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LETTERS

Sterically encumbered triarylcorroles from aryldipyrromethanes and aromatic aldehydes

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Abstract—A two-step synthesis of corroles from dipyrromethanes and aromatic aldehydes has been achieved. Acid-catalyzed [2+2] condensation of (2,6-dichlorophenyl)dipyrromethane with electron deficient aldehydes in CH_2Cl_2 followed by cyclization and oxidation in propionitrile or CH_2Cl_2, in the presence of DDQ or chloranil gave corroles in good yields. © 2001 Elsevier Science Ltd. All rights reserved.

Corroles are porphyrin analogues, lacking one *meso* carbon. Until recently, they were rather rare chemicals, formed either as side products in porphyrin synthesis[1] or by multistep procedures.[2] In the last few years a number of publications have appeared describing the synthesis of corroles and core-modified corroles. The procedures start from (i) pyrrole and 2,6-substituted electron poor benzaldehydes (e.g. pentafluorobenzaldehyde)[3,4] (ii) dipyrromethanes[5,6] or (iii) higher oligopyrroles.[7] Paolesse et al. have also developed a modified Rothemund condensation reaction of pyrrole with aromatic aldehydes to give corroles.[8,9] This has made these compounds much more available than before, allowing the study of their coordination chemistry,[10,11] applications of metallocorroles in catalysis and their photophysical behavior.[12] *N*-Substituted corroles have also been shown to be useful as chiral ligands.[13]

As part of a project to prepare porphyrin derivatives of 4,6-dichloropyrimidine-5-aldehyde **1a**[14,15] we tried the McDonald condensation of a 1:1 mixture of **1a** and (2,6-dichlorophenyl) dipyrromethane **2a**. To our surprise the only identifiable product formed (in 25% yield) after *p*-chloranil oxidation was the corrole **3aa**, without any trace of the expected porphyrin **4aa** detected. (Note: a compound with numbering **Nxy** is derived from an aldehyde **1x** and a dipyrromethane **2y**). On the other hand, the same reaction with **1a** and mesityldipyrromethane **2b** gave only the porphyrin **4ab**. This intriguing result bears some analogy to the literature data describing preferential formation of corroles from pyrrole and electron poor *ortho,ortho′*-disubstituted benzaldehydes.[3,4] We decided to carry out a systematic study of this reaction with the aim to obtain sterically encumbered triarylcorroles. Metal complexes of these corroles could be of use as stable catalysts for oxidation reactions and cyclopropanations.[16–18] While these studies were being completed, several authors published closely related work on corrole synthesis from dipyrromethanes **2** and benzaldehydes **1**,[5,6] or from the intermediate tetrapyrroles **5**[7] (Scheme 1). The recently published work of Gryko[6] may be considered the closest to our results. Gryko used a non-catalyzed condensation reaction of sterically encubered (mesityl) aryldipyrromethane and 2,6-difluorobenzaldehyde (1:1 ratio at high concentration), followed by DDQ oxidation, and was able to obtain an optimized yield of 19% of the corresponding unsymmetrically substituted corrole. However, yields go down when other, less electron rich dipyrromethanes or other aldehydes were used.[6] In our hands, using the Gryko conditions, we could obtain no corrole **3ca** from the reaction of (2,6-dichlorophenyl)-dipyrromethane **2a** and pentafluorobenzaldehyde **1c**. Even more recently, Brückner et al. were able to prepare corroles in good yields (18–40%) from an excess of (4-substituted aryl)dipyrromethane and 4-substituted benzaldehydes (6:1 ratio), by a trifluoroacetic acid (TFA)-catalyzed condensation followed by chloranil oxidation.[5] No report was made on sterically encumbered aldehydes or dipyrromethanes, while the modified Rothemund condensation reaction[8] did not give corrole from *ortho*-substituted benzaldehydes and the Brückner method wastes a lot of dipyrromethane. The dipyrromethanes are still expensive chemicals to prepare, although

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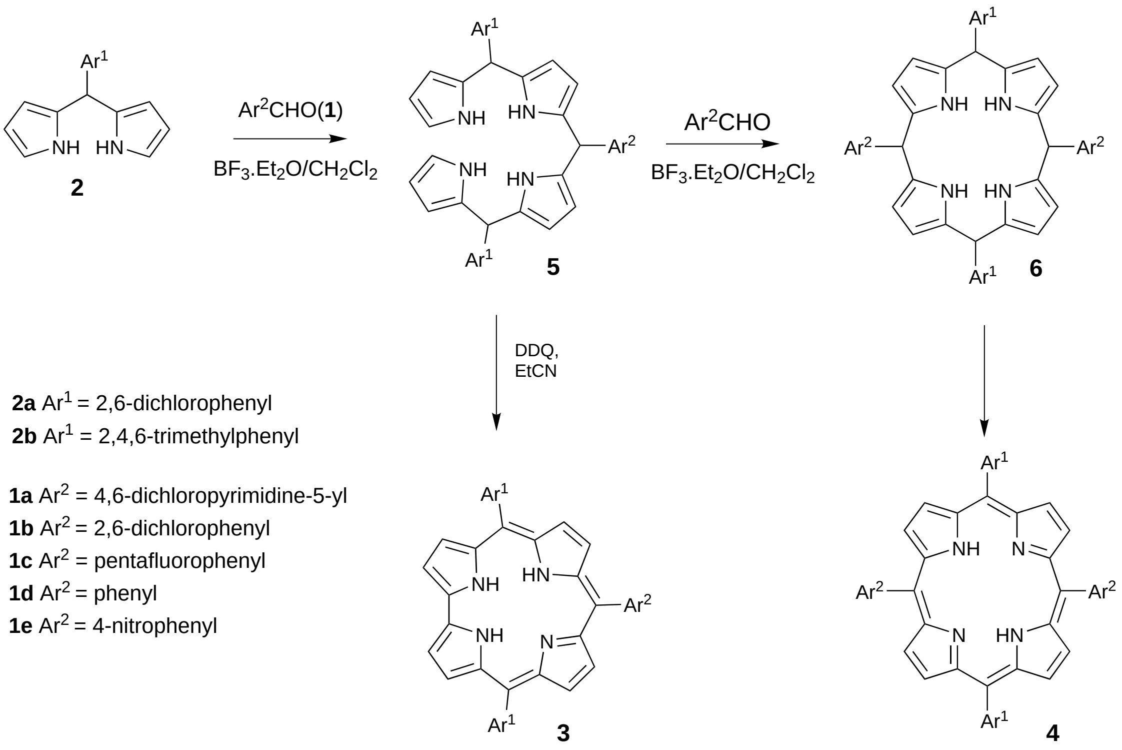


Scheme 1.

improved procedures have been reported in recent years.[19]

We have first carried out the condensation of dipyrromethane **2a** with the 2,6-dichloropyrimidine carbaldehyde **1a**, in the stochiometric ratio of 1:1 under the reaction conditions of the Lindsey porphyrin synthesis (i. dichloromethane, $BF_3\cdot Et_2O$, ii. chloranil).[20] The corrole **3aa** was obtained as mentioned earlier (Table 1). When the reaction was repeated by changing the molar ratio of dipyrromethane **2a** and the aldehyde **1a** to 2:1, under identical conditions, the corrole **3aa** was formed in a similar yield. However, the reaction of **2b** with **1a**, under these conditions gave only traces of corrole **3ab** and porphyrin **4ab** while the reaction of **2b** and **1a** in the stochiometric ratio 1:1 is known to afford the 5,15-bis(pyrimidinyl)porphyrin **4ab** in 53% yield.[14] The reaction of dipyrromethane **2a** with 2,6-dichlorobenzaldehyde **1b** in the ratio 2:1 also gave only traces of corrole **3ba** along with small amounts of porphyrin **4ba**. Examination of the product mixture obtained by the $BF_3\cdot Et_2O$-catalyzed condensation of **2a** and **1b** in the ratio 2:1 in methylene chloride has indicated the presence of the desired tetrapyrrole intermediate **5ba** which could be isolated by flash chromatography over silica-gel [eluent: CH_2Cl_2/hexane (1:1)+Et_3N (1%)] in 55% yield. Other than porphyrinogen **6ba**, a dark yellow powder also was obtained from

Table 1. Yield of corroles from various dipyrromethanes and aldehydes

Entry	DPM	Aldehyde	Ratio (2:1)	Method	Yield of corrole **3** (%)
1	**2a**	**1a**	1:1	A[a]	25
2	**2a**	**1a**	2:1	A	25
3	**2b**	**1a**	1:1	A	0[d]
4	**2b**	**1a**	2:1	A	0
5	**2a**	**1b**	2:1	A	0
6	**2a**	**1b**	2:1	B[b]	48[e]
7	**2a**	**1b**	2:1	C[c]	22
8	**2a**	**1c**	2:1	C	18
9	**2a**	**1d**	2:1	C	0[f]
10	**2a**	**1e**	2:1	C	0

[a] Method A: (i) $BF_3\cdot Et_2O/CH_2Cl_2$, rt, 1 h; (ii) Chloranil/reflux 1 h.

[b] Method B: (i) $BF_3\cdot Et_2O/CH_2Cl_2$, rt, 1 h (isolated tetrapyrrole **5**); (ii) EtCN/NH_4Cl/DDQ, rt, 1 h.

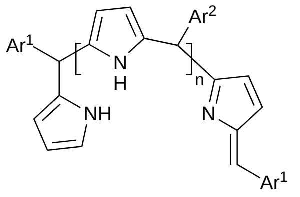
[c] Method C: (i) $BF_3\cdot Et_2O/CH_2Cl_2$, rt, 1 h; (ii) EtCN/NH_4Cl/DDQ, rt, 1 h.

[d] Porphyrin **4ab** obtained in 53% yield.

[e] Based on tetrapyrrole **5ba**.

[f] Porphyrin **4da** was obtained in 20% yield.

this reaction which appears to be a mixture of oligopyrroles **7** on the basis of electrospray mass analysis.



7 $Ar^1 = Ar^2$ = 2,6-dichlorophenyl, n = 4-6

Lee et al. have described the oxidation of tetrapyrroles **5** with DDQ in propionitrile as an effective strategy towards triarylcorroles. However, these tetrapyrroles were prepared in low yields after painstaking separation from oligopyrroles, from the condensation of benzaldehydes and pyrrole. We have oxidized the tetrapyrrole **5ba** with the Lee method to the corrole **3ba** in 48% yield. The reaction proceeded efficiently even when the crude product obtained from the condensation of dipyrromethane **2a** and the aldehyde **1b** was directly subjected to oxidation without the isolation of **5ba**, under Lee conditions, to afford the corrole **3ba** in an overall 22% yield.[21] Nevertheless, removal of the porphyrinogen from the crude tetrapyrromethane by flash chromatography avoids the need of separating corrole from porphyrin, after the oxidation, which is difficult due to their similar R_f values. Similarly, corrole **3ca** was obtained from pentafluorobenzaldehyde **1c** and dipyrromethane **2a** in 18% yield. The pyrimidinyl corrole **3aa** was also obtained with this method albeit only in 8% yield. This disappointing result is probably due to the partial decomposition of the reactive 4,6-dichloropyrimidinyl unit of **5aa** with the base (0.1 M NaOH) used for quenching of the acid-catalyzed condensation reaction.

The success of the procedure described in this letter seems to be restricted to 2,6-disubstituted, electron poor benzaldehydes. Reaction in the same conditions of benzaldehyde **1d** or even 4-nitrobenzaldehyde **1e** with dipyrromethane **2a** gave only the porphyrins **4da** and **4ea** and no corroles. In this case, the porphyrinogen is rapidly formed (a 'kinetic trap') via acid-catalyzed exchange reactions.

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21. **Typical procedure:** The solution of aldehyde **1b** (175 mg, 1 mmol) and dipyrromethane **2a** (592 mg, 2 mmol), in 80 mL CH_2Cl_2 was stirred for 15 min at room temperature under argon atmosphere and boron trifluoride etherate (0.085 mL, 0.067 mmol) was added. The mixture was stirred for 30 min and was then quenched with aqueous NaOH (0.1N, 30 mL). The organic layer was separated, washed with water and dried ($MgSO_4$) and filtered through a small column of neutral alumina. The solvent was evaporated under vacuum and the residue was dissolved in propionitrile (500 mL). Ammonium chloride (535 mg, 10 mmol) was added to the solution followed by DDQ (681 mg, 3 mmol). The mixture was stirred for 1 h, then the solvent was removed in vacuum. Column chromatography over neutral alumina (CH_2Cl_2) gave 5,10,15-tris(2,6-dichlorophenyl)corrole **3ba** (162 mg, 22%).