

Refined methods for the synthesis of meso-substituted A₃- and *trans*-A₂B-corroles †

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We have refined a one-pot synthesis of A₃-corroles via “3+4” condensation of an aldehyde with a pyrrole followed by macrocyclization mediated by DDQ. After thorough examination of various reaction parameters (reactivity of an aldehyde, catalyst, solvent, concentration, time *etc.*) we have elaborated three different sets of conditions for different types of aromatic aldehydes—highly reactive, moderately reactive and sterically hindered. Thanks to the identification of the key factors influencing the yield of bilanes and the yield of their conversion to corroles we were able to improve yields to *ca.* 17% for highly reactive aldehydes and *ca.* 13% for moderately reactive aldehydes. Altogether fourteen A₃-corroles have been prepared in 7–21% yield. 5,10,15-Trimesitylcorrole has been obtained for the first time. [2+1] Condensation between sterically hindered dipyrromethanes and aldehydes has also been refined and yields of *trans*-A₂B-corroles have been improved by *ca.* 10%.

Introduction

Corroles^{1,2} are aromatic tetrapyrrole macrocycles bearing a direct pyrrole–pyrrole link, and only in recent years has this area of research begun to attract attention as an independent rapidly evolving field. Interest in corroles was induced by the discovery of their remarkable ability to stabilize higher oxidation states of metals³ and by enormous synthetic developments made during the last four years.² Progress in coordination chemistry of corroles^{4,5} has led to the use of their complexes as catalysts in hydrocarbon oxidations,⁶ as well as to the controversy over the ‘innocence’ of their core.^{5,7}

The acid-catalyzed reaction of aldehydes with pyrrole was known for years to give only porphyrins accompanied by linear side-products.⁸ However, recent discoveries proved that apparently small changes in the reaction conditions can furnish corroles,^{9,10} *N*-confused porphyrins,¹¹ pentaphyrins,¹² hexaphyrins^{12,13} or even bigger macrocyclic structures.¹² Disclosure of the first simple methods for the one-pot synthesis of meso-substituted corroles^{9,10} has prompted several groups to undertake synthetic activity in this area.^{14–21} Altogether four different procedures have been proposed for the direct reaction of aromatic aldehydes with pyrrole leading to A₃-corroles.^{9,10,17,20} The first method published by Gross *et al.*,¹⁰ which involves heating a mixture of both reactants supported on alumina, is suitable only for the synthesis of corroles from aldehydes with strong electron-withdrawing substituents.²² Meanwhile, Paolesse and co-workers¹⁹ showed that the modification of Adler–Longo conditions by changing the ratio of pyrrole to aldehyde from 1 : 1 to 3 : 1 results in the formation of an appreciable amount of corrole. Paolesse’s conditions, although quite versatile, failed to yield any corroles using sterically hindered aldehydes. Furthermore, in this method corroles are usually accompanied by substantial amounts of porphyrins and it can be envisioned that some aldehydes are not stable in boiling HOAc. The procedure of Lee and co-workers²⁰ involves the TFA catalyzed reaction of an aldehyde with pyrrole, subsequent purification of a bilane (5,10,15,20,22,23-hexahydrodipyrromethane) and its conversion into corrole (DDQ action). This method has one major bottleneck *i.e.* the purification of bilanes. It should be pointed out that the total yield of syn-

thesized corroles were not reported. The current synthetic needs of corrole chemistry are thus only partially satisfied by these methodologies, which are subject to limitations. This fact provided us with the motivation to develop a more comprehensive procedure for the synthesis of A₃-corroles.

Our strategy is centered around the following observations and hypotheses.

(1) Over the years, yields of meso-substituted A₄-porphyrin were improved by up to ~50%,⁸ while yields of the analogous corroles are at a level of ~10%. It is reasonable, therefore, to assume that there is still scope for the optimization of corrole synthesis.

(2) Detailed consideration of previous endeavors leading to A₃-corroles and to A₄-porphyrins clearly indicates that there is a key difference between the structure of both intermediates formed in the acid-catalyzed first step of the synthesis. The precursor of porphyrin—porphyrinogen is already a macrocyclic compound while bilanes, in all probability precursors of corroles, are linear oligomers. Moreover, while the conversion of porphyrinogen to porphyrin is almost quantitative, it is unreasonable to expect the yield of radical oxidative macrocyclization of bilanes to exceed 60%.²⁰ The above mentioned reasons clearly indicate that a strategy used for maximization of the yield of porphyrins has to be completely changed in order to increase the yield of corrole. Bearing in mind that oligomer distribution is inevitable in the acid-catalyzed condensation of aldehydes with pyrrole, we might assume that the yield of bilane can probably reach at best ~30%. If so, one can calculate that a total yield of corroles of *ca.* 20% should be accessible. Maximizing the bilane formation at the cost of dipyrromethane, tripyrromethane and higher oligomers is a difficult task since aldehydes react faster with dipyrromethanes than with pyrrole. Independent improvement of both processes (*e.g.* bilane formation and its macrocyclization) is the key to success but optimization of the first step seems to be more crucial.

(3) There are huge differences in the reactivity of various aromatic aldehydes and one cannot expect the same conditions to work equally well for all of them. Systematic changes of various reaction factors should lead to the development of several sets of reaction conditions which will be effective for different groups of aldehydes.

In this paper we would like to present the results of the research which eventually led to a substantial improvement in the yield of both A₃- and *trans*-A₂B-corroles.

† Electronic supplementary information (ESI) available: table describing attempts to optimize the reaction of MesDPM 30 with aldehyde 11. See <http://www.rsc.org/suppdata/ob/b2/b208950e/>

Table 1 Optimization of conditions for the reaction of aldehyde **1** with pyrrole^a

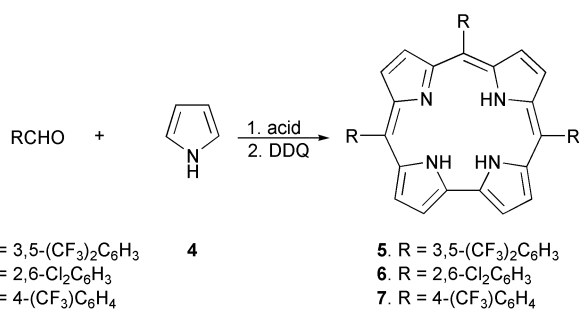
Entry	TFA/mmol : Ald. 1 /mmol	Pyrrole/mmol : ald. 1 /mmol	Solvent/ mL per mmol of ald. 1	DDQ/mmol : ald. 1 /mmol	Yield of corrole 4 (%) ^b
1	0.1	3	10	1	10
2	0.1	1.5	10	1	12
3	0.012	1.5	10	1	14
4 ^c	0.012	1.5	10	1	14
5	0.012	1.5	10	1.2	17
6	0.012	1.5	10	1.4	8
7	0.012	1.5	10 ^d	1.2	14
8	0.012	1.5	100	1.2	16
9	0.008 ^e	1.5	10	1.2	12
10	8 × 10 ^{-4e}	1.5	10	1.2	16

^a All reactions were performed under the following constant conditions. For 1st step: neat, *t* = 10 min, RT. For 2nd step: CH₂Cl₂, RT. ^b Isolated yields. ^c In this case the reaction time was 20 min. ^d EtCN was used. ^e BF₃·Et₂O was used instead of TFA.

Results and discussion

Synthesis of A₃-corroles from highly reactive aldehydes

We considered and evaluated a variety of strategies that seemed to hold promise for efficient synthesis of A₃-corroles^{9,10,17,20} and we have chosen the approach proposed by Lee *et al.*²⁰ as the most promising starting point. This method originates from dipyrromethane synthesis and involves the TFA catalyzed reaction of aldehydes with pyrrole followed by bilane conversion to corroles. Since the reaction was carried out neat, porphyrinogen formation was limited and thereby the amount of porphyrin, the most notorious side-product, was minimized. In comparison to Lee's method we wanted to avoid both purification of bilanes and the use of toxic and expensive EtCN in the second step. At the beginning we resolved to concentrate our efforts on the condensation of pyrrole with highly reactive aldehydes—the precursors of corroles with electron-withdrawing groups. Such corroles are the most stable ones and thereby potentially the most important. For the reaction of 3,5-bis(trifluoromethyl)benzaldehyde (**1**) with pyrrole (chosen as the first model system for the optimization study) the initial reaction conditions were based on Lee's results.²⁰ A mixture²³ of aldehyde **1** and pyrrole was treated with TFA (0.1 eq. *versus* the amount of aldehyde used) for 10 min and then the reaction mixture was dissolved in CH₂Cl₂.²⁴ Subsequent addition of DDQ gave corrole **5** in 10% yield (Scheme 1, Table 1, entry 1).

**Scheme 1**

Since the ratio of aldehyde : pyrrole, 1 : 3, is far from the reaction stoichiometry we were interested in whether a substantial decrease in the above-mentioned ratio to the more stoichiometric one would affect the yield of corrole. Indeed, when the amount of pyrrole was decreased to 1.5 eq. (*versus* aldehyde) the yield of corrole **5** increased to 12% (entry 2). In this process the first step was extremely vigorous which might lead to the undesired formation of higher oligomers. Therefore the effect of a lower concentration of TFA on the yield was examined. Additionally we came to the conclusion that adding very small amounts of pure TFA is both inconvenient and disadvan-

tageous due to the fact that, regardless of the rate of stirring, centres of very fast oligomerization form. Consequently the solution of TFA in CH₂Cl₂ has been used in the following experiments. A decrease in the amount of TFA to 0.012 eq. led to an appreciable increase in yield of up to 14% (Table 1, entry 3). Hence, for further reactions the amount of TFA was kept constant (0.012 eq.) and was added as a solution. Subsequent extension of the reaction time to 20 min did not improve the outcome of the process (Table 1, entry 4). We considered the possibility that a certain amount of DDQ can be consumed by the excess of pyrrole present in the reaction mixture leading to so-called 'pyrrole-red'.²⁵ The use of 1.2 eq. DDQ (*versus* aldehyde) resulted in a substantial increase in the yield while a further increase to 1.4 eq. caused a sudden drop in the yield of corrole **5** (Table 1, entries 5 and 6). The replacement of CH₂Cl₂ with EtCN (recommended by Lee and co-workers²⁰ as a solvent for the second step) resulted in a decline in the yield of corrole **5** compared with the optimum (Table 1, entry 7). The idea of diluting the reaction mixture before DDQ addition was inspired by the mechanistic hypotheses²⁰ (DDQ mediated cyclization) and by our earlier results.¹⁶ Surprisingly 10-fold dilution did not alter the yield (Table 1, entry 8). Finally, a control experiment using BF₃·Et₂O as a catalyst did not improve the yield although the use of a smaller amount of the acid was beneficial (Table 1, entries 9 and 10). It should be emphasized that exceptionally straightforward purification of corrole **5** (silica pad filtration and single 'crystallization') combined with its high stability in solution makes this molecule the best candidate for extensive coordination and physicochemical studies in the near future.

Subsequent experiments with a considerable number of representative highly reactive aldehydes were carried out using the optimized procedure [first step: neat, TFA : ald = 0.012, pyrrole : ald = 1.5, 10 min, room temperature; second step: the reaction mixture is dissolved in CH₂Cl₂ and then DDQ is added (1.2 eq *versus* aldehyde)] (Table 2, method A). We employed not only commercially available aldehydes **8** and **11–13** but also derivatives **9** and **10** prepared for the purpose of this study. All these aldehydes gave rise to corresponding A₃-corroles **19–24** in very good yield (13–21%). It is worth emphasizing that the yield of corrole **19**, recently the most important molecule in the field, was improved almost 2-fold in comparison with the yield previously reported.¹⁰ Aldehyde **9**, possessing four fluorine atoms and one N₃ group is expected to be even more reactive than pentafluorobenzaldehyde (**8**) and indeed the condensation under the latter conditions was very fast (15% yield). A decrease in the amount of TFA (2-fold) resulted in an appreciable increase in the yield of corrole **20** (Table 2, 19%) which confirms that the higher the reactivity of the aldehyde the smaller the amount of TFA required to maximize the yield of bilane. As a general rule Method A is applicable to the synthesis of corroles starting from aldehydes possessing one or more NO₂, CN or other strongly electron-withdrawing substituents or several F

Table 2 Comparison of reaction yields of different meso- A_3 -corroles

Aromatic aldehyde	Method	Corrole	Yield (%) ^a
3,5-(CF ₃) ₂ C ₆ H ₄ CHO, 1	A	5	17
C ₆ F ₅ CHO, 8	A	19	21(11) ^b
4-N ₃ C ₆ F ₄ CHO, 9	A	20	15(19) ^c
4-(SCH ₂ CO ₂ tBu)C ₆ F ₄ CHO, 10	A	21	17
4-CNC ₆ H ₄ CHO, 11	A	22	13
4-NO ₂ C ₆ H ₄ CHO, 12	A	23	19(22) ^b
3-NO ₂ C ₆ H ₄ CHO, 13	A	24	14(15) ^b
2,6-Cl ₂ C ₆ H ₃ CHO, 2	B	6	9(1) ^b
2,4,6-Me ₃ C ₆ H ₂ CHO, 14	B	25	7
4-CF ₃ C ₆ H ₄ CHO, 3	C	7	19
3-CNC ₆ H ₄ CHO, 15	C	26	15
4-(CO ₂ Me)C ₆ H ₄ CHO, 16	C	27	14(~4) ^b
2,6-F ₂ C ₆ H ₄ CHO, 17	C	28	8(6) ^b
4-CH ₃ C ₆ H ₄ CHO, 18	C	29	9(7) ^b

^a Isolated yields. ^b Values in parentheses indicate the highest yields obtained using previous methods. ^c Value in parentheses indicates the yield obtained when the amount of TFA was reduced 2-fold.

and CF₃ substituents. The presence of functional groups such as CN, CO₂tBu or N₃ in the starting aldehyde did not interfere with the outcome of the studied reaction. In order to prove the scalability of this process, a large scale synthesis of corrole **5** was attempted. The reactions of aldehyde **1** with pyrrole performed in the 15 mmol scale furnished 630 mg of corrole **5** in essentially the same yield as in the small scale experiment (15%).

Synthesis of A_3 -corroles from sterically hindered aldehydes

The second important group of A_3 -corroles we distinguished comprises compounds that bear sterically hindered substituents in the meso positions. Such molecules are of interest owing to the strong influence of their hindrance on the absorption spectra. Until now the only example of such types of corroles, namely 5,10,15-tris(2,6-dichlorophenyl)corrole (**6**), was obtained by Gross and co-workers (in 1% yield).¹⁰ Moreover, Paolesse *et al.*¹⁹ have reported that their method does not work for any sterically hindered aldehydes. The reaction of 2,6-dichlorobenzaldehyde (**2**) with pyrrole has been chosen as the second model system (Scheme 1, Table 3). As might be expected the conditions optimized for highly reactive aldehydes were not suitable for the preparation of corrole **6** (Table 3, entries 1 and 2). An increase in the amount of TFA combined with an increase in the amount of pyrrole resulted in corrole **6** in 1% yield (Table 3, entry 4). Real progress (4% yield) was achieved by extending the reaction time from 10 min to 16 h as well as by increasing the amount of pyrrole (while maintaining the same 'concentration' of TFA) (entry 6). In analogy to earlier studies dilution of the reaction mixture before the second step was

investigated (Table 3, entry 7) and resulted in an increase in the yield to 9%. Large volumes of solvents are required for the preparative-scale synthesis if 10-fold dilution precedes DDQ addition. To eliminate this disadvantage while at the same time maintaining high dilution conditions, simultaneous addition of the reaction mixture (after the 1st step) and DDQ solution to a small amount of vigorously stirred CH₂Cl₂ was examined. To our delight the yield of corrole **6** remained at the same level (Table 3, entry 11).

The optimized procedure (first step: neat, TFA : ald = 0.21, pyrrole : ald = 5, 16 h, room temperature; second step: simultaneous addition of the reaction mixture dissolved in CH₂Cl₂ and DDQ solution to CH₂Cl₂, 1.0 eq of DDQ *versus* aldehyde) was subsequently used for the preparation of 5,10,15-trimesitylcorrole (**25**), a compound unknown to date. After careful purification corrole **25** was obtained in 7% yield (Table 2, Method B).

Synthesis of A_3 -corroles from moderately reactive aldehydes

Attempts to apply Method A to less reactive aldehydes (yet bearing electron-withdrawing groups) like 4-trifluoromethylbenzaldehyde (**3**), 3-cyanobenzaldehyde (**15**) or 4-(methoxycarbonyl)benzaldehyde (**16**) resulted in the synthesis of corroles **7**, **26** and **27** albeit in low or moderate yields (4%, 9% and 3% respectively). Therefore methodological studies have been pursued to identify conditions suitable for a broad range of aromatic aldehydes with moderate reactivity to be used in corrole synthesis. The reaction of 4-(trifluoromethyl)benzaldehyde (**3**) with pyrrole has been chosen as a model system in this optimization study (Scheme 1, Table 4). As a result of the combined effect of an increase in a ratio of pyrrole : aldehyde to 3 : 1 (suggested earlier by Lee *et al.*²⁰ and Paolesse *et al.*¹⁹), extending the reaction time to 1 h and diluting the reaction mixture before DDQ addition, the yield was increased 5-fold to reach 19% (Table 4, entry 5). It is worth emphasizing that an increase in the amount of TFA to the level suggested by Lee *et al.*²⁰ (ald : TFA = 10 : 1) leads to a lower yield of corrole **7** (Table 4, entry 4). Until this point of our study, in all the reactions involving aldehydes **2**, **14** and **3**, the excess pyrrole has always been evaporated from the reaction mixture before DDQ addition. The inconvenience of this procedure prompted us to investigate the influence of the presence of pyrrole in the reaction mixture at the moment of DDQ addition on the yield of corrole **7**. To our delight the yield was essentially the same as in the absence of pyrrole (although 1 eq. of DDQ was used instead of the 1.2 eq.) which indicates that DDQ reacts much faster with oligomers than with pyrrole itself (Table 4, entry 7). Hence for further experiments pyrrole was not evaporated.

By using these conditions (first step: neat, TFA : ald = 0.023, pyrrole : ald = 3, 1 h, room temperature; second step: simultaneous addition of the reaction mixture dissolved in CH₂Cl₂

Table 3 Optimization of conditions for the reaction of aldehyde **2** with pyrrole^a

Entry	TFA/mmol : Ald. 2 /mmol	Pyrrole/mmol : ald. 2 /mmol	Time of acid catalyzed step	Solvent/ mL per mmol of ald. 2	Yield of corrole 6 (%) ^b
1	0.012	1.5	10 min	10	0
2	0.012	1.5	16 h	10	0
3	0.065	1.5	16 h	10	0
4	0.3	3	10 min	10	1
5	0.13	3	16 h	10	2
6	0.21	5	16 h	10	4
7	0.21	5	16 h	100	9
8	0.21	5	2 h	100	6
9	0.21	5	5 h	100	8
10	0.3	7	16 h	100	9
11	0.21	5	16 h	^c	9

^a All reactions were performed under the following constant conditions. For 1st step: neat, ald : DDQ = 1 : 1, RT. For 2nd step: CH₂Cl₂, RT. ^b Isolated yields ^c The reaction mixture dissolved in CH₂Cl₂ and the solution of DDQ were added simultaneously to CH₂Cl₂ over 10 min.

Table 4 Optimization of conditions for the reaction of aldehyde **3** with pyrrole^a

Entry	TFA/mmol : Ald. 3 /mmol	Pyrrole/mmol : ald. 3 /mmol	Time of acid catalyzed step	Solvent/mL per mmol of ald. 3	Yield of corrole 7 (%) ^b
1	0.012	1.5	10 min	10	4
2	0.023	3	4 h	10	11
3 ^c	0.023	3	4 h	100	16
4	0.1	3	20 min	10	8
5	0.023	3	1 h	100	19
6	0.023	3	30 min	100	15
7 ^{c,d}	0.023	3	1 h	100	19
8 ^{c,d}	0.023	3	1 h	^e	18

^a All reactions were performed under the following constant conditions. For 1st step: neat, RT. For 2nd step: CH₂Cl₂, Ald. **3** : DDQ = 1 : 1.2, RT.

^b Isolated yields. ^c In this case Ald. **3** : DDQ = 1 : 1. ^d Pyrrole was not evaporated after the first step. ^e The reaction mixture dissolved in CH₂Cl₂ and the solution of DDQ were added simultaneously to CH₂Cl₂ over 10 min.

Table 5 The comparison of optimized reaction conditions for the synthesis of meso-substituted A₃-corroles from various aldehydes

Entry	Type of aldehyde	TFA/mmol : ald./mmol	Pyrrole/mmol : ald./mmol	Time of acid catalyzed step	CH ₂ Cl ₂ /ml per mmol of ald.	DDQ/mmol : ald./mmol
1	Highly reactive aldehydes	0.012	1.5	10 min	10 mL	1.2
2	Sterically hindered aldehydes	0.21	5	16 h	^a	1
3	Moderately reactive aldehydes	0.023	3	1 h	^a	1

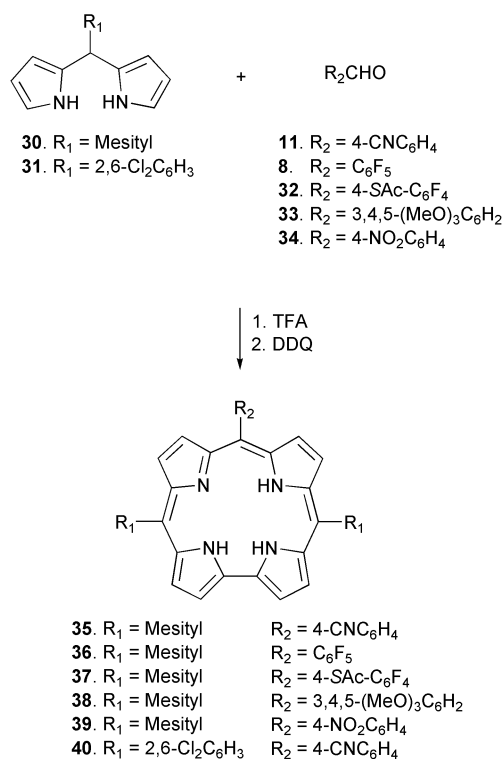
^a The reaction mixture dissolved in CH₂Cl₂ and the solution of DDQ were added simultaneously to CH₂Cl₂ over 10 min.

and DDQ solution to CH₂Cl₂, 1.0 eq of DDQ *versus* aldehyde), we synthesized corroles from several aromatic aldehydes. A few exemplary corroles **26–29** were obtained from aldehydes **15–18** in 8–15% yield (Table 2, Method C). All attempts to improve the unsatisfactory yield of corrole **29** derived from *p*-tolylaldehyde **18** failed.

Our detailed optimization study eventually led to significant improvements in corrole yield in most of the cases studied. The overview of optimized reaction conditions for the synthesis of meso-substituted A₃-corroles from various types of aromatic aldehydes is given in Table 5. In comparison to Paolesse's method, our procedure (1) gives better yields, (2) results in yields of porphyrins that are often below the limit of detection (for highly reactive aldehydes) and in all cases are below 2%, which greatly simplifies corrole purification, (3) is potentially more versatile due to the milder reaction conditions. We did not use aromatic aldehydes less reactive than **18** due to the low stability of corroles possessing only electron-donating substituents in due meso positions.

Synthesis of *trans*-A₂B-corroles

meso-substituted *trans*-A₂B-corroles are accessible *via* a [2+1] approach from dipyrromethanes and aldehydes.^{14–18} Among these compounds, those bearing two mesityl groups in positions 5 and 15 are of special interest for the following reasons: (1) steric congestion causes significant changes in the absorption spectrum (pink–violet color of solutions instead of green; the Soret band has a characteristic splitting); (2) in their NMR spectra line broadening is not observed; (3) they can be synthesized in relatively high yield. Although the formation of corroles from 5-mesityldipyrromethane (MesDPM, **30**) and aromatic aldehydes has already been extensively studied,¹⁵ in view of our recent findings concerning the synthesis of corroles bearing pyridyl units,¹⁶ we came to the conclusion that there is an opportunity for further improvement of the yield. We have chosen the reaction of MesDPM (**30**) with 4-cyanobenzaldehyde (**11**) as a model system (Scheme 2, Table 6). In theory 1.5 eq. of DDQ (*versus* dipyrromethane) is needed to fully oxidize bilane to corrole. Yet, in preliminary experiments¹⁴ it was found that a better yield was obtained when only 1 eq. of DDQ was used, which is probably associated with incomplete DPM conversion and the formation of a charge-transfer

**Scheme 2**

complex (corrole–DDQ). Therefore we revisited this issue and we found that an increase in the amount of DDQ afforded an increase in the yield from 18% to 24% (Table 6, entry 2). The dilution of the reaction mixture before DDQ addition further improved the yield of corrole **35** by an additional 4% (entry 3). Numerous subsequent attempts to improve the yield (shown in detail in the supplementary information finally led to the elaboration of two sets of conditions giving corrole **35** in 29% and 31% yield, respectively (Table 6, entries 4 and 5).

The optimized procedure (first step: CH₂Cl₂, [DPM] = 133 mM, [aldehyde] = 67 mM, [TFA] = 1.3 mM, 5 h, room temperature; second step: simultaneous addition of the reaction mixture and DDQ solution to CH₂Cl₂, 1.3 eq. of DDQ *versus* DPM) was then applied to the synthesis of other corroles from

Table 6 Optimization of conditions for the reaction of dipyrromethane **30** with aldehyde **11**^a

Entry	TFA/mM	Time of acid catalyzed step	DPM 30 /mM	DDQ/mmol : 30 /mmol	<i>x</i> -fold dilution ^b	Yield of corrole 35 (%) ^c
1	1.3	5 h	33	1	—	18
2	1.3	5 h	33	1.3	—	24
3	1.3	5 h	33	1.3	27	28
4	13	10 min	133	1.3	—	29
5	1.3	5 h	133	1.3	^d	31

^a All reactions were performed under the following constant conditions. For 1st step: CH₂Cl₂, MesDPM : aldehyde **11** = 2 : 1, RT. For 2nd step: RT.

^b Where *x* indicates how many times the reaction mixture was diluted before the addition of DDQ. ^c Isolated yields. ^d The reaction mixture dissolved in CH₂Cl₂ and the solution of DDQ were added simultaneously to CH₂Cl₂ over 10 min.

MesDPM (**30**) and aromatic aldehydes (Scheme 2). All reactions afforded corroles **36–39** in good yields (32%, 25%, 23% and 26% respectively) which gave an average improvement of 9%.

Given the weak electron-donating character of the mesityl group and thereby moderate stability of the respective corroles, we found it important to extend our study to 5-(2,6-dichlorophenyl)dipyrromethane (**31**). The reaction of **31** with 4-cyanobenzaldehyde (**11**) under conditions optimized for the condensation of MesDPM gave corrole **40** in 13% yield (Scheme 2).

Conclusions

In conclusion, the direct “3+4” condensation of aldehyde with pyrrole has been studied in-depth and, as a result, a broad variety of A₃-corroles has been synthesized in good yields using simple reaction conditions. By identifying the issue of the different reactivity of various aldehydes and by tailoring reaction conditions accordingly, yields of a broad range of A₃-corroles have been improved by a factor of 1.5–9 fold. The most notable findings are as follows. (1) A small amount of TFA favors bilane formation, the likely precursors of corroles. (2) The degree of improvement in corrole yield upon dilution of the reaction mixture before DDQ addition strongly depends on the particular case, which raises questions regarding the mechanism of this reaction. (3) The lower the reactivity of an aldehyde the higher the amount of pyrrole needed to achieve the maximal yield of corroles. (4) In larger scale experiments, simultaneous addition of both reactants (*e.g.* bilane and DDQ) to a small amount of CH₂Cl₂ can efficiently replace ‘classical’ high-dilution conditions. (5) Under elaborated conditions DDQ does not react with excess pyrrole to form ‘pyrrole-red’. As a result there is no need to evaporate pyrrole. (6) The use of EtCN as a solvent for radical oxidative cyclization does not lead to an increase in the yield of corroles as compared with CH₂Cl₂. Though the yield of corroles was not improved in every single case, such tailored procedures provide a new insight into factors influencing the course of the reaction of pyrrole with aldehydes leading to linear oligomers and macrocyclic structures. The efficiency of the synthesis of meso-substituted *trans*-A₂B-corroles from sterically hindered dipyrromethanes has also been improved by combining the effects of various factors.

This paper establishes the foundation for the first comprehensive method for the synthesis of A₃- and *trans*-A₂B-corroles that can serve as an ideal platform for coordination and physicochemical studies.

Experimental

General

All chemicals were used as received unless otherwise noted. Reagent grade solvents (CH₂Cl₂, hexanes) were distilled prior to use. All reported ¹H NMR and ¹³C NMR spectra were collected using a Bruker AM 500MHz spectrometer. *J* values

are given in Hz. UV-Vis absorption spectra were recorded in toluene (Cary). Chromatography was performed on silica (Kieselgel 60, 200–400 mesh) or alumina (Fluka). Preparative scale size exclusion chromatography (SEC) was performed using BioRad Bio-Beads SX-1 with THF as eluent. Mass spectra were obtained *via* electrospray MS (ESI-MS). The following compounds were prepared as described in the literature: aldehydes **9**,²⁶ and **32**,²⁷ and dipyrromethanes **30–31**.²⁸ The purity of all new corroles and porphyrins was established based on ¹H NMR spectra, elemental analyses and ESI-MS spectra.

4-(*tert*-Butoxycarbonylmethylthio)-2,3,5,6-tetrafluorobenzaldehyde **10**

Following a previously developed procedure,²⁷ potassium thioacetate (1.28 g, 11.2 mmol) was added to a solution of pentafluorobenzaldehyde (1.24 mL, 10.2 mmol) in anhydrous DMF (15 mL). After the exotherm subsided, the mixture was stirred at RT for 30 min. Then BrCH₂CO₂*t*-Bu (3.3 mL, 22.4 mmol) was added and the mixture was stirred for another 1 h. Subsequently, the reaction mixture was poured into water and extracted with ether. The combined organic extracts were washed with water, dried (Na₂SO₄) and evaporated to obtain an orange oil, which was chromatographed (silica, hexanes : ethyl acetate, 9 : 1) to afford a pale-yellow oil. Crystallization from pentane gave white crystals (1.454 g, 44%): mp 43–44 °C (Found: C, 48.3; H, 3.95; S, 10.1. Calc. for C₁₃H₁₂F₄O₃S: C, 48.15; H, 3.7; S, 9.9%); ν_{\max} (KBr)/cm⁻¹ 3411, 2982, 1725, 1711, 1638, 1472, 1295, 1281, 1132 and 971; δ_{H} (500 MHz; CDCl₃; Me₄Si) 1.40 (9 H, s, *t*-Bu), 3.70 (2 H, s, CH₂), 10.29 (1 H, s, CHO); δ_{C} (125 MHz; CDCl₃; Me₄Si) 27.8, 36.1, 82.9, 114.2, 121.9, 145.3, 147.4, 166.9, 182.1; *m/z* (EI) obsd 324.0458 (M⁺, C₁₃H₁₂F₄O₃S requires 324.0443).

Method A: general procedure for the preparation of A₃-corroles starting from very reactive aldehydes and pyrrole

A sample of the aldehyde (1.00 mmol) was dissolved in pyrrole (105 μ L, 1.50 mmol) at room temperature (in the case of some solid aldehydes gentle heating to 40 °C was necessary) and 10 μ L (12 μ mol) of the pre-prepared solution of TFA (10 mL) in CH₂Cl₂ (100 mL) was added while stirring. After 10 min at room temperature, the reaction mixture was dissolved in CH₂Cl₂ (10 mL) and a solution of DDQ (273 mg, 1.20 mmol) in toluene–THF (2 mL) was added, and the reaction mixture was stirred at room temperature for a further 5 min. The purification details are described for each case as follows.

5,10,15-Tris[3,5-bis(trifluoromethyl)phenyl]corrole **5.** The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 1 : 3) and all fractions containing corrole **5** were combined and evaporated to dryness. Hot hexanes were added and the suspension was left overnight in the refrigerator. Filtration afforded pure corrole **5** (52 mg, 17%) as a dark violet solid: *R*_f = 0.49 (CH₂Cl₂ : hexanes, 1 : 3); mp > 360

°C (Found: C, 55.3; H, 2.35; N, 6.1. Calc. for $C_{43}H_{20}F_{18}N_4$: C, 55.3; H, 2.2; N, 6.0%); λ_{\max} (toluene)/nm 423 ($\epsilon \times 10^{-3}/\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ 130), 580 (21), 615 (12), 647 (7.8); δ_{H} (500 MHz; C_6D_6 -THF- d_8 ; Me₄Si) -3.35 (1 H, br s, NH), -1.85 (2 H, br s, NH), 8.29 (2 H, br s, Ar), 8.36 (4 H, br s, Ar), 8.67 (4 H, br s, Ar), 8.81 (5 H, br s, Ar), 8.90 (2 H, br s, Ar); m/z (ESI) 935.1475 (M + H⁺, $C_{43}H_{21}F_{18}N_4$ requires 935.1473).

5,10,15-Tris(pentafluorophenyl)corrole 19. In this case TFA solution was added to the aldehyde just before the pyrrole in order to avoid an uncontrolled reaction. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 2 : 3) to give corrole **19** contaminated with porphyrin and unidentified compounds. Subsequent chromatography (silica, hexanes, then CH₂Cl₂ : hexanes, 1 : 4) afforded pure corrole **19** (57 mg, 21%) which was recrystallized from hexanes to give dark crystals. Spectral and physical properties concur with published data.¹⁰ Mp > 360 °C.

5,10,15-Tris(4-azido-2,3,5,6-tetrafluorophenyl)corrole 20. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 3 : 2) and all fractions containing corrole **20** were combined and evaporated. Subsequent chromatography (silica, toluene : hexanes, 3 : 7) afforded corrole contaminated with yellow impurities which were removed *via* crystallization from hexanes. Corrole **20** was obtained as very dark crystals (55 mg, 19%). $R_f = 0.49$ (CH₂Cl₂ : hexanes, 1 : 1); mp > 360 °C (Found: C, 51.4; H, 1.1; N, 20.8. Calc. for $C_{37}H_{11}F_{12}N_{13}$: C, 51.3; H, 1.3; N, 21.0%); λ_{\max} (toluene)/nm 422 ($\epsilon \times 10^{-3}/\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ 107), 571 (19), 608 (9.5); δ_{H} (500 MHz; C_6D_6 ; Me₄Si) -5.87 (3 H, br s, NH), 8.39 (2 H, br s, β -H), 8.51 (2 H, d, J 4.0, β -H), 8.69 (2 H, m, β -H), 8.76 (2 H, br s, β -H); m/z (ESI) 866.1153 (M + H⁺, $C_{37}H_{12}F_{12}N_{13}$ requires 866.1142).

5,10,15-Tris[4-(*tert*-butoxycarbonylmethylthio)-2,3,5,6-tetrafluorophenyl]corrole 21. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 3 : 2) and all fractions containing corrole **21** were combined and evaporated. Subsequent chromatography (silica, toluene) afforded pure corrole **21** as a violet glass (67 mg, 17%) which could not be transformed into crystals regardless of the conditions used. $R_f = 0.52$ (toluene : EtOAc, 9 : 1) (Found: C, 56.2; H, 3.8; N, 4.55; S, 8.1. Calc. for $C_{55}H_{44}F_{12}N_4O_6S_3$: C, 55.9; H, 3.75; N, 4.7; S, 8.1%); λ_{\max} (toluene)/nm 424 ($\epsilon \times 10^{-3}/\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ 104), 570 (19), 608 (9.7); δ_{H} (500 MHz; C_6D_6 ; Me₄Si) -5.80 (3 H, br s, NH), 1.44 (18 H, s, *t*-Bu), 1.45 (9 H, s, *t*-Bu), 3.41 (2 H, s, SCH₂), 3.42 (4 H, s, SCH₂), 8.37 (2 H, br s, β -H), 8.46 (2 H, d, J 3.5, β -H), 8.61 (2 H, m, β -H), 8.70 (2 H, br s, β -H); m/z (ESI) 1181.2344 (M + H⁺, $C_{55}H_{45}F_{12}N_4O_6S_3$ requires 1181.2304).

5,10,15-Tris(4-cyanophenyl)corrole 22. The reaction mixture was chromatographed (silica, toluene) affording pure corrole **22** (25 mg, 13%) which was recrystallized (THF-hexanes) to give a violet solid: $R_f = 0.58$ (toluene : EtOAc, 9 : 1); mp > 360 °C (Found: C, 79.7; H, 3.95; N, 16.25. Calc. for $C_{40}H_{23}N_7$: C, 79.6; H, 3.85; N, 16.3%); λ_{\max} (toluene)/nm 431 ($\epsilon \times 10^{-3}/\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ 125), 586 (21), 621 (15), 647 (11); δ_{H} (500 MHz; C_6D_6 -THF- d_8 ; Me₄Si) -3.40 (1 H, br s, NH), -1.70 (2 H, br s, NH), 7.80, 8.07 (2 × 2 H, AA'BB', J 7.5, C_6H_4), 7.82, 8.22 (2 × 4 H, AA'BB', J 8.0, C_6H_4), 8.32-8.50 (4 H, m, β -H), 8.69 (2 H, d, J 4.5, β -H), 8.89 (2 H, br s, β -H); m/z (ESI) 602.2084 (M + H⁺, $C_{40}H_{24}N_7$ requires 602.2088).

5,10,15-Tris(4-nitrophenyl)corrole 23. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 1 : 1). In the subsequent chromatography (silica, CH₂Cl₂ : hexanes, 1 : 1, then 3 : 2) corrole **23** contaminated with

unidentified compounds comprised the first dark green band. The dark green residue was triturated with hot hexanes-acetone and cooled down. Subsequently the solution was filtered to afford corrole **23** as a dark powder (42 mg, 19%). Spectral and physical properties concur with published data.¹⁹ Mp > 360 °C.

5,10,15-Tris(3-nitrophenyl)corrole 24. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂). Corrole **24** contaminated with unidentified compounds comprised the first green band. Subsequent chromatography (silica, toluene) afforded pure corrole **24** (32 mg, 14%) which was recrystallized (CH₂Cl₂-hexanes) to give dark crystals. Spectral and physical properties concur with published data.¹⁹ Mp > 360 °C.

Method B: general procedure for the preparation of A₃-corroles starting from sterically hindered aldehydes and pyrrole

A sample of the aldehyde (1.00 mmol) was dissolved in pyrrole (350 μ L, 5.00 mmol) at room temperature and then TFA (16 μ L, 0.21 mmol) was added while stirring. After 16 h, the reaction mixture was diluted with 10 mL of CH₂Cl₂, neutralized with NEt₃ (29 μ L, 0.21 mmol) and added to vigorously stirred CH₂Cl₂ (40 mL) simultaneously with the solution of DDQ (227mg, 1.00 mmol) in THF (10 mL) over 10 min, and the reaction was stirred at room temperature for a further 5 min. The purification details are described for each case as follows.

5,10,15-Tris(2,6-dichlorophenyl)corrole 6. After evaporation to dryness, the reaction mixture was redissolved (CH₂Cl₂-THF) and chromatographed (silica, CH₂Cl₂ : hexanes, 2 : 3) to afford pure corrole **6** (21 mg, 9%) which was recrystallized from cyclohexane. Spectral and physical properties concur with published data.¹⁰ Mp > 360 °C.

5,10,15-Trimesitylcorrole 25. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 2 : 3). Corrole **25** contaminated with porphyrin and a few unidentified compounds comprised the first violet band. Subsequent chromatography (silica, CH₂Cl₂ : hexanes, 2 : 3) afforded corrole **25** contaminated with tetramesitylporphyrin (TMP) which could not be separated on silica in any eluent mixture. The presence of TMP can be easily observed on an alumina plate (CH₂Cl₂ : hexanes, 1 : 4) but corrole **25** does not survive chromatography on alumina. Therefore SEC was performed. Two repetitive SEC (3 × 40 cm) afforded pure corrole **25** (15 mg, 7%). $R_f = 0.57$ (CH₂Cl₂ : hexanes, 1 : 1); mp > 360 °C (Found: C, 84.5; H, 6.7; N, 8.3. Calc. for $C_{46}H_{44}N_4$: C, 84.6; H, 6.8; N, 8.6%); λ_{\max} (toluene)/nm 409 ($\epsilon \times 10^{-3}/\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$ 109), 427 (82), 568 (16), 607 (11), 656 (5.4); δ_{H} (500 MHz; CDCl₃; Me₄Si) -0.5(-3.0) (3 H, br s, NH), 1.88 (6 H, s, *o*-Me-mesityl), 1.94 (12 H, s, *o*-Me-mesityl), 2.59 (3 H, s, *p*-Me-mesityl), 2.59 (6 H, s, *p*-Me-mesityl), 7.24 (6 H, s, *m*-H-mesityl), 8.25 (2 H, d, J 4.5, β -H), 8.29 (2 H, br s, β -H), 8.41 (2 H, d, J 4.5, β -H), 8.84 (2 H, d, J 4.5, β -H); m/z (ESI) 653.3636 (M + H⁺, $C_{46}H_{45}N_4$ requires 653.3639).

Method C: general procedure for the preparation of A₃-corroles starting from the rest of aromatic aldehydes and pyrrole

Sample of an aldehyde (2.00 mmol) was dissolved in pyrrole (420 μ L, 6.00 mmol) at room temperature and then 40 μ L (47 μ mol) of the pre-prepared solution of TFA (10 mL) in CH₂Cl₂ (100 mL) was added while stirring. After 10 min at room temperature, the reaction mixture was dissolved in CH₂Cl₂ (10 mL) and added to vigorously stirred CH₂Cl₂ (40 mL) simultaneously with the solution of DDQ (454 mg, 2.00 mmol) in THF (10 mL) over 10 min. Then the reaction was stirred at room temperature for a further 5 min. The purification details are described for each case as follows.

5,10,15-Tris[(4-trifluoromethyl)phenyl]corrole 7. The reaction mixture was concentrated to half the volume and passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 2 : 3). Subsequent chromatography (silica, toluene : hexanes, 3 : 7) afforded pure corrole **7** (92 mg, 19%) which was recrystallized (CH₂Cl₂-hexanes) to give dark violet crystals. *R*_f = 0.35 (toluene : hexanes, 1 : 3); mp > 360 °C (Found: C, 65.4; H, 2.85; N, 7.4. Calc. for C₄₀H₂₃F₉N₄: C, 65.8; H, 3.15; N, 7.7%); λ_{max}(toluene)/nm 422 (ε × 10⁻³/dm³ mol⁻¹ cm⁻¹ 110), 580 (17), 616 (11), 650 (8.8); δ_H(500 MHz; C₆D₆; Me₄Si) -2.0(-4.5) (3 H, br s, NH), 7.82, 8.07 (2 × 2 H, AA'BB', *J* 8.0, C₆H₄), 7.85, 8.20 (2 × 4 H, AA'BB', *J* 8.0, C₆H₄), 8.37 (4 H, br s, β-H), 8.67 (2 H, br s, β-H), 8.73 (2 H, br s, β-H); *m/z* (ESI) 731.1862 (M + H⁺, C₄₀H₂₄F₉N₄ requires 731.1852).

5,10,15-Tris(3-cyanophenyl)corrole 26. The reaction mixture was concentrated to half the volume and passed over a chromatography column (silica, toluene). Subsequent chromatography (silica, toluene) afforded pure corrole **26** (30 mg, 15%) which was recrystallized (THF-Et₂O) to give dark violet crystals. *R*_f = 0.50 (toluene : EtOAc, 9 : 1); mp > 360 °C (Found: C, 79.5; H, 3.55; N, 16.1. Calc. for C₄₀H₂₃N₇: C, 79.85; H, 3.85; N, 16.3%); λ_{max}(toluene)/nm 422 (ε × 10⁻³/dm³ mol⁻¹ cm⁻¹ 92), 580 (14), 616 (9.0), 647 (7.4); δ_H(500 MHz; C₆D₆-THF-d₈; Me₄Si) -3.50 (1 H, br s, NH), -1.85 (2 H, br s, NH), 7.50-7.63 (3 H, m, CNC₆H₄), 7.73 (2 H, d, *J* 7.5, CNC₆H₄), 7.78 (1 H, d, *J* 8.0, CNC₆H₄), 8.20 (1 H, d, *J* 8.0, CNC₆H₄), 8.30-8.45 (7 H, m, 2β-H + 5 CNC₆H₄), 8.51 (2H, br s, β-H), 8.65 (2 H, d, *J* 4.5, β-H), 8.85 (2 H, br s, β-H); *m/z* (ESI) 602.2085 (M + H⁺, C₄₀H₂₄N₇ requires 602.2088).

5,10,15-Tris(4-methoxycarbonylphenyl)corrole 27. The reaction mixture was concentrated to half the volume and passed over a chromatography column (silica, toluene). Subsequent chromatography (silica, toluene, then toluene : EtOAc, 99 : 1, then 97 : 3) afforded pure corrole **27** (64 mg, 14%) which was recrystallized (CH₂Cl₂-hexanes) to give a dark green powder. Spectral and physical properties concur with published data.²⁰ Mp > 360 °C.

5,10,15-Tris(2,6-difluorophenyl)corrole 28. The reaction mixture was concentrated to half the volume and passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 1 : 1). Subsequent chromatography (silica, CH₂Cl₂ : hexanes, 1 : 3) afforded pure corrole **28** (36 mg, 8%) as a pink-violet powder. Spectral and physical properties concur with published data.¹⁰ Mp > 360 °C.

5,10,15-Tris(4-methylphenyl)corrole 29. The reaction mixture was concentrated to half the volume and passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 2 : 3). Subsequent dry column vacuum chromatography²⁹ (silica, CH₂Cl₂ : hexanes, 2 : 3) afforded pure corrole **29** (34 mg, 9%) which was recrystallized from CH₂Cl₂-hexanes. Spectral and physical properties concur with published data.¹⁹ Mp > 360 °C.

Method D: general procedure for the preparation of corroles starting from 5-mesityldipyromethane **30**

Samples of 5-mesityldipyromethane **30** (210 mg, 0.80 mmol) and an aldehyde (0.40 mmol) were added to 6 mL of the pre-prepared solution of TFA (10 μL, 0.13 mmol) in CH₂Cl₂ (100 mL). The reaction was left at room temperature for 5 h. Then, the reaction mixture was diluted to 10 mL with CH₂Cl₂ and added to vigorously stirred CH₂Cl₂ (40 mL) simultaneously with the solution of DDQ (236 mg, 1.04 mmol) in THF (10 mL) over 10 min, and the reaction was stirred at room temperature for a further 5 min. The purification details are described for each case as follows.

10-(4-Cyanophenyl)-5,15-dimesitylcorrole 35. The reaction mixture was evaporated to dryness and chromatographed (silica, toluene) to afford pure corrole **35** (79 mg, 31%). Spectral and physical properties concur with published data.¹⁵ Mp > 360 °C.

5,15-Dimesityl-10-(pentafluorophenyl)corrole 36. The reaction mixture was evaporated to dryness and chromatographed (silica, CH₂Cl₂ : hexanes, 1 : 4) to afford pure corrole **36** (44 mg, 32%). Spectral and physical properties concur with published data.¹⁵ Mp > 360 °C.

10-(4-Acetylthio-2,3,5,6-tetrafluorophenyl)-5,15-dimesitylcorrole 37. The reaction mixture was evaporated to dryness and chromatographed (silica, toluene : hexanes, 1 : 1) to afford pure corrole **37** (39 mg, 25%). Spectral and physical properties concur with published data.¹⁵ Mp > 360 °C.

10-(3,4,5-Trimethoxyphenyl)-5,15-dimesitylcorrole 38. Directly after DDQ addition only a green non-fluorescent spot was present on a TLC plate. After 1 h a pink-violet highly fluorescent spot of corrole appeared just below the green spot. The reaction mixture was evaporated to dryness and chromatographed (silica, CH₂Cl₂ : hexanes, 1 : 1, then 2 : 1) to afford pure corrole **38** (33 mg, 23%). Spectral and physical properties concur with published data.¹⁵ Mp > 360 °C.

10-(4-Nitrophenyl)-5,15-dimesitylcorrole 39. The reaction mixture was evaporated to dryness and chromatographed (silica, toluene : hexanes, 1 : 1 then 2 : 1) to afford pure corrole **39** (34 mg, 26%). Spectral and physical properties concur with published data.¹⁵ Mp > 360 °C.

10-(4-Cyanophenyl)-5,15-(2,6-dichlorophenyl)corrole 40. The reaction mixture was passed over a chromatography column (silica, CH₂Cl₂ : hexanes, 3 : 2). Corrole **40** contaminated with unidentified compounds comprised the first violet band. This mixture was chromatographed (silica, acetone : hexanes, 1 : 9 then 1 : 4) and a broad violet band was collected. After evaporation, 45 mg (13%) of pure corrole **40** was obtained and subsequently recrystallized (CH₂Cl₂ : hexanes). *R*_f = 0.30 (hexanes : acetone, 4 : 1); mp > 360 °C (Found: C, 65.9; H, 3.3; N, 10.05. Calc. for C₃₈H₂₁Cl₄N₅: C, 66.2; H, 3.1; N, 10.2%); λ_{max}(toluene)/nm 414 (ε × 10⁻³/dm³ mol⁻¹ cm⁻¹ 100), 430 (91), 569 (16), 609 (9.5), 638 (3.6); δ_H(500 MHz; CDCl₃; Me₄Si) -2.20 (3 H, br s, NH), 7.68 (2 H, t, *J* 8.5, 2,6-dichlorophenyl), 7.79 (4 H, d, *J* 8.0, 2,6-dichlorophenyl), 8.04, 8.33 (2 × 2H, AA'BB', *J* 8.0, C₆H₄), 8.44 (2 H, d, *J* 3.5, β-H), 8.51 (2 H, d, *J* 4.5, β-H), 8.58 (2 H, d, *J* 4.5, β-H), 9.02 (2 H, d, *J* 4.0, β-H); *m/z* (ESI) 688.0624 (M + H⁺, C₃₈H₂₂Cl₄N₅ requires 688.0624).

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