FORMATION CONSTANTS IN C—H HYDROGEN BONDING. 2. ALKYNES AND POLYHALOBENZENES WITH HEXAMETHYLPHOSPHORIC TRIAMIDE IN CYCLOHEXANE SOLUTION

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Formation constants, K, for hydrogen bonding of weak C—H donors with hexamethylphosphoric triamide were measured in cyclohexane at 35 °C by PMR spectroscopy; data were analyzed by the Higuchi method. Donors include terminal alkynes and series of polyfluoro-, polychloro- and polybromobenzenes. The K values for many of these are too small to measure in CCl4. For RC≡CH, K decreases in the order R = BrCH2 > C6H5 > C2H5O > *tert-butyl*. For polyhalobenzenes, K is generally larger for F than Cl or Br, and *meta* halogens facilitate hydrogen bonding most effectively. Among tetrahalobenzenes, 1,2,3,4-isomers show the least evidence of 2:1 complex formation. Pentachlorobenzene has a smaller K than its 1,2,3,4-tetrachloro analog even after statistical correction; for C_6HX_5, K decreases in the order F > Cl > Br; the K values for 1,3,5-trihalobenzenes are closely similar; and 1,3,5-tribromo-2,4-dimethylbenzene shows no evidence of hydrogen bonding by PMR. The last three observations suggest that buttressing is important in the C_6HX_5 structure, at least with Cl and Br. A value of K for benzene was measured, suggesting for the first time that the H atoms of benzene engage in hydrogen bonding. The result compares well with values extrapolated from data for polyfluoro- but not polychlorobenzenes, again probably because of buttressing in the latter.

INTRODUCTION

A wide variety of compounds participate in C—H hydrogen bonding, encompassing alkyl, vinylic, aromatic and acetylenic hydrogens; certain electronegative substituents must usually be present.[1] To date, the only hydrocarbons known to serve as proton donors in hydrogen bonding are terminal alkynes.

Previously we measured C—H hydrogen bond strengths with the strong acceptor hexamethylphosphoric triamide (HMPA) by PMR spectroscopy[2] using the Higuchi method.[3] We found that formation constants, K, as calculated do not correlate with shifts in the fundamental infrared stretching frequencies of the corresponding C—H bonds nor, in the aliphatic series, with inductive substituent constants. α-Cyano and -nitro groups facilitate hydrogen bonding far more than halogens. Significant K values are also observed for benzenes and terminal alkynes, molecules which cannot have an α-substituent. The relative effectiveness of F and Cl substituents depends on their location and

the type of compound in which they occur: α-Cl is more effective at sp³-hybridized carbon, whereas β-F is more effective at sp²-hybridized carbon, as in halobenzenes.

Several other quantitative studies of C—H hydrogen-bonding have appeared. Dale[4] reported K and ΔH values, calculated by the Higuchi method, from PMR data for chloroform and pentafluorobenzene with HMPA in CCl4 (cf. Table 1). Both K values at 35 °C are in excellent agreement with those reported, both previously and in this paper. The ΔH values are −2·7 and −1·7 kcal mol⁻¹, respectively. LeNours *et al.*,[5] using infrared spectroscopy, measured K (l mol⁻¹) for the acceptor dimethyl sulfoxide (DMSO) in CCl4 at 25 °C with 2,3,5-tribromothiophene (0·3), trichloroethylene (0·4), pentafluoro- and pentachlorobenzene (both 0·6) and 3-nitro-1,2,4,5-tetrachlorobenzene (0·7). Their values are of a reasonable order of magnitude, but larger than our values with HMPA,[2] even though DMSO is a weaker acceptor than HMPA.[6] Domke and Lippert[7] applied a statistical method to PMR shifts to estimate hydrogen bonding energies for all the polychlorobenzenes that have three or more Cl atoms, in the presence of HMPA

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in CCl₄. Complex formation appears to be more strongly enhanced by *meta-* than *para*-Cl, but impeded by *ortho*-Cl. Murdoch and Streitwieser,[8] using both infrared and PMR spectroscopy, obtained $K = 0.36 \pm 0.12 \, l\,mol^{-1}$ for pentafluorobenzene and pyridine-d_5 in CCl₄. In the absence of CCl₄, K rose to about $1.7 \, l\,mol^{-1}$. Finally, Miura *et al.*[9] determined K values for association of both CHCl₃ and CHBr₃ with tetrabutylammonium chloride in four different solvents at $22.2\,^\circ C$ using NMR methods. The K values are closely similar for the two compounds, and those in CCl₄ are the same as measured at $35\,^\circ C$ with HMPA.[2]

Previous efforts[2] to measure K for certain compounds, viz. 3,3-dimethylbut-1-yne and 1,3,5-trichlorobenzene, with HMPA in CCl₄ were unsuccessful because changes in δ_{obs}, the proton chemical shift, were small and scattered. This contrasts with the reported measurement of K for other alkynes and tetra- and pentahalobenzenes.[2,4] However, both compounds must form hydrogen bond complexes with strong acceptors, since both show sizable shifts (82 and 27 cm⁻¹, respectively) of their C–H stretching bands in the presence of DMSO-d_6.[2] Therefore, a way of measuring their K values by PMR should exist. Indeed, in agreement with other reports,[3,10] K is usually[2] 4–5 times greater in cyclohexane than in CCl₄. (CCl₄ may suppress K values by competing with HMPA for the proton donor, whereas cyclohexane, lacking lone pairs, presumably does not. Alternatively, a solvent effect may be operating.) Whatever the origin of this effect, it may well cause K for the two donors in question, and many others, to be large enough to measure in cyclohexane.

We decided to measure complex formation constants of a series of substituted terminal alkynes and polyhalobenzenes with HMPA in cyclohexane by PMR. The absence of CCl₄ enhanced the chemical shifts, and we

succeeded in measuring K for four alkynes and in separating the effects of *ortho*, *meta* and *para* substituents. We also attempted to measure for the first time the benzene–HMPA formation constant. The result is compared with values extrapolated from those for the polyhalobenzenes.

RESULTS

Measurement of formation constants, K

The Higuchi iterative method[3] was used to caculate both K and $\delta_c - \delta_a$, the limiting shift, from equation (1). This method is particularly useful for identifying and eliminating deviant data points.

$$\frac{C_b}{\delta_{obs} - \delta_a} = \frac{C_a + C_b - C_c}{\delta_c - \delta_a} + \frac{1}{K(\delta_c - \delta_a)} \quad (1)$$

where C_a and C_b are total concentrations of donor ('acid') and acceptor ('base,' i.e. HMPA), respectively, C_c is the equilibrium concentration of the hydrogen bond complex, δ_{obs} is the chemical shift at equilibrium, δ_c and δ_a are the chemical shifts of the fully formed complex and free donor, respectively, and K is the formation constant. The Higuchi equation is derived exclusively for 1 : 1 complex formation. The problem of 2 : 1 complex formation by donors with two or more equivalent protons is discussed below.

Solvent effects and small K

If K is smaller than *ca* $0.5 \, l\,mol^{-1}$ as measured by the Higuchi method, K becomes the lower limit to the 'true' K.[2] In the Higuchi method $K = slope/intercept$. When K is small, δ_{obs} is small and strongly affected by miscellaneous solvent effects. The left-hand side of

Table 1. Formation constants in CCl₄ vs cyclohexane at $35\,^\circ C$[a]

Donor (Registry No.)	K (l mol⁻¹) in		Ratio, $\dfrac{K(CH)}{K(CCl_4)}$	$\delta_c - \delta_a$ (ppm)	
	CCl₄	CH[b]		CCl₄	CH[b]
Br₂CHCN(3252-43-5)	16·8	71	4·2	2·22	2·39
CHCl₃ (67-66-3)	2·4	12·0	5·0	1·79	1·90
	2·36[c]			1·80[c]	
C₆HF₅ (363-72-4)	0·53[c]	2·2[d]	4·2	2·13	1·94
1,2,3,4-C₆H₂Cl₄[d](634-66-2)	0·54	2·1	3·9	0·87	0·82
C₆HCl₅(608-93-5)	0·09	0·68	7·5	3·2	1·58
C₆H₅C≡CH(536-74-3)	0·15	1·0	6·7	4·1	2·1

[a] From Ref. 2, except as noted.
[b] CH = cyclohexane.
[c] Ref. 4.
[d] This work.

equation (1) increases too slowly, the slope is too small and the intercept is too large. As a result, the measured K is too small and the measured limiting shift is too large.

The data in Table 1 illustrate these trends for six donors in CCl_4 and cyclohexane. For Br_2CHCN and $CHCl_3$, which show $K > 1 \cdot 0 \, l \, mol^{-1}$ in CCl_4, the K values in cyclohexane are 4–5 times those in CCl_4, while values of $\delta_c - \delta_a$ in the two solvents differ by less than 10%. For pentafluorobenzene and 1,2,3,4-tetrachlorobenzene the K values are likewise ca four times as great in cyclohexane as in CCl_4, while the $\delta_c - \delta_a$ values are again only slightly different. For pentachlorobenzene and phenylacetylene, however, the K values in cyclohexane are ca seven times those in CCl_4, and the $\delta_c - \delta_a$ values are twice as great in CCl_4. For small K, then, as measured by PMR in a given solvent, quantitative comparisons may lack rigor.

Effect of water on K

Water is a strong proton donor and would certainly alter the concentration of free HMPA. The water content of a freshly opened bottle of HMPA was found by gas–liquid chromatography (GLC) to be ca $0 \cdot 2$ mol-%, and 9 months later was still less than $1 \cdot 0$ mol-%. The K values for polyhalobenzenes and for chloroform measured using this material agreed well with earlier values, particularly for donors containing only one proton, or for which 2 : 1 complexing could be ruled out. For example, K for chloroform and HMPA was $2 \cdot 31$, comparing very favorably with published values of $2 \cdot 35^2$ and $2 \cdot 36;^4$ K for pentachlorobenzene was $0 \cdot 77 \pm 0 \cdot 01$ (mean of two runs), while $0 \cdot 69$ had been obtained previously.[2] The agreement was unexpected because the water content had been found[2]

by Karl Fischer titration to be 2–6 mol-%. These results may mean that the Fischer results were in error.

K for 1,2,3,4-tetrachlorobenzene was $2 \cdot 10 \pm 0 \cdot 08$ (mean of five runs). However, addition of ca 6 mol-% water to HMPA resulted in a decrease in K to $1 \cdot 17 \pm 0 \cdot 02$. Hence, the presence of water in HMPA can be critical, but with the samples available evidently is not.

The amount of water present in spectroscopic-grade cyclohexane, and presumably CCl_4, had no effect on the K values for C—H hydrogen bonding with HMPA. Identical K values, within the experimental precision, were obtained for 1,2,3,4-tetrachlorobenzene with HMPA in cyclohexane, whether this solvent had been dried over Type 3A molecular sieves or not. The K values were $2 \cdot 02 \pm 0 \cdot 03$ and $2 \cdot 06 \pm 0 \cdot 02$, respectively; these are also indistinguishable from the mean value given above.

Terminal alkynes

Formation constants for phenylacetylene and three other alkynes in CCl_4 were reported earlier.[2] Values for 3,3-dimethylbut-1-yne (tert-butylacetylene) and ethoxyacetylene have now been measured in cyclohexane, and are given in Table 2. The formation constants decrease in the order NC— > $BrCH_2$— > C_6H_5— > C_2H_5O— > tert-Butyl—. The inductive substitutent constants,[11] σ_I, however, decrease in the order NC— > C_2H_5O— > $BrCH_2$— > C_6H_5— > tert-Butyl— (Cf. Table 2). Ethoxy shows a much smaller K than is consistent with its inductive constant. The reason is probably lone pair p–π conjugation with the triple bond. With this exception, K values correlate well with σ_I.

Table 2. Formation constants of alkyne–HMPA complexes at $35 \, ^\circ C^a$

Alkyne: R in RC≡CH (Reg. No.)	Concentration (M) [AH]	Concentration (M) [HMPA]	Solvent[b]	No. of points	σ_I	K (l mol⁻¹)	$\delta_c - \delta_a$ (ppm)	Source
$(CH_3)_3C$— (917-92-0)	0·25	0·4–1·0	CH	6	−0·07	0·44 ± 0·02	1·68 ± 0·07	This work
C_2H_5O— (927-80-0)	0·3	1·5–3·2	CH	7	0·27[d]	0·60 ± 0·03	1·92 ± 0·02	This work
C_6H_5— (536-74-3)	0·2	0·2–1·8	CH	6	0·10	1·00 ± 0·01	2·07 ± 0·01	This work
	0·2	0·2–1·7	CCl_4	7	0·10	0·15 ± 0·01	4·07 ± 0·16	Ref. 2
$BrCH_2$— (106-96-7)	—	—	CH	—	0·10	2·12	—	Est.[e]
	0·08	0·6–1·4	CCl_4	5	0·16[f]	0·53	2·1	Ref. 2
NC— (1070-71-9)	—	—	CH	—	0·16[f]	48·4	—	Est.[e]
	0·08	0·3–1·0	CCl_4	7	0·56	12·1	3·08	Ref. 2

[a] NMR method: CW at 60 MHz.
[b] CH = Cyclohexane.
[c] Source: Ref. 11.
[d] For methoxy.
[e] From K in CCl_4, assuming K in cyclohexane is four times greater.
[f] From $\sigma_I = 0 \cdot 44$ for Br, dividing by $2 \cdot 8$.

Polyhalobenzenes

Measured values of K in cyclohexane for a variety of polychloro- and polybromobenzenes with HMPA are presented in Table 3, together with published results for comparison. A value for benzene is included.

Formation constants were also 'statistically corrected' by dividing by the number of equivalent hydrogens, and the results are listed in Table 3 as K/H. This procedure is essential for comparing K values for compounds with differing numbers of equivalent hydrogens. The presence of two or more equivalent hydrogens multiplies the probability of complex formation, an entropy effect which is of no interest in itself.

For 1,2,3,4-tetrachlorobenzene, data were obtained at three temperatures, 35, 45 and 55 °C, and ΔH was found to be $-3 \cdot 6 \pm 0 \cdot 2$ kcal mol^{-1}. Chemical shifts for 1,2,3-trichlorobenzene were measured at 360 MHz (see Experimental); K values were extrapolated from 300 to 308 K using the above ΔH value.

K for 1,3,5-tribromo-2,4-dimethylbenzene could not be measured because its chemical shift was virtually insensitive to added HMPA. Substitution of methyl groups for two of the three Hs in 1,3,5-tribromobenzene had been expected both to prevent higher order complexing and to increase observed shifts.

Results for polyfluorobenzenes are given in Table 4. These are less precise, probably because of extensive splitting of their proton signals by ^{19}F. Data in CCl$_4$ are included where the measurements are sufficiently precise. Formation constants in Table 4, as in Table 3, are also listed on a per hydrogen basis as K/H.

Table 3. K values for polychloro- and polybromobenzenes with HMPA at 35 °C

| | | Concentration (M) | | | NMR | | K/H | $\delta_c - \delta_a$ |
Donor, AH (Registry No.)	No. of points	[AH]	[HMPA]	Solvent[a]	method	K (l mol^{-1})	(l mol^{-1})	(ppm)
C$_6$HCl$_5$(608-93-5)	7	0·05	0·5–2·0	CH	CW	0·69		1·57
	5	0·2	0·2–1·7	CH	FT	0·77 ± 0·01	0·77[b]	1·53 ± 0·02
C$_6$HBr$_5$(608-90-2)	3	0·1	2·2–4·2	CH	CW	0·060 ± 0·002	0·06	2·57 ± 0·10
1,2,3,4-C$_6$H$_2$Cl$_4$(634-66-2)	7	0·1	0·5–2·5	CH	CW	2·20 ± 0·13		0·82 ± 0·01
	6	0·2	0·2–2·7	CH	FT	2·19 ± 0·06	1·05[c]	0·81 ± 0·01
	7	0·08	0·1–1·8	CH	FT	2·06 ± 0·04		0·836 ± 0·006
	7	0·08	0·1–1	CH	FT	1·73 ± 0·03[d]		0·828 ± 0·006[d]
	7	0·08	0·1–1	CH	FT	1·44 ± 0·02[e]		0·836 ± 0·007[e]
	6	0·2	0·2–2·6	CCl$_4$	FT	0·54 ± 0·01	0·27	0·87 ± 0·01
1,2,3,5-C$_6$H$_2$Cl$_4$(634-90-2)	6	0·1	0·8–2·6	CH	CW	0·40 ± 0·02		1·19 ± 0·04
	6	0·05	0·1–0·6	CH	CW	0·76 ± 0·02	0·38[f]	0·82 ± 0·02
	4	0·1	1·3–2·3	CH	CW	0·47 ± 0·02[g]		1·10 ± 0·03[g]
1,2,4,5-C$_6$H$_2$Cl$_4$(95-94-3)	5	0·1	0·7–1·8	CH	CW	0·59[h]		1·02[h]
	5	0·05	0·1–1·5	CH	FT	0·93 ± 0·03	0·47	0·76 ± 0·02
1,2,4,5-C$_6$H$_2$Br$_4$(636-28-2)	6	0·05	1·0–3·6	CH	CW	0·57 ± 0·02		0·67 ± 0·01
1,3,5-C$_6$H$_3$Cl$_3$(108-70-3)	5	0·1	0·5–2·5	CH	CW	0·34 ± 0·01		0·75
	6	0·06	0·2–1·2	CH	FT	0·62 ± 0·02	0·21	0·55 ± 0·02
1,3,5-C$_6$H$_3$Br$_3$(626-39-1)	5	0·1	0·5–2·5	CH	CW	0·42 ± 0·05		0·53
	7	0·06	0·2–1·5	CH	FT	0·68 ± 0·02	0·23	0·41 ± 0·01
1,2,3-C$_6$H$_3$Cl$_3$(87-61-6):								
H-5	7	0·15	0·2–1·0	CH	FT[i]	1·74 ± 0·02[j]	1·49[k]	0·755 ± 0·004[j]
H-4,6	7	0·15	0·2–1·0	CH	FT[i]	1·41 ± 0·04[j]	0·60[k]	0·504 ± 0·010[j]
1,4-C$_6$H$_4$Cl$_2$(106-46-7)	7	0·13	0·3–1·7	CCl$_4$	FT	0·23 ± 0·02	0·05	0·50 ± 0·04
	7	0·13	0·3–1·6	CH	FT	0·90 ± 0·03	0·23	0·46 ± 0·01

[a] CH = cyclohexane.
[b] Mean of 2 runs.
[c] Mean of 5 runs.
[d] At 45·0 ± 0·5 °C.
[e] At 55·0 ± 0·5 °C.
[f] Mean of 3 runs.
[g] Highest concentration points of a run of 7 points; original plot concave down.
[h] Source: Ref. 2.
[i] At 360 MHz.
[j] Run conducted at 300 K (27 °C).
[k] Extrapolated from 300 to 308 K, assuming $\Delta H^0 = -3 \cdot 6$ kcal mol^{-1}.

Table 4. K values for polyfluorobenzenes with HMPA at 35 $^\circ$C

| Donor, AH (Registry No.) | No. of points | Concentration (M) | | Solvent[a] | NMR method | K (l mol^{-1}) | $K/$H (l mol^{-1}) | $\delta_c - \delta_a$ (ppm) |
		[AH]	[HMPA]					
C$_6$HF$_5$(363-72-4)	8	0·2	0·2–1·6	CCl$_4$	FT	0·56 ± 0·01	0·50[b]	2·20 ± 0·03
	3	0·3	0·4–1·7	CH	CW	2·15 ± 0·32	2·15	1·94 ± 0·10
1,2,3,4-C$_6$H$_2$F$_4$(551-62-2)	7	0·1	0·1–0·5	CCl$_4$	FT	0·76 ± 0·04	0·38	0·82 ± 0·04
	8	0·14	0·2–2·7	CCl$_4$	FT	0·71 ± 0·02		0·85 ± 0·02
	4[c]	0·14	0·2–1·1	CCl$_4$	FT	0·78 ± 0·01		0·80 ± 0·01
1,2,3,5-C$_6$H$_2$F$_4$(2367-82-0)	5	0·2	0·2–1·4	CCl$_4$	FT	0·13 ± 0·02	0·065	2·40 ± 0·26
	4[d]	0·3	1·7–3·2	CH	CW	0·73 ± 0·05		1·61 ± 0·05
	4[d]	0·3	1·0–1·7	CH	CW	1·11 ± 0·03	0·56	1·37 ± 0·02
1,2,4,5-C$_6$H$_2$F$_4$(327-54-8)	5	0·05	0·3–1·0	CCl$_4$	CW	0·45 ± 0·01[e]		1·27[e]
	6	0·1	0·1–0·5	CCl$_4$	CW	0·64 ± 0·05	0·32	1·01 ± 0·07
	3	0·02	0·1–0·3	CH	CW	2·6[e]	1·3	1·11[e]
	7	0·2	0·2–1·2	CH	FT	1·38 ± 0·03		1·64 ± 0·02
1,3,5-C$_6$H$_3$F$_3$(372-38-3)	4	0·15	0·6–2·0	CH	CW	0·57 ± 0·05		0·86 ± 0·06
	3[f]	0·15	0·6–1·5	CH	CW	0·67 ± 0·05	0·22	0·77 ± 0·04
1,4-C$_6$H$_4$F$_2$(540-36-3)	5	0·4	1·1–3·2	CH	CW	0·70 ± 0·02	0·18	0·53 ± 0·01

[a] CH = cyclohexane.
[b] Mean of 2 runs.
[c] First four points of preceding run; plot of all 8 points is curved, concave down.
[d] From set of 7 points giving a curved plot, concave down; one point common to both entries.
[e] Source: Ref. 2.
[f] First three points of preceding run; four points give a curved plot, concave down.
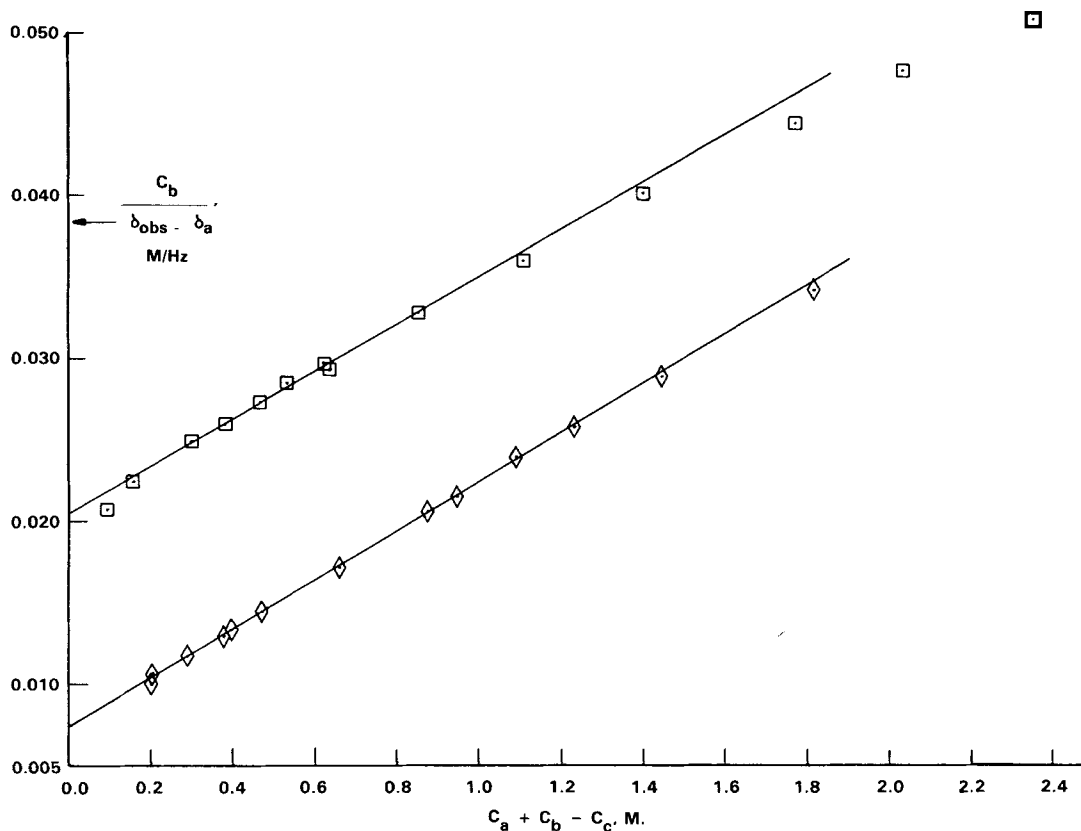

Figure 1. Higuchi plots for association of tetrachlorobenzenes with HMPA in cyclohexane. $\diamond$, 1,2,3,4-Isomer, $K = 2\cdot06$ lmol^{-1}, $\delta_c - \delta_a = 0\cdot84$ ppm; $\square$, 1,2,3,5-isomer, $K = 0\cdot76$ lmol^{-1}, $\delta_c - \delta_a = 0\cdot82$ ppm (from low concentration points)

Benzene

The measured formation constant, $0 \cdot 17 \, \mathrm{l \, mol}^{-1}$, is small (see above), so the true value is probably closer to $0 \cdot 3$ and K/H close to $0 \cdot 05 \, \mathrm{l \, mol}^{-1}$. The largest shift was only 8 Hz, and modest scatter obscured any curvature due to 2 : 1 complex formation (see below).

2 : 1 Complex formation by polyhalobenzenes

Since the Higuchi method applies only to 1 : 1 complex formation, data for donors having two equivalent protons will be meaningful only if 2 : 1 complex

formation can be ruled out. Higher order complex formation increases δ_{obs} further, causing the left-hand side of equation (1) to increase too slowly. The Higuchi plot becomes concave downward, particularly at higher concentrations of HMPA, where the limiting shift (the reciprocal of the slope) becomes too large. Measured K values thus increase as [HMPA] *decreases*, and should approach limiting values. Malononitrile and fumaronitrile are cases in point.[2]

Measurements for the tetrahalobenzenes and 1,3,5-trichlorobenzene were undertaken in the lowest practical range of [HMPA]. Figures 1 and 2 show
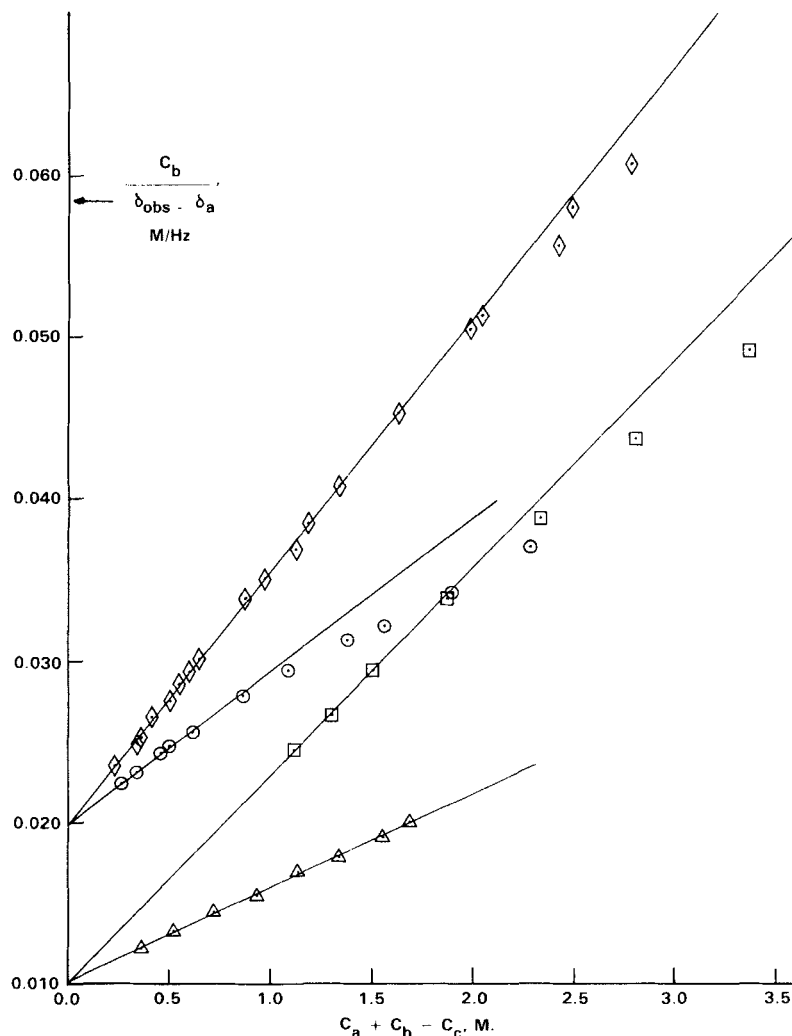

Figure 2. Higuchi plots for association of polyfluorobenzenes with HMPA. Δ, C_6HF_5 in CCl_4, $K = 0 \cdot 56 \, \mathrm{l \, mol}^{-1}$, $\delta_c - \delta_a = 2 \cdot 20$ ppm; □, 1,2,3,5-$C_6H_2F_4$ in cyclohexane, $K = 1.11 \, \mathrm{l \, mol}^{-1}$, $\delta_c - \delta_a = 1 \cdot 37$ ppm (from low concentration points); ○, 1,2,3,4,-$C_6H_2F_4$ in CCl_4, $K = 0.64 \, \mathrm{l \, mol}^{-1}$, $\delta_c - \delta_a = 1 \cdot 01$ ppm (from low concentration points); ◇, 1,2,3,4,-$C_6H_2F_4$ in CCl_4, $K = 0.71 \, \mathrm{l \, mol}^{-1}$, $\delta_c - \delta_a = 0.85$ ppm

typical Higuchi plots for most of the tetrahalobenzenes studied, and also for pentafluorobenzene. The plot for pentafluorobenzene is strictly linear, as expected. Those for the 1,2,3,5- and 1,2,4,5-tetrahalobenzenes are clearly curved at high [HMPA], whereas those for the 1,2,3,4-isomers are only slightly curved. Except for 1,2,3,4-tetrachlorobenzene, K was indeed higher at lower [HMPA], and the limiting shifts were smaller. For all isomers, K remained constant for [HMPA] below $1 \cdot 0$ M, consistent with $1:1$ complex formation. The plot for 1,3,5-trichlorobenzene was also curved, and K nearly doubled when measured at lower [HMPA].

K for 1,2,3,4-tetrachlorobenzene in CCl_4 was almost exactly one quarter of that in cyclohexane, consistent with the K values being correct and uncomplicated by $2:1$ complex formation. The limiting shift for 1,2,3,4-tetrafluorobenzene was the lowest of the three isomers, close to the lowest values observed for the tetrachloro analogs. We conclude that $2:1$ complexing is also negligible in this case. The shifts for 1,2,3,5- and 1,2,4,5-tetrafluorobenzenes were much larger, consistent with some $2:1$ complexing. The limiting shifts for 1,2,3,5-tetrafluoro- and pentafluorobenzene were very large because of relatively low K values (see above).

The limiting shifts of the 1,3,5-trihalobenzenes are similar and approximately one third of those for the pentahalobenzenes. The limiting shifts of the tetrachlorobenzenes at low [HMPA] are all nearly half of that for pentachlorobenzene. Such relationships would be expected if the shifts for complexed aromatic protons were all alike, while those for uncomplexed protons in the same molecules were essentially unaffected.

Overall, the evidence is strong for the tetrachlorobenzenes and suggestive for the tetrafluorobenzenes that the 1,2,3,4-isomers undergo negligible $2:1$ complexing with HMPA, and that their measured K values are correct. In contrast, the 1,2,3,5- and 1,2,4,5-isomers do appear to form $2:1$ complexes, but the true K values for $1:1$ complexing of the tetraclorobenzenes have been closely approached. In the following analysis it must be borne in mind that the true K values of the tetrafluorobenzenes and the 1,3,5-trihalobenzenes may not have been reached.

DISCUSSION

Effects of chlorine and bromine

For the chloro- and bromobenzenes the K values are generally smaller than those for the corresponding fluorobenzenes, but the difference is small for the 1,3,5-trihalobenzenes. Thus, the halobenzenes *appear* to show behavior opposite to that of the few aliphatic compounds examined to date, the dihaloacetonitriles,

where replacement of Cl by F *decreases K* (however, we have found K for 1,1,1-trifluoro-2-bromo-2-chloroethane to be[12] $2 \cdot 5$ times greater than for pentabromoethane,[12] showing the effect of β-F to be opposite to that of α-F in C—H hydrogen bonding.) Evidently aliphatic α-F is unable to exert on the hydrogen bond complex a stabilizing effect in keeping with its high electronegativity and the fact that it shows the largest σ value of all the halogens. This may be attributed to the nearness and hardness of the α-F lone pairs, in contrast to those of α-Cl and α-Br.

Chloro and bromo analogs show virtually identical K values under identical conditions, except for pentabromobenzene, where $K = 0 \cdot 06$ $1 mol^{-1}$, only one tenth of the value for pentachlorobenzene. The correct value is likely to be in excess of $0 \cdot 10$ $1 mol^{-1}$ (see above).

K/H is smaller for 1,2,4,5- and 1,2,3,5-tetrachlorobenzenes than for pentachlorobenzene, in agreement with Domke and Lippert's finding that *meta*- and *para*-chlorines facilitate hydrogen bonding.[7] However, K/H is significantly *greater* for 1,2,3,4-tetrachlorobenzene than for pentachlorobenzene, and K for H-5 of 1,2,3-tetrachlorobenzene, which has no Cl atoms *ortho* to it, is even greater. Clearly, *ortho*-chlorines in the isomers studied hinder hydrogen-bonding, again in agreement with Domke and Lippert.[7] They assigned a polar origin to the *ortho* effect: the C—Cl dipole is in the opposite direction relative to those of *meta* and *para* C—Cl bonds. This effect should then be greater for F than for Cl, a conclusion not supported by our data (see below).

A series of apparently self-consistent substituent factors or s_x values can be calculated from ratios of formation constants for certain polyhalobenzenes [equation (2)]. [These are analogous to $K(X)/K(H)$ for ionization of substituted benzoic acids, the decadic logarithms of which are, of course, the Hammett substituent constants; we compare log s_x values with Hammett constants below.] The procedure is illustrated for p-Cl. The value of s_p is obtained from the formation constant ratio of pentachlorobenzene to 1,2,4,5-tetrachlorobenzene, representing replacement of H by Cl in the *para* position:

$$s_p = K(C_6HCl_5)/ [K(1,2,4,5-C_6H_2Cl_4)/2]$$

$$= 0 \cdot 77/0 \cdot 47 = 1 \cdot 6_4 \quad (2)$$

Similarly, data for pentachloro- and 1,2,3,5-tetrachlorobenzene give $s_{m2} = 2 \cdot 0$, while data for pentachloro- and 1,3,5-trichlorobenzene give $s_{m2} \times s_{m1} = 3 \cdot 7$, so that $s_{m1} = 1 \cdot 8$. Finally, data for 1,2,3,4-tetrachlorobenzene and H-5 of 1,2,3-trichlorobenzene give $s_{o2} = 0 \cdot 73$ and $s_{o1} = 0 \cdot 71$. These last two are identical within the experimental precision. The s_x values are given in Table 5.

These s_x values are applicable to other polychlorobenzenes, e.g. to estimate K for Hs at positions 4 and

Table 5. Substituent factors s_x in aromatic C—H hydrogen bonding

| Ring position | Sources | | | s_x [b] | Log s_x | σ |
| | K/H (l mol^{-1})[a] | | Other | | | |
	C_6HX_5	$C_6H_iX_6{}^{-i}$				
Br in Cyclohexane solution:						
para	0·06	0·3	—	$s_p = 0\cdot2$	$(-0\cdot7)$	0·23
Cl in cyclohexane solution:						
ortho	0·77	1·05	—	$s_{o2} = 0\cdot73$	$-0\cdot14$	$(1\cdot28)^c$
ortho	0·77	1·49	s_{o2}	$s_{o1} = 0\cdot71$	$-0\cdot15$	$(1\cdot28)^c$
meta	0·77	0·38	—	$s_{m2} = 2\cdot0_2$	0·30	0·37
meta	0·77	0·21	s_{m2}	$s_{m1} = 1\cdot8_2$	0·26	0·37
para	0·77	0·47	—	$s_p = 1\cdot6_4$	0·21	0·23
F in cyclohexane solution:						
ortho	2·2	1·5^d	—	$s_{o2} = 1\cdot5$	0·18	$(0\cdot93)^c$
meta	2·2	0·56	—	$s_{m2} = 3\cdot9$	0·59	0·34
meta	2·2	0·22	s_{m2}	$s_{m1} = 2\cdot6$	0·41	0·34
para	2·2	1·3	—	$s_p = 1\cdot7$	0·23	0·06
F in CCl$_4$ solution:						
ortho	0·50	0·38	—	$s_{o2} = 1\cdot3$	0·11	$(0\cdot93)^c$
meta	0·50	0·10^e	—	$s_{m2} = 5\cdot0$	0·70	0·34
para	0·50	0·32	—	$s_p = 1\cdot6$	0·20	0·06

[a] Cf. Tables 3 and 4.
[b] s_{o2} is the effect of adding a second *ortho*-halogen when one is already present; s_{o1} is the effect of adding the first *ortho* halogen; see text.
[c] $pK_a(C_6H_5CO_2H) - pK_a(o\text{-}XC_6H_5CO_2H)$.
[d] Estimated assuming K/H in cyclohexane is four times K/H in CCl$_4$.
[e] Estimated; measured $K/H \ll 0\cdot5$ l mol^{-1}; see text.

6 of 1,2,3-trichlorobenzene. This compound can be compared with pentachlorobenzene by removing one *ortho*-Cl and the adjacent *meta*-Cl, and $K/H = 0\cdot77/(0\cdot7 \times 2\cdot0) = 0\cdot55$ l mol^{-1}. The measured value of K/H, extrapolated to 308 K, is $0\cdot60$ l mol^{-1}. The excellent agreement also suggests that 2:1 complexing by H-4 and H-6 is negligible.

Effect of fluorine

Pentafluorobenzene shows a larger K/H than all other polyfluorobenzenes, including 1,2,3,4-tetrafluorobenzene. Substitution of F at *any* position thus increases K/H.

Substituent factors are not as easy to calculate as for Cl because of the uncertainty and precision of several of the K values and the fact that K for pentafluorobenzene is *ca* $0\cdot5$ l mol^{-1}. The series of s_x values in Table 5 are based on $K(C_6HF_5) = 2\cdot2$ in cyclohexane and $0\cdot50$ in CCl$_4$; the latter is the mean of our two determinations, and is close to Dale's value.[4]

Despite their uncertainties, these s_x values suggest that F is most effective in facilitating hydrogen bonding when *meta*, not *ortho*, to an H, in agreement with Domke and Lippert's findings for polychlorobenzenes.[7] The small effect of the second *ortho*-F probably results from the opposition of two factors: polarity probably

promotes hydrogen bonding, while the size of F inhibits approach of HMPA to the proton.

Measurement of a value of s_{o1} will require the study of 1,2,3-trifluorobenzene, whose H at C-5 has no *ortho*-F neighbors. The complex PMR spectrum of this molecule[13] will require decoupling of the Fs.

The above s_x values may be used to predict K/H for any additional polyfluorobenzene. To obtain K/H for *p*-difluorobenzene, one *ortho*- and one *meta*-F are removed from 1,2,4,5-tetrafluorobenzene, decreasing K/H by the factor $s_{o2} \times s_{m2} = 1\cdot5 \times 3\cdot9 = 5\cdot9$. K/H in cyclohexane should be $1\cdot3/5\cdot9 = 0\cdot22$ l mol^{-1}, which is reasonably close to the measured value of $0\cdot18$ l mol^{-1}.

The s_x values for F and Cl will be compared with Hammett σ values after the following discussion of steric effects.

Steric effects

The K values for chloro- and bromobenzenes reflect two sizable steric effects. First, a pair of *ortho*-Cl or -Br atoms sterically hinder the approach of the O atom of an HMPA molecule. Second, buttressing, deformation of C—C—X bond angles by bulky neighboring atoms,[14] brings the *ortho*-chlorines or -bromines even closer to the proton and to the Lewis base. This effect should increase with increasing size of the halogen

substituent. Steric hindrance, aggravated by buttressing, explains the fact that 1,3,5-tribromo-2,4-dimethylbenzene showed virtually no change in its chemical shift even in 2·0 M HMPA (in CCl₄). Buttressing should be severe in pentabromobenzene, but unimportant in the 1,2,4,5-tetrahalo- and 1,3,5-trihalobenzenes.

The buttressing hypothesis is supported by the modest amount of available x-ray diffraction data. Hexafluorobenzene is planar within ±0·01 Å, according to Boden *et al.*[15] Hexachloro-[16] and hexaiodobenzene,[17] however, display deviation of halogen atoms alternately above and below the ring plane: Cl atoms deviate by 0·014–0·020 Å and I atoms deviate by *ca* 0·04 Å. Marsh and Williams' study of pentachlorobenzene[18] also showed deviations of Cl atoms. Unexpectedly, Cl-1 and Cl-4, not Cl-5, lie above the plane, while Cl-2 and Cl-5 lie below the plane, and Cl-3 lies within ±0·005 Å of the ring plane; the deviations range from 0·025 to 0·039 Å. Moreover, the C-1−C-6 and C-5−C-6 bonds are shorter than the other four by nearly 0·03 Å (1·363 Å vs a mean of 1·391 Å). Presumably the latter effect will bring the *ortho*-Cl atoms closer to the H atom, thus blocking a base molecule more severely. Similar deformation and bond shortening are likely in pentabromobenzene, thus explaining the larger differences among our *K* values for C_6HX_5 molecules than 1,2,4,5-tetrahalo- or 1,3,5-trihalobenzenes. Finally, 1,3,5-tribromo-2,4-dimethylbenzene, which hydrogen bonds negligibly to HMPA, experiences strong buttressing but lacks the crucial *meta*-bromines of pentabromobenzene.

A second steric effect, not involving buttressing, is discernible in the absence of 2 : 1 complex formation with the donors having two *ortho*-H atoms, viz. the 1,2,3,4-tetrahalobenzenes. In a 2 : 1 complex two HMPA molecules would have to be prohibitively close together.

Comparison of s_x with Hammett σ

To facilitate this comparison, Table 5 includes log s_x values, σ_m and σ_p values, and 'σ_o' values calculated from pK_a values of ortho-substituted benzoic acids.

Clearly no correlation exists between log s_x and σ, and should not, because of the well known sensitivity of reactions of *ortho*-substituted compounds to steric effects. Although the strengthening of benzoic acids by *ortho*-halogens is not attenuated by their steric bulk, we have seen that aromatic C−H hydrogen bonding is.

Log s_m and log s_p values also fail to correlate with Hammett σ values: those for Cl are smaller than σ, whereas those for F are larger. This inconsistency again reflects steric effects, which are larger for Cl than F. When *m*-Cl is substituted, for example, in 1,2,3,5-tetrachlorobenzene, a buttressing effect attenuates an expected large polar effect. With F, the buttressing

effect is smaller or absent, and a larger polar effect is observed.

Estimation of K/H for benzene

Our measurement of K for benzene strongly suggests that benzene represents a second class of hydrocarbons, in addition to the terminal alkynes, which undergoes C−H hydrogen bonding. This is not surprising, in view of hydrogen bonding by polyhalobenzenes. To gain an insight into whether the measured K is 'reasonable,' we calculated K/H by extrapolation from K/H values for polyhalobenzenes, using the s_x values derived above. For example, for polychlorobenzenes in cyclohexane,

$$K/H(C_6H_6) = K(H\text{-}5)(1,2,3\text{-}C_6H_3Cl_3)/(s_{m2} \times s_{m1} \times s_p)$$
$$= 1·49/(2·02 \times 1·82 \times 1·64)$$
$$= 0·25 \, \text{l mol}^{-1} \tag{3}$$

K for benzene would then be 1·50 l mol⁻¹ for all six positions. Other polychlorobenzenes give virtually identical estimates, as expected, because the same s_x values are used repeatedly. This large estimate is clearly inconsistent with the measured value.

An analogous estimate using polyfluorobenzenes gives a much smaller estimate of K/H = 0·05 l mol⁻¹, which is much closer to the measured value. The discrepancy between the two extrapolated values of K/H is serious, and must be explained if this evidence for C−H hydrogen bonding by benzene is to be taken seriously.

The key is again likely to be the buttressing effect. With all the polychlorobenzenes studied except 1,3,5-trichlorobenzene, two or more chlorines occupy adjacent positions. When one chlorine is substituted into 1,3,5-trichlorobenzene, the product has chlorines in *three* consecutive positions, introducing strong buttressing which counteracts a favorable polar effect. We have already argued that this is why s_m is so much smaller for Cl than F (and why $s_o < 1·0$ for Cl). The present data by no means show that the same value of s_{m2} would be obtained by comparing H-5 of 1,2,3-trichlorobenzene with H-4 (and H-5) of 1,2-dichlorobenzene, nor the same value of s_{o2} by comparing the 1,3,5-trichloro isomer with H-4 (and H-6) of 1,3-dichlorobenzene. It is very likely that *larger* values of s_{m2} and s_{o2} would result. These would bring the extrapolated value of K/H for benzene into line with those from polyfluorobenzenes and from experiment. These experiments might be readily performed at high field, or if first-order spectra could not be obtained, with deuterium-labeled polychlorobenzenes.

CONCLUSIONS

The interaction of polyhalogenated benzenes with the very strong Lewis base HMPA meets two of the most

important tests of hydrogen bonding proposed by
Pimentel and McClellan [1a] and others, viz. a shift of the
fundamental stretching frequencies [1b,2,5,7] of their
C—H bonds and downfield shifts of their proton
resonances in PMR.[2,4,6,7] We have no illusions that
these hydrogen bond interactions are strong. They
clearly are weak, and the blend of Coulombic and
quantum mechanical contributions must be different
from that for O—H⋯O or other strong hydrogen
bonds. However, the weak interactions examined show
more specificity than van der Waals interactions and
therefore their designation as hydrogen bonds is fully
justified.

The present data show that formation constants in
aromatic C—H hydrogen bonding are measurable by
PMR, and that 2 : 1 complexing by donors with two or
more equivalent hydrogens can be virtually eliminated.
Although it should be possible to measure formation
constants by infrared methods, the authors believe that
this approach would probably be more tedious and less
precise than PMR.

The constants appear to be influenced as much by
steric factors, including buttressing, as by polar factors.
Steric hindrance increases as expected in the order
F > Cl > Br, to the point that, in the presence of but-
tressing, *ortho*-Cl (and presumably Br) *decrease* K/H,
although *ortho*-F *increases* K/H slightly. Highly substi-
tuted polyfluorobenzenes show larger K/H values than
their chloro analogs, contrary to expectation based on
ionization of substituted benzoic acids. The apparent
superiority of F results from buttressing in polychloro-
benzenes. Consistent with their polarity as measured by
Hammett constants, *meta*-halogens enhance hydrogen
bonding more than *para*-halogens. A deeper under-
standing of these substituent effects might emerge from
measurements of the enthalpy and entropy contribu-
tions to complex formation.

The chemical shift of benzene increased sufficiently
regularly in the presence of HMPA to permit the
measurement of K. It has thus been shown for the first
time that the hydrogen atoms of benzene engage in
hydrogen bonding. This conclusion is supported by an
extrapolated value of K/H for benzene from
polyfluorobenzene data, in fair agreement with the
experimental value.

EXPERIMENTAL

Materials. Most compounds and solvents were of
reagent grade and were used as received. Freshly
purchased HMPA (Aldrich) contained *ca* 0·2 mol-%
water (GLC) and, after 9 months, less than 1·0 mol-%
water.

A sample of 1,3,5-tribromo-2,4-dimethylbenzene was
prepared starting from 2·0 g (16·5 mmol) 3,5-
dimethylaniline (Aldrich), following a procedure for
1,3,5-tribromobenzene;[19] yield, 0·66 g, 1·9 mmol,

12%; m.p. 80·5–83·0 °C (lit.[20] m.p., 85 °C); pmr
(CCl₄, TMS, 60 MHz; arom. H): [HMPA] (M), δ_{obs}
(ppm): 0·0, 7·72; 0·5, 7·72; 2·0, 7·74.

NMR Measurements and calculations. Solutions
were prepared in either 2- or 5-ml volumetric flasks
which had been calibrated with water at 25 °C; penta-
and 1,2,4,5-tetrabromobenzene were dissolved in
HMPA with mild heating before adding the
cyclohexane or CCl₄. Aliquots of solutions were
transferred to 5-mm NMR tubes, stoppered and
analyzed on the same day. TMS was usually employed
for internal locking and chemical shift reference in
continuous-wave (CW) experiments (Varian T-60
spectrometer, probe temperature 35·5 ± 1·0 °C). In a
few cases cyclohexane was the internal standard. In
pulsed Fourier transform (FT) experiments
(IBM—Bruker NR-80 pulsed FT spectrometer,
35·0 ± 0·5 °C, 4 or 16 pulses), TMS was added only to
CCl₄ solutions; deuterium locking was accomplished
using chloroform-*d* in a concentric 10-mm tube.

The FT spectrometer was employed for
reinvestigating K values at lower [HMPA] because the
CW instrument had become less precise. However, with
pulsed FT the cyclohexane signal masked those of the
aromatic substrates at concentrations below *ca* 0·1 M
and, in the cases of the highly split tetrafluoro
compounds, much higher. Attempts to overcome this
interference by irradiating the cyclohexane protons
were unsuccessful; the use of completely deuterated
cyclohexane as solvent should succeed, but this material
is prohibitively expensive on the scale needed. For these
reasons the decision was made to employ CCl₄ for
reinvestigation of polyfluorobenzenes. Even so,
extensive splitting of most signals prevented precise
work below 0·1 M donor. The FT results were all
obtained using HMPA containing less than 1·0 mol-%
water; HMPA used earlier was not analyzed by GLC.

Formation constants and limiting shifts were
calculated via the Higuchi equation. The slope was
calculated by the least-squares method after each
iteration using a preprogrammed pocket calculator or a
specially written program in Fortran IV. Data points
deviating more than *ca* 1·5 standard deviations from
the least-squares line were rejected and the calculation
was repeated. No more than two points were rejected.

The chemical shifts for 1,2,3-trichlorobenzene were
measured at 360 MHz, because the spectrum was first
order: 5·524 ppm, triplet, 1H, $J = 7·94$ Hz;
5·803 ppm, doublet, 2H, $J = 7·94$ Hz. At 60 HMz, the
nine-line AB pattern[21] depended on HMPA
concentration, making accurate measurements of δ_{obs}
impossible.

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