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An efficient entry to pyrrolo[1,2-*b*]isoquinolines and related systems through Parham cyclisation

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Abstract—Aryllithiums generated by lithium–iodine exchange undergo intramolecular cyclisation to give pyrrolo[1,2-*b*]isoquinolines, in high yields. The best results were obtained when Weinreb or morpholine amides were used as internal electrophiles. The procedure has been extended to the preparation of seven and eight membered rings, opening a route to benzazepine and benzazocine skeletons.

1. Introduction

Aryl and heteroaryllithium compounds[1] are interesting building blocks in synthetic organic chemistry because by reaction with carbon electrophiles they produce, together with the formation of a carbon–carbon bond, the transference of functionality to the electrophilic reagent, so polyfunctionalised molecules can be prepared in one step. Lithium–halogen exchange, though mechanistically controversial,[2] is a particularly useful tactic for the metalation of aromatic substrates, because metal–halogen exchange can effectively compete with the organolithium reaction with internal electrophiles.[3] Once generated, the aryllithiums may react with internal or external electrophiles and give rise to cyclisation reactions.

The intramolecular cyclisations that employ aryllithiums generated by lithium–halogen exchange are known as Parham cyclisations. Thus, the aromatic metalation–cyclisation sequence has become a valuable protocol for the regiospecific construction of carbocyclic and heterocyclic systems.[4] When the internal electrophile is a carboxylate, this anionic cyclisation could be considered as an anionic Friedel–Crafts equivalent, with the advantage that it lacks the electronic requirements of the classical reaction. The complementary character of the anionic and classical cyclisations is exemplified by the synthesis of azafluorenone alkaloids.[5] Acid derivatives, such as amides and carbamates constitute even more effectively used internal electrophiles than the carboxylates in Parham-type cycliacylations.[6] For instance, Avendaño[7] has applied this protocol to the synthesis of 1,8-diazanthracene-9,10-diones using a tandem directed *ortho*-metalation/metal–halogen exchange reactions. Various amides can be used for these reactions and, in some cases, it has been reported that there is an influence of the nature of the susbstituents at nitrogen in the course of the cyclisation reaction. Thus, Quallich[8] has prepared azatetralones starting from 3-bromopyridines with a *N*,*N*-dialkylaminocarbonylpropyl substituent at C-2. Although three different amides (dimethyl, diisopropyl, and pyrrolidine) were tested as substrates for this carbanionic ring annelation, best results were obtained with the *N*,*N*-dimethyl derivative. However, when Wu et al.[9] applied a similar Parham cyclisation protocol to the synthesis of dibenzocycloheptenone derivatives, they found no significant influence of the nitrogen substitution pattern in the cyclisation yields.

On the other hand, Weinreb[10] amides have been widely used in synthesis, although their use in Parham cyclisations is scarce. Thus, aryl and heteroaryllithium compounds have been generated in the presence of this group to give access to benzocyclobutenones,[11] thieno[2,3-*b*]thiophenes,[12] or methylideneindanones.[13] Weinreb amides have also been successfully used as internal electrophiles in cyclisation reactions of organolithiums derived from alkyl iodides, accessing cyclic ketones,[14] or vinyl iodides, in the synthesis of (−)-Brunsvigine,[15] or the hexahydrobenzofuran subunit of Avermeticin.[16]

In connection with our interest in aromatic lithiation,[17] we decided to develop an anionic cyclisation approach toward

Keywords: Lithiation; Lithium–halogen exchange; Parham cyclisation; Pyrrolo[1,2-*b*]isoquinoline.
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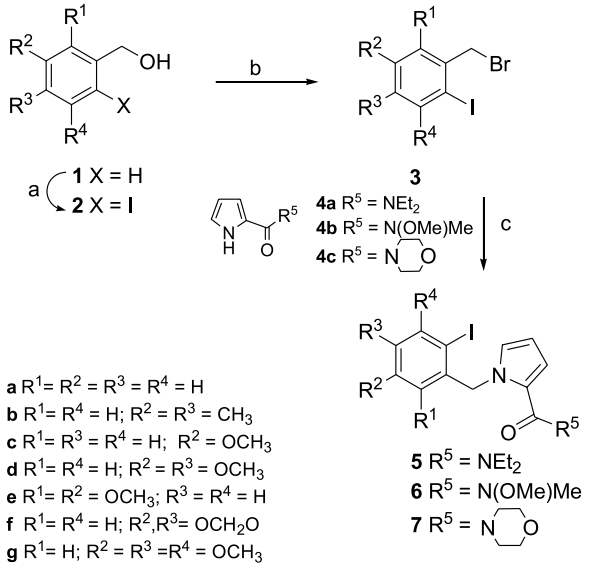
the construction of the pyrrolo[1,2-*b*]isoquinolone core present in some natural products such as the lycorine class of *Amaryllidaceae* alkaloids[18] and the phenanthroindolizidine alkaloids.[19] In the planned synthetic strategy, an aryllithium would be generated from a *N*-(*o*-halobenzyl)-pyrrole-2-carboxamide, that is expected to undergo a 6-*exo*-trig cyclisation onto the amide carbonyl of the pyrrole ring to provide the target heterocycle. A key feature of this synthetic approach is the ability of the amide moiety to intercept the aryllithium in an intramolecular fashion. Therefore, in order to study the influence of the nature of the substituents at the amide nitrogen atom on Parham-type cyclisations, this metalation–cyclisation sequence would be tested using different types of amides (*N*,*N*-dialkyl, Weinreb amides and morpholine amides) as internal electrophiles. It should be pointed out that, although morpholine amides are expected to be good electrophiles, and have been used in acylation reaction with organometallic reagents,[20] they have not been used in Parham-type cyclisations. However, the low cost of the morpholine, compared to the MeONHMe·HCl that is needed to make the Weinreb amides, led us to test the morpholine amides as internal electrophiles. Herein, we provide the full account of our investigations in this area,[21] including the extension of this strategy to the construction of seven and eight membered rings.



Scheme 1. Synthesis of *N*-benzylpyrroles **5**–**7**. Reagents: (a) I_2, CF_3CO_2Ag, $CHCl_3$, rt; (b) PBr_3, rt or HBr (45%), 0 °C; (c) KOH, DMSO, rt.

2. Results

2.1. Synthesis of *N*-benzylpyrroles

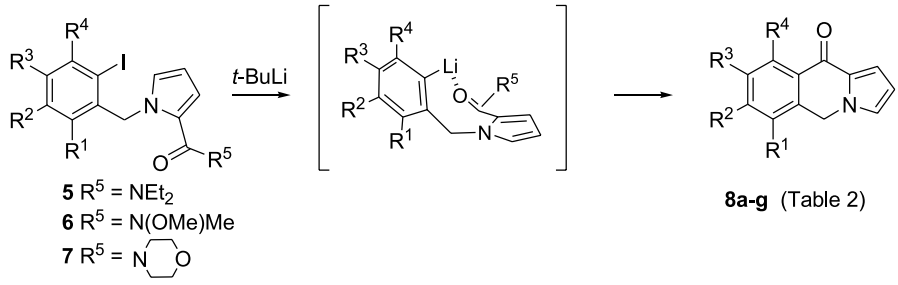
The study started with the synthesis of the substrates **5**–**7** with different substituents at the aromatic ring to prove the generality of the approach. Thus, *N*-(*o*-iodobenzyl)pyrroles were prepared by alkylation of the corresponding pyrrole-2-carboxamide **4a**–**c** under standard conditions (Scheme 1, Table 1). Iodobenzyl bromides **3a**–**g** were obtained from the corresponding benzylic alcohols **1** in two steps. Aromatic iodination of benzylic alcohols **1b**–**g** with I_2/CF_3CO_2Ag in $CHCl_3$ afforded alcohols **2b**–**g** in good yields (64–94%). In all cases the reaction was completely regioselective, except in **e**, where a minor amount of the 5-iodo regioisomer was obtained (see Section 3). Subsequent treatment with PBr_3 for cases **a**–**f**, or with HBr for **g** afforded bromides **3a**–**g** (86–99%).

2.2. Parham cyclisation of *N*-benzylpyrroles

We started studying the *N*,*N*-diethylcarbamoyl group as an internal electrophile. The metalation–cyclisation sequence was carried out under several conditions, using *t*-BuLi (2.2 equiv). Cyclisation conditions had to be optimised for each substrate **5a**–**g**, and minor amounts of deiodinated *N*-benzylpyrroles **9a**–**g** were always isolated together with the pyrrolisoquinolines **8**. For instance, when benzylpyrrole **5d** was treated with *t*-BuLi (2.2 equiv) at −78 °C for 3 h, and the reaction was quenched at 0 °C, pyrrolosoquinoline **8d** was obtained in 49% yield, together with **9d** (24%) (Fig. 1). However, if the reaction mixture was allowed to reach rt, and stirred for 3 h, the pyrroloisoquinoline **8d** was obtained in 79% yield (Table 2, entry 4). Thus, iodine–lithium exchange took place efficiently at −78 °C, but higher temperature was required for cyclisation. As shown in Table 2, some of the substrates required even longer periods at room temperature (entry 6), or the use of *n*-BuLi as metalating agent (entry 2). Thus, when **5f** or **5b** were treated with *t*-BuLi under the standard conditions (Method A), the corresponding deiodinated benzylpyrroles **9f** or **9b** were obtained (39 and 33% respectively). Under all conditions tested, no cyclisation product was obtained from **5g** which, under standard conditions gave only deiodinated product **9g** (81%, entry 7). In general, only moderate yields of pyrroloisoquinolines were obtained when the aromatic ring is activated by donor groups. Although in related Parham-type cyclisations no influence of the aromatic ring substitution pattern has been observed,[22] it seems that, once the iodine–lithium exchange

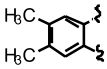
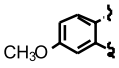
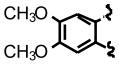
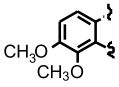
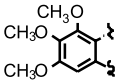
Table 1. Synthesis of benzylpyrroles **5**, **6**, and **7** by alkylation of **4**

Entry	$R^5=NEt_2$		$R^5=N(OMe)Me$		$R^5=N\square O$	
	Product	Yield (%)	Product	Yield (%)	Product	Yield (%)
1	**5a**	60	**6a**	90	**7a**	63
2	**5b**	83	**6b**	78	**7b**	98
3	**5c**	94	**6c**	83	**7c**	86
4	**5d**	73	**6d**	95	**7d**	93
5	**5e**	25	**6e**	61	**7e**	50
6	**5f**	84	**6f**	77	**7f**	68
7	**5g**	56	**6g**	73	**7g**	40



Scheme 2. Parham cyclisation of benzylpyrroles **5**–**7**.

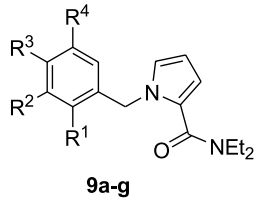
Table 2. Synthesis of pyrrolo[1,2-*b*]isoquinolines

Entry	Product		$R^5=NEt_2$	$R^5=N(OMe)Me$		$R^5=N\square O$	
			Method A[a], yield (%)	Method A[a], yield (%)	Method B[b], yield (%)	Method A[a], yield (%)	Method B[b], yield (%)
1	**8a**		28[c]	83	87	73	63
2	**8b**		10[c]	60	80	60	98
3	**8c**		54	77	69	81	77
4	**8d**		79	70	86	60	88
5	**8e**		40	24	62	40	76
6	**8f**		34[d]	62	73	60	63
7	**8g**		[e]	15	68	—	59

[a] Method A: *t*-BuLi (2.2 equiv), −78 °C, 3 h; →rt, 4 h.
[b] Method B: *t*-BuLi (2.2 equiv), −78 °C, 3 h.
[c] *n*-BuLi (3 equiv), −78 °C, 3 h; →rt, 4 h.
[d] *t*-BuLi (2.2 equiv), −78 °C, 3 h; →rt, 16 h.
[e] 81% of deiodinated benzylpyrrole **9g** was obtained.

has occurred, the more reactive aryllithium compounds lead to better yields of pyrroloisoquinolines **8** (Scheme 2).

We next focused our attention on the metalation–cyclisation sequence using Weinreb amides **6** and morpholine amides **7**. As shown in Table 2, both types of amides gave moderate to good yields of pyrroloisoquinolines **8** under Method A conditions, except when the aromatic ring bears methoxy groups on C-6 or C-3 (entries 5 and 7). However, when the reactions were quenched at −78 °C (Method B), yields of pyrroloisoquinolines **8** were consistently improved. Most significant is the improvement of the yield of pyrroloisoquinolines **8e** (24% vs. 62% from **6e** and 40% vs. 76% from **7e**) and **8g** (15% vs. 68% from **6g** and 0% vs. 59% from **7g**) (Table 2, entries 5 and 7). In these cases, the poor results obtained when the reactions are quenched at room temperature might be due to an equilibration of the intermediate organolithium prior to cyclisation. Thus, as shown in Table 2, in all cases the use of Weinreb amides or morpholine amides as internal electrophiles clearly improved the results obtained with diethyl amides. The most significant results would be the synthesis of pyrroloisoquinolines **8a**, **8b**, or **8g**.



a $R^1=R^2=R^3=R^4=H$
b $R^1=R^4=H$; $R^2=R^3=CH_3$
c $R^1=R^3=R^4=H$; $R^2=OCH_3$
d $R^1=R^4=H$; $R^2=R^3=OCH_3$
e $R^1=R^2=OCH_3$; $R^3=R^4=H$
f $R^1=R^4=H$; $R^2,R^3=OCH_2O$
g $R^1=H$; $R^2=R^3=R^4=OCH_3$

Figure 1. Deiodinated *N*-benzylpyrroles **9a**–**g**.

Amides are generally useful electrophiles in Parham cyclisations due to a complex induced proximity effect (CIPE).[23,24] Thus, lithium–iodine exchange could be favoured first by coordination of the organolithium to the

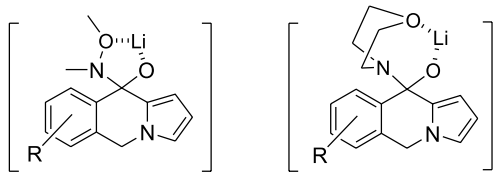
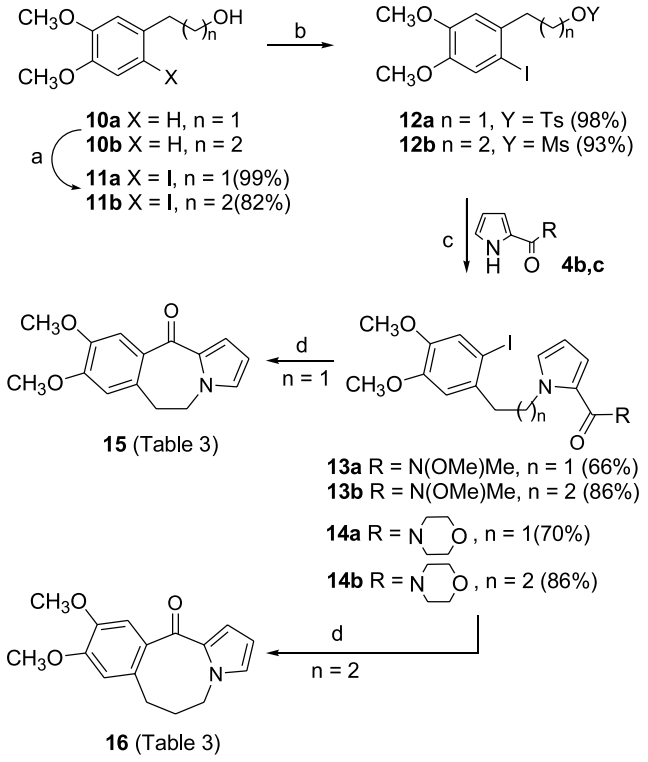


Figure 2.

amide group, and second, by stabilisation of the resulting aryllithium. Although there is no significant difference in the efficiency of Weinreb amides and morpholine amides as internal electrophiles, the better behaviour of both compared to *N*,*N*-diethyl amides could be attributed to the extra stabilisation of the intermediate generated after cyclisation by formation of an internal chelate, as depicted in Figure 2.

2.3. Parham cyclisation of *N*-phenethyl- and *N*-phenylpropylpyrroles

In view of the excellent results obtained in the formation of pyrrolosoquinoline ring system with Weinreb amides or morpholine amides, we decided to investigate the feasibility of using this type of Parham cyclisation to construct a seven or an eight-membered ring, opening a new access to the pyrrolobenzoazepine and pyrrolobenzoazocine skeletons. The pyrrolobenzoazepine core is present in *Cephalotaxus* alkaloids,[25] and some pyrrolobenzoazepines have muscle relaxant, antihypertensive or antipsychotic properties.[26] Thus, the required pyrrole-2-carboxamides **13** and **14** and were obtained from 3,4-dimethoxyphenethyl alcohol **10a** and 3,4-dimethoxyphenylpropan-1-ol **10b** in three steps, as described in Scheme 3. Parham cyclisation was carried out



Scheme 3. Parham cyclisation of *N*-phenethyl and *N*-phenylpropylpyrroles. Reagents: (a) I_2, CF_3CO_2Ag, $CHCl_3$, rt; (b) TsCl or MsCl, Et_3N, CH_2Cl_2, 0 °C; (c) KOH, DMSO, rt; (d) *t*-BuLi, −78 °C, 3 h.

Table 3. Synthesis of **15** and **16**

Substrate	Method[a]	Product	Yield, %
13a	B	**15**	59
14a	B	**15**	58
13b	B	**16**	55
14b	B	**16**	57

[a] Method B: *t*-BuLi (2.2 equiv), −78 °C, 3 h.

using 2.2 equiv of *t*-BuLi at −78 °C. As shown in Table 3, moderate to good yields of the pyrrolo[1,2-*a*]benzo[*d*]-azepine-11-one **15** and pyrrolo[1,2-*a*]benzo[*d*]azozin-12-one **16** were obtained when the reaction was quenched at low temperature.

In summary, it has been shown that *N*-(*o*-iodobenzyl)-pyrrole-2-carboxamides tolerate lithium–iodine exchange reaction conditions, allowing the efficient synthesis of the pyrrolo[1,2-*b*]isoquinoline nucleus. The *N*-methoxy-*N*-methyl and morpholine amides behave as excellent internal electrophiles, improving the results obtained with *N*,*N*-diethyl amides. This procedure has also been extended to the construction of fused seven and eight membered rings, opening also new routes to other heterocyclic systems (pyrrolo[1,2-*a*]benzazepines and pyrrolo[1,2-*a*]benzo-azocines) with potential pharmacological properties that could compete with previously reported strategies.[27]

3. Experimental

3.1. Iodination reactions. General procedure

A solution of I_2 (250 mg, 1 mmol) in dry $CHCl_3$ (30 mL) was added over a suspension of CF_3COOAg (220 mg, 1 mmol) and alcohols **1b–g**, or **10a**,**b** (1 mmol) in $CHCl_3$ (5 mL). The reaction mixture was stirred at rt during 30 min, the resulting AgI precipitate was filtered, and the resulting solution was washed with saturated $Na_2S_2O_3$. Evaporation of the solvent afforded iodinated alcohols **2b–g**, or **11a**,**b**, which were crystallised from Et_2O.

3.1.1. 2-Iodo-4,5-dimethylbenzyl alcohol (2b). According to the general procedure, alcohol **1b** (136 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, alcohol **2b** was recrystallised from Et_2O (183 mg, 70%): mp (Et_2O) 110–112 °C; IR (KBr) 3260 cm^{-1}; ^1H NMR ($CDCl_3$) 2.20 (s, 3H), 2.21 (s, 3H), 4.58 (s, 2H), 7.17 (s, 1H), 7.57 (s, 1H); ^{13}C NMR ($CDCl_3$) 18.9, 19.3, 68.9, 93.8, 129.8, 137.1, 138.2, 139.7, 139.8. MS (EI) *m*/*z* (rel intensity) 262 (M^+, 78), 245 (11), 135 (30), 133 (21), 107 (84), 106 (31), 105 (37), 103 (17), 92 (33), 91 (100), 85 (28), 83 (42), 79 (32), 78 (14), 77 (35), 65 (20), 63 (17), 53 (11), 51 (23). Anal. Calcd for $C_9H_{11}IO$: C, 41.24; H, 4.23. Found: C, 41.59; H, 3.94.

3.1.2. 2-Iodo-5-methoxybenzyl alcohol (2c).[28] According to the general procedure, alcohol **1c** (136 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, alcohol **2c** was recrystallised from Et_2O (167 mg, 64%): mp (Et_2O) 64–65 °C; IR (KBr) 3260 cm^{-1}; ^1H NMR ($CDCl_3$) 3.10 (s, 1H), 3.75 (s, 3H), 4.54 (s, 2H), 6.54 (dd, J=8.7, 2.8 Hz, 1H),

7.01 (d, $J=2.8$ Hz, 1H), 7.60 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 55.2, 68.7, 85.1, 113.8, 115.0, 139.3, 143.4, 159.9. The rest of the spectroscopic and physical data are consistent with those described in the literature.[28]

3.1.3. 2-Iodo-4,5-dimethoxybenzyl alcohol (2d).[29] According to the general procedure, alcohol **1d** (168 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, alcohol **2d** was recrystallised from Et_2O (188 mg, 64%): mp (Et_2O) 83–85 °C; IR (KBr) 3270 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.40 (s, 1H), 3.84 (s, 6H), 4.56 (s, 2H), 6.97 (s, 1H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$) 55.8, 56.1, 68.9, 85.2, 111.4, 121.3, 135.1, 148.7, 149.3. The rest of the spectroscopic and physical data are consistent with those described in the literature.[29]

3.1.4. 6-Iodo-2,3-dimethoxybenzyl alcohol (2e) and 5-iodo-2,3-dimethoxybenzyl alcohol (2e′). According to the general procedure, alcohol **1d** (168 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, flash column chromatography afforded a mixture of **2e** and **2e′** in a 3:1 ratio, that could not be separated. Data of the mixture is given (178 mg, 73 and 83% conversion); IR (neat) 3422 cm^{-1}; ^{1}H NMR ($CDCl_3$) 3.42 (s, 1H, both isomers), 3.71 (s, 3H, minor), 3.73 (s, 3H, both isomers), 3.77 (s, 3H, major), 4.51 (s, 2H, minor), 4.68 (s, 2H, major), 6.53 (d, $J=$ 8.7 Hz, 1H, major), 7.03 (d, $J=2.0$ Hz, 1H, minor), 7.22 (d, $J=2.0$ Hz, 1H, minor), 7.40 (d, $J=8.7$ Hz, 1H, major); ^{13}C NMR ($CDCl_3$) 55.7 (major), 55.8 (minor), 59.6 (minor), 60.6 (minor), 61.5 (major), 64.2 (major), 86.8, 88.5 (major, minor), 113.9 (major), 120.7, 129.0 (minor), 134.3 (major), 136.3 (major), 136.5 (minor), 146.2 (minor), 147.9 (major), 152.7 (minor), 152.9 (major). MS (EI) *m/z* (rel intensity) 295 ($M^+ +1$, 10), 294 (M^+, 100), 279 (13), 152 (19), 139 (24), 124 (39), 109 (30), 108 (12), 106 (10), 85 (11), 83 (17), 81 (19), 79 (13), 78 (11), 77 (19), 65 (11), 63 (17), 53 (23), 52 (10), 51 (20).

3.1.5. 2-Iodo-4,5-methylendioxybenzyl alcohol (2f).[30] According to the general procedure, alcohol **1f** (152 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, alcohol **2f** was recrystallised from Et_2O (211 mg, 76%): mp (Et_2O) 107–109 °C; IR (KBr) 3200 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.31 (s, 1H), 4.55 (s, 2H), 5.96 (s, 2H), 6.96 (s, 1H), 7.21 (s, 1H); ^{13}C NMR ($CDCl_3$) 69.1, 85.3, 101.6, 109.0, 118.4, 136.1, 147.8, 148.5. The rest of the spectroscopic and physical data are consistent with those described in the literature.[30]

3.1.6. 2-Iodo-3,4,5-trimethoxybenzyl alcohol (2g).[31] According to the general procedure, alcohol **1g** (198 mg, 1 mmol) was treated with I_2 (250 mg, 1 mmol) and CF_3COOAg (220 mg, 1 mmol) in $CHCl_3$ (30 mL). After work-up, alcohol **2g** was recrystallised from Et_2O (305 mg, 94%): mp (Et_2O) 52–54 °C; IR (neat) 3420 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.75 (s, 1H), 3.83 (s, 6H), 3.84 (s, 3H), 4.59 (s, 2H), 6.89 (s, 1H); ^{13}C NMR ($CDCl_3$) 56.0, 60.7, 60.9, 69.1, 84.2, 107.6, 138.3, 141.0, 152.7, 153.7. The rest of the spectroscopic and physical data are consistent with those described in the literature.[31]

3.1.7. 2-(2-Iodo-4,5-dimethoxyphenyl)ethanol (11a).[32] According to the general procedure, alcohol **10a** (1 g, 6 mmol) was treated with I_2 (1.5 g, 6 mmol) and CF_3COOAg (1.33 g, 6 mmol) in $CHCl_3$ (100 mL). After work-up, alcohol **11a** was recrystallised from Et_2O (1.8 g, 99%): mp (Et_2O) 53–54 °C; IR (neat) 3580 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.27 (s, 1H), 2.87 (t, $J=6.7$ Hz, 2H,), 3.75 (t, $J=$ 6.7 Hz, 2H), 3.78(s, 3H), 3.79 (s, 3H), 6.73 (s, 1H), 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$) 43.1, 55,8, 56.0, 62.2, 88.1, 112.9, 121.5, 133.3, 147.9, 149.0. The rest of the spectroscopic and physical data are consistent with those described in the literature.[32]

3.1.8. 3-(2-Iodo-4,5-dimethoxyphenyl)propan-1-ol (11b). According to the general procedure, alcohol **10b** (6.3 g, 32 mmol) was treated with I_2 (8.2 g, 32 mmol) and CF_3COOAg (7.14 g, 32 mmol) in $CHCl_3$ (100 mL). After work-up, alcohol **11a** was recrystallised from Et_2O (8.5 g, 82%): mp (Et_2O) 107–108 °C; IR (neat) 3381 cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.52 (s, 1H), 1.79–1.90 (m, 2H), 2.75 (t, $J=$ 7.8 Hz, 2H), 3.71 (t, $J=6.3$ Hz, 2H), 3.84 (s, 3H), 3.85 (s, 3H), 6.75 (s, 1H), 7.20 (s, 1H); ^{13}C NMR ($CDCl_3$) 33.2, 36.5, 55.8, 56.0, 61.8, 87.8, 112.1, 121.5, 136.7, 147.6, 149.2. MS (EI) *m/z* (rel intensity) 322 (M^+, 64), 277(36), 167(16), 152(12), 151(100).

3.2. Synthesis of bromides 3a–g. General procedure

PBr_3 (0.19 mL, 2 mmol) was added over a solution of alcohols **2a–g** (1 mmol) in dry CH_2Cl_2 (10 mL), and the reaction mixture was stirred at rt for 16 h. Solvent was evaporated, and the resulting oil was treated with saturated $NaHCO_3$. The resulting aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo, yielding bromides **3a–g**, which were crystallised from Et_2O.

3.2.1. 2-Iodobenzyl bromide (3a).[33] According to the general procedure, alcohol **2a** (234 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2 (10 mL). After work-up, bromide **3a** was recrystallised from Et_2O (291 mg, 98%): mp (Et_2O) 56–58 °C; ^{1}H NMR ($CDCl_3$) 4.60 (s, 2H), 6.98 (td, $J=7.7$, 1.5 Hz, 1H), 7.34 (td, $J=7.5$, 0.9 Hz, 1H), 7.47 (dd, $J=7.6$, 1.5 Hz, 1H), 7.86 (d, $J=7.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 38.8, 100.1, 128.8, 130.1, 130.4, 140.0, 140.1. The rest of the spectroscopic and physical data are consistent with those described in the literature.[33]

3.2.2. 2-Iodo-4,5-dimethylbenzyl bromide (3b). According to the general procedure, alcohol **2b** (262 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2 (10 mL). After work-up, bromide **3b** was recrystallised from Et_2O (325 mg, 99%): mp (Et_2O) 76–78 °C; IR (KBr) 3260 cm^{-1}; ^{1}H NMR ($CDCl_3$) 2.21 (s, 6H), 4.56 (s, 2H), 7.24 (s, 1H), 7.62 (s, 1H); ^{13}C NMR ($CDCl_3$) 19.0, 19.3, 38.9, 96.3, 131.4, 137.3, 137.5, 139.4, 140.5. MS (EI) *m/z* (rel intensity) 326 ($M^+ +2$, 10), 324 (M^+, 9), 246 (10), 245 (100), 118 (41), 117 (24), 115 (15), 91 (14), 85 (30), 83 (46), 51 (12).

3.2.3. 2-Iodo-5-methoxybenzyl bromide (3c).[34] According to the general procedure, alcohol **2c** (264 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2

(10 mL). After work-up, bromide **3c** was recrystallised from Et_2O (280 mg, 86%): mp (Et_2O) 111–113 °C; ^1H NMR ($CDCl_3$) 3.80 (s, 3H), 4.54 (s, 2H), 6.59 (dd, $J=8.7$, 2.8 Hz, 1H), 7.03 (d, $J=2.8$ Hz, 1H), 7.70 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 38.7, 55.4, 88.3, 116.0, 116.3, 140.4, 140.9, 160.0. The rest of the spectroscopic and physical data are consistent with those described in the literature.[34]

3.2.4. 2-Iodo-4,5-dimethoxybenzyl bromide (3d).[33] According to the general procedure, alcohol **2d** (294 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2 (10 mL). After work-up, bromide **3d** was recrystallised from Et_2O (339 mg, 95%): mp (Et_2O) 74–75 °C; ^1H NMR ($CDCl_3$) 3.86 (s, 3H), 3.87 (s, 3H), 4.58 (s, 2H), 6.96 (s, 1H), 7.22 (s, 1H); ^{13}C NMR ($CDCl_3$) 39.4, 56.0, 56.2, 88.5, 112.7, 121.8, 132.5, 149.6. The rest of the spectroscopic and physical data are consistent with those described in the literature.[33]

3.2.5. 6-Iodo-2,3-dimethoxybenzyl bromide (3e) and 5-iodo-2,3-dimethoxybenzyl bromide (3e′). According to the general procedure, a mixture of alcohols **2e/2e′** in a 3:1 ratio (294 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2 (10 mL). After work-up, a mixture of bromides **3e/3e′** in a 3:1 ratio was obtained, that could not be separated by chromatographic methods (332 mg, 93%). Data of the mixture are given: ^1H NMR ($CDCl_3$) 3.84 (s, 3H both isomers), 3.92 (s, 3H minor), 3.95 (s, 3H, major), 4.44 (s, 2H, minor), 4.70 (s, 2H, major), 6.64 (d, $J=8.7$ Hz, 1H, major), 7.13 (d, $J=2.0$ Hz, 1H, minor), 7.28 (d, $J=2$ Hz, 1H, minor), 7.51 (d, $J=8.7$ Hz, 1H, major); ^{13}C NMR ($CDCl_3$) 26.6 (minor), 33.5 (major), 55.8, 61.0 (major), 56.0, 60.8 (minor), 86.4 (minor), 89.1 (major), 114.5 (major), 121.9, 131.1 (minor), 133.6, 134.2 (major, minor), 134.5 (major), 147.3 (minor), 148.1, 153.1 (major), 153.3 (minor). MS (EI) *m/z* (rel intensity) 358 ($M^+ +2$, 16), 356 (M^+, 15), 277 (80), 262 (58), 232 (10), 92 (17), 90 (24), 87 (12), 85 (68), 83 (100), 77 (15), 64 (22), 63 (20).

3.2.6. 2-Iodo-4,5-methylendioxybenzyl bromide (3f).[30] According to the general procedure, alcohol **2f** (278 mg, 1 mmol) was treated with PBr_3 (0.19 mL, 2 mmol) in dry CH_2Cl_2 (10 mL). After work-up, bromide **3f** was recrystallised from Et_2O (310 mg, 91%): mp (Et_2O) dec.; ^1H NMR ($CDCl_3$) 4.55 (s, 2H), 5.99 (s, 2H), 6.96 (s, 1H), 7.24 (s, 1H); ^{13}C NMR ($CDCl_3$) 39.5, 88.8, 102.0, 110.0, 119.0, 133.3, 148.6. The rest of the spectroscopic and physical data are consistent with those described in the literature.[30]

3.2.7. 2-Iodo-3,4,5-trimethoxybenzyl bromide (3g). Alcohol **2g** (324 mg, 1 mmol) was treated with HBr (45%) (10 mL) at −10 °C under argon for 48 h. The precipitate obtained was filtered and washed with H_2O. The resulting bromide **3g** was recrystallised from Et_2O (298 mg, 77%): mp (Et_2O) 78–80 °C; ^1H NMR ($CDCl_3$) 3.86 (s, 9H), 4.62 (s, 2H), 6.88 (s, 1H); ^{13}C NMR ($CDCl_3$) 39.5, 56.1, 60.7, 60.9, 88.3, 109.5, 135.3, 142.0, 153.4, 153.6. MS (EI) *m/z* (rel intensity) 388 ($M^+ +2$, 4), 386 (M^+, 4), 165 (21), 135 (11), 90 (13), 79 (16), 77 (11), 66 (10), 63 (12), 53 (10), 51 (25).

3.2.8. 2-(2-Iodo-4,5-dimethoxyphenyl)ethyl *p*-toluensulfonate (12a). Et_3N (4.6 mL, 32.9 mmol) and tosyl chloride (6.3 g, 32.9 mmol) were added over a solution of alcohol **11a** (8.45 g, 27.4 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C, and the reaction mixture was stirred at rt for 30 min. The reaction mixture was washed with HCl (5 M, 5 mL). The resulting aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo, yielding **12a**, which was crystallised from Et_2O (12.5 g, 98%): mp (Et_2O) 109–110 °C; ^1H NMR ($CDCl_3$) 2.42 (s, 3H), 3.01 (t, $J=6.9$ Hz, 2H), 3.81, 3.83 (s, 3H), 4.20 (t, $J=6.9$ Hz, 2H), 6.67 (s, 1H), 7.11 (s, 1H), 7.27 (d, $J=7.9$ Hz, 2H), 7.68 (d, $J=7.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$) 21.3, 39.2, 55.6, 55.8, 69.0, 87.6, 112.8, 121.2, 127.4, 129.5, 130.9, 132.5, 144.4, 148.2, 148.9. MS (EI) *m/z* (rel intensity) 462 (M^+, 27), 291 (11), 290 (100), 277 (26), 151 (14), 91 (25), 65 (10).

3.2.9. 3-(2-Iodo-4,5-dimethoxyphenyl)propyl methanesulfonate (12b). Et_3N (1.9 mL, 13.6 mmol) and mesyl chloride (1.06 mL, 13.6 mmol) were added over a solution of alcohol **11b** (3.66 g, 11.4 mmol) in dry CH_2Cl_2 (40 mL) at 0 °C, and the reaction mixture was stirred at rt for 30 min. The reaction mixture was washed with saturated $NaHCO_3$ (15 mL). The resulting aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo, yielding **12b** (4.1 g, 93%); ^1H NMR ($CDCl_3$) 1.79–1.90 (m, 2H), 2.75 (t, $J=7.8$ Hz, 2H), 2.91 (s, 3H), 3.71 (t, $J=6.3$ Hz, 2H), 3.84, 3.85 (s, 3H), 6.75 (s, 1H), 7.20 (s, 1H); ^{13}C NMR ($CDCl_3$) 33.2, 36.5, 37.1, 55.8, 56.0, 65.8, 87.8, 112.1, 121.5, 136.7, 147.6, 149.2. MS (EI) *m/z* (rel intensity) 400 (M^+, 100), 304 (22), 289 (10), 277 (92), 177 (39), 151 (31), 146 (22), 91 (18).

3.3. Alkylation reactions. General procedure for the synthesis of *N*-benzyl-, *N*-phenethyl-, and *N*-phenylpropylpyrroles 5–7, 13, and 14

Pyrrole-2-carboxamide **4a**, **4b** or **4c** (1 mmol) was added over a suspension of powdered KOH (224 mg, 4 mmol) in DMSO (5 mL). The mixture was stirred at rt for 2 h, bromide **3a–g**, tosylate **12a**, or mesylate **12b** (2 mmol) was added, and the reaction mixture was stirred for 3 h. H_2O (10 mL) was added and the resulting aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were washed with brine (3×10 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash column chromatography (silicagel) afforded *N*-benzylpyrroles **5**, **6**, and **7**, *N*-phenethylpyrroles or *N*-phenylpropylpyrroles **13** or **14**.

3.3.1. 1-(2-Iodobenzyl)pyrrole-2-carboxylic acid diethyl amide (5a). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (165 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3a** (595 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **5a** as a colourless oil (227 mg, 60%); IR ($CHCl_3$) 1616 cm^{-1}; ^1H NMR ($CDCl_3$) 1.10 (t, $J=7.1$ Hz, 6H), 3.43 (q, $J=7.1$ Hz, 4H), 5.32 (s, 2H), 6.13 (dd, $J=3.7$, 2.6 Hz, 1H), 6.38 (dd, $J=3.7$, 1.7 Hz, 1H), 6.69 (dd, $J=7.7$, 1.3 Hz, 1H), 6.74 (dd, $J=2.6$, 1.7 Hz, 1H), 6.91 (td, $J=7.7$, 1.4 Hz, 1H), 7.21 (td, $J=7.7$, 1.3 Hz, 1H), 7.79 (dd, $J=7.7$, 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.4, 41.4, 56.2, 97.5, 107.2, 111.0,

125.1, 126.2, 128.2, 128.3, 128.9, 139.1, 140.8, 163.4. MS (EI) *m/z* (rel intensity) 383 ($M^+ + 1$, 8), 382 (M^+, 39), 282 (15), 256 (13), 255 (70), 217 (28), 184 (25), 183 (100), 182 (42), 156 (29), 155 (19), 154 (22), 127 (13), 100 (16), 91 (12), 90 (37), 89 (17), 72 (34). Anal. Calcd for $C_{16}H_{19}IN_2O$: C, 50.28; H, 5.01; N, 7.33. Found: C, 49.99; H, 5.10; N, 7.29.

3.3.2. 1-(2-Iodo-4,5-dimethylbenzyl)pyrrole-2-carboxylic acid diethyl amide (5b). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (260 mg, 1.6 mmol) was treated with KOH (340 mg, 6.1 mmol) in DMSO (6 mL), and bromide **3b** (1.03 g, 3.2 mmol). After work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **5b** as a colourless oil (530 mg, 83%); IR ($CHCl_3$) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.11 (t, $J=7.1$ Hz, 6H), 2.09 (s, 3H), 2.13 (s, 3H), 3.45 (q, $J=7.1$ Hz, 4H), 5.25 (s, 2H), 6.09 (dd, $J=4.0$, 2.8 Hz, 1H), 6.35 (dd, $J=4.0$, 2.0 Hz, 1H), 6.59 (s, 1H), 6.72 (dd, $J=2.8$, 2.0 Hz, 1H), 7.55 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.5, 18.8, 19.4, 41.3, 55.6, 94.4, 107.0, 110.9, 124.9, 126.1, 129.9, 139.8, 136.9, 137.9, 163.6. MS (EI) *m/z* (rel intensity) 410 (M^+, 17), 284 (23), 283 (100), 245 (31), 212 (17), 211 (57), 210 (44), 196 (17), 190 (17), 184 (19), 183 (13), 168 (12), 119 (10), 118 (23), 117 (17), 115 (13), 100 (17), 91 (12), 85 (10), 83 (16), 72 (29). Anal. Calcd for $C_{18}H_{23}IN_2O$: C, 52.69; H, 5.65; N, 6.83. Found: C, 52.44; H, 5.21; N, 7.02.

3.3.3. 1-(2-Iodo-5-methoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (5c). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (150 mg, 0.9 mmol) was treated with KOH (250 mg, 4.4 mmol) in DMSO (5 mL), and bromide **3c** (610 mg, 1.9 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **5c** as a colourless oil (350 mg, 94%); IR ($CHCl_3$) 1617 cm^{-1}; ^1H NMR ($CDCl_3$) 1.10 (t, $J=7.1$ Hz, 6H), 3.45 (q, $J=7.1$ Hz, 4H), 3.64 (s, 3H), 5.27 (s, 2H), 6.12 (dd, $J=3.6$, 2.8 Hz, 1H), 6.26 (d, $J=2.8$ Hz, 1H), 6.38 (dd, $J=3.6$, 1.6 Hz, 1H), 6.50–6.52 (m, 1H), 6.73 (dd, $J=2.8$, 1.6 Hz, 1H), 7.63 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.4, 41.3, 55.1, 56.1, 85.8, 107.2, 111.1, 114.5, 125.1, 126.1, 139.5, 141.9, 160.0, 163.3. MS (EI) *m/z* (rel intensity) 412 (M^+, 3), 286 (24), 285 (100), 214 (14), 213 (41), 212 (23), 192 (23), 186 (13), 170 (17), 120 (15), 100 (14), 85 (23), 83 (39), 72 (20). Anal. Calcd for $C_{17}H_{21}IN_2O_2$: C, 49.52; H, 5.13; N, 6.79. Found: C, 49.23; H, 5.41; N, 6.59.

3.3.4. 1-(2-Iodo-4,5-dimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (5d). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (884 mg, 2.0 mmol) was treated with KOH (448 mg, 8.0 mmol) in DMSO (20 mL), and bromide **3d** (1.5 g, 4.2 mmol). After work-up, flash column chromatography (silicagel, 40% hexane/AcOEt) afforded **5d** as a colourless oil (1.72 mg, 73%); IR ($CHCl_3$) 1616 cm^{-1}; ^1H NMR ($CDCl_3$) 1.11 (t, $J=7.1$ Hz, 6H), 3.44 (q, $J=7.1$ Hz, 4H), 3.68 (s, 3H), 3.80 (s, 3H), 5.24 (s, 2H), 6.08–6.09 (m, 1H), 6.34 (dd, $J=3.6$, 1.5 Hz, 1H), 6.44 (s, 1H), 6.72 (dd, $J=2.5$, 1.5 Hz, 1H), 7.17 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.5, 41.2, 55.6, 55.6, 56.0, 86.1, 107.1, 111.0, 111.9, 121.3, 124.8, 126.2, 133.2, 148.7, 149.4, 163.5. MS (EI) *m/z* (rel intensity) 442 (M^+, 2), 316 (21), 315 (100), 277 (62), 244 (22), 243 (22), 242 (33), 222 (29), 200 (12), 150 (18), 107 (15), 100 (36), 94 (11), 92 (15), 85 (10), 83 (13), 79 (10), 77 (20), 72 (56), 64 (14), 63 (13), 56 (14), 51 (12). Anal. Calcd for $C_{18}H_{23}IN_2O_3$: C, 48.88; H, 5.24; N, 6.33. Found: C, 48.60; H, 5.36; N, 6.24.

3.3.5. 1-(6-Iodo-2,3-dimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (5e). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (600 mg, 3.6 mmol) was treated with KOH (780 mg, 13.9 mmol) in DMSO (15 mL), and a mixture of bromides **3e/3e′** in a 2:1 ratio (2.5 g, 7 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **5e** as a colourless oil (400 mg, 25%); IR ($CHCl_3$) 1613 cm^{-1}; ^1H NMR ($CDCl_3$) 1.23 (t, $J=7.1$ Hz, 6H), 3.57 (q, $J=7.1$ Hz, 4H), 3.68 (s, 3H), 3.81 (s, 3H), 5.39 (s, 2H), 5.97 (dd, $J=4.0$, 2.8 Hz, 1H), 6.29 (dd, $J=4.0$, 1.6 Hz, 1H), 6.49 (dd, $J=2.8$, 1.6 Hz, 1H), 6.64 (d, $J=8.7$ Hz, 1H), 7.51 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.5, 41.9, 50.5, 55.7, 60.8, 89.6, 106.6, 110.0, 114.1, 123.1, 126.7, 133.5, 134.5, 148.6, 153.1, 164.0. MS (EI) *m/z* (rel intensity) 442 (M^+, 16), 262 (15), 87 (11), 85 (64), 83 (100), 72 (13). Anal. Calcd for $C_{18}H_{23}IN_2O_3$: C, 48.88; H, 5.24; N, 6.33. Found: C, 49.03; H, 4.89; N, 5.90.

3.3.6. 1-(2-Iodo-4,5-methylendioxybenzyl)pyrrole-2-carboxylic acid diethyl amide (5f). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (710 mg, 4.3 mmol) was treated with KOH (1.05 g, 18.7 mmol) in DMSO (6 mL), and bromide **3f** (2.9 g, 8.6 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **5f** as a colourless oil (1.53 mg, 84%); IR ($CHCl_3$) 1615 cm^{-1}; ^1H NMR ($CDCl_3$) 1.14 (t, $J=7.1$ Hz, 6H), 3.46 (q, $J=7.1$ Hz, 4H), 5.22 (s, 2H), 5.89 (s, 2H), 6.10 (dd, $J=4.0$, 2.8 Hz, 1H), 6.34 (s, 1H), 6.36 (dd, $J=4.0$, 1.6 Hz, 1H), 6.73 (dd, $J=2.8$, 1.6 Hz, 1H), 7.19 (s, 1H); ^{13}C NMR ($CDCl_3$) 13.2, 41.0, 55.7, 85.4, 101.3, 107.0, 108.5, 110.8, 118.0, 124.6, 125.7, 134.0, 147.3, 148.3, 163.1. MS (EI) *m/z* (rel intensity) 426 (M^+, 2), 299 (45), 261 (23), 227 (15), 226 (16), 206 (9), 100 (9), 87 (13), 85 (69), 83 (100), 76 (11), 72 (13). Anal. Calcd for $C_{17}H_{19}IN_2O_3$: C, 47.90; H, 4.49; N, 6.57. Found: C, 48.01; H, 4.65; N, 6.12.

3.3.7. 1-(2-Iodo-3,4,5-trimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (5g). According to the general procedure, *N*,*N*-diethyl-pyrrole-2-carboxamide **4a** (150 mg, 0.9 mmol) was treated with KOH (240 mg, 4.3 mmol) in DMSO (6 mL), and bromide **3g** (700 mg, 1.8 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **5g** as a colourless oil (240 mg, 56%); IR ($CHCl_3$) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (t, $J=7.1$ Hz, 6H), 3.43 (q, $J=7.1$ Hz, 4H), 3.63 (s, 3H), 3.78 (s, 3H), 3.81 (s, 3H), 5.27 (s, 2H), 6.08–6.10 (m, 1H), 6.15 (s, 1H), 6.34–6.36 (m, 1H), 6.73 (broad s, 1H); ^{13}C NMR ($CDCl_3$) 13.4, 41.4, 55.7, 56.2, 60.6, 60.7, 85.4, 107.1, 107.8, 111.0, 125.0, 126.1, 136.4, 141.0, 152.6, 153.6, 163.2. MS (EI) *m/z* (rel intensity) 346 (12), 345 (38), 307 (16), 252 (48), 181 (24), 100 (18), 87 (12), 85 (72), 83 (100), 72 (25). Anal. Calcd for $C_{19}H_{25}IN_2O_4$: C, 48.32; H, 5.33; N, 5.93. Found: C, 48.17; H, 5.01; N, 5.12.

3.3.8. 1-(2-Iodobenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6a). According to the general

procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3a** (594 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **6a** as a colourless oil, that was crystallised from Et_2O (333 mg, 90%): mp (Et_2O) 100–102 °C; IR ($CHCl_3$) 1623 cm^{-1}; ^1H NMR ($CDCl_3$) 3.27 (s, 3H), 3.66 (s, 3H), 5.52 (s, 2H), 6.23(dd, $J=4.0$, 2.8 Hz, 1H), 6.48 (dd, $J=7.9$, 1.2 Hz, 1H,), 6.79 (dd, $J=2.8$, 1.8 Hz), 6.90–6.93 (m, 1H), 7.02 (dd, $J=4.0$, 1.8 Hz, 1H), 7.18–7.24 (m, 1H), 7.82 (dd, $J=7.9$, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) 33.5, 57.3, 60.8, 96.9, 108.2, 116.6, 123.1, 127.1, 127.5, 128.3, 128.6, 138.9, 161.8. MS (EI) *m/z* (rel intensity) 370 (M^+, 5), 311 (7), 310 (51), 217 (15), 184 (12), 183 (10), 182 (10), 154 (10), 127 (5), 90 (14), 89 (7). Anal. Calcd for $C_{14}H_{15}IN_2O_2$: C, 45.42; H, 4.08; N, 7.57. Found: C, 45.42; H, 4.27; N, 7.25.

3.3.9. 1-(2-Iodo-4,5-dimethylbenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6b). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3b** (645 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 10% hexane/AcOEt) afforded **6b** as a colourless oil, that was crystallised from Et_2O (310 mg, 78%): mp (Et_2O) 76–79 °C; IR ($CHCl_3$) 1625 cm^{-1}; ^1H NMR ($CDCl_3$) 2.08 (s, 3H), 2.16 (s, 3H), 3.30 (s, 3H), 3.66 (s, 3H,), 5.46 (s, 2H), 6.19 (dd, $J=4.0$, 2.4 Hz, 1H), 6.38 (s, 1H), 6.76 (dd, $J=2.4$, 1.8 Hz, 1H), 6.99 (dd, $J=4.0$, 1.8 Hz, 1H), 7.59(s, 1H); ^{13}C NMR ($CDCl_3$) 18.8, 19.5, 33.7, 56.8, 60.9, 93.7, 108.8, 116.5; 123.3, 127.3, 128.9; 137.1, 137.8, 138.3, 139.8, 162.1. MS (EI) *m/z* (rel intensity) 398 (M^+, 1), 338 (25), 245 (19), 241 (8), 221 (18), 211 (100), 210 (7), 196 (24), 168 (6), 118 (15), 117 (11), 115 (8), 91 (7), 83 (6).

3.3.10. 1-(2-Iodo-5-methoxybenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6c). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3c** (654 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **6b** as a colourless oil, that was crystallised from Et_2O (332 mg, 83%): mp (Et_2O) 84–85 °C; IR ($CHCl_3$) 1663 cm^{-1}; ^1H NMR ($CDCl_3$) 3.28 (s, 3H), 3.64 (s, 3H), 3.66 (s, 3H,), 5.48 (s, 2H), 6.07 (d, $J=3.0$ Hz, 1H), 6.22 (dd, $J=4.0$, 2.6 Hz, 1H), 6.53 (dd, $J=8.7$, 3.0 Hz, 1H), 6.80 (dd, $J=2.6$, 1.8 Hz, 1H), 7.02 (dd, $J=4.0$, 1.8 Hz, 1H), 7.67 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 33.7, 55.1, 57.3, 61.0, 85.3, 108.3, 113.8, 114.3, 116.8, 123.3, 127.7, 139.5, 142.5, 160.2, 162.0. MS (EI) *m/z* (rel intensity) 400 (M^+, 2), 340 (21), 273 (6), 247 (6), 214 (15), 213 (100), 212 (9), 182 (5), 170 (11), 120 (6), 93 (5), 77 (5). Anal. Calcd for $C_{15}H_{17}IN_2O_3$: C, 45.02; H, 4.28; N, 7.00. Found: C, 44.73; H, 4.20; N, 6.94.

3.3.11. 1-(2-Iodo-4,5-dimethoxybenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6d). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3d** (714 mg, 2 mmol) after work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **6d** as a colourless oil, that was crystallised from pentane (409 g, 95%); IR ($CHCl_3$) 1623 cm^{-1}; ^1H NMR ($CDCl_3$) 3.30 (s, 3H), 3.65 (s, 3H), 3.67 (s, 3H), 3.84 (s, 3H), 5.46 (s, 2H), 6.19 (dd, $J=4.0$, 2.8 Hz, 1H), 6.28 (s, 1H), 6.82 (dd, $J=2.8$, 1.8 Hz, 1H), 6.97 (dd, $J=4.0$, 1.8 Hz, 1H), 7.22 (s, 1H); ^{13}C NMR ($CDCl_3$) 33.7, 55.6, 56.1, 56.6, 60.9, 85.6, 108.1, 111.1, 116.6, 121.3, 123.2, 127.4, 133.6, 148.6, 149.5, 162.2. MS (EI) *m/z* (rel intensity) 430 (M^+, 6), 370 (22), 243 (100), 83 (29). Anal. Calcd for $C_{16}H_{19}IN_2O_4$: C, 44.67; H, 4.45; N, 6.51. Found: C, 45.12; H, 4.44; N, 5.96.

3.3.12. 1-(6-Iodo-2,3-dimethoxybenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6e). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and a mixture of bromides **3e/3e′** in a 3:1 ratio (714 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **6e** as a colourless oil, that was crystallised from pentane (262 mg, 61%): mp (pentane) 94–96 °C; IR (KBr) 1622 cm^{-1}; ^1H NMR ($CDCl_3$) 3.39 (s, 3H), 3.70 (s, 3H), 3.72 (s, 3H), 3.84 (s, 3H), 5.62 (s, 2H), 6.03 (dd, $J=4.0$, 2.6 Hz, 1H), 6.52 (dd, $J=2.6$, 1.8 Hz, 1H), 6.68 (d, $J=8.7$ Hz, 1H), 6.86 (dd, $J=4.0$, 1.8 Hz, 1H), 7.56 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 34.1, 51.2, 56.7, 60.8, 60.9, 89.9, 107.3, 114.2, 115.5, 123.9, 125.0, 133.5, 134.5, 148.7, 153.1, 162.7. MS (EI) *m/z* (rel intensity) 430 (M^+,1), 370 (25), 262 (14), 244 (16), 243 (100), 228 (17), 212 (25), 200 (7), 108 (8), 92 (7), 90 (8). Anal. Calcd for $C_{16}H_{19}IN_2O_4$: C, 44.67; H, 4.45; N, 6.51. Found: C, 44.55; H, 4.46; N, 6.34.

3.3.13. 1-(2-Iodo-4,5-methylendioxybenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6f). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3f** (682 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **6f** as a colourless oil (319 mg, 77%); IR (KBr) 1624 cm^{-1}; ^1H NMR ($CDCl_3$) 3.30 (s, 3H), 3.67 (s, 3H), 5.43 (s, 2H), 5.90 (s, 2H), 6.10 (s, 1H), 6.21 (dd, $J=4.0$, 2.8 Hz, 1H), 6.78 (dd, $J=2.8$, 1.6 Hz, 1H), 7.01 (dd, $J=4.0$, 1.6 Hz, 1H), 7.23 (s, 1H); ^{13}C NMR ($CDCl_3$) 33.6, 57.2, 61.0, 84.8, 101.5, 107.9, 108.4, 116.8, 118.3, 123.1, 127.4, 134.8, 147.5, 148.7, 161.3. MS (EI) *m/z* (rel intensity) 414 (M^+, 2), 354 (21), 287 (11), 261 (15), 227 (100), 134 (6), 76 (8). Anal. Calcd for $C_{15}H_{15}IN_2O_4$: C, 43.50; H, 3.65; N, 6.76. Found: C, 43.53; H, 3.69; N, 6.54.

3.3.14. 1-(2-Iodo-3,4,5-trimethoxybenzyl)pyrrole-2-carboxylic acid methoxy methyl amide (6g). According to the general procedure, *N*-methoxy-*N*-methylpyrrole-2-carboxamide **4b** (154 mg, 1 mmol) was treated with KOH (224 mg, 4 mmol) in DMSO (5 mL), and bromide **3g** (756 mg, 2 mmol). After work-up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **6g** as a colourless oil, that was crystallised from pentane (336 mg, 73%): mp (pentane) 80–82 °C; IR (KBr) 1624 cm^{-1}; ^1H NMR ($CDCl_3$) 3.30 (s, 3H), 3.63 (s, 3H), 3.67 (s, 3H), 3.83 (s, 3H), 3.88 (s, 3H), 5.50 (s, 2H), 5.98 (s, 2H), 6.22 (dd, $J=4.0$, 2.6 Hz, 1H), 6.82 (dd, $J=2.6$, 1.8 Hz, 1H), 7.00 (dd, $J=4.0$, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) 33.4, 55.5, 57.1,

60.4, 60.6, 60.7, 84.5, 106.8, 108.0, 116.4, 123.0, 127.5, 140.7, 156.8, 152.5, 153.7, 161.8. MS (EI) *m/z* (rel intensity) 460 (M^+,1), 400 (12), 334 (8), 333 (39), 307 (21), 274 (17), 273 (100), 272 (6), 259 (13), 258 (83), 240 (22), 230 (7), 227 (12), 210 (8), 165 (6). Anal. Calcd for $C_{17}H_{21}IN_2O_5$: C, 44.36; H, 4.60; N, 6.09. Found: C, 45.13; H, 4.64; N, 5.71.

3.3.15. 1-(2-Iodobenzyl)pyrrole-2-carboxylic acid morpholine amide (7a). According to the general procedure, pyrrole-2-carboxamide **4c** (1.34 g, 7.4 mmol) was treated with KOH (1.66 g, 29.7 mmol) in DMSO (35 mL), and bromide **3a** (4.41 g, 14.8 mmol) after work-up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **7a** as a colourless oil, that was crystallised from ethyl ether (2.00 g, 63%): mp (Et_2O) 96–98 °C; IR ($CHCl_3$) 1619 cm^{-1}; ^1H NMR ($CDCl_3$) 3.54–3.58 (m, 4H), 3.67–3.71 (m, 4H), 5.35 (s, 2H), 6.16 (dd, J=3.8, 2.8 Hz, 1H), 6.37 (dd, J=3.8, 1.6 Hz, 1H), 6.68 (dd, J=7.9, 1.2 Hz, 1H), 6.97 (dd, J=2.8, 1.6 Hz, 1H), 6.95 (td, J=7.9, 1.2 Hz, 1H), 7.22 (td, J=7.5, 1.2 Hz, 1H), 7.82 (dd, J=7.5, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) 45.5, 56.3, 66.8, 97.6, 107.5, 112.0, 124.8, 125.9, 128.2, 128.4, 129.1, 139.3, 140.7, 162.7. MS (EI) *m/z* (rel intensity) 397 (M^++1, 10), 396 (M^+, 55), 282 (15), 269 (70), 217 (23), 184 (24), 183 (100), 182 (42), 155 (15), 154 (17), 90 (31), 70 (17). Anal. Calcd for $C_{16}H_{17}IN_2O_2$: C, 48.50; H, 4.32; N, 7.07. Found: C, 48.21; H, 4.43; N, 6.72.

3.3.16. 1-(2-Iodo-4,5-dimethylbenzyl)pyrrole-2-carboxylic acid morpholine amide (7b). According to the general procedure, pyrrole-2-carboxamide **4c** (118 mg, 0.65 mmol) was treated with KOH (147 mg, 2.6 mmol) in DMSO (10 mL), and bromide **3b** (425 mg, 1.31 mmol). After work-up, flash column chromatography (silicagel, 40% hexane/AcOEt) afforded **7b** as a colourless oil (271 mg, 95%); IR ($CHCl_3$) 1621 cm^{-1}; ^1H NMR ($CDCl_3$) 2.09 (s, 3H), 2.14 (s, 3H), 3.52–3.56 (m, 4H), 3.66–3.69 (m, 4H), 5.26 (s, 2H), 6.10 (dd, J=3.6, 2.7 Hz, 1H), 6.32 (dd, J=3.6, 1.6 Hz, 1H), 6.54 (s, 1H), 6.75 (dd, J=2.7, 1.6 Hz, 1H), 7.56 (s, 1H); ^{13}C NMR ($CDCl_3$) 18.6, 19.3, 45.4, 55.4, 66.6, 94.2, 107.1, 112.5, 124.6, 125.6, 129.6, 136.8, 137.6, 137.9, 139.7, 162.7. MS (EI) *m/z* (rel intensity) 424 (M^+, 9), 298 (21), 297 (100), 245 (21), 212 (11), 211 (46), 210 (29), 204 (21), 196 (11), 118 (11), 70 (9). Anal. Calcd for $C_{18}H_{21}IN_2O_2$: C, 50.96; H, 4.99; N, 6.60. Found: C, 50.87; H, 4.63; N, 6.72.

3.3.17. 1-(2-Iodo-5-methoxybenzyl)pyrrole-2-carboxylic acid morpholine amide (7c). According to the general procedure, pyrrole-2-carboxamide **4c** (597 mg, 3.3 mmol) was treated with KOH (744 mg, 13.2 mmol) in DMSO (15 mL), and bromide **3c** (2.17 g, 6.6 mmol). After work-up, flash column chromatography (silicagel, 40% hexane/AcOEt) afforded **7c** as a white solid, that was crystallised from ethyl ether (1.22 g, 86%): mp (Et_2O) 96–98 °C; IR (KBr) 1619 cm^{-1}; ^1H NMR ($CDCl_3$) 3.49–3.53 (m, 4H), 3.62 (s, 3H), 3.64–3.67 (m, 4H), 5.27 (s, 2H), 6.11 (dd, J=3.7, 2.8 Hz, 1H), 6.22 (d, J=2.8 Hz, 1H), 6.32 (dd, J=3.7, 1.6 Hz, 1H), 6.51 (dd, J=8.7, 2.8 Hz, 1H), 6.76 (dd, J=2.8, 1.6 Hz, 1H), 7.63 (d, J=8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) 45.7, 55.3, 56.3, 67.0, 85.8, 107.4, 112.9, 114.3, 114.9, 124.7, 125.9, 139.7, 141.8, 160.1, 162.7. MS (EI) *m/z* (rel intensity) 426 (M^+, 11), 299 (100), 214 (11), 213 (37), 212 (16), 206 (25), 170 (11), 120 (10), 114 (10), 70 (13). Anal. Calcd for $C_{17}H_{19}IN_2O_3$: C, 47.90; H, 4.49; N, 6.57. Found: C, 47.81; H, 4.42; N, 6.45.

3.3.18. 1-(2-Iodo-4,5-dimethoxybenzyl)pyrrole-2-carboxylic acid morpholine amide (7d). According to the general procedure, pyrrole-2-carboxamide **4c** (446 mg, 2.5 mmol) was treated with KOH (560 mg, 9.9 mmol) in DMSO (5 mL), and bromide **3d** (1.77 g, 4.9 mmol) after work-up, flash column chromatography (silicagel, 70% hexane/AcOEt) afforded **7d** as a colourless oil (1.05 g, 93%); IR ($CHCl_3$) 1619 cm^{-1}; ^1H NMR ($CDCl_3$) 3.42–3.43 (m, 4H), 3.52–3.54 (m, 4H), 3.55 (s, 3H), 3.67 (s, 3H), 5.13 (s, 2H), 5.97 (dd, J=3.6, 2.8 Hz, 1H), 6.19 (dd, J=3.6, 1.6 Hz, 1H), 6.34 (s, 1H), 6.66 (dd, J=2.8, 1.6 Hz, 1H), 7.08 (s, 1H); ^{13}C NMR ($CDCl_3$) 45.0, 55.1, 55.2, 55.6, 66.3, 85.8, 106.9, 111.6, 112.3, 120.9, 124.3, 125.3, 132.5, 148.4, 148.9, 162.3. MS (EI) *m/z* (rel intensity) 456 (M^+, 3), 330 (19), 329 (100), 277 (52), 243 (17), 242 (16), 236 (26), 150 (10), 114 (11), 70 (14).

3.3.19. 1-(6-Iodo-2,3-dimethoxybenzyl)pyrrole-2-carboxylic acid morpholine amide (7e). According to the general procedure, pyrrole-2-carboxamide **4c** (321 mg, 1.8 mmol) was treated with KOH (400 mg, 7.1 mmol) in DMSO (10 mL), and a mixture of bromides **3e/3e′** in a 2.2/1 ratio (1.27 g, 3.5 mmol). After work-up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **7e** as a white solid that was crystallised from pentane. (413 mg, 50%): mp (pentane) 148–150 °C; IR (KBr) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 3.68 (s, 3H), 3.68–3.70 (m, 4H), 3.75–3.77 (m, 4H), 3.79 (s, 3H), 5.42 (s, 2H), 5.97 (dd, J=3.6, 2.4 Hz, 1H), 6.23 (dd, J=3.6, 1.6 Hz, 1H), 6.59 (dd, J=2.4, 1.6 Hz, 1H), 6.63 (d, J=8.7 Hz, 1H), 7.50 (d, J=8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) 45.8, 50.4, 55.8, 60.9, 66.9, 89.5, 107.1, 112.1, 114.3, 124.1, 125.4, 133.6, 134.7, 148.8, 153.2, 163.5. MS (EI) *m/z* (rel intensity) 456 (M^+, 6), 330 (22), 391 (100), 262 (10), 243 (13), 236 (24), 114 (11), 70 (15).

3.3.20. 1-(2-Iodo-4,5-methylendioxybenzyl)pyrrole-2-carboxylic acid morpholine amide (7f). According to the general procedure, pyrrole-2-carboxamide **4c** (53 mg, 0.3 mmol) was treated with KOH (66 mg, 1.2 mmol) in DMSO (5 mL), and bromide **3f** (200 mg, 0.6 mmol). After work-up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **7f** as a colourless oil that was crystallised from diethyl ether (90 mg, 68%): mp (Et_2O) 134–138 °C; IR ($CHCl_3$) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 3.58–3.62 (m, 4H), 3.70–3.73 (m, 4H), 5.25 (s, 2H), 5.91 (s, 2H), 6.13 (dd, J=3.8, 2.8 Hz, $1H_l$), 6.31 (s, 1H), 6.33 (dd, J=3.8, 1.6 Hz, 1H), 6.77 (dd, J=2.8, 1.6 Hz, 1H), 7.22 (s, 1H); ^{13}C NMR ($CDCl_3$) 45.5, 55.9, 66.8, 85.6, 101.6, 107.5, 108.6, 112.9, 118.4, 124.6, 125.7, 134.1, 147.7, 148.6, 162.7. MS (EI) *m/z* (rel intensity) 440 (M^+, 2), 314 (21), 313 (100), 261 (44), 227 (31), 226 (22), 220 (23), 134 (12), 114 (12), 76 (15), 70 (15). Anal. Calcd for $C_{17}H_{17}IN_2O_4$: C, 46.38; H, 3.89; N, 6.36. Found: C, 46.02; H, 3.74; N, 5.96.

3.3.21. 1-(2-Iodo-3,4,5-trimethoxybenzyl)pyrrole-2-carboxylic acid morpholine amide (7g). According to the general procedure, pyrrole-2-carboxamide **4c** (354 mg, 1.9 mmol) was treated with KOH (441 mg, 7.8 mmol) in

DMSO (10 mL), and bromide **3g** (1.52 mg, 3.9 mmol). After work-up, flash column chromatography (silicagel, 60% hexane/AcOEt) afforded **7g** as a colourless oil (374 mg, 40%); IR ($CHCl_3$) 1620 cm^{-1}; ^1H NMR ($CDCl_3$) 3.57–3.61 (m, 4H), 3.67 (s, 3H), 3.68–3.72 (m, 4H), 3.83 (s, 3H), 3.86 (s, 3H), 5.31 (s, 2H), 6.14 (dd, J= 4.0, 2.8 Hz, 1H), 6.21 (s, 1H), 6.35 (dd, J=4.0, 1.6 Hz, 1H, H), 6.78 (dd, J=2.8, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 45.6, 55.9, 56.3, 60.7, 60.9, 66.8, 85.6, 107.5, 108.2, 113.0, 124.9, 126.0, 136.3, 141.3, 152.9, 153.8, 162.8. MS (EI) *m/z* (rel intensity) 486 (M^+, 3), 360 (23), 359 (100), 307 (17), 273 (6), 267 (9), 266 (55), 114 (7), 70 (8).

3.3.22. 1-[2-(2-Iodo-4,5-dimethoxyphenyl)ethyl]-pyrrole-2-carboxylic acid methoxy methyl amide (13a). According to the general procedure, pyrrole-2-carboxamide **4b** (150 mg, 1 mmol) was treated with KOH (220 mg, 4 mmol) in DMSO (10 mL), and tosylate **12a** (440 mg, 1 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **13a** as a colourless oil (290 mg, 67%); IR ($CHCl_3$) 1620 cm^{-1}; ^1H NMR ($CDCl_3$) 3.13 (t, J=6.9 Hz, 2H), 3.33 (s, 3H), 3.68 (s, 3H), 3.72 (s, 3H), 3.83 (s, 3H), 4.46 (t, J=6.9 Hz, 2H), 6.04 (dd, J=4.0, 2.6 Hz, 1H), 6.45 (s, 1H), 6.57 (dd, J=2.6, 1.8 Hz, 1H), 6.91 (dd, J=4.0, 1.8 Hz, 1H), 7.19 (s, 1H); ^{13}C NMR ($CDCl_3$) 33.7, 42.1, 49.2, 55.6, 55.9, 60.8, 87.8, 107.1, 112.7, 116.5, 121.0, 122.1, 127.8, 133.6, 147.9, 148.9, 162.3. MS (EI) *m/z* (rel intensity) 444 (M^+, 1), 317 (54), 286 (10), 257 (100), 230 (10), 191 (15), 164 (6).

3.3.23. 1-[3-(2-Iodo-4,5-dimethoxyphenyl)-propyl]-pyrrole-2-carboxylic acid methoxy methyl amide (13b). According to the general procedure, pyrrole-2-carboxamide **4b** (440 mg, 2.8 mmol) was treated with KOH (650 mg, 11.5 mmol) in DMSO (10 mL), and mesylate **12b** (1.15 mg, 2.8 mmol). After work-up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **13b** as a colourless oil (1.14 g, 86%); IR ($CHCl_3$) 1622 cm^{-1}; ^1H NMR ($CDCl_3$) 1.95–2.11 (m, 2H), 2.64 (t, J=7.4 Hz, 2H), 3.31 (s, 3H), 3.69 (s, 3H), 3.81, 3.84 (s, 3H), 4.38 (t, J=6.3 Hz, 2H), 6.11 (dd, J=4.0, 2.6 Hz, 1H), 6.71 (s, 1H), 6.81 (dd, J=2.6, 1.8 Hz, 1H), 6.91 (dd, J=4.0, 1.8 Hz, 1H), 7.19 (s, 1H); ^{13}C NMR ($CDCl_3$) 32.5, 34.0, 37.6, 48.8, 55.9, 56.1, 61.0, 87.9, 107.5, 112.0, 116.5, 121.6, 122.6, 127.3, 136.4, 147.8, 149.3, 162.6. MS (EI) *m/z* (rel intensity) 458 (M^+, 13), 427 (13), 370 (13), 331 (27), 272 (20), 271 (100), 243 (21), 199 (11), 176 (22), 120 (10), 109 (12), 108 (14), 106 (13), 80 (61).

3.3.24. 1-[2-(2-Iodo-4,5-dimethoxyphenyl)-ethyl]-pyrrole-2-carboxylic acid morpholine amide (14a). According to the general procedure, pyrrole-2-carboxamide **4c** (480 mg, 2.7 mmol) was treated with KOH (600 mg, 10.7 mmol) in DMSO (10 mL), and tosylate **12a** (1.06 g, 2.7 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **14a** as a colourless oil (880 mg, 70%); IR ($CHCl_3$) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 3.12 (t, J=6.9 Hz, 2H), 3.69–3.73 (m, 8H), 3.73 (s, 3H), 3.84 (s, 3H), 4.34 (t, J=6.9 Hz, 2H), 6.03 (dd, J=4.0, 2.6 Hz, 1H), 6.27 (dd, J=4.0, 1.6 Hz, 1H), 6.45 (s, 1H), 6.61 (dd, J=2.6, 1.6 Hz, 1H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$) 42.4, 45.6, 48.0, 55.8, 56.0, 66.9, 87.9, 107.0, 112.8, 113.0, 121.2, 124.0, 125.7, 133.5, 148.1, 149.1, 162.9. MS (EI) *m/z* (rel intensity) 470 (M^+, 1), 344 (18), 343 (75), 290 (16), 256 (27), 114 (20), 97 (14), 85 (20), 83 (21), 71 (20), 70 (33), 69 (12).

3.3.25. 1-[3-(2-Iodo-4,5-dimethoxyphenyl)-propyl]-pyrrole-2-carboxylic acid morpholine amide (14b). According to the general procedure, pyrrole-2-carboxamide **4c** (900 mg, 5 mmol) was treated with KOH (1.22 mg, 20 mmol) in DMSO (20 mL), and mesylate **12b** (2.0 g, 5 mmol). After work-up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **14b** as a colourless oil (1.94 g, 86%); IR ($CHCl_3$) 1616 cm^{-1}; ^1H NMR ($CDCl_3$) 1.85–2.05 (m, 2H), 2.67 (t, J=7.4 Hz, 2H), 3.61–3.68 (m, 4H), 3.71–3.80 (m, 4H), 3.86 (s, 3H), 3.88 (s, 3H), 4.25 (t, J=6.3 Hz, 2H), 6.09 (dd, J=4.0, 2.6 Hz, 1H), 6.31 (dd, J=4.0, 1.6 Hz, 1H), 6.66 (s, 1H), 6.80 (dd, J=2.6, 1.6 Hz, 1H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$) 32.3, 37.7, 45.6, 47.6, 55.9, 56.1, 67.1, 87.8, 107.1, 112.0, 113.0, 121.7, 124.1, 125.3, 136.2, 147.9, 149.4, 163.2. MS (EI) *m/z* (rel intensity) 484 (M^+, 7), 370 (8), 358 (24), 357 (100), 271 (18), 270 (39), 243 (10), 207 (10), 177 (25), 151 (10), 120 (11), 114 (71), 108 (13), 80 (19), 70 (16).

3.4. Parham cyclisation reactions. General procedure

Method A. To a solution of iodinated pyrrole-2-carboxamides **5**–**7**, **13** or **14** (1 mmol) in dry THF (15 mL), *t*-BuLi (2.2 mmol) was added at −78 °C, and the resulting mixture was stirred at this temperature for 3 h, allowed to reach rt, and stirred for 4 h. The reaction was quenched by the addition of sat. NH_4Cl (10 mL). Et_2O (15 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. Flash column chromatography afforded **8a**–**g**, **15** or **16**.

Method B. To a solution of iodinated pyrrole-2-carboxamides **5**–**7**, **13** or **14** (1 mmol) in dry THF (15 mL), *t*-BuLi (2.2 mmol) was added at −78 °C, and the resulting mixture was stirred at this temperature for 3 h. The reaction was quenched by the addition of sat. NH_4Cl (10 mL). Et_2O (15 mL) was added, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. Flash column chromatography afforded pyrroloisoquinolones **8a**–**g**, **15** or **16**.

3.4.1. 5*H*-Pyrrolo[1,2-*b*]isoquinolin-10-one (8a). According to the general procedure B pyrrole-2-carboxamide **6a** (288 mg, 0.78 mmol) was treated with *t*-BuLi (1.07 mL of a 1.6 M solution in pentane, 1.72 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **8a** as a colourless oil (125 mg, 87%); IR (neat) 1642 cm^{-1}; ^1H NMR ($CDCl_3$) 5.38 (s, 2H), 6.44 (dd, J= 4.0, 2.4 Hz, 1H), 7.08–7.09 (m, 1H,), 7.20 (dd, J=4.0, 1.5 Hz, 1H), 7.33 (dd, J=7.6, 0.9 Hz, 1H), 7.47 (td, J=7.3, 0.9 Hz, 1H), 7.56 (td, J=7.3, 1.4 Hz, 1H), 8.30 (dd, J=7.6, 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) 46.9, 111.6, 113.6, 125.6, 127.1, 127.8, 129.6, 130.5, 132.4, 135.6, 174.7. MS (EI) *m/z* (rel intensity) 183 (M^+, 100), 182 (58), 155 (11), 154 (51), 128 (12), 127 (30), 89 (16), 77 (20), 63 (20), 51 (13). Anal. Calcd for $C_{12}H_9NO$: C, 78.67; H, 4.95; N, 7.65. Found: C, 78.88; H, 4.82; N, 7.54.

3.4.2. 7,8-Dimethyl-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8b). According to the general procedure B pyrrole-2-carboxamide **7b** (122 mg, 0.29 mmol) was treated with *t*-BuLi (0.72 mL of a 1.05 M solution in pentane, 0.81 mmol). After work up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **8b** as a colourless oil (63 mg, 98%); IR (neat) 1638 cm^{-1}; ^1H NMR ($CDCl_3$) 2.35 (s, 6H), 5.33 (s, 2H), 6.43 (dd, $J=4.0$, 2.8 Hz, 1H), 7.06 (dd, $J=2.8$, 1.6 Hz, 1H), 7.10 (s, 1H), 7.18 (dd, $J=4.0$, 1.6 Hz, 1H), 8.06 (s, 1H); ^{13}C NMR ($CDCl_3$) 19.5, 20.1, 46.6, 111.4, 113.2, 125.3, 126.6, 127.6, 128.3, 129.7, 133.2, 136.6, 142.2, 175.1. MS (EI) *m/z* (rel intensity) 211 (M^+, 100), 210 (28), 197 (12), 196 (80), 168 (13), 167 (15). Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.51; H, 6.17; N, 6.51.

3.4.3. 7-Methoxy-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8c). According to the general procedure A pyrrole-2-carboxamide **7c** (261 mg, 0.61 mmol) was treated with *t*-BuLi (1.68 mL of a 0.8 M solution in pentane, 1.3 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **8c** as a colourless oil (105 mg, 81%); IR (neat) 1638 cm^{-1}; ^1H NMR ($CDCl_3$) 3.88 (s, 3H), 5.34 (s, 2H), 6.41 (dd, $J=4.0$, 2.4 Hz, 1H), 6.78 (dd, $J=2.4$, 1.2 Hz, 1H), 6.98 (dd, $J=8.7$, 2.4 Hz, 1H), 7.04 (dd, $J=2.4$, 1.6 Hz, 1H), 7.16 (dd, $J=4.0$, 1.2 Hz, 1H), 8.25 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 47.0, 55.5, 110.1, 111.4, 113.1, 114.0, 123.9, 125.2, 129.4, 129.6, 137.9, 162.8, 174.3. MS (EI) *m/z* (rel intensity) 213 (M^+, 100), 182 (24), 170 (41), 169 (14), 142 (13), 141 (13), 115 (10), 87 (14), 85 (66), 83 (94). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.22; H, 5.20; N, 6.57. Found: C, 73.14; H, 5.27; N, 6.41.

3.4.4. 7,8-Dimethoxy-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8d). According to the general procedure B pyrrole-2-carboxamide **7d** (425 mg, 0.93 mmol) was treated with *t*-BuLi (2.0 mL of a 1.3 M solution in pentane, 2.61 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **8d** as a colourless oil (199 mg, 88%); IR (neat) 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 3.90 (s, 3H), 3.92 (s, 3H), 5.17 (s, 2H), 6.35 (dd, $J=4.0$, 2.4 Hz, 1H), 6.64 (s, 1H), 6.95–6.97 (m, 1H), 7.08 (dd, $J=4.0$, 1.5 Hz, 1H), 7.63 (s, 1H); ^{13}C NMR ($CDCl_3$) 46.4, 56.0, 56.0, 107.1, 107.9, 111.1, 112.7, 123.7, 125.2, 129.2, 129.7, 148.7, 152.8, 174.1. MS (EI) *m/z* (rel intensity) 243 (M^+, 100), 242 (22), 228 (21), 212 (28), 200 (13), 199 (13). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.24; H, 5.41; N, 5.84.

3.4.5. 6,7-Dimethoxy-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8e). According to the general procedure B pyrrole-2-carboxamide **7e** (140 mg, 0.31 mmol) was treated with *t*-BuLi (0.77 mL of a 1.12 M solution in pentane, 0.86 mmol). After work up, flash column chromatography (silicagel, 20% hexane/AcOEt) afforded **8e** as a white powder, that was crystallised from Et_2O (53 mg, 76%): mp(Et_2O) 177–179 °C; IR (KBr) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 3.94 (s, 3H), 3.97 (s, 3H), 5.37 (s, 2H), 6.43 (dd, $J=4.0$, 2.4 Hz, 1H), 7.05 (d, $J=8.7$ Hz, 1H), 7.10 (dd, $J=2.4$, 1.6 Hz, 1H), 7.17 (dd, $J=4.0$, 1.6 Hz, 1H), 8.09 (d, $J=8.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 43.4, 55.9, 60.3, 111.5, 113.1, 123.9, 124.1, 125.7, 129.3, 129.9, 143.8, 155.6, 174.2. MS (EI) *m/z* (rel intensity) 243 (M^+, 100), 242 (12), 213 (16), 212 (63), 198 (10), 185 (16), 157 (16). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.79; H, 5.48; N, 5.72.

3.4.6. 7,8-Methylenedioxy-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8f). According to the general procedure B pyrrole-2-carboxamide **6f** (159 mg, 0.38 mmol) was treated with *t*-BuLi (0.52 mL of a 1.6 M solution in pentane, 0.84 mmol). After work up, flash column chromatography (silicagel, 30% hexane/AcOEt) afforded **8f** as a white powder, that was crystallised from Et_2O (163 mg, 73%): mp(Et_2O) 181–183 °C; IR (KBr) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 5.24 (s, 2H), 6.03 (s, 2H), 6.38 (dd, $J=4.0$, 2.8 Hz, 1H), 6.69 (s, 1H), 7.02 (broad s, 1H), 7.10 (dd, $J=4.0$, 1.2 Hz, 1H), 7.64 (s, 1H); ^{13}C NMR ($CDCl_3$) 46.9, 101.9, 105.0, 105.9, 111.3, 112.9, 125.2, 129.2, 131.7, 147.8, 151.5, 173.8. MS (EI) *m/z* (rel intensity) 227 (M^+, 66), 226 (M^+-1, 26), 169 (17), 141 (14), 87 (14), 85 (72), 83 (100). Anal. Calcd for $C_{13}H_9NO_3$: C, 68.72; H, 3.99; N, 6.16. Found: C, 68.28; H, 3.86; N, 5.94.

3.4.7. 7,8,9-Trimethoxy-5*H*-pyrrolo[1,2-*b*]isoquinolin-10-one (8g). According to the general procedure B pyrrole-2-carboxamide **6g** (202 mg, 0.43 mmol) was treated with *t*-BuLi (0.59 mL of a 1.6 M solution in pentane, 0.95 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **8g** as a colourless oil that was crystallised from Et_2O (80 mg, 68%): mp(Et_2O) 144–145 °C; IR (neat) 1639 cm^{-1}; ^1H NMR ($CDCl_3$) 3.91 (s, 3H), 3.94 (s, 3H), 3.97 (s, 3H), 5.30 (s, 2H), 6.38 (dd, $J=4.0$, 2.4 Hz, 1H), 6.60 (s, 1H), 6.97 (dd, $J=2.4$, 1.6 Hz, 1H), 7.10 (dd, $J=4.0$, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 47.0, 56.0, 61.2, 61.7, 104.3, 111.1, 112.7, 118.4, 124.0, 130.4, 133.8, 142.6, 155.5, 156.6, 174.0. MS (EI) *m/z* (rel intensity) 273 (M^+, 76), 272 (6), 259 (14), 258 (100), 256 (12), 240 (9), 230 (11), 228 (8), 227 (14), 215 (17), 213 (6), 212 (14), 207 (9), 198 (8), 197 (6), 184 (6), 170 (6), 137 (17), 94 (15), 85 (7), 83 (8), 51 (7). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.12. Found: C, 66.17; H, 5.65; N, 5.12.

3.4.8. 8,9-Dimethoxy-5,6-dihydropyrrolo[1,2-*a*]benzo-[*d*]azepin-11-one (15). According to the general procedure B pyrrole-2-carboxamide **14a** (108 mg, 0.23 mmol) was treated with *t*-BuLi (0.57 mL of a 1.0 M solution in pentane, 0.57 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **15** as a colourless oil that was crystallised from pentane (23 mg, 58%): mp (pentane) 122–124 °C; IR (neat) 1639 cm^{-1}; ^1H NMR ($CDCl_3$) 3.24–3.28 (m, 2H), 3.93 (s, 6H), 4.30–4.34 (m, 2H), 6.20 (dd, $J=4.0$, 2.4 Hz, 1H), 6.63 (s, 1H), 6.82 (dd, $J=2.4$, 2.0 Hz, 1H), 7.36 (dd, $J=4.0$, 2.0 Hz, 1H), 7.75 (s, 1H); ^{13}C NMR ($CDCl_3$) 35.6, 50.0, 56.0, 109.4, 111.7, 113.6, 121.0, 127.9, 129.5, 133.5, 133.6, 147.9, 151.9, 179.4. MS (EI) *m/z* (rel intensity) 258 ($M^+ +1$; 18), 257 (M^+, 100), 256 (15), 242 (10), 191 (35), 164 (12). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.87; N, 5.44. Found: C, 69.98; H, 5.43; N, 5.37.

3.4.9. 9,10-Dimethoxy-6,7-dihydro-5*H*-pyrrolo[1,2-*a*]-benzo[*d*]azocin-12-one (16). According to the general procedure B pyrrole-2-carboxamide **13b** (269 mg, 0.59 mmol) was treated with *t*-BuLi (1.36 mL of a 1.08 M

solution in pentane, 1.47 mmol). After work up, flash column chromatography (silicagel, 40% hexane/AcOEt) afforded **16** as a colourless oil (88 mg, 55%); IR (neat) 1590 cm^{-1}; ^1H NMR ($CDCl_3$) 1.85–2.01 (m, 2H), 2.66 (t, $J=7.4$ Hz, 2H), 3.31 (s, 3H), 3.69 (s, 3H), 3.81, 3.84 (s, 3H), 4.38 (t, $J=6.3$ Hz, 2H), 6.22 (dd, $J=4.0$, 2.6 Hz, 1H), 6.57 (s, 1H), 6.76 (dd, $J=2.6$, 1.8 Hz, 1H), 7.24 (dd, $J=4.0$, 1.8 Hz, 1H), 7.31 (s, 1H); ^{13}C NMR ($CDCl_3$) 29.6, 32.8, 45.6, 55.9, 109.4, 111.1, 112.6, 119.3, 128.0, 131.2, 132.4, 135.7, 147.6, 152,0, 183.1. MS (EI) *m/z* (rel intensity) 271 (M^+, 100), 254 (10), 243 (27), 242 (15), 228 (17), 212 (17), 191 (30), 163 (12), 106 (12). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.31; N, 5.16. Found: C, 70.53; H, 6.20; N, 5.22.

3.4.10. 1-Benzylpyrrole-2-carboxylic acid diethyl amide (9a). Obtained as a by-product (14 mg, 13%) when, according to the general procedure A, pyrrole-2-carboxamide **5a** (160 mg, 0.4 mmol) was treated with *t*-BuLi (0.6 mL of a 1.6 M solution in pentane, 0.9 mmol); IR (neat) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.02 (t, $J=7.1$ Hz, 6H), 3.32 (q, $J=7.1$ Hz, 4H), 5.31 (s, 1H), 6.10 (dd, $J=3.6$, 2.4 Hz, 1H), 6.33 (dd, $J=3.6$, 1.6 Hz, 1H), 6.81 (dd, $J=2.4$, 1.6 Hz, 1H), 7.06–7.10 (m, 2H), 7.17–7.29 (m, 3H); ^{13}C NMR ($CDCl_3$) 13.5, 42.1, 51.5, 106.6, 111.1, 124.9, 125.9, 127.1, 127.3, 128.3, 138.5, 163.8. MS (EI) *m/z* (rel intensity) 256 (M^+, 15), 184 (38), 183 (14), 156 (25), 91 (100), 72 (16), 65 (26).

3.4.11. 1-(3,4-Dimethylbenzyl)pyrrole-2-carboxylic acid diethyl amide (9b). Obtained as a by-product (10 mg, 18%) when, according to the general procedure A, pyrrole-2-carboxamide **5b** (80 mg, 0.2 mmol) was treated with *t*-BuLi (0.4 mL of a 1.0 M solution in pentane, 0.4 mmol); IR (neat) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.04 (t, $J=7.1$ Hz, 6H), 2.19 (s, 3H), 2.20 (s, 3H), 3.35 (q, $J=7.1$ Hz, 4H), 5.23 (s, 2H), 6.08 (dd, $J=4.0$, 2.8 Hz, 1H), 6.32 (dd, $J=4.0$, 1.6 Hz, 1H), 6.78–6.84 (m, 2H), 6.89 (s, 1H), 7.01 (d, $J=8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.3, 19.4, 19.7, 41.4, 51.3, 106.6, 111.0, 124.8, 125.9, 128.7, 129.6, 135.6, 135.9, 136.5, 164.0. MS (EI) *m/z* (rel intensity) 284 (M^+, 18), 212 (25), 211 (24), 196 (16), 184 (21), 120 (12), 119 (100), 91 (23), 77 (11), 72 (20).

3.4.12. 1-(3-Methoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (9c). Obtained as a by-product (13 mg, 39%) when, according to the general procedure A, pyrrole-2-carboxamide **5c** (48 mg, 0.1 mmol) was treated with *t*-BuLi (0.2 mL of a 1.0 M solution in pentane, 0.2 mmol); IR (neat) 1604 cm^{-1}; ^1H NMR ($CDCl_3$) 1.04 (t, $J=7.1$ Hz, 6H), 3.35 (c, $J=7.1$ Hz, 4H), 3.74 (s, 3H), 5.28 (s, 2H), 6.10 (dd, $J=3.6$, 2.8 Hz, 1H), 6.33 (dd, $J=3.6$, 1.6 Hz, 1H), 6.62–6.80 (m, 4H), 7.17 (t, $J=7.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.3, 40.5, 51.5, 55.1, 106.8, 111.2, 112.7, 112.8, 119.4, 125.0, 126.0, 129.4, 140.2, 159.7, 163.9 (CO). MS (EI) *m/z* (rel intensity) 286 (M^+, 61), 215 (16), 214 (86), 213 (51), 187 (26), 186 (41), 170 (11), 122 (15), 121 (100), 94 (10), 91 (34), 78 (18), 77 (16), 72 (24), 65 (12).

3.4.13. 1-(3,4-Dimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (9d). Obtained as a by-product (30 mg, 24%) when, according to the general procedure A, pyrrole-2-carboxamide **5d** (176 mg, 0.4 mmol) was treated with *t*-BuLi (0.5 mL of a 1.6 M solution in pentane, 0.8 mmol); IR (neat) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.03 (t, $J=7.1$ Hz, 6H), 3.34 (q, $J=7.1$ Hz, 4H), 3.78 (s, 3H), 3.81 (s, 3H), 5.22 (s, 2H), 6.07 (dd, $J=3.6$, 2.8 Hz, 1H), 6.31 (dd, $J=3.6$, 1.6 Hz, 1H), 6.62–6.66 (m, 2H), 6.72–6.75 (m, 1H), 6.78 (dd, $J=2.8$, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.3, 42.0, 51.3, 55.7, 55.8, 106.6, 110.5, 110.9, 119.6, 124.7, 125.8, 131.1, 148.2, 148.8, 163.9. MS (EI) *m/z* (rel intensity) 316 (M^+, 18), 244 (6), 243 (18), 216 (8), 152 (12), 151 (100), 107 (11), 72 (9). Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.64; N, 8.85. Found: C, 68.54; H, 7.46; N, 8.77.

3.4.14. 1-(2,3-Dimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (9e). Obtained as a by-product (41 mg, 35%) when, according to the general procedure A, pyrrole-2-carboxamide **5e** (162 mg, 0.4 mmol) was treated with *t*-BuLi (0.5 mL of a 1.6 M solution in pentane, 0.8 mmol); IR (neat) 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 1.09 (t, $J=7.1$ Hz, 6H), 3.42 (q, $J=7.1$ Hz, 4H), 3.76 (s, 3H), 3.83 (s, 3H), 5.34 (s, 2H), 6.07 (dd, $J=4.0$, 2.8 Hz, 1H), 6.31 (dd, $J=4.0$, 1.6 Hz, 1H), 6.52 (d, $J=7.9$ Hz, 1H), 6.79 (dd, $J=2.8$, 1.6 Hz, 1H), 6.82 (s, 1H), 6.93 (t, $J=7.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.4, 46.5, 55.7, 60.4, 106.6, 110.8, 111.7, 120.7, 123.8, 125.2, 126.0, 132.3, 146.6, 152.4, 164.0. MS (EI) *m/z* (rel intensity) 316 (M^+, 56), 285 (21), 245 (10), 244 (57), 243 (15), 229 (10), 228 (39), 216 (16), 214 (17), 212 (16), 186 (13), 165 (10), 152 (11), 151 (76), 137 (13), 136 (100), 135 (11), 122 (16), 106 (13), 100 (13), 94 (14), 91 (58), 80 (11), 78 (11), 77 (11), 72 (29), 65 (22).

3.4.15. 1-(3,4-Methylendioxybenzyl)pyrrole-2-carboxylic acid diethyl amide (9f). Obtained as a by-product (11 mg, 14%) when, according to the general procedure A, pyrrole-2-carboxamide **5f** (112 mg, 0.3 mmol) was treated with *t*-BuLi (0.4 mL of a 1.6 M solution in pentane, 0.6 mmol); ^1H NMR ($CDCl_3$) 1.08 (t, $J=7.1$ Hz, 6H), 3.37 (q, $J=7.1$ Hz, 4H), 5.20 (s, 2H), 5.90 (s, 2H), 6.08 (dd, $J=4.0$, 2.4 Hz, 1H), 6.32 (dd, $J=4.0$, 1.6 Hz, 1H), 6.61–6.69 (m, 2H), 6.71–6.74 (m, 1H), 6.78 (dd, $J=2.4$, 1.6 Hz, 1H).

3.4.16. 1-(3,4,5-Trimethoxybenzyl)pyrrole-2-carboxylic acid diethyl amide (9g). According to the general procedure A pyrrole-2-carboxamide **5g** (140 mg, 0.3 mmol) was treated with *t*-BuLi (0.7 mL of a 1.0 M solution in pentane, 0.7 mmol). After work up, flash column chromatography (silicagel, 50% hexane/AcOEt) afforded **9g** as a colourless oil (83 mg, 81%); IR (neat) 1616 cm^{-1}; ^1H NMR ($CDCl_3$) 1.02 (t, $J=7.1$ Hz, 6H), 3.35 (q, $J=7.1$ Hz, 4H), 3.75 (s, 6H), 3.77 (s, 3H), 5.24 (s, 2H), 6.09 (dd, $J=3.6$, 2.8 Hz, 1H), 6.29 (s, 2H), 6.33 (dd, $J=3.6$, 1.6 Hz, 1H), 6.80 (dd, $J=2.4$, 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) 13.3, 40.9, 51.7, 55.9, 60.7, 104.0, 106.7, 111.4, 125.0, 125.8, 134.3, 153.1, 163.7. MS (EI) *m/z* (rel intensity) 346 (M^+, 39), 273 (11), 242 (38), 182 (16), 181 (100), 137 (11), 83 (14).

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