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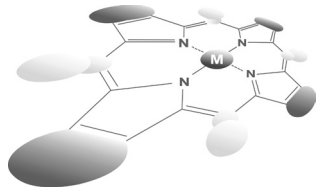

Synthesis and functionalization of β-alkyl-*meso*-triarylcorroles

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ABSTRACT: After the definition of efficient synthetic routes for the preparation of triarylcorroles, the functionalization of these macrocycles is becoming a necessary and challenging field of research. One important synthetic step is the introduction of substituents able to influence the electronic distribution in the macrocyclic ring. A valuable target would be a corrole macrocycle with some β-pyrrole positions occupied by methyl groups, while exploiting other positions to introduce electron-withdrawing substituents. To explore the scope of this approach, we investigated the bromination and the nitration of the corrole ring and the desired products have been obtained in moderate to good yield. The successful preparation of selectively halogenated corroles is particularly interesting since they are suitable substrates for the preparation of more complex partially alkylated structures using modern cross coupling methodologies.

KEYWORDS: corrole, bromination, nitration.

INTRODUCTION

The accomplishment of synthetic procedures for the preparation of 5,10,15-triarylcorroles starting from commercially available precursors [1, 2] has permitted widespread investigation of the functionalization of the macrocycle [3]. Whereas the developed synthetic chemistry of porphyrins offers a wide choice of methodology, in the case of corrole this chemistry is more challenging, since the reduced symmetry for corrole can afford a complex mixture of regioisomers [4]. However, unexpected regioselectivity has been often observed, which simplifies corrole functionalization: since the pyrroles directly linked, designated A and D, are usually more reactive than those next to the 10 *meso*-position (called B and C), the introduction of functional groups on carbons 2, 3, 17 or 18 occurs much more readily than on positions 7, 8, 12 and 13.

Taking in account the potential application of corroles in different fields, such as for example optical and photovoltaic devices, we have been interested in exploiting regioselectivity of electrophilic aromatic substitution found in corrole chemistry.

To fulfil this synthetic target, an interesting target could be a β-alkyl-*meso*-aryl corrole, *i.e.* a macrocycle having some β-pyrrolic positions functionalized with alkyl groups. Since in the corrole ring the A and D pyrroles are the most reactive for functionalization reactions, we have focused on the preparation of a corrole (Fig. 1), which, to the best of our knowledge, has not been previously reported.

Once the target macrocycle has been synthesized, a second step in our work would be investigation of the functionalization reactions of such an electronically lopsided species. Among the different substitutions of corroles, those convenient for our goal are the bromination and the nitration reactions. Both these modification of tetrapyrrole

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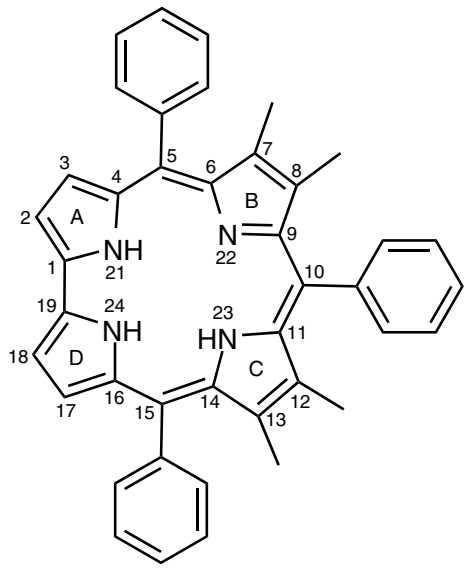


Fig. 1. Molecular structure of the target corrole **1**

peripheral positions strongly influence the electronic structure of the macrocycle [5, 6] and allow the preparation of substrates to be exploited in the formation of more complex architectures by a bottom-up approach: in the case of brominated compounds, these are common substrates for the palladium catalyzed cross-coupling reactions [7], such as those developed by Heck [8], Stille [9], Suzuki [10] and Sonogashira [11]. The nitration is the first step to prepare new substrates useful for so-called "click chemistry" [12, 13]. For this last reaction, different conditions have been mainly optimized [14, 15] for the preparation of the 3-NO_2, and 3,17-$(NO_2)_2$ derivatives, either using the free base or Cu complexes, even though a wide range of differently mono or polynitrated products have been obtained by changing the reaction conditions [16, 17].

The regioselective bromination of corrole is more difficult and the complete substitution of the ring is usually observed, thus avoiding the separation of complex regioisomers [5]. However some examples of synthetic routes for the preparation of selectively brominated corroles have been recently reported [18].

In this work we present the synthesis of the target 7,8,12,13-tetramethyl-5,10,15-triphenylcorrole **1**, together with some related *bromo*- and *nitro*-derivatives.

EXPERIMENTAL

General

Silica gel 60 (70-230 mesh, Sigma Aldrich) or basic alumina oxide (Type T, Merck) were used for column chromatography. Reagents and solvents (Aldrich) were of the highest grade available and were used without further purification. UV-vis spectra were recorded in CH_2Cl_2 on a Cary 50 spectrophotometer. ^{1}H NMR spectra were recorded at 300 K either using a Bruker AV300 spectrometer operating at 300 MHz or with a Bruker Avance 600 spectrometer operating at 600 MHz with a 5 mm inverse broad-band equipped with z-axis gradients. Chemical shifts are given in ppm relative to residual $CHCl_3$ (7.26 ppm for ^{1}H and 77.16 ppm MHz for ^{13}C). All data were processed with TopSpin. Mass spectra (FAB mode) were recorded on a VGQuattro spectrometer in the positive-ion mode using *m*-nitrobenzyl alcohol (Aldrich) as matrix.

Synthesis

2-Benzoyl-3,4-dimethyl-pyrrole(3). 2-Carboxyethyl-3,4-dimethyl-5-benzoylpyrrole (**2**) (800 mg, 2.95 mmol) and NaOH (1.41 g, 35.4 mmol) were dissolved in ethylene glycol (30 mL), and the mixture was stirred at reflux under nitrogen for 90 min. After this period, the mixture was cooled down, diluted with water (100 mL) and extracted with $CHCl_3$. The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue oil was directly used for the following step. ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.90 (br s, 1 H, NH pyrrole), 7.66 (d, 2 H, J = 6.72 Hz, *o*-H benzoyl), 7.49–7.44 (m, 3 H, *m, p*-H benzoyl), 6.84 (s, 1 H, *a*-H pyrrole), 2.10 (s, 3 H, β-methyl), 1.89 (s, 3 H, β-methyl). Anal. calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03%. Found C, 78.42; H, 6.64; N, 7.00%. Yield 85% (496 mg).

1,9-Dibenzoyl-2,3,7,8-tetramethyl-5-phenyldipyrromethane (4). Pyrrole **3** (800 mg, 4.04 mmol) was dissolved in ethanol (10 mL) and stirred to reflux; a solution of benzaldehyde (205 μL, 2.02 mmol) in ethanol (2 mL) was added dropwise, and then few drops of concentrated HCl were added and the solution color turned from orange to purple. The solvent was removed under reduced pressure and the residue was purified by chromatography using a short silica gel column eluted with $CHCl_3$; the eluted product was examined by exposure of the TLC plate to bromine vapor, whereupon the dipyrromethane appeared as a red-pink spot, while the tripyrrane is violet. The final product was obtained as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.57 (s, 2 H, NH pyrrole), 7.59 (d, 4 H, J = 6.81 Hz, *o*-H benzoyl), 7.51–7.35 (m, 9 H, *m, p*-H benzoyl + *m, p*-H *meso* phenyl), 7.17 (d, 2 H, J = 6.84 Hz *o*-H *meso* phenyl), 5.60 (s, 1 H, *meso* H), 1.92 (s, 6 H, β-methyl), 1.84 (s, 6 H, β-methyl). Anal. calcd. for $C_{33}H_{30}N_2O_2$: C, 81.45; H, 6.21; N, 5.76%. Found C, 81.51; H, 6.26; N, 5.72%. Yield 70% (687 mg).

1,9-Bis(benzoylcarbinol)-2,3,7,8-tetramethyl-5-phenyldipyrromethane (5). Dipyrromethane **4** (600 mg, 1.23 mmol) was dissolved in THF/methanol (50 + 17 mL) and $NaBH_4$ (50 equiv, 2.32 g) was added in small portions during 30 min under vigorous stirring at room temperature. The mixture was stirred for a further 90 min and then water

was added. The solvent was reduced to a small volume and extracted with $CHCl_3$. The organic phase was dried over anhydrous Na_2SO_4 and immediately used for the corrole synthesis. Yield 90% (542 mg).

7,8,12,13-Tetramethyl-5,10,15-triphenylcorrole (1). Compound **5** (281 mg, 0.65 mmol) was dissolved in 50 equiv. (2.26 mL) of pyrrole and 130 μL of a solution of TFA in CH_3CN (10 μL in 1 mL) was added and the resulting solution was stirred at room temperature for 10 min. The solution was transferred to a larger flask containing 260 mL of CH_2Cl_2, and after 10 min a solution of DDQ (442 mg) in THF (2 mL) was added under vigorous stirring. After 1 h the solvent was removed under vacuum and the residue was purified by passage through a silica gel plug eluted with chloroform; the fractions containing the porphyrinoid derivatives were collected and purified again by column chromatography (basic Al_2O_3 grade T) eluted with CH_2Cl_2. The first green band was collected and crystallized from CH_2Cl_2/CH_3OH, yielding 15 mg (4%) of the titled corrole. mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 429 (4.31), 575 (3.56), 658 (3.53). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.88 (d, 2 H, J = 3.96 Hz, β-pyrrole), 8.45 (d, 2 H, J = 3.45 Hz, β-pyrrole), 8.20 (d, 4 H, J = 7.15 Hz, phenyl), 8.14–8.09 (m, 2 H, phenyl), 7.77–7.69 (m, 9 H, phenyl), 2.40 (s, 6 H, β-methyl), 2.10 (s, 6 H, β-methyl). Anal. calcd. for $C_{41}H_{34}N_4$: C, 84.51; H, 5.88; N, 9.61%. Found C, 84.58; H, 5.83; N, 9.55%.

[7,8,12,13-Tetramethyl-5,10,15-triphenylcorrolato] Cu (6). ***Method A.*** This corrole was prepared similarly as described for **1**, but a saturated solution of $Cu(AcO)_2$ in methanol was added 30 min after the oxidant addition; the mixture was then stirred at reflux for 20 min. The solvent was removed under vacuum and the residue was purified by passage through a silica gel plug eluted with $CHCl_3$; the fraction containing the corrole contaminated with the Cu complex of porphyrin **7** (5:1 ratio) was collected, the solvent reduced to a small volume and purified again by a silica gel TLC with CH_2Cl_2/hexane (2:3) as eluting system. The brown fraction containing the corrole was collected and crystallized from CH_2Cl_2/CH_3OH. Yield 5% (21 mg). ***Method B.*** Dipyrromethane **5** (281 mg, 0.65 mmol) and 50 equiv. of pyrrole (2.26 mL) were dissolved in CH_3OH (70 mL), then 0.25 M HCl (70 mL) was added and the mixture was stirred for 2 h. After this period the suspension was extracted with $CHCl_3$, the organic phase was washed with water, dried over anhydrous Na_2SO_4, diluted up to 120 mL with $CHCl_3$ and 630 mg of chloranil (630 mg) was added. The mixture was stirred for 30 min, and then a satured solution of $Cu(OAc)_2$ in methanol was added and the resulting mixture was stirred at reflux for a further 20 min. The solvent was removed and the residue was purified as above. Yield 4% (17 mg). ***Method C.*** Dipyrromethane **5** (281 mg, 0.65 mmol) was dissolved in 50 equiv. (2.26 mL) of pyrrole and stirred under nitrogen flux for 10 min; then 8 μL of a solution of CH_2Cl_2/TFA mixture (10 μL of TFA + 40 μL of CH_2Cl_2) were added and the mixture was stirred under nitrogen for a further 30 min. The mixture was diluted with CH_2Cl_2 (10 mL) and after 10 min chloranil (167 mg) was added. The mixture was stirred for 20 min before the addition of a satured solution of $Cu(OAc)_2$ in methanol. The final solution was stirred at reflux for 20 min. The solvent was removed and the residue was purified as above. Yield 12% (50 mg), mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 410 (4.50), 560 (3.46), 623 (3.22). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 7.76 (d, 2 H, J = 4.33 Hz, β-pyrrole), 7.69 (d, 4 H, J = 7.22 Hz, phenyl), 7.62 (d, 2 H, J = 4.33 Hz, β-pyrrole), 7.58–7.53 (m, 5 H, phenyl), 7.51–7.42 (m, 6 H, phenyl), 1.61 (s, 6 H, β-methyl), 1.34 (s, 6 H, β-methyl). MS (FAB): *m/z* (%) 642 $[M]^+$ (100). Anal. calcd. for $C_{41}H_{31}CuN_4$: C, 76.55; H, 4.86; N, 8.71%. Found C, 76.60; H, 4.92 N, 8.64.

2,3,7,8,12,13-Hexamethyl-5,10,15,20-tetraphenylporphyrin (7). mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 439 (5.37), 537 (4.13), 586 (3.91), 612 (3.74) 669 (3.49). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.34 (br s, 2 H, β-pyrrole), 8.30–8.27 (m, 4 H, phenyl), 8.23–8.20 (m, 4 H, phenyl), 7.78–7.75 (m, 12 H, phenyl), 2.13 (s, 6 H, β-methyl), 2.03 (s, 6 H, β-methyl), 1.85 (s, 6 H, β-methyl), -2.37 (br s, 2 H, inner NH). Anal. calcd. for $C_{50}H_{42}N_4$: C, 85.93; H, 6.06; N, 8.02%. Found C, 85.88; H, 6.01; N, 8.07.

[2,3,7,8,12,13-Hexamethyl-5,10,15,20-tetraphenylporphyrinato]Zn. mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 444 (5.37), 581 (4.39). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.34 (br s, 2 H, β-pyrrole), 8.29–8-27 (m, 4 H, phenyl), 8.22–8.21 (m, 4 H, phenyl), 7.77–7.52 (m, 12 H, phenyl), 2.13 (s, 6 H, β-methyl), 2.03 (s, 6 H, β-methyl), 1.85 (s, 6 H, β-methyl). Anal. calcd. for $C_{50}H_{40}N_4Zn$: C, 78.78; H, 5.29; N, 7.35%. Found C, 78.87; H, 5.36; N, 7.30.

Nitration of [7,8,12,13-tetramethyl-5,10,15-triphenylcorrolato]Cu. Copper corrole **6** (34 mg, 0.053 mmol) was dissolved in DMF (8 mL) and the mixture was heated to reflux. $AgNO_2$ (8 mg, 0.053 mmol, 1 equiv) and $NaNO_2$ (33 mg, 0.477 mmol, 9 equiv) were added and the reaction progress was monitored by UV-vis spectrometry and TLC analysis (silica gel/CH_2Cl_2). After 8 min brine was added to quench the reaction and the precipitate filtered off on paper. The residue was dissolved in $CHCl_3$, dried over anhydrous Na_2SO_4, and purified using a silica gel column eluted with CH_2Cl_2. A first olive green fraction was the mononitroderivative **8** and the following bright green fraction was the dinitroderivative **9**.

[3-NO_2-7,8,12,13-tetramethyl-5,10,15-triphenylcorrolato]Cu (8). Crystallized from CH_2Cl_2/CH_3OH. Yield 34% (12 mg), mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 381 (sh), 420 (4.64), 591 (3.95), 671 (3.80). ^{1}H NMR (600 MHz, $CDCl_3$): δ, ppm 8.14 (s, 1 H, β-pyrrole H-2), 7.76 (d, 1 H, J = 4.32 Hz, β-pyrrole H-18), 7.69 (d, 1 H, J = 4.32 Hz, β-pyrrole H-17), 7.65 (d, 4 H, J = 8.55 Hz, 5,15-*o*-phenyl), 7.62–7.58

(m, 3 H, 5,10,15-*p*-phenyl), 7.55 (d, 2 H, J = 6.85 Hz, 10-*o*-phenyl), 7.51 (t, 2 H, J = 8.22 Hz, 15-*m*-phenyl), 7.47 (t, 2 H, J = 7.92 Hz, 10-*m*-phenyl), 7.42 (t, 2 H, J = 8.86 Hz, 5-*m*-phenyl), 1.62 (s, 3 H, β-methyl C-13), 1.46 (s, 3 H, β-methyl C-7), 1.41 (s, 3 H, β-methyl C-8), 1.30 (s, 3 H, β-methyl C-12). ^{13}C NMR (600 MHz, $CDCl_3$): δ, ppm 158.89 (α-pyrrole C-9), 157.13 (α-pyrrole C-6), 156.35 (α-pyrrole C-14), 153.03 (α-pyrrole C-11), 150.40 (α-pyrrole C-16), 144.43 (α-pyrrole C-19), 143.47 (β-pyrrole C-7 or C-8), 143.26 (β-pyrrole C-12 or C-13), 142.66 (10-phenyl C-*ipso*), 142.78 (β-pyrrole C-7 or C-8), 141.70 (α-pyrrole C-1 or C-4), 141.69 (5-phenyl C-*ipso*), 140.73 (α-pyrrole C-1 or C-4), 140.54 (β-pyrrole C-12 or C-13), 140.51 (β-pyrrole C-3), 139.72 (15-phenyl C-*ipso*), 131.35 (*meso* C-5 or C-15), 129.52 (5 or 15-phenyl C-*orto*), 129.01 (5,10,15-phenyl C-*para*), 128.94 (10-phenyl C-*orto*), 128.69 (5-phenyl C-*meta*), 128.60 (10-phenyl C-*meta*), 128.44 (15-phenyl C-*meta*), 128.33 (β-pyrrole C-17), 127.59 (5 or 15-phenyl C-*orto*), 124.51 (*meso* C-10), 123.73 (*meso* C-5 or C-15), 121.07 (β-pyrrole C-18) 114.32 (β-pyrrole C-2), 13.56 (β-Methyl C-7), 13.30 (β-Methyl C-12), 12.79 (β-Methyl C-13), 12.61 (β-Methyl C-8). MS (FAB): *m/z* (%) 690 $[M + H]^+$ (100). Anal. calcd. for $C_{41}H_{30}CuN_5O_2$: C, 71.55; H, 4.39; N, 10.18%. Found C, 71.51; H, 4.33 N, 10.22%.

[3,17-$(NO_2)_2$-7,8,12,13-tetramethyl-5,10,15-triphenylcorrolato]Cu (9). Crystallized from CH_2Cl_2/CH_3OH. Yield 23% (9 mg), mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 430 (4.72), 605 (4.02), 685 (3.86). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.04 (s, 2 H, β-pyrrole H-2, 18), 7.66–7.58 (m, 8 H, phenyl), 7.51–7.44 (m, 7 H, phenyl), 1.52 (s, 6 H, β-methyl), 1.38 (s, 6 H, β-methyl). MS (FAB): *m/z* (%) 734 $[M]^+$. Anal. calcd. for $C_{41}H_{29}CuN_6O_4$: C, 67.16; H, 3.99; N, 11.46%. Found C, 67.02; H, 4.04 N, 11.52%.

Bromination of [7,8,12,13-tetramethyl-5,10,15-triphenylcorrolato]Cu. Copper corrole **6** (60 mg, 0.093 mmol) was dissolved in spectroscopic grade $CHCl_3$ (ethanol free) (20 mL) and a solution of Br_2 in $CHCl_3$ (70 μL/4 mL) was added dropwise, monitoring the course of the reaction by UV-vis spectrometry and TLC analysis (silica gel/CH_2Cl_2). After 5 min the reaction was quenched with a few drops of pyridine, then washed with an aqueous solution of $Na_2S_2O_5$ (20% w/v), dried over anhydrous Na_2SO_4, solvent reduced to a small volume and residue purified using a silica gel column eluted with CH_2Cl_2. The first olive green fraction was collected and identified as the tetrabrominated copper derivative **10**, while the second fraction, bright green in color, as the corresponding free base **11**.

[2,3,17,18-Br_4-7,8,12,13-tetramethyl-5,10,15-triphenylcorrolato]Cu (10). Crystallized from CH_2Cl_2/CH_3OH. Yield 21% (16 mg), mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 414 (4.81), 570 (4.06), 646 (3.77). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 7.62–7.38 (m, 15 H, phenyl), 1.53–1.41 (m, 12 H, β-methyl). MS (FAB): *m/z* (%) 959 $[M]^+$ (100). Anal. calcd. for $C_{41}H_{27}Br_4CuN_4$: C, 51.36; H, 2.84; N, 5.84%. Found C, 51.31; H, 2.76 N, 5.90%.

2,3,17,18-Br_4-7,8,12,13-tetramethyl-5,10,15-triphenylcorrole (11). Crystallized from CH_2Cl_2/CH_3OH. Yield 18% (5 mg), mp >300 °C. UV-vis (CH_2Cl_2): λ_{max}, nm (log ε) 425 (4.76), 450 (4.68), 589 (4.03), 670 (4.28). ^{1}H NMR (300 MHz, $CDCl_3$): δ, ppm 8.02–7.97 (m, 6 H, phenyl), 7.76–7.68 (m, 9 H, phenyl), 2.10 (s, 6 H, β-methyl), 1.91 (s, 6 H, β-methyl). MS (FAB): *m/z* (%) 897 $[M]^+$ (100). Anal. calcd. for $C_{41}H_{27}Br_4CuN_4$: C, 54.82; H, 3.37; N, 6.24%. Found C, 54.90; H, 3.43 N, 6.18%.

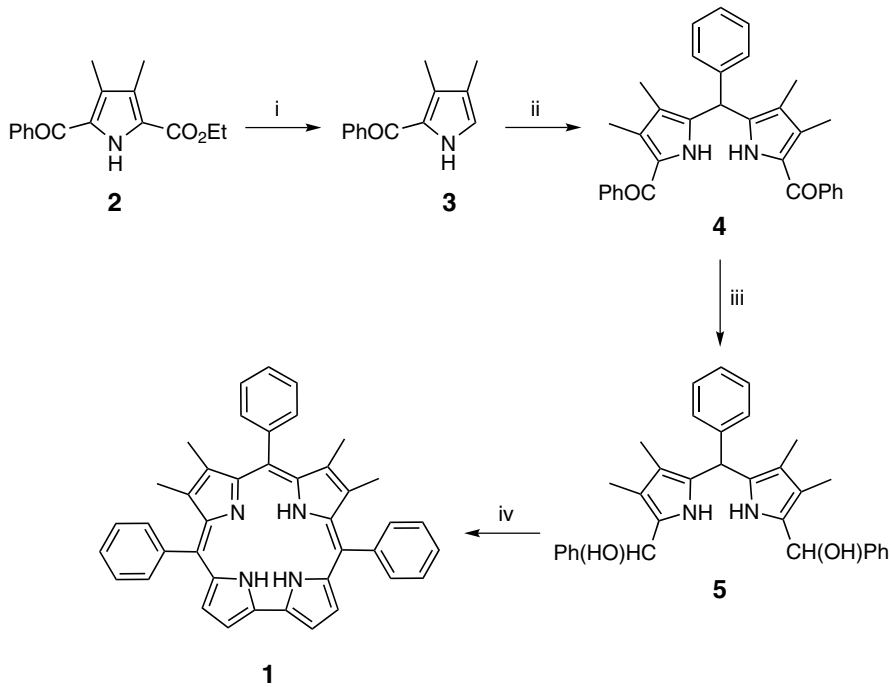
RESULTS AND DISCUSSION

The first step of our work was the preparation of the target corrole; we choose to modify the corrole framework by introducing methyl groups at β-positions of pyrroles B and C, with the aim to obtain the 7,8,12,13-tetramethyl-5,10,15-triphenylcorrole **1** (Fig. 1), which keeps the more reactive pyrrole positions (2, 3, 17 and 18) still available for the introduction of other substituents. The synthetic pathway for the preparation of the target molecule is shown in Scheme 1.

Since the desired corrole cannot be obtained by a statistical approach (one pot condensation of pyrrole, dialkylpyrrole and arylaldehyde), due to the different reactivity of unsubstituted and 3,4-disubstituted pyrrole, a rational approach was applied. The procedure for the formation of **1** can be divided in two main steps, where the first is the preparation of a suitable dipyrromethane-biscarbinol (**5**) followed by the cyclization of this intermediate with an excess of pyrrole. This synthetic pathway resembles the procedure reported for the preparation of arylcorroles or arylporphyrins bearing different *meso*-substituents by a dipyrromethane-diketone precursor [19–21].

The multistep procedure leading to **1** starts with the preparation of **2** [22], which then underwent decarboxylation under alkaline conditions. The α-free pyrrole **3** thereby obtained was reacted with a stoichiometric amount of benzaldehyde in acidic ethanol, and following purification yielded the desired dipyrromethane **4**. The two benzoyl groups were reduced to the more reactive carbinol moieties by reaction with $NaBH_4$ [23], giving the dipyrromethane **5**.

We initially adopted the same reaction conditions reported for the preparation of corrole bearing three different aryl groups [20]. Biscarbinol (**5**) was dissolved in 50 equivalents of pyrrole and a solution of TFA in CH_3CN was added; after 10 min the mixture was diluted with CH_2Cl_2, stirred for a further 10 min, and then a solution of DDQ in THF was added to induce the oxidation of bilane to corrole **1**. The UV-vis spectrum of the reaction mixture did not provide evidence of the corrole formation because of the presence of many by-products, mainly



Scheme 1. Synthetic pathway for the preparation of corrole **1**. Reaction conditions: (i) NaOH, ethylene glycol, reflux, 90 min; (ii) benzaldehyde, ethanol, reflux, HCl; (iii) $NaBH_4$, THF/CH_3OH, r.t., 90 min; (iv) pyrrole, catalyst, solvent, oxidant, r.t.

open chain derivatives; a first chromatographic separation was done using a silica gel plug eluted with $CHCl_3$. The fractions collected were subject to a second purification on basic alumina, which yielded a small amount of a green compound characterized by a large Soret band and two Q-bands at 429, 575 and 658 nm, respectively. The pattern of the ^{1}H NMR signals was in agreement with the corrole formation: namely, two doublets (2 protons each) at 8.45 and 8.88 ppm, with *J* values consistent with those of β-pyrrolic protons of arylcorrole, and two sharp singlets (6 protons each) at 2.40 and 2.10 ppm for the methyl substituents.

Attempts to grow single crystals for a definitive characterization of **1** failed. After a few days the color of the corrole solution turned from green to pink, and the UV-vis spectrum revealed the decomposition of the product. This result showed that **1** was sensitive to ambient light and to the presence of air that trigger the decomposition process, forming a biliverdine-like product [24]. Corroles are generally sensitive to oxidation and/or photodecomposition, and in the case of **1** this feature was even increased by the presence of the alkyl groups. To circumvent this drawback the reaction was repeated introducing a simple variation that was successful in the preparation of triaryl-tetrabenzocorrole or the 5,10,15-triferrocenylcorrole [25, 26]: instead of isolating the free base, the corresponding Cu complex was prepared by addition of a methanolic solution of $Cu(OAc)_2$ just after the oxidation of the bilane to corrole. The coordination of the copper cation increases the stability of the macrocycle, allowing the isolation of the desired product. A subsequent chromatographic separation afforded the product **6**, contaminated with a small amount of another compound having a very similar R_f as revealed by TLC analysis (silica gel, CH_2Cl_2/hexanes 2:3).

The identification of the reaction by-product was done by separation of it on preparative TLC. The first red band fraction was characterized as a Cu-porphyrin ($R_f = 0.67$), due to its Soret band at 428 nm and only one Q-band at 561 nm, which closely resembles the UV-vis spectrum of a Cu-tetraphenylporphyrin. The second brown band corresponded to the desired Cu-corrole **6** ($R_f = 0.64$), as confirmed by the UV-vis (Fig. 2) and ^{1}H NMR spectra (see Supporting information). The formation of **6** was also confirmed by X-ray analysis, although only a low resolution structure was obtained due to incomplete data acquistion due to instrument failure during data collection. Although the structure is not of adequate quality for publication, it was good enough to clearly indicate the formation of **6** (Fig. 3), and to demonstrate that the corrole framework has a "saddled" conformation similar to previously published structures [27, 29]. During the attempt to prepare the corrole free base, no porphyrin-like product was collected. A plausible explanation for the different results obtained is possibly due to the larger basicity reported for the highly substituted porphyrins [30, 31], which are easily protonated even in the mild acid conditions. The mixture leading to corrole and porphyrin was initially purified on silica gel (an acid support) possibly forming a dicationic species not eluted during the chromatographic step. The formation of this

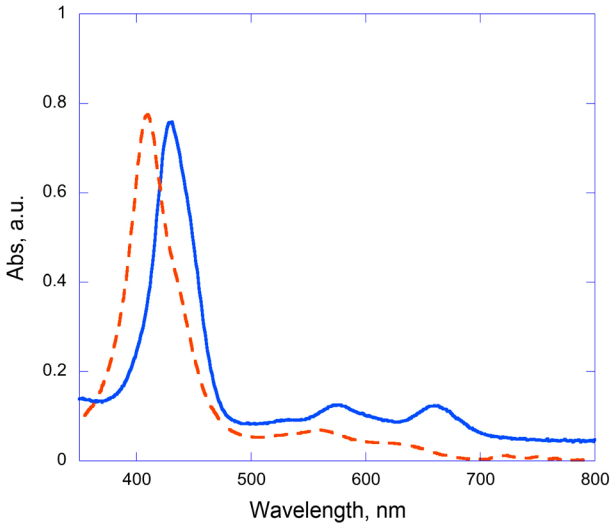


Fig. 2. UV-vis spectra in CH_2Cl_2 of **1** (full line) and **6** (dashed line)

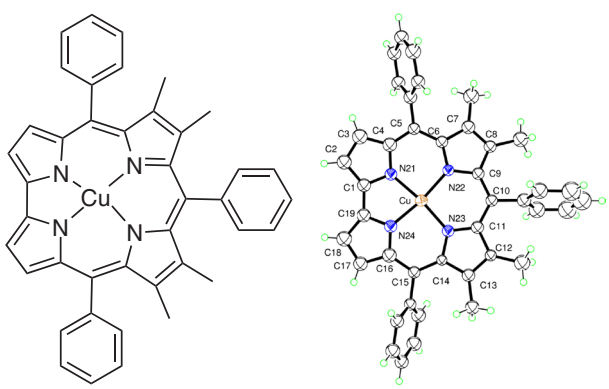


Fig. 3. Molecular and X-ray structure of **6**

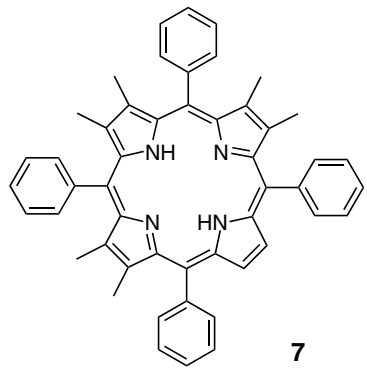


Fig. 4. Structure of the hexamethyl-tetraphenylporphyrin **7**

porphyrin-like product is due to the reaction between dipyrromethane-biscarbinol and pyrrole under reversible conditions [32].

The paramagnetic nature of the Cu-porphyrin ruled out its ^{1}H NMR characterization; to confirm the nature of the macrocycles, the mixture containing the porphyrin and the corrole was subject to Cu demetalation by the procedure reported for accomplishing this with corrole complexes [33], and also works for Cu-porphyrins.

The purification carried out by a basic alumina column eluted with CH_2Cl_2 afforded two fractions: the first (green) fraction was characterized as **1** by comparison of UV-vis and ^{1}H NMR spectra with those previously obtained. The second fraction, red in color, was identified as the porphyrin derivative **7** (Fig. 4); the red-shift for the Soret band (17 nm with respect to β-unsubstituted tetraphenylporphyrin) suggests a certain degree of distortion of the macrocycle due to the crowding of the peripheral positions. The ^{1}H NMR spectrum of this compound did not unequivocally clarify its structure: three broad singlets at 1.85, 2.03 and 2.13 ppm (6H each) suggested the presence of three pyrrole rings bearing the methyl groups and only one β-unsubstituted pyrrole, while the typical broad signal centerd at -2.37 ppm for the inner NH confirms the free base nature of the macrocycle. In the aromatic region, three not well-resolved signals, integrating 2, 4 and 4 H, respectively, were assigned to the β-pyrrole and some phenyl ring protons. The low resolution is due either to steric hindrance between alkyl and aryl substituents, or by some conformational equilibrium of the macrocycle [34]. The coordination of Zn gave a better-resolved spectrum, showing a singlet (2H) at 8.34 ppm that can be attributed to the unsubstituted β-pyrrole; the ^{1}H NMR spectrum obtained for this compound is very similar to that reported in the literature for the hexaethyl-tetraphenylporphyrin [35]. The regioselective formation of this porphyrin is quite surprising, since its formation could be reasonably attributed to the ring-scrambling that occurred under the reaction conditions. Nevertheless, the formation could be of synthetic interest since the multi-step methodology reported in the literature is quite complicated, but the overall yields are quite comparable.

Once the corrole formation had been confirmed, we tried alternative synthetic routes for the preparation of this macrocycle, with the aim to improve the yields of the reaction. Two different procedures were investigated; in both cases the Cu-complex was prepared to take advantage of the higher stability of the metal-derivative compared with the corresponding free base. The second method tested was one reported by Gryko [36] for the preparation of triarylcorrole in a methanol–water solvent mixture; the procedure was adapted to our starting material. Dipyrromethane **5** and a 50-fold excess of pyrrole were dissolved in the solvent mixture and HCl was added. The solution became purple and after a few minutes, the formation of a white suspension was observed. Work up of the reaction, followed by the oxidation of the bilane to corrole and by Cu insertion, afforded corrole **6** in comparable yield to that reported for the previously described method.

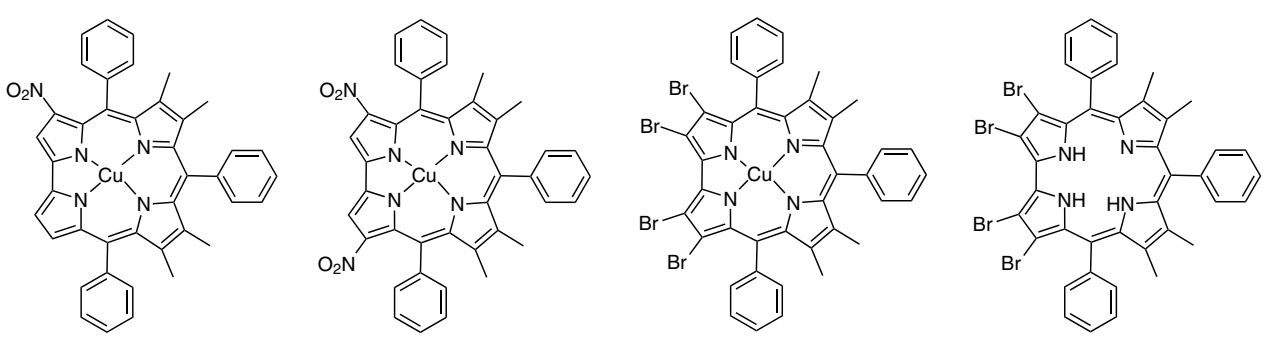
Finally we tested the effectiveness of the procedure previously reported for the preparation of triarylcorrole [37]; even if this method is based on the reaction of a 10 fold excess of pyrrole *vs*. aldehyde, for sake of consistency with the other investigations, a 50 fold excess of pyrrole (*vs.* dipyrromethane-biscarbinol) was employed. The target corrole was also obtained using this procedure, and it gave the best results in terms of yield (12%). Although not exciting, it is noteworthy that the yield calculated with respect to **5** is not unusual in the case of corrole and comparable with those reported for some triarylcorroles obtained by a one-step condensation of arylaldehyde and pyrrole [5, 37].

Two different functionalization reactions were successfully carried out on corrole **6**: the nitration and the bromination reactions (Fig. 5). The nitration reaction was performed following the method recently reported [15], which drives the reaction toward the formation of the mononitro derivative as the main product, together with a small amount of dinitro substituted corrole. Compound **6** was reacted with 1 equivalent of $AgNO_2$ and 9 equivalents of $NaNO_2$ in refluxing DMF. The silver nitrite acts as oxidant, promoting the formation of a π radical cation species that undergoes nucleophilic attack by the nitrite anion from the $NaNO_2$. The UV-vis spectrum and TLC analysis after a few minutes showed almost complete disappearance of the starting material. Purification of the reaction mixture afforded a first, major band (silica gel, CH_2Cl_2: R_f 0.86), olive green in color, which was collected and characterized by UV-vis (Fig. 6), ^{1}H NMR, and mass spectrometry. The ^{1}H NMR analysis showed one singlet and two doublets (1H each) in the region of the β-pyrrole protons, which suggested the formation of a mono-nitroderivative; this was confirmed by the mass analysis where a peak at $m/z^+ = 689$ was observed. Although we did not obtain a suitable crystal to confirm on which carbon the substitution had taken place, it can be presumed that the nitration occurred on C-3 because of the higher reactivity observed for this position in previous cases of the nitration reaction. To confirm this hypothesis, a 2D NMR analysis was performed. In the ROESY spectrum a dipolar interaction between the singlet belonging to the H close the $–NO_2$ group and a doublet of one of the hydrogens on the unsubstituted pyrrole was observed (see Supporting information). Since this interaction can occur only between atoms spatially close to each other (H2–H18), we can deduce that the functionalization occurred on position 3, leading to the formation of corrole **8**. Furthermore, the interaction between the H17 and the *ortho* protons of the adjacent phenyl ring, furnished further proof of the site of nitration.

A second emerald green fraction was also isolated (R_f: 0.81) from the reaction. The higher polarity of this product with respect to **8** suggested the formation of a polynitrated product, as corroborated by the mass spectrum, where a peak at *m/z* 734 was present. In this case it is expected that substitution likely occurs at position 3 and 17. The singlet (2 H) at 8.04 ppm confirmed the formation of the symmetrical disubstituted nitro derivative **9**. It should be noted that the product yields were lower than those obtained for the analogous triarylcorrole complex [15] and that the mono- and bis-substituted product ratio was also different, with an increase of the bis-nitro corrole product. Both results could be attributed to the presence of the peripheral methyl groups, making **6** more liable to the oxidation, which is the initial step for the reaction.

Finally the bromination reaction of **6** was initially investigated using a mild reagent such as NBS (Fig. 5). A small excess of NBS (with respect the four positions to be functionalized) was reacted with the Cu-corrole in refluxing $CHCl_3$. After a few minutes a severe broadening of the Soret band and the complete disappearance of the Q-bands was observed. TLC analysis showed the presence of only base-line material; these results suggested the complete decomposition of the Cu-corrole. Similar results were obtained when the reaction was repeated at room temperature. We can again attribute this result to the sensitivity of **6** to the oxidative conditions of the reaction.

A different approach was then carried out using elemental bromine. The procedure for the complete bromination of Cu-corrole [5, 38] was slightly modified



8 **9** **10** **11**

Fig. 5. Products of the nitration (**8**, **9**) and bromination (**10**, **11**) of **6**

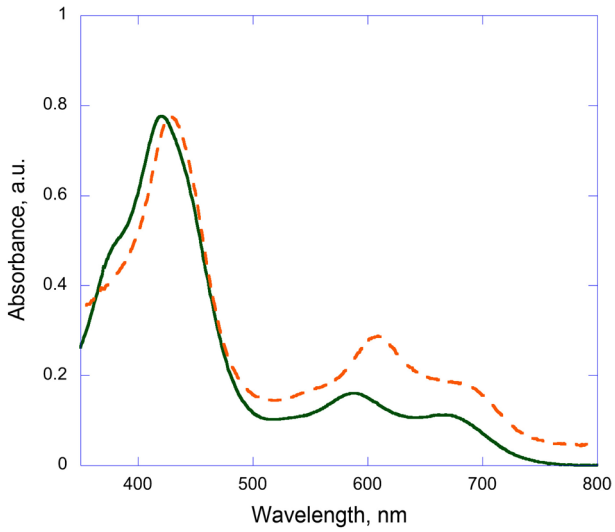


Fig. 6. UV-vis spectra in CH_2Cl_2 of **8** (full line) and **9** (dashed line)

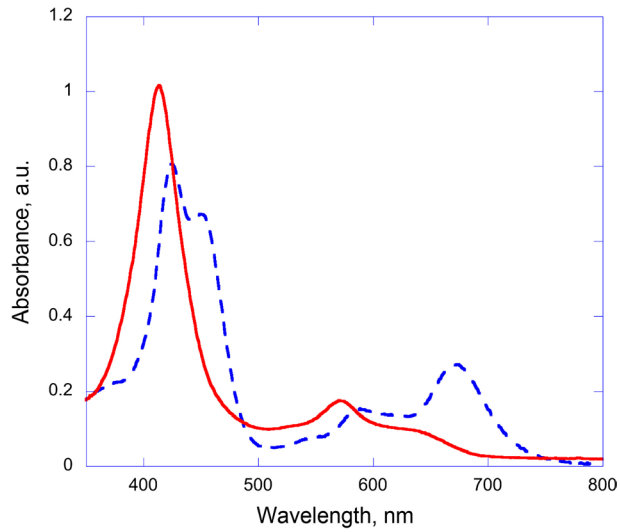


Fig. 7. UV-vis spectra in CH_2Cl_2 of **10** (full line) and **11** (dashed line)

by decreasing the equivalents of Br_2, since the positions available for the bromination were four instead of eight; for this reason we used half of the equivalent compared with those reported in the original paper. Br_2 was added dropwise and after 5 min no more starting material was detected by TLC. The reaction was immediately quenched by addition of pyridine; chromatographic purification (silica gel, CH_2Cl_2) afforded two products. The first band, olive green in color was identified as the desired tetrabrominated derivative **10**, characterized by a low solubility that negatively affected the characterization of the product. The ^{1}H NMR spectrum was quite broad, but is was however possible to determine the complete bromination of the β-pyrrolic positions, since only the multiplets for the phenyl rings were observed around 7.50 ppm; a complex pattern of singlets for the methyl groups were present at 1.53–1.41 ppm. The second fraction showed a split Soret band and two Q-bands in the UV-vis spectrum (Fig. 7). Also in this case the ^{1}H NMR analysis confirmed that bromination had taken place on all four β-pyrrole positions available, while the FAB mass spectrum showed a molecular peak corresponding the free base **11**, suggesting an unexpected demetalation of **10** in the bromination reaction conditions. It is important to note that the low solubility of **10** requires particular care in the reaction work-up. At the end of the reaction the solvent should be reduced to a small volume to carry out the chromatographic separation; if the reaction mixture is led to dryness, it is difficult to redissolve **10** in CH_2Cl_2 and most of the corrole derivative is irreversibly adsorbed on the top of the column. In this case the chromatographic purification afforded only **11**, strongly reducing the reaction yields. We would like to thank a referee that helped us to clarify this point.

To confirm the nature of both the substances, free base **11** was reacted with $Cu(OAc)_2$ in refluxing chloroform/methanol solution. The product obtained has the same spectroscopical pattern of **10**, confirming that **11** is derived from the demetallation of **10** in the reaction conditions. The reaction yields were however lower than those of the corresponding triarylcorroles, and this result could be reasonably attributed to the sensitivity of **6** to oxidative decomposition and to its low solubility as previously described.

CONCLUSION

A synthetic route for the preparation of β-alkyl-*meso*-arylcorroles has been investigated, and the first example of such a corrole has been synthesized. The route involves the preparation of a methyl-substituted dibenzoyl dipyrromethane, which was reduced and then the corresponding biscarbinol was reacted with pyrrole to obtain the bilane precursor of the target corrole. The addition of copper ion after the oxidation step resulted in a significant increase of the reaction yields, due to protection of the corrole ring from oxidative decomposition. Nitration and bromination reactions were performed on the copper corrole complex, giving the corresponding functionalized corroles in moderate yields.

The developed synthetic routes open the way for the preparation of novel corrole derivatives that could be of interest for opto-electronic applications and these studies are ongoing in our laboratories.

Supporting information

^{1}H and ^{13}C NMR, FAB mass spectra of compounds and low resolution crystal data of **6** (Table S1, Figs S1–S16) are given in the supplementary material. This material is available free of charge *via* the Internet at http://www.worldscinet.com/jpp/jpp.shtml.

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