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Synthesis and characterization of a novel three-dimensional oligopyrrole: tris(bipyrro)methane†

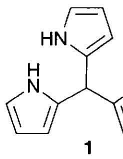
Jonathan L. Sessler,* Michael C. Hoehner, Darren W. Johnson, Andreas Gebauer and Vincent Lynch

Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712, USA

The synthesis, characterization and X-ray structure of the novel three dimensional tris(bipyrro)methane 3 is reported; this species is predisposed to self-assemble into a cryptand-like dimer in both organic solution and the solid state.

Compounds containing three pyrrole units bonded *via* the α-position to an sp^3 hybridized carbon have been known for at least 80 years.[1] Dubbed tripyrrylmethanes (*e.g.* **1**) Corwin and co-workers[2] proposed these species as intermediates in the formation of dipyrromethenes after the initial work of Piloty, Krannich and Will.[1a] They found that the condensation of an α-free pyrrole with a 2-formylpyrrole could give rise to several different dipyrromethanes, presumably through an intermediary tripyrrylmethane, which was never characterized beyond its elemental composition and melting point. The finding that the bacterial pigment prodigiosin,[3] originally proposed as being a tripyrrylmethane,[4] was actually a pyrryldipyrromethene (*e.g.* **2**) further complicates this issue. On the other hand, Wang and Bruce[5] have recently put forward NMR spectral evidence that supports the conclusion that three pyrroles are bound to a sp^3 hybridized carbon in species **1** and are connected, presumably, *via* the respective α-positions. Inspired by these historical findings, we decided to explore whether it might not be possible to stabilize a tripyrrylmethane-like species using higher order pyrrolic precursors. Here we demonstrate that this can in fact be done; we report the synthesis and characterization of the tris(bipyrro)methane species **3** and **8** and the single crystal X-ray structure of the first of these 'tripod'-type oligopyrroles.

Scheme 1 illustrates the synthesis of the tripod **3**. The sequence commences with the monosaponification of the known, symmetrical 2,2′-bipyrrole **4**, obtained *via* standard literature procedures.[6] This was done by heating **4** at reflux in a mixture of sodium hydroxide dissolved in benzyl alcohol and water. The differing solubilities of the starting materials and products allows for the facile separation and purification of the crude product **5**. In fact, this monosodium salt is routinely prepared in yields on the order of 40%. Decarboxylation of **5**, effected by treatment with TFA, generates the mono α-free bipyrrole **6** in nearly quantitative yields after flash chromatographic purification over silica gel. Some portion of this intermediate was then subjected to Clezy formylation.[7] This gives the monoformyl bipyrrole **7** in yields of about 90%. From the acid-catalysed condensation of 1 equiv. of **7** with 2 equiv. of **6** in ethanol, the target tripod **3** is isolated in yields of up to 60%. Compound **8** was prepared in a similar manner.‡ In the case of compound **3**, purification was realized by simply filtering the crude mixture (**3** is insoluble in ethanol). Purification of **8**, being soluble in ethanol, was effected *via* chromatographic means (silica gel, dichloromethane eluent).§



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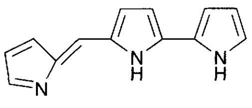

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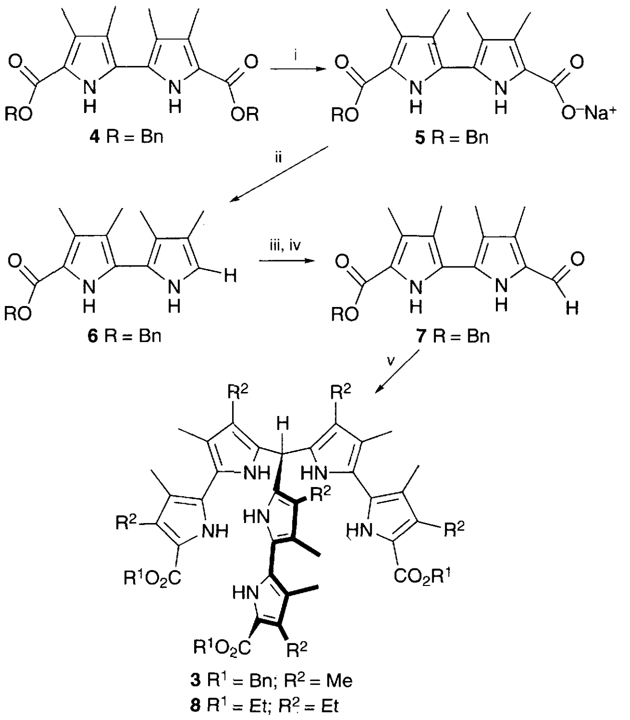
The novel tripod **3** was first characterized *via* ^1H NMR spectroscopy. Here, the most distinctive feature was found to be the AB pattern displayed by the methylene protons of the benzyl ester. Such a pattern is anomalous in our experience with bipyrroles[6] and tetrapyrroles[8] and leads us to suggest that these methylene protons are held in a diastereotopic environment. Heating to 60 °C effects coalescence of these signals and gives rise, in turn, to the conclusion that the stereodifferentiating environment of the benzyl methylene protons is well-maintained at room temperature.

A single crystal X-ray structure study of **3** provided support for the above inferences.¶ In the solid state, this compound exists as a dimer (Fig. 1) wherein each individual monomer possesses either a right or left handed twist (identical twists pertain for each subunit of the dimer). This shape is maintained in the solid state by twelve hydrogen bonds involving the carbonyl oxygens of the benzyl ester and the N–H protons of the pyrroles. Each carbonyl oxygen on one molecule is within H-bonding distance of two pyrroles on the adjacent tripod. One of these contacts exists between the carbonyl and one of the outermost pyrroles, and the other contact involves an interior pyrrole on a neighbouring arm of the tripod. The N···O H-bonding contacts range from 2.85(2)–3.11(2) Å, with N–H···O bond angles ranging from 134(1) to 159(1)°. The H···O···H angles range from 100.7(6) to 113.0(6)°.

This diastereogenic dimer appears to be retained under a range of solution phase conditions. For instance, an ion peak



Scheme 1 *Reagents and conditions*: i, NaOH, ROH; ii, TFA; iii, TFA, $CH(OEt)_3$; iv, H_2O; v, **6** (2 equiv.), EtOH, HCl (cat.)

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corresponding to the dimer was seen in the FAB mass spectrum of **3**. Furthermore, a proton NMR spectrum acquired in a 1 : 1 $CD_3OD–CDCl_3$ solution proved identical to that recorded in pure $CDCl_3$. In particular, none of the peaks appeared shifted to either higher or lower field. Also, all the N–H signals remained well-resolved and clear. The further addition of Me_2SO to this mixed solvent sample (*ca.* 5% by volume) also failed to engender changes in the ^1H NMR spectrum. This leads us to conclude that the dimeric form of **3** is stable in protic solvents and that dimerization not only 'protects' the pyrrolic hydrogens from deuterium exchange but also imparts a twist-like structure to the ensemble that mirrors the one seen in the solid state.||

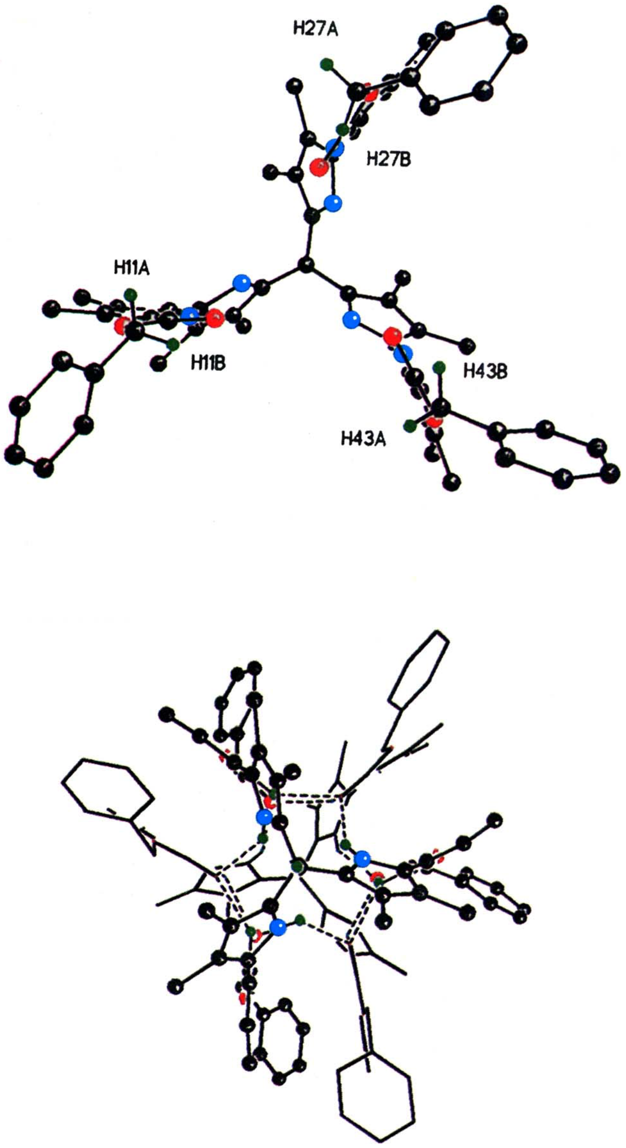

Fig. 1 Two views of the X-ray structure of tripod **3**. The top view shows the diastereotopic benzyl protons [designated as H(11a and b), H(27a and b) and H(43a and b), respectively]. The remaining hydrogen atoms have been omitted for clarity. The lower view shows the dimer formed between two molecules of **3** in the solid state, with one molecule of the dimer represented as a line drawing for clarity. Dashed lines indicate a H-bonding interaction. Each carbonyl oxygen atom of one molecule is held within H-bonding distance of two pyrrolic N–H groups of the second molecule. Carbon atoms are shown in black, oxygen atoms in red, nitrogen atoms in dark blue and hydrogen atoms in green.

The exciting result that compound **3** is stabilized as a hydrogen bonded dimer interests us from several perspectives. First, it leads us to propose that species such as **3** could serve as receptors for various other non-tripod substrates provided these latter act as good hydrogen bond donors and/or acceptors. Second, this stabilization illustrates how polypyrrole frameworks that are intrinsically non-planar can potentially be made to be non-racemic by virtue of appropriate self-organization processes. Finally, the very fact that **3** dimerizes provides a non-covalent 'hint' that it might be possible to fuse building blocks such as **3** together *via* prudently chosen synthetic connections. This would provide three-dimensional cryptand-like materials wherein oligopyrrolic entities act as the key bridging subunits.

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Footnotes

† A multimedia version of this article will be temporarily available from the CLIC page http://chemistry.rsc.org/rsc/clic.htm

‡ The systematic names for compounds **3** and **8** are tris(benzyl 3,3′,4,4′-tetramethyl-2,2′-bipyrrole-5,5′-carboxylate)methane and tris(ethyl 4,4′-diethyl-3,3′-dimethyl-2,2′-bipyrrole-5,5′-carboxylate)methane, respectively.

§ Satisfactory elemental analyses, spectroscopic data and high resolution mass spectroscopic data were obtained for all new compounds.

¶ *Crystal data* for **3**. Colourless plates were grown from a reddish coloured $CHCl_3$–ethanol solution of **3**. Orthorhombic crystals, space group *Pbca*, $Z = 16$, cell dimensions: $a = 23.833(5)$, $b = 29.771(8)$, 30.476(11) Å, $V = 21624(10)$ Å^3, $\rho_{calc} = 1.20$ g cm^{-3}, $F(000) = 8320$. A total of 14 126 unique reflections were measured using ω scans on a Siemens P3 diffractometer utilizing graphite monochromatized Mo-Kα radiation ($\lambda = 0.71073$ Å) at −90 °C. In the solid state **3** exists as a H-bound dimer, with the arms of one tripod molecule interleaved between the arms of the second tripod. The structure was refined on F^2 to an $R_W = 0.242$, with a conventional $R = 0.157$, and a goodness of fit = 1.112 for 1274 parameters.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/186.

|| ^1H NMR spectroscopic studies were performed using the lanthanide shift reagent Eu-FOD. Adding this reagent failed to produce any significant peak shifts. This is consistent with the carbonyl oxygen being shielded from the shift reagent by, *e.g.*, steric hindrance. These experiments thus provide further support for the proposed dimer.

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