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SYNTHESIS AND PROPERTIES OF PARTIALLY FLUORINATED 4-ALKYL-4'-CYANOBIPHENYLS - PART I. 4'-ALKYL-4-CYANO-2',3',5',6'-TETRAFLUOROBIPHENYLS.¶

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A general synthetic route to 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls has been developed and used to prepare compounds with unbranched alkyl chains ranging from 4 to 8 carbon atoms. The compounds were characterised by ^{19}F, ^{13}C and ^{1}H NMR spectroscopy.

The 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls synthesised are crystalline solids which melt at temperatures 20-50°C higher than the corresponding fully protonated analogues. None of the 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls synthesised give rise to a liquid crystalline phase on melting.

4-Alkyl-4'-cyanobiphenyls are a well known class of compounds which exhibit liquid crystalline properties.[1] Such compounds have found applications in electronic display devices as well as providing aligned media for the examination of solutes by various forms of spectroscopy.

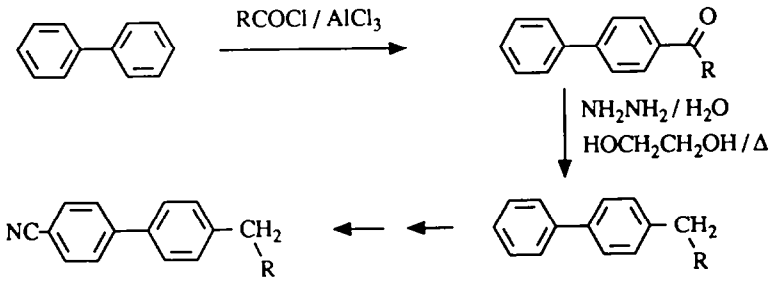
In a continuing project involving NMR spectroscopy of molecules aligned in liquid crystalline solvents,[2] we have the requirement for liquid crystalline solvents with a reduced concentration of protons as well as an increased chemical stability towards reactive solutes. Liquid crystalline solvents used in ^{1}H NMR spectroscopy have typically been taken directly from commercial sources and the signals of the solvents themselves often dominate or contribute significantly to the observable NMR spectrum. The problem becomes particularly acute as the number of interacting spins in the solute increases and the required spectrum increases in complexity such that it is difficult to distinguish weaker transitions from the background signals of the liquid crystal solvent. In this paper we report the synthesis and properties of 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls¶ with a view to using these as "proton-depleted" liquid crystalline compounds or as "proton-depleted" components of liquid crystalline mixtures.

The synthesis of a series of monofluorinated 4'-alkyl-4-cyanobiphenyls has been reported by Fearon *et al.*[3] These compounds were thermotropic liquid crystals but monofluoro substitution was found to depress the nematic to isotropic transition temperature, compared to the non-fluorinated parent compounds.

Results and Discussion.

In the synthesis of the 4'-alkyl-4-cyanobiphenyl framework, there are three critical bonds that must be made *(i)* the aryl-aryl bond, *(ii)* the aryl-alkyl bond and *(iii)* the aryl-C≡N bond. Published syntheses typically begin from biphenyl[4-10] or 4-bromobiphenyl[3] *i.e.* with the aryl-aryl bond already in place. The

alkyl chain is introduced by acylation ($RCOCl/AlCl_3$) followed by reduction of the ketone to give a 4-alkylbiphenyl. The cyano group is typically built up by initial acetylation of the biphenyl followed by haloform oxidation to give the carboxylic acid. Subsequent formation of the amide followed by dehydration affords the desired 4'-alkyl-4-cyanobiphenyl (Scheme 1).

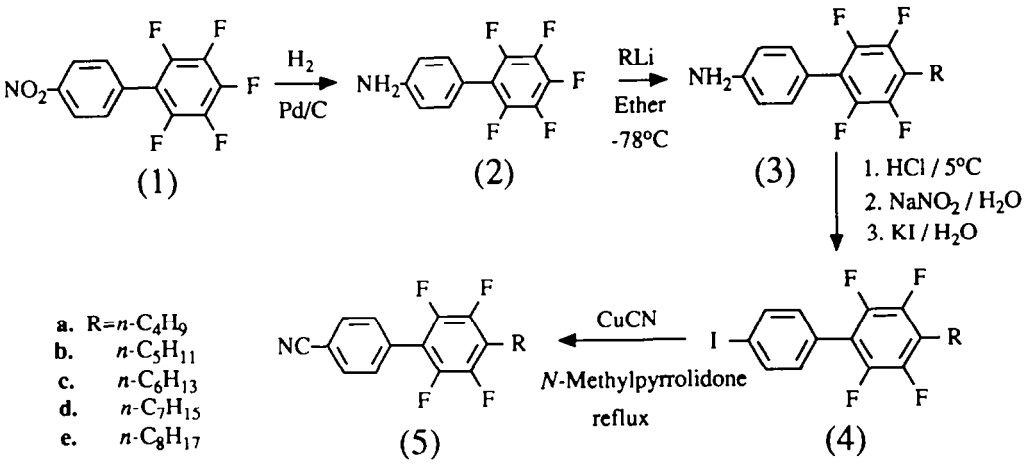


Scheme 1.

The main variations to this approach have been in the method of introducing the $-C{\equiv}N$ group. Halogenation at the 4'-position by bromine[11] or iodine[12] and substitution of the halide by cyanide provides a more direct method of introducing the cyanide but involves the use of CuCN which can be difficult to handle safely in large scale preparations. Alternatively, the $-C{\equiv}N$ has been introduced by formylation of the biphenyl, formation of the oxime followed by dehydration.[5]

This general scheme is inappropriate for the synthesis of 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls since fluorination of one of the aromatic rings dictates that an alkyl or acyl chain cannot be introduced onto that ring by an electrophilic substitution. Furthermore, fluorination on one of the aromatic rings sufficiently deactivates the system that electrophilc substitution of the non-fluorinated ring is difficult. Substitution of the 4-position of the fluorinated ring can be best achieved by direct substitution by a suitable nucleophile[13] and for this reason, the 4-position of the non-fluorinated ring must be substituted before the biphenyl skeleton is assembled.

In our approach, the aryl-aryl bond was made by coupling 4-iodonitrobenzene and bromopentafluorobenzene over copper powder at high temperature. The unsymmetrical product, 4-nitro-2',3',4',5',6'-pentafluorobiphenyl, (**1**), was the major component of the product mixture (>50%) and was easily isolated by fractional distillation. The nitro group was reduced quantitatively to the amine using hydrogen over a palladium on charcoal catalyst and this provides a reactive functionality which can be elaborated, at a later point in the synthesis, to the required cyano group. The alkyl chain was introduced at the 4-position of the fluorinated aromatic ring by direct displacement of the fluoride at the 4-position by an alkyllithium at low temperature. In this reaction, only the *para*-fluoride was displaced and the reaction afforded the 4'-alkyl-4-amino-2',3',5',6'-tetrafluorobiphenyl in high yields (typically >80%). The amino group was converted into an iodide via the diazonium salt and displacement of iodide by cuprous cyanide in *N*-methylpyrrolidone at reflux afforded the required cyano-substituted biphenyls (Scheme 2).



Scheme 2.

The conversion of the 4'-alkyl-4-amino-2',3',5',6'-tetrafluorobiphenyl **(3)** to the nitrile **(5)** typically proceded in 60–70% isolated yield. The 4'-alkyl-2',3',5',6'-tetrafluorobiphenyl was a significant by product in the conversion of **(3)** to **(5)**.

Physical properties of 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls. 4'-Alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls containing 4, 5, 6, 7 and 8 membered *n*-alkyl chains were synthesised in the same manner (according to Scheme 2). All are colourless crystalline solids at room temperature with melting points 20 to 50°C higher than the corresponding fully protonated analogues (Table 1). None of the compounds exhibited a liquid crystalline phase which could be detected by slow melting and solidification of the pure materials.

Table 1. MELTING POINTS[a] OF 4'-ALKYL-4-CYANO-2',3',5',6'-TERTAFLUOROBIPHENYLS AND THEIR PROTONATED ANALOGUES.

Alkyl chain	Fully protonated[b] °C	Partially fluorinated °C	
n-Butyl	46 (46–16)[c]	71–73	**(5a)**
n-Pentyl	23[d] (23–35)	65–66	**(5b)**
n-Hexyl	15[d] (15–30)	56–58	**(5c)**
n-Heptyl	29[d] (29–43)	52–53	**(5d)**
n-Octyl	21[d] (21–41)	64–65	**(5e)**

a. solid → isotropic transition temperature.
b. From ref. 14, liquid crystal range (°C) is in parenthesis.
c. From ref. 15.
d. solid → nematic transition temperature.

NMR spectroscopy. The products of the syntheses as well as various key intermediates in the synthetic schemes were characterised routinely by ^{19}F, ^{1}H and ^{13}C NMR spectroscopy.

The ^{19}F NMR spectra of the 4'-alkyl-4-substituted-2',3',5',6'-tetrafluorobiphenyls (Table 2) have resonances in the expected region for ^{19}F in polyfluorinated aromatic compounds. For all of the 4'-alkyl-4-amino-2',3',5',6'-tetrafluorobiphenyls (3) synthesised, the ^{19}F NMR spectra appeared as only a single resonance at about δ-142 ppm (in $CDCl_3$ solution) due to accidental equivalence of the chemical shifts of the 3',5'- and 2',6'-fluorine nuclei. The 4'-alkyl-4-iodo-2',3',5',6'-tetrafluorobiphenyls (4) and 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls (5) exhibited two sets of multiplets in the ^{19}F spectrum with a typical AA'XX' coupling pattern.

Table 2. ^{19}F NMR SHIFTS[a] OF 4'-R-4-X-2',3',5',6'-TETRAFLUOROBIPHENYLS.

Compound	X	R	$\delta^{19}F$ F2',F6'	$\delta^{19}F$ F3',F5'
1	NO_2	F[b]	-137.8	-156.1
2	NH_2	F[c]	-139.2	-158.2
3a	NH_2	*n*-Butyl	-141.3	-141.3
4a	I	*n*-Butyl	-142.4	-141.7
5a	CN	*n*-Butyl	-140.7	-141.5
3b	NH_2	*n*-Pentyl	-142.5	-142.5
5b	CN	*n*-Pentyl	-140.7	-141.6
3c	NH_2	*n*-Hexyl	-142.5	-142.5
5c	CN	*n*-Hexyl	-140.7	-141.6
3d	NH_2	*n*-Heptyl	-142.5	-142.5
5d	CN	*n*-Heptyl	-104.7	-141.6
3e	NH_2	*n*-Octyl	-142.5	-142.5
5e	CN	*n*-Octyl	-140.7	-141.6

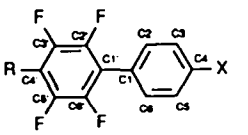
a. ^{19}F NMR shifts are referenced to neat external C_6F_6 taken as δ-163.0 ppm.
b. F4' shift = -147.8 ppm.
c. F4' shift = -152.8 ppm.

The ^{13}C NMR spectra of the 4'-alkyl-4-substituted-2',3',5',6'-tetrafluorobiphenyls (Table 3) exhibited strong resonances for the protonated carbons. ^{13}C resonances of the fluorinated rings were difficult to observe (without ^{19}F decoupling) due to the lack of NOE and the presence of direct and long range ^{19}F-^{13}C couplings. The fluorinated aromatic carbons appear characteristically 10 to 20 ppm to lower field than the protonated aromatic carbons with one-bond fluorine-carbon splittings of about 250 Hz. Both of the quaternary carbons of the fluorinated aromatic ring appear as narrow triplets (15-20 Hz) due to two-bond coupling to the fluorine nuclei at C2',6' and C3',5'.

Conclusions.

A general synthetic route to 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls has been developed and used to prepare compounds with *n*-alkyl chains ranging from 4 to 8 carbon atoms. The approach can be varied easily to introduce alkyl substituents via the appropriate alkyllithium reagent.

Table 3. ^{13}C CHEMICAL SHIFTS and COUPLING CONSTANTS OF FLUORINATED COMPOUNDS[a]



Compound	X	C4	C3,C5	C2,C6	C1	C1' ($^2J_{C-F}$)	C2',C6' ($^1J_{C-F}$)	C3',C5' ($^1J_{C-F}$)	C4' ($^2J_{C-F}$)	C≡N	
2	NH_2	147.4	114.8	131.2	115.7	-[b]	144.2 (243.0)	137.9 (249.8)	139.7 (252.5)[d]		
5a	CN	112.9	132.2	131.0	132.7	116.1 (15.9)	145.3 (250.0)	143.4 (247.3)	121.6 (16.8)	118.2	C1"-31.3, C2",C3"-22.7, 22.4, CH_3-13.6
3b	NH_2	147.0	114.8	131.2	117.4	-[b]	145.2 (239.7)	143.6 (249.8)	118.8 (18.1)		C1"-31.4, C2"-C4"-29.0, 22.7, 22.3, C5"-13.9.
5b	CN	112.9	132.2	131.0	132.6	116.1 (15.7)	145.3 (251.0)	143.4 (246.2)	121.7 (18.5)	118.3	C1"-31.4, C2"-C4"-28.9, 22.9, 22.4, CH_3-13.9
3c	NH_2	147.0	114.7	131.2	117.2	-[b]	145.2 (241.9)	143.6 (250.0)	118.7		C1"-31.4, C2"-C5"-29.3, 28.9, 22.7, 22.5, CH_3-13.9
5c	CN	112.8	132.3	131.0	132.6	116.0 (15.1)	145.3 (248.0)	143.4 (244 0)	121.6 (18.1)	118.3	C1"-31.4, C2"-C5"-29.2, 28.9, 23.0, 22.5, CH_3-13.9
3d	NH_2	147.0	114.8	131.2	117.4	-[b]	145.2 (250.3)	143.7 (248.0)	118.7		C1"-31.8, C2"-C6"-29.4, 29.2, 28.9, 22.8, 22.6, CH_3-14.0
5d	CN	112.8	132.2	130.9	132.6	116.0 (15.9)	145.2 (248.4)	143.0 (245.2)	121.6 (18.2)	118.3	C1"-31.7, C2"-C6"-29.2, 29.1, 28.9, 23.0, 22.6, CH_3-14.0
3e	NH_2	147.0	114.8	131.3	117.4	-[b]	145.2 (246.0)	143.1 (246.0)	118.8		C1"-31.6, C2"-C7"-29.3, 29.2, 29.1, 29.1, 22.8, 22.7, CH_3-14.0
5e	CN	112.9	132.3	131.0	132.6	116.1 (14.9)	145.2 (245.2)	143.2 (258.1)	121.7 (17.9)	118.3	C1"-31.7, C2"-C7"-29.3, 29.3, 29.2, 29.2, 23.0, 22.7, CH_3-14.1

a. $CDCl_3$ solution, 300K, $CDCl_3$ taken as δ77.0 ppm, coupling constants in Hz. b. not observed.

The 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls synthesised were all crystalline solids which melt at temperatures 20-50°C higher than the corresponding fully protonated analogues. None of the 4'-alkyl-4-cyano-2',3',5',6'-tetrafluorobiphenyls synthesised gave rise to a liquid crystalline phase on melting.

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Experimental Section.

Synthesis of Compounds. Ethyl acetate and light petroleum (b.p. 60-70°) were distilled prior to use. Bromopentafluorobenzene was obtained from Aldrich and used without further purification. Chromatography was performed on Merck flash silica (230-400 mesh). Ether was dried over sodium wire, and copper cyanide was prepared according to literature procedures.[16] NMR spectra were recorded in $CDCl_3$ solution at 300K unless otherwise noted. ^1H (400.1 MHz) and ^{13}C (100.6 MHz) NMR spectra were recorded on a Bruker WM-400 spectrometer and were referenced to residual solvent resonances. ^{19}F (376.3 MHz) NMR spectra were recorded on a Varian XL-400 spectrometer and were referenced to external neat C_6F_6 (taken as -163.0 ppm).

Alkyllithiums were prepared by the general procedures of Gilman *et al.*[17a] and Freeman *et al.*[17b] For the lower alkyllithiums (< 6 carbon chain) the alkyl bromide (*ca.* 150 mmol) was added to a suspension of lithium pieces (2.8g, 400 mmol) in ether (100 mls) at room temperature and stirred for 3 hours under argon. The supernatant was drawn off by canula and used directly. For higher alkyllithiums (> 6 carbons) a small amount of the alkyl bromide was added at room temperature to initiate the reaction and the temperature was lowered to -78°C before the remainder of the bromide was added. The mixture was stirred at -78°C for 3 hours, the supernatant was removed by cold canula and the reagent stored below 5°C until it was used.

4-Nitro-2',3',4',5',6'-pentafluorobiphenyl (1). A mixture of 4-iodonitrobenzene (1g, 4 mmol), bromopentafluorobenzene (1g, 4 mmol) and copper powder (2g) was heated in a stainless steel reaction bomb at 190°C for 18 hours. The bomb was cooled and the contents extracted exhaustively with dichloromethane. The solvent was removed and the residue was extracted with boiling light petroleum and filtered while hot. The solvent was removed and the resulting brown oil was distilled (Kugelrohr, 160°C/1mm). The yellow oil solidified on cooling to yield 4-nitro-2',3',4',5',6'-pentafluorobiphenyl **(1)** as a yellow solid (0.66g, 57%) mp: 93-94°C (Lit.[18,19] mp 92-93°C). ^1H NMR δ8.38, 2H, Ar$\underline{H}$3 Ar$\underline{H}$5; 7.65, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6.

4-Amino-2',3',4',5',6'-pentafluorobiphenyl (2). 4-Nitro-2',3',4',5',6'-pentafluorobiphenyl **(1)**, (1g, 3.45 mmol) was dissolved in absolute ethanol (75 ml) and stirred under a hydrogen atmsophere over a palladium on charcoal catalyst at atmospheric pressure until the hydrogen uptake ceased. The solution was filtered and solvent was removed. The crude product was recrystallized from light petroleum to give 4-amino-2',3',4',5',6'-pentafluorobiphenyl **(2)** as a white crystalline solid (0.84g, 95%) mp: 129-130°C (Lit.[19] mp 129-130°C). ^1H NMR δ7.23, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6; 6.78, 2H, Ar$\underline{H}$3 Ar$\underline{H}$5; 3.85, 2H, -N$\underline{H}_2$.

4-Amino-4'-butyl-2',3',5',6'-tetrafluorobiphenyl (3a). *n*-Butyllithium (2.5M, 2.68 ml, 13.4mmol) was added slowly to a solution of 4-amino-2',3',4',5',6'-pentafluorobiphenyl **(2)** (1.75g, 6.7 mmol) in dry ether (100 ml) at -78°C. The solution was stirred at this temperature for 2 hours and then allowed to warm to room temperature over a period of 5 hours. Hydrochloric acid (3M, 50ml) was added, the organic layer was separated and the aqueous layer was extracted with ether; the combined extracts were dried and solvent removed. The crude product was distilled (Kugelrohr, 200°C/1mm) to give 4-amino-4'-butyl-2',3',5',6'-tetrafluorobiphenyl **(3a)** as a white solid (1.65g, 83%) mp: 56-57°C. ^{1}H NMR δ7.28, m, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6; 6.78, m, 2H, Ar$\underline{H}$3 Ar$\underline{H}$5; 3.85, (bs), 2H, -N$\underline{H}_2$; 2.75, t, 2H, Ar-C$\underline{H}_2$; 1.60, m, 2H, Ar-CH$_2$-C$\underline{H}_2$; 1.40, m, 2H, Ar-(CH$_2$)$_2$-C$\underline{H}_2$; 0.97, t, 3H, Ar-(CH$_2$)$_3$-C$\underline{H}_3$. Anal. calcd. for $C_{16}H_{15}F_4N$: C, 64.63%; H, 5.08%; N, 4.71%. Found: C, 64.2%; H, 4.7%; N, 4.4%. High-resolution mass spectrum calculated for $C_{16}H_{15}F_4N$ (M^+) 297.1140, found 297.1121.

4'-Butyl-4-iodo-2',3',5',6'-tetrafluorobiphenyl (4a). Hydrochloric acid (5M, 5 ml) was added to a solution of 4-amino-4'-butyl-2',3',5',6'-tetrafluorobiphenyl **(3a)** (0.56g, 1.9 mmol) in dioxane (1 ml). The mixture was cooled with stirring to below 5°C and a solution of sodium nitrite (6.2M, 0.35 ml) was added slowly, maintaining the temperature below 5°C. A solution of potassium iodide (4M, 0.6 ml) was added as quickly as possible, the reaction was heated on a steam bath for 20 minutes, cooled and extracted with ether. The combined ether extracts were washed with sodium metabisulfite, dried and the solvent removed to yield the crude product as a brown solid. A sample was purified by column chromatography with light petroleum as eluent. The bulk of the sample was used without purification for the preparation of 4'-butyl-4-cyano-2',3',5',6'-tetrafluorobiphenyl. ^{1}H NMR δ7.84, m, 2H, Ar$\underline{H}$3 Ar$\underline{H}$5; 7.21, m, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6; 2.79, t, 2H, Ar-C$\underline{H}_2$; 1.63, m, 2H, Ar-CH$_2$-C$\underline{H}_2$; 1.42, m, 2H, Ar-(CH$_2$)$_2$-C$\underline{H}_2$; 0.97, t, 3H, Ar-(CH$_2$)$_3$-C$\underline{H}_3$.

4'-Butyl-4-cyano-2',3',5',6'-tetrafluorobiphenyl (5a). Copper(I) cyanide (0.25g) was added to a solution of the crude iodide **(4a)** in freshly distilled *N*-methylpyrrolidone (10 ml). The reaction mixture was refluxed for 2 hours, cooled and poured into a solution of iron(III) chloride (4g) in water (60 ml). Hydrochloric acid (10M, 2 ml) was added and the solution was extracted with ether. The solvent was removed and the crude product was purified by column chromatography (7% ethyl acetate/light petroleum) and recrystallized from light petroleum. 4'-Butyl-4-cyano-2',3',5',6'-tetrafluorobiphenyl **(5a)** was obtained as a white crystalline solid (0.36g, 61% with respect to 4-amino-4'-butyl-2',3',5',6'-tetrafluorobiphenyl) mp: 71-73°C. ^{1}H NMR δ7.78, m, 2H, Ar$\underline{H}$3 Ar$\underline{H}$5; 7.60, m, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6; 2.80, t, 2H, Ar-C$\underline{H}_2$; 1.64, m, 2H, Ar-CH$_2$-C$\underline{H}_2$; 1.42, m, 2H, Ar-(CH$_2$)$_2$-C$\underline{H}_2$; 0.97, t, 3H, Ar-(CH$_2$)$_3$-C$\underline{H}_3$. IR (KBr disc) 2963(m), 2933(m), 2874(w), 2239(m, -C≡N), 1477(s), 1405(m), 1193(w), 1103(w), 972(s), 960(m), 846(s). Mass Spectrum: *m/z* 307(M^+, 37%), 264(43), 43(100). High-resolution mass spectrum calculated for $C_{17}H_{13}F_4N$ (M^+) 307.0983, found 307.0979.

4-Amino-4'-pentyl-2',3',5',6'-tetrafluorobiphenyl (3b). A solution of *n*-pentyllithium (>2 equiv.) in dry ether was added slowly to a solution of 4-amino-2',3',4',5',6'-pentafluorobiphenyl **(2)** (1.90g, 7.3 mmol) in dry ether (100 ml) at -78°C. Using a procedure identical to that described for preparation of **(3a)**, 4-amino-4'-pentyl-2',3',5',6'-tetrafluorobiphenyl **(3b)** was obtained as a white crystalline solid (2.05g, 90%) and was used without further purification. ^{1}H NMR δ7.29, m, 2H, Ar$\underline{H}$2 Ar$\underline{H}$6; 6.78, m, 2H, Ar$\underline{H}$3

ArH5; 3.88, (bs), 2H, $-NH_2$; 2.75, t, 2H, Ar–CH_2; 1.63, m, 2H, Ar–CH_2–CH_2; 1.40–1.37, m, 4H, Ar–$(CH_2)_2$–CH_2–CH_2; 0.95, t, 3H, Ar–$(CH_2)_4$–CH_3. IR (KBr disc) 3422(w), 3333(w), 2955(w), 2936(w), 1629(w), 1610(w), 1524(m), 1477(s), 1425(m), 1404(w), 1292(w), 1267(w), 1176(m), 1126(w), 1101(w), 984(w), 929(m), 827(w). Mass spectrum: *m/z* 312(M+1, 20%), 311(M^+, 95), 267(5), 255(18), 254(100), 207(5), 127(4), 57(10), 43(12), 41(17).

4–Cyano–4'–pentyl–2',3',5',6'–tetrafluorobiphenyl (5b). 4–Amino–4'–pentyl–2',3',5',6'–tetrafluorobiphenyl (**3b**) was diazotized and treated with a solution of potassium iodide as described for the preparation of (**4a**). Copper(I) cyanide (2g) was added to a solution of crude 4–iodo–4'–pentyl–2',3',5',6'–tetrafluorobiphenyl in freshly distilled *N*–methylpyrrolidone (15 ml). The reaction mixture was refluxed for 2 hours and the product was extracted and purified as described for (**5a**). 4–Cyano–4'–pentyl–2',3',5',6'–tetrafluorobiphenyl (**5b**) was obtained as a white crystalline solid (1.55g, 73% with respect to 4–amino–4'–pentyl–2',3',5',6'–tetrafluorobiphenyl) mp: 65–66°C. ^{1}H NMR δ7.78, m, 2H, ArH3 ArH5; 7.57, m, 2H, ArH2 ArH6; 2.80, t, 2H, Ar–CH_2; 1.65, m, 2H, Ar–CH_2–CH_2; 1.42–1.39, m, 4H, Ar–$(CH_2)_2$–CH_2–CH_2; 0.97, t, 3H, Ar–$(CH_2)_4$–CH_3. IR (KBr disc) 2964(m), 2953(m), 2933(w), 2854(w), 2235(m, –C≡N), 1479(s), 1402(m), 1315(w), 1296(w), 1186(w) 1132(m), 1105(w), 982(s), 939(s), 862(w), 852(m), 833(s). Mass Spectrum: *m/z* 322(M+1, 20%), 321(M^+, 100), 277(8), 265(50), 264(55), 244(8), 57(65), 55(12), 44(17), 43(12), 41(43). Anal. calcd. for $C_{18}H_{15}F_4N$: C, 67.28%; H, 4.71%; N, 4.36%. Found: C, 67.1%; H, 4.6%; N, 4.1%.

4–Amino–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl (3c). A solution of *n*–hexyllithium (>2 equiv.) in dry ether was added slowly to a solution of 4–amino–2',3',4',5',6'–pentafluorobiphenyl (**2**) (1.00g, 3.9 mmol) in dry ether (100 ml) at -78°C. 4–Amino–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl was obtained as a white crystalline solid (1.15g, 92%) mp: 32–33°C using a procedure identical to that described for the preparation of (**3a**). 4–Amino–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl was used without further purification. ^{1}H NMR δ7.30, m, 2H, ArH2 ArH6; 6.77, m, 2H, ArH3 ArH5; 3.88, (bs), 2H, $-NH_2$; 2.78, t, 2H, Ar–CH_2; 1.67, m, 2H, Ar–CH_2–CH_2; 1.50–1.30, m, 6H, Ar–$(CH_2)_2$–CH_2–CH_2–CH_2; 0.93, t, 3H, Ar–$(CH_2)_5$–CH_3. IR (KBr disc) 3423(w), 3330(w), 2958(m), 2932(m), 2873(w), 2858(w), 2851(w) 1628(m), 1619(m), 1482(s), 1475(s), 1426(m), 1177(m), 952(s), 828(m). Mass spectrum: *m/z* 312(M+1, 17%), 325(M^+, 78), 267(4), 255(17), 254(100), 69(6), 57(7), 55(16), 44(49), 43(22).

4–Cyano–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl (5c). 4–Amino–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl (**3c**) was diazotized and treated with a solution of potassium iodide as described for the preparation of (**4a**). The crude 4'–hexyl–4–iodo–2',3',5',6'–tetrafluorobiphenyl was used without further purification. Copper(I) cyanide (1.2g) was added to a solution of the crude iodide in freshly distilled *N*–methylpyrrolidone (15 ml). The reaction mixture was refluxed for 2 hours and the product was extracted and purified as described for (**5a**). 4–Cyano–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl (**5c**) was obtained as a white crystalline solid (0.77g, 65% with respect to 4–amino–4'–hexyl–2',3',5',6'–tetrafluorobiphenyl) mp: 56–58°C. ^{1}H NMR δ7.79, m, 2H, ArH3 ArH5; 7.60, m, 2H, ArH2 ArH6; 2.78, t, 2H, Ar–CH_2; 1.65, m, 2H, Ar–CH_2–CH_2; 1.45–1.30, m, 6H, Ar–$(CH_2)_2$–CH_2–CH_2–CH_2; 0.92, t, 3H, Ar–$(CH_2)_5$–CH_3. IR (KBr disc) 2958(m), 2926(m), 2858(w), 2237(w, –C≡N), 1481(s), 1475(s), 1406(m), 960(w), 947(m), 842(m).

High-resolution mass spectrum calculated for $C_{19}H_{17}F_4N$ (M^+) 335.1296, found 335.1285.

4-Amino-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl (3d). A solution of *n*-heptyllithium (>2 equiv.) in dry ether was added slowly to a solution of 4-amino-2',3',4',5',6'-pentafluorobiphenyl **(2)** (0.55g, 2.12 mmol) in dry ether (100 ml) at -78°C. 4-Amino-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl was obtained as a white crystalline solid (0.64g, 89%) using a procedure identical to that described for the preparation of **(3a)**. 4-Amino-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl was used without further purification. ^{1}H NMR δ7.28, m, 2H, ArH2 ArH6; 6.77, m, 2H, ArH3 ArH5; 3.84, (bs), 2H, $-NH_2$; 2.75, t, 2H, Ar-CH_2; 1.5, m, 2H, Ar-CH_2-CH_2; 1.45-1.25, m, 8H, Ar-$(CH_2)_2$-CH_2-CH_2-CH_2-CH_2; 0.93, t, 3H, Ar-$(CH_2)_6$-CH_3.

4-Cyano-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl (5d). 4-Amino-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl **(3d)** was diazotized and treated with a solution of potassium iodide as described for the preparation of **(4a)**. 4'-Heptyl-4-iodo-2',3',5',6'-tetrafluorobiphenyl **(4d)** was used without further purification. Copper(I) cyanide (0.6g) was added to a solution of the crude iodide in freshly distilled *N*-methylpyrrolidone (10 ml). The reaction mixture was refluxed for 2 hours and worked up as in procedure described for **(5a)** to give 4-cyano-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl **(5d)** as a white crystalline solid (0.55g, 84% with respect to 4-amino-4'-heptyl-2',3',5',6'-tetrafluorobiphenyl) mp: 52-53°C. ^{1}H NMR δ7.79, m, 2H, ArH3 ArH5; 7.60, m, 2H, ArH2 ArH6; 2.79, t, 2H, Ar-CH_2; 1.67, m, 2H, Ar-CH_2-CH_2; 1.45-1.20, m, 8H, Ar-$(CH_2)_2$-CH_2-CH_2-CH_2-CH_2; 0.97, t, 3H, Ar-$(CH_2)_6$-CH_3. IR (KBr disc) 2957(s), 2918(s), 2850(s), 2238(m, -C≡N), 1475(s), 1406(m), 961(m), 950(m), 854(w), 826(w). Mass Spectrum: *m/z* 350(M+1, 55%), 349(M^+, 100), 265(61), 264(56), 85(7), 57(13), 43(83), 41(19). High-resolution mass spectrum calculated for $C_{20}H_{19}F_4N$ (M^+) 349.1453, found 349.1451.

4-Amino-4'-octyl-2',3',5',6'-tetrafluorobiphenyl (3e). A solution of *n*-octyllithium (>2 equiv.) in dry ether was added slowly to a solution of 4-amino-2',3',4',5',6'-pentafluorobiphenyl **(2)** (1.5g, 5.79 mmol) in dry ether (100 ml) at -78°C. 4-Amino-4'-octyl-2',3',5',6'-tetrafluorobiphenyl was obtained as a white crystalline solid (1.91g, 93%) using a procedure identical to that described for the preparation of **(3a)**. 4-Amino-4'-octyl-2',3',5',6'-tetrafluorobiphenyl was used without further purification in subsequent preparations. ^{1}H NMR δ7.30, m, 2H, ArH2 ArH6; 6.77, m, 2H, ArH3 ArH5; 3.85, (bs), 2H, $-NH_2$; 2.75, t, 2H, Ar-CH_2; 1.64, m, 2H, Ar-CH_2-CH_2; 1.50-1.27, m, 10H, Ar-$(CH_2)_2$-CH_2-CH_2-CH_2-CH_2-CH_2; 0.92, t, 3H, Ar-$(CH_2)_7$-CH_3. IR (KBr disc) 3417(w), 3325(w), 2957(m), 2923(m), 2852(m) 1630(w), 1611(w), 1524(m), 1477(s), 1426(m), 1267(m), 1178(m), 1128(m), 962(s), 923(m), 828(m), 719(m). Mass spectrum: *m/z* 354(M+1, 17%), 353(M^+, 76), 255(17), 254(100), 73(17), 71(11), 57(30), 43(48), 41(46).

4-Cyano-4'-octyl-2',3',5',6'-tetrafluorobiphenyl (5e). 4-Amino-4'-octyl-2',3',5',6'-tetrafluorobiphenyl **(3e)** was diazotized and treated with a solution of potassium iodide as described for **(4a)**. 4-Octyl-4'-iodo-2',3',5',6'-tetrafluorobiphenyl **(4e)** was used without further purification in subsequent preparations. Copper(I) cyanide (2.0g) was added to a solution of the crude iodide in freshly distilled *N*-methylpyrrolidone (10 ml). The reaction mixture was refluxed for 2 hours and worked up as in procedure described for **(5a)** to give 4-cyano-4'-octyl-2',3',5',6'-tetrafluorobiphenyl **(5e)** as a white

crystalline solid (1.44g, 73% with respect to 4-amino-4'-octyl-2',3',5',6'-tetrafluorobiphenyl) mp: 64-65°C. ^{1}H NMR δ7.79, m, 2H, ArH3 ArH5; 7.60, m, 2H, ArH2 ArH6; 2.79, t, 2H, Ar-CH_2; 1.65, m, 2H, Ar-CH_2-CH_2; 1.45-1.25, m, 10H, Ar-$(CH_2)_2$-CH_2-CH_2-CH_2-CH_2-CH_2; 0.97, t, 3H, Ar-$(CH_2)_7$-CH_3. IR (KBr disc) 2962(m), 2952(m), 2915(s), 2848(m), 2232(w, -C≡N), 1474(s), 1406(m), 1313(w), 1126(w), 961(m), 953(s), 925(m), 841(s). Mass Spectrum: *m/z* 363(M^+, 56), 265(38), 264(32), 57(100), 43(63), 41(20). Anal. calcd. for $C_{21}H_{21}F_4N$: C, 69.40%; H, 5.82%; N, 3.85%. Found C, 69.7%; H, 5.6%; N, 4.2%.

References and Notes.

¶ The correct systematic numbering of the substituted biphenyl skeleton according to IUPAC rules for nomenclature, depends on the priority of the substituents. However, *in this paper* for clarity and consistency throughout the series of compounds, the substituents on the fluorinated ring have *always* been numbered with primes.

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