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Facile Syntheses of Quater-, Penta-, and Sexipyrroles

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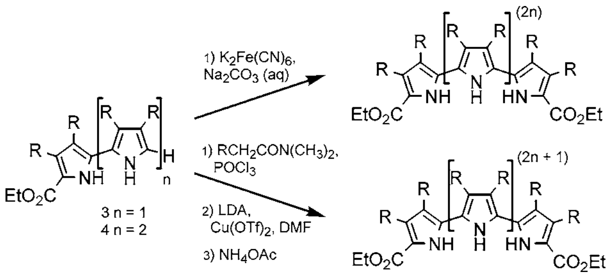
ABSTRACT



α,α-Linked oligopyrroles are attractive precursors for both expanded porphyrin and conducting polymer chemistry. We demonstrate facile methods for synthesizing quater-, penta-, and sexipyrroles from more readily available bi- and terpyrrole intermediates. These products demonstrate stability in their brightly colored oxidized forms, while reduction using borohydride reagents gives the corresponding all-pyrrole oligomers, which oxidize readily in air. The oxidized quater- and sexipyrroles were characterized by single-crystal X-ray diffraction analysis.

α,α-Linked oligopyrroles comprise an important family of compounds that have found applications in materials chemistry as conducting polymers[1] and in synthesis as precursors for porphyrins and related macrocycles.[2] They originally sparked interest as intermediates for pyrrole-containing natural products, including vitamin B_{12}, melanin, and the prodigiosins.[3] Increasingly, however, open-chain oligopyrroles are attracting attention as potential building blocks for new expanded porphyrins.[4] This has stimulated our interest in molecules of this generalized class. With new, synthetically viable approaches to oligopyrroles, it is possible to conceive of further advances in expanded porphyrin chemistry. Historically, bipyrroles, terpyrroles, and quaterpyrroles have been synthesized by performing Vilsmeier condensations and subsequent dehydrogenation of the cyclic imine intermediates.[3] Ullman coupling of iodopyrroles,[5] and the cyclization of pyrrolic 1,4-diketones[6] have also proven popular methods for their synthesis. More recently, procedures based on nickel[7] and palladium[8] chemistry have been

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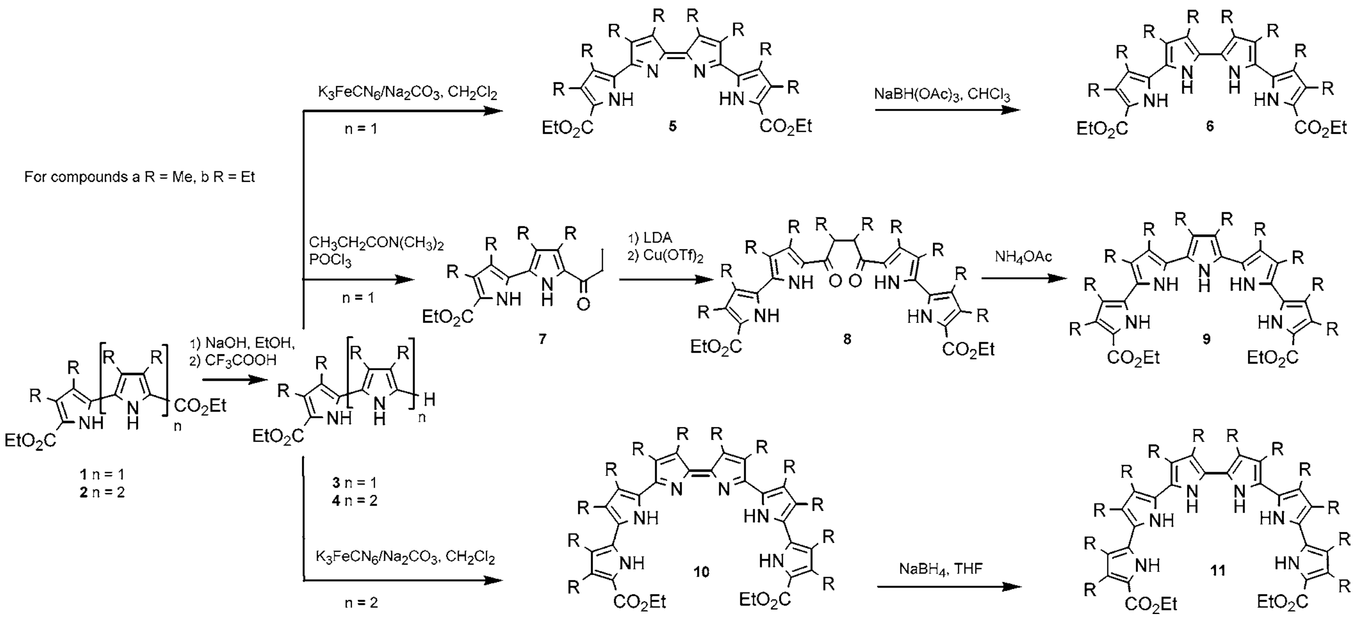
Scheme 1



applied. Unfortunately, all these methodologies require relatively elaborate multistep syntheses.

In 1988, Falk et al.[9] proposed that oxidative coupling could be used to obtain bipyrroles. We found that treatment of an α-free pyrrole with FeCl$_3$ or Na$_2$Cr$_2$O$_7$ yielded an azafulvalene, which, after NaBH$_4$ reduction, furnished the corresponding bipyrrole in moderate yields. The use of similar oxidative couplings with open-chain pyrrole precursors by Sessler et al. has allowed the preparation of new porphyrin analogues, including isoamethyrin,[10] [28]heptaphyrin(1.0.0.1.0.0.0), and [32]octaphyrin(1.0.0.0.1.0.0.0),[11] and more recently a series of cyclo[*n*]pyrroles.[12] Inspired by these developments, we sought to test whether oligopyrroles larger than bipyrroles could be synthesized using an oxidative dimerization strategy. However, we also appreciated that such an approach would only be useful for the preparation of even-numbered oligopyrroles. We were thus keen to explore whether the enolate coupling, 1,4-dicarbonyl cyclization method used to generate terpyrrole as described previously[6,13] could be generalized so as to construct higher-order odd-numbered oligopyrroles. This would provide a second general strategy for obtaining oligopyrroles that would be complementary to methods based on oxidative dimerization.

In this paper, we report the first results of efforts along these lines. Specifically, we describe the synthesis and structural characterization of quater- and sexipyrroles obtained via the oxidative homocoupling of mono-α-free bi- and terpyrroles using potassium ferricyanide, as well as the synthesis of pentapyrrole obtained through enolate coupling, and Knorr-like cyclization of the resulting 1,4-diketones. The relevant chemistry is outlined in Scheme 1.

The precursors for formation of the quaterpyrrole and the sexipyrrole are the mono-α-free bipyrroles **3** and terpyrroles **4**, respectively. To obtain these materials, the known diesters **1** and **2** were subjected to monosaponification[14] and decarboxylation using procedures described previously with good to moderate yields of up to 77 and 54%, respectively.

Compounds **3** and **4** were dissolved in methylene chloride and treated with a solution of potassium ferricyanide dissolved in saturated aqueous sodium bicarbonate. Stirring this biphasic mixture at room temperature afforded the oxidized quaterpyrroles **5** and sexipyrroles **10** in relatively good yields (e.g., 49% for **5b** and 72% for **10a**). The relatively good yields seen in these reactions are thought to reflect, in part, the use of precursors that are fully *β*-substituted and contain only one free α-pyrrolic position. This, we propose, limits the possibility of side reactions such as *β*-pyrrolic coupling. Such unwanted couplings are always seen, even in the case of controlled electropolymerization.[15] Consistent with the clean nature of the present reaction, both sets of products, namely, **5** and **10**, proved to be relatively stable at ambient temperature, even in the presence of air.

Unambiguous proof for the synthesis of quaterpyrrole **5** and sexipyrrole **10** was provided by X-ray diffraction analyses of the octaethyl and dodecamethyl derivatives of these two products (compounds **5b** and **10a**, respectively). To the best of our knowledge, these structures (cf. Figures

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(13) This procedure involves formation of the enolate of the pyrrolic ketone followed by coupling in the presence of Cu(triflate)$_2$ and subsequent treatment with neat ammonium acetate. Here, we have recently found that the use of an ammonium acetate melt results in clean formation of the pyrrole and avoids furan formation.

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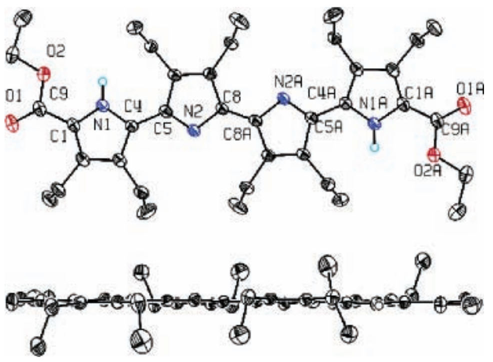


Figure 1. View of **5b** showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. The molecule resides on a crystallographic inversion center at 1/2, 1/2, 1/2. Atoms with labels appended by an "A" are related by 1 − *x*, 1 − *y*, 1 − *z*.

1 and 2) are the first structurally characterized directly linked open-chain oligopyrroles containing more than three pyrrolic subunits.

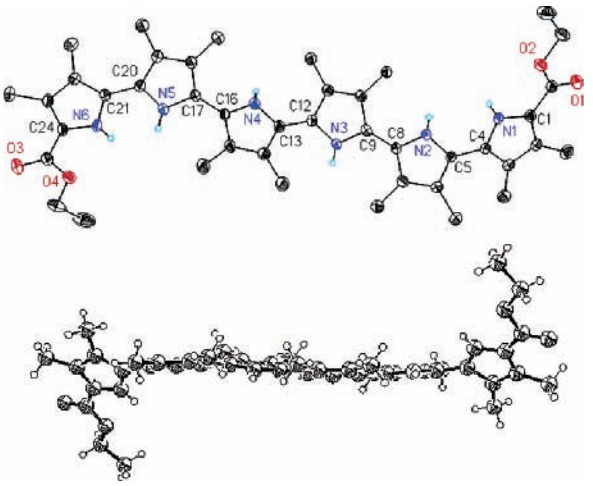


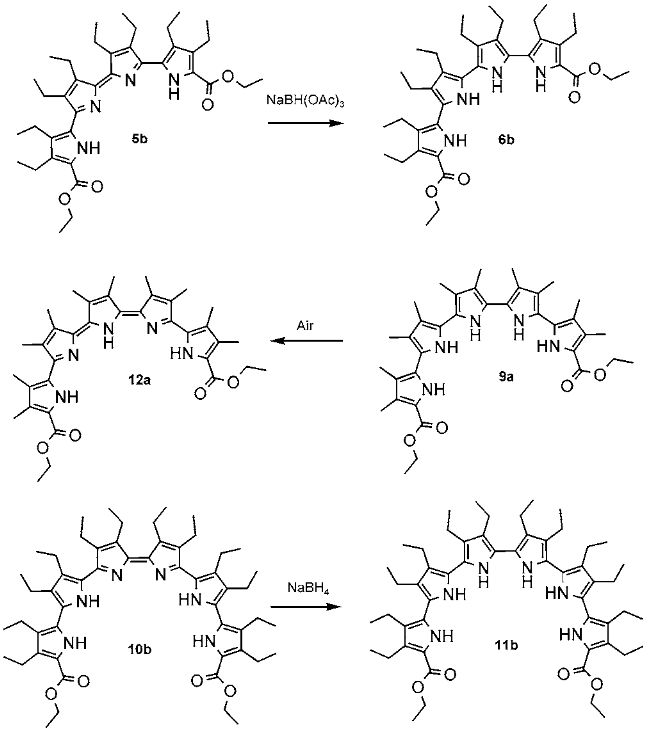
Figure 2. View of the diprotonated form of **10a** showing partial numbering scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. Although omitted for clarity, the molecule crystallized with four molecules of TFA and two trifluoroacetate counterions (as judged by C−O bond lengths).

The solid-state structure of **5b** is characterized by its almost perfect planarity [relevant torsion angles are O2−C9−C1−N1 (0.7°), N1−C4−C5−N2 (3.4°), and N2−C8−C8a−CN2a (0.0°)]. The distance (1.38 Å) between C8 and C8a is consistent with the existence of a double bond between these two linking carbon atoms. In comparison, the bond length of C4−C5 was found to be 1.45 Å.

The sexipyrrole **10a** crystallized as a dication with the two central pyrroles protonated and two trifluoroacetate counteranions. Four neutral trifluoroacetic acid molecules were also found in the solid state. Unlike **5b**, the pyrrole units in **10a** are slightly tilted relative to one another [relevant torsional angles are N1−C4−C5−N2 (42.0°), N2−C8−C9−N3 (0.3°), N3−C12−C13−N4 (4.7°), N4−C16−C17−N5 (15.7°), and N5−C20−C21−N6 (39.0°)]; this is especially true in the case of the terminal pyrrole moieties, which are twisted out of the RMS plane by about 40°. The distance between C12 and C13 (the two middle pyrroles) is 1.39 Å, which is considerably shorter than the average distance of 1.45 Å between the outer pyrrole units. This is in accord with the ^{1}H NMR spectroscopic findings and the UV−vis data and is consistent with the proposal that compound **10a** is an oxidized sexipyrrole. In this case, the double-bond character is distributed somewhat more evenly over the bonds between pyrroles 3 and 4 and between pyrroles 5 and 6. The effects of oxidation thus appear to be less localized in sexipyrrole **10a** than in the corresponding quaterpyrrole, **5b**.

Pentapyrrole **9a** was synthesized using a modified 1,4-diketone cyclization strategy first described for the synthesis of terpyrrole by LeGoff[6a] and then subsequently optimized and employed by our group.[6b,13] Thus, bipyrrole **3** was first acylated using Vilsmier conditions with dimethyl propionamide to give the ketone **7**. This differentially functionalized system was then treated with lithium diisopropylamide to form the corresponding lithium enolate. Subsequent addition of copper(II) triflate then effected C−C coupling, generating the 1,4-diketone **8** in 26% yield. Although this latter compound is obtained as a mixture of isomers, treatment with neat ammonium acetate at reflux leads to the formation of pentapyrrole **9a** in 82% yield. This material, although it could be isolated, is unstable and undergoes oxidation to the

Scheme 2



corresponding oxidized pentapyrrole **12a** when exposed to air. At ambient temperature, this process is essentially complete within 12 h.

It is interesting to note that all three of the higher order oligopyrroles described in this paper are more stable in their oxidized forms. These oxidized forms are brightly colored. This stands in contrast to the reduced species, **6**, **9**, and **11** (Scheme 2), which are colorless. The strong color seen for **5**, **12**, and **10** is consistent with the presence of an extended conjugation pathway. In accord with such a conclusion, a bathochromic shift in the absorption maximum was seen as the size of the oligopyrrole was allowed to increase. For instance, the absorption maximum (CH_2Cl_2) was seen to shift from 502 (37 900) to 625 (23 100) to 649 (18 700) nm (ϵ), in the case of quaterpyrrole **5b**, pentapyrrole **12a**, and sexipyrrole **10b**, respectively.

While the oxidized forms are more stable, it is also important to appreciate that the corresponding reduced forms could be obtained, either directly as in the case of **9**, or by treatment of **5** with $NaBH(OAc)_3$ and **10** with $NaBH_4$, giving **6** and **11**, respectively. Unfortunately, the stability of the resulting species was generally sufficient only to allow for characterization via the most basic of spectroscopic means. Nonetheless, the fact that these reduced species can be obtained “in situ” allows for their consideration as possible precursors for use in the synthesis of more elaborated products, including new expanded porphyrins. Currently, studies of reduced species **6**, **9**, and **11** as “building blocks” for this purpose are in progress, as are studies targeting the use of the corresponding oxidized oligopyrroles **5**, **12**, and **10**.

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Supporting Information Available: Experimental procedures and full spectroscopic data, including crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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