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New synthesis of methyl 5-aryl or heteroaryl pyrrole-2-carboxylates by a tandem Sonogashira coupling/5-*endo*-*dig*-cyclization from β-iododehydroamino acid methyl esters and terminal alkynes

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ABSTRACT

A new and versatile 'Pd'/CuI catalyzed protocol was developed for the synthesis in good to high yields of substituted pyrroles from *N*-Boc-β-iododehydroamino acid methyl esters and several terminal alkynes. This one-pot, two-step procedure occurs by a Sonogashira coupling followed by a 5-*endo*-*dig*-cyclization, which involves the nitrogen atom of the dehydroamino acid. After several experiments using different Pd(0) and Pd(II) species it was possible to establish the more general reaction conditions, which are: the use of a Pd(II) catalyst, CuI and Cs_2CO_3 as base in dry DMF at 70 °C. The best yields were obtained with arylacetylenes bearing electron-donating groups and with electron-rich heteroarylacetylenes.

1. Introduction

Pyrrole rings are of great interest in organic chemistry as they can be found in several natural products,[1] organic materials[2] and bioactive molecules.[3] Especially substituted pyrroles present antibacterial,[4a–d] antiviral,[5a,b] anti-inflammatory and antioxidant activities.[6] The development of practical methods for the preparation of pyrroles bearing various substituents has become a critical goal in organic synthesis.[7,8a–d] The most recent methods are based on metal-catalyzed reactions.[9a–g]

Crawley et al. synthesized substituted methyl pyrrole-2-carboxylates from *N*-acetyl or *N*-benzyloxycarbonyl-(*Z*)-β-iododehydroamino acid derivatives and internal alkynes by a palladium-catalyzed cyclization.[9g]

Buchwald et al. have developed a domino Cu-catalyzed C–N coupling/hydroamidation reaction for the synthesis of pyrroles via an intramolecular cyclization of enyne intermediates obtained from haloenynes and *tert*-butylcarbamate by a Cu-catalyzed amidation. Only the combination of the catalyst with the base was effective, suggesting that the intramolecular hydroamidation is both a copper-catalyzed and a base-assisted process.[9f]

The synthesis of indoles using a Sonogashira coupling[10] can also be performed following one-pot methodologies, since Sakamoto et al. observed that the treatment of terminal alkynes with *o*-iodo-*N*-mesylanilide afforded indole products in a single step through a domino process.[11]

For some years now, our research group has been interested in the linkage of heterocycles to dehydroamino acid derivatives by palladium-catalyzed Suzuki cross-couplings using either β-bromo or β,β-dibromo dehydroamino acids as starting materials. The coupling products gave fused heterocycles like indoles, tri- and tetracyclic heteroaromatic compounds using a new metal-assisted C–N intramolecular cyclization involving the nitrogen atom of the dehydroamino acid derivative.[12a–e]

Herein we describe a new approach for the synthesis of *N*-(*tert*-butoxycarbonyl)-2,3,5-substituted pyrroles by a one-pot two-step reaction: Sonogashira coupling of the methyl ester of *N*-Boc-(*Z*)-β-iododehydrophenylalanine (Boc-*Z*-ΔPhe(β-I)-OMe) **1a** or of *N*-Boc-(*Z*)-β-iododehydroaminobutyric acid (Boc-*Z*-ΔAbu-(β-I)-OMe)[13] **1b** with several terminal aryl- and heteroarylacetylenes, followed by a 5-*endo*-*dig*-cyclization (Scheme 1).

To our knowledge this is the first time that dehydroamino acids and terminal alkynes were used to synthesize substituted pyrroles.

2. Results and discussion

The dehydroamino acid **1a** was prepared stereoselectively from the corresponding (*Z*)-dehydrophenylalanine, Boc-*Z*-ΔPhe-OMe,[14] with *N*-iodosuccinimide followed by treatment with NEt_3.

We studied the Sonogashira coupling of **1a** with phenylacetylene to determine the most effective conditions that allowed

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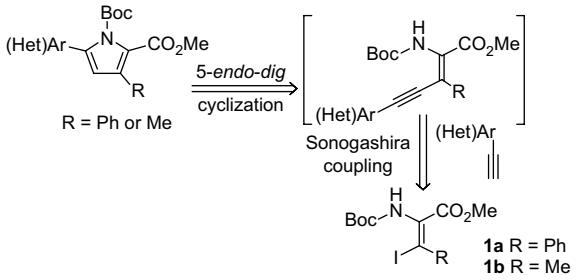
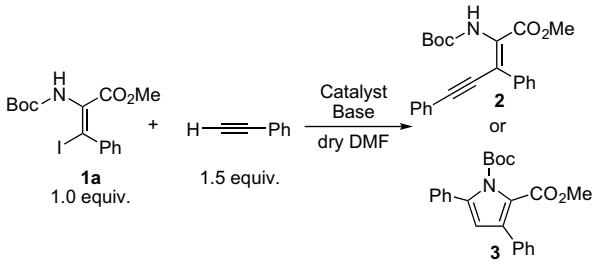


Scheme 1. Retrosynthetic analysis of our pyrrole synthesis.

the intramolecular cyclization to occur (Table 1). In all reactions an excess of phenylacetylene was used, as it is well known that an important side reaction, namely the Glaser-type oxidative dimerization of the alkyne, usually occurs in the presence of Cu(I).[15] We first chose Pd(0) instead of Pd(II) as we have previously noticed that the use of the latter sometimes favours the isomerization of the dehydroamino acid double bond.[12e] When the triphenylphosphine ligand was used (Table 1, entries 1–3) only by-products, resulting from the hydrodehalogenation of the amino acid derivative and from the oxidative dimerization of the phenylacetylene, were isolated and no starting materials were recovered at the end of the reaction. In the latter cases we used NEt_3 (18 equiv) as base as in the classical Sonogashira coupling conditions.[16] We then tried to perform this reaction under amine- and phosphine-free conditions using Pd_2dba_3 and Cs_2CO_3 as base, at rt (Table 1, entry 4). Thus it was possible to isolate the Sonogashira coupling product **2** in 30% yield together with the side products referred above. To promote the formation of pyrrole **3**, the mixture was heated at 50 °C and the pyrrole was obtained in 35% yield (Table 1, entry 5), resulting from a 5-*endo*-*dig*-cyclization of the intermediate alkyne **2**. Heating at 70 °C did not increase the pyrrole yield (Table 1, entry 6). As the yield for pyrrole **3** was not very high, it was decided to use Pd(II) catalysts: $PdCl_2(PPh_3)_2$ (Table 1, entry 7) and $PdCl_2(dppf)\cdot CH_2Cl_2$ 1:1 (Table 1, entry 8) and both afforded the corresponding pyrrole in good yields. The best conditions proved to be those using $PdCl_2(PPh_3)_2$ (Table 1, entry 7) but Pd(0) proved also to be efficient at 50 °C or at 70 °C in the tandem reaction, despite giving the pyrrole **3** in a lower yield (Table 1, entries 5 and 6).

Table 1
Optimization of the reaction conditions



Entry	Catalytic system	Base	*T* (°C)/*t* (h)	Yields (%) for **2** or **3**
1	$Pd(PPh_3)_4$ 4 mol % CuI 8 mol %	Et_3N 18 equiv	rt/21	—[a]
2	$Pd(PPh_3)_4$ 4 mol % CuI 8 mol %	Et_3N 18 equiv	70/3	—[a]
3	Pd/C 6 mol % PPh_3 24 mol % CuI 12 mol %	Et_3N 18 equiv	70/3	—[a]
4	Pd_2dba_3 10 mol % CuI 20 mol %	Cs_2CO_3 2 equiv	rt/24	**2**, 30
5	Pd_2dba_3 10 mol % CuI 20 mol %	Cs_2CO_3 2 equiv	50/4	**3**, 35
6	Pd_2dba_3 10 mol % CuI 20 mol %	Cs_2CO_3 2 equiv	70/4	**3**, 33
7	$PdCl_2(PPh_3)_2$ 5 mol % CuI 10 mol %	Cs_2CO_3 2 equiv	70/4	**3**, 60
8	$PdCl_2(dppf)\cdot CH_2Cl_2$ 5 mol % CuI 10 mol %	Cs_2CO_3 2 equiv	70/4	**3**, 54

[a] Only by-products were isolated like phenylacetylene dimers and dehalogenated dehydrophenylalanine.

Having these results in hands, it was decided to use both $Pd_2(dba)_3$ (conditions **A**) and $PdCl_2(PPh_3)_2$ (conditions **B**) as the catalytic species in the reaction of compound **1a** with several aryl- and heteroarylacetylenes in order to compare the results (Table 2).

The best yields were obtained with arylacetylenes bearing electron-donating groups in the phenyl ring. Thus, pyrroles **4**–**6** (Table 2, entries 1–3), resulting from the reaction of aminophenylacetylenes, were obtained in the highest yields. The amino groups of pyrroles **5** and **6** may allow further functionalization. The reaction involving 4-ethynylanisole required the use of higher temperature (Table 2, entry 4). Using conditions **A** at 50 °C both Sonogashira coupling product **7** and pyrrole **8** were obtained whereas increasing the temperature up to 70 °C provided the sole pyrrole **8** in 50% yield. Almost the same result was obtained with conditions **B**. With 2-ethynylanisole (Table 2, entry 5) using conditions **A** at 70 °C also afforded the two products, the intermediate **9** in poor yield (8%) and the corresponding pyrrole **10** in good yield. In this case however conditions **B** were much more efficient as they afforded pyrrole **10** in 65% yield and the intermediate in only 6% yield. Using 3-ethynylanisole and conditions **B**, pyrrole **11** was obtained as the only product in good yield (Table 2, entry 6).

The reactions with 4-fluoro and 4-bromophenylacetylenes afforded the corresponding pyrroles **12** and **13** in moderate yields using conditions **A** and **B** (Table 2, entries 7 and 8). These pyrroles are also interesting as they may be further functionalized by nucleophilic substitution or cross-coupling reactions.

With heteroarylalkynes it was found that the reaction with the electron-rich 3-ethynylthiophene afforded the expected pyrrole **14** in good yield, using both conditions (Table 2, entry 9). Electron-poor ethynylpyridines however were much less reactive: the reaction with 3-ethynylpyridine (Table 2, entry 10) gave pyrrole **15** in moderate yields (30–35%) using both conditions, whereas 2-ethynylpyridine did not react, starting materials being isolated.

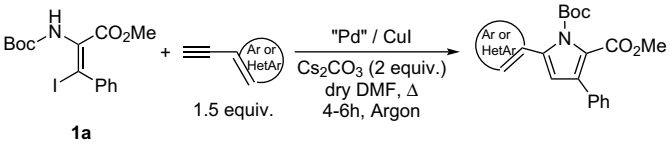
The Boc group of the synthesized pyrroles can be easily removed with TFA at rt, thus pyrrole **16** was obtained in quantitative yield from the corresponding *N*-protected pyrrole **8** (Scheme 2).

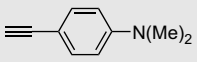
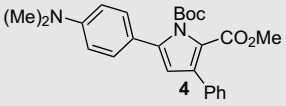
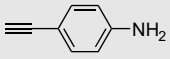
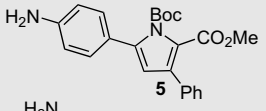
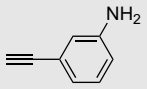
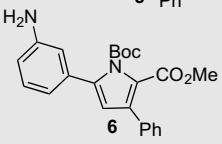
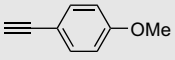
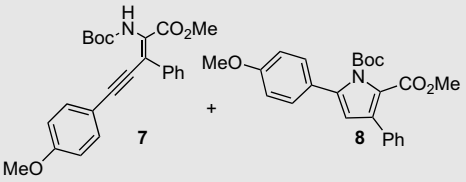
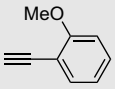
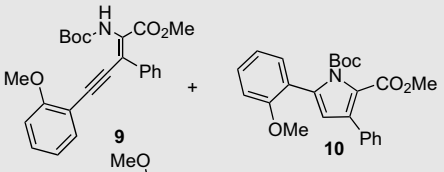
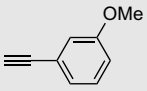
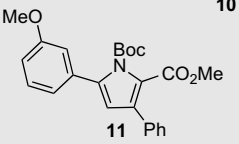
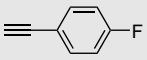
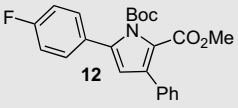
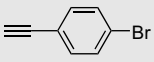
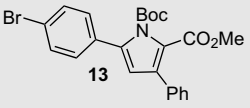
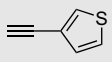
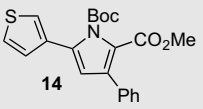
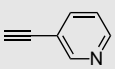
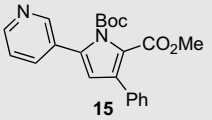
We have also applied conditions **B**, as they seem to be more general, to the reaction of Boc-*Z*-ΔAbu(β-I)-OMe **1b**[13] with aryl or heteroarylacetylenes (Scheme 3). In this case the pyrroles obtained bear a methyl group in position 3 instead of the phenyl group.

Reactions of **1b** with 4-ethynyl-*N*,*N*-dimethylaniline and 4-ethynylanisole gave pyrroles **17** and **18** in good to high yields comparable with those obtained from compound **1a** in the synthesis of pyrroles **4** and **8** (Table 2, entries 1 and 4). Reaction of **1b** with 3-ethynylthiophene gave pyrrole **19** in a lower yield (33%) comparing with the one for pyrrole **14** (55%) obtained from the dehydrophenylalanine derivative **1a** (Table 2, entry 9).

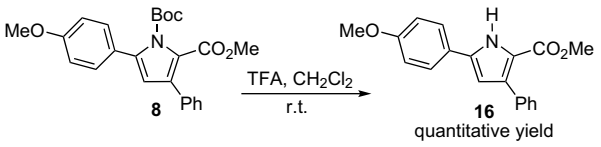
In summary, we have developed a new convenient regioselective method for the synthesis of methyl *N*-Boc-3,5-substituted pyrrole-2-carboxylates using a tandem Sonogashira coupling/5-*endo*-*dig*-cyclization by reacting *N*-Boc-β-iododehydroamino acid methyl esters with terminal aryl or heteroarylalkynes, under 'Pd' and Cu(I) catalysis and using Cs_2CO_3 as base. Both Pd(0) (conditions **A**) and Pd(II) species (conditions **B**) are efficient, although the use of Pd(II) provides higher yields in some cases. The pyrroles obtained present an aryl or a heteroaryl substituent in position 5. Some of them may be further functionalized due to the presence of different

Table 2
One-pot two-step pyrrole synthesis from the methyl ester of *N*-Boc-(*Z*)-β-iododehydrophenylalanine (**1a**) and several aryl and heteroarylacetylenes

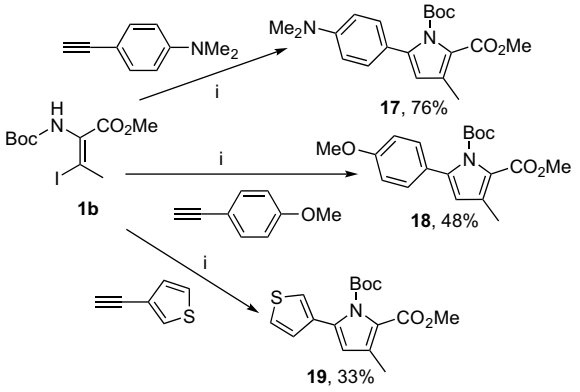


Entry	Phenylacetylenes	Conditions	Time	Product	Yield (%)
1		**A** **B**	5 h 5 h	 **4**	70 70
2		**A** **B**	5 h 5 h	 **5**	60 62
3		**A** **B**	4 h 4 h	 **6**	61 63
4		**A** **A** **B**	4 h 70 °C/5 h 5 h	 **7** + **8**	**7**: 15, **8**: 30 **7**: 0, **8**: 50 **7**: 0, **8**: 48
5		**A** **A** **B**	5 h 70 °C/6 h 6 h	 **9** + **10**	**9**: 14, **10**: 25 **9**: 8, **10**: 49 **9**: 6, **10**: 65
6		**B**	6 h	 **11**	55
7		**A** **B**	6 h 6 h	 **12**	40 43
8		**A** **B**	6 h 6 h	 **13**	36 41
9		**A** **B**	6 h 6 h	 **14**	53 55
10		**A** **B**	70 °C/6 h 3 h	 **15**	30 35

A: amino acid (1.0 equiv), Pd_2dba_3 (10 mol %), CuI (20 mol %), terminal alkyne (1.5 equiv), Cs_2CO_3 (2 equiv), dry DMF, under argon, at 50 °C or at 70 °C when specified.
B: $PdCl_2(PPh_3)_2$ (5 mol %) and CuI (10 mol %) were used as the catalytic system heating at 70 °C.



Scheme 2. Removal of the *N*-protecting group using TFA.



Scheme 3. (i) Amino acid (1.0 equiv), $PdCl_2(PPh_3)_2$ (5 mol %), CuI (10 mol %), terminal alkyne (1.5 equiv), Cs_2CO_3 (2 equiv), dry DMF, under argon, at 70 °C.

substituents in the aryl moiety. The Boc group is easily removed to give the *N*-unprotected pyrroles.

3. Experimental

3.1. General

Melting points were determined on a Stuart SMP3 apparatus and are uncorrected. The ^{1}H NMR spectra were measured on a Varian Unity Plus 300 or on an Avance III 400 Bruker. The ^{13}C NMR spectra were measured on the same instruments at 75.4 MHz or 100.6 MHz, respectively. ^{1}H–^{1}H spin–spin decoupling technique was used to attribute some signals. Heteronuclear correlations ^{1}H, ^{13}C, HMQC and HMBC were also performed. Mass spectra (EI or ESI) and HRMS were performed by the mass spectrometry service of University of Vigo, Spain (CACTI). Elemental analysis was performed in a LECO CHNS 932 instrument. Column chromatography was performed on Macherey–Nagel silica gel 230–400 mesh. Petroleum ether refers to the boiling range 40–60 °C. Ether refers to diethyl ether. When solvent gradient was used the increase of polarity was done gradually from neat petroleum ether to mixtures of ether/petroleum ether increasing 5% of ether until the isolation of the product.

3.2. Synthesis of Boc-*Z*-ΔPhe(β-I)-OMe (1a)

Boc-*Z*-ΔPhe-OMe[14] (1.39 g, 5.00 mmol) was dissolved in dichloromethane (0.1 M) and 2.5 equiv of *N*-iodosuccinimide was added with vigorous stirring. After reacting for 16 h, triethylamine (1.5 equiv) was added and stirring continued for 30 min. The solvent was then evaporated at reduced pressure and the residue partitioned between 100 mL of dichloromethane and 50 mL of $KHSO_4$ (1 M). The organic phase was washed with $KHSO_4$ (1 M), $NaHCO_3$ (1 M) and brine (3×30 mL). After drying over $MgSO_4$ the extract was taken to dryness at reduced pressure and the residue was submitted to column chromatography in diethyl ether/petroleum ether (1:4) to afford Boc-*Z*-ΔPhe(β-I)-OMe (1.75 g, 87%) as a yellow solid. Recrystallization from ether/*n*-hexane gave yellow crystals, mp 126–127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49 (s, 9H, CH_3 Boc), 3.48 (s, 3H, OCH_3), 6.39 (s, 1H, NH), 7.26–7.31 (br s, 5H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 28.06 (CH_3 Boc), 52.36 (OCH_3), 82.14 ($CO_2C(CH_3)_3$), 91.78 (C), 128.14 (2×CH), 128.69 (2×CH), 128.81 (CH), 129.49 (C), 140.66 (C), 152.08 (C=O Boc), 162.27(CO_2CH_3) ppm. Anal. Calcd for $C_{15}H_{18}INO_4$ (403.21): C 44.68; H 4.50; N 3.47. Found: C 44.70; H 4.64; N 3.78.

3.3. General procedures for the synthesis of pyrroles

Conditions **A**. In a Schlenk tube, Pd_2dba_3 (10 mol %) was added under argon to a solution of *N*-Boc-(*Z*)-β-iododehydroamino acid methyl ester in dry DMF (1–2 mL) and the reaction was left stirring for about 5 min at rt. Then the aryl or heteroarylacetylene (1.5 equiv), CuI (20 mol %) and Cs_2CO_3 (2.0 equiv) were successively added and the solution was stirred at 50 °C for several hours. The reaction was monitored by TLC, following the disappearance of the dehydroamino acid. After cooling, the reaction mixture was diluted with ether and washed three times with water. Then the organic layer was collected, dried over $MgSO_4$, filtered and concentrated under reduced vacuum. The resulting oil was purified by column chromatography.

Conditions **B**. The same as conditions **A** but using $PdCl_2(PPh_3)_2$ (5 mol %) and CuI (10 mol %) as catalytic system and heating at 70 °C.

*3.3.1. Methyl ester of N-Boc-(Z)-β-(phenylethynyl)-α,β-dehydrophenylalanine (**2**)*

From compound **1a** (80.0 mg, 0.244 mmol) and phenylacetylene (61.0 mg, 0.367 mmol) following conditions **A**, but stirring at rt for 24 h, and after purification by column chromatography using a solvent gradient from neat petroleum ether to 25% ether/petroleum ether, compound **2** was obtained as a yellow solid (28 mg, 30%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 68–69 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (s, 9H, CH_3 Boc), 3.62 (s, 3H, OCH_3), 6.93 (br s, 1H, NH), 7.32–7.41 (m, 8H, 8×ArH), 7.48–7.51 (m, 2H, 2×ArH) ppm. *m*/*z* EI (%) 377.16 (M^+, 2), 277.11 (M^+−Boc, 78), 217.09 (82), 216.08 (88), 190.08 (75), 189.07 (100). HRMS: Calcd for $C_{23}H_{23}NO_4$ [M^+] 377.1627. Found [M^+] 377.1628.

*3.3.2. Methyl N-Boc-3,5-diphenyl-1H-pyrrole-2-carboxylate (**3**)*

From compound **1a** (150 mg, 0.456 mmol) and phenylacetylene (69.0 mg, 0.688 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 15% ether/petroleum ether, pyrrole **3** was obtained as a beige solid (conditions **A**: 61.0 mg, 35%; conditions **B**: 105.0 mg, 60%). Recrystallization from ether/petroleum ether gave beige pale crystals, mp 71–73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (s, 9H, CH_3 Boc), 3.77 (s, 3H, OCH_3), 6.30 (s, 1H, 4-H), 7.33–7.47 (m, 8H, ArH), 7.51–7.55 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.24 (CH_3 Boc), 51.82 (OCH_3), 85.16 ($CO_2C(CH_3)_3$), 113.14 (4-CH), 120.81 (C), 127.41 (CH), 127.97 (4×CH), 128.27 (CH), 129.07 (2×CH), 129.16 (2×CH), 132.16 (C), 132.23 (C), 134.09 (C), 137.65 (C), 149.19 (C=O Boc), 162.12 (CO_2CH_3) ppm. *m*/*z* EI (%) 377.16 (M^+, 1), 277.11 (M^+−Boc, 100), 245.08 (95), 217.09 (96). HRMS: Calcd for $C_{23}H_{23}NO_4$ [M^+] 377.1627. Found [M^+] 377.1629.

*3.3.3. Methyl N-Boc-5-[4-(N,N-dimethylamino)phenyl]-3-phenyl-1H-pyrrole-2-carboxylate (**4**)*

From compound **1a** (80.0 mg, 0.244 mmol) and 4-ethynyl-*N*,*N*-dimethylaniline (53.0 mg, 0.367 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% ether/petroleum ether, compound **4** was obtained as a beige solid (conditions **A** or **B**: 71.0 mg, 70%). Recrystallization from ether/petroleum ether gave beige crystals, mp 138–140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (s, 9H, CH_3 Boc), 3.01 (s, 6H, $N(CH_3)_2$), 3.75 (s, 3H, OCH_3), 6.23 (s, 1H, 4-H), 6.74 (d, *J*=8.7 Hz, 2H, 3′-H and 5′-H), 7.33–7.42 (m, 5H, ArH), 7.52–7.56 (m,

2H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 27.35 (CH_3 Boc), 40.38 ($N(CH_3)_2$), 51.57 (OCH_3), 84.86 ($CO_2C(CH_3)_3$), 111.54 (3′-CH and 5′-CH), 112.34 (4-CH), 119.47 (C), 119.85 (C), 127.26 (CH), 127.82 (2×CH), 129.23 (2×CH), 130.04 (2×CH), 132.92 (C), 134.50 (C), 138.92 (C), 149.69 (C=O Boc), 150.4 (4′-C), 161.92 (CO_2CH_3) ppm. *m*/*z* EI (%) 420.21 (M^+, 2), 320.15 (M^+−Boc, 76), 288.12 (100), 260.13 (76), 259.12 (54), 216.08 (22). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 420.2049. Found [M^+] 420.2045.

3.3.4. Methyl N-Boc-5-(4-aminophenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**5**)

From compound **1a** (80.0 mg, 0.244 mmol) and 4-ethynylaniline (43.0 mg, 0.367 mmol), and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% ether/petroleum ether, compound **5** was obtained as a beige solid (conditions **A**: 57.0 mg, 60%; conditions **B**: 59.0 mg, 62%). Recrystallization from ether/petroleum ether gave beige crystals, mp 114–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 9H, CH_3 Boc), 3.75 (s, 3H, OCH_3), 3.80 (br s, 2H, NH_2), 6.22 (s, 1H, 4-H), 6.70 (d, *J*=8.4 Hz, 2H, 3′-H and 5′-H), 7.26 (d, *J*=8.4 Hz, 2H, 2′-H and 6′-H), 7.32–7.41 (m, 3H, ArH), 7.52–7.54 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.31 (CH_3 Boc), 51.60 (OCH_3), 84.95 ($CO_2C(CH_3)_3$), 112.47 (4-CH), 114.30 (3′-CH and 5′-CH), 119.98 (C), 121.85 (C), 127.28 (CH), 127.83 (2×CH), 129.17 (2×CH), 130.33 (2′-CH and 6′-CH), 132.69 (C), 134.37 (C), 138.48 (C), 146.69 (C), 149.58 (C=O Boc), 162.92 (CO_2CH_3) ppm. *m*/*z* EI (%) 392.17 (M^+, 12), 292.09 (M^+−Boc, 92), 260.06 (98), 232.07 (100), 231.07 (84). HRMS: Calcd for $C_{23}H_{24}N_2O_4$ [M^+] 392.1736. Found [M^+] 392.1731.

3.3.5. Methyl N-Boc-5-(3-aminophenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**6**)

From compound **1a** (80.0 mg, 0.244 mmol) and 3-ethynylaniline (43.0 mg, 0.367 mmol), and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% ether/petroleum ether, compound **6** was obtained as a brown oil (conditions **A**: 58.0 mg, 61%; conditions **B**: 60.0 mg, 63%). Recrystallization from ether/petroleum ether gave brown crystals, mp 83–86 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (s, 9H, CH_3 Boc), 3.76 (s, 3H, OCH_3), 6.27 (s, 1H, 4-H), 6.70–6.77 (m, 2H, ArH), 6.82–6.86 (m, 1H, ArH), 7.16–7.21 (dd, *J*=8.1 and 8.1 Hz, 1H, Ar-H), 7.34–7.42 (m, 3H, ArH), 7.51–7.54 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.31 (CH_3 Boc), 51.84 (OCH_3), 85.31 ($CO_2C(CH_3)_3$), 113.26 (4-CH), 117.50 (CH), 118.25 (CH), 120.91 (C), 122.83 (CH), 127.43 (CH), 127.98 (2×CH), 129.07 (2×CH), 129.15 (CH), 132.12 (C), 133.56 (C), 134.01 (C), 137.03 (C), 140.85 (C), 149.13 (C=O Boc), 162.08 (CO_2CH_3) ppm. *m*/*z* ESI (%) 393.18 (M^++H, 56), 337.12 (58), 293.13 (M^++H-Boc, 100). HRMS: Calcd for $C_{23}H_{24}N_2O_4$ [M^++H] 393.1809. Found [M^++H] 393.1818.

3.3.6. Methyl ester of N-Boc-(Z)-β-(4-methoxyphenylethynyl)-α,β-dehydrophenylalanine (**7**)

Following conditions **A**, from compound **1a** (100 mg, 0.306 mmol) and 4-ethynylanisole (61.0 mg, 0.459 mmol), heating at 50 °C for 4 h and after purification by column chromatography using a solvent gradient from neat petroleum ether to 10% ether/petroleum ether, the most polar product isolated as a yellow solid was shown to be compound **7** (19.0 mg, 15%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 119–121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 9H, CH_3 Boc), 3.81 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 6.22 (br s, 1H, NH), 6.84 (d, *J*=8.8 Hz, 2H, 3′-H and 5′-H), 7.34–7.39 (m, 3H, Ar-H), 7.42–7.46 (m, 2H, ArH), 7.50–7.53 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 28.05 (CH_3 Boc), 52.39 (OCH_3), 55.28 (CO_2CH_3), 81.84 ($CO_2C(CH_3)_3$), 86.19 (C), 95.60 (C), 113.95 (3′-CH and 5′-CH), 115.18 (C), 128.48 (C), 128.58 (CH), 128.62 (2×CH), 128.97 (2×CH), 131.77 (C), 133.10 (2×CH), 135.63 (C), 151.83 (C=O Boc), 159.84 (4′-C), 164.97 (CO_2CH_3) ppm. *m*/*z* EI (%) 407.17 (M^+, 3), 307.12 (M^+−Boc, 72), 275.09 (40), 247.10 (65), 246.09 (100), 220.09 (42), 203.07 (42), 176.06 (43). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 407.1733. Found [M^+] 407.1730.

As the less polar, compound **8** was isolated as a yellow solid (38.0 mg, 30%) (Table 2) described below.

3.3.7. Methyl N-Boc-5-(4-methoxyphenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**8**)

From compound **1a** (150 mg, 0.456 mmol) and 4-ethynylanisole (91.0 mg, 0.688 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 25% ether/petroleum ether, compound **8** was obtained as a yellow solid (conditions **A** heating at 70 °C: 94.0 mg, 50%; conditions **B**: 90.0 mg, 48%). Recrystallization from ether/petroleum ether gave yellow pale crystals, mp 94–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 9H, CH_3 Boc), 3.76 (s, 3H, CO_2CH_3), 3.86 (s, 3H, OCH_3), 6.25 (s, 1H, 4-H), 6.94 (d, *J*=8.8 Hz, 2H, 3′-H and 5′-H), 7.33–7.41 (m, 5H, ArH), 7.52–7.53 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.31 (CH_3 Boc), 51.71 (CO_2CH_3), 55.30 (OCH_3), 85.07 ($CO_2C(CH_3)_3$), 112.89 (4-CH), 113.39 (3′-CH and 5′-CH), 120.42 (C), 124.41 (C), 127.36 (CH), 127.91 (2×CH), 129.12 (2×CH), 130.53 (2×CH), 132.45 (C), 134.21 (C), 137.77 (C), 149.38 (C=O Boc), 159.73 (4′-C), 162.02 (CO_2CH_3) ppm. *m*/*z* EI (%) 407.17 (M^+, 1), 307.12 (M^+−Boc, 88), 275.09 (100), 247.10 (38), 232.08 (36), 204.08 (32). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 407.1733. Found [M^+] 407.1729.

3.3.8. Methyl ester of N-Boc-(Z)-β-(2-methoxyphenylethynyl)-α,β-dehydrophenylalanine (**9**) and methyl N-Boc-5-(2-methoxyphenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**10**)

From compound **1a** (150 mg, 0.456 mmol) and 2-ethynylanisole (91.0 mg, 0.688 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 30% ether/petroleum ether compounds **9** and **10** were obtained, the most polar product isolated as a yellow solid was shown to be compound **9** (conditions **A**: 26.0 mg, 14%; conditions **A** heating at 70 °C: 15.0 mg, 8%; conditions **B**: 11.0 mg, 6%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 68–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (s, 9H, CH_3 Boc), 3.87 (s, 3H, OCH_3), 3.96 (s, 3H, CO_2CH_3), 6.25 (br s, 1H, NH), 6.85–6.92 (m, 2H, 2×ArH), 7.26–7.47 (m, 5H, 5×ArH), 7.57 (d, *J*=7.2 Hz, 2H, 2×ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 28.07 (CH_3 Boc), 52.43 (CO_2CH_3), 55.73 (OCH_3), 81.87 ($CO_2C(CH_3)_3$), 92.05 (C), 110.33 (C), 110.71 (CH), 120.39 (CH), 128.20 (C), 128.25 (CH), 128.56 (CH), 128.80 (2×CH), 128.91 (2×CH), 129.96 (CH), 130.23 (C), 133.41 (5′-CH), 135.45 (C), 151.79 (C=O Boc), 160.08 (2′-C), 164.90 (CO_2CH_3) ppm. *m*/*z* EI (%) 407.17 (M^+, 3), 333.10 (M^+−74, 21), 307.12 (M^+−100, 100), 247.09 (M^+−160, 39), 246.09 (M^+−161, 92), 232.08 (M^+−175, 34), 191.09 (M^+−216, 39), 176.06 (M^+−231, 36). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 407.1733. Found [M^+] 407.1724.

As the less polar, compound **10** was obtained as a yellow solid (conditions **A**: 47.0 mg, 25%; conditions **A** heating at 70 °C: 92.0 mg, 49%; conditions **B**: 122.0 mg, 65%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 127–129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (s, 9H, CH_3 Boc), 3.78 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 6.26 (s, 1H, 4-H), 6.91 (dd, *J*=8.0 and 0.8 Hz, 1H, 3′-H), 7.02 (ddd, *J*=7.4, 7.4 and 0.8 Hz, 1H, 5′-H), 7.32–7.41 (m, 5H, 5×ArH), 7.55 (d, *J*=7.4 Hz, 2H, 2×ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.21 (CH_3 Boc), 51.93 (OCH_3), 55.24 (OCH_3), 84.09 ($CO_2C(CH_3)_3$), 110.01 (3′-CH), 113.33 (4-CH), 120.39 (5′-CH), 121.13 (C), 122.36 (C), 127.25 (CH), 128.02 (2×CH), 128.83 (2×CH), 129.75 (CH), 130.77 (CH), 131.14 (C), 134.03 (C), 148.66 (C=O Boc), 156.99 (2′-C), 162.78 (CO_2CH_3) ppm. *m*/*z* EI (%) 407.17 (M^+, 2), 307.12 (100), 247.10 (35), 246.09 (75), 176.06 (12), 118.05 (14). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 407.1733. Found [M^+] 407.1739.

*3.3.9. Methyl N-Boc-5-(3-methoxyphenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**11**)*

From compound **1a** (80.0 mg, 0.244 mmol) and 3-ethynylanisole (49.0 mg, 0.367 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 25% ether/petroleum ether, compound **11** was obtained as a yellow oil (conditions **B**: 55.0 mg, 55%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (s, 9H, CH_3 Boc), 3.77 (s, 3H, CO_2CH_3), 3.84 (s, 3H, OCH_3), 6.31 (s, 1H, 4-H), 6.92–7.05 (m, 3H, ArH), 7.27–7.43 (m, 4H, ArH), 7.52–7.55 (m, 2H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 27.25 (CH_3 Boc), 51.81 (CO_2CH_3), 55.20 (OCH_3), 85.17 ($CO_2C(CH_3)_3$), 113.05 (4-CH), 114.04 (CH), 114.61 (CH), 120.71 (C), 121.53 (CH), 127.41 (CH), 127.95 (2×CH), 129.01 (2×CH), 129.07 (CH), 132.14 (C), 133.40 (C), 134.07 (C), 137.42 (C), 149.17 (C=O Boc), 159.15 (4′-C), 162.05 (CO_2CH_3) ppm. *m*/*z* ESI (%) 408.18 (M^++H, 46), 384.11 (3), 352.11 (18), 320.18 (13), 255.16 (71), 233.18 (100). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^++H] 408.1806. Found [M^++H] 408.1799.

*3.3.10. Methyl N-Boc-5-(4-fluorophenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**12**)*

From compound **1a** (100 mg, 0.306 mmol) and 1-fluoro-4-ethynylbenzene (55.0 mg, 0.459 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 20% ether/petroleum ether, compound **12** was obtained as a yellow solid (conditions **A**: 49.0 mg, 40%; conditions **B**: 53.0 mg, 43%). Recrystallization from ether/petroleum ether gave yellow pale crystals, mp 89–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.41 (s, 9H, CH_3 Boc), 3.78 (s, 3H, OCH_3), 6.28 (s, 1H, 4-H), 7.11 (m, 2H, 3′-H and 5′-H), 7.32–7.46 (m, 5H, ArH), 7.51–7.54 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.30 (CH_3 Boc), 51.86 (OCH_3), 85.33 ($CO_2C(CH_3)_3$), 113.39 (4-CH), 114.98 (d, *J*=22 Hz, 3′-CH and 5′-CH), 121.01 (C), 127.49 (CH), 128.01 (2×CH), 129.00 (2×CH), 131.07 (d, *J*=8 Hz, 2′-CH and 6′-CH), 131.15 (C), 132.07 (C), 133.91 (C), 136.59 (C), 149.08 (C=O Boc), 162.11 (CO_2CH_3), 162.79 (d, *J*=248.5 Hz, CF) ppm. *m*/*z* EI (%) 395.15 (M^+, 1), 295.10 (M^+−Boc, 100), 263.07 (100), 235.08 (98). HRMS: Calcd for $C_{23}H_{23}NO_4$ [M^+] 395.1533. Found [M^+] 395.1535.

*3.3.11. Methyl N-Boc-5-(4-bromophenyl)-3-phenyl-1H-pyrrole-2-carboxylate (**13**)*

From compound **1a** (100 mg, 0.306 mmol) and 1-bromo-4-ethynylbenzene (86.0 mg, 0.459 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 20% ether/petroleum ether, compound **13** was obtained as a yellow solid (conditions **A**: 50.0 mg, 36%; conditions **B**: 57.0 mg, 41%). Recrystallization from ether/petroleum ether gave off-white crystals, mp 89–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H, CH_3 Boc), 3.77 (s, 3H, OCH_3), 6.30 (s, 1H, 4-H), 7.32–7.41 (m, 5H, ArH), 7.50–7.56 (m, 4H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.32 (CH_3 Boc), 51.92 (OCH_3), 85.51 ($CO_2C(CH_3)_3$), 113.53 (4-CH), 121.37 (C), 122.55 (C), 127.53 (CH), 128.03 (2×CH), 128.96 (2×CH), 130.76 (2×CH), 131.14 (2×CH), 132.01 (C), 133.80 (C), 136.36 (C), 148.96 (C=O Boc), 162.13 (CO_2CH_3) ppm. *m*/*z* EI (%) 457.07 (M^+ ^{81}Br, 11), 455.05 (M^+ ^{79}Br, 10), 357.01 (M^+ ^{81}Br-Boc, 65), 355.01 (M^+ ^{79}Br-Boc, 71), 324.98 (M^+ ^{81}Br-132, 73), 322.99 (M^+ ^{79}Br-132, 80), 216.08 (100). HRMS: Calcd for $C_{23}H_{22}BrNO_4$ [M^+ ^{81}Br] 457.0712, [M^+ ^{79}Br] 455.0732. Found [M^+ ^{81}Br] 457.0690, [M^+ ^{79}Br] 455.0723.

*3.3.12. Methyl N-Boc-5-(thien-3-yl)-3-phenyl-1H-pyrrole-2-carboxylate (**14**)*

From compound **1a** (100 mg, 0.306 mmol) and 3-ethynylthiophene (50.0 mg, 0.459 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 10% ether/petroleum ether, compound **14** was obtained as a yellow solid (conditions **A**: 63.0 mg, 53%; conditions **B**: 65.0 mg, 55%). Recrystallization from ether/petroleum ether gave yellow crystals, mp 69–71 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47 (s, 9H, CH_3 Boc), 3.76 (s, 3H, OCH_3), 6.33 (s, 1H, 4-H), 7.23 (dd, *J*=5.0 and 1.2 Hz, 1H, ArH), 7.33–7.45 (m, 5H, ArH), 7.50–7.53 (m, 2H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 27.33 (CH_3 Boc), 51.77 (OCH_3), 85.31 ($CO_2C(CH_3)_3$), 113.31 (4-CH), 120.60 (C), 124.51 (CH), 124.95 (CH), 127.44 (CH), 127.94 (2×CH), 128.87 (CH), 129.10 (2×CH), 131.90 (C), 132.42 (C), 132.77 (C), 134.06 (C), 149.38 (C=O Boc), 161.93 (CO_2CH_3) ppm. *m*/*z* EI (%) 383.12 (M^+, 5), 341.32 (32), 327.26 (25), 283.06 (M^+−Boc, 30), 251.04 (35), 81.07 (84), 69.07 (100). HRMS: Calcd for $C_{21}H_{21}NO_4S$ [M^+] 383.1191. Found [M^+] 383.1202.

*3.3.13. Methyl N-Boc-5-(pyridin-3-yl)-3-phenyl-1H-pyrrole-2-carboxylate (**15**)*

From compound **1a** (100 mg, 0.306 mmol) and 3-ethynylpyridine (48.0 mg, 0.459 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% ether/petroleum ether, compound **15** was obtained as a yellow solid (conditions **A**: 34.0 mg, 30%; conditions **B**: 40.0 mg, 35%). Recrystallization from ether/petroleum ether gave yellow pale crystals, mp 89–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (s, 9H, CH_3 Boc), 3.79 (s, 3H, OCH_3), 6.37 (s, 1H, 4-H), 7.32–7.42 (m, 4H, ArH), 7.50–7.53 (m, 2H, ArH), 7.80 (br d, *J*=8.1 Hz, 1H, ArH), 8.63–8.71 (m, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 27.35 (CH_3 Boc), 52.10 (OCH_3), 85.78 ($CO_2C(CH_3)_3$), 114.48 (4-CH), 122.30 (C), 122.95 (CH), 127.66 (CH), 128.16 (2×CH), 128.80 (2×CH), 131.70 (C), 133.48 (C), 133.83 (C), 136.92 (CH), 148.66 (C=O Boc), 148.90 (CH), 149.55 (CH), 162.33 (CO_2CH_3) ppm. *m*/*z* EI (%) 378.16 (M^+, 8), 278.10 (M^+−Boc, 100), 246.07 (78), 218.08 (59). HRMS: Calcd for $C_{24}H_{25}NO_5$ [M^+] 378.1580. Found [M^+] 378.1567.

*3.3.14. Methyl N-Boc-5-[4-(N,N-dimethylamino)phenyl]-3-methyl-1H-pyrrole-2-carboxylate (**17**)*

From compound **1b** (80.0 mg, 0.235 mmol) and 4-ethynyl-*N*,*N*-dimethylaniline (51.0 mg, 0.352 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 25% ether/petroleum ether, compound **17** was obtained as a yellow pale solid (conditions **B**: 64.0 mg, 76%). Recrystallization from ether/petroleum ether gave white crystals, mp 114–115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (s, 9H, CH_3 Boc), 2.32 (s, 3H, 3-CH_3), 2.99 (s, 6H, $N(CH_3)_2$), 3.86 (s, 3H, OCH_3), 5.99 (s, 1H, 4-H), 6.71 (d, *J*=8.8 Hz, 2H, ArH), 7.31 (d, *J*=8.8 Hz, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 12.86 (3-CH_3), 27.33 (CH_3 Boc), 40.39 ($N(CH_3)_2$), 51.20 (OCH_3), 84.46 ($CO_2C(CH_3)_3$), 111.60 (2×CH), 112.79 (4-CH), 119.47 (C), 120.59 (C), 129.93 (2×CH), 133.60 (C), 139.41 (C), 150.21 (C), 150.34 (C=O Boc), 161.65 (CO_2CH_3) ppm. *m*/*z* ESI (%) 381.18 (M^++Na, 4), 359.20 (M^++H, 100), 303.13 (16), 259.14 (M^++H-Boc, 14). HRMS: Calcd for $C_{20}H_{26}N_2O_4$ [M^++H] 359.1965. Found [M^++H] 359.1976.

*3.3.15. Methyl N-Boc-5-(4-methoxyphenyl)-3-methyl-1H-pyrrole-2-carboxylate (**18**)*

From compound **1b** (80.0 mg, 0.235 mmol) and 4-ethynylanisole (47.0 mg, 0.352 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 15% ether/petroleum ether, compound **18** was obtained as a yellow pale solid (conditions **B**: 27.0 mg, 33%). Recrystallization from ether/petroleum ether gave white crystals, mp 110–111 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (s, 9H, CH_3 Boc), 2.32 (s, 3H, 3-CH_3), 3.84 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.00 (s, 1H, 4-H), 6.91 (d, *J*=9.0 Hz, 2H, ArH), 7.35 (d, *J*=9.0 Hz, 2H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 12.77 (3-CH_3), 27.28 (CH_3 Boc), 51.33 (OCH_3), 55.28 (OCH_3), 84.68 ($CO_2C(CH_3)_3$), 113.34 (4-CH), 113.37 (2×CH), 121.02 (C), 124.23 (C), 130.40 (2×CH), 130.41 (C), 138.34 (C), 149.91 (C), 159.68 (C=O), 161.64 (C=O) ppm. Anal. Calcd for $C_{19}H_{23}NO_5$: C, 66.07; H, 6.71; N, 4.06. Found: C, 66.11; H, 6.75; N, 4.04.

*3.3.16. Methyl N-Boc-5-(thien-3-yl)-3-methyl-1H-pyrrole-2-carboxylate (**19**)*

From compound **1b** (80.0 mg, 0.235 mmol) and 3-ethynylthiophene (38.0 mg, 0.352 mmol) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 25% ether/petroleum ether, compound **19** was obtained as a yellow oil (conditions **B**: 36.0 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (s, 9H, CH_3 Boc), 2.31 (s, 3H, 3-CH_3), 3.86 (s, 3H, OCH_3), 6.09 (s, 1H, 4-H), 7.19 (dd, J=5.2 and 1.2 Hz, 2H, ArH), 7.32 (dd, J=5.2 and 3.2 Hz, 2H, ArH), 7.41 (dd, J=3.2 and 1.2 Hz, 2H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 12.74 (3-CH_3), 27.31 (CH_3 Boc), 51.37 (OCH_3), 84.93 ($CO_2C(CH_3)_3$), 113.62 (4-CH), 121.19 (C), 124.20 (CH), 124.95 (CH), 128.66 (CH), 130.28 (C), 131.17 (C), 133.29 (C), 149.99 (C=O Boc), 161.56 (CO_2CH_3) ppm. m/z ESI (%) 344.09 (M^++Na, 18), 318.08 (26), 279.09 (15), 238.05 (49), 222.06 (M^++H-Boc, 83), 190.04 (100). HRMS: Calcd for $C_{16}H_{19}NO_4S$ [M^++Na] 344.0927. Found [M^++Na] 344.0929.

3.4. Synthesis of methyl 5-(4-methoxyphenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (16)

To a solution of *N*-protected pyrrole **8** (40.0 mg, 0.0980 mmol) in CH_2Cl_2 (3 mL), TFA (1 mL) was added and the reaction mixture was then stirred at rt for about 2 h. Then, the solution was diluted with more CH_2Cl_2, washed with $NaHCO_3$ 1 M (3×10 mL) and brine, dried over $MgSO_4$, filtered and concentrated under vacuum. Pyrrole **16** was obtained as a beige solid (30.0 mg, quantitative yield). Recrystallization from ether/petroleum ether gave beige crystals, mp 134–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H, CO_2CH_3), 3.86 (s, 3H, OCH_3), 6.54 (d, J=3.2 Hz, 1H, 4-H), 6.98 (d, J=8.8 Hz, 2H, 3′-H and 5′-H), 7.31–7.43 (m, 3H, ArH), 7.54 (d, J=8.8 Hz, 2H, 2′-H and 6′-H), 7.59–7.62 (m, 2H, ArH), 9.21 (br s, 1H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 51.30 (CO_2CH_3), 55.38 (OCH_3), 109.15 (4-CH), 114.54 (3′ and 5′-CH), 117.59 (C), 123.82 (C), 126.14 (2′ and 6′-CH), 127.12 (CH), 127.77 (2×CH), 129.38 (2×CH), 133.73 (C), 135.07 (C), 135.56 (C), 159.56 (4′-C), 161.53 (CO_2CH_3) ppm. m/z EI (%) 307.12 (M^+, 1), 81.07 (73), 69.06 (100). HRMS: Calcd for $C_{19}H_{17}NO_3$ [M^+] 307.1208. Found [M^+] 307.1209.

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