.30 (m, 5 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.9, 16.0, 29.5, 31.0, 31.7, 32.4, 40.6, 44.6, 55.4, 103.4, 111.8, 127.6, 128.7, 131.6, 133.6, 137.4, 138.7, 164.4 ppm. ES/MS: *m*/*z* = 369 [M + 1]<sup>+</sup>. C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>2</sub>: C 74.96, H 8.75, N 7.60; found C 74.88, H 8.70, N 7.63.

*N*,1-Dibenzyl-5-ethyl-2-phenylpyrrole-3-carboxamide (90): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.25 (t, *J* = 7 Hz, 3 H, Me), 2.45 (q, *J* = 7 Hz, 2 H, CH<sub>2</sub>-pyrrole), 3.98 (s, 2 H, CH<sub>2</sub>N), 4.97 (s, 2 H, CH<sub>2</sub>N), 6.60 (s, 1 H, 4-H), 6.84–7.43 (m, 16 H, Ar) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 11.9, 19.4, 47.3, 60.4, 106.8, 112.3, 125.3, 127.0, 127.6, 128.0, 128.5, 130.4, 131.8, 135.3, 137.7, 138.6, 165.3 ppm. ES/MS: *m*/*z* = 395 [M + 1]<sup>+</sup>. C<sub>27</sub>H<sub>26</sub>N<sub>2</sub>O: calcd. C 82.20, H 6.64, N 7.10; found C 82.11, H 6.59, N 7.13.

**5**-*tert*-**Buty**I-*N*-(**3**-methylpropyl)-**2**-phenylthiophene-**3**-carboxamide (**91**): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.89$  and 0.92 (d, J = 8 Hz, 6 H, Me<sub>2</sub>), 1.13 (s, 9 H, *t*Bu), 1.98 (m, 1 H, CH), 3,77 (m, 2 H, CH<sub>2</sub>), 7.30 (m, 7 H, Ar + 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.9$ , 15.7, 29.4, 31.3, 36.8, 44.9, 108.8, 120.2, 123.3, 126.6, 127.6, 127.8, 130.8, 135.7, 167.5 ppm. ES/MS: *m*/*z* = 316 [M + 1]<sup>+</sup>. C<sub>19</sub>H<sub>25</sub>NOS: calcd. C 72.34, H 7.99, N 4.44; found C 72.28, H 7.95, N 4.42.

**5**-*tert*-**Butyl**-*N*-**(2**-morpholinoethyl)-2-phenylthiophene-3-carboxamide (92): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.13 (s, 9 H, *t*Bu), 2.88 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 3.00 (m, 4 H, CH<sub>2</sub>N), 3.77 (m, 4 H, CH<sub>2</sub>O), 4.01 (t, *J* = 8 Hz, 2 H, CH<sub>2</sub>N), 7.30 (m, 6 H, Ar + 4-H), 7.71 (br. s, 1 H, NH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 29.4, 31.3, 44.9, 48.9, 51.8, 55.9, 107.8, 120.2, 123.3, 126.6, 127.6, 127.8, 130.8, 135.7, 167.5 ppm. ES/MS: *m*/*z* = 373 [M + 1]<sup>+</sup>. C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>2</sub>S: calcd. C 67.71, H 7.58, N 7.52; found C 67.66, H 7.55, N 7.50.

**5-Methyl-***N*-(**3-methylpropyl**)-**2-propylthiophene-3-carboxamide** (**93**): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.84$  (t, J = 7 Hz, 3 H, Me), 1.01 (d-like, 6 H, Me<sub>2</sub>), 1.24 (m, 2 H, CH<sub>2</sub>), 1.98 (m, 1 H, CH), 2.33 (s, 3 H, Me), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.90 (d, J = 7 Hz, 2 H, CH<sub>2</sub>N) 7.03 (br. s, 1 H, NH), 7.23 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 18.3$ , 20.2, 21.3, 29.6, 29.9, 30.7, 38.1, 56.7, 60.1, 109.8, 120.2, 121.9, 135.7, 165.6 ppm. ES/MS: m/z = 240 [M + 1]<sup>+</sup>. C<sub>13</sub>H<sub>21</sub>NOS: calcd. C 65.23, H 8.84, N 5.85; found C 65.26, H 8.80, N 5.88.

**5-Methyl-***N*-(**2-phenylethyl)-2-propylthiophene-3-carboxamide (94):** <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.84$  (t, J = 7 Hz, 3 H, Me), 1.24 (m, 2 H, CH<sub>2</sub>), 2.33 (s, 3 H, Me), 2.67 (t, J = 7 Hz, 2 H, CH<sub>2</sub>Ar), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-furan), 3.99 (d, J = 7 Hz, 2 H, CH<sub>2</sub>N), 7.20–7.40 (s, 7 H, Ar, 4-H and NH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 21.3$ , 29.6, 30.7, 38.1, 39.9, 47.8, 56.7, 60.1, 109.8, 120.2, 121.9, 135.7, 165.6 ppm. ES/MS: m/z = 285 [M + 1]<sup>+</sup>. C<sub>17</sub>H<sub>21</sub>NOS: calcd. C 71.04, H 7.36, N 4.87; found C 71.09, H 7.33, N 4.83.

**5-Methyl-***N***-(2-morpholinoethyl)-2-propylthiophene-3-carboxamide** (95): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.89$  (t, J = 7 Hz, 3 H, Me), 1.25 (m, 2 H, CH<sub>2</sub>), 2.33 (s, 3 H, Me), 2.86 (m, 2 H, CH<sub>2</sub>N), 3.02 (m, 4 H, CH<sub>2</sub>N), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>-thiophene), 3.80 (m, 4 H, CH<sub>2</sub>O), 4.01 (m, 2 H, CH<sub>2</sub>N), 7.19 (br. s, 1 H, NH), 7.23 (s, 1 H, 4-H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 21.3$ , 29.6, 30.7, 38.1, 40.5, 46.9, 55.9, 58.7, 109.8, 120.2, 121.9, 135.7, 165.6 ppm. ES/MS: m/z = 297 [M + 1]<sup>+</sup>. C<sub>15</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub>S: calcd. C 60.78, H 8.16, N 9.45; found C 60.69, H 8.13, N 9.41.

*N*-(*p*-Methoxyphenyl)-5-methyl-2-propylthiophene-3-carboxamide (96): <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta = 0.89$  (t, J = 7 Hz, 3 H, Me), 1.25 (m, 2 H, CH<sub>2</sub>), 2.33 (s, 3 H, Me), 3.09 (t, J = 7 Hz, 2 H, CH<sub>2</sub>thiophene), 3.68 (s, 3 H, MeO), 6.87 (m, 2 H, Ar), 7.30 (m, 4 H, Ar, 4-H and NH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 21.3$ , 30.7, 38.1, 55.9, 58.7, 109.8, 120.2, 121.9, 126.7, 128.3, 128.9, 133.2, 135.7, 165.6 ppm. ES/MS: *m*/*z* = 288 [M + 1]<sup>+</sup>. C<sub>16</sub>H<sub>19</sub>NO<sub>2</sub>S: calcd. C 66.41, H 6.22, N 4.84; found C 66.35, H 6.26, N 4.80.

Compound 97: Pyrrole 58 (0.1 g, 0.2 mmol) was dissolved in a solution of EtOH (5 mL) that contained NaOH (50 mg). The mixture was stirred at room temperature for 12 h. The solvent was evaporated, and HCl (5% in H<sub>2</sub>O, 2 mL) was added. The aqueous layer was extracted three times with EtOAc, the extracts were combined, and the solvent was evaporated. The crude was dissolved in THF (5 mL), and HValOMe·HCl (35 mg, 0.2 mmol) was added to this solution followed by DMTMM (82 mg, 0.3 mmol) and NMM (60 mg, 0.6 mmol). The mixture was stirred at room temperature for 12 h. The solid was filtered off, and the THF solution was diluted with EtOAc (5 mL) and washed with HCl (5%, 10 mL), Na<sub>2</sub>CO<sub>3</sub> (10%, 10 mL) and brine. The organic layer was separated and dried, and the solvent was evaporated. The product 97 was isolated by column chromatography on silica gel (eluting with EtOAc/hexane, 1:1) to yield 0.103 g, 89%. <sup>1</sup>H NMR (600 MHz,  $CDCl_3$ ):  $\delta = 1.086$  (d, J = 7 Hz, 3 H, MeAla), 2.086 (s, 3 H, Me), 3.144 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar), 3.390 (AB part of an ABX system, 2 H, CH<sub>2</sub>-pyrrole), 3.555 (s, 3 H, COOMe), 4.061 (AB system, 2 H,  $CH_2N$ ), 4.389 (qd, J = 7 and 12 Hz, 1 H, CHN-Ala), 4.510 (m, 1 H, CHNHCbz), 4,885 (s, CH2-N), 5.122 (s, 2 H, OCH<sub>2</sub>Ph), 6.210 (br. s, 1 H, NH), 6.550 (s, 1 H, 4-H), 7.304 (m, 16 H, Ar and NH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 15.2, 24.3, 33.4, 41.7, 44.6, 49.6, 52.7, 61.4, 103.4, 111.8, 126.3, 127.4, 127.6, 128.6, 128.7, 128.9, 131.6, 133.6, 135.7, 134.6, 138.7, 155.7, 165.4, 167.9 ppm. ES/MS:  $m/z = 568 [M + 1]^+$ .

Compound 98: Product 97 (0.10 g, 0.18 mmol) was dissolved in iPr-OH (3 mL), and HCOONH<sub>4</sub> (20 mg) was added followed by Pd/C (10%, 10 mg). The mixture was heated inside a microwave cavity at 140 °C for 4 min. After cooling, EtOAc (10 mL) was added, and the residue was filtered. The solvent was evaporated, and the crude was dissolved in THF followed by addition of DMTMM (110 mg, 0.4 mmol), BocPheOH (53 mg, 0.2 mmol) and NMM (30 mg). The mixture was stirred at room temperature for 12 h. The solid was filtered off, and the THF solution was diluted with EtOAc (5 mL) and washed with HCl (5%, 10 mL), Na<sub>2</sub>CO<sub>3</sub> (10%, 10 mL) and brine. The organic layer was separated and dried, and the solvent was evaporated. The crude was dissolved in THF/H<sub>2</sub>O, 1:1 (5 mL, containing LiOH, 810 mg), and the mixture was stirred at room temperature for 2 h. HCl (5% in H<sub>2</sub>O, 1 mL) was added, the solvent was evaporated under vacuum, and the product 98 was isolated by column chromatography on silica gel (eluting with EtOAc/ hexane, 4:1) to yield 94 mg, 79%. An analytical sample was isolated by preparative HPLC. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>):  $\delta = 1.054$  (d, J = 7 Hz, 3 H, MeAla), 1.45 (s, 9 H, tBu), 2.091 (s, 3 H, Me), 2.986 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar, Phe), 3.155 (AB part of an ABX system, 2 H, CH<sub>2</sub>-Ar), 3.408 (AB part of an ABX system, 2 H, CH<sub>2</sub>-pyrrole), 4.123 (AB system, 2 H, CH<sub>2</sub>N), 4.389 (qd, J = 7 and 12 Hz, 1 H, CHNH), 4.511 (m, 1 H, CHNH), 4.567 (m, 1 H, CHNH), 4.779 (s, 2 H, CH<sub>2</sub>–N), 6.331 (br. s, 1 H, NH), 6.554 (s, 1 H, 4-H), 7.20–7.50 (m, 15 H, Ar), 10.8 (s, 1 H, COOH) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 11.7$ , 15.2, 24.3, 33.4, 41.7, 44.6, 49.6, 50.8, 52.7, 61.3, 70.9, 103.4, 111.8, 126.3, 127.4, 127.6 (2 C), 128.6, 128.7, 128.9, 131.6, 133.6, 135.7, 134.6, 138.7, 155.7, 165.4, 167.9, 171.8 ppm. ES/MS: calcd. for C<sub>39</sub>H<sub>46</sub>N<sub>4</sub>O<sub>6</sub> 666.3417; found 666.3419.

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