Supporting Information

A Survey of Acid Catalysis and Oxidation Conditions in the Two-Step, One-Flask Synthesis of meso-Substituted Corroles via Dipyrrromethane-Dicarbinols and Pyrrole

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Table of Contents

	<u>Page</u>
Experimental section	
General experimental methods	S2
Synthesis of dipyrrromethane-dicarbinol precursors	S2-S3
Oxidant screening experiments	S3
Comparison of DDQ and <i>p</i> -Chloranil Oxidation in the synthesis of TPC under conditions reported by Guilard, Gryko and coworkers	S4
Correction factors for spectrophometric analysis of corroles	S4-S5
Plots of the yield of TPC as a function of acid concentration	S5-S6
Investigation of TFA/acetonitrile condensation conditions	S7
Timecourse experiments for reactions leading to corroles 2b,d,e	S8
Stability of corroles 2a-e	S9
¹ H NMR spectra of diacyl dipyrrromethanes	
1a	S10
1c	S11
¹ H NMR spectra of corroles	
2a	S12
2b	S13
2c	S14
2d	S15
2e	S16
COSY spectra of corroles	
2b	S17
2c	S18
2d	S19

Experimental Section

General Experimental Methods.

^1H NMR (400 MHz), ^{13}C NMR (100 MHz), and absorption spectra were collected routinely. Melting points are uncorrected. Column chromatography was performed on silica (Merck, 230-400 mesh, 60 Å). CH_2Cl_2 used in corrole forming reactions was distilled from potassium carbonate and stored over 4-Å Linde molecular sieves. CH_2Cl_2 used in spectrophotometric determination of yield of corrole was passed through a pad of basic alumina prior to use. THF used in the reduction of diacyl dipyrromethanes was stored over 4-Å Linde molecular sieves. Toluene used in the preparation of diacyl dipyrromethanes was distilled from calcium hydride. Pyrrole was distilled from calcium hydride and stored at $-15\text{ }^\circ\text{C}$ until use. The distilled pyrrole was used prior to the appearance of any discoloration. The sodium dithionite is technical grade, 85%. All other chemicals are reagent grade and were used as obtained. Diacyl dipyrromethanes **1b**,¹ **1d**,¹ and **1e**,¹ and their precursors [5-phenyldipyrromethane,² 5-(4-methoxyphenyl)dipyrromethane,² S-2-pyridyl 4-benzothioate,³ and 1-benzoyl-5-(4-methoxyphenyl)dipyrromethane³] were prepared as described in the literature. Authentic TPC **2a**⁴ and TpFPC **2e**⁵ for use in the development of a spectrophotometric method for the determination of the yield of corrole were prepared as described in the literature.

Synthesis of Dipyrromethane-Dicarbinol Precursors.

1,9-Bis(benzoyl)-5-phenyldipyrromethane (1a). Following a standard procedure,¹ a solution of EtMgBr (50 mL, 50 mmol, 1 M in THF) was added to a solution of 5-phenyldipyrromethane (2.22 g, 10.0 mmol) in toluene (200 mL) under argon. The mixture was stirred for 30 min at rt followed by the addition of a solution of benzoyl chloride (2.90 mL, 25.0 mmol) in toluene (25 mL) over 10 min. The mixture was stirred at rt for 20 min. The reaction was quenched by the addition of satd aq NH_4Cl (150 mL) and extracted with ethyl acetate (200 mL). The organic layer was separated and dried over Na_2SO_4 . Removal of solvent afforded a dark red/orange oil. The oil was triturated with hot ethyl acetate (3-5 mL). The mixture was cooled in an ice bath, and the solid was collected by filtration yielding a light grey powder and a maroon filtrate. The trituration was performed 2-4 times until there was no evidence for 5-phenyldipyrromethane or 1-benzoyl-5-phenyldipyrromethane by TLC [silica, CH_2Cl_2 /ethyl acetate (25:1), visualization with Br vapor] or ^1H NMR (CDCl_3). **1a** [(2.0 g, 47%, mp 231-232 $^\circ\text{C}$ (lit mp 232 $^\circ\text{C}$)⁶] was obtained as a light gray to white powder. Anal. Calcd for $\text{C}_{30}\text{H}_{24}\text{N}_2\text{O}_2$: C, 80.91; H, 5.15; N, 6.51. Found: C, 80.66; H, 5.17; N, 6.47. Analytical data are consistent with literature values.⁶

1-Benzoyl-5-phenyl-9-(4-methylbenzoyl)dipyrromethane (1c). Following a standard procedure,¹ a solution of EtMgBr (34.8 mL, 34.8 mmol, 1 M THF) was added to a solution of 1-

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benzoyl-5-(4-methoxyphenyl)dipyrromethane (2.00 g, 5.88 mmol) in toluene (10 mL) under argon. The mixture was stirred for 10 min at rt followed by the slow addition of benzoyl chloride (2.01 mL, 17.3 mmol). The mixture was stirred at rt for 1 h. The reaction was quenched by the addition of satd aq NH_4Cl (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was separated, dried (Na_2SO_4) and concentrated. Column chromatography of the residue [silica, CH_2Cl_2 /ethyl acetate (95:5)] afforded 0.71 g (27%) of a tan amorphous powder. mp 116-117 °C; ^1H NMR (CDCl_3) δ 2.40 (s, 3H), 5.67 (s, 1H), 5.98 (m, 2H), 6.59 (m, 2H), 7.20 (d, J = 7.9 Hz, 2H), 7.33 (m, 1H), 7.40 (m, 4H), 7.50 (m, 3H), 7.69 (d, J = 8.1 Hz, 2H), 7.78 (m, 2H), 11.1 (br s, 2H); ^{13}C NMR (CDCl_3) δ 21.3, 45.3, 111.4, 111.5, 120.6, 121.0, 128.0, 128.4, 129.1, 129.3, 129.8, 130.0, 131.4, 131.5, 132.0, 135.9, 138.7, 140.5, 140.6, 141.0, 142.6, 184.7, 184.9; HRMS (FAB) obsd 445.1898 (MH^+), calcd 445.1916 (MH^+); Anal. Calcd for $\text{C}_{30}\text{H}_{24}\text{N}_2\text{O}_2$: C, 81.06; H, 5.44; N, 6.30. Found: C, 80.77; H, 5.46; N, 6.17.

Oxidant Screening Experiments.

Analytical Scale (DDQ). Aliquots (200 μL) of the reaction of **1a-OH** (2.5 mM) with pyrrole (250 mM) catalyzed by $\text{Dy}(\text{OTf})_3$ (1.0 mM) at rt for 2 h were transferred to microcentrifuge tubes containing DDQ (0.5 to 80 equiv. relative to **1a-OH**) in toluene (300 μL). The mixtures were vortex mixed and monitored for yield of corrole (UV/Vis). TLC was performed on the crude, oxidized mixtures [silica, CH_2Cl_2 /hexanes (1:1)] after washing with the aq dithionite solution.

Analytical Scale (*p*-Chloranil). Aliquots (10 mL) of the reaction of **1a-OH** (2.5 mM) with pyrrole (250 mM) catalyzed by $\text{Dy}(\text{OTf})_3$ (1.0 mM) at rt for 1.2 h and treated with triethylamine (5 equiv. relative to acid) were transferred to 25 mL pear shaped flasks containing *p*-chloranil (0.25 to 16 equiv. relative to **1a-OH**). Each flask was equipped with a condenser and the mixtures were heated to reflux open to the air. The oxidation reactions were monitored for yield of corrole from 15 min to 2 h [UV/Vis, with the exception that an aliquot of the reaction mixture (200 μL) was transferred to a microcentrifuge tube containing toluene (300 μL) rather than DDQ solution]. TLC was performed directly from the crude, oxidized mixtures [silica, CH_2Cl_2 /hexanes (1:1)].

Semi-Preparative Scale. Aliquots (50-100 mL) of the reaction of **1a-OH** (2.5 mM) with pyrrole (250 mM) catalyzed by $\text{Dy}(\text{OTf})_3$ (1.0 mM) at rt for 1.5 h and treated with triethylamine (5 equiv. relative to acid) were transferred to flasks containing *p*-chloranil (1.5, 1.75, 1.9, or 2.0 equiv. relative to **1a-OH**) or DDQ (3 equiv. relative to **1a-OH**). The flasks containing *p*-chloranil were heated to reflux open to the air for 45 min, and the flask containing DDQ was stirred at rt for 45 min. The contents of each flask were filtered through a pad of silica gel (CH_2Cl_2), followed by chromatography [silica, CH_2Cl_2 /hexanes (1:1)]. Fractions containing TPC were combined, concentrated, dried under vacuum, and the mass was recorded. TLC was performed on the crude mixtures after oxidation and on the purified TPC samples [silica, CH_2Cl_2 /hexanes (1:1)].

Comparison of DDQ and *p*-Chloranil Oxidation in the Synthesis of TPC from **1a-OH** Under Conditions Reported by Guillard, Gryko and coworkers.⁷

The condensation of **1a-OH** (0.40 mmol) with pyrrole (20 mmol) mediated by TFA (0.010 mmol) was performed in accordance with the published procedure.⁷ After mixing at rt for 10 min, the contents were diluted by the addition of CH₂Cl₂ (160 mL) and divided evenly between two flasks. To one flask, DDQ (0.60 mmol, 3 equiv. per **1a-OH**) dissolved in THF (0.6 mL) was added. The mixture was allowed to stir at rt for 1 h. To the other flask, triethylamine (5 equiv. relative to acid) and *p*-chloranil (0.40 mmol, 2 equiv. per **1a-OH**) were added. The mixture was heated at reflux for 45 min. The TPC was isolated from the two reactions in identical fashion by filtration through a silica pad (eluting with CH₂Cl₂) followed by chromatography [silica, CH₂Cl₂/hexanes (1:1)]. While spectral monitoring of the two oxidation reactions provided similar results, DDQ oxidation afforded the isolation of 11.2 mg of TPC (11% yield) whereas *p*-chloranil oxidation provided 50.0 mg of TPC (50% yield). The purity of the isolated TPC was assessed by TLC analysis [silica, CH₂Cl₂/hexanes (1:1)].

Correction Factors for Spectrophometric Analysis of Corroles.

Retention of eluent on silica pipet. To account for the portion of CH₂Cl₂ eluent that is retained by the silica pipet (thereby increasing the concentration of the eluted corrole relative to simple dilution in 3 mL of CH₂Cl₂) CH₂Cl₂ (3 mL) was passed through a pipet containing silica gel and collected in a tared vial or directly transferred to a tared vial. The mass of the solvent in the vials were recorded and compared. The ratio of the mass of CH₂Cl₂ dispensed directly into a vial compared to the mass of CH₂Cl₂ passed through the silica pad was found to be 1.30. Multiple trials provided consistent results. This correction is applied to the calculation of the theoretical absorbance to account for the fact that a portion of the CH₂Cl₂ used to elute the corrole from the silica pad remains on the pad and does not dilute the corrole. A similar correction factor was applied in a reported pre-HPLC work-up for the analysis of porphyrin, N-confused porphyrin, and sapphyrin in reactions of pyrrole + benzaldehyde.⁸

Attenuation of the absorbance of the Soret band in the presence of pyrrole and DDQ. To account for the attenuation of the Soret band under conditions encountered in the crude reaction mixtures, stock solutions of TPC (200 μ L, mimicking yields of corrole of 10, 20, 30, 40, 50, and 60%) were doped with pyrrole (0 mM, 62.5 mM, 125 mM, or 250 mM), treated with DDQ (300 μ L of a 10 mM solution in toluene), followed by washing with aq sodium dithionite, filtration through a silica pad, and UV-Vis analysis. The absorbance of the Soret band was compared, and the ratio of the absorbance in the presence of pyrrole to the absorbance in the absence of pyrrole was calculated. The mean ratio was found to be 0.306. This correction factor is applied to adjust the calculated theoretical absorbance due to the effects of pyrrole in crude reaction mixtures. The raw data leading to the correction factor is provided in Table S1. A consistent effect of pyrrole in the presence of DDQ on the absorbance of the Soret band was observed across the various concentrations of corrole and pyrrole that were investigated. This

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suggests that the yield of TPC can be quantified across a broad range of conditions and yields of TPC despite the alteration of the appearance of the UV/Vis spectrum by pyrrole.

Table S1. A summary of the data leading to the correction factor accounting for the attenuation of the Soret band by pyrrole in the crude reaction mixtures.^a

Entry	[TPC], mM	[pyrrole], mM	λ_{max} , nm	A	$A_{\text{pyrrole}} : A_{\text{no pyrrole}}^b$
1	0.25 ^c	0	415	0.167	-----
2	0.25	62.5	409	0.0425	0.254
3	0.25	125	405	0.0484	0.290
4	0.25	250	409	0.0452	0.271
5	0.50	0	415	0.346	-----
6	0.50	62.5	409	0.103	0.298
7	0.50	125	405	0.106	0.306
8	0.50	250	408	0.109	0.315
9	0.75	0	414	0.612	-----
10	0.75	62.5	409	0.184	0.301
11	0.75	125	405	0.182	0.297
12	0.75	250	405	0.186	0.304
13	1.0	0	415	0.763	-----
14	1.0	62.5	409	0.241	0.316
15	1.0	125	406	0.249	0.326
16	1.0	250	407	0.246	0.322
17	1.25	0	414	1.085	-----
18	1.25	62.5	408	0.328	0.302
19	1.25	125	405	0.327	0.301
20	1.25	250	406	0.323	0.298
21	1.5	0	415	1.241	-----
22	1.5	62.5	409	0.377	0.304
23	1.5	125	406	0.386	0.311
24	1.5	250	406	0.358	0.288
				Mean	0.306 ^d
				Std. Dev.	0.010 ^d

^aA solution of TPC and pyrrole (200 μL) was transferred to a microcentrifuge tube containing a solution of DDQ (300 μL , 10 mM in toluene). The mixture was treated with dithionite wash and filtration through a silica pad followed by analysis by UV/Vis. ^bRatio of the absorbance of a TPC solution treated with pyrrole to the absorbance of the same TPC solution not treated with pyrrole (*e.g.*, entry 2 provides the ratio of the absorbance of entry 2 to the absorbance of entry 1). ^cA concentration of TPC of 0.25 mM mimics a 10% yield of corrole in a reaction involving 2.5 mM of dipyrromethane-dicarbonyl. ^dThe mean and standard deviation do not include entries 2-4 as the absorbance recorded in the presence of pyrrole was too low to be reliable. Including those values provides a mean of 0.300 and standard deviation of 0.017.

Plots of Yield of TPC as a Function of Acid Concentration from Acid Screening Experiments.

Figure S1 provides plots of the spectral yield of TPC as a function of acid concentration for reaction conditions that provided TPC devoid of *meso*-tetraphenylporphyrin (TPP). The yield of TPC could not be determined for conditions that also afforded TPP, as the Soret band of TPP interferes with that of TPC.

Figure S1. Yield of TPC as a function of acid concentration for reactions of dipyrromethane-diol **1a-OH** (2.5 mM) + pyrrole (125, 250, or 500 mM) in CH₂Cl₂ at rt. Reactions were monitored at 15 min (○) and 1 h (■) by removing an aliquot of the reaction mixture, oxidizing with DDQ, washing with aq dithionite, filtering through a silica pad, and analyzing spectrophotometrically for yield of TPC.

Investigation of TFA/Acetonitrile Condensation Conditions.^{1,3}

TFA catalysis requirement. Analytical scale reactions (5 mL) of dipyrromethane-dicarbinol **1a-OH** (2.5 mM) + pyrrole (125, 250, or 500 mM) catalyzed by TFA (0.10, 0.32, 1.0, 3.2, 10, 32, 100 mM) in acetonitrile at rt were performed in order to identify the best catalytic conditions. The yield of corrole was monitored spectrophotometrically at condensation times of 15 min and 1 h. The presence of a brown/red pigment that eluted with the green band of TPC through the silica pad prevented the precise determination of the yield of TPC. Qualitative comparisons based on the UV/Vis spectra and TLC analysis [silica, CH₂Cl₂/hexanes (2:1)] found a concentration of TFA of 0.32 mM and pyrrole of 250 mM to provide the best result.

Oxidant screening experiments. Aliquots (8 mL) of the condensation of dipyrromethane-dicarbinol **1a-OH** (0.213 mmol, 2.5 mM) + pyrrole (250 mM) catalyzed by TFA (0.32 mM) in acetonitrile at rt for 25 min followed by addition of triethylamine (5 equiv. relative to acid) were transferred to flasks containing DDQ or *p*-chloranil (1, 2, 3, 4, or 8 equiv. relative to **1a**). DDQ oxidations were performed at rt and *p*-chloranil reactions were performed at reflux. The oxidation reactions were monitored for yield of TPC spectrophotometrically, and for complexity of the reaction mixture by TLC [silica, CH₂Cl₂/hexanes (1:1)] from 30 min to 2 h. The best oxidation conditions for each oxidant were 3 equiv. of DDQ and 2 equiv. of *p*-chloranil—in agreement with reactions performed in CH₂Cl₂. Reactions involving DDQ provided an olive green spot of slightly lower *R_f* than that of TPC and *p*-chloranil in quantities ≥ 2 equiv. provided a tan spot of slightly greater *R_f* than that of TPC. DDQ was observed to cause less interference with the detection of TPC in acetonitrile solvent than in CH₂Cl₂.

Semi preparative reactions comparing TFA/acetonitrile and Dy(OTf)₃/CH₂Cl₂ conditions. Condensation reactions of **1a-OH** (0.25 mmol, 2.5 mM) + pyrrole (250 mM) catalyzed by TFA (0.32 mM in acetonitrile or by Dy(OTf)₃ (1.0 mM) in CH₂Cl₂ were performed at rt. At a condensation time of 45 min, triethylamine (5 equiv. relative to acid and *p*-chloranil (1.9 equiv. relative to **1a-OH** were added to the reaction catalyzed by TFA. At a condensation time of 90 min, triethylamine (5 equiv. relative to acid and *p*-chloranil (1.9 equiv. relative to **1a-OH** were added to the reaction catalyzed by Dy(OTf)₃. Both reactions were heated at reflux for 45 min, followed by purification by passing through a silica pad (CH₂Cl₂) and chromatography [silica gel, CH₂Cl₂/hexanes (1:1)]. The fraction from each reaction containing TPC was concentrated, dried under vacuum, and weighed. Purity of the samples was compared by TLC analysis [silica, CH₂Cl₂/hexanes (1:1)]. The TFA/acetonitrile condition afforded TPC (35 mg, 26%) that was contaminated with a low level of a tan pigment of slightly greater *R_f* than that of TPC as well as by a low level of baseline material. The Dy(OTf)₃ condition afforded TPC (71 mg, 54%) containing a trace level of a tan pigment of slightly greater *R_f* than that of TPC.

Taken together, these results suggest that a TFA/acetonitrile condition can provide TPC, however conditions involving mild acids in CH₂Cl₂ provide better yields of TPC with a higher level of purity.

Timecourse Experiments for Reactions Leading to Corroles 2b,d,e.

The yield of corroles **2b,d,e** as a function of condensation time are summarized in Figure S2.

Figure S2. Percent yield of corrole as a function of condensation time for reactions of dipyrromethane-dicarbinol (2.5 mM) + pyrrole in CH_2Cl_2 at rt. Reactions were monitored by removing an aliquot of the reaction mixture, oxidizing with DDQ, washing with aq dithionite, filtering through a silica pad, and analyzing spectrophotometrically for yield of TPC. Note the log scale for time.

Stability of Corroles 2a-e.

The stability of dilute solutions of corroles **2a-e** as assessed by changes in the absorbance of the Soret band as a function of exposure to light is summarized in Figure S3.

Figure S3. Absorbance of the Soret band as a function of time for dilute solutions corroles **2a-e** in toluene in the presence of ambient light. The λ_{max} of the Soret band of **2a** shifted from 420 to 401 nm during the experiment, **2b-c** shifted from 421 to 402 nm, **2d** shifted from 421 to 404 nm, and the λ_{max} of the Soret band of **2e** was 414 nm.

CDCl_3

CDCl₃

CD₃OD (0.6%) in CDCl₃
 N-H signals are not detected
 due to exchange with CD₃OD