Synthesis of non-symmetrical 3,4-diaryl-substituted pyrroles: implementation for the preparation of lamellarin R

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A straightforward method for synthesising symmetrical and non-symmetrical 3,4-diaryl-substituted pyrroles is proposed, consisting of (i) the condensation reaction between phenylacetonitriles and aldehydes to give acrylonitriles, (ii) the conjugate addition of cyanide to afford succinonitriles, and (iii) reduction of the succinonitriles with DIBAL-H to provide the target pyrroles in good overall yields. The implementation of this technology for the preparation of lamellarin R is presented.

Keywords: heterocyclic compounds, pyrroles, lamellarins, *N*-arylation of pyrroles, natural products

In recent years, an increasing number of alkaloids with different molecular architectures containing a pyrrole ring have been isolated from marine organisms,[1–3] mainly from ascidians and sponges, as well as from other sources.[4] Among these natural products, lamellarins (Fig. 1) are an important group of pyrrole-containing compounds first isolated by Faulkner in 1985 from the marine mollusc *Lamellaria* sp.[5] Since the isolation of lamellarins A–D, an increasing number of structurally related compounds have been reported.[6] For instance, in 1988 lamellarins E–H were isolated from the marine ascidian *Didemnum chartaceum*.[7] In 1992, the structurally related compounds lukianol A and B were recovered from an unidentified tunicate,[8] and in 1993 lamellarins I–N were reported from an Australian colonial ascidian *Didemnum* sp.[9] Later, in 1994, lamellarins O and P,[10] and in 1995, lamellarins Q and R[11] were obtained from different geographically located specimens of the marine sponge *Dendrilla cactos*. Currently, more than 70 different lamellarins and structurally related 3,4-diaryl-substituted pyrrole-derived compounds, isolated from diverse marine organisms, have been reported. Remarkably, a significant number of the members of this group of alkaloids exhibit different kinds of biological activities, including antitumour,[12] reversal of multidrug resistance (MDR), antiviral and HIV inhibition.[13] Until now, lamellarin D has been the most studied and promising member of this family of compounds.[14–17]

All lamellarins possess aryl substituents at C-3 and C-4 of the pyrrole moiety, and they can be classified into three groups according to their structural features. In the first group, the central pyrrole ring is unfused. In the second group, the pyrrole moiety is fused to an isoquinoline ring with an unsaturated C5–C6 bond, whereas in the third group the pyrrole contains a quinoline ring with a saturated C5–C6 bond.[18,19]

In recent decades, different approaches have been reported for the synthesis of lamellarins.[6,19,20] For instance, 10 years after the isolation of lamellarins A–D, Fürstner and co-workers[21] employed the reductive cleavage of the N–O bond of a 2,3-diarylisoxazole, followed by a McMurry cyclisation as the fundamental transformation, to accomplish the first total synthesis of the *O*-dimethyl ether of lamellarin O. Starting from this compound, they were able to obtain lamellarin O and lukianol A. Similarly, Boger reported the synthesis of lamellarin O using an elegant aza-Diels-Alder strategy combining a 1,2,4,5-tetrazine and a 1,2-diaryl acetylene[22]. Several subsequent syntheses of non-fused pyrrole lamellarins focused instead on lamellarin Q dialkyl ethers as the key intermediate for further

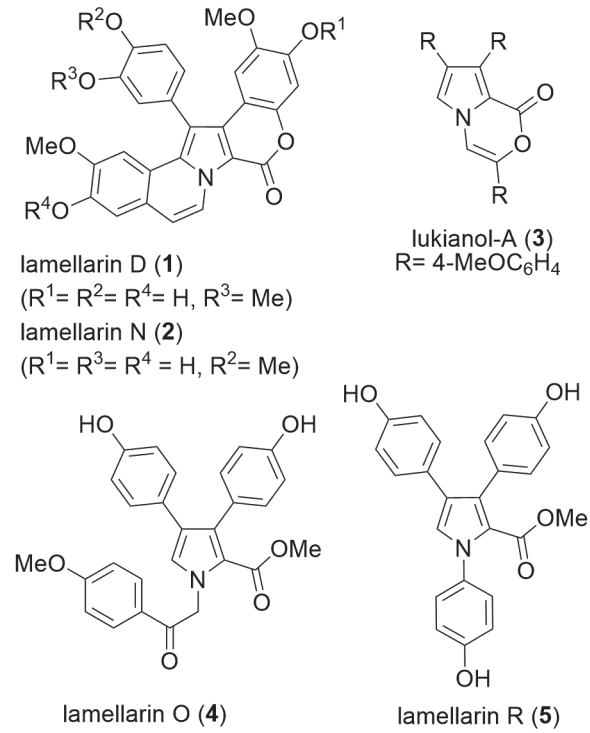

Fig. 1. Structures of lamellarins D, N, O, R and lukianol A.

transformations. Examples include the works of Banwell[23] on the synthesis of lamellarin O, Alvarez[24] for lamellarine Q, and Iwao[25] for lamellarins P and R by constructing the pyrrole nucleus first, followed by the introduction of the phenyl rings using cross-coupling procedures.[26-28]. More recently, our group used a Paal–Knorr approach for the preparation of 3,4-disubstitued pyrroles starting from succinonitriles as 1,4-dicarbonyl precursors (Scheme 1). Thus, we were able to prepare lamellarins Q and O quite easily.[29]

The wide variety of biological activities displayed by lamellarins continues to elicit the interest of synthetic chemists in developing new and more efficient methodologies for obtaining these compounds in the quantities required for extensive biological studies. Herein, we disclose the scope of our previously reported methodology, as well as its implementation, by making a series of non-symmetrical 3,4-diarylpyrroles in combination with a copper-catalysed cross-coupling reaction in a new synthesis of lamellarin R.

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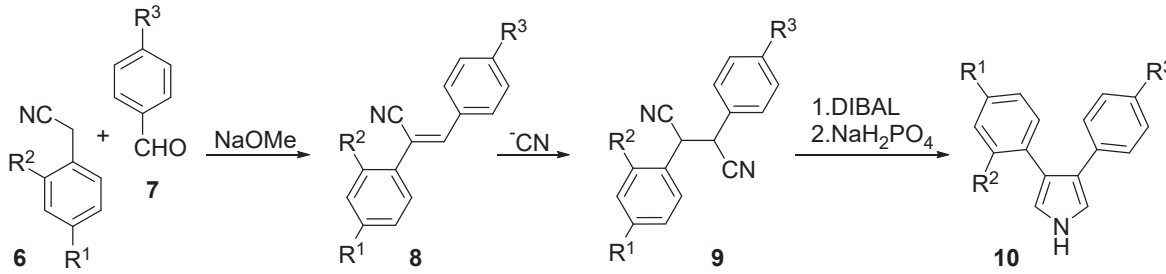


Scheme 1 Methodology for the synthesis of non-symmetrical 3,4-diaryl-substituted pyrroles.

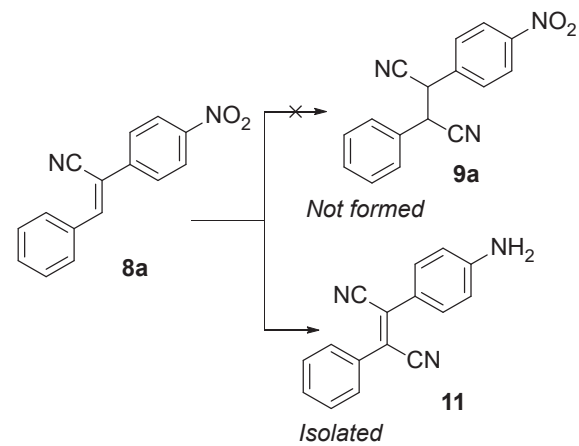
Results and discussion

From a general viewpoint, two approaches can be envisioned for the synthesis of a heterocyclic compound: (i) modification on an existing heterocyclic ring, usually through substitution reactions, and (ii) synthesis of the heterocyclic core from an acyclic precursor.[29] Even though pyrroles undergo electrophilic substitution in a straightforward manner, this process takes place preferentially or exclusively at C2/C5, and some additional manipulations might be required to introduce substituents selectively at C3/C4 (*e.g.* introduction of a triisopropylsilyl ether (TIPS) protecting group at the nitrogen atom).[30]

Knoevenagel condensation between benzaldehyde and phenylacetonitriles **6a–h**, according to a reported methodology,[29] afforded the desired acrylonitrile derivatives **8a–h**, in a straightforward fashion (Table 1, entries 2–8). However, the reaction between (4-nitrophenyl)acetonitrile and benzaldehyde did not occur under the conditions mentioned above (sodium methoxide, 1.2 equiv. in methanol), leading only to complete consumption of (nitrophenyl)acetonitrile, presumably due to the high stability of the corresponding anion. To overcome this obstacle, acrylonitrile **8a** was prepared using K_3PO_4 as a solid basic catalyst, as reported by Saad[31] (Table 1, entry 1). For the formation of succinonitriles, we used standard conditions (KCN/NH_4Cl; DMF/H_2O). Unfortunately, nitroacrylonitrile **8a** did not react to form succinonitrile **9a**, and compound **11** was the only isolated product (Table 2, entry 1). We believe that compound **11** might be formed by a formal redox reaction. Experiments to investigate the mechanism for this transformation are currently underway, and the results will be published elsewhere.

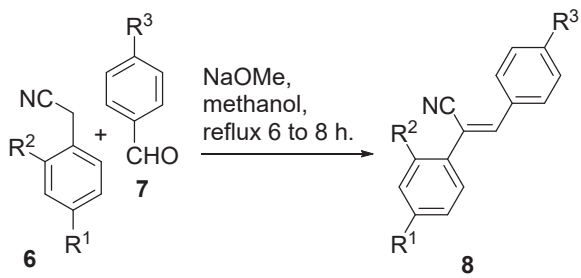
Finally, treatment of succinonitriles **9b–h** with diisobutylaluminium hydride (DIBAL) (2.5 equiv) followed by aqueous NaH_2PO_4 afforded the desired pyrroles in good overall yields (Table 3).

After proving the generality of our method, we explored the functionalisation of the N atom in the pyrrole ring. Base on a report by Buchwald and co-workers, where they performed copper-mediated cross-couplings between N–H heterocycles and aromatic iodides in the presence of diamine ligands in excellent yields,[32] we explored the arylation of 3,4-diphenylpyrrole **12** using commercially available 4-iodoanisole under Buchwald's conditions (Scheme 3). In our first experiment, ethylenediamine, an inexpensive ligand for this reaction, was



Scheme 2 Formal redox reaction of **8a**.

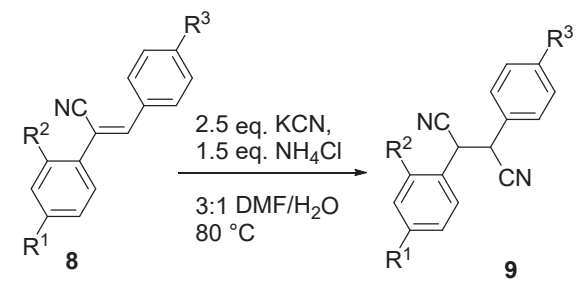
Table 1 Knoevenagel condensation



Entry	R^1	R^2	R^3	Product	Yield (%)
1[a]	NO_2	H	H	**8a**	91
2	Cl	H	H	**8b**	95
3	Me	H	H	**8c**	95
4	OMe	H	H	**8d**	87
5	H	OMe	H	**8e**	98
6	NMe_2	H	H	**8f**	84
7	NBn_2	H	H	**8g**	98
8	NBn_2	H	Cl	**8h**	95

[a]4 equiv. of K_3PO_4 were used as the base.

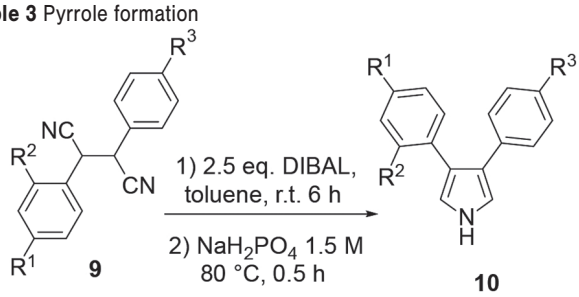
Table 2 Michael addition of cyanide to obtain succinonitriles



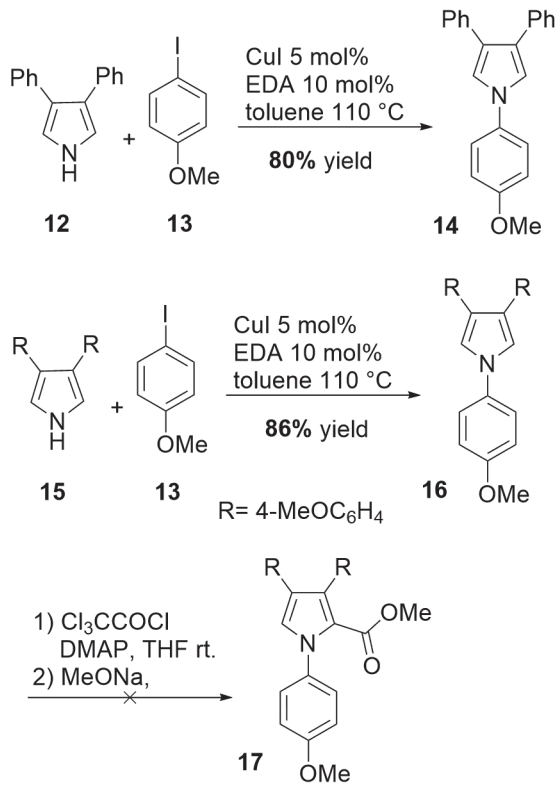
Entry	R^1	R^2	R^3	Product	Yield (%)
1	NO_2	H	H	**9a**	ND
2	Cl	H	H	**9b**	86
3	Me	H	H	**9c**	89
4	OMe	H	H	**9d**	89
5	H	OMe	H	**9e**	79
6	NMe_2	H	H	**9f**	94
7	NBn_2	H	H	**9g**	90
8	NBn_2	H	Cl	**9h**	92

ND, not determined.

Table 3 Pyrrole formation

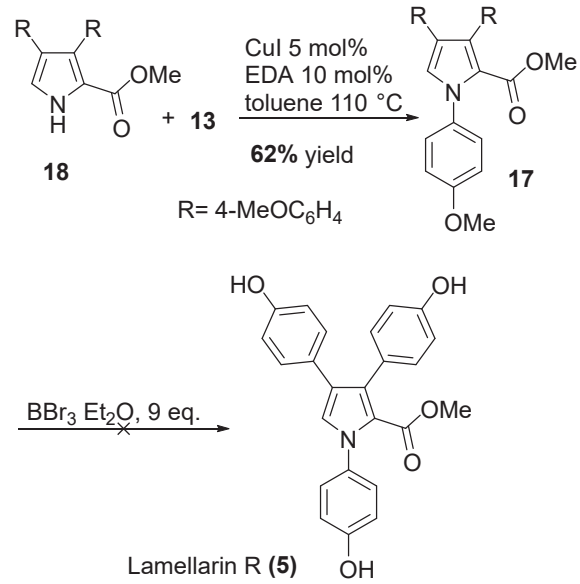


Entry	R^1	R^2	R^3	Product	Yield (%)
1	Cl	H	H	**10b**	70
2	Me	H	H	**10c**	73
3	OMe	H	H	**10d**	70
4	H	OMe	H	**10e**	62
5	NMe_2	H	H	**10f**	64
6	NBn_2	H	H	**10g**	72
7	NBn_2	H	Cl	**10h**	70



Scheme 3 *N*-arylation of 3,4-diaryl-substituted pyrroles under Buchwald's conditions.

used instead of Buchwald's *N,N'*-dimethylethylenediamine. After 18 h of reaction, we were delighted to isolate the desired 1,3,4-triarylpyrrole **14** in 80% yield. When 3,4-bis(4-methoxyophenyl)pyrrole **15**[29] was coupled to 4-iodoanisole **13** under the above conditions, 1,3,4-triarylpyrrole **16** was isolated in 86% yield in a reproducible manner. Jia was able to introduce the carboxymethyl functionality into the pyrrole moiety using a Vilsmeier–Haack formylation, oxidation and esterification sequence of reactions[33]. Since we were able to introduce the same functionality into a 3,4-diaryl-substituted pyrrole with trichloroacetyl chloride in the presence of 4-dimethylaminopyridine (DMAP), followed by methanolysis,[29] compound **16** was subjected to our conditions to obtain the desired trimethoxy lamellarin R **17**. Unfortunately, this reaction



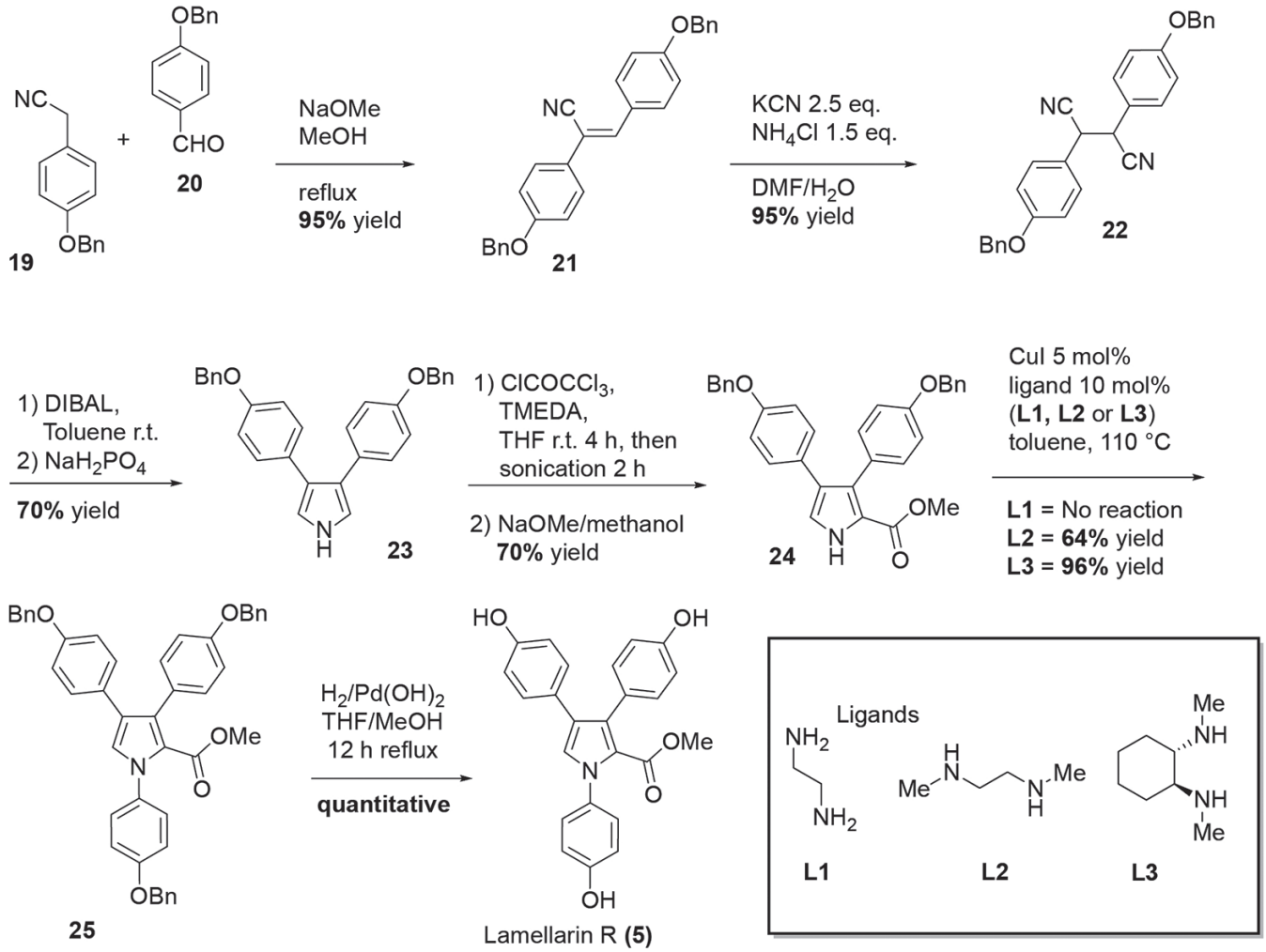
Scheme 4 Attempts to obtain lamellarin R.

did not take place, and we recovered only unreacted pyrrole **16** (Scheme 3).

Our unsuccessful attempts to acylate **16** prompted us to modify the order of the transformations. Thus, we decided to prepare the Fürstner intermediate **18** first, using our reported porcedure,[29] and then to perform the coupling between **18** and 4-iodoanisole **13** (Scheme 4). With this modification, we were able to obtain trimethoxy lamellarin R **17** in 62% yield. Despite the fact that deprotection of trimethoxy lamellarin R with BBr_3 has been reported,[33] we were unable to reproduce the procedure to deprotect **17** (Scheme 4). To circumvent the problem of deprotection, benzylated pyrrole **23** was prepared in three steps (62% yield). The yield for the carboxymethylation step (**23** to **24**, Scheme 5), previously described by our group,[29] was improved from 56% to 70% by performing the reaction under sonication for 1 h, followed by stirring the reaction mixture for 5 h at room temperature (Scheme 5).

Surprisingly, **24** did not react under the conditions used to arylate **18** (Scheme 4). Buchwald reported[32] that the best results for this transformation are obtained when *N,N'*-dimethylcyclohexan-1,2-diamine (**L3**) and *N,N'*-dimethylethylenediamine (**L2**) are used as the ligands. Indeed, when **23** was subjected to Buchwald's conditions using these ligands, **25** was readily obtained in 96% (*N,N'*-dimethylcyclohexan-1,2-diamine) and 64% (*N,N'*-dimethylethylenediamine) yields (Scheme 5). Finally, removal of the benzyl protective groups was conducted with $H_2/Pd(OH)_2$ in methanol to afford lamellarin R (**5**) in quantitative yield. All of the intermediates and products were satisfactorily characterised, and the ^{1}H NMR chemical shifts for compound **5** compared favourably with those reported in the literature[25,33].

Originally, ^{1}H and ^{13}C NMR spectra for lamellarin R prepared by us were recorded in $CDCl_3$; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.14 (d, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 8.6 Hz, 2H), 6.92 (s, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 6.60 (d, *J* = 8.7 Hz, 2H), 3.40 (s, 3H)]. Some differences in chemical shifts were observed between the spectra in $CDCl_3$ and those collected in deuterated acetone reported by Iwao.[25] When we recorded the spectra in deuterated acetone, our ^{13}C NMR spectrum was identical to Iwao's spectrum. However, our ^{1}H NMR spectrum showed some minor differences in the chemical shifts for the OH



Scheme 5 Synthesis of lamellarin R.

signals compared to Iwao's spectrum, which we attributed to differences in concentration.

To the best of our knowledge, two routes have been reported for the synthesis of lamellarin R. The first, in 2008, by Iwao[25] relies on Pd-mediated coupling reactions between 3,4-dibromopyrrole and the corresponding aryl derivative to obtain lamellarin R in 8% yield over eight steps. In 2011, Jia[33] reported a biomimetic approach for lamellarin R (five steps, 53% overall yield) consisting of oxidative transformations. The introduction of the carboxyl functionality was achieved *via* a sequence of Vilsmeier–Haack formylation, oxidation and esterification reactions. However, 2-(4-methoxyphenyl)acetaldehyde is not readily available, and some additional steps are required for its preparation, which has a detrimental effect on the overall yield.

Conclusions

A simple procedure for the preparation of non-symmetrical 3,4-diarylpyrroles in excellent yields employing readily available starting materials has been developed. Our method is amenable to scaling and starts from easily prepared succinonitriles as 1,4-dicarbonyl surrogates. Using our protocol, we were able to synthesise lamellarin R (**5**) in 42% overall yield. We believe that this methodology might be of practical use for synthetic chemists and can be implemented with suitable modifications for the preparation of other 3,4-diarylpyrrole structural motifs commonly present in the lamellarin family of alkaloids.

Experimental

Commercial reagents were purchased from Sigma-Aldrich and were used without further purification. Solvents were purified by distillation and were dried using Na/benzophenone when required. All reactions were monitored by TLC. Crude-mixture purifications were performed by flash column chromatography (FCC) on silica gel 60 mesh. NMR measurements were performed on a Varian Inova 300 MHz instrument using Me_4Si as internal standard. Infrared (IR) spectra were recorded on a PerkinElmer IR-FT with ATR Spectrum 400 spectrophotometer. High-resolution mass spectra (HRMS) were collected using a JEOL SMX-102a spectrometer. Melting points were obtained on a MeltTemp apparatus and are uncorrected.

Synthesis of 2,3-diarylacrylonitrile derivatives; general procedure

2-(4-Chlorophenyl)-3-phenylacrylonitrile (**8b**)

A 30% solution of NaOMe in MeOH (2.86 mL, 16 mmol) was added to a mixture of 4-chlorophenylacetonitrile (2.00 g, 13.27 mmol) and benzaldehyde (1.41 g, 13.27 mmol) in MeOH (90 mL), at room temperature under nitrogen. The mixture was refluxed for 12 h. The reaction mixture was cooled to room temperature, diluted with 50% EtOAc–hexanes (100 mL), washed successively with H_2O (3 × 30 mL) and brine (30 mL), dried over Na_2SO_4 and the solvent removed *in vacuo* to afford 3.00 g (95% yield) of the desired product (used without further purification in the next reaction): White solid; m.p. 89–91 °C; IR (ν_{max}/cm^{-1}): 3057, 2217, 1598, 1492, 821, 750; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92–7.85 (m, 2H), 7.61 (d, J = 8.7 Hz, 2H), 7.51 (s, 1H), 7.49–7.44 (m, 3H), 7.41 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.9, 142.6, 135.3, 133.5, 133.0 130.8, 129.4, 129.1, 127.3, 117.7,

110.5; MS *m/z* (relative intensity): 204 (100%), 239 (60%), 240 (11%) (M^+), 241 (19%).

*3-Phenyl-2-(*p*-tolyl)acrylonitrile* (**8c**) $C_{16}H_{13}N$, from 4-methylphenylacetonitrile (3.00 g, 22.9 mmol) and benzaldehyde (2.43 g, 22.9 mmol) gave 4.76 g (95% yield): Pale yellow powder; m.p. 38–39 °C; IR (ν_{max}/cm^{-1}): 3054, 3030, 2216, 1605, 1445, 909, 689; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.93–7.87 (m, 2H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.51 (s, 1H), 7.49–7.41 (m, 3H), 7.26 (d, *J* = 7.9 Hz, 2H), 2.41 (s, 3H); ^{13}CNMR ($CDCl_3$, 75 MHz): δ 141.1, 139.3, 133.8, 131.6, 130.3, 129.7, 129.1, 128.8, 125.8, 118.1, 111.5, 21.2; MS *m/z:* 219 (M^+).

2-(4-Methoxyphenyl)-3-phenylacrylonitrile (**8d**) $C_{16}H_{13}NO$, from 4-methoxyphenylacetonitrile (2.00 g, 13.6 mmol) and benzaldehyde (1.44 g, 13.6 mmol) gave 2.80 g (87% yield): Pale yellow solid; m.p. 71–74 °C; IR (ν_{max}/cm^{-1}): 2964, 2843, 2208, 1510, 1253, 1179, 692; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.89–7.81 (m, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.45 (s, 1H), 7.48–7.35 (m, 3H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.4, 141.8, 134.8, 131.1, 128.9, 128.7, 126.4, 125.7, 118.5, 114.3, 108.6, 55.4; MS *m/z*: 235 (M^+).

2-(2-Methoxyphenyl)-3-phenylacrylonitrile (**8e**) $C_{16}H_{13}NO$, from 2-methoxyphenylacetonitrile (1.00 g, 7.35 mmol) and benzaldehyde (861 mg, 7.35 mmol) gave 1.69 g (98% yield): Amber oil; IR (ν_{max}/cm^{-1}): 2838, 2212, 1596, 1245, 748; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.97 (s, 1H), 7.75–7.66 (m, 2H), 7.49–7.34 (m, 5H), 7.07 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 131.9, 128.9, 129.0, 128.57, 126.1, 124.2, 123.1, 123.1, 120.8, 119.4, 119.4, 110.7, 110.7, 55.64; MS *m/z*: 235 (M^+).

2-(4-(Dimethylamino)phenyl)-3-phenylacrylonitrile (**8f**) $C_{17}H_{16}N_2$, from 4-(dimethylamino)phenylacetonitrile (5.46g, 34.1 mmol) and benzaldehyde (3.60 g, 34.1 mmol) gave 7.12 g (84% yield): Bright yellow solid; m.p. 103–104 °C; IR (ν_{max}/cm^{-1}): 3031, 2900, 2198, 1525, 1371, 1172; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.86 (d, *J* = 8.7 Hz, 2H), 7.69–7.59 (m, 2H), 7.41 (s, 1H), 7.45–7.28 (m, 3H), 6.73 (d, *J* = 9.1 Hz, 2H), 3.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.6, 135.6, 131.3, 128.9, 128.0, 125.5, 121.6, 119.5, 111.6, 104.6, 104.5, 40.1; MS *m/z*: 248 (M^+).

2-[4-(Dibenzylamino)phenyl]-3-phenylacrylonitrile (**8g**) $C_{29}H_{24}N_2$, from 4-(*N,N*-dibenzylamino)phenylacetonitrile (1.00 g, 3.2 mmol) and benzaldehyde (343 mg, 3.2 mmol) gave 1.26 g (98% yield): Bright orange powder; m.p. 81–82 °C; IR (ν_{max}/cm^{-1}): 3028, 2211, 1607, 1519, 1241; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.86–7.78 (m, 2H), 7.49 (d, *J* = 9.0 Hz, 2H), 7.44–7.21 (m, 13H), 6.77 (d, *J* = 9.0 Hz, 2H), 4.71 (s, 3H); ^{13}C NMR ($CDCl_3$ 75 MHz): δ 149.7, 137.8, 137.7, 137.6, 134.4, 129.7, 128.9, 128.9, 127.2, 127.2, 126.5, 122.7, 118.3, 112.5, 111.6, 54.3; MS *m/z* 400 (M^+).

3-(4-Chlorophenyl)-2-[4-(dibenzylamino)phenyl]acrylonitrile (**8h**) $C_{29}H_{23}N_2Cl$, from 4-(*N,N*-dibenzylamino)phenylacetonitrile (2 g, 4.6 mmol) and 4-chlorobenzaldehyde (646 mg, 4.6 mmol) gave 2.01 g (95% yield): Orange-brownish powder; m.p. 97–99 °C; IR (ν_{max}/cm^{-1}): 3058, 3027, 2212, 1519, 1200, 729; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.38 (s, 1H), 7.37–7.19 (m, 12H), 6.75 (d, *J* = 9.0 Hz, 2H), 4.70 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.9, 137.7, 135.9, 135.4, 132.9, 130.1, 129.1, 128.9, 127.2, 126.5, 122.4, 118.1, 112.5, 112.2, 105.0, 54.3; MS *m/z* (relative intensity): 91 (100%), 203 (18%), 343 (23%), 434 (46%), 435 (14%) (M^+), 436 (15%).

2,3-Bis[4-(benzyloxy)phenyl]acrylonitrile (**20**) $C_{29}H_{23}NO_2$, from 4-(benzyloxy)phenylacetonitrile (500 mg, 2.24 mmol) and 4-(benzyloxy) benzaldehyde (475 mg, 2.24 mmol) gave 890 mg (95% yield): Yellow solid; m.p.130–131 °C; IR (ν_{max}/cm^{-1}): 3063, 3032, 2216, 1248; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.84 (d, *J* = 9 Hz, 2H), 7.57 (d, *J* = 9 Hz, 2H), 7.45–7.33 (m, 11 H), 7.02 (d, *J* = 9 Hz, 2H), 7.00 (d, *J* = 9 Hz, 2H), 5.11 (s, 2H), 5.09 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.2, 159.2, 157.7, 139.9, 136.5, 136.3, 130.9, 128.6, 128.2, 128.1, 127.5, 127.4, 127.0, 126.9, 118.6, 115.3, 115.3, 115.1, 108.4, 70.1, 70.0. MS: *m/z:* 417 (M^+).

Synthesis of 2,3-diarylsuccionontrile derivatives; general procedure

2-(4-Chlorophenyl)-3-phenylsuccinonitrile (**9b**) $C_{16}H_{11}ClN_2$

A solution of KCN (2.00 g, 30.7 mmol) and NH_4Cl (1.00 g, 18.8 mmol) in H_2O (27 mL) was added dropwise to a solution of 2-(4-chlorophenyl)-3-phenylacrylonitrile **8b** (2.9 g, 12.1 mmol) in DMF (81 mL) at room temperature. After the addition was completed, the resultant mixture was heated at 100 °C (oil bath) for 6 h. The reaction mixture was then poured into ice-water (ca. 150 mL) to precipitate the product. The solid was filtered and rinsed with H_2O (100 mL). The product was then dried *in vacuo* to afford the desired succinonitrile: Yellow-cream solid (2.77 g, 86% yield), m.p. 172–173 °C; IR (ν_{max}/cm^{-1}): 2941, 2247, 1492, 1097, 702; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.52 (d, *J* = 8.5 Hz, 2H), 7.50–7.41 (m, 5H), 7.39 (d, *J* = 8.5 Hz, 2H), 5.25–5.15 (m, *J* = 8.3, 4.3 Hz, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 134.4, 134.3, 132.4, 132.4, 131.6, 131.6, 130.9, 130.6, 129.6, 129.5, 128.9, 128.6; MS *m/z* (relative intensity): 116 (72%), 150 (100%), 204 (28%), 266 (7%) (M^+), 267 (1%), 268 (2%).

*2-Phenyl-3-(*p*-tolyl)succinonitrile* (**9c**) $C_{17}H_{14}N_2$, from 3-phenyl-2-(*p*-tolyl)acrylonitrile **8c** (2 g, 9.1 mmol) gave 2.00 g (89% yield): Pale yellow powder; m.p. 166–171 °C; IR (ν_{max}/cm^{-1}): 3059, 2941, 2246, 1494, 1454, 1025, 751, 698; ^{1}H NMR (acetone-d_6 300 MHz,): δ 7.53–7.38 (m, 5H), 7.33–7.22 (m, 4H), 5.01–4.80 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 139.1, 139.0, 132.8, 132.7, 132.7, 130.0, 129.8, 129.6, 129.6, 129.5, 129.5, 129.0, 128.9, 128.7, 128.6, 119.2, 119.1, 119.1, 118.9, 105.1, 41.8, 21.3. MS *m/z*: 246 (M^+).

2-(4-Methoxyphenyl)-3-phenylsuccinonitrile (**9d**) $C_{17}H_{14}N_2O$, from 2-(4-methoxyphenyl)-3-phenylacrylonitrile **8d** (2.5 g, 10.6 mmol) gave 2.53 g (89% yield): Yellow powder; m.p. 152–154 °C; IR (ν_{max}/cm^{-1}): 2938, 2246, 1516, 1250, 1029, 747; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.46–7.36 (m, 5H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 6.97 (d, *J* = 7.2 Hz, 2H), 5.15–4.91 (m, 2H), 3.75 (s, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 159.6, 159.5, 132.3, 132.2, 129.7, 129.5, 128.9, 128.5, 128.2, 124.0, 118.7, 118.6, 118.5, 114.3, 55.2. MS *m/z:* 262 (M^+).

2-(2-Methoxyphenyl)-3-phenylsuccinonitrile (**9e**) $C_{17}H_{14}N_2O$, from 2-(2-methoxyphenyl)-3-phenylacrylonitrile **8e** (3.9g, 16.6 mmol) gave 3.43g (79% yield): Light yellow oil; IR (ν_{max}/cm^{-1}): 2946, 2244, 1597, 1492, 1245, 1020, 697; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60 (d, *J* = 7.4 Hz, 2H), 7.48 (t, *J* = 8.3 Hz, 1H), 7.49–7.38 (m, 5H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 4.62 (d, *J* = 4.6 Hz, 1H), 4.43 (d, *J* = 4.7 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.1, 155.7, 132.3, 131.0, 129.7, 129.4, 129.3, 129.2, 128.9, 128.5, 127.7, 121.4, 121.0, 119.9, 117.1, 117.0, 110.9, 55.9, 55.7, 41.5, 40.1, 39.3, 37.9. MS *m/z*: 262 (M^+).

2-[4-(Dimethylamino)phenyl]-3-phenylsuccinonitrile (**9f**) $C_{18}H_{17}N_3$; from 2-(4-(dimethylamino)phenyl)-3-phenylacrylonitrile **8f** (2.35g, 9.5 mmol) gave 2.46 g (94% yield): Brick-red powder; m.p. 145–147 °C; IR (ν_{max}/cm^{-1}): 2923, 2249, 1618, 1528, 1367, 697; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 7.50–7.39 (m, 5H), 7.25 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 1H), 6.74 (d, *J* = 8.9 Hz, 2H), 6.73 (d, *J* = 8.9 Hz, 2H), 5.05 (t, 1H), 4.96 (t, 1H), 2.94 (s, 6H);^{13}C NMR (DMSO-d_6, 75 MHz): δ 150.9, 150.9, 133.1, 132.9, 129.6, 129.4, 129.3, 129.0, 128.7, 119.5, 119.3, 119.2, 119.2, 119.1, 112.6, 112.5, 112.1, 40.4, 40.3, MS *m/z*: 275 (M^+).

2-[4-(Dibenzylamino)phenyl]-3-phenylsuccinonitrile (**9g**) $C_{30}H_{25}N_3$, from 2-(4-(dibenzylamino)phenyl)-3-phenylacrylonitrile **8g** (2.00 g, 5 mmol) gave 1.92 g (90% yield): Orange powder; m.p. 115–117 °C; IR (ν_{max}/cm^{-1}): 2863, 2244, 1613, 1520, 721; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.45–7.19 (m, 13H), 6.77 (d, *J* = 8.5 Hz, 2H), 4.84–4.62 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.8, 137.8, 131.3, 129.4, 129.3, 129.1, 128.9, 128.8, 128.4, 128.2, 127.1, 127.0, 126.5, 118.2, 117.6, 117.6, 112.8, 112.6, 54.2, 43.7, 42.7. MS m/z: 427 (M^+).

2-(4-Chlorophenyl)-3-[4-(dibenzylamino)phenyl]succinonitrile (**9h**) $C_{30}H_{24}N_3Cl$, from 3-(4-chlorophenyl)-2-(4-(dibenzylamino) phenyl)acrylonitrile **8h** (1 g, 2.3 mmol) gave 980 mg (92% yield): Orange powder; m.p. 137–140 °C; IR (ν_{max}/cm^{-1}): 3029, 2244, 2195, 1612, 1520, 1355, 729; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39–7.18 (m, 12H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.69 (d, *J* = 8.9 Hz, 2H), 4.67 (s, 4H), 4.12 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.9, 137.8, 135.7, 129.8, 129.7, 129.4, 129.3, 128.8, 127.2, 126.6, 117.7, 117.4, 117.3, 112.7, 54.3, 43.1, 42.6; MS *m/z* (relative intensity): 91 (100%), 149 (66%), 311 (58%), 434 (16%), 461 (3%)(M^+), 462 (1%), 463 (1%).

2,3-Bis[4-(benzyloxy)phenyl]succinonitrile (**21**) $C_{30}H_{24}N_2O_2$, from 2,3-bis[4-(benzyloxy)phenyl]acrylonitrile **20** (1.8 g, 4.3 mmol)

gave 1.80 g (95% yield): Yellow-brownish powder; m.p. 240–244 °C; IR (ν_{max}/cm^{-1}): 3070, 3032, 2936, 2880, 2244, 1514, 1247; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.42–7.35 (m, 10H), 7.13 (d, *J* =8.7 Hz, 4H), 6.96 (d, *J* = 8.7 Hz, 4H), 5.07 (s, 4H), 4.16 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.0, 136.4, 129.7, 128.7, 128.2, 127.5, 122.9, 117.5, 115.4, 70.1; MS: *m/z* = 444 (M^+).

Synthesis of 3,4-diraylpyrroles; typical procedure

*3-(4-Chlorophenyl)-4-phenyl-1*H*-pyrrole* (**10b**) $C_{16}H_{12}ClN$

A 1.0 M solution of DIBAL-H in toluene (9.5 mL, 9.5 mmol) was added dropwise to a suspension of 2-(4-chlorophenyl)-3-phenylsuccinonitrile **9b** (1.00 g, 3.8 mmol) in anhydrous toluene (25 mL) at room temperature under nitrogen. After the addition was completed, the mixture was stirred at room temperature for 6 h and then quenched with aqueous 1.5 M NaH_2PO_4 (80 mL). The resulting heterogeneous mixture was stirred at 100 °C for an additional period of 1 h, cooled to room temperature, diluted with 50% EtOAc–hexanes (150 mL) and filtered through Celite®. The two layers were separated and the organic phase was washed with H_2O (2 × 30 mL), brine (30 mL), and then dried (Na_2SO_4). After removal of the solvent *in vacuo*, the residue was fractionated by FCC (SiO_2, 30% EtOAc–hexanes) to obtain the product (672 mg, 70% yield): Brown solid; m.p. 73–75 °C; IR (ν_{max}/cm^{-1}): 3422, 1671, 1532, 1487, 1090, 698, 518; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.22 (br s, 1H), 7.44–7.12 (m, 9H), 6.94–6.78 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.5, 134.3, 131.5, 129.8, 128.6, 128.4, 128.4, 126.0, 123.6, 122.5, 117.7, 117.5; MS *m/z* (relative intensity): 217 (50%), 253 (100%), 254 (22%) (M^+), 255 (31%); HRMS (EI) *m/z:* (M^+) calcd for $C_{16}H_{12}ClN$: 253.0658; found: 253.0663.

*3-Phenyl-4-(*p*-tolyl)-1*H*-pyrrole* (**10c**) $C_{17}H_{15}N$, from 2-(4-methylphenyl)-3-phenylbutanedinitrile **9c** (500 mg, 2.03 mmol) gave 346 mg (73% yield): Brown solid; m.p. 51–52 °C; IR (ν_{max}/cm^{-1}): 3416, 3024, 2918, 1712, 1535, 1439, 1082, 770, 697; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (s, 1H), 7.38–7.25 (m, 5H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.95–6.91 (m, 2H), 3.42 (s, 3H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 136.0, 135.3, 132.9, 129.9, 129.0, 128.6, 128.5, 128.2, 125.7, 123.5, 117.5, 117.4, 21.2; HRMS (EI) *m/z:* (M^+) calcd for $C_{17}H_{15}N$: 233.1204; found: 233.1205.

*3-(4-Methoxyphenyl)-4-phenyl-1*H*-pyrrole* (**10d**) $C_{17}H_{15}NO$, from 2-(4-methoxyphenyl)-3-phenylsuccinonitrile **9d** (524 mg, 2 mmol) gave 349 mg (70% yield): Yellow solid; m.p.100–102 °C; IR (ν_{max}/cm^{-1}): 3418, 1499, 1240, 1174, 1025, 698; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (br s, 1H), 7.37–7.27 (m, 4H), 7.29–7.20 (m, 3H), 6.94 (s, 1H), 6.91–6.83 (m, 3H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.8, 130.0, 129.6, 128.4, 127.9, 123.19, 118.2, 116.8, 116.8, 113.6, 55.2; MS: *m/z:* 249 (M^+); HRMS (ESI) *m/z:* (M^+H) calcd for $C_{17}H_{15}NO$: 250.1231; found: 250.1233.

*3-(2-Methoxyphenyl)-4-phenyl-1*H*-pyrrole* (**10e**) $C_{17}H_{15}NO$, from 2-(2-methoxyphenyl)-3-phenylsuccinonitrile **9e** (500 mg, 1.9 mmol) gave 294 mg (62% yield): Yellow oil; IR (ν_{max}/cm^{-1}): 3374, 2935, 1702, 1433, 1239, 1022, 749, 697; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (br s, 1H), 7.33–7.12 (m, 6H), 7.19–7.05 (m, 2H), 6.98–6.77 (m, 3H), 3.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.9, 137.0, 136.9, 131.6, 128.0, 127.6, 127.4, 125.3, 120.5, 118.7, 116.5, 111.1, 55.1; HRMS (EI) *m/z:* (M^+) calcd for $C_{17}H_{15}NO$: 249.1154; found: 249.1157.

N,N-*Dimethyl-4-(4-phenyl-1*H*-pyrrol-3-yl)aniline* (**10f**) $C_{18}H_{18}N_2$, from 2-[4-(dimethylamino)phenyl]-3-phenylsuccinonitrile **9f** (600 mg, 2.18 mmol) gave 366 mg (64% yield): Brown-red solid; m.p. 25–27 °C; IR (ν_{max}/cm^{-1}): 3404, 2882, 1614, 1534, 1505, 1057, 770, 550; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.23 (s, br, 1H), 7.38–7.22 (m, 5H), 7.16 (d, *J* = 8.9 Hz, 3H), 6.82 (s, 1H), 6.82 (s, 1H), 6.67 (d, *J* = 8.9 Hz, 2H), 2.93 (s, 6H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 148.9, 136.2, 129.4, 128.5, 128.1, 125.5, 124.2, 123.3, 120.6, 117.2, 116.7, 112.7, 40.8; HRMS (EI) *m/z:* (M^+) calcd for $C_{18}H_{18}N_2$: 262.1470; found: 262.1464.

N,N-*Dibenzyl-4-(4-phenyl-1*H*-pyrrol-3-yl)aniline* (**10g**) $C_{30}H_{26}N_2$, from 2-[4-(dibenzylamino)phenyl]-3-phenylsuccinonitrile **9g** (1.09 g, 2.55 mmol) gave 762 mg (72% yield): Yellow solid; m.p.116–118 °C; IR (ν_{max}/cm^{-1}): 3426, 3027, 1507, 1356, 1238, 730, 694; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.19 (s, br, 1H), 7.39–7.23 (m, 5H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.89–6.84 (m, 1H), 6.82–6.79 (m, 1H), 6.65 (d, *J* = 8.8 Hz, 2H), 4.62 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.6, 138.9, 136.2, 129.3, 128.6, 128.6, 128.1, 126.9, 126.9, 125.6, 124.4, 123.5, 123.3, 117.2, 116.7, 112.6, 54.3; HRMS (EI) *m/z*: (M^+) calcd for $C_{30}H_{26}N_2$: 414.2096; found: 414.2087.

N,N-*Dibenzyl-4-[4-(4-chlorophenyl)-1*H*-pyrrol-3-yl]aniline* (**10h**) $C_{30}H_{25}ClN_2$, from 2-(4-chlorophenyl)-3-[4-(dibenzylamino)phenyl] succinonitrile **9h** (690 mg, 1.5 mmol) gave 471 mg (70% yield): Yellow solid; m.p. 145–147 °C; IR (ν_{max}/cm^{-1}): 3426, 3025, 1614, 1506, 1354, 735, 551; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.19 (s, br, 1H), 7.36–7.29 (m, 6H), 7.28–7.23 (m, 6H), 7.22–7.19 (m, 2H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.86–6.82 (m, 1H), 6.81–6.78 (m, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 4.63 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.7, 138.8, 134.7, 131.2, 129.7, 129.4, 128.6, 128.3, 126.9, 126.8, 123.9, 123.5, 122.2, 117.1, 116.8, 112.6, 54.3; MS *m/z* (relative intensity): 217 (27%), 357 (100%), 448 (96%), 449 (28%) (M^+), 450 (32%); HRMS (EI) *m/z:* (M^+) calcd for $C_{30}H_{25}ClN_2$: 449.1784; found: 449.1774.

*3,4-Bis[4-(benzyloxy)phenyl]-1*H*-pyrrole* (**23**) $C_{30}H_{25}NO_2$, from 2,3-bis[4-(benzyloxy)phenyl]succinonitrile **21** (1.8 g, 4 mmol) gave 1.21 g (70% yield): Yellow solid; m.p. 120–140 °C; IR (ν_{max}/cm^{-1}): 3443, 3061, 3030, 2883, 2852, 2549, 1696, 1593, 1497, 1247; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.19 (br s, 1H), 7.45–7.31 (m, 10H), 7.19 (d, *J* = 9 Hz, 4H), 6.88 (d, *J* = 9 Hz, 4H), 6.81 (d, *J* = 3 Hz, 2H), 5.03 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.1, 137.2, 129.6, 128.6, 128.5, 127.9, 127.6, 123.0, 116.8, 114.5, 69.9; MS: *m/z* = 431 (M^+).

*Methyl-3,4-bis(4-benzyloxyphenyl)-1*H*-pyrrole-2-carboxylate* (**24**) $C_{32}H_{27}NO_4$

A solution of trichloroacetyl chloride (230 μL, 2.06 mmol) in anhydrous THF (2 mL) was added dropwise to a mixture of pyrrole **23** (587, 1.36 mmol) and DMAP (268 mg, 2.2 mmol) in anhydrous THF (2 mL) at 0 °C. After the addition was completed, the resultant mixture was stirred at room temperature for 4 h. The mixture was then transfer to an ultrasound bath and sonicated for three periods of 45 min each. The reaction was quenched by the addition of 30% NaOMe in MeOH (1 mL, 5.5 mmol) and MeOH (7 mL) and the sonication was continued for 30 minutes. The mixture was diluted with 50% EtOAc–hexanes (50 mL) and washed successively with H_2O (3 × 20 mL) and brine (20 mL), dried over Na_2SO_4 and the solvent evaporated *in vacuo*. The residue was fractionated by FCC (SiO_2, 30% EtOAc–hexanes) to afford 466 mg (70% yield) of the desired product: Pale yellow solid; m.p.166–168 °C; IR (ν_{max}/cm^{-1}): 3307, 3000, 2947, 2832, 1674, 1246; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.24 (br s, 1H), 7.16 (d, *J* = 9 Hz, 2H), 7.00–7.03 (m, 3H), 6.81 (d, *J* = 9 Hz, 2H), 6.72 (d, *J* = 9 Hz, 2H), 3.79 (s, 3H), 3.73 (s, 3H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.5, 158.5, 158.0, 131.8, 129.5, 127.1, 126.5, 120.0, 119.4, 113.7, 113.1, 55.2, 55.1, 51.2; MS: *m/z* = 489 (M^+).

N-*Arylation of 3,4-diraylpyrroles; general procedure*

*1-(4-Methoxyphenyl)-3,4-diphenyl-1*H*-pyrrole* (**14**) $C_{23}H_{19}NO$

CuI (5 mg, 5 mol%), 3,4-diphenyl-1*H*-pyrrole **12** (100 mg, 0.46 mmol) and anhydrous K_3PO_4 (212 mg, 0.96 mmol) were added to a Schlenck flask. The reaction vessel was evacuated and back-filled with nitrogen. This sequence was repeated two more times. 1-(Methoxy)-4-iodobenzene (130 mg, 0.55 mmol), ethylenediamine (5 mg, 90 μmol) and toluene (1 mL) were then added simultaneously under a stream of nitrogen. The reaction vessel was sealed and stirred in a pre-heated oil bath at 120 °C for 18 h. The reaction mixture was allowed to cool to room temperature and diluted with ethyl acetate, filtered through Celite®, and the filter rinsed with ethyl acetate. The solvent was evaporated *in vacuo* and the residue was fractionated by FCC (SiO_2, 20% EtOAc–hexanes) to afford 119 mg (80% yield) of the desired product: White-yellow solid; m.p. 82–84 °C; IR (ν_{max}/cm^{-1}): 3056, 1602, 1516, 1247, 1027, 695; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.37 (d, *J* = 8.9 Hz, 2H), 7.34–7.30 (m, 4H), 7.30–7.25 (m, 4H), 7.25–7.19 (m, 2H), 7.10 (s, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 3.822 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.9, 135.5, 133.9, 128.5, 128.3, 125.9, 125.1, 121.9, 119.0, 114.8, 55.6.

*1,3,4-Tris(4-methoxyphenyl)-1*H*-pyrrole* (**16**) $C_{25}H_{23}NO_3$, from 3,4-bis(4-methoxyphenyl)-1*H*-pyrrole **15** (201 mg, 0.72 mmol) gave

236 mg (86% yield): White-yellow solid; m.p. 59–63 °C; IR (ν_{max}/cm^{-1}): 2956, 2832, 1706, 1515, 1239, 1029, 826; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.37 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 8.8 Hz, 4H), 7.05 (s, 1H), 6.96 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 4H), 3.83 (s, 3H), 3.80 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.0, 157.7, 134.1, 129.6, 128.1, 124.7, 121.7, 118.3, 114.8, 113.7, 55.6, 55.2; HRMS (EI) *m/z*: (M^+) calcd for $C_{25}H_{23}NO_3$: 358.1678; found: 385.1684.

*Methyl-1,3,4-tris[4-(methoxy)phenyl]-1*H*-pyrrole-2-carboxylate (Trimethoxy lamellarin R)* (**17**) $C_{27}H_{25}NO_5$, from 3,4-bis(4-methoxyphenyl)-1*H*-pyrrole-2-carboxylate **18** (30 mg, 90 μmol) gave 25 mg (62% yield): Yellow solid; m.p. 42–44 °C; IR (ν_{max}/cm^{-1}): 2949, 1702, 1512, 1240, 832; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.31 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.9 Hz, 2H), 7.00 (s, 1H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H), 3.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.3, 161.7, 158.9, 158.4, 158.0, 134.0, 131.8, 131.0, 129.4, 127.3, 127.1, 126.8, 126.5, 124.9, 113.8, 113.6, 113.0, 55.5, 55.2, 55.2, 50.9; HRMS (EI) *m/z;* (M^+) calcd for $C_{27}H_{25}NO_5$: 443.1733; found: 443.1731.

*Methyl-1,3,4-tris[4-(benzyloxy)phenyl]-1*H*-pyrrole-2-carboxylate (Tribenzyloxy lamellarin R)* (**25**) $C_{45}H_{37}NO_5$, from methyl-3,4-bis(4-benzyloxyphenyl)-1*H*-pyrrole-2-carboxylate **24** (95 mg, 0.19 mmol) gave 125 mg (96% yield) as a white solid; m.p. 69–72 °C; IR (ν_{max}/cm^{-1}): 3031, 1702, 1510, 1220, 1010, 832, 695; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.41–7.23 (m, 15H), 7.21 (d, *J* = 9.0 Hz, 2H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.94 (dd, *J* = 8.9, 1.5 Hz, 4H), 6.90 (s, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 8.9 Hz, 2H), 5.00 (s, 2H), 4.97 (s, 2H), 4.90 (s, 2H), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.7, 158.2, 157.8, 157.3, 137.1, 137.1, 136.7, 134.2, 131.9, 131.0, 129.4, 128.7, 128.6, 128.2, 128.0, 128.0, 127.7, 127.7, 127.6, 127.1, 127.1, 126.6, 125.0, 121.3, 114.8, 114.6, 114.1, 70.3, 70.0, 51.0; HRMS (ESI) *m/z*: (M^+H) calcd for $C_{45}H_{37}NO_5$: 672.2750; found: 672.2726.

*Methyl-1,3,4-tris(4-hydroxyphenyl)-1*H*-pyrrole-2-carboxylate (Lamellarin R)* (**5**) $C_{24}H_{19}NO_5$

A mixture of methyl-1,3,4-tris(4-(benzyloxy)phenyl)-1*H*-pyrrole-2-carboxylate (tribenzyloxy lamellarin R) **25** (100 mg, 0.15 mmol) and $Pd(OH)_2$ (10 mol%) in MeOH (1 mL) was stirred over night under a hydrogen atmosphere (balloon). The reaction mixture was filtered through Celite®, the filter was rinsed with EtOAc, and the solvent was evaporated under reduced pressure to afford 60 mg (quantitative yield) of the desired product (not purified further): Yellow-brownish oil; ^{1}H NMR (acetone-d_6, 300 MHz): δ 8.54 (s, 1H), 8.23 (s, 2H), 7.23 (d, *J* = 8.8 Hz, 2H), 7.11 (s, 1H), 7.08 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 8.7 Hz, 2H), 3.40 (s, 3H); ^{13}C NMR (acetone-d_6, 75 MHz): δ 162.2, 157.6, 157.1, 156.7, 134.1, 132.8, 131.3, 130.3, 127.6, 127.2, 126.9, 126.7, 125.8, 116.1, 115.9, 115.3, 51.0.

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