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Expedient synthesis of corroles by oxidant-mediated, direct α-α′ coupling of tetrapyrromethanes

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Abstract

Oxidant mediated coupling of tetrapyrromethanes resulted in the exclusive formation of *meso*-substituted corroles in more than 60% yields. The similar coupling reaction of 1,14-unsubstituted 16-oxatripyrromethane with 5-tolyldipyrromethane carried out in acetonitrile also gave expanded corroles as a single product. In both cases acid catalysts are not necessary for the direct α-α′ coupling reaction. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: corroles; tetrapyrromethanes; oxidative-coupling; smaragdyrin.

The metal complexes of corroles and corrins are important biological cofactors and the study of their physicochemical properties has contributed to the development of the chemistry of corrinoid macrocycles.[1] A recent report[2] indicated the potential utilities of metallocorroles as catalysts for oxygen activation and for cyclopropanation reaction. The more flexible nature of the corrin ring system allows it to change the steric environment around the central metal ion easily in comparison to the reduced porphyrins. This versatility is well adapted in vitamin B_{12}.[3,4] One of the well known synthetic methods of corroles is the cyclization of tetrapyrrolic precursors. Paolesse et al. reported the acid-catalyzed cyclization of *a*,*c*-biladiene in various solvents claiming that the conformational factors control the cyclization processes.[5] More recently, corrole has been isolated from the solventless condensation of aldehydes and pyrrole.[6] It has been known that square-planar forming metal ions show a template effect and usually enhance the yield of corroles.[7] The mechanistic insight for the biladiene cyclization was also investigated by Woodward and Hoffman.[8] Previously, we reported a synthetic method for core-modified corrole by a '2+2' approach starting from two different dipyrromethanes.[9] The reaction involves acid-catalyzed condensation followed by direct intramolecular coupling. Current results indicate that simple oxidative cyclization is operating in the intramolecular coupling of tetrapyrrolic precursors and an acid catalyst is not necessary. Direct coupling of oligopyrromethanes in the presence of oxidizing agents resulted in the formation of corroles as a single product with high yields. The oxidant-mediated intermolecular coupling of dipyrromethanes

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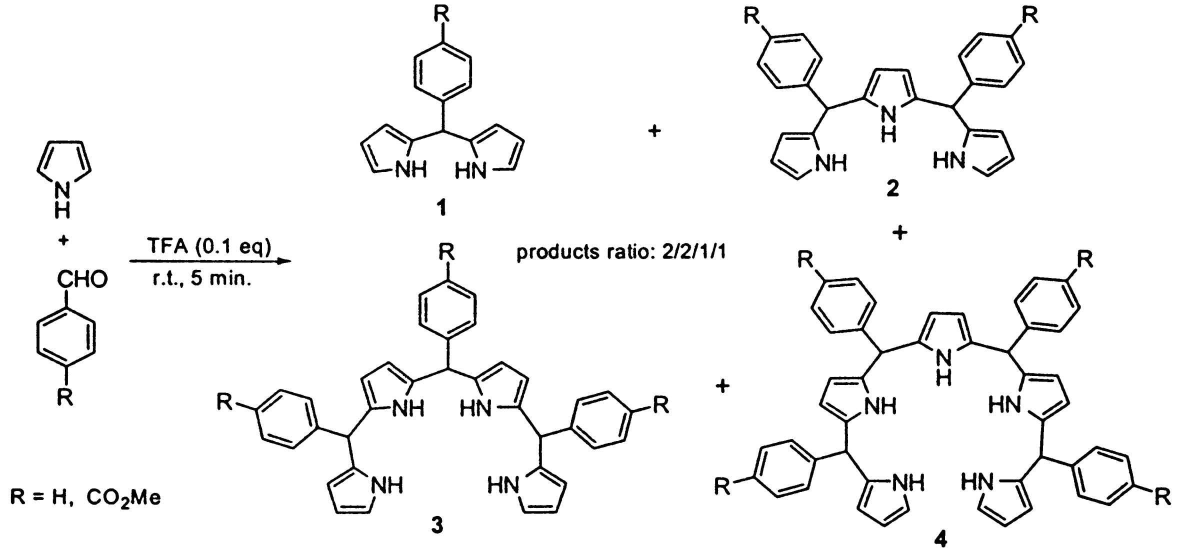
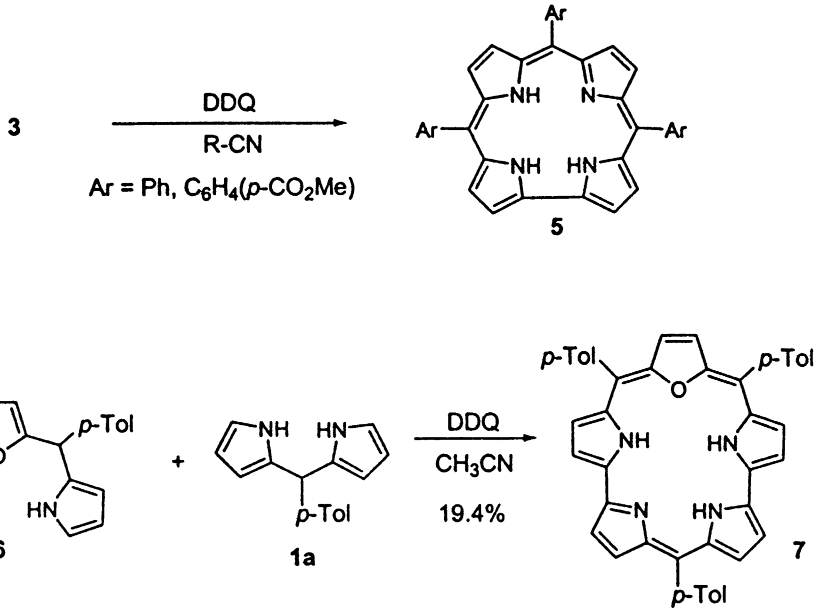
with tripyrromethanes also afforded smaragdyrin, an expanded corrole as a single product. Herein, we report a convenient, rational synthesis of *meso*-substituted corroles as well as expanded corroles by direct coupling of oligopyrromethanes.

The tetrapyrromethanes (**3**) are synthesized in reasonable yields (Scheme 1) by direct condensation of aldehydes and pyrrole as reported previously.[10] Improved yields of tetrapyrromethane was achieved by reducing the pyrrole/aldehyde ratio to 3/1. The typical product ratios (**1**/**2**/**3**/**4**) of 2/2/1/1 was obtained when benzaldehyde and pyrrole were condensed. Single column chromatography is good enough to separate all the components. The oxidative coupling reaction of (**3**) to obtain corroles was carried out as shown in Scheme 2.[11]



Scheme 1.



Scheme 2.

The reaction gave desired corroles in a range of solvents and in the presence of inorganic additives, including NH_4Cl, KCl, NaCl, KBr and NH_4NO_3. No corroles were obtained when pure dichloromethane was used as a solvent, while 16% of corrole was isolated by adding excess NH_4Cl. Low yield (~6%) of corrole was obtained in protic solvents such as methanol.

Acetonitrile usually gave ~30% yield of corrole in the presence of inorganic additives, but only ~4% of corrole was isolated in the absence of the additives. Attempted coupling in propionitrile dramatically improved the yield up to 65% and the addition of additives did not alter the yield appreciably. Butyronitrile was also a good solvent for the coupling, but without the improvement in yield (Table 1). The reaction proceeds smoothly in all cases and acid catalysts are not necessary in the reaction. Corrole (**5**) was easily separated by column chromatography on neutral alumina. Significant peak broadening of all the resonance lines was observed when proton NMR spectra were taken in pure $CDCl_3$. On the other hand, adding a drop of methanol-d_4 resulted in fully resolved spectra. This result indicates the flexible nature of the molecule. Pyrrolic N–H signals were not detected in either solvents, but the spectra taken in DMSO-d_6 show broad signal at –2.67 ppm. The reaction carried out in the presence of *p*-chloranil afforded only 10% of corroles and the reaction was much slower.

Table 1
Isolated yields of corrole in various solvents and inorganic additives[a]

R	Solvent	Additives	Yield (%)
$COOCH_3$	CH_3CN	NH_4Cl	30
H	CH_3OH	NH_4Cl	6
H	CH_2Cl_2	NH_4Cl	16[b]
H	$CH_3CH_2CH_2CN$	NH_4Cl	61
H	CH_3CN	None	4
H	CH_3CN	NH_4Cl	30
H	CH_3CN	KCl	28
H	CH_3CN	NaCl	26
H	CH_3CN	KBr	26
H	CH_3CN	NH_4NO_3	22
H	CH_3CH_2CN	None	53
H	CH_3CH_2CN	NH_4Cl	60
H	CH_3CH_2CN	NaCl	61
H	CH_3CH_2CN	NH_4NO_3	65

[a] The reaction time was 60 min and the reactant concentration was 5×10^{-3} M. Ten equivalents of inorganic additives were used in all cases.

[b] In this particular case, only trace amount of corrole was isolated in the absence of additives.

Similar oxidant-mediated coupling of dipyrromethane (**1a**) with 16-oxatripyrromethanes (**6**)[12] resulted in the formation of smaragdyrin (**7**).[13] The acid is not necessary in this reaction and this '3+2' type coupling gave expanded corrole (**7**) exclusively in 19.4% yield. Compound (**7**) did not show any fluorescence on TLC under UV-light and appeared as a yellowish spot. Attempted coupling of *meso*-tolyltripyrromethane or 16-thiatripyrromethane with *meso*-

tolyldipyrromethane did not give corresponding expanded corroles. Obviously, the presence of furanyl oxygen is essential in the case of '3+2' type oxidative coupling. The template effect of a Lewis acid must be involved in the coupling as previously indicated.[14] The effect of inorganic additives were not obvious, but somewhat related with applied solvent.

In conclusion, the direct oxidative coupling of tetrapyrromethanes is a convenient method of obtaining high yields of corroles as the single product. In addition, the acid-free condition is advantageous due to the lack of scrambling resulting from the reversible cleavage of starting material. The preferable formation of corrole may be related with minimum macrocyclic angle strain of the intermediate corrinogen. Due to the smaller cavity of corroles, their metal complexes are even more efficient catalysts for various catalytic reactions than those mediated by metalloporphyrins. The synthetic method described here could be an expedient way to the various *meso*-substituted corroles and expanded corroles. The coupling of pentapyrromethanes and other higher oligomers are under extensive investigation accompanying the studies of physico-chemical properties of various metallocorroles.

Supplementary material

Proton NMR spectra, carbon spectra and MS data for compounds **3**, **5** and **7** is available electronically.

Acknowledgements

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11. Typical procedure for the coupling: 5,10,15-triphenyltetrapyrromethane (50 mg, 0.094 mmol) and ammonium chloride (49 mg, 0.94 mmol) was dissolved in propionitrile (47 mL), then DDQ (64 mg, 0.28 mmol) was added

with stirring. The mixture was stirred for 1 h then the solvent was removed in vacuo. The pure corrole was obtained by column chromatography of the remaining dark black solid on neutral alumina (CH_2Cl_2). Fast moving light brown pigment, which is provisionally assigned as a bilatriene derivative, is eluted first, then the desired corrole is eluted as a green pigment. Yield 30 mg (60%); ^{1}H NMR ($CDCl_3$+CD_3OD) δ 7.73–7.81 (m, 9H, Ar–H), 8.15 (d, 2H, Ar(*o*)–H), 8.35 (d, 4H, Ar(*o*)–H), 7.62 (bs, 4H, pyrrole-H), 8.85 (bs, 4H, pyrrole-H); UV–vis. (CH_2Cl_2) λ_{max} ($\varepsilon\times10^3$) 645 (14), 613 (16.5), 575 (20.7), 414 (137.8); FAB-MS calcd for $C_{37}H_{26}N_4$ 526.22, found 527.32 (M^++H).

12. 5,10-Di(*p*-tolyl)-16-oxatripyrromethane (**6**): 2,5-[α-hydroxy-α-(*p*-tolyl)]methylfuran (1.47 g, 4.78 mmol) was dissolved in pyrrole (26.5 mL, 0.32 mol) under N_2 and $BF_3\cdot OEt_2$ (0.61 mL, 4.78 mmol) was added. The mixture was stirred for 30 min at room temperature. The reaction was then quenched by adding aq. NaOH (0.1N, 20 mL). The mixture was extracted with CH_2Cl_2 (30 mL×3) and washed with water (30 mL). The organic layer was dried (Ns_2SO_4) and the solvent and excess pyrrole was removed in vacuo and the remaining brown oil was purified by column chromatography on silica (CH_2Cl_2/hexanes = 2/1). Yield: 1.65 g (84.8%); R_f 0.45 (CH_2Cl_2/hexanes = 2/1); ^{1}H NMR ($CDCl_3$) δ 7.95 (bs, 2H, N–H), 7.11–7.06 (m, 8H, Ar–H), 6.62–6.61 (m, 2H, pyrrole-H), 6.12–6.11 (m, 2H, pyrrole-H), 5.94 (d, J = 2.4 Hz, 2H, furan-H), 5.90–5.87 (m, 2H, pyrrole-H), 5.35 (s, 2H, *meso*-H), 2.33 (s, 6H, Ar–CH_3).
13. '3+2' coupling to give (**7**): 5,10-di(*p*-tolyl)-16-oxatripyrromethane (0.17 g, 0.42 mmol), *p*-tolyldipyrromethane (0.10 g, 0.42 mmol) and ground NH_4Cl (0.23 g, 4.22 mmol) were dissolved in acetonitrile (42.2 mL) in ice bath. Then $BF_3\cdot OEt_2$ (stock solution of 1 mM in acetonitrile, 5.4 μL, 0.43 mmol) was added and the mixture was stirred for 60 min in ice-bath. DDQ (0.19 g, 0.84 mmol) was added and the mixture was stirred for 60 min at room temperature. The mixture was combined with water and extracted with ethyl acetate (50 mL×3). The organic layer was dried (Na_2SO_4) and the solvent was evaporated in vacuo. The resulting solid was purified by column chromatography on silica (CH_2Cl_2/hexanes = 2/1). Recrystallization from methanol afforded pure product. Yield: 52 mg (19.4%); ^{1}H NMR ($CDCl_3$) δ 9.44 (s, 2H), 9.34 (s, 2H), 8.94 (s, 2H), 8.73 (s, 2H), 8.42 (s, 2H), 8.27 and 7.65 (two doublets, J = 6.8 Hz, 4H, Ar–H), 8.07 and 7.60 (two doublets, J = 6.8 Hz, 8H, Ar–H), 2.72 (s, 9H, Ar–CH_3), −3.03 (bs, 3H, N–H); UV–vis (CH_2Cl_2/EtOH = 3/1, base) λ_{max} ($\varepsilon\times10^3$): 444 (187), 457 (99), 556 (12), 597 (10), 636 (9.6), 697 (14); (CH_2Cl_2/EtOH = 3/1, acid) λ_{max} ($\varepsilon\times10^3$): 422 (49), 447 (175), 480 (75), 604 (13), 659 (18), 721 (40); FAB calcd for $C_{44}H_{34}N_4O$ 634.27, found 635.23.
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