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Direct Synthesis of Aryldipyrromethanes

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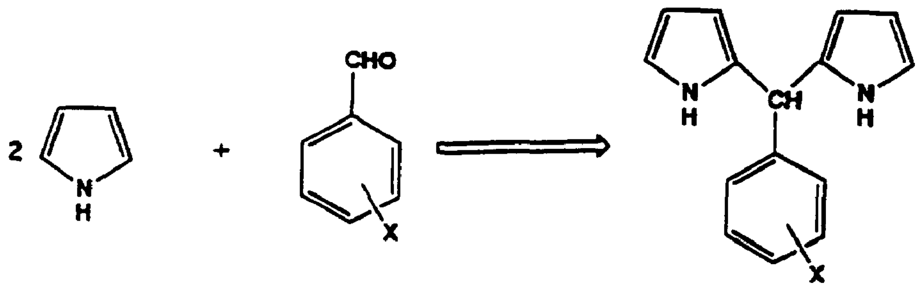
Abstract: The synthesis of aryldipyrromethanes from the direct condensation of pyrroles with aromatic aldehydes is described. Yields are improved with strong electronegative substituents on the aromatic aldehyde.

The development of pyrrole chemistry has largely been associated with the synthesis of natural products. However, with the discovery of the unique properties of organic polymers, an increased range of pyrrole-based monomers are being sought that will create polymers with improved characteristics. We wish to design polymer supports with a range of functionalities in order to immobilise specific receptors for chemical sensor applications and aryldipyrromethanes provide a basic structure for a series of compounds incorporating various functional groups which can be polymerised.

Syntheses of aryldipyrromethanes have thus far been indirect, requiring either the elimination of a protecting ester group from the pyrrole segment[1,2] or through the formation of a Grignard reagent.[3] The reaction of pyrrole derivatives with a variety of aromatic and heterocyclic aldehydes has been described[4-6] but the major products appear to be azafulvenes. The formation of dipyrromethanes in acetic acid has been reported when the starting 1H-pyrroles are strongly basic or the aldehyde component carries an electron-donating substituent[6] but the earlier work by Treibs *et al.*[5] demonstrates that the formation of dipyrromethanes is unfavourable in the presence of acids. The direct condensation of aromatic aldehydes with unsubstituted pyrrole under a variety of conditions (refluxing in acetic acid[7,8], in the presence of a Lewis acid[9] or with microwave irradiation[10]) has resulted in tetraaryl porphyrins. Therefore, further work is necessary to determine the experimental conditions required to obtain desired products from pyrrole condensations.



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X=H(a);4-Me(b);4-NMe$_2$(c);
4-Cl(d);4-CN(e);4-NO$_2$(f);2-NO$_2$(g)

In the general procedure, a solution of pyrrole (5g) in acetic acid (20 mL) was cooled in an ice-bath. The appropriate aldehyde (0.5 molar equivalents), dissolved in a solution of THF and acetic acid (9:1), was added dropwise to the pyrrole over a period of 1 hour. After the addition, the mixture was stirred in the ice-bath for 30 min and then for an additional 2 hours at room temperature. The mixture was poured over ice-water (250 mL) with stirring and the dark-coloured suspension was then extracted with dichloromethane. The organic layer was washed thoroughly with sodium bicarbonate (1% aq.), then with water and finally dried over sodium sulfate. Upon removing the solvent with a rotary evaporator, a dark-coloured solid is obtained (70-75% yield). A purity check of this material by TLC in toluene-ethyl acetate (9:1) shows three spots; the top one is due to traces of unreacted aldehyde, the middle one from the desired aryldipyrromethane and the lower one results from oligomeric byproducts. Purification of the crude product was effected by column chromatography using silica gel with either pure toluene or toluene-ethyl acetate (9:1) as the eluent. The middle fraction was concentrated to recover the light-coloured aryldipyrromethane in each case. In some instances, the middle fraction had to be rechromatographed to eliminate traces of larger oligomeric products from the dipyrromethanes.

As the aryldipyrromethanes undergo slow polymerization upon standing at room temperature, elemental analyses were not attempted. Characterisation of freshly-prepared samples by low/high resolution mass spectrometry and NMR[11] confirmed that the desired products were obtained and indicated no discernable impurities.

Table 1: Yields and Analyses of Aryldipyrromethanes

Compound	Substituent	Yield (%)	Melting Point	High Resolution M.S. Molecular Peak (Deviation from Calculated M.W.)
3a	H	20	liquid*	222.1162 (2.3 ppm)
3b	4-Me	25	75°C	236.1316 (1.2 ppm)
3c	4-NMe_2	15-20	124°C	265.1579 (0.2 ppm)
3d	4-Cl	35	112°C	256.0758 (-3.7 ppm)
3e	4-CN	45	161°C	247.1107 (-0.8 ppm)
3f	4-NO_2	35	148°C	267.0995 (-4.7 ppm)
3g	2-NO_2	35	liquid*	267.1003 (-2.0 ppm)

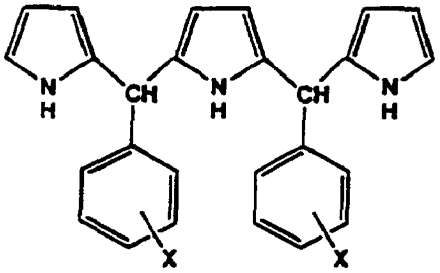
*decomposes above 150°C

For all the products except **3g**, the base peak in the mass spectra arises from the molecular ion (electron impact source used). With **3g** there is still a significant molecular ion peak (33%) but due to the *ortho*-nitro substituent, the base peak originates from the ion after loss of water and NO. FTIR of the aryldipyrromethanes **3a-g** show a strong band centered around 3415 cm^{-1} from the imino group. Peaks of medium intensity near 1117, 1093 and 1030 cm^{-1} match those values reported for the in-plane deformation of 2-substituted pyrroles.

The series of compounds also shows strong absorption bands between 1600 and 1630 cm^{-1} from C-C ring deformation and near 1500 cm^{-1} arising from the C-phenyl stretch.

A selection of aldehydes was chosen so as to permit a study of the electronic effect of the substituents on the reaction. The results indicate that higher yields of aryldipyrromethanes were obtained in the presence of strong electronegative substituents. It has been previously reported that electron-withdrawing groups on the pyrrole ring provide a stabilising influence while electron-donating groups on the aromatic ring, such as dimethylamino, favour the formation of azafulvene-type structures.[6] Under the conditions described here, no azafulvene was isolated from any of the reactions.

The major byproducts obtained from the condensation of pyrrole with aromatic aldehydes are the oligomers 4 and 5, deduced from mass spectrometric analysis. The two products are obtained in significantly higher yields (30%) with 4-dimethylaminobenzaldehyde, which was the reagent leading to the lowest yield of dipyrromethane. With an increase in the molar ratio of 4-dimethylaminobenzaldehyde (to 1 mole per mole of pyrrole), 4 and 5 become the major products and there is a sharp decrease in the yield of 3c. When pyrrole was used in large excess (4 moles per mole of the aldehyde), the combined yield of 3c, 4 and 5 was less than 10%. Therefore, controlling the degree of condensation requires careful adjustment of the concentrations of the reactants.



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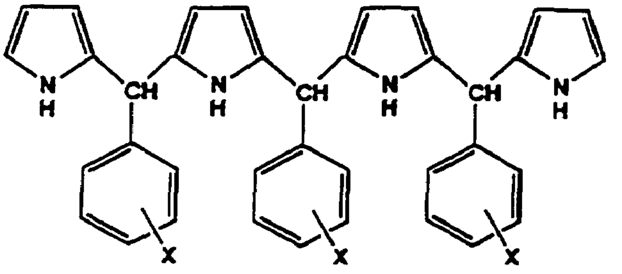

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The procedure described here allows one to synthesise a series of pyrrole-based monomers possessing an assortment of substituents on the aromatic aldehyde. These compounds will allow a study of the changes in the properties of the resulting polymers as the electronic states are altered. The electrochemical oxidation of the aryldipyrromethanes 3a-g will be the subject of a separate publication.

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11. ^{13}C NMR chemical shift data: **3a:** 43.67 (methine), 129.47, 107.00, 107.96, 117.03 (pyrrole carbons), 141.97, 128.16, 128.08, 132.00 (aldehyde carbons); **3b:** 43.35 (methine), 128.11, 106.99, 108.14, 117.04 (pyrrole carbons), 139.02, 128.92, 136.28 (aldehyde carbons); **3c:** 42.94 (methine), 132.71, 106.67, 108.00, 116.69 (pyrrole carbons), 133.40, 112.63, 128.91, 149.40 (aldehyde carbons), 40.60 (amino carbons); **3d:** 43.22 (methine), 131.76, 107.31, 108.35, 117.37 (pyrrole carbons), 132.52, 131.76, 128.50 140.21 (aldehyde carbons); **3e:** 43.88 (methine), 130.76, 107.81, 108.43, 117.86 (pyrrole carbons), 147.71, 129.08, 132.12, 107.54 (aldehyde carbons), 118.72 (cyano); **3f:** 43.78 (methine), 130.77, 107.80, 108.78, 117.95 (pyrrole carbons), 149.63, 123.79, 129.22, 146.89 (aldehyde carbons); **3g:** 38.89 (methine), 130.77, 107.38,108.56, 117.65 (pyrrole carbons), 148.78, 124.49, 130.95, 137.24, 132.94, 127.73 (aldehyde carbons).

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