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# Metal/organo relay catalysis in a one-pot synthesis of methyl 4-aminopyrrole-2-carboxylates from 5-methoxyisoxazoles and pyridinium ylides

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Methyl 4-aminopyrrole-2-carboxylates were synthesized in one-pot mode by the relay catalytic cascade reaction of 5-methoxyisoxazoles with pyridinium ylides by use of a $FeCl_2$/$Et_3N$ binary catalytic system leading to 1-(5-methoxycarbonyl-1*H*-pyrrol-3-yl)pyridinium salts followed by hydrazinolysis. The approach permits the introduction of a substituent at the pyrrole nitrogen via a nucleophilic reaction of the pyrrolylpyridinium ylide derived from the salt. Catalytic reduction of the ylides gives methyl 4-piperidinopyrrole-2-carboxylates.

## Introduction

Derivatives of 4-aminopyrrole-2-carboxylic acid demonstrate various biological activities. We mention here only recently published works on the topic. 4-Aminopyrrole-2-carboxylates are particularly important building blocks for synthesis[1] and biosynthesis[2] of pyrrole-based polyamides possessing antibiotic, antiviral and cytotoxic properties.[3] The use of derivatives of 4-aminopyrrole-2-carboxylic acid in the synthesis of various heterocycles or ensembles with other heterocyclic systems, permits the preparation of such compounds as poly(ADP-ribosyl) polymerase-1 inhibitors,[4] dual inhibitors of Aurora kinases and cyclin dependent kinase 1,[5] androgen receptor antagonists,[6] inhibitors of the phosphodiesterase 4 enzyme.[7]

4-Aminopyrrole-2-carboxylates can be synthesized by reduction of the corresponding nitro-,[1c, 4, 8] nitroso-,[9] azo-compounds[10] and azides[11] or by aminodecarboxylation of alkyl 4-carboxypyrrole-2-carboxylates via the Curtius rearrangement.[12] A series of benzyl 4-(N-substituted-amino)-1*H*-pyrrole-2-carboxylates was synthesized by treatment of *N*-(9-phenylfluoren-9-yl)-4-oxoproline benzyl ester with primary and secondary amines. Benzyl 4-aminopyrrole-2-carboxylate was prepared by $Pd(PPh_3)_4$/*N*,*N*-dimethylbarbituric acid induced deprotection of the corresponding *N*-allyl derivative.[13] An example of the formation of a 3-aminopyrrole derivative from an acyclic precursor is the cyclization of dimethyl 2-((cyano(phenyl)methyl)amino)butenedioate, providing dimethyl 4-amino-5-phenyl-1*H*-pyrrole-2,3-dicarboxylate.[14]

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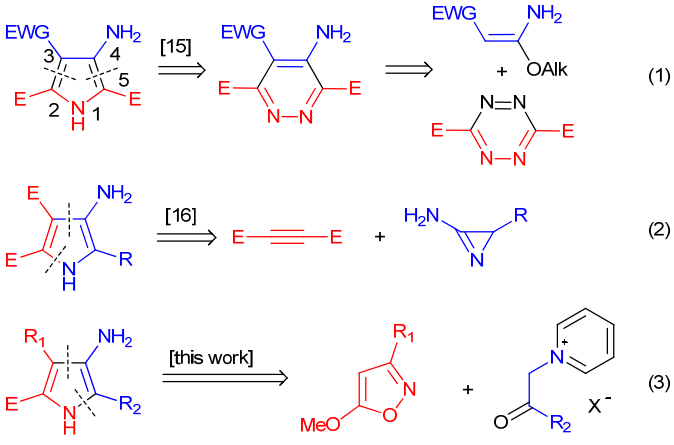
Two approaches to 4-aminopyrrole-2-carboxylates involving the formation of two bonds of the pyrrole ring were also reported. In the first, the C2-C3 and C4-C5 bonds of the aminopyrrole system were formed via a two-step procedure. The EWG-substituted primary ketene *N*,*O*-acetals react with dimethyl tetrazine-3,6-dicarboxylate to furnish tetrafunctionalized pyridazines via [4+2] cycloaddition (Scheme 1, reaction 1).




E = $CO_2$Me, EWG = Electron Withdrawing Group

**Scheme 1** Convergent synthetic approaches to 4-aminopyrrol-2-carboxylates

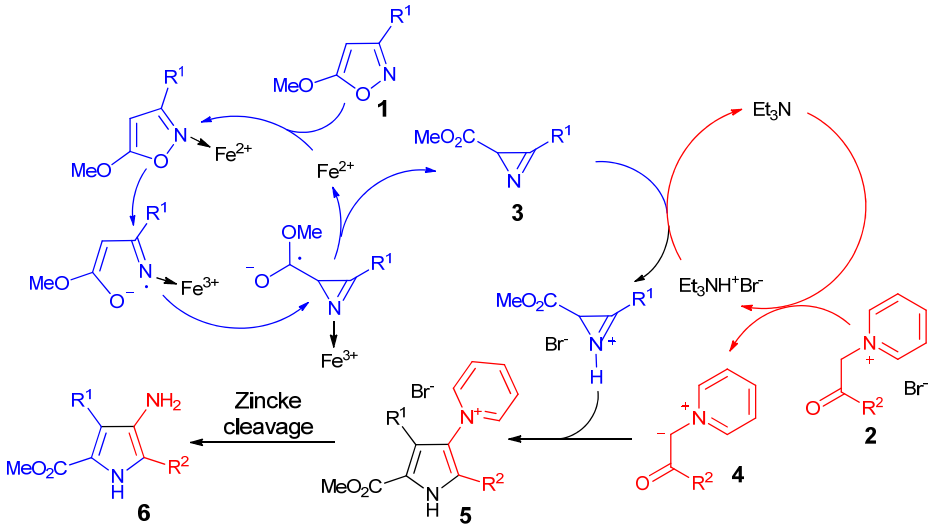
The latter, possessing an EWG, primary amino- and two ester groups, undergoes reductive ring contraction to give the corresponding 4-aminopyrrole-2,5-dicarboxylates.[15] In the second approach, the N-C2 and C3-C4 bonds of the pyrrole ring were formed by the reaction of 3-amino-2-phenylcarbamoyl-2*H*-azirine with dimethyl acetylenedicarboxylate, giving 3-amino-4,5-dimethoxycarbonyl-2-phenylcarbamoylpyrrole, albeit in low yield (Scheme 1, reaction 2).[16] To expand the use of the valuable pyrrole derivatives discussed above for medicinal

chemistry, there is still a need to develop new methods for the preparation of 4-aminopyrrole-2-carboxylates because the known methods often do not tolerate a wide range of functional groups and have limitations in changing the substituents at positions 1, 3 and 5.

We report here a new approach for the construction of the 4-aminopyrrole-2-carboxylate backbone via the formation of the C3-C4 and N-C5 pyrrole bonds from 5-methoxyisoxazoles and pyridinium salts, which can be performed as a one-pot procedure (Scheme 1, reaction 3).

## Results and discussion

Earlier we disclosed the reaction of 2*H*-azirines with pyridinium ylides leading to 1-(1*H*-pyrrol-3-yl)pyridinium salts.[17] It is also known, that $FeCl_2 \cdot 4H_2O$ effectively catalyzes the isomerization of 3-aryl-5-methoxyisoxazoles to methyl 3-aryl-2*H*-azirine-2-carboxylates.[18] Recently this transformation was used to prepare 4-acylpyrrole-2-carboxylic acid derivatives by the domino reaction of 3-aryl-5-methoxyisoxazoles with 1,3-dicarbonyl compounds under relay catalysis.[19] Taking into account all these facts, we envisioned that the synthesis of alkyl 3-alkyl/aryl-4-amino-5-arylpyrrole-2-carboxylates could be carried out starting from easily available 3-alkyl/aryl-5-alkoxyisoxazoles **1**[20] and *N*-phenacylpyridinium salts **2** according to Scheme 2. This synthetic scheme implies the possibility of an implementation of parallel and sequential stages (*a:* the generation of azirine **3** from isoxazole **1** under $FeCl_2 \cdot 4H_2O$ catalysis; *b:* the formation of phenacylpyridinium ylide **4** catalyzed by $Et_3N$; *c:* activation of azirine with $Et_3HN^+Br^-$; *d:* reaction of the activated azirine with the pyridinium ylide **4**, leading to 1-(1*H*-pyrrol-3-yl)pyridinium salt **5**) as a domino process under relay catalysis,[21] which does not involve isolation of the often unstable 2*H*-azirines.[22] The last stage on the way to aminopyrroles **6**, a Zincke cleavage of the pyridinium salts **5**, can hardly be coupled with the previously mentioned domino process, because there is a possibility that a Zincke ring opening reaction of salt **2** will occur, but the implementation of Scheme 2 as a one-pot procedure is not excluded.



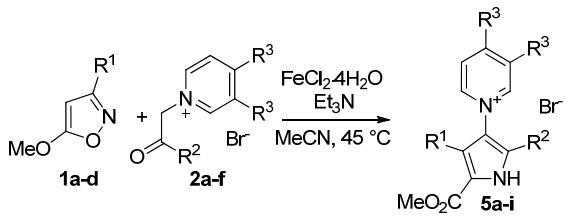

**Scheme 2.** The mechanistic representation of the synthetic route to methyl 4-aminopyrrole-2-carboxylates **6**

The reaction of aryl-substituted 2*H*-azirines with pyridinium ylides leading to 1-(1*H*-pyrrol-3-yl)pyridinium salts is usually performed in $CH_2Cl_2$ at room temperature.[17] Since acetonitrile is the solvent of choice[18,19] for the transformation of 3-aryl-5-methoxyisoxazoles to alkyl 3-aryl-2*H*-azirine-2-carboxylates **3** under $FeCl_2 \cdot 4H_2O$ catalysis, the test reaction of methyl 3-phenyl-2*H*-azirine-2-carboxylate **3a**, which is the product of catalytic isomerization of 3-phenyl-5-methoxyisoxazole **1a** with *N*-[2-(2-bromophenyl)-2-oxoethyl]pyridinium bromide **2a** was carried out in MeCN at 20 °C. The 1-(1*H*-pyrrol-3-yl)pyridinium bromide **5a** was obtained in 40% yield after stirring for 36 h. It was decided to be performed the reaction of the isoxazoles with the pyridinium salts at a slightly higher temperature (45 °C) to accelerate the reaction of the pyridinium ylide **4** with transient azirine **3** and thus prevent its decomposition. A very simple procedure, consisting of stirring a mixture of isoxazole **1**, pyridinium salt **2**, $FeCl_2 \cdot 4H_2O$ and $Et_3N$ in MeCN at 45 °C gave compounds **5** in reasonable yields, except for the isoquinolinium derivative **5h** (Table 1). All new compounds were characterized by $^1H$ and $^{13}C$ NMR, IR spectroscopy, and mass-spectrometry.

According to a recent paper[23] 2*H*-chromen-3-pyridinium chlorides can be efficiently transformed via the Zincke ring opening reaction into the corresponding amino-substituted heterocycles using *N*-methylpiperazine. The reaction of pyridinium salt **5b** with *N*-methylpiperazine led, however, to the tarring of the reaction mixture and only traces of the corresponding amine were detected. We tested, therefore, the traditional reagent, hydrazine hydrate, to induce Zincke cleavage of the *N*-heterocyclyl-pyridinium salts, affording the corresponding heterocyclylamines.[24] The reaction of hydrazine hydrate with pyridinium salt **5b** led cleanly to the corresponding amine and consequently this reagent was used in the developed one-pot transformation of 5-

methoxyisoxazoles **1** and *N*-(2-aryl-2-oxoethyl)pyridinium bromides **2** to methyl 4-aminopyrrole-2-carboxylates **6**.

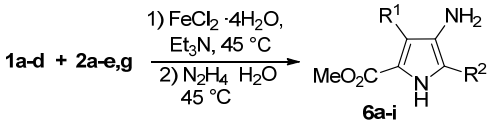
**Table 1** Synthesis of 1-(1*H*-pyrrol-3-yl)pyridinium bromides **5** by the reaction of 5-methoxyisoxazoles **1** and *N*-(2-aryl-2-oxoethyl)pyridinium bromides **2**




| Entry | $R^1$ | $R^2$ | $R^3$/ $R^3$+ $R^3$ | **1+2** | **5**, yield, % |
|---|---|---|---|---|---|
| 1 | Ph | 2-$BrC_6H_4$ | H | **1a+2a** | **5a**, 71 |
| 2 | Ph | Ph | H | **1a+2b** | **5b**, 84 |
| 3 | Ph | 4-$ClC_6H_4$ | H | **1a+2c** | **5c**, 75 |
| 4 | Ph | 4-$NO_2C_6H_4$ | H | **1a+2d** | **5d**, 64 |
| 5 | 4-$BrC_6H_4$ | 3-$BrC_6H_4$ | H | **1b+2e** | **5e**, 71 |
| 6 | 4-$MeOC_6H_4$ | 3-$BrC_6H_4$ | H | **1c+2e** | **5f**, 70 |
| 7 | Me | Ph | H | **1d+2b** | **5g**, 49 |
| 8 | Me | 4-$ClC_6H_4$ | H | **1d+2c** | **5h**, 66 |
| 9 | Me | 4-$MeOC_6H_4$ | H | **1d+2f** | **5i**, 63 |
| 10 | Ph | 4-$ClC_6H_4$ | $(CH=CH)_2$ | **1a+2g** | **5j**, 34 |

Hydrazine hydrate was added to the reaction mixture obtained as described above and the mixture was stirred for an additional period at 45 °C to give methyl 4-aminopyrrole-2-carboxylates **6** in reasonable yields (Table 2).

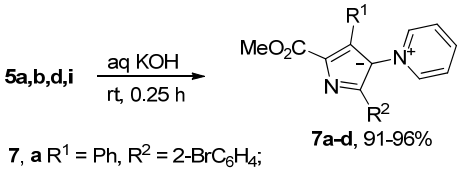
**Table 2** Synthesis of 4-aminopyrrole-2-carboxylates **6** via the one-pot procedure




| Entry | $R^1$ | $R^2$ | **1+2** | **6**, yield, % |
|---|---|---|---|---|
| 1 | Ph | 2-$BrC_6H_4$ | **1a+2a** | **6a**, 64 |
| 2 | Ph | Ph | **1a+2b** | **6b**, 63 |
| 3 | Ph | 4-$ClC_6H_4$ | **1a+2c** | **6c**, 52 |
| 4 | Ph | 4-$NO_2C_6H_4$ | **1a+2d** | **6d**, 42 |
| 5 | Ph | 2,4-$Me_2C_6H_3$ | **1a+2g** | **6e**, 53 |
| 6 | 4-$BrC_6H_4$ | 3-$BrC_6H_4$ | **1b+2e** | **6f**, 55 |
| 7 | 4-$MeOC_6H_4$ | 3-$BrC_6H_4$ | **1c+2e** | **6g**, 63[a] |
| 8 | Me | Ph | **1d+2b** | **6h**, 43 |
| 9 | Me | 4-$ClC_6H_4$ | **1d+2c** | **6i**, 38 |

[a] Step wise procedure.

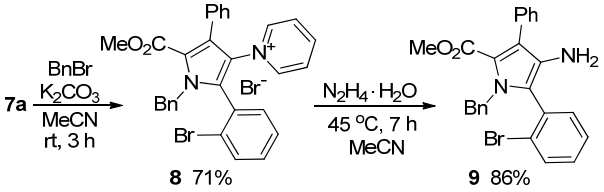
This approach has an important advantage over the above mentioned methodologies 1 and 2 (Scheme 1) since only here is it possible to make the simple introduction of a substituent at the pyrrole nitrogen of compounds **6** via nucleophilic reaction of the corresponding pyridinium ylide. Pyridinium salts **5** were converted in high yield into the corresponding stable pyridinium ylides **7** by the action of potassium hydroxide under very mild conditions (Scheme 3). The ester group remains intact under this procedure.




**7**, **a** $R^1$ = Ph, $R^2$ = 2-$BrC_6H_4$;
**b** $R^1$ = $R^2$ = Ph; **c** $R^1$ = Ph, $R^2$ = 4-$NO_2C_6H_4$;
**d** $R^1$ = Me, $R^2$ = 4-$MeOC_6H_4$

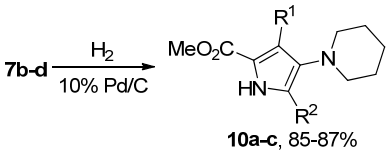
**Scheme 3**. The preparation of ylides **7**

The alkylation provides a good yield of the *N*-alkylation product being produced prior to the deprotection of the amino group by hydrazinolysis. Thus, pyridinium ylide **7a** was converted into *N*-benzyl derivative with benzyl bromide in the presence of potassium carbonate. The deprotection of the *N*-benzylpyridinium salt **8** gave aminopyrrole **9** in high yield (Scheme 4)




**Scheme 4**. The introduction of a substituent at the pyrrole nitrogen

Ylides **7** can be easily transformed in high yield into 4-piperidino-substituted methyl 1*H*-pyrrole-2-carboxylates **10** by hydrogenation on Pd/C (Scheme 5). While the ester group was stable under the reduction of the pyridinium moiety, the nitro-substituent in compound **7c** was reduced to amino group to give compound **10b**.




**10**, **a** $R^1$ = $R^2$ = Ph; **b** $R^1$ = Ph, $R^2$ = 4-$NH_2C_6H_4$;
**c** $R^1$ = Me, $R^2$ = 4-$MeOC_6H_4$

**Scheme 5**. The preparation of methyl 4-(piperidin-1-yl)-1H-pyrrole-2-carboxylates **10**

## Conclusions

A convenient and efficient approach was developed for the synthesis of methyl 4-aminopyrrole-2-carboxylates from easily available compounds, 5-methoxyisoxazoles and phenacylpyridinium salts. The innovation of this synthetic route consists in an implementation of parallel and sequential reaction stages (the generation of an azirine from isoxazoles, the formation of phenacylpyridinium ylide, the activation of azirine, the reaction of the activated azirine with pyridinium ylide) as a domino process under relay catalysis, followed by a one-pot Zincke cleavage of the resulting pyridinium salts. The approach permits the introduction of a substituent at the pyrrole nitrogen via a nucleophilic reaction of the corresponding pyrrolylpyridinium ylide under very mild

conditions. Catalytic hydrogenation of the pyrrolylpyridinium ylides gave 4-piperidino-substituted methyl 1*H*-pyrrole-2-carboxylates.

## Experimental

### General

Melting points were determined on a capillary melting point apparatus Stuart® SMP30. $^1$H (400 MHz) and $^{13}$C (100 MHz) NMR spectra were determined in $CDCl_3$ or DMSO-$d_6$ with Bruker AVANCE III 400. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS δ = 0.00); $^1$H NMR spectra were calibrated according to the residual peak of $CDCl_3$ (7.26 ppm) or DMSO-$d_6$ (2.50 ppm). For all new compounds $^{13}$C{$^1$H} and $^{13}$C DEPT135 were recorded and calibrated according to the peak of $CDCl_3$ (77.00 ppm) or DMSO-$d_6$ (39.51 ppm). Mass spectra were recorded on a Bruker maXis HRMS-ESI-QTOF, electrospray ionization, positive mode. IR-spectra were recorded on a Bruker FT-IR spectrometer Tensor 27 for tablets in KBr, only characteristic absorption is indicated. Thin-layer chromatography (TLC) was conducted on aluminium sheets with 0.2 mm silica gel (fluorescent indicator, Macherey-Nagel). The pyridinium salts[25] and isoxazoles[26] were synthesized by known literature procedures.

### Synthesis of *N*-pyrrolylpyridinium salts 5

**General procedure for the synthesis of *N*-pyrrolylpyridinium salts 5 from isoxazoles 1 and *N*-phenacylpyridinium bromides 2.**

Isoxazole **1** (1.2–1.5 mmol) and pyridinim salt **2** (1.0 mmol) were suspended in MeCN (4 mL), $FeCl_2{\cdot}4H_2O$ (0.06–0.08 mmol, 5 mol% calcd on isoxazole) and $Et_3N$ (3.0 mmol) were added, and the mixture was stirred at 45 °C (6–7 h, monitored by TLC). Reaction mixture was evaporated to dryness, ethyl acetate was added and the precipitate formed was filtered off and washed with ethyl acetate or ethyl acetate/$CH_2Cl_2$ mixture. The residue was purified by column chromatography on silica gel ($CH_2Cl_2$/MeOH 12:1), additionally washed with ethyl acetate or ethyl acetate/$CH_2Cl_2$ mixture and dried to give analytically pure compound **5**.

**1-(2-(2-Bromophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5a).** Compound **5a** (292 mg, 71%) was obtained from 5-methoxy-3-phenylisoxazole (**1a**) (175 mg, 1.00 mmol), 1-(2-(2-bromophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2a**) (286 mg, 0.801 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol) and $Et_3N$ (245 mg, 2.42 mmol) according to the general procedure. Light rose solid, mp 185–187 °C (ethyl acetate). $^1$H NMR (DMSO-$d_6$): δ = 3.72 (s, 3H), 7.25-7.29 (m, 2H), 7.30 (m, 3H), 7.40-7.44 (m, 1H), 7.50-7.54 (m, 1H), 7.65-7.69 (m, 2H), 8.07-8.11 (m, 2H), 8.60-8.65 (m, 1H), 8.85-8.87 (m, 2H), 13.31 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.6, 118.1, 123.3, 125.0, 125.7, 128.0, 128.1, 128.15, 128.22, 128.3, 129.6, 129.7, 129.9, 132.0, 132.7, 133.5, 147.0, 147.5, 160.0. ESI/HRMS (m/z): 433.0546 calcd for $C_{23}H_{18}BrN_2O_2^+$ [M – Br]$^+$, found 433.0563. IR (KBr, cm$^{-1}$): ν 3403, 2998, 1714, 1625.

***1*-(5-(Methoxycarbonyl)-2,4-diphenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5b).** Compound **5b** (294 mg, 84%) was obtained from 5-methoxy-3-phenylisoxazole (**1a**) (175 mg, 1.00 mmol), 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide (**2b**) (223 mg, 0.802 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol) and $Et_3N$ (245 mg, 2.42 mmol) according to the general procedure. Light rose solid, mp 240–243 °C (dec.) (ethyl acetate/$CH_2Cl_2$). $^1$H NMR (DMSO-$d_6$): δ = 3.70 (s, 3H), 7.22-7.24 (m, 2H), 7.27-7.30 (m, 5H), 7.38-7.41 (m, 3H), 8.15-8.19 (m, 2H), 8.69-8.73 (m, 1H), 9.10-9.12 (m, 2H), 13.18 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.6, 118.0, 124.8, 126.7, 127.1, 127.9, 127.99, 128.02, 128.4, 128.9, 129.3, 129.7, 129.9, 130.9, 147.6, 147.7, 160.2. ESI/HRMS (m/z): 355.1441 calcd for $C_{23}H_{19}N_2O_2^+$ [M – Br]$^+$, found 355.1438. IR (KBr, cm$^{-1}$): ν 3397, 2986, 1707, 1626.

**1-(2-(4-Chlorophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5c).** Compound **5c** (280 mg, 75%) was obtained from 5-methoxy-3-phenylisoxazole (1a) (175 mg, 1.00 mmol), 1-(2-(4-chlorophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2c**) (248 mg, 0.793 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol, 5% mol) and $Et_3N$ (245 mg, 2.42 mmol) according to the general procedure. Light rose solid, mp 245–246 °C (dec.) (ethyl acetate/$CH_2Cl_2$). $^1$H NMR (DMSO-$d_6$): δ = 3.71 (s, 3H), 7.20-7.23 (m, 2H), 7.29-7.32 (m, 5H), 7.46-7.49 (m, 2H), 8.69-8.73 (m, 1H), 9.07-9.08 (m, 2H), 13.27 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.6, 118.2, 124.9, 126.0, 126.7, 128.1, 128.1, 128.5, 129.0, 129.6, 129.7, 129.78, 129.83, 134.1, 147.5, 147.8, 160.2. ESI/HRMS (m/z): 389.1051 calcd for $C_{23}H_{18}ClN_2O_2^+$ [M – Br]$^+$, found 389.1052. IR (KBr, cm$^{-1}$): ν 3398, 3000, 1703, 1626.

**1-(5-(Methoxycarbonyl)-2-(4-nitrophenyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5d).** Compound **5d** (247 mg, 64%) was obtained from 5-methoxy-3-phenylisoxazole (**1a**) (175 mg, 1.00 mmol), 1-(2-(4-nitrophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2d**) (259 mg, 0.802 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol) and $Et_3N$ (245 mg, 2.42 mmol) according to the general procedure. Light rose solid, mp 249–250 °C (dec.) (ethyl acetate/$CH_2Cl_2$). $^1$H NMR (DMSO-$d_6$): δ = 3.73 (s, 3H), 7.21-7.24 (m, 2H), 7.29-7.31 (m, 3H), 7.54-7.56 (m, 2H), 8.18-8.21 (m, 2H), 8.22-8.24 (m, 2H), 8.72-7.76 (m, 1H), 9.12-9.13 (m, 2H), 13.53 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.8, 119.3, 124.0, 125.7, 127.0, 128.1, 128.2, 128.5, 128.7, 129.1, 129.6, 129.7, 133.4, 147.3, 147.4, 148.0, 160.1. ESI/HRMS (m/z): 400.1292 calcd for $C_{23}H_{18}N_3O_4^+$ [M – Br]$^+$, found 400.1293. IR (KBr, cm$^{-1}$): ν 3419, 2997, 1724.

**1-(2-(3-Bromophenyl)-4-(4-bromophenyl)-5-(methoxycarbonyl)-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5e).** Compound **5e** (339 mg, 71%) was obtained from 3-(4-bromophenyl)-5-methoxyisoxazole (**1b**) (254 mg, 1.00 mmol), 1-(2-(3-bromophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2e**) (286 mg, 0.801 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol) and $Et_3N$ (245 mg, 2.4 mmol) according to the general procedure. Light rose solid, mp 232–236 °C (dec.) (ethyl acetate/ $CH_2Cl_2$). $^1$H NMR (DMSO-$d_6$): δ = 3.74 (s, 3H), 7.06-7.08 (m, 1H), 7.17-7.19 (m, 2H), 7.28-7.32 (m, 1H), 7.49-7.52 (m, 2H), 7.60-7.62 (m. 1H), 7.67-7.68 (m, 1H), 8.19-8.22 (m, 2H), 8.73-8.76 (m,

1H), 9.08-9.09 (m, 2H), 13.35 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.7, 118.5, 121.7, 122.1, 124.8, 125.3, 126.5, 128.6, 129.0, 129.2, 129.3, 130.96, 131.01, 131.1, 131.9, 132.0, 147.4, 148.0, 160.0. ESI/HRMS (m/z): 510.9651 calcd for $C_{23}H_{17}Br_2N_2O_2^+$ [M – Br]$^+$, found 510.9675. IR (KBr, cm$^{-1}$): ν 3404, 2947, 1699, 1626.

**1-(2-(3-Bromophenyl)-5-(methoxycarbonyl)-4-(4-methoxyphenyl)-1*H*-pyrrol-3-yl)pyridin-1-ium bromide (5f).** Compound **5f** (306 mg, 70%) was obtained from 5-methoxy-3-(4-methoxyphenyl)isoxazole (**1c**) (205 mg, 1.00 mmol), 1-(2-(3-bromophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2e**) (286 mg, 0.801 mmol), $FeCl_2{\cdot}4H_2O$ (10 mg, 0.05 mmol) and $Et_3N$ (245 mg, 2.4 mmol) according to the general procedure. Light yellow solid, mp 211–212 °C. $^1$H NMR (DMSO-$d_6$): δ = 3.73 (s, 6H), 6.84-6.87 (m, 2H), 7.06-7.08 (m, 1H), 7.11-7.12 (m, 1H), 7.28-7.32 (m, 1H), 7.60-7.62 (m, 1H), 7.68 (s, 1H), 8.18-8.22 (m, 2H), 8.72-8.76 (m, 1H), 9.06-9.08 (m, 2H), 13.22 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.7, 55.0, 113.6, 118.4, 121.5, 122.1, 125.1, 126.4, 126.5, 128.6, 129.0, 129.4, 130.95, 130.98, 131.02, 132.0, 147.5, 147.8, 158.9, 160.2. ESI/HRMS (m/z): 465.0633 calcd for $C_{24}H_{20}BrN_2O_3^+$ [M – Br]$^+$, found 465.0655. IR (KBr, cm$^{-1}$): ν 3634, 3337, 1697, 1450.

**1-(5-(Methoxycarbonyl)-4-methyl-2-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5g).** Compound **5g** (181 mg, 49%) was obtained from 5-methoxy-3-methylisoxazole (**1d**) (170 mg, 1.5 mmol), 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide (**2b**) (278 mg, 1.00 mmol), $FeCl_2{\cdot}4H_2O$ (15 mg, 0.08 mmol) and $Et_3N$ (300 mg, 3.0 mmol) according to the general procedure. Before chromatography crude residue was washed with $CH_2Cl_2$. Light rose solid, mp 252–253 °C (dec.) (ethyl acetate/$CH_2Cl_2$). $^1$H NMR (DMSO-$d_6$): δ = 2.21 (s, 3H), 3.88 (s, 3H), 7.19-7.21 (m, 2H), 7.33-7.37 (m, 3H), 8.28-8.31 (m, 2H), 8.80-8.84 (m, 1H), 9.14-9.16 (m, 2H), 12.81 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 8.8, 51.6, 118.2, 122.4, 125.6, 127.3, 127.8, 128.8, 128.9, 129.1, 130.7, 147.3, 137.4, 160.8. ESI/HRMS (m/z): 293.1285 calcd for $C_{18}H_{17}BrN_2O_2^+$ [M – Br]$^+$, found 293.1291. IR (KBr, cm$^{-1}$): ν 3060, 2987, 2861, 1697, 1626.

**1-(2-(4-Chlorophenyl)-5-(methoxycarbonyl)-4-methyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (5h).** Compound **5h** (267 mg, 66%) was obtained from 5-methoxy-3-methylisoxazole (**1d**) (170 mg, 1.50 mmol), 1-(2-(4-chlorophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2c**) (313 mg, 1.00 mmol), $FeCl_2{\cdot}4H_2O$ (15 mg, 0.08 mmol) and $Et_3N$ (300 mg, 3.0 mmol) according to the general procedure. Before the chromatography crude residue was washed with $CH_2Cl_2$. Light yellow solid, mp 232–234 °C (dec.) (ethyl acetate). $^1$H NMR (DMSO-$d_6$): δ = 2.21 (s, 3H), 3.88 (s, 3H), 7.20-7.24 (m, 2H), 7.42-7.45 (m, 2H), 8.28-8.32 (m, 2H), 8.80-8.84 (m, 1H), 9.13-9.14 (m, 2H), 12.87 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 8.9, 51.7, 118.5, 122.4, 125.8, 126.2, 128.9, 129.0, 129.5, 129.7, 133.8, 147.2, 147.4, 160.8. ESI/HRMS (m/z): 327.0895 calcd for $C_{18}H_{16}ClN_2O_2^+$ [M – Br]$^+$, found 327.0901. IR (KBr, cm$^{-1}$): ν 3423, 3112, 3040, 1709, 1624.

**1-(5-(Methoxycarbonyl)-2-(4-methoxyphenyl)-4-methyl-1*H*-pyrrol-3-yl)pyridin-1-ium bromide (5i).** Compound **5i** (504 mg, 63%) was obtained from 5-methoxy-3-methylisoxazole (**1d**) (340 mg, 3.00 mmol), 1-(2-(4-methoxyphenyl)-2-oxoethyl)pyridin-1-ium bromide (**2f**) (616 mg, 2.00 mmol), $FeCl_2{\cdot}4H_2O$ (30 mg, 0.16 mmol) and $Et_3N$ (600 mg, 6.0 mmol) according to the general procedure. Bright yellow solid, mp 205–207 °C (dec.) (ethyl acetate). $^1$H NMR (DMSO-$d_6$): δ = 2.20 (s, 3H), 3.74 (s, 3H), 3.87 (s, 3H), 6.91 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.6 Hz, 2H), 8.27-8.31 (m, 2H), 8.79-8.83 (m, 1H), 9.11-9.12 (m, 2H), 12.68 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 8.9, 51.5, 55.2, 114.4, 117.7, 119.5, 122.3, 125.2, 128.8, 129.3, 130.8, 147.2, 147.3, 159.8, 160.9. ESI/HRMS (m/z): 323.1390 calcd for $C_{19}H_{19}N_2O_3^+$ [M – Br]$^+$, found 323.1401. IR (KBr, cm$^{-1}$): 3408, 3368, 3115, 3057, 1705, 1616.

**2-(2-(4-Chlorophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)isoquinolin-2-ium bromide (5j).** Compound **5j** (175 mg, 34%) was obtained from 5-methoxy-3-phenylisoxazole (**1a**) (210 mg, 1.20 mmol), 1-(2-(4-chlorophenyl)-2-oxoethyl)isoquinolin-1-ium bromide (**2g**) (363 mg, 1.00 mmol), $FeCl_2{\cdot}4H_2O$ (12 mg, 0.06 mmol) and $Et_3N$ (300 mg, 3.0 mmol) according to the general procedure. Light yellow solid, mp 226–230 °C (dec.) (water). $^1$H NMR (DMSO-$d_6$): δ = 3.72 (s, 3H), 7.21-7.25 (m, 5H), 7.33-7.35 (m, 2H), 7.42-7.44 (m, 2H), 8.05-8.09 (m, 1H), 8.30-8.33 (m, 1H), 8.36-8.40 (m, 2H), 8.58-8.59 (m, 1H), 8.71-8.73 (m, 1H), 10.12 (s, 1H), 13.29 (br s, 1H). $^{13}$C NMR (DMSO-$d_6$): δ = 51.7, 118.4, 124.9, 126.1, 126.2, 127.0, 127.1, 127.5, 128.0, 128.0, 129.1, 129.75, 129.79, 129.84, 131.0, 131.9, 134.0, 137.2, 137.3, 138.5, 152.6, 160.2. ESI/HRMS (m/z): 439.1208 calcd for $C_{27}H_{20}ClN_2O_2^+$ [M – Br]$^+$, found 439.1211. IR (KBr, cm$^{-1}$): ν 3398, 2997, 1708, 1637.

**Synthesis of aminopyrroles 6**

**General procedure for the one-pot synthesis of aminopyrroles 6 by the reaction of isoxazoles 1 with pyridinium bromides 2 followed by the treatment with hydrazine.**

Isoxazole (1.2–1.5 mmol) **1** and pyridinium bromide (1.0 mmol) **2** were suspended in MeCN (4 mL), $FeCl_2{\cdot}4H_2O$ (0.06–0.08 mmol, 5% mol) and $Et_3N$ (3.0 mmol) were added, and the mixture obtained was stirred at 45°C till the completion of the reaction (6–7 h, monitored by TLC). Hydrazine hydrate (10.0 mmol, 10 equiv) was added and the mixture was stirred at 45°C (6–7 h, monitored by TLC). Then the reaction mixture was evaporated to dryness. The residue was purified by column chromatography on silica gel ($CH_2Cl_2$/MeOH 40:1), additionally washed with $Et_2O$ or water and dried to give analytically pure compound **6**.

**Methyl 4-amino-5-(2-bromophenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (6a).** Compound **6a** (341 mg, 64%) was obtained from 5-methoxy-3-phenylisoxazole (**1a**) (304 mg, 1.74 mmol), 1-(2-(2-bromophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2a**) (516 mg, 1.445 mmol), FeCl2·4H2O (18 mg, 0.09 mmol), Et3N (450 mg, 4.52 mmol) and hydrazine hydrate (750 mg, 15.0 mmol) according to the general procedure. Light yellow solid, mp 138–140 °C (water). 1H NMR (CDCl3): δ = 3.16 (br s, 2H), 3.71 (s, 3H), 7.20-7.24 (m, 1H), 7.32-7.50 (m, 6H), 7.58-7.60 (m, 1H), 7.69-7.71 (m, 1H), 8.95 (br s, 1H). 13C NMR (CDCl3): δ = 51.2, 116.7, 119.3, 120.9, 122.5, 127.1, 127.8, 128.2, 129.5, 129.8, 130.3, 131.5, 132.3, 133.1, 133.8, 161.4. ESI/HRMS (m/z): 371.0390 calcd for $C_{18}H_{16}BrN_2O_2^+$ [M + H]+, found 371.0385. IR (KBr, cm-1): ν 3297, 1677, 1604.

**Methyl 4-amino-3,5-diphenyl-1*H*-pyrrole-2-carboxylate (6b).** Compound **6b** (183 mg, 63%) was obtained from 5-methoxy-3-phenylisoxazole **(1a)** (210 mg, 1.20 mmol), 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **(2b)** (278 mg, 1.00 mmol), $FeCl_2{\cdot}4H_2O$ (12 mg, 0.06 mmol), $Et_3N$ (300 mg, 3.0 mmol) and hydrazine hydrate (500 mg, 10.0 mmol) according to the general procedure. Before chromatography the crude residue was washed with EtOH. Light yellow solid, mp 151–153 °C (ether). $^1$H NMR (DMSO-$d_6$): δ = 3.61 (s, 3H), 3.66 (br s, 2H), 7.23-7.27 (m, 1H), 7.29-7.37 (m, 3H), 7.40-7.44 (m, 4H), 7.76-7.77 (m, 2H), 11.37 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 50.6, 116.1, 121.1, 121.3, 126.1, 126.2, 126.5, 127.9, 128.4, 129.5, 130.2, 131.8, 133.6, 160.7. ESI/HRMS (m/z): 293.1285 calcd for $C_{18}H_{17}N_2O_2^+$ [M + H]$^+$, found 293.1277. IR (KBr, cm$^{-1}$): ν 3302, 1674.

**Methyl 4-amino-5-(4-chlorophenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (6c).** Compound **6c** (156 mg, 52%) was obtained from 5-methoxy-3-phenylisoxazole **(1a)** (194 mg, 1.11 mmol), 1-(2-(4-chlorophenyl)-2-oxoethyl)pyridin-1-ium bromide **(2c)** (288 mg, 0.921 mmol), $FeCl_2{\cdot}4H_2O$ (11 mg, 0.06 mmol, 5% mol), $Et_3N$ (300 mg, 3.0 mmol) and hydrazine hydrate (500 mg, 10.0 mmol) according to the general procedure. Before chromatography the crude residue was washed with EtOH. Light yellow solid, mp 160–162 °C (ether). $^1$H NMR (DMSO-$d_6$): δ = 3.61 (s, 3H), 3.70 (br s, 2H), 7.30-7.35 (m, 3H), 7.39-7.43 (m, 2H), 7.44-7.46 (m, 2H), 7.80-7.82 (m, 2H), 11.44 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 50.7, 116.6, 120.0, 121.5, 126.6, 127.8, 127.9, 128.3, 129.9, 130.1, 130.3, 130.7, 133.5, 160.7. ESI/HRMS (m/z): 327.0895 calcd for $C_{18}H_{16}ClN_2O_2^+$ [M + H]$^+$, found 327.0886. IR (KBr, cm$^{-1}$): ν 3268, 1664.

**Methyl 4-amino-5-(4-nitrophenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (6d).** Compound **6d** (90 mg, 42%) was obtained from 5-methoxy-3-phenylisoxazole **(1a)** (135 mg, 0.771 mmol), 1-(2-(4-nitrophenyl)-2-oxoethyl)pyridin-1-ium bromide **(2d)** (205 mg, 0.634 mmol), $FeCl_2{\cdot}4H_2O$ (8 mg, 0.04 mmol), $Et_3N$ (180 mg, 1.8 mmol) and hydrazine hydrate (300 mg, 6.0 mmol) according to the general procedure. Before chromatography the crude residue was washed by EtOH. Bright red solid, mp 211–216 °C (ether). $^1$H NMR (DMSO-$d_6$): δ = 3.64 (s, 3H), 4.05 (br s, 2H), 7.33-7.35 (m, 3H), 7.41-7.45 (m, 2H), 8.05 (m, 2H), 8.22-8.24 (m, 2H), 11.64 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 51.0, 118.7, 119.1, 121.1, 123.7, 125.9, 126.8, 128.0, 130.1, 132.8, 132.9, 138.5, 144.1, 160.6. ESI/HRMS (m/z): 338.1135 calcd for $C_{18}H_{16}N_3O_4^+$ [M + H]$^+$, found 338.1126. IR (KBr, cm$^{-1}$): ν 3410, 3323, 1670.

**Methyl 4-amino-5-(2,4-dimethylphenyl)-3-phenyl-1*H*-pyrrole-2-carboxylate (6e).** Compound **6e** (203 mg, 53%) was obtained from 5-methoxy-3-phenylisoxazole **(1a)** (247 mg, 1.41 mmol), 1-(2-(2,4-dimethylphenyl)-2-oxoethyl)pyridin-1-ium bromide **(2g)** (368 mg, 1.20 mmol), $FeCl_2{\cdot}4H_2O$ (14 mg, 0.07 mmol), $Et_3N$ (300 mg, 3.0 mmol) and hydrazine hydrate (600 mg, 12.0 mmol) according to the general procedure. Colorless solid, mp 164–165 °C (ether-hexane). $^1$H NMR ($CDCl_3$): δ = 2.39 (s, 6H), 2.95 (br s, 2H), 3.69 (s, 3H), 7.09-7.11 (m, 2H), 7.16 (s, 1H), 7.31-7.35 (m, 2H), 7.43-7.47 (m, 2H), 7.52-7.54 (m, 2H), 8.80 (br s, 1H).$^{13}$C NMR ($CDCl_3$): δ = 19.6, 21.1, 51.0, 115.8, 120.9, 121.3, 126.8, 126.9, 127.6, 128.0, 128.7, 130.0, 130.2, 131.5, 133.4, 137.2, 138.3, 161.6. ESI/HRMS (m/z): 321.1598 calcd for $C_{20}H_{21}N_2O_2^+$ [M + H]$^+$, found 321.1657. IR (KBr, cm$^{-1}$): ν 3310, 1670, 1452.

**Methyl 4-amino-3-(4-bromophenyl)-5-(3-bromophenyl)-1*H*-pyrrole-2-carboxylate (6f).** Compound **6f** (249 mg, 55%) was obtained from 3-(4-bromophenyl)-5-methoxyisoxazole (**1b**) (305 mg, 1.20 mmol), 1-(2-(3-bromophenyl)-2-oxoethyl)pyridin-1-ium bromide (**2e**) (357 mg, 1.00 mmol), $FeCl_2{\cdot}4H_2O$ (12 mg, 0.06 mmol), $Et_3N$ (300 mg, 3.0 mmol) and hydrazine hydrate (500 mg, 10.0 mmol) according to the general procedure. Before chromatography the crude residue was washed by EtOH. Light grey solid, mp 169–170 °C (ether). $^1$H NMR (DMSO-$d_6$): δ = 3.63 (s, 3H), 3.81 (br s, 2H), 7.29-7.31 (m, 2H), 7.33-7.37 (m, 1H), 7.40-7.42 (m, 1H), 7.57-7.59 (m, 1H), 7.78-7.80 (m, 1H), 8.00-8.01 (m, 1H), 11.56 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 50.8, 116.9, 119.6, 119.9, 120.1, 122.0, 124.9, 128.47, 128.53, 130.3, 130.4, 130.8, 132.4, 132.7, 134.0, 160.5. ESI/HRMS (m/z): 448.9495 calcd for $C_{18}H_{15}Br_2N_2O_2^+$ [M + H]$^+$, found 448.9485. IR (KBr, cm$^{-1}$): ν 3306, 1685.

**Methyl 4-amino-5-(3-bromophenyl)-3-(4-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (6g).**

Compound **6g** (17 mg, 63%) was obtained from 1-(2-(3-bromophenyl)-5-(methoxycarbonyl)-4-(4-methoxyphenyl)-1*H*-pyrrol-3-yl)pyridin-1-ium bromide (**5f**) (36 mg, 0.0661 mmol) and hydrazine hydrate (66 mg, 1.322 mmol). Colorless solid, mp 138–140 °C (ether-hexane). $^1$H NMR ($CDCl_3$): δ = 3.24 (br s, 2H), 3.72 (s, 3H), 3.86 (s, 3H), 6.98 (d, *J* = 7.7 Hz, 2H), 7.26-7.30 (m, 1H), 7.32-7.39 (m, 3H), 7.54 (d, *J* = 8.7 Hz, 1H), 7.78 (s, 1H), 8.87 (br s, 1H).$^{13}$C NMR ($CDCl_3$): δ = 51.3, 55.2, 113.7, 117.3, 119.1. 121.9, 123.4, 123.9, 124.8, 128.2, 129.63, 129.69, 130.7, 131.3, 133.8, 158.9, 161.5. ESI/HRMS (m/z): 403.0520 calcd for $C_{19}H_{18}BrN_2O_3^+$ [M + H]$^+$, found 403.0476. IR (KBr, cm$^{-1}$): ν 3314, 1662, 1450.

**Methyl 4-amino-3-methyl-5-phenyl-1*H*-pyrrole-2-carboxylate (6h).** Compound **6h** (149 mg, 43%) was obtained from 5-methoxy-3-methylisoxazole **(1c)** (230 mg, 2.03 mmol), 1-(2-oxo-2-phenylethyl)pyridin-1-ium bromide **(2b)** (415 mg, 1.49 mmol), $FeCl_2{\cdot}4H_2O$ (20 mg, 0.10 mmol), $Et_3N$ (450 mg, 4.5 mmol) and hydrazine hydrate (750 mg, 15.0 mmol) according to the general procedure. Colorless solid, mp 119–120 °C (ether/hexane). $^1$H NMR ($CDCl_3$): δ = 2.28 (s, 3H), 3.13 (br s, 2H), 3.85 (s, 3H), 7.25-7.29 (m, 1H), 7.41-7.44 (m, 2H), 7.53-7.55 (m, 2H), 8.67 (br s, 1H).$^{13}$C NMR ($CDCl_3$): δ = 9.1, 51.1, 117.3, 117.7, 121.4, 125.6, 126.8, 129.2, 131.9, 162.1. ESI/HRMS (m/z): 231.1128 calcd for $C_{13}H_{15}N_2O_2^+$ [M + H]$^+$, found 231.1134. IR (KBr, cm$^{-1}$): ν 3344, 1673.

**Methyl 4-amino-5-(4-chlorophenyl)-3-methyl-1*H*-pyrrole-2-carboxylate (6i).** Compound **6i** (149 mg, 38%) was obtained from 5-methoxy-3-methylisoxazole **(1c)** (230 mg, 2.03 mmol), 1-(2-(4-chlorophenyl)-2-oxoethyl)pyridin-1-ium bromide **(2c)** (469 mg, 1.50 mmol), $FeCl_2{\cdot}4H_2O$ (20 mg, 0.10 mmol), $Et_3N$ (450 mg, 4.5 mmol) and hydrazine hydrate (750 mg, 15.0 mmol) according to the general procedure. according to the general procedure. Colorless solid, mp 148–151 °C (ether/hexane). $^1$H NMR (DMSO-$d_6$): δ = 2.17 (s, 3H), 3.76 (s, 3H), 3.92 (s, 2H), 7.39-7.42 (m, 2H), 7.74-7.76 (m, 2H), 10.97 (br s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 9.2, 50.6, 116.9, 117.0,

119.9, 127.5, 128.2, 129.9, 131.03, 131.04, 161.3. ESI/HRMS (m/z): 265.0738 calcd for $C_{13}H_{14}ClN_2O_2^+$ [M + H]$^+$, found 265.0734. IR (KBr, cm$^{-1}$): ν 3347, 1690, 1650.

**General procedure for the synthesis of pyrrolylpyridinium ylides 7 from *N*-pyrrolylpyridinium salts 5**

*N*-pyrrolylpyridinium salt **5** (1 mmol) was suspended in water (2 mL) and the excess of 2-5% aq KOH (2-4 mmol) was added. The suspension was stirred for 15 min, the solid was filtered off, washed with water and dried to give analytically pure compound.

**5-(2-Bromophenyl)-2-(methoxycarbonyl)-3-phenyl-4-(pyridine-1-ium-1-yl)pyrrol-1-ide (7a).** Compound **7** (324 mg, 96%) was obtained from 1-(2-(2-bromophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide **(5a)** (400 mg, 0.78 mmol) and aq solution of KOH (84 mg, 1.50 mmol, 4 mL $H_2O$). Bright orange solid, mp 160 °C. $^1$H NMR ($CDCl_3$): δ = 3.77 (s, 3H), 7.10-7.14 (m, 1H), 7.20-7.26 (m, 5H), 7.35-7.40 (m, 2H), 7.57-7.61 (m, 2H), 7.87-7.89 (m, 1H), 8.05-8.09 (m, 1H), 8.16-8.17 (m, 2H).$^{13}$C NMR ($CDCl_3$): δ = 50.8, 123.0, 124.5, 125.2, 126.6, 126.9, 128.1, 128.3, 128.4, 129.0, 130.3, 132.2, 134.1, 134.3, 135.6, 136.1, 140.9, 144.3, 165.1. ESI/HRMS (m/z): 433.0546 calcd for $C_{23}H_{18}BrN_2O_2^+$ [M + H]$^+$, found 433.0534. IR (KBr, cm$^{-1}$): ν 3067, 1678.

**2-(Methoxycarbonyl)-3,5-diphenyl-4-(pyridine-1-ium-1-yl)pyrrol-1-ide (7b).** Compound **7b** (324 mg, 96%) was obtained from 1-(5-(methoxycarbonyl)-2,4-diphenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (**5b**) (240 mg, 0.55 mmol) and aq solution of KOH (100 mg, 1.79 mmol, 2mL $H_2O$). Bright orange solid, dec. >213 °C without melting. $^1$H NMR (DMSO-$d_6$): δ = 3.56 (s, 3H), 7.08-7.20 (m, 10H), 8.01-8.04 (m, 2H), 8.53-8.56 (m, 1H), 8.86-8.88 (m, 2H).$^{13}$C NMR (DMSO-$d_6$): δ = 49.9, 125.1, 125.8, 125.8, 125.9, 126.8, 127.5, 127.9, 128.4, 129.7, 134.15, 134.24, 134.9, 145.3, 147.2, 164.2. ESI/HRMS (m/z): 355.1441 calcd for $C_{23}H_{19}N_2O_2^+$ [M + H]$^+$, found 355.1456. IR (KBr, cm$^{-1}$): ν 3356, 3065, 1670.

**2-(Methoxycarbonyl)-5-(4-nitrophenyl)-3-phenyl-4-(pyridine-1-ium-1-yl)pyrrol-1-ide (7c).** Compound **7c** (144 mg, 91%) was obtained from 1-(5-(methoxycarbonyl)-2-(-4-nitrophenyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (**5d**) (190 mg, 0.40 mmol) and aq solution of KOH (50 mg, 0.90 mmol, 1mL $H_2O$). Bright orange solid, dec. >300 °C without melting. $^1$H NMR (DMSO-$d_6$): δ = 3.58 (s, 3H), 7.06-7.08 (m, 2H), 7.13-7.17 (m, 3H), 7.31 (d, J = 8.8 Hz, 2H), 8.04 (d, J = 8.8 Hz, 2H), 8.07-8.10 (m, 2H), 8.60-8.64 (m, 1H), 8.97-8.99 (m, 2H).$^{13}$C NMR (DMSO-$d_6$): δ = 50.0, 124.0, 125.4, 126.1, 126.6, 127.5, 127.8, 128.0, 128.2, 129.6, 131.8, 133.9, 142.1, 144.2, 145.9, 147.2, 164.3. ESI/HRMS (m/z): 400.1292 calcd for $C_{23}H_{18}N_3O_4^+$ [M + H]$^+$, found 400.1306. IR (KBr, cm$^{-1}$): ν 3319, 3065. 1692.

**2-(Methoxycarbonyl)-5-(4-methoxyphenyl)-3-methyl-4-(pyridine-1-ium-1-yl)pyrrol-1-ide (7d).** Compound **7d** (140 mg, 91%) was obtained from 1-(5-(methoxycarbonyl)-2-(-4-methoxyphenyl)-4-methyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (**5i**) (193 mg, 0.48 mmol) and aq solution of KOH (75 mg, 1.34 mmol, 1.5 mL $H_2O$). Bright yellow solid, dec. >203 °C without melting. $^1$H NMR (DMSO-$d_6$): δ = 2.13 (s, 3H), 3.65 (s, 3H), 3.68 (s, 3H), 6.73 (d, J = 8.7 Hz, 2H), 6.97 (d, J = 8.7 Hz), 2H), 8.11-8.14 (m, 2H), 8.57-8.61 (m, 1H), 8.87-8.89 (m, 2H).$^{13}$C NMR (DMSO-$d_6$): δ = 10.2, 49.5, 54.9, 113.7, 121.1, 125.5, 125.7, 126.8, 128.1, 128.9, 134.4, 144.2, 146.5, 157.1, 165.4. ESI/HRMS (m/z): 323.1390 calcd for $C_{19}H_{19}N_2O_3^+$ [M + H]$^+$, found 323.1401. IR (KBr, cm$^{-1}$): ν 3528, 3393, 1670

**Introduction of a substituent at the pyrrole nitrogen**

**1-(1-Benzyl-2-(2-bromophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide (8).** A mixture of 5-(2-bromophenyl)-2-(methoxycarbonyl)-3-phenyl-4-(pyridine-1-ium-1-yl)pyrrol-1-ide (**7a**) (324 mg, 0.748 mmol), benzyl bromide (256 mg, 1.50 mmol) and $K_2CO_3$ (207 mg, 1.50 mmol) was stirred in MeCN (15 mL) for 3 h at room temperature. The solvent was removed on a rotary evaporator and the residue was purified by column chromatography ($CH_2Cl_2$/MeOH 15:1) to give analytically pure compound as bright orange solid, 320 mg (71%), mp 188–189 °C. $^1$H NMR ($CDCl_3$): δ = 3.54 (s, 3H), 5.31 (d, *J* = 15.6 Hz, 1H), 5.72 (d, *J* = 15.6 Hz, 1H), 6.99-7.01 (m, 2H), 7.22-7.32 (m, 9H), 7.40-7.44 (m, 1H), 7.50-7.52 (m, 1H), 7.84-7.86 (m, 1H), 8.06-8.09 (m, 2H), 8.47-8.51 (m, 1H), 8.95-8.96 (m, 2H).$^{13}$C NMR ($CDCl_3$): δ = 50.5, 51.5, 120.0, 124.8, 125.7, 126.6, 126.8, 126.9, 127.6, 128.4, 128.5, 128.6, 128.7, 128.8, 129.9, 130.0, 132.6, 132.9, 133.2, 134.7, 136.1, 146.5, 146.6, 160.70. ESI/HRMS (m/z): 523.1016 calcd for $C_{30}H_{24}BrN_2O_2^+$ [M – Br]$^+$, found 523.1033. IR (KBr, cm$^{-1}$): ν 3028, 1709, 1626.

**Methyl 4-amino-1-benzyl-5-(2-bromophenyl)-3-phenyl-1*H*-pyrrol-2-carboxylate (9).** A solution of 1-(1-benzyl-2-(2-bromophenyl)-5-(methoxycarbonyl)-4-phenyl-1*H*-pyrrol-3-yl)pyridine-1-ium bromide **(8)** (300, 0.496 mmol) and hydrazine hydrate (250 mg, 5.00 mmol) in MeCN (10 mL) was stirred at 45 °C for 7 h. Then the reaction mixture was evaporated to dryness. The residue was purified by column chromatography on silica gel ($CH_2Cl_2$/MeOH 40:1), additionally washed with hexane and dried to give analytically pure compound as light yellow oil, 196 mg (86%). $^1$H NMR ($CDCl_3$): δ = 2.90 (br s, 2H), 3.49 (s, 3H), 5.15 (d, *J* = 15.9 Hz, 1H), 5.63 (d, *J* = 15.9 Hz, 1H), 6.85-6.87 (m, 2H), 7.13-7.34 (m, 7H), 7.39-7.43 (m, 4H), 7.66-7.68 (m, 1H).$^{13}$C NMR ($CDCl_3$): δ = 49.4, 50.7, 117.6, 122.5, 124.9, 126.0, 126.1, 126.7, 126.8, 127.6, 128.0, 128.2, 128.9, 130.2, 130.4, 131.6, 133.2, 133.6, 134.5, 139.0, 162.0. ESI/HRMS (m/z): 461.0859 calcd for $C_{25}H_{22}BrN_2O_2^+$ [M + H]$^+$, found 461.0869. IR (KBr, cm$^{-1}$): ν 3415, 3343, 3029, 2948, 1695, 1604.

**General procedure for the preparation of methyl 4-(piperidin-1-yl)-1H-pyrrole-2-carboxylates 10 by hydrogenation of pyrrolylpyridinium ylides 7**

Hydrogen was passed through a suspension of ylide (100 mg) and Adams' catalyst (10 mg, 10% w/w) in MeOH (2 mL) till the completion of the reaction (0.5-1.5 h, monitored by TLC). Then the reaction mixture was evaporated to dryness. The residue was purified by column chromatography on silica gel ($CH_2Cl_2$/MeOH 40:1), additionally washed with hexane and dried to give analytically pure compound **10**.

**Methyl 3,5-diphenyl-4-(piperidine-1-yl)-1*H*-pyrrole-2-carboxylate (10a).** Compound **10a** (107 mg, 88%) was obtained

from ylide **7b** (120 mg) and Adams' catalyst (12 mg) for 0.5 h. Colorless solid, mp 172-174 °C ($CH_2Cl_2$-hexane). $^1$H NMR ($CDCl_3$): δ = 1.31-1.35 (m, 2H), 1.41-1.47 (m, 4H), 2.70-2.73 (m, 4H), 3.63 (s, 3H), 7.31-7.44 (m, 8H), 7.85-7.86 (m, 2H), 8.98 (br s, 1H).$^{13}$C NMR ($CDCl_3$): δ = 24.1, 26.7, 51.1, 53.7, 116.7, 126.6, 126.9, 127.2, 127.4, 128.0, 128.5, 129.8, 130.7, 131.9, 135.5, 136.6, 161.5. ESI/HRMS (m/z): 361.1911 calcd for $C_{23}H_{25}N_2O_2^+$ $[M + H]^+$, found 361.1929. IR (KBr, $cm^{-1}$): ν 3323, 2940, 1674.

**Methyl 5-(4-aminophenyl)-3-phenyl-4-(piperidine-1-yl)-1*H*-pyrrole-2-carboxylate (10b).** Compound **10b** (111mg, 87%) was obtained from ylide **7c** (135mg) and Adams' catalyst (14mg) for 1.5 h. Colorless solid, mp 195-197 °C ($CH_2Cl_2$-hexane). $^1$H NMR (DMSO-$d_6$): δ = 1.21-1.24 (m, 2H), 1.30-1.35 (m, 4H), 3.50 (s, 3H), 5.19 (s, 2H), 6.58 (d, J = 8.5 Hz, 2H), 7.26-7.34 (m, 5H), 7.58 (d, J = 8.5 Hz, 2H), 11.18 (s, 1H).$^{13}$C NMR (DMSO-$d_6$): δ = 23.7, 26.2, 50.4, 53.3, 113.2, 114.8, 119.3, 126.4, 127.0, 128.5, 129.2, 130.0, 130.6, 134.2, 136.1, 148.0, 160.6. ESI/HRMS (m/z): 376.2020 calcd for $C_{23}H_{26}N_3O_2^+$ $[M + H]^+$, found 376.2035. IR (KBr, $cm^{-1}$): ν 3312, 2930, 1676.

**Methyl 5-(4-methoxyphenyl)-3-methyl-4-(piperidine-1-yl)-1*H*-pyrrole-2-carboxylate (10c).** Compound **10c** (104 mg, 85%) was obtained from ylide **7c** (120 mg) and Adams' catalyst (12 mg) for 0.5 h. Colorless solid, mp 140-141 °C ($CH_2Cl_2$-hexane). $^1$H NMR ($CDCl_3$): δ = 1.50-1.54 (m, 2H), 1.58-1.64 (m, 4H), 2.40 (s, 3H), 2.97-2.99 (m, 4H), 3.84 (s, 3H), 3.84 (s, 3H), 6.92-6.95 (m, 2H), 7.65 -7.67 (m, 2H), 8.62 (br s, 1H).$^{13}$C NMR ($CDCl_3$): δ = 11.3, 24.3, 27.0, 51.0, 52.9, 55.3, 113.8, 116.4, 124.8, 126.5, 128.4, 129.2, 135.7, 159.0, 162.1. ESI/HRMS (m/z): 329.1860 calcd for $C_{19}H_{25}N_2O_3^+$ $[M + H]^+$, found 329.1873. IR (KBr, $cm^{-1}$): ν 3335, 2930, 1670.

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