Synthesis and characterization of monosubstituted hexapyrrolylbenzene derivatives

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Abstract
Six new monosubstituted hexapyrrolylbenzene derivatives 3a–c, 4a–c have been synthesized based on the multiple nucleophilic substitution reaction of appropriate 1-pentafluorophenyl-1H-pyrrole derivatives 1a–c, 2a–c with the sodium salt of pyrrole in dry DMF.

Keywords: Propeller-shaped hexapyrrolylbenzenes, S_NAr reaction, \( \pi \)-conjugation

Introduction
It is well known that oligomers and polymers with extended \( \pi \)-conjugation serve as important active components of electronic and opto-electronic devices. Currently a growing interest has been directed towards the design of molecular wires and rods, since such structures may serve as building blocks for nanoscale chemical entities that are geometrically and dimensionally confined. They may act as connectors in molecular and supramolecular electronic and photonic devices. The interest in chemically functionalized conductive materials continues to expand and currently encompasses electronic and opto-electronic devices, energy storage systems, bio-electrochemical sensors etc. Detecting single molecule properties, however, leads to completely new functional concept, and benzene-based compounds are particularly well-suited subjects for this developing technology. In these compounds is a synergism through which spectroscopic techniques are improved and in the course greater understanding of structure-property relationships is gained. The study of stereochemistry of molecules is a relatively mature field.

Highly symmetrical, propeller-shaped, hexasubstituted benzenes have received considerable interest due to their intriguing properties as sterically congested polycyclic aromatic compounds. Any aromaticity discussion will soon rise the awareness that benzene chemistry is
a starting point for polymer chemistry and in turn, that π-conjugated polymers contribute tremendously to theories of π-bonding structures. While the electronic design of conjugated polymers will appear to be an important concern below, it should be mentioned that benzene-based polymers should be looked at not only from the point of view of extended π-conjugation. Other important aspects of introducing benzene-based units into polymers are the high chemical and thermal stability of the building block and their easy chemical functionalization with all of the additional properties brought in by adding an appropriate group.

Pyrroles are very often used as a conducting interface because the substitution chemistry of the monomer is well defined and chemical and electrochemical polymerization is easy and the resulting polymers form robust and even films.

Monosubstituted hexapyrrolylbenzenes are unknown. Electrophilic substitution reactions of hexapyrrolylbenzene such as Vilsmeier-Haack formylation and electrophilic acylation failed to lead to the formation of monosubstituted derivatives 3a–c, 4a–c.

Results and Discussion

The 2-substituted products 1a–c could be selectively converted with high yields into the 3-substituted products 2a–c by treatment with trifluoromethanesulphonic acid. We now tried new synthetic route to 3a–c, 4a–c starting from monosubstituted derivatives of 1-pentafluorophenyl-1H-pyrrole 1a–c and 2a–c by SNAr reaction with pyrrole sodium salt. The one-pot synthesis of compounds 3a–c, 4a–c is based on the multiple nucleophilic substitution of the pentafluorophenyl group with 7.0 equivalents of pyrrolyl sodium salt in DMF (Scheme 1).

Since it is known that the rate of an SNAr reaction increases by the use of a more polar aprotic solvent, we performed the reaction of sodium salt of pyrrole with 1a-c and 2a-c in dry DMF at ambient temperature.

![Scheme 1](image-url)
Mono α-derivatives 1a–c of hexapyrrolylbenzene afforded of requested products 3a–c only in low yields. In our opinion this is due to steric hindrance by the substituent in α-position of pyrrole. This suggestion was confirmed by S_N Ar of mono β-derivative 2a–c, which gave the corresponding 4a–c in much higher yields. In both of cases the products were separated by column chromatography. Physical and chemical properties of 3a–c and 4a–c compounds are collected in Table 1.

Table 1. Selected physical data and yields of 3a–c and 4a–c

<table>
<thead>
<tr>
<th>Product</th>
<th>R</th>
<th>Eluant^a</th>
<th>R_f</th>
<th>mp [°C]</th>
<th>color</th>
<th>Yield^b [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>toluene</td>
<td>0.07</td>
<td>300–303</td>
<td>colorless</td>
<td>7</td>
</tr>
<tr>
<td>3b</td>
<td>Me</td>
<td>toluene</td>
<td>0.11</td>
<td>253–254</td>
<td>yellow</td>
<td>6</td>
</tr>
<tr>
<td>3c</td>
<td>Et</td>
<td>toluene</td>
<td>0.11</td>
<td>208–212</td>
<td>yellow</td>
<td>8</td>
</tr>
<tr>
<td>4a</td>
<td>H</td>
<td>toluene/EtOAc 20:1</td>
<td>0.31</td>
<td>209–215</td>
<td>light yellow</td>
<td>39</td>
</tr>
<tr>
<td>4b</td>
<td>Me</td>
<td>toluene/EtOAc 20:1</td>
<td>0.13</td>
<td>271–272</td>
<td>light yellow</td>
<td>55</td>
</tr>
<tr>
<td>4c</td>
<td>Et</td>
<td>toluene/EtOAc 20:1</td>
<td>0.21</td>
<td>239–240</td>
<td>light yellow</td>
<td>47</td>
</tr>
</tbody>
</table>

^a Eluant used for column chromatography. ^b Isolated yield after column chromatography.

We were not able to identify any by-products due to the difficult separation of the crude S_N Ar reaction mixtures. For confirmation of any atom of fluorine appears in desired products 3a–c and 4a–c, ^19_F NMR spectroscopy was utilized.

Conclusions

We have presented a facile and convenient synthetic method for the synthesis of monosubstituted hexapyrrolylbenzenes. Due to their sterically congested structures they may be regarded as building blocks for larger π-conjugated systems possessing propeller-shaped molecules with interesting optoelectronic properties.

Products 3a–c and 4a–c were synthesized in order to study their conductive properties. We observed interesting results which will published as part of a full paper.

Acknowledgments

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Experimental Section

**General Procedures.** Derivatives 1a–c and 2a–c were prepared according to the literature. A 60% dispersion of sodium hydride in mineral oil was used after removal of mineral oils with hexane. DMF was distilled at reduced pressure and kept in a dark bottle over 4 Å molecular sieves. Pyrrole was used after distillation under reduced pressure and kept in a freezer. Thin layer chromatography (TLC) was carried out on silica gel 60 F254 (Merck) and ALUGRAM® SIL UV (Macherey-Nagel). All products were separated by column chromatography packed with silica gel 60 (0.040–0.063 mm, Merck). The $^1$H and $^{13}$C NMR spectra (DMSO-$d_6$ solutions) were recorded either with a Varian VX-R-300 spectrometer (operating frequencies 295.0 MHz for $^1$H and 75.12 MHz for $^{13}$C) or with a Bruker DRX-500 instrument (operating frequencies 500.13 MHz for $^1$H and 125.76 MHz for $^{13}$C). Mass spectra (AEI) were measured with a GC/MS 25 RFA instrument (Kratos Analytical, Manchester) equipped with a direct inlet system at 70 eV, trap current 100 µA at temperature of the ion source 200 °C. IR spectra (KBr pellets) were measured on spectrometer PU 9800 FTIR and Impact 400 (Nicolet). Melting points were measured on a Kofler block.

1-[2,3,4,5,6-Penta($^{1}$H-pyrrol-1-yl)phenyl]-$^{1}$H-pyrrole-2-carbaldehyde (3a). **Typical procedure**

In a 25 mL two-necked flask under an argon atmosphere the mixture of NaH (1.03 g, 27.0 mmol) and DMF (30 mL) was stirred, and pyrrole (1.80 g, 27.0 mmol) was added through a dropping funnel. After the liberation of H$_2$ had ceased the reaction mixture was stirred for 130 min. and the solution of 1-penta($^{1}$H-pyrrol-1-yl)phenyl-$^{1}$H-pyrrole-2-carbaldehyde (1a; 1.0 g, 3.83 mmol) in DMF (10 mL) was added dropwise within 15 min. The reaction mixture was stirred for 24 h before it was poured into iced water (100 mL). The colorless precipitate formed was filtered off, washed with water (5x30 mL) and air dried overnight. Separation by column chromatography on silica gel (toluene) afforded the colorless product 3a. $^1$H NMR (300 MHz, DMSO-$d_6$): δ 9.23 (1H, s), 7.04 (1H, s), 6.89 (1H, s), 6.31–6.21 (10H, m), 5.90–5.86 (11H, m). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 178.8, 135.2, 135.0, 134.6, 134.1, 132.8, 132.6, 123.4, 121.4, 121.3, 111.1, 109.6, 109.5, 109.2. MS: m/z (%) 496 (100) [M$^+$], 469 (17) [M–CHO], 404 (11) [M–C$_4$H$_3$NCHO], 77 (6) [C$_6$H$_5$]. IR (KBr): ~ν 3150, 3100, 1670, 1550, 1530, 1510, 1450 cm$^{-1}$. Anal. Calcd for C$_{31}$H$_{24}$N$_6$O (496.20): C, 74.98; H, 4.87; N, 16.92. Found: C, 74.81; H, 4.85; N, 16.77.

Products 3b–c and 4a–c were prepared according to this procedure.

Selected physical data and yields: Table 1.

1-[2,3,4,5,6-Penta($^{1}$H-pyrrol-1-yl)phenyl]-$^{1}$H-pyrrole-2-yl]ethanone (3b). $^1$H NMR (300 MHz, DMSO-$d_6$): δ 6.90–6.88 (2H, m), 6.32 (2H, m), 6.26 (4H, m), 6.19 (4H, m), 6.10 (1H, dd, J = 3.6, 3.0 Hz), 5.92–5.89 (6H, m), 5.86 (4H, m), 2.07 (3H, s). $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ 178.2, 135.5, 134.7, 134.5, 134.4, 132.2, 130.9, 121.4, 121.3, 111.9, 110.1, 109.5, 109.1, 26.4. MS: m/z (%) 510 (100) [M$^+$], 494 (7) [M–CH$_4$], 466 (26) [M–COCH$_3$], 77 (7) [C$_6$H$_5$]. IR

1-[1-(2,3,4,5,6-Penta(1H-pyrrol-1-yl)phenyl)]-1H-pyrrolyl-2-y]propan-1-one (3c). ¹H NMR: (300 MHz, DMSO-d₆): δ 6.75–6.76 (2H, m), 6.20 (2H, t, J = 2.1 Hz, 3.1 Hz), 6.14 (4H, m), 6.04–6.05 (4H, m), 5.96 (1H, dd, J = 3.6 Hz, 3.0 Hz), 5.79–5.77 (10H, m), 2.32 (2H, q, J = 7.2 Hz), 0.76 (3H, t, J = 7.2 Hz). ¹³C NMR (75 MHz, DMSO-d₆): δ 190.7, 135.6, 134.8, 134.5, 134.4, 131.9, 130.7, 121.4, 121.3, 119.5, 118.8, 110.1, 110.9, 109.2, 31.1, 8.2. MS: m/z (%): 524 (100) [M⁺], 495 (13) [M–CH₃], 467 (37) [M–COCH₂CH₃], 77 (4) [C₆H₅]. IR (KBr): ν 3130, 3110, 2980, 2890, 1665, 1540, 1520, 1530, 1440 cm⁻¹. Anal. Calcd. for C₃₃H₂₈N₆O (524.20): C, 75.55; H, 5.38; N, 16.02. Found: C, 75.30; H, 5.18; N, 16.12.

1-[2,3,4,5,6-Penta(1H-pyrrol-1-yl)phenyl]-1H-pyrrolyl-3-carbaldehyde (4a). ¹H NMR (500 MHz, DMSO-d₆): δ 9.47 (1H, s), 7.17 (1H, broad s), 6.34–6.37 (5H, m), 6.26–6.29 (7H, m), 5.88–5.95 (10H, m). ¹³C NMR (125 MHz, DMSO-d₆): δ 185.2, 135.3, 135.0, 134.8, 133.9, 131.8, 127.0, 125.3, 121.8, 121.5, 121.4, 110.2, 109.8, 109.7, 107.4. MS: m/z (%): 496 (100) [M⁺], 469 (10) [M–CHO], 401 (50) [M–C₆H₅NCHO], 77 (10) [C₆H₅]. IR (KBr): ν 3160, 3150, 1650, 1550, 1480, 1520, 1500 cm⁻¹. Anal. Calcd. for C₃₁H₂₉N₆O (496.20): C, 74.98; H, 4.87; N, 16.92. Found: C, 74.83; H, 4.83; N, 16.80.

1-[1-(2,3,4,5,6-Penta(1H-pyrrol-1-yl)phenyl)-1H-pyrrolyl-3-yl]ethanone (4b). ¹H NMR (500 MHz, DMSO-d₆): δ 7.01 (1H, dd, J = 1.7, 1.7 Hz), 6.35–6.38 (5H, m), 6.26–6.30 (7H, m), 5.94–5.96 (4H, m), 5.92–5.94 (6H, m), 2.07 (3H, s). ¹³C NMR (125 MHz, DMSO-d₆): δ 191.8, 135.0, 134.9, 134.5, 134.0, 127.8, 126.3, 123.7, 121.7, 121.4, 121.3, 109.74, 109.69, 109.63, 108.8, 26.8. MS: m/z (%): 510 (100) [M⁺], 495 (15) [M–CH₃], 466 (8) [M–COCH₃], 77 (7) [C₆H₅]. IR (KBr): ν 3160, 3150, 2950, 2810, 1650, 1600, 1530, 1500, 1450 cm⁻¹. Anal. Calcd. for C₃₃H₂₈N₆O (510.20): C, 75.27; H, 5.13; N, 16.46. Found: C, 75.22; H, 5.15; N, 16.70.

1-[1-(2,3,4,5,6-Penta(1H-pyrrol-1-yl)phenyl)-1H-pyrrolyl-3-yl]propan-1-one (4c). ¹H NMR (500 MHz, DMSO-d₆): δ 7.01 (1H, dd, J = 1.9, 1.9 Hz), 6.33–6.36 (5H, m), 6.25–6.29 (7H, m), 5.92–5.95 (4H, m), 5.90–5.92 (6H, m), 2.45 (2H, q, J = 7.2 Hz), 0.99 (3H, t, J = 7.2 Hz). ¹³C NMR (125 MHz, DMSO-d₆): δ 195.2, 135.1, 134.9, 134.5, 134.0, 127.3, 125.6, 123.7, 121.7, 121.5, 121.4, 109.74, 109.68, 108.8, 31.9, 8.7. MS: m/z (%): 524 (100) [M⁺], 495 (44) [M–CH₂CH₃], 467 (8) [M–COCH₂CH₃], 77 (5) [C₆H₅]. IR (KBr): ν 3130, 3100, 3000, 2950, 1670, 1530, 1520, 1500, 1420 cm⁻¹. Anal. Calcd. for C₃₃H₂₈N₆O (524.20): C, 75.55; H, 5.38; N, 16.02. Found: C, 75.33; H, 5.20; N, 16.10.

References