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Hexapyrrolylbenzene and Octapyrrolylnaphthalene

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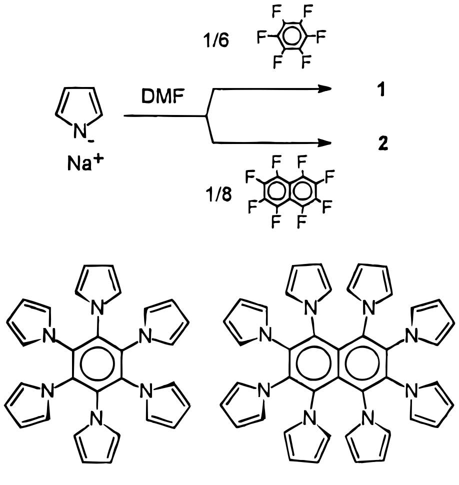
Introduction

Highly symmetrical, propeller-shaped, hexasubstituted benzenes have received considerable interest due to their intriguing properties as sterically congested polycyclic aromatic compounds.[1] Recently, octasubstituted naphthalenes and decasubstituted anthracenes were studied as well.[2] An interesting one-pot synthesis for some selected structures is based on the multiple nucleophilic substitution of perfluoroaromatics with the corresponding nucleophile. Nitrogen-containing nucleophiles that have been reacted six times with hexafluorobenzene comprise 4-(dimethylamino)pyridine,[3] imidazole,[4,5] pyrazole,[4] and dimethylpyrazole.[4,6,7] In some of these cases an unexplained autoacceleration is suggested in the synthesis, since hexasubstitution seems to be favored over partial substitution.[3,4] Remarkably, the synthesis of hexapyrrolylbenzene is reported to be unsuccessful when using pyrrolylsodium and hexafluorobenzene in THF.[4] Since hexapyrrolylbenzene **1** and octapyrrolylnaphthalene **2** are expected to be useful as building blocks for larger π-conjugated systems, we have investigated the synthesis and properties of these molecules. In this communication we report on a convenient and general synthesis toward **1** and **2**, present evidence for the absence of an autoacceleration in the nucleophilic aromatic substitution of hexafluorobenzene, and discuss the crystal structures of **1** and **2**.

Results and Discussion

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 pyrrolylsodium with hexafluorobenzene at ambient temperature in DMF (Scheme 1). Pyrrolylsodium was prepared by the addition of pyrrole in dry DMF to sodium hydride in dry DMF. To this 1 M light-brown solution was added dropwise a stoichiometric amount of hexafluorobenzene in dry DMF. The noticeable exothermic reaction yielded, after precipitation in water, hexapyrrolylbenzene **1** as a white solid in 86% yield. Crystallization from acetonitrile produced large crystals of **1** from which the crystal structure was determined (Figure 1). The crystals are orthorhombic, space group $Pna2_1$ with 1 molecule per asymmetric unit.

Scheme 1. Synthesis of Hexapyrrolylbenzene (1) and Octapyrrolylnaphthalene (2)



1 **2**

In the crystal the dihedral angles between the least squares planes through the pyrrole rings and the central phenyl ring in the "propeller-shaped" molecule range between 48° and 69°. Comparing these values to those found for other hexasubstituted benzenes (hexaphenyl:[8] 64° to 69°; hexakis(3,5-dimethylpyrazolyl):[6,7] 85° or between 51−122° and hexakis(4-(dimethylamino)-1-pyridinium):[3] 80°), we conclude that the pyrroles are able to become more coplanar with the central phenyl ring than any other substituent known today. The broad range in which the dihedral angles are found is also somewhat wider, reflecting the greater conformational freedom in the hexapyrrolylbenzene. On the other hand, the UV/vis spectrum of **1** in acetonitrile shows the presence of some π-stacking between the pyrrole units (Figure 2), as is concluded from the small shoulder at $\lambda = 300$ nm on the low-energy side of the main absorption band at $\lambda_{\max} = 254$ nm.

In order to investigate the previously suggested autoacceleration effect,[3,4] an experiment was conducted in which 1 equimolar amount of hexafluorobenzene was added to 2 equimolar amounts of pyrrolylsodium (instead of 6 needed for a stoichiometric and complete reaction). After the usual workup, the reaction mixture was subjected to column chromatography. The five main products could be isolated, and their structures were elucidated using GC/MS, ^{1}H, ^{13}C, and ^{19}F NMR spectroscopy (Table 1). The chemical shifts determined with ^{1}H NMR are surprisingly consistent throughout the series. When a pyrrole substituent has two fluorine neighbors, the

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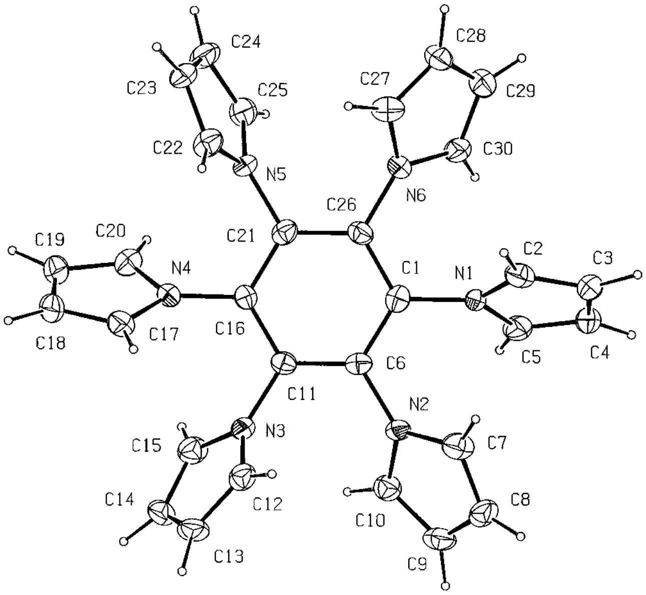

Figure 1. ORTEP drawing (50% probability level) of hexapyrrolylbenzene (**1**).

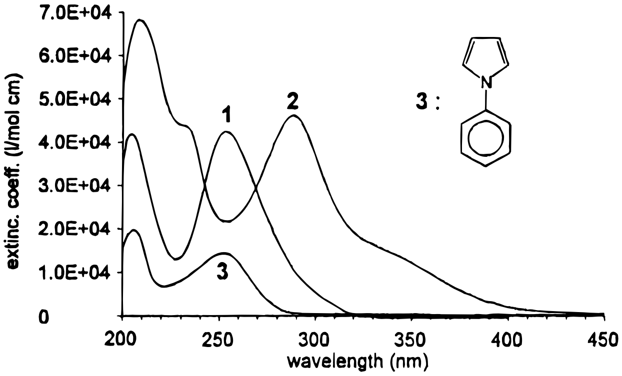

Figure 2. UV/vis spectra of **1**, **2**, and phenylpyrrole measured in acetonitrile.

signals of the two different pyrrole protons are centered around 6.96 and 6.43 ppm. If a pyrrole unit is neighbored by one fluorine atom and another pyrrole unit, its chemical shifts are approximately 6.52 and 6.26 ppm, and if the pyrrole unit is sandwiched between two other pyrrole rings the chemical shifts are 6.18 and 6.08 ppm, respectively. The products found reflect the expected ortho-para activation, while indeed a preferred formation of the highly substituted compounds is found. That preference for **1** is even more pronounced, when hexafluorobenzene was added very slowly to pyrrolylsodium; the product consisted of >90% hexapyrrolylbenzene (as determined by ^{1}H-NMR). Apparently, these experimental results are indicative of the autoacceleration effect as suggested by other authors.[3,4] However, when the *addition sequence is reversed* by the slow addition of 2 equimolar amounts of pyrrolylsodium to 1 equimolar amount of hexafluorobenzene, the product consists of >90% of 1,4-dipyrrolyl-2,3,5,6-tetrafluorobenzene. This result clearly contradicts autoacceleration, where, irrespective of the addition sequence, a preferred formation of hexapyrrolylbenzene would have to take place. An instantaneous exothermic reaction between pyrrolylsodium and hexafluorobenzene, however, accounts for all the results found, and we are prompted to conclude that the proposed autoaccelerated synthesis is incorrect.

The reactivity of pyrrolylsodium toward other fluorinated aromatics was tested by the reaction with octafluoronaphthalene as the core molecule (Scheme 1). Octapyrrolylnaphthalene (**2**) was obtained as a yellow solid in 80% yield by using the conditions as described for the synthesis of **1**. It was crystalized from acetonitrile, producing large crystals from which the crystal structure was determined (Figure 3).

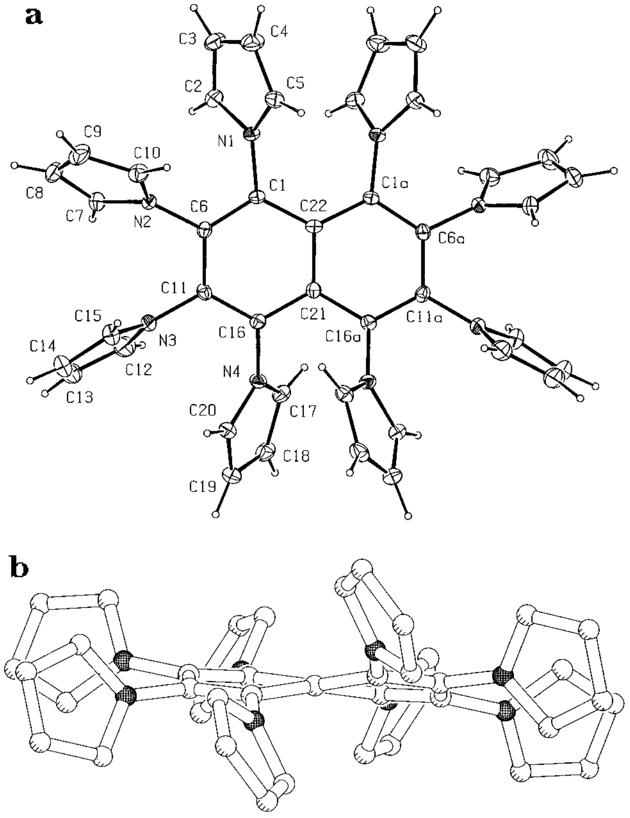

Figure 3. Octapyrrolylnaphthalene (**2**). (a) Top view, ORTEP drawing at 50% probability level with atom labeling scheme. (b) Side view, PLUTON drawing.

The crystals are tetragonal, space group $P4_12_12$ and the unit cell contains four molecules. Each molecule lies upon a crystallographic two-fold rotation axis. As expected, the dihedral angles between the least squares planes through the pyrrole rings and the acene in **2** range between 59° and 78°. Again, the pyrroles can obviously be more coplanar with the central naphthalene unit as compared to octaphenylnaphthalene[2] (68° to 69°). As in the case of octaphenylnaphthalene,[2] the naphthalene unit is twisted and the pyrroles neighboring the central C(21)−C(22) bond are displaced above and below the plane. The twist of the naphthalene core, expressed as the angle between the two symmetry-related C(6)−C(11) bonds, amounts to 21.84(12)°. NMR and UV/vis spectroscopy of **2** in solution clearly shows the presence of stacking of the pyrrole units in **2** ($\lambda_{\text{shoulder}} = 340$ nm, $\lambda_{\text{max}} = 288$ nm, Figure 2). The effect is even more pronounced here than in the case of **1**.

Conclusion

We have demonstrated the great ease with which multiple-pyrrolyl aromatic compounds can be synthesized. Due to their sterically congested structure, they may be regarded as building blocks for larger π-conjugated systems aiming at star-shaped molecules with new electrooptical properties.[9]

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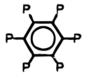
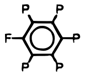
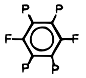
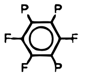
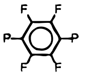
Table 1. Selected Data of Main Reaction Products Obtained after Addition of 1 Equimolar Amount of Hexafluorobenzene to 2 Equimolar Amounts of Pyrrolylsodium in DMF

Compound	GC/MS (M/Z)	Yield[a]	^{1}H-NMR[b] (400 MHz)	^{13}C-NMR (100 MHz)	^{19}F-NMR[c] (375 MHz)	Structure[d]
6 pyrroles	468	50	6.08[1] 6.18[1]	110.6 120.8 134.2	-	
5 pyrroles	421	9	6.08[3] 6.18[3] 6.26[2] 6.52[2]	110.5 110.6 110.8 120.9 121.1 121.7 126.4 126.5 133.7 151.1 (J_{CF}=256Hz)	-127	
4 pyrroles	373	36	6.26[1] 6.53[1]	110.8 121.6 125.4 148.4 (J_{CF}=252Hz)	-133	
3 pyrroles	326	3	6.26[2] 6.43[1] 6.50[2] 6.97[1]	110.8 110.8 110.9 119.2 121.6 121.8 122.4 125.4 133.7 142.5 (J_{CF}=247Hz) 144.6 (J_{CF}=256Hz) 147.7 (J_{CF}=252Hz)	-134(d, J=10.7Hz) -143(d, J=22.0Hz) -148(dd, J=10.7Hz, J=22.0Hz)	
2 pyrroles	280	2	6.43[1] 6.96[1]	110.9 118.7 122.3 142.0 (J_{CF}=255Hz)	-148	

[a] As determined by GC. [b] The values between brackets indicate the relative intensities of the signals. [c] Hexafluorobenzene was used as external reference (−162 ppm). [d] The P stands for a pyrrole unit.

Experimental Section

General Information. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a 400 MHz spectrometer operating at 400.13, 100.62, and 376.48 MHz, respectively. Analytical gas chromatography was done using a CPSIL5CB column (length 25 m, diameter 0.32 mm, film 0.12 μm).

Chemical reagents and solvents were purchased from commercial sources and used as received with the exception of DMF which was dried over barium oxide.

Hexapyrrolylbenzene (1). A 0.43 g (17.9 mmol) amount of NaH was stirred in 15 mL of DMF using a 25 mL two-necked flask fitted with a calcium chloride tube. Through a dropping funnel was added 1.20 g (17.9 mmol) of pyrrole. After the liberation of H_2 gas had ceased, the reaction mixture was stirred for an additional 30 min. Then a solution of 0.5 g (2.69 mmol) of hexafluorobenzene in 5 mL of DMF was added dropwise in 15 min, and the reaction mixture was stirred for an additional 2 h. It was poured into 100 mL of ice−water, and the white precipitate was filtered and dried overnight in air yielding 1.08 g (86%). Crystallization from acetonitrile yielded large colorless crystals from which the crystal structure was determined. $C_{30}H_{24}N_6$, $M = 468.57$; elemental analysis: C 76.94 (76.90), N 17.83 (17.94), H 6.05 (5.16); GC/MS (m/z) 468; ^{1}H NMR ($CDCl_3$) δ 6.17 (12H, dd, $J = 2.2$ Hz, $J = 2.2$ Hz), 6.07 (12H, dd, $J = 2.1$ Hz, $J = 2.1$ Hz); ^{13}C NMR ($CDCl_3$) δ 134.3, 120.9, 110.6; mp > 350 °C; crystal data of **1**: colorless, block-shaped crystal (0.35 × 0.35 × 0.30 mm), orthorhombic, space group $Pna2_1$ (no. 33) with $a = 10.2570(12)$, $b = 19.797(2)$, $c = 11.811(2)$ Å, $V = 2398.3(5)$ Å^3, $Z = 4$, $D_x = 1.298$ g cm^{-3}, $F(000) = 984$, μ(Mo Kα) = 0.8 cm^{-1}, 2914 reflections measured, 2675 independent, (1.03° < θ < 27.49°, ω scan, $T = 150$ K, Mo Kα radiation, graphite monochromator, $\lambda = 0.71073$ Å) on an Enraf-Nonius CAD4 Turbo diffractometer on rotating anode. Data were corrected for Lp effects and for a linear decay of 1% of the reference reflections, but not for absorption. The structure was solved by automated direct methods (SHELXS86). Refinement on F^2 was carried out by full-matrix least-squares techniques (SHELXS-93); no observance criterium was applied during refinement. Refinement converged at a final $wR2$ value of 0.1370, $R1 = 0.0635$ (for 1653 reflections with $F_o > 4\sigma(F_o)$) $S = 1.040$, for 349 parameters. Hydrogen atoms were included in the refinement on calculated positions riding on their carrier atoms. A final difference Fourier showed no residual density outside −0.25 and 0.27 e Å^{-3}.

Partial Substitution of Hexafluorobenzene by Pyrrole. A 0.125 g (5.2 mmol) amount of NaH was stirred in 5 mL of DMF using a 25 mL two-necked flask fitted with a calcium chloride tube. Through a dropping funnel was added 0.35 g (5.2 mmol) of pyrrole. After the liberation of H_2 gas had ceased, the reaction mixture was stirred for an additional 30 min. Then 0.49 g (2.63 mmol) of hexafluorobenzene in 5 mL of DMF was added in one batch and the mixture was stirred for an additional 2 h. It was poured into 100 mL ice−water, and the white precipitate was filtered and dried overnight in air yielding 0.36 g. The mixture was subjected to column chromatography using silica and CH_2Cl_2/hexanes as eluent (from a 1/3 ratio to 1/1 ratio).

Five products were isolated and characterized:

1,4-Di(N-pyrrolyl)tetrafluorobenzene: GC-yield: 2%; GC/MS (m/z) 280; ^{1}H NMR ($CDCl_3$) δ 6.43, 6.96; ^{13}C NMR ($CDCl_3$) δ 110.9, 118.7, 122.3, 142.0; ^{19}F NMR ($CDCl_3$) δ −148.

1,2,4-Tri(N-pyrrolyl)trifluorobenzene: GC-yield: 3%; GC/MS (m/z) 326; ^{1}H NMR ($CDCl_3$) δ 6.26 (4H), 6.43 (2H), 6.50 (4H), 6.97 (2H); ^{13}C NMR ($CDCl_3$) δ 110.8, 110.8, 110.9, 119.2, 121.6, 121.8, 122.4, 125.4, 133.7, 142.5, 144.6, 147.7; ^{19}F NMR ($CDCl_3$) δ −134, −143, −148.

1,2,4,5-Tetra(*N*-pyrrolyl)difluorobenzene: GC-yield: 36%; GC/MS (m/z) 373; ^{1}H NMR ($CDCl_3$) δ 6.26 (8H), 6.53 (8H); ^{13}C NMR ($CDCl_3$) δ 110.8, 121.6, 125.4, 148.4; ^{19}F NMR ($CDCl_3$) δ −133.

1,2,3,4,5-Penta(*N*-pyrrolyl)fluorobenzene: GC-yield: 9%; GC/MS (m/z) 421; ^{1}H NMR ($CDCl_3$) δ 6.08 (6H), 6.18 (6H), 6.26 (4H), 6.52 (4H); ^{13}C NMR ($CDCl_3$) δ 110.5, 110.6, 110.8, 120.9, 121.1, 121.7, 126.4, 126.5, 133.7, 151.1; ^{19}F NMR ($CDCl_3$) δ −127.

1: GC yield 50%; other data are given above.

Octapyrrolylnaphthalene (2). A 0.71 g (29.6 mmol) amount of NaH was stirred in 25 mL of DMF using a 50 mL two-necked flask fitted with a calcium chloride tube. Through a dropping funnel was added 2.00 g (29.8 mmol) of pyrrole. After the liberation of H_2 gas had ceased, the reaction mixture was stirred for an additional 30 min. Then a solution of 0.6 g (2.21 mmol) of hexafluorobenzene in 10 mL of DMF was added dropwise in 15 min, and the reaction mixture was stirred overnight. It was poured into 100 mL ice−water, and the yellow precipitate was filtered and dried overnight in air yielding 1.15 g (80%). Crystallization from acetonitrile yielded large yellow crystals from which the crystal structure was determined. $C_{42}H_{32}N_8$, M = 648.78; elemental analysis: C 76.35 (77.76), N 17.20 (17.27), H 5.14 (4.97); GC/MS (m/z) 648; ^{1}H NMR ($CDCl_3$) δ 6.19 (8H, m), 5.98 (16H, m), 5.82 (8H, m); ^{13}C NMR ($CDCl_3$) δ 135.9, 133.5, 127.7, 124.3, 121.0, 110.0, 109.8; mp > 350 °C; crystal data of **2** (unless stated otherwise, the same procedure has been followed as for compound **1**): yellow, block-shaped crystal (0.4 × 0.3 × 0.2 mm), tetragonal, space group $P4_12_12$ (no. 92) with a = 11.5659(11), c = 25.680(9) Å, V = 3435.2(13) Å^3, Z = 4, D_x = 1.254 g cm^{-3}, $F(000)$ = 1360, μ(Mo Kα) = 0.8 cm^{-1}, 15226 reflections measured, 4791 independent, R_{int} = 0.0925, (1.1° < θ < 29.99°, T = 100K) on an Enraf-Nonius FAST area detector on rotating anode. A disordered solvent area (V = 243 Å^3, 11.7 electrons, probably partially occupied by water) was treated with the SQUEEZE/BYPASS[10] procedure. Where relevant, data are given without disordered solvent contribution. Refinement converged at a final $wR2$ value of 0.1432, $R1$ = 0.0570 (for 4144 reflections with $F_o > 4\sigma(F_o)$) S = 1.123, for 227 parameters. A final difference Fourier showed no residual density outside −0.29 and 0.36 e Å^{-3}. Atomic coordinates, bond lengths and angles, and thermal parameters of both structure determinations have been deposited at the Cambridge Crystallographic Data Centre.

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