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One-Pot Three-Component Catalytic Synthesis of Fully Substituted Pyrroles from Readily Available Propargylic Alcohols, 1,3-Dicarbonyl Compounds and Primary Amines

Victorio Cadierno,* José Gimeno,* and Noel Nebra[a]

Dedicated to Professor Miguel Yus and Professor Juan Forniés on the occasion of their 60th birthdays

Abstract: A simple and highly efficient method for the preparation of fully substituted pyrroles, from readily accessible secondary propargylic alcohols, 1,3-dicarbonyl compounds and primary amines, has been developed. The one-pot multicomponent reaction, which is catalysed by the system [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6]/CF_3CO_2H (dppf: 1,1′-bis(diphenylphosphanyl)ferrocene), involves initial propargylation of the 1,3-dicarbonyl compound promoted by CF_3CO_2H and subsequent condensation between the resulting γ-keto alkyne and the primary amine to afford a propargylated β-enamino ester or ketone, which undergoes a ruthenium-catalysed 5-*exo-dig* annulation to form the final pyrrole.

Keywords: alkynes · annulation · multicomponent reactions · nitrogen heterocycles · ruthenium

Introduction

The pyrrole ring is not only a key structural attribute of many bioactive natural products,[1] pharmaceutical substances[2] and organic conducting materials, such as polypyrroles,[3] but is also a useful and versatile building block in organic synthesis.[4] Although several general approaches to these compounds are presently available, such as the classical Hantzsch and Paal–Knorr procedures, most of them involve tedious multistep synthetic operations.[4] The most recent strategies are based on palladium-, platinum-, copper- and gold-catalysed cycloisomerisation or cyclisation reactions of a variety of acyclic precursors, such as alkynylimines,[5a,b] (*Z*)-(2-en-4-ynyl)amines[5c] or homopropargyl azides,[5d,e] among others.[5f,g] Nevertheless, despite the new useful developments, difficult access to the appropriate starting materials limits the scope of these reactions. In particular, the design of a pyrrole ring with a varied set of substituents may be a critical target. In order to overcome these difficulties, the application of multicomponent reactions (MCRs) is a very appealing strategy since it allows the use of readily available and simple precursors, with the transformations being performed in a single step.[6] Herein, we describe a novel method for the preparation of fully substituted pyrroles, through a one-pot three-component coupling reaction in which easily accessible terminal secondary propargylic alcohols, commercially available 1,3-dicarbonyl compounds and primary amines are used as the starting materials. This methodology represents a highly efficient synthetic route to pentasubstituted pyrroles for which catalytic approaches are scarce.

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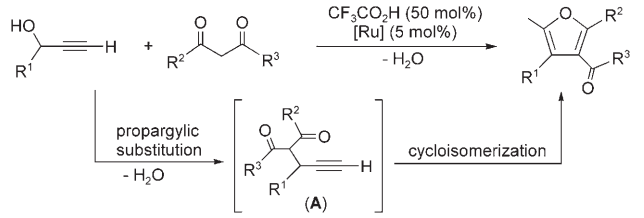
Results and Discussion

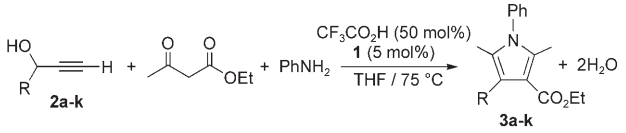
We recently described a straightforward catalytic approach to the synthesis of tetrasubstituted furans from terminal secondary propargylic alcohols and 1,3-dicarbonyl compounds (Scheme 1).[7] The process, which proceeds in a one-pot manner, involves initial trifluoroacetic acid promoted propargylic substitution of the alkynol by the 1,3-dicarbonyl compound[8] and subsequent cycloisomerisation of the resulting γ-keto alkyne **A** catalysed by the 16-electron allyl–ruthenium(II) complex [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] (**1**). We have now found that when a primary amine is introduced into the reaction medium pyrroles are selectively formed instead of furans. The results obtained for the cou-



Scheme 1. Direct synthesis of furans from propargylic alcohols and 1,3-dicarbonyl compounds. [Ru] = [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] (**1**; dppf: 1,1′-bis(diphenylphosphanyl)ferrocene).

pling of several monosubstituted propargylic alcohols with ethyl acetoacetate and aniline are collected in Table 1. The reactions were performed in THF at 75 °C (sealed tube)

Table 1. Synthesis of pyrroles **3a**–**k**.[a]



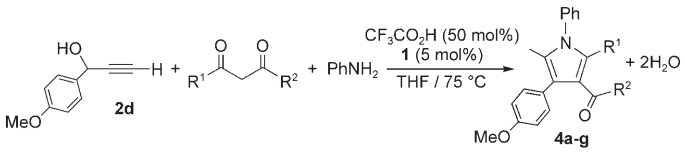
Entry	R; propargylic alcohol	*t* [h]	Pyrrole	Yield [%][b]
1	Ph; **2a**	3	**3a**	70
2	2-C_6H_4OMe; **2b**	2	**3b**	87
3	3-C_6H_4OMe; **2c**	6	**3c**	81
4	4-C_6H_4OMe; **2d**	2	**3d**	94
5	2-C_6H_4Cl; **2e**	7	**3e**	78
6	3-C_6H_4Cl; **2f**	7	**3f**	82
7	4-C_6H_4Cl; **2g**	7	**3g**	73
8	1-naphthyl; **2h**	3	**3h**	72
9	2-naphthyl; **2i**	3	**3i**	71
10	(*E*)-CH=CHPh; **2j**	8	**3j**	68
11	2-thienyl; **2k**	6	**3k**	94

[a] Reactions performed in tetrahydrofuran (THF; 0.5 mL) at 75 °C with the appropriate propargylic alcohol (**2a**–**k**; 1 mmol), ethyl acetoacetate (1 mmol) and aniline (1 mmol). [b] Yield of isolated product.

with 1 mmol of the alkynol ([alkynol]:[ethyl acetoacetate]:[aniline] ratio = 1:1:1) in the presence of 50 mol% of CF_3CO_2H and 5 mol% of complex **1**. This three-component coupling reaction can be successfully applied to secondary aryl alkynols, independently of the substitution pattern and electronic properties of the aromatic ring (**2a**–**i**; entries 1–9 in Table 1), as well as to alkenyl (**2j**; entry 10 in Table 1) and heteroaromatic (**2k**; entry 11 in Table 1) alkynols, with the corresponding pyrroles **3a**–**k** being obtained in 68–94% yield (isolated product) with complete regioselectivity after 2–8 h. No formation of the corresponding furans or other regioisomers of **3** was observed by GC/MS. By contrast, with alkyl-monosubstituted alkynols such as 1-octyn-3-ol or 3-butyn-2-ol, mixtures containing the expected pyrroles are obtained, albeit in very low yields (<15% yield as determined by GC). The formation of several major uncharacterised byproducts prevented the isolation of the pyrroles in these cases.

The generality of this transformation has been also studied by using other 1,3-dicarbonyl compounds (see Table 2).

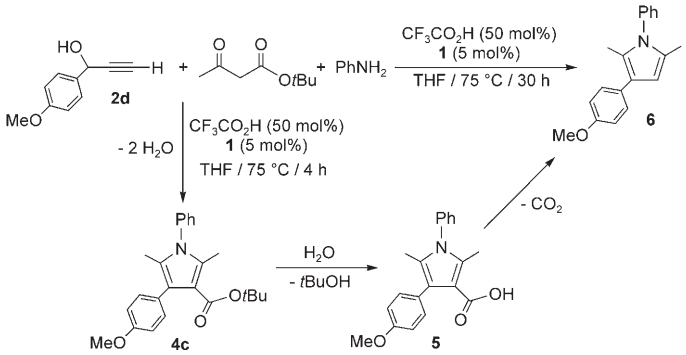
Table 2. Synthesis of pyrroles **4a**–**g**.[a]



Entry	R^1; R^2	*t* [h]	Pyrrole	Yield [%][b]
1	Me; OMe	4	**4a**	93
2	Me; OBn	6	**4b**	87
3	Me; O*t*Bu	4	**4c**	84
4	Me; Me	6	**4d**	88
5	Et; Et	12	**4e**	83
6	Ph; Ph	9	**4f**	84
7	Me; Ph	6	**4g**	91

[a] Reactions performed in THF (0.5 mL) at 75 °C with propargylic alcohol **2d** (1 mmol), the appropriate 1,3-dicarbonyl compound (1 mmol) and aniline (1 mmol). Bn: benzyl. [b] Yield of isolated product.

Thus, under the same reaction conditions, other β-keto esters (entries 1–3 in Table 2) as well as a variety of 1,3-diketones (entries 4–7 in Table 2) also reacted with alkynol **2d** and aniline to afford the corresponding pyrroles **4a**–**g** in excellent yields (83–93%) after 4–12 h. Interestingly, when the nonsymmetric diketone 1-phenyl-1,3-butanedione (entry 7 in Table 2) was used as the substrate, pyrrole **4g** is chemoselectively formed, that is, only the more activated acetyl group, as opposed to the benzoyl unit, participates in the condensation process. The behaviour of alkynol **2d** towards aniline and *tert*-butyl acetoacetate also merits a comment (entry 3 in Table 2). Although the reaction leads to the expected pyrrole **4c** in 4 h (84% yield of isolated product), it further evolves into the 1,2,4,5-tetrasubstituted derivative **6** (78% yield) after 30 h (Scheme 2). Pyrrole **6** results from the ini-

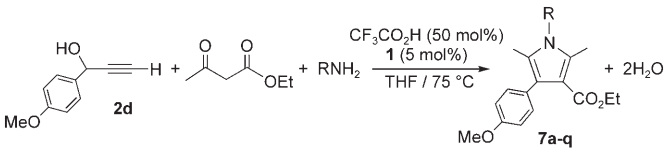


Scheme 2. Synthesis of the tetrasubstituted pyrrole **6**.

tial CF_3CO_2H-mediated hydrolysis of the *tert*-butyl ester (Boc) group and subsequent ruthenium-catalysed decarboxylation of the resulting carboxylic acid **5**.[9] Therefore, this MCR methodology with Boc-containing 1,3-dicarbonyl substrates discloses a synthetic route to 1,2,4,5-tetrasubstituted pyrroles.

More attractive is the wide scope of the process with respect to the nature of the amine (Table 3). Thus, we have

Table 3. Synthesis of pyrroles **7a–q**.[a]



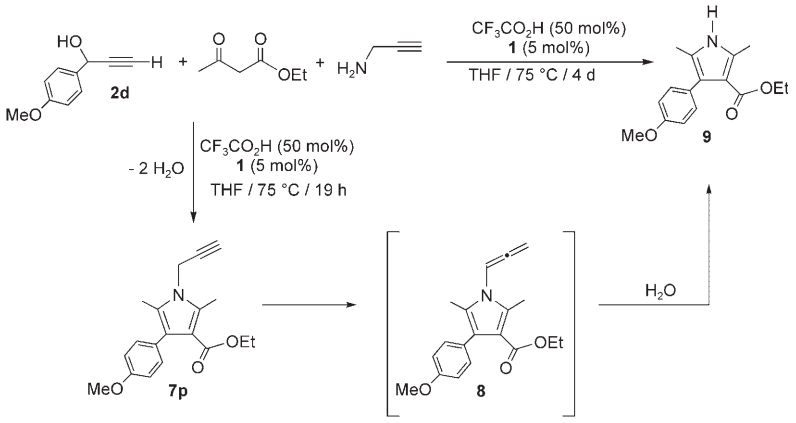
Entry	R	*t* [h]	Pyrrole	Yield [%][b]
1	4-C_6H_4OMe	3	**7a**	94
2	3-C_6H_4OMe	3	**7b**	90
3	2-C_6H_4OMe	3	**7c**	95
4	4-C_6H_4Cl	4	**7d**	94
5	4-C_6H_4I	6	**7e**	78
6	4-$C_6H_4NO_2$	3	**7f**	92
7	4-$C_6H_4CO_2Et$	3	**7g**	85
8	4-C_6H_4OH	8	**7h**	88
9	3-$C_6H_4C(=O)Me$	6	**7i**	87
10	4-$C_6H_4C(=O)NH_2$	5	**7j**	73
11	2-$C_6H_4C(Me)=CH_2$	3	**7k**	92
12	Et	40	**7l**	75
13	Bn	9	**7m**	72
14	furfuryl	20	**7n**	78
15	$CH_2CH=CH_2$	21	**7o**	74
16	$CH_2C\equiv CH$	19	**7p**	56
17	(*S*)-CHMePh	44	**7q**	76

[a] Reactions performed in THF (0.5 mL) at 75 °C with propargylic alcohol **2d** (1 mmol), ethyl acetoacetate (1 mmol) and the appropriate primary amine (1 mmol). [b] Yield of isolated product.

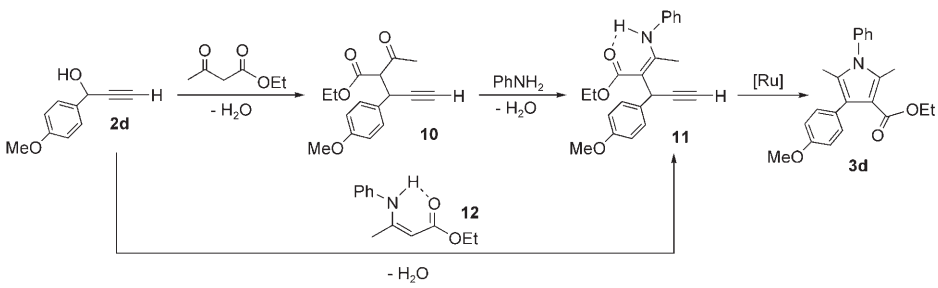
found that, with alkynol **2d** and ethyl acetoacetate as model compounds, several aromatic (entries 1–11 in Table 3) and aliphatic (entries 12–16 in Table 3) primary amines can be successfully employed in this transformation to afford the corresponding pyrroles **7a–p** in moderate to good yields (56–95%). With respect to the functional-group tolerance, this methodology is compatible with the presence in the amino framework of alkoxy (**7a–c**), hydroxy (**7h**), halide (**7d**,**e**), nitro (**7f**), ester (**7g**), ketone (**7i**), amide (**7j**), olefin (**7k**,**o**), propargyl (**7p**) and heteroaromatic (**7n**) substituents. It should be noted that longer reaction times are required when aliphatic amines are employed (entries 12–17 in Table 3). In addition, the enantiomerically pure pyrrole **7q** (entry 17 in Table 3) could be easily prepared from commercially available (*S*)-(−)-α-methylbenzylamine, with the stereogenic centre in the initial amine not being affected during the transformation.[10]

Remarkably, our MCR can be also applied to the preparation of N–H pyrroles. Although all attempts to generate these species by using NH_4OH or NH_4Cl as sources of the NH unit failed, these compounds are accessible by using propargylamine. Thus, we have found that treatment of **2d** with ethyl acetoacetate and propargylamine, under the standard reaction conditions, leads to the slow but clean formation of **9** after 4 days (74% yield of isolated product; Scheme 3). The reaction proceeds through the expected propargylic pyrrole **7p** (isolated in 56% yield after 19 h; entry 16 in Table 3), which further undergoes scission of the C–N bond,[11] a transformation probably involving the hydrolysis of the allenyl intermediate **8** (not detected by GC/MS).

A mechanistic proposal for this three-component coupling reaction, exemplified by the formation of pyrrole **3d**, is depicted in Scheme 4. Two competitive pathways occur simultaneously. The first one involves an initial acid-promoted propargylation of the β-keto ester to afford the γ-keto alkyne **10**. In fact, this intermediate could be isolated (91% yield) by treatment of a THF solution of **2d** with ethyl acetoacetate (1 equiv) and CF_3CO_2H (0.5 equiv) at 75 °C for 3 h (details are given in the Experimental Section). Subsequent condensation between **10** and aniline generates the propargylated β-enamino ester **11** which undergoes a ruthenium-catalysed 5-*exo-dig* annulation to form the final pyrrole **3d**.[12,13] Alternatively, intermediate **11** can be also generated through propargylic substitution of **2d** by the β-enamino



Scheme 3. Synthesis of the N–H pyrrole **9**.



Scheme 4. Proposed mechanism for the reaction.

ester **12** (detected in the reaction medium by monitoring the course of the reaction by GC/MS), which results from the initial condensation between ethyl acetoacetate and aniline. In this respect, we have confirmed that treatment of **2d** with independently synthesised compound **12**,[14] in THF at 75 °C in the presence of 50 mol % of CF_3CO_2H and 5 mol % of complex **1**, cleanly generates pyrrole **3d** in > 95 % yield (as determined by GC) after 2 h.

Conclusion

In summary, an operationally simple and highly efficient one-pot multicomponent reaction for the synthesis of fully substituted pyrroles from secondary propargylic alcohols,[15,16] 1,3-dicarbonyl compounds and primary amines has been developed in this work. The transformation constitutes a straightforward alternative to the limited catalytic approaches to the synthesis of pentasubstituted pyrroles that are presently available.[5c,16,17] The following points merit highlighting: 1) the procedure stems from readily available and inexpensive precursors, 2) it allows the direct introduction of carbonyl functionalities onto the pyrrolic skeleton, 3) this methodology is tolerant to the presence of a wide variety of functional groups in the starting materials, and 4) it is highly selective and allows the isolation of the desired pyrroles in good to excellent yields (56–95 %). In conclusion, selectivity, time/cost savings and experimental simplicity, concepts that are considered by modern academic and industrial synthetic chemists in reaching the maximum efficiency of a process, are clearly represented in this one-pot catalytic transformation that provides an appealing methodology for the synthesis of highly functionalised pyrroles.

Experimental Section

General methods: Infrared spectra were recorded on a Perkin–Elmer 1720-XFT spectrometer. NMR spectra were recorded on a Bruker DPX-300 instrument at 300 MHz (^{1}H) or 75.4 MHz (^{13}C). The chemical shift values (δ) are given in parts per million (ppm) and are referred to the residual peak of the deuterated solvent ($CDCl_3$). DEPT experiments have been carried out for all of the compounds reported. GC/MS measurements were performed on Agilent 6890N equipment coupled to a 5973 mass detector (70 eV electron-impact ionisation) by using an HP-1MS column. High-resolution mass spectra were recorded on a Finnigan-Mat 95 spectrometer. Elemental analyses were performed with a Perkin–Elmer 2400 microanalyser. Optical rotations were measured by using a Perkin–Elmer 241 polarimeter and are quoted in units of 10^{-1} deg cm^2 g^{-1}. Flash chromatography was performed with Merck silica gel 60 (230–400 mesh). All reagents were obtained from commercial suppliers and used without any further purification, with the exception of the complex $[Ru(\eta^3\text{-}2\text{-}C_3H_4Me)(CO)(dppf)][SbF_6]$ (**1**),[18] propargylic alcohols **2b–k**[19] and 3-phenylamino-2-butenoic acid ethyl ester (**12**),[14] which were prepared by following the methods reported in the literature.

General procedure for the catalytic reactions: The appropriate propargylic alcohol **2a–k** (1 mmol), 1,3-dicarbonyl compound (1 mmol) and primary amine (1 mmol) were introduced into a sealed tube under a nitrogen atmosphere. THF (0.5 mL), $[Ru(\eta^3\text{-}2\text{-}C_3H_4Me)(CO)(dppf)][SbF_6]$ (**1**; 0.049 g, 0.05 mmol) and CF_3CO_2H (37 μL, 0.5 mmol) were then added at room temperature, and the resulting solution was heated at 75 °C for the indicated time (see Tables 1–3 and Schemes 2 and 3; the course of the reactions was monitored by regular sampling and analysis by GC/MS). After removal of volatiles under vacuum, the residue was purified by column chromatography (silica gel) with a mixture EtOAc/hexanes (1:15) as the eluent (except for pyrroles **7h** and **7j**, which required a 1:1 mixture of EtOAc/hexanes). Analytical and spectroscopic data for all of the compounds synthesised are reported below.

2,5-Dimethyl-1,4-diphenylpyrrole-3-carboxylic acid ethyl ester (3a):[17b] Yellow oil; yield: 70 % (0.223 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.11 (q, $J = 7.2$ Hz, 2H, CH_2), 7.26 (m, 3H, CH_{arom}), 7.51 (m, 3H, CH_{arom}), 7.34 ppm (m, 4H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.9$, 12.3, 13.6 (s, CH_3), 58.9 (s, CH_2), 111.8, 122.1, 126.5, 135.4, 136.1, 137.5 (s, =C, C_{arom}), 125.6, 127.1, 127.9, 128.3, 129.1, 130.1 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu} = 1698$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): *m*/*z* (%): 319 (100) [M^+], 290 (85) [M^+−Et], 274 (20) [M^+−OEt], 244 (15) [M^+−OEt−2Me], 230 (20) [M^+−CO_2Et−Me]; HRMS (EI): *m*/*z*: calcd for $C_{21}H_{21}O_2N$: 319.15668; found: 319.15636.

4-(2-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3b):[17b] Yellow oil; yield: 87 % (0.304 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.00$ (t, $J = 7.0$ Hz, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.06 (q, $J = 7.0$ Hz, 2H, CH_2), 6.96 (m, 2H, CH_{arom}), 7.25 (m, 4H, CH_{arom}), 7.47 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 11.0$, 12.2, 13.6 (s, CH_3), 55.0 (s, OCH_3), 58.6 (s, CH_2), 109.9, 119.6, 127.2, 128.0, 128.1, 128.9, 131.4 (s, CH_{arom}), 111.6, 117.4, 125.2, 126.6, 134.8, 137.6, 157.2 (s, =C, C_{arom}), 165.8 ppm (s, C=O); IR (Nujol): $\tilde{\nu} = 1695$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): *m*/*z* (%): 349 (100) [M^+], 320 (35) [M^+−Et], 304 (10) [M^+−OEt], 288 (20) [M^+−OMe−2Me], 276 (60) [M^+−CO_2Et], 260 (15) [M^+−OEt−3Me]; HRMS (EI): *m*/*z*: calcd for $C_{22}H_{23}O_3N$: 349.16724; found: 349.16680.

4-(3-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3c): Yellow oil; yield: 81 % (0.283 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (t, $J = 7.2$ Hz, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 4.10 (q, $J = 7.2$ Hz, 2H, CH_2), 6.81–6.93 (m, 3H, CH_{arom}), 7.25 (m, 3H, CH_{arom}), 7.44–7.55 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.9$, 12.2, 13.6 (s, CH_3), 54.8 (s, OCH_3), 58.8 (s, CH_2), 111.2, 115.7, 122.7, 127.9, 128.3, 129.1 (s, CH_{arom}), 110.7, 121.8, 126.5, 135.3, 137.4, 137.5, 158.5 (s, =C, C_{arom}), 165.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu} = 1683$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): *m*/*z* (%): 349 (100) [M^+], 320 (55) [M^+−Et], 304 (20) [M^+−OEt], 288 (5) [M^+−OMe−2Me], 274 (15) [M^+−OEt−2Me], 260 (10) [M^+−OEt−3Me]; HRMS (EI): *m*/*z*: calcd for $C_{22}H_{23}O_3N$: 349.16724; found: 349.16705.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3d): Yellow oil; yield: 94 % (0.328 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.09$ (t, $J = 7.0$ Hz, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 4.12 (q, $J = 7.0$ Hz, 2H, CH_2), 6.92 (m, 2H, CH_{arom}), 7.24 (m, 4H, CH_{arom}), 7.48 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 10.9$, 12.3, 13.8 (s, CH_3), 54.9 (s, OCH_3), 58.8 (s, CH_2), 110.7, 121.6, 126.4, 128.4, 135.2, 137.6, 157.6 (s, =C, C_{arom}), 112.6, 127.9, 128.2, 129.1, 131.1 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu} = 1698$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): *m*/*z* (%): 349 (100) [M^+], 320 (60) [M^+−Et], 304 (15) [M^+−OEt], 274 (10) [M^+−OEt−2Me], 260 (10) [M^+−OEt−3Me]; HRMS (EI): *m*/*z*: calcd for $C_{22}H_{23}O_3N$: 349.16724; found: 349.16680.

4-(2-Chlorophenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3e): Yellow oil; yield: 78 % (0.276 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.1$ Hz, 3H, CH_3), 1.81 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 4.05 (q, $J = 7.1$ Hz, 2H, CH_2), 7.22–7.32 (m, 6H, CH_{arom}), 7.47 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 11.1$, 12.5, 13.7 (s, CH_3), 59.0 (s, CH_2), 111.2, 119.3, 127.1, 134.9, 135.7, 135.9, 137.6 (s, =C, C_{arom}), 125.8, 127.6, 128.5, 128.8, 129.3, 132.9 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu} = 1682$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): *m*/*z* (%): 353 (40) [M^+], 318 (100) [M^+−Cl], 289 (90) [M^+−Et−Cl], 272 (10) [M^+−OEt−Cl], 245 (20) [M^+−CO_2Et−Cl]; HRMS (EI): *m*/*z*: calcd for $C_{21}H_{20}O_2ClN$: 353.11771; found: 353.11752.

4-(3-Chlorophenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3f): Yellow oil; yield: 82 % (0.290 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.06$ (t, $J = 7.1$ Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 2.32 (s, 3H, CH_3),

4.11 (q, $J=7.1$ Hz, 2H, CH_2), 7.19–7.31 (m, 6H, CH_{arom}), 7.51 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.5, 13.8 (s, CH_3), 59.1 (s, CH_2), 110.7, 120.9, 127.0, 129.2, 132.9, 137.5, 138.4 (s, =C, C_{arom}), 125.5, 127.8, 128.0, 128.1, 128.2, 129.0, 130.2 (s, CH_{arom}), 165.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 353 (100) [M^+], 324 (80) [M^+−Et], 308 (20) [M^+−OEt], 278 (10) [M^+−OEt−2Me], 245 (30) [M^+−CO_2Et−Cl]; HRMS (EI): *m/z*: calcd for $C_{21}H_{20}O_2ClN$: 353.11771; found: 353.11756.

4-(4-Chlorophenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3g): Yellow oil; yield: 73% (0.258 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (t, $J=7.1$ Hz, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.10 (q, $J=7.1$ Hz, 2H, CH_2), 7.23–7.34 (m, 6H, CH_{arom}), 7.50 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.6, 14.0 (s, CH_3), 59.2 (s, CH_2), 110.8, 121.1, 126.9, 134.9, 136.0, 137.4, 137.6 (s, =C, C_{arom}), 127.5, 128.2, 128.6, 129.4, 131.7 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1699\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 353 (100) [M^+], 324 (80) [M^+−Et], 308 (30) [M^+−OEt], 280 (10) [M^+−CO_2Et], 278 (10) [M^+−OEt−2Me], 245 (15) [M^+−CO_2Et−Cl]; HRMS (EI): *m/z*: calcd for $C_{21}H_{20}O_2ClN$: 353.11771; found: 353.11796.

4-(1-Naphthyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3h): Orange solid; yield: 72% (0.266 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.44$ (t, $J=7.0$ Hz, 3H, CH_3), 1.81 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 3.76 (q, $J=7.0$ Hz, 2H, CH_2), 7.32–7.56 (m, 9H, CH_{arom}), 7.83 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.8$, 12.2, 12.8 (s, CH_3), 58.4 (s, CH_2), 111.9, 120.2, 127.1, 133.1, 133.5, 134.7, 135.7, 137.5 (s, =C, C_{arom}), 124.8, 124.9, 125.0, 126.2, 126.4, 127.4, 127.6, 128.0, 128.2, 129.1 (s, CH_{arom}), 165.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1690\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 369 (100) [M^+], 340 (60) [M^+−Et], 309 (10) [M^+−OEt−Me], 294 (15) [M^+−OEt−2Me], 280 (15) [M^+−CO_2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{25}H_{23}O_2N$: 369.17233; found: 369.17244; elemental analysis calcd (%) for $C_{25}H_{23}O_2N$: C 81.27, H 6.27, N 3.79; found: C 81.13, H 6.31, N 3.83.

4-(2-Naphthyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3i): Orange solid; yield: 71% (0.262 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.98$ (t, $J=7.0$ Hz, 3H, CH_3), 1.96 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 4.09 (q, $J=7.0$ Hz, 2H, CH_2), 7.28 (m, 2H, CH_{arom}), 7.44–7.56 (m, 6H, CH_{arom}), 7.77 (s, 1H, CH_{arom}), 7.85 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.0$, 12.3, 13.7 (s, CH_3), 58.9 (s, CH_2), 110.7, 121.8, 126.7, 131.7, 132.9, 133.8, 135.7, 137.5 (s, =C, C_{arom}), 124.9, 125.3, 126.2, 127.2, 127.4, 128.0, 128.3, 129.1, 129.5 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1683\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 369 (100) [M^+], 340 (50) [M^+−Et], 324 (15) [M^+−OEt], 294 (20) [M^+−OEt−2Me], 280 (15) [M^+−CO_2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{25}H_{23}O_2N$: 369.17233; found: 369.17252; elemental analysis calcd (%) for $C_{25}H_{23}O_2N$: C 81.27, H 6.27, N 3.79; found: C 81.40, H 6.14, N 3.88.

2,5-Dimethyl-1-phenyl-4-styrylpyrrole-3-carboxylic acid ethyl ester (3j): Yellow oil; yield: 68% (0.235 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.38$ (t, $J=7.1$ Hz, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 4.33 (q, $J=7.1$ Hz, 2H, CH_2), 6.60 (d, $J=16.5$ Hz, 1H, =CH), 7.17–7.38 ppm (m, 11H, CH_{arom}, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=12.6$, 12.8, 14.5 (s, CH_3), 59.4 (s, CH_2), 111.3, 127.1, 135.1, 136.2, 137.5, 138.6 (s, =C, C_{arom}), 120.4, 123.5, 125.9, 128.3, 128.5, 128.7, 129.3, 129.5 (s, CH_{arom}, =CH), 166.1 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1699\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 345 (100) [M^+], 330 (2) [M^+−Me], 316 (20) [M^+−Et], 285 (10) [M^+−OEt−Me], 270 (20) [M^+−OEt−2Me], 257 (15) [M^+−CO_2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{23}H_{23}O_2N$: 345.17233; found: 345.17218.

4-(2-Thienyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid ethyl ester (3k): Orange oil; yield: 94% (0.306 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.12$ (t, $J=7.1$ Hz, 3H, CH_3), 1.94 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.15 (q, $J=7.1$ Hz, 2H, CH_2), 6.94 (dd, $J=3.4$, 1.1 Hz, 1H, =CH), 7.04 (dd, $J=5.1$, 3.4 Hz, 1H, =CH), 7.24 (m, 2H, CH_{arom}), 7.29 (dd, $J=5.1$, 1.1 Hz, 1H, =CH), 7.50 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.3$, 12.5, 14.0 (s, CH_3), 59.3 (s, CH_2), 111.8, 114.1, 120.6, 128.8, 135.8, 137.5 (s, =C, C_{arom}), 124.6, 126.2, 126.9, 128.1, 128.6, 129.4 (s, =CH, CH_{arom}), 165.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1697\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 325 (100) [M^+], 296 (60) [M^+−Et], 281 (20) [M^+−Et−Me], 250 (15) [M^+−OEt−2Me], 237 (10) [M^+−CO_2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{19}H_{19}O_2NS$: 325.11310; found: 325.11300.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid methyl ester (4a): Yellow oil; yield: 93% (0.312 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.90$ (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.95 (m, 2H, CH_{arom}), 7.25 (m, 4H, CH_{arom}), 7.49 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.2$, 12.8 (s, CH_3), 50.4, 55.1 (s, OCH_3), 110.6, 121.9, 126.7, 128.4, 135.6, 137.8, 157.9 (s, =C, C_{arom}), 112.9, 128.2, 128.5, 129.4, 131.3 (s, CH_{arom}), 166.4 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1699\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 335 (100) [M^+], 320 (20) [M^+−Me], 304 (15) [M^+−OMe], 274 (10) [M^+−OMe−2Me], 260 (10) [M^+−OMe−3Me], 244 (5) [M^+−2OMe−2Me]; HRMS (EI): *m/z*: calcd for $C_{21}H_{21}O_3N$: 335.15159; found: 335.15125.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid benzyl ester (4b): Yellow solid; yield: 87% (0.358 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.88$ (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 5.14 (s, 2H, CH_2), 6.87 (d, $J=8.2$ Hz, 2H, CH_{arom}), 7.06 (m, 2H, CH_{arom}), 7.24 (m, 6H, CH_{arom}), 7.49 ppm (m, 4H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.7 (s, CH_3), 55.1 (s, OCH_3), 65.1 (s, CH_2), 110.7, 121.9, 126.8, 128.7, 136.1, 136.5, 137.8, 158.0 (s, =C, C_{arom}), 113.0, 127.4, 127.7, 128.0, 128.2, 128.5, 129.4, 131.4 (s, CH_{arom}), 166.4 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1694\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 411 (40) [M^+], 334 (5) [M^+−Ph], 320 (100) [M^+−Bn], 304 (10) [M^+−OBn], 276 (10) [M^+−CO_2Bn], 246 (10) [M^+−CO_2Bn−2Me]; HRMS (EI): *m/z*: calcd for $C_{27}H_{25}O_3N$: 411.18289; found: 411.18278; elemental analysis calcd (%) for $C_{27}H_{25}O_3N$: C 78.81, H 6.12, N 3.40; found: C 78.96, H 6.05, N 3.55.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole-3-carboxylic acid *tert*-butyl ester (4c): Yellow oil; yield: 84% (0.317 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.31$ (s, 9H, $C(CH_3)_3$), 1.87 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.92 (m, 2H, CH_{arom}), 7.23 (m, 4H, CH_{arom}), 7.48 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.4 (s, CH_3), 28.0 (s, $C(CH_3)_3$), 55.2 (s, OCH_3), 79.2 (s, $C(CH_3)_3$), 112.6, 120.5, 126.4, 129.2, 134.9, 137.9, 157.8 (s, =C, C_{arom}), 112.9, 128.2, 128.4, 129.3, 131.2 (s, CH_{arom}), 165.5 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 377 (20) [M^+], 320 (100) [M^+−*t*Bu], 304 (10) [M^+−O*t*Bu], 276 (10) [M^+−CO_2*t*Bu], 260 (5) [M^+−O*t*Bu−3Me]; HRMS (EI): *m/z*: calcd for $C_{24}H_{27}O_3N$: 377.19854; found: 377.19802.

1-[4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenyl-3-pyrrolyl]-ethanone (4d): Yellow oil; yield: 88% (0.281 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.84$ (s, 3H, CH_3), 1.97 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.94 (m, 2H, CH_{arom}), 7.24 (m, 4H, CH_{arom}), 7.49 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 13.1, 30.7 (s, CH_3), 55.1 (s, OCH_3), 113.6, 128.1, 128.6, 129.4, 131.4 (s, CH_{arom}), 121.5, 121.7, 126.8, 128.8, 135.3, 137.5, 158.4 (s, =C, C_{arom}), 197.9 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1651\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 319 (20) [M^+], 304 (100) [M^+−Me], 289 (5) [M^+−2Me], 276 (5) [M^+−COMe], 261 (10) [M^+−COMe−Me]; HRMS (EI): *m/z*: calcd for $C_{21}H_{21}O_2N$: 319.15668; found: 319.15641.

1-[2-Ethyl-4-(4-methoxyphenyl)-5-methyl-1-phenyl-3-pyrrolyl]-propan-1-one (4e): Yellow oil; yield: 83% (0.288 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=0.93$ (t, $J=7.4$ Hz, 3H, CH_3), 1.03 (t, $J=7.4$ Hz, 3H, CH_3), 1.80 (s, 3H, CH_3), 2.22 (q, $J=7.4$ Hz, 2H, CH_2), 2.67 (q, $J=7.4$ Hz, 2H, CH_2), 3.85 (s, 3H, OCH_3), 6.93 (m, 2H, CH_{arom}), 7.25 (m, 4H, CH_{arom}), 7.49 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=8.6$, 11.0, 14.7 (s, CH_3), 19.5, 35.6 (s, CH_2), 55.1 (s, OCH_3), 113.5, 128.4, 128.6, 129.2, 131.3 (s, CH_{arom}), 120.7, 121.0, 126.5, 128.2, 137.7, 140.5, 158.2 (s, =C, C_{arom}), 200.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1651\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 347 (50) [M^+], 332 (15) [M^+−Me], 318 (100) [M^+−Et], 303 (5) [M^+−Et−Me], 274 (10) [M^+−2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{23}H_{25}O_2N$: 347.18798; found: 347.18765.

[4-(4-Methoxyphenyl)-5-methyl-1,2-diphenyl-3-pyrrolyl]-phenylmethanone (4f): Orange solid; yield: 84% (0.372 g); ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.17$ (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 6.82 (d, $J=8.2$ Hz, 2H, CH_{arom}), 6.97–7.35 (m, 15H, CH_{arom}), 7.72 ppm (d, $J=7.4$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.6$ (s, CH_3), 55.0 (s, OCH_3), 113.4, 126.9, 127.4, 127.5, 127.8, 128.7, 128.9, 129.8, 130.1, 130.7, 131.7 (s,

CH_{arom}), 122.2, 122.8, 127.6, 127.9, 131.0, 135.7, 138.3, 138.8, 157.8 (s, =C, C_{arom}), 194.5 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1661\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 443 (100) [M^+], 366 (20) [M^+−Ph], 338 (5) [M^+−COPh]; HRMS (EI): *m/z*: calcd for $C_{31}H_{25}O_2N$: 443.18798; found: 443.18768; elemental analysis calcd (%) for $C_{31}H_{25}O_2N$: C 83.95, H 5.68, N 3.16; found: C 83.77, H 5.76, N 3.27.

[4-(4-Methoxyphenyl)-2,5-dimethyl-1-phenyl-3-pyrrolyl]-phenylmethanone (4g): Orange solid; yield: 91% (0.347 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.01$ (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 3.71 (s, 3H, OCH_3), 6.68 (m, 2H, CH_{arom}), 7.67 (m, 2H, CH_{arom}), 7.01–7.35 (m, 7H, CH_{arom}), 7.50 ppm (m, 3H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.5$, 12.8 (s, CH_3), 55.1 (s, OCH_3), 113.1, 127.5, 128.2, 128.5, 129.4, 129.7, 131.0, 131.3 (s, CH_{arom}), 120.5, 121.9, 126.0, 128.0, 134.4, 137.8, 139.7, 157.4 (s, =C, C_{arom}), 194.1 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1652\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 381 (100) [M^+], 366 (10) [M^+−Me], 304 (10) [M^+−Ph], 289 (5) [M^+−Ph−Me], 276 (5) [M^+−COPh]; HRMS (EI): *m/z*: calcd for $C_{26}H_{23}O_2N$: 381.17233; found: 381.17073; elemental analysis calcd (%) for $C_{26}H_{23}O_2N$: C 81.86, H 6.08, N 3.67; found: C 82.03, H 6.15, N 3.59.

3-(4-Methoxyphenyl)-2,5-dimethyl-1-phenylpyrrole (6): Yellow oil; yield: 72% (0.199 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.09$ (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 6.12 (s, 1H, =CH), 6.95 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.28 (d, $J=7.1$ Hz, 2H, CH_{arom}), 7.36–7.52 ppm (m, 5H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=12.1$, 12.8 (s, CH_3), 55.2 (s, OCH_3), 106.4 (s, =CH), 113.7, 127.7, 128.3, 128.8, 129.0 (s, CH_{arom}), 120.6, 124.5, 128.4, 129.9, 138.8, 157.3 ppm (s, =C, C_{arom}); LRMS (EI, 70 eV): *m/z* (%): 277 (100) [M^+], 262 (60) [M^+−Me], 246 (5) [M^+−OMe], 233 (5) [M^+−3Me]; HRMS (EI): *m/z*: calcd for $C_{19}H_{19}NO$: 277.14611; found: 277.14591.

1,4-Bis(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7a): Orange oil; yield: 94% (0.356 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.11 (q, $J=7.1$ Hz, 2H, CH_2), 6.90 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.22 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.00 (d, $J=8.8$ Hz, 2H, CH_{arom}), 7.15 ppm (d, $J=8.8$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.6, 14.1 (s, CH_3), 55.1, 55.4 (s, OCH_3), 59.1 (s, CH_2), 110.7, 121.5, 126.9, 128.7, 130.5, 135.8, 157.8, 159.4 (s, =C, C_{arom}), 112.8, 114.5, 129.2, 131.4 (s, CH_{arom}), 166.0 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1694\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 379 (100) [M^+], 364 (5) [M^+−Me], 350 (30) [M^+−Et], 334 (15) [M^+−OEt], 320 (5) [M^+−Et−2Me], 304 (10) [M^+−OEt−2Me]; HRMS (EI): *m/z*: calcd for $C_{23}H_{25}O_4N$: 379.17781; found: 379.17766.

4-(4-Methoxyphenyl)-1-(3-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7b): Orange oil; yield: 90% (0.341 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.90 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.11 (q, $J=7.1$ Hz, 2H, CH_2), 6.78–7.02 (m, 5H, CH_{arom}), 7.22 (d, $J=8.7$ Hz, 2H, CH_{arom}), 7.40 ppm (m, 1H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.6, 14.0 (s, CH_3), 55.1, 55.4 (s, OCH_3), 59.1 (s, CH_2), 110.9, 121.7, 126.6, 128.6, 135.5, 138.9, 157.8, 160.2 (s, =C, C_{arom}), 112.8, 113.9, 114.2, 120.4, 130.0, 131.4 (s, CH_{arom}), 165.9 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1699\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 379 (100) [M^+], 364 (5) [M^+−Me], 350 (30) [M^+−Et], 334 (10) [M^+−OEt], 320 (5) [M^+−Et−2Me], 304 (5) [M^+−OEt−2Me]; HRMS (EI): *m/z*: calcd for $C_{23}H_{25}O_4N$: 379.17781; found: 379.17709.

4-(4-Methoxyphenyl)-1-(2-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7c): Orange oil; yield: 95% (0.360 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.83 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 4.12 (q, $J=7.1$ Hz, 2H, CH_2), 6.90 (d, $J=8.8$ Hz, 2H, CH_{arom}), 7.25 (d, $J=8.8$ Hz, 2H, CH_{arom}), 7.04–7.19 (m, 3H, CH_{arom}), 7.43 ppm (m, 1H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.7$, 12.3, 14.1 (s, CH_3), 55.1, 55.6 (s, OCH_3), 59.0 (s, CH_2), 110.5, 121.4, 126.3, 127.0, 128.9, 136.2, 155.6, 157.7 (s, =C, C_{arom}), 112.0, 112.7, 120.7, 130.0, 130.1, 131.5 (s, CH_{arom}), 166.1 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 379 (100) [M^+], 364 (5) [M^+−Me], 350 (25) [M^+−Et], 334 (15) [M^+−OEt], 320 (5) [M^+−Et−2Me], 306 (10) [M^+−CO_2Et]; HRMS (EI): *m/z*: calcd for $C_{23}H_{25}O_4N$: 379.17781; found: 379.17740.

1-(4-Chlorophenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7d): Yellow oil; yield: 94% (0.360 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 4.12 (q, $J=7.1$ Hz, 2H, CH_2), 6.91, 7.19, 7.22 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.50 ppm (d, $J=8.5$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.7, 13.9 (s, CH_3), 55.2 (s, OCH_3), 59.6 (s, CH_2), 111.1, 122.2, 126.7, 128.3, 134.6, 135.7, 136.2, 157.9 (s, =C, C_{arom}), 112.9, 129.5, 129.7, 131.3 (s, CH_{arom}), 166.5 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1699\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 383 (100) [M^+], 368 (5) [M^+−Me], 354 (30) [M^+−Et], 338 (15) [M^+−OEt]; HRMS (EI): *m/z*: calcd for $C_{22}H_{22}O_3ClN$: 383.12827; found: 383.12751.

1-(4-Iodophenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7e): Yellow solid; yield: 78% (0.371 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (t, $J=7.1$ Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.11 (q, $J=7.1$ Hz, 2H, CH_2), 6.90 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.20 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.00 (d, $J=8.2$ Hz, 2H, CH_{arom}), 7.85 ppm (d, $J=8.2$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.2$, 12.6, 14.0 (s, CH_3), 55.2 (s, OCH_3), 59.3 (s, CH_2), 94.0, 112.3, 122.2, 126.5, 128.3, 135.4, 137.5, 157.9 (s, =C, C_{arom}), 112.9, 130.1, 131.3, 138.6 (s, CH_{arom}), 166.1 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 475 (100) [M^+], 446 (30) [M^+−Et], 430 (15) [M^+−OEt], 400 (5) [M^+−OEt−2Me], 348 (10) [M^+−I]; HRMS (EI): *m/z*: calcd for $C_{22}H_{22}O_3IN$: 475.06388; found: 475.06343; elemental analysis calcd (%) for $C_{22}H_{22}O_3IN$: C 55.59, H 4.67, N 2.95; found: C 55.42, H 4.75, N 3.08.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-(4-nitrophenyl)pyrrole-3-carboxylic acid ethyl ester (7f): Red solid; yield: 92% (0.363 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.12 (q, $J=7.1$ Hz, 2H, CH_2), 6.91 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.20 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.46 (d, $J=8.8$ Hz, 2H, CH_{arom}), 8.41 ppm (d, $J=8.8$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.3$, 12.7, 14.0 (s, CH_3), 55.2 (s, OCH_3), 59.4 (s, CH_2), 112.3, 120.4, 126.2, 127.9, 134.9, 143.4, 147.4, 158.1 (s, =C, C_{arom}), 112.9, 124.8, 129.2, 131.3 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1697\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 394 (100) [M^+], 379 (5) [M^+−Me], 365 (50) [M^+−Et], 349 (20) [M^+−OEt], 319 (10) [M^+−OEt−2Me]; HRMS (EI): *m/z*: calcd for $C_{22}H_{22}O_5N_2$: 394.15232; found: 394.15109; elemental analysis calcd (%) for $C_{22}H_{22}O_5N_2$: C 66.99, H 5.62, N 7.10; found: C 66.83, H 5.70, N 7.06.

1-(4-Ethoxycarbonylphenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7g): Orange solid; yield: 85% (0.358 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (t, $J=7.1$ Hz, 3H, CH_3), 1.42 (t, $J=7.1$ Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 4.07 (q, $J=7.1$ Hz, 2H, CH_2), 4.42 (q, $J=7.1$ Hz, 2H, CH_2), 6.90 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.21 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.33 (d, $J=8.5$ Hz, 2H, CH_{arom}), 8.20 ppm (d, $J=8.5$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.2$, 12.6, 14.0, 14.2 (s, CH_3), 55.1 (s, OCH_3), 59.2, 61.3 (s, CH_2), 111.6, 113.4, 122.4, 126.3, 130.6, 135.1, 141.7, 157.9 (s, =C, C_{arom}), 112.9, 128.2, 130.7, 131.3 (s, CH_{arom}), 165.6, 165.8 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698\ cm^{-1}$ (s, C=O); LRMS (EI, 70 eV): *m/z* (%): 421 (100) [M^+], 406 (5) [M^+−Me], 392 (15) [M^+−Et], 376 (15) [M^+−OEt], 348 (10) [M^+−CO_2Et], 333 (5) [M^+−CO_2Et−Me]; HRMS (EI): *m/z*: calcd for $C_{25}H_{27}O_5N$: 421.18837; found: 421.18848; elemental analysis calcd (%) for $C_{25}H_{27}O_5N$: C 71.24, H 6.46, N 3.32; found: C 71.01, H 6.57, N 3.45.

1-(4-Hydroxyphenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7h): Yellow oil; yield: 88% (0.321 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.11$ (t, $J=7.1$ Hz, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 4.15 (q, $J=7.1$ Hz, 2H, CH_2), 5.98 (br, 1H, OH), 6.90 (d, $J=8.5$ Hz, 4H, CH_{arom}), 7.05 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.23 ppm (d, $J=8.5$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 12.7, 14.0 (s, CH_3), 55.2 (s, OCH_3), 59.5 (s, CH_2), 110.3, 121.5, 127.3, 128.7, 129.8, 136.3, 156.4, 157.8 (s, =C, C_{arom}), 112.9, 116.1, 129.2, 131.4 (s, CH_{arom}), 166.8 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1663$ (s, C=O), 3295 cm^{-1} (m, O−H); LRMS (EI, 70 eV): *m/z* (%): 365 (100) [M^+], 336 (50) [M^+−Et], 320 (20) [M^+−OEt], 292 (10) [M^+−CO_2Et], 275 (5) [M^+−CO_2Et−OH]; HRMS (EI): *m/z*: calcd for $C_{22}H_{23}O_4N$: 365.16216; found: 365.16238.

1-(3-Acetylphenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7i): Orange oil; yield: 87% (0.340 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (t, $J=7.0$ Hz, 3H, CH_3), 1.87 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 4.10 (q, $J=7.0$ Hz, 2H, CH_2), 6.90 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.21 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.46 (d, $J=7.9$ Hz, 1H, CH_{arom}), 7.63 (dd, $J=7.9$, 7.9 Hz, 1H, CH_{arom}), 7.84 (s, 1H, CH_{arom}), 8.05 ppm (d, $J=7.9$ Hz, 1H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.9$, 12.4, 13.7 and 26.4 (s, CH_3), 54.9 (s, OCH_3), 58.9 (s, CH_2), 111.2, 122.0, 126.2, 128.1, 135.0, 138.0, 138.1, 157.7 (s, =C, C_{arom}), 112.6, 127.6, 128.0, 129.5, 131.1, 132.4 (s, CH_{arom}), 165.6, 196.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1651$, 1694 cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 391 (100) [M^+], 376 (5) [M^+-Me], 362 (20) [M^+-Et], 346 (15) [M^+-OEt], 316 (10) [M^+-OEt−2Me], 303 (15) [M^+-CO_2Et−Me]; HRMS (EI): m/z: calcd for $C_{24}H_{25}O_4N$: 391.17781; found: 391.17699.

1-(4-Carbamoylphenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7j): Orange solid; yield: 73% (0.286 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.08$ (t, $J=7.1$ Hz, 3H, CH_3), 1.88 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.11 (q, $J=7.1$ Hz, 2H, CH_2), 6.20 (br, 2H, NH_2), 6.90 (d, $J=8.7$ Hz, 2H, CH_{arom}), 7.21 (d, $J=8.7$ Hz, 2H, CH_{arom}), 7.33 (d, $J=8.4$ Hz, 2H, CH_{arom}), 7.97 ppm (d, $J=8.4$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.8$, 12.3, 13.6 (s, CH_3), 54.8 (s, OCH_3), 58.8 (s, CH_2), 111.2, 122.0, 126.0, 127.9, 133.0, 134.7, 140.6, 157.5 (s, =C, C_{arom}), 112.5, 128.1, 128.2, 130.9 (s, CH_{arom}), 165.4, 168.0 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1625$, 1691 cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 392 (100) [M^+], 363 (30) [M^+-Et], 347 (20) [M^+-OEt], 332 (5) [M^+-OEt−Me], 319 (10) [M^+-CO_2Et], 304 (10) [M^+-CO_2Et−Me]; HRMS (EI): m/z: calcd for $C_{23}H_{24}O_4N_2$: 392.17306; found: 392.17327; elemental analysis calcd (%) for $C_{23}H_{24}O_4N_2$: C 70.39, H 6.16, N 7.14; found: C 70.15, H 6.09, N 7.23.

1-(2-Isopropenylphenyl)-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7k): Yellow oil; yield: 92% (0.358 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.09$ (t, $J=7.1$ Hz, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 4.10 (q, $J=7.1$ Hz, 2H, CH_2), 4.91 (br, 1H, $=CH_2$), 5.07 (br, 1H, $=CH_2$), 6.89 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.14–7.26 (m, 4H, CH_{arom}), 7.42 ppm (m, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.7$, 12.3, 13.7, 21.4 (s, CH_3), 54.9 (s, OCH_3), 58.7 (s, CH_2), 110.5, 121.9, 126.5, 128.5, 134.5, 135.4, 141.8, 142.9, 157.5 (s, =C, C_{arom}), 112.4, 127.8, 128.6, 129.0, 129.5, 131.2 (s, CH_{arom}), 116.6 (s, $=CH_2$), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1681$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 389 (100) [M^+], 374 (50) [M^+-Me], 360 (15) [M^+-Et], 344 (15) [M^+-OEt], 329 (20) [M^+-OEt−Me], 316 (25) [M^+-CO_2Et], 301 (15) [M^+-CO_2Et−Me], 286 (10) [M^+-CO_2Et−2Me]; HRMS (EI): m/z: calcd for $C_{25}H_{27}O_3N$: 389.19854; found: 389.19791.

1-Ethyl-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7l): Yellow oil; yield: 75% (0.226 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.04$ (t, $J=7.1$ Hz, 3H, CH_3), 1.29 (t, $J=7.3$ Hz, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 3.89 (q, $J=7.3$ Hz, 2H, CH_2), 4.05 (q, $J=7.1$ Hz, 2H, CH_2), 6.88 (d, $J=8.7$ Hz, 2H, CH_{arom}), 7.14 ppm (d, $J=8.7$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=9.8$, 10.9, 13.7, 15.3 (s, CH_3), 38.1, 58.6 (s, CH_2), 54.8 (s, OCH_3), 110.0, 121.5, 124.7, 128.8, 133.6, 157.5 (s, =C, C_{arom}), 112.4, 131.2 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1694$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 301 (100) [M^+], 286 (5) [M^+-Me], 272 (90) [M^+-Et], 256 (15) [M^+-OEt], 226 (10) [M^+-OEt−2Me]; HRMS (EI): m/z: calcd for $C_{18}H_{23}O_3N$: 301.16724; found: 301.16721.

1-Benzyl-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7m): Yellow oil; yield: 72% (0.261 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.06$ (t, $J=7.2$ Hz, 3H, CH_3), 2.03 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.08 (q, $J=7.2$ Hz, 2H, CH_2), 5.10 (s, 2H, NCH_2), 6.83–6.97 (m, 4H, CH_{arom}), 7.18–7.35 ppm (m, 5H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.0$, 11.2, 13.7 (s, CH_3), 46.7 (s, NCH_2), 54.9 (s, OCH_3), 58.7 (s, CH_2), 110.5, 121.9, 125.7, 128.6, 134.5, 136.7, 157.5 (s, =C, C_{arom}), 112.5, 125.3, 127.1, 128.6, 131.2 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1698$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 363 (100) [M^+], 348 (2) [M^+-Me], 334 (5) [M^+-Et], 318 (10) [M^+-OEt], 290 (5) [M^+-CO_2Et], 226 (50) [M^+-Ph−4Me]; HRMS (EI): m/z: calcd for $C_{23}H_{25}O_3N$: 363.18289; found: 363.18284.

1-Furfuryl-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7n): Orange oil; yield: 78% (0.275 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.05$ (t, $J=7.1$ Hz, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 4.07 (q, $J=7.1$ Hz, 2H, CH_2), 4.99 (s, 2H, NCH_2), 6.12 (d, $J=3.1$ Hz, 1H, =CH), 6.31 (dd, $J=3.1$, 2.0 Hz, 1H, =CH), 6.88 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.15 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.35 ppm (d, $J=2.0$ Hz, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.2$, 11.4, 13.9 (s, CH_3), 40.7 (s, NCH_2), 55.1 (s, OCH_3), 58.9 (s, CH_2), 107.6, 110.3, 142.5 (s, =CH), 110.8, 122.0, 125.8, 128.9, 134.7, 150.1, 157.8 (s, =C, C_{arom}), 112.7 and 131.5 (s, CH_{arom}), 165.8 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1679$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 353 (100) [M^+], 324 (5) [M^+-Et], 308 (10) [M^+-OEt], 280 (5) [M^+-CO_2Et], 226 (80) [M^+-Fu−4Me]; HRMS (EI): m/z: calcd for $C_{21}H_{23}O_4N$: 353.16216; found: 353.16182.

1-Allyl-4-(4-methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (7o): Yellow oil; yield: 74% (0.231 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.05$ (t, $J=7.1$ Hz, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.06 (q, $J=7.1$ Hz, 2H, CH_2), 4.45 (br, 2H, NCH_2), 4.82 (d, $J=17.0$ Hz, 1H, $=CH_2$), 5.16 (d, $J=10.5$ Hz, 1H, $=CH_2$), 5.90 (m, 1H, =CH), 6.86 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.15 ppm (d, $J=8.5$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.0$, 11.2, 14.0 (s, CH_3), 45.7 (s, NCH_2), 55.1 (s, OCH_3), 58.9 (s, CH_2), 110.4, 121.8, 125.7, 129.0, 134.5, 157.7 (s, =C, C_{arom}), 112.7, 131.4 (s, CH_{arom}), 116.2 (s, $=CH_2$), 132.7 (s, =CH), 165.9 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1694$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 313 (100) [M^+], 298 (5) [M^+-Me], 284 (30) [M^+-Et], 268 (15) [M^+-OEt], 238 (10) [M^+-OEt−2Me], 225 (30) [M^+-CO_2Et−Me]; HRMS (EI): m/z: calcd for $C_{19}H_{23}O_3N$: 313.16724; found: 313.16721.

4-(4-Methoxyphenyl)-2,5-dimethyl-1-propargylpyrrole-3-carboxylic acid ethyl ester (7p): Yellow oil; yield: 56% (0.174 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.04$ (t, $J=7.1$ Hz, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 2.32 (t, $J=2.3$ Hz, 1H, C≡CH), 3.78 (s, 3H, OCH_3), 4.06 (q, $J=7.1$ Hz, 2H, CH_2), 4.58 (d, $J=2.3$ Hz, 2H, NCH_2), 6.87 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.14 ppm (d, $J=8.5$ Hz, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=10.1$, 11.3, 13.9 (s, CH_3), 33.1 (s, NCH_2), 55.1 (s, OCH_3), 59.0 (s, CH_2), 72.6 (s, ≡CH), 77.6 (s, ≡C), 111.0, 122.1, 125.4, 128.6, 134.2, 157.9 (s, =C, C_{arom}), 112.7, 131.4 (s, CH_{arom}), 165.7 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1693$ (s, C=O), 2122 (w, C≡C), 3279 cm^{-1} (m, ≡C−H); LRMS (EI, 70 eV): m/z (%): 311 (100) [M^+], 296 (5) [M^+-Me], 282 (40) [M^+-Et], 266 (20) [M^+-OEt], 236 (15) [M^+-OEt−2Me].

4-(4-Methoxyphenyl)-2,5-dimethyl-1-[(*S*)-1-phenylethyl]pyrrole-3-carboxylic acid ethyl ester (7q): Orange oil; yield: 76% (0.287 g); $[\alpha]^{20}=-41.0$ [$c=1.0$ in $CHCl_3$]; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.04$ (t, $J=7.1$ Hz, 3H, CH_3), 1.93 (d, $J=7.4$ Hz, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.07 (q, $J=7.1$ Hz, 2H, CH_2), 5.65 (q, $J=7.4$ Hz, 1H, NCH), 6.90 (d, $J=7.4$ Hz, 2H, CH_{arom}), 7.13–7.38 ppm (m, 7H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.5$, 12.4, 14.0, 18.9 (s, CH_3), 52.8 (s, NCH), 55.1 (s, OCH_3), 59.0 (s, CH_2), 111.2, 122.6, 125.9, 129.2, 134.7, 141.1, 157.8 (s, =C, C_{arom}), 112.7, 125.8, 127.1, 128.6, 131.5 (s, CH_{arom}), 166.1 ppm (s, C=O); IR (Nujol): $\tilde{\nu}=1693$ cm^{-1} (s, C=O); LRMS (EI, 70 eV): m/z (%): 377 (100) [M^+], 332 (5) [M^+-OEt], 272 (70) [M^+-OEt−4Me], 244 (30) [M^+-CO_2Et−4Me], 227 (30) [M^+-CO_2Et−Ph]; HRMS (EI): m/z: calcd for $C_{24}H_{27}O_3N$: 377.19854; found: 377.19835. The enantiomeric excess of this compound (>99% *ee*) was determined by chiral HPLC analysis on a Hewlett–Packard 1100 LC apparatus by using a CHIRACEL OD column (250×4.6 mm; mobile phase: *n*-hexane/isopropanol 90:10; flow rate: 0.4 mL min^{-1}; $T=30$ °C; detection wavelength: 227 nm). To this end, a racemic mixture of **7q** was prepared from racemic α-methylbenzylamine and the chromatograms were compared (Figure 1).

4-(4-Methoxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid ethyl ester (9): Yellow oil; yield: 74% (0.201 g); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=1.11$ (t, $J=7.1$ Hz, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 4.10 (q, $J=7.1$ Hz, 2H, CH_2), 6.88 (d, $J=8.5$ Hz, 2H, CH_{arom}), 7.18 (d, $J=8.5$ Hz, 2H, CH_{arom}), 8.26 ppm (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=11.1$, 13.7, 14.1 (s, CH_3), 55.1 (s, OCH_3), 59.0 (s, CH_2), 110.4, 121.9, 123.3, 128.5, 133.8, 157.7 (s, =C, C_{arom}), 112.8,

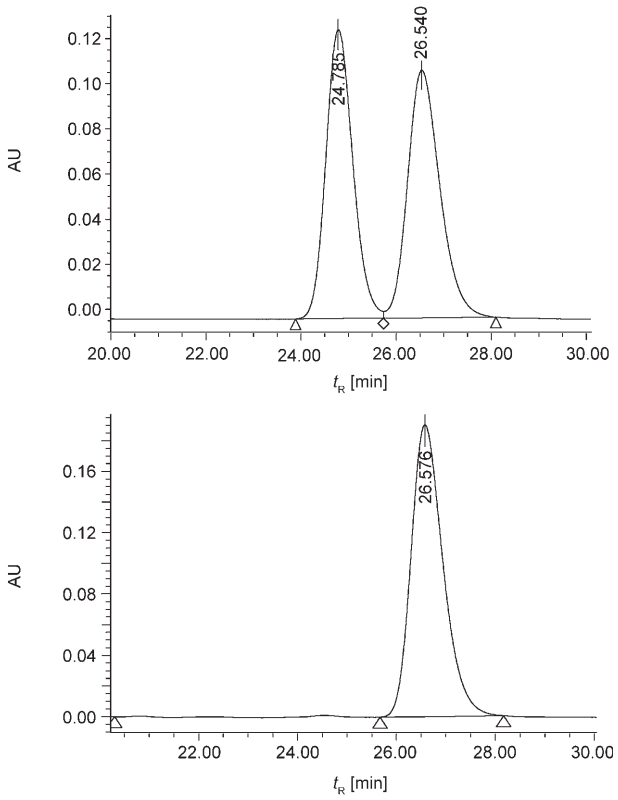


Figure 1. Chromatograms of racemic **7q** (top) and the enantiomerically pure **7q** (bottom) obtained from (*S*)-(−)-α-methylbenzylamine.

131.3 (s, CH_{arom}), 165.9 ppm (s, C=O); IR (Nujol): $\tilde{\nu}$ = 1702 (s, C=O), 3255 cm^{-1} (m, N–H); LRMS (EI, 70 eV): *m*/*z* (%): 273 (100) [M^+], 258 (5) [M^+−Me], 244 (80) [M^+−Et], 228 (20) [M^+−OEt], 213 (5) [M^+−OEt−Me], 198 [M^+−OEt−2Me], 184 (10) [M^+−OEt−3Me].

2-Acetyl-3-(4-methoxyphenyl)pent-4-ynoic acid ethyl ester (10): A solution of 1-(4-methoxyphenyl)prop-2-yn-1-ol (**2d**; 0.162 g, 1 mmol), ethyl acetoacetate (0.130 g, 1 mmol) and CF_3CO_2H (37 μL, 0.5 mmol) in THF (0.5 mL) was heated at 75 °C for 3 h (in a sealed tube). After removal of volatiles under vacuum, the residue was purified by column chromatography (silica gel) with a mixture EtOAc/hexanes (1:20) as the eluent. Alkyne **10** was isolated as a nonseparable mixture of two diastereoisomers in approximately 1.2:1 ratio: yellow oil; yield: 91 % (0.249 g); NMR data for the major diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3H, CH_2CH_3), 1.96 (s, 3H, $COCH_3$), 2.26 (d, *J* = 2.5 Hz, 1H, C≡CH), 3.75 (s, 3H, OCH_3), 3.97 (m, 3H, CH_2, *CH*CHC≡CH), 4.19 (m, 1H, C*H*C≡CH), 6.82 (m, 2H, CH_{arom}), 7.26 ppm (m, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (s, CH_2CH_3), 30.6 (s, $COCH_3$), 36.0 (s, *C*HC≡CH), 55.1 (s, OCH_3), 61.7 (s, CH_2), 66.1 (s, *C*HCHC≡CH), 71.8 (s, ≡CH), 83.3 (s, ≡C), 114.0, 129.2 (s, CH_{arom}), 129.5, 158.9 (s, C_{arom}), 166.9, 200.3 ppm (s, C=O); NMR data for the minor diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.0 Hz, 3H, CH_2CH_3), 2.27 (d, *J* = 2.2 Hz, 1H, C≡CH), 2.34 (s, 3H, $COCH_3$), 3.75 (s, 3H, OCH_3), 3.97 (m, 3H, CH_2, *CH*CHC≡CH), 4.32 (m, 1H, C*H*C≡CH), 6.82 (m, 2H, CH_{arom}), 7.26 ppm (m, 2H, CH_{arom}); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7 (s, CH_2CH_3), 30.0 (s, $COCH_3$), 36.0 (s, *C*HC≡CH), 55.1 (s, OCH_3), 61.5 (s, CH_2), 66.6 (s, *C*HCHC≡CH), 72.3 (s, ≡CH), 83.1 (s, ≡C), 113.9, 129.1 (s, CH_{arom}), 129.5, 159.0 (s, C_{arom}), 166.5, 200.6 ppm (s, C=O); IR (Nujol): $\tilde{\nu}$ = 1722, 1738 (s, C=O), 2118 (w, C≡C), 3290 cm^{-1} (m, ≡C-H); LRMS (EI, 70 eV): *m*/*z* (%): 274 (5) [M^+], 245 (5) [M^+−Et], 230 (30) [M^+−Et−Me], 201 (90) [M^+−CO_2Et], 186 (40) [M^+−CO_2Et−Me], 145 (100) [M^+−CH(CO_2Et)(COMe)]; HRMS (EI): *m*/*z*: calcd for $C_{16}H_{18}O_4$: 274.11996; found: 274.11979.

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[9] This unusual transformation has been previously observed by us while studying the coupling process depicted in Scheme 1 (see reference [7]). The intermediate carboxylic acid **5** could not be detected by GC/MS, which indicates that its decarboxylation is a highly favoured process.

[10] The enantiomeric excess of **7q** (>99% *ee*; determined by chiral HPLC analysis) was identical to that of the starting amine, a result that confirms the complete stereospecificity of the reaction sequence.

[11] Metal-mediated cleavage of propargylic C–N bonds is a well-documented process. For a review on this topic, see: S. Escoubet, S. Gastaldi, M. Bertrand, *Eur. J. Org. Chem.* **2005**, 3855–3873.

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[13] We have observed that transformation of **10** into **3d** is a highly favoured process that can be exclusively promoted by CF_3CO_2H (50 mol%, in THF at 75°C). Nevertheless, under these conditions, the sequential amination/annulation reaction takes place very slowly and yields **3d** in only 43% yield (as determined by GC) after 24 h (compare with entry 4 in Table 1). This fact clearly indicates an active role of the Lewis acid–ruthenium species in the reaction sequence. We note that related sequential amination/annulation reactions of 2-propynyl-1,3-dicarbonyl compounds with amines catalysed by trifluoroacetic acid have been described: A. S. Demir, A. Aybey, M. Kayalar, *ARKIVOC* **2005**, *15*, 105–116. It is also interesting to note that treatment of **10** with aniline, in THF at 75°C, in the absence of both CF_3CO_2H and complex **1** leads directly to pyrrole **3d** without detection of the intermediate β-enamino ester **11**, albeit in very low yield (approximately 20%; as determined by GC) after 24 h (compare with the catalysed reaction in entry 4 in Table 1; 2 h, 94% yield of isolated product).

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[15] A one-pot four-component synthesis of 1,2,3,5-tetrasubstituted pyrroles from secondary propargylic alcohols, aryl halides, aldehydes and primary amines has been reported. The process, which is catalysed by a Pd/Cu/thiazolium salt/acetic acid system, generates the corresponding tetrasubstituted pyrroles only in moderate yields (49–59%): R. U. Braun, K. Zeitler, T. J. J. Müller, *Org. Lett.* **2001**, *3*, 3297–3300.

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