

## Formation constants in C–H hydrogen bonding. 4. Effects of cyano, nitro, and trifluoromethyl substituents in aromatic compounds

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### Abstract

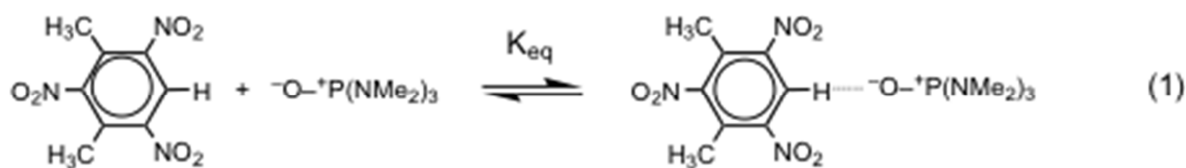
Formation constants ( $K_{eq}$ ) have been measured using  $^1\text{H}$  NMR for H–bond complexes with HMPA in  $\text{CCl}_4$  of 35 aromatic compounds variously substituted with cyano, nitro, and trifluoromethyl groups; several compounds contained F and Cl. The three strongly polar groups enhance H–bonding significantly, usually in the order  $\text{NO}_2 > \text{CN} > \text{CF}_3$ ; all are superior to Cl and F. 1,3,5–Trinitrobenzene fails to H–bond at all; however, TNT, its tert–butyl analog, and trinitro–m–xylene show significant  $K_{eq}$  values. Coplanarity of nitro groups with the ring blocks approach of HMPA, probably *via* intramolecular H–bonds. The buttressing effect is evident in some crowded compounds.

**Keywords:** C–H hydrogen bonding, polysubstituted benzenes, formation constants, Higuchi equation, substituent constants, intramolecular hydrogen bonding

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### Introduction

Hydrogen bonds involving C–H groups have proven to be not uncommon. Formation of a C–H H–bond is illustrated by Equation 1. Examples include the well known exothermic mixing of acetone with chloroform; the strong shift of the infrared  $\text{C}(\text{sp})\text{--H}$  stretching band of alkynes in the presence of bases; and certain crystal structures, e.g. malononitrile–crown ether compounds,<sup>1</sup> and pyrrolylpyridine Pt(II) complexes.<sup>2</sup> Benzhydryltriphenylphosphonium ions form H–bonds with  $\text{Cl}^-$  and  $\text{Br}^-$ , but not with  $\text{BF}_4^-$  nor  $\text{SbF}_6^-$ .<sup>3</sup> Certain substituted trioxanes form trifurcated C–H H–bonds with anions in solution.<sup>4</sup>  $\text{C--H}\cdots\text{F}$  “jousting” interactions occur in certain fused doubly bicyclic systems.<sup>5</sup> Benzyloxy radical, having  $\alpha$ –hydrogens which may form H–bonds, abstracts H atoms very much faster than cumyloxy, which lacks  $\alpha$ –H’s.<sup>6</sup>



Previous surveys of the strength of C–H H-bonding with hexamethylphosphorotriamide, HMPA, in terms of formation constants,  $K_{\text{eq}}$ , have shown that electron withdrawing groups significantly increase  $K_{\text{eq}}$  when the carbon atom is part of an aromatic ring, as well as when it is  $\text{sp}^3$  or  $\text{sp}$  hybridized or vinylic.<sup>7</sup> At first we reported on F, Cl, Br, and  $\text{NO}_2$ , but only one nitro compound had been included, *i.e.* 2,3,5,6-tetrachloronitrobenzene: Substituting  $\text{NO}_2$  for one H in 1,2,4,5-tetrachlorobenzene increased  $K_{\text{eq}}$  by a factor of ca. 6.5. For the halogens, the order had been found to be  $\text{F} > \text{Cl} \sim \text{Br}$ ; I was not studied. In a subsequent study polyhalobenzenes with no other substituents were examined.<sup>8</sup> Recently we reported a Hammett correlation of  $K_{\text{eq}}$  values for a series of 3-X-substituted 1,2,4,5-tetrafluorobenzenes, where  $\text{X} = \text{CN}$ ,  $\text{CF}_3$ , F,  $\text{CH}_3\text{O}$ , and  $\text{CH}_3$ .<sup>9</sup> In virtually all these cases  $K_{\text{eq}}$  values exceeded the value of ca.  $0.08 \text{ M}^{-1}$  shown by Abraham, *et al.*,<sup>10</sup> to be the minimum attributable to H-bonding.

We have now surveyed a wider range of aromatic compounds containing  $\text{NO}_2$ , CN,  $\text{CF}_3$ , F, and Cl, alone and in combination. One compound with  $\text{F}_3\text{C-SO}_2$  groups was also studied.

## Results and Discussion

Equilibrium constants,  $K_{\text{eq}}$ , and limiting chemical shift changes,  $\delta_{\text{c}} - \delta_{\text{a}}$ , were measured using the Higuchi Equation, as described in the Experimental section. The chemical shifts,  $\delta$ , are that of the H nucleus in the complex and in the free donor, respectively.

Tables 1–3 display these values for 35 aromatic compounds, **1–31** & **33–36**, reported for the first time. New results for 1,2,3,4-tetrafluorobenzene, (**38**),<sup>8</sup> 1,2,4,5-tetrafluorobenzene, (**39**),<sup>8</sup> and published results for four polychlorobenzenes, **37** and **40–42**,<sup>8</sup> are shown for comparison.  $K_{\text{eq}}/\text{H}$ , or  $K_{\text{eq}}$  divided by the number of equivalent H's, is also shown, whenever two or more such H's are present. We assume, and in some cases have shown,<sup>8</sup> that at sufficiently low concentrations of both donor and HMPA the extent of complexing of the second proton is negligible.

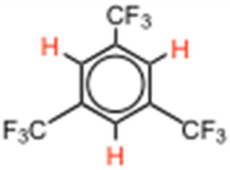
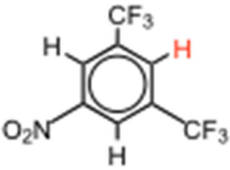
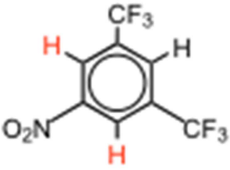
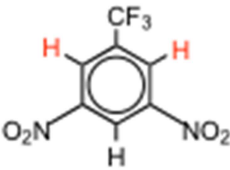
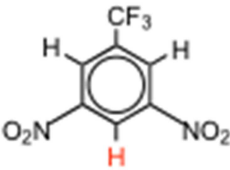
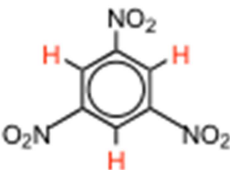
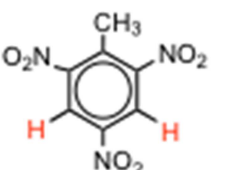
Table 1 shows the trifluoromethyl compounds studied (except **27** & **28**; *cf.* Table 3), nitro compounds lacking other polar groups, and 2,4,6-tris-trifluoromethanesulfonyltoluene (**12**).

Table 2 shows all the cyano compounds; the dinitrobenzenes, **21–23**, are included for ready comparison with the dicyanobenzenes, **16–18**.

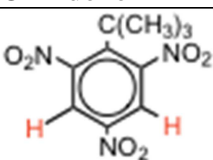
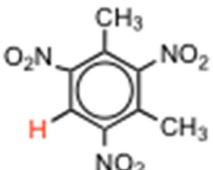
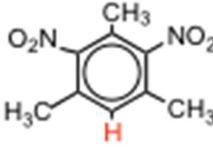
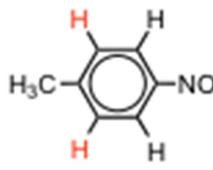
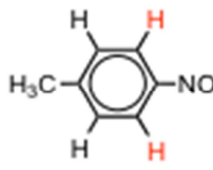
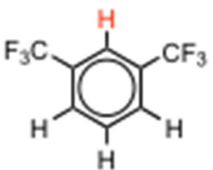
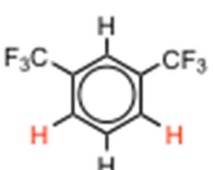
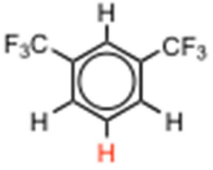
Table 3 shows all the nitrohalobenzenes, **24–36**, and the polyhalobenzenes, **37–42**. HMPA appeared to react too rapidly with **25** and **27** to permit observation of their  $\delta$  values. This is consistent with the report by Bunnett, *et al.*, of the much greater rate of aromatic nucleophilic

substitution of F than Cl.<sup>11</sup> DMF reacted much more slowly, and  $K_{eq}$  values were readily measured for **25–28**.  $K_{eq}$ 's with DMF were 2 to 3 times smaller for **26** and **28** than with HMPA.

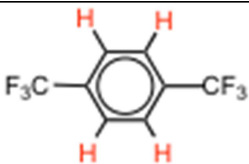
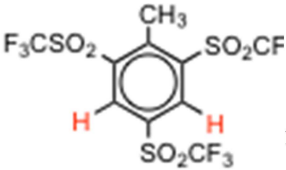
**Table 1.**  $K_{eq}$ 's of aromatic NO<sub>2</sub> and CF<sub>3</sub> compounds with HMPA in CCl<sub>4</sub> at 22° C

No.	C–H donor	$K_{eq}, M^{-1}$	$K_{eq}/H, M^{-1}$	$\delta_c - \delta_a, ppm$
1	 1,3,5-tris-Trifluoro- methylbenzene	2.7(0.1)	0.9	0.107(0.003)
2	 1,3-bis-Trifluoromethyl-5- nitrobenzene	0.52(0.03)	0.52	0.81(0.04)
2	 	1.4(0.2)	0.7	0.110(0.007)
3	 3,5-Dinitrotrifluoro- methylbenzene	2.84(0.06)	1.42	0.058(0.001)
3	 	0 <sup>a</sup>	0	n.a. <sup>b</sup>
4	 1,3,5-Trinitrobenzene	0 <sup>a</sup>	0	n.a. <sup>b</sup>
5	 2,4,6-Trinitrotoluene	6.1(0.3)	3.0	0.358(0.012)

**Table 1 (cont'd.).**  $K_{eq}$ 's of aromatic  $\text{NO}_2$  and  $\text{CF}_3$  compounds w. HMPA in  $\text{CCl}_4$  at 22° C

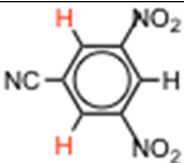
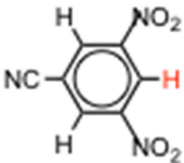
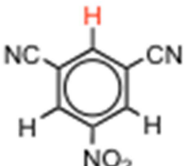
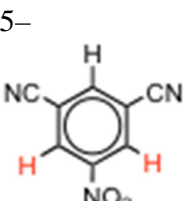
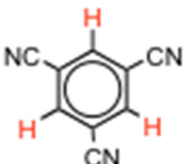
No.	C-H donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
6	 2,4,6-Trinitro-tert-butylbenzene	3.88(0.06)	1.94	0.504(0.004)
7	 2,4,6-Trinitro-m-xylene	3.3(0.1)	3.3	0.365(0.004)
8	 2,4-Dinitro-1,3,5-trimethylbenzene	0.70(0.02)	0.70	1.00(0.02)
9	 p-Nitrotoluene	0.63(0.06)	0.32	0.307(0.024)
9	 p-Nitrotoluene	0 <sup>a</sup>	0	n.a. <sup>b</sup>
10	 1,3-bis-Trifluoromethylbenzene	0 <sup>a</sup>	0	n.a. <sup>b</sup>
10	 1,3-bis-Trifluoromethylbenzene	0.96(0.12)	0.48	0.26(0.02)
10	 1,3-bis-Trifluoromethylbenzene	0.75(0.05)	0.75	0.69(0.03)

**Table 1 (cont'd.).**  $K_{eq}$ 's of aromatic  $\text{NO}_2$  and  $\text{CF}_3$  compounds w. HMPA in  $\text{CCl}_4$  at  $22^\circ\text{C}$ 

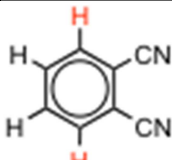
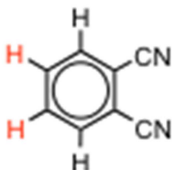
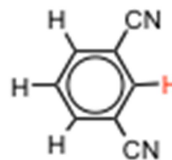
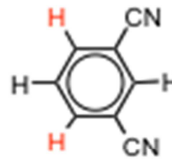
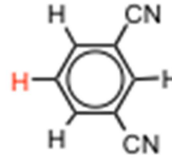
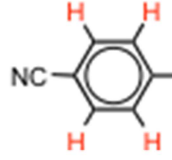
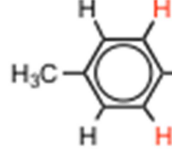
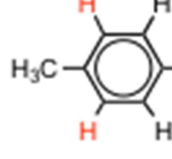
No.	C-H donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
11	 1,4-bis-Trifluoro- methylbenzene	1.8(0.2)	0.45	0.19(0.01)
12	 2,4,6-tris-Trifluoro- methanesulfonyltoluene	0 <sup>a</sup>	0	n.a. <sup>b</sup>

<sup>a</sup>NMR signal ( $^1\text{H}$ ) moves to higher field, not lower. <sup>b</sup>Could not be measured; *cf.* text.

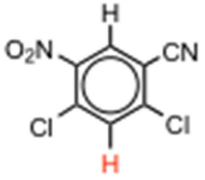
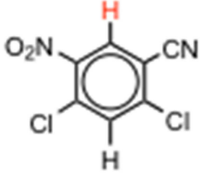
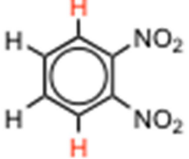
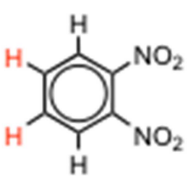
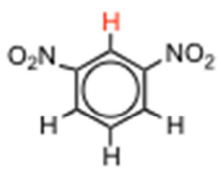
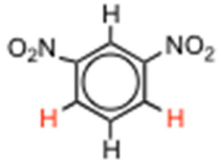
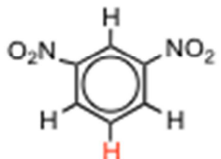
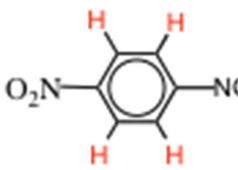
**Table 2.**  $K_{eq}$ 's of aromatic CN and  $\text{NO}_2$  compounds with HMPA in  $\text{CCl}_4$  at  $22^\circ\text{C}$ 

No.	C-H Donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
13	 3,5-Dinitrobenzonitrile	9.93(0.34)	5.0	0.337(0.005)
13	 3,5-Dinitrobenzonitrile	0 <sup>a</sup>	0	n.a. <sup>b</sup>
14	 5-Nitroisophthalonitrile	12.7(0.05)	12.7	0.726(0.005)
14	 5-Nitroisophthalonitrile	12.6(0.6)	6.3	0.184(0.003)
15	 1,3,5-Tricyanobenzene	9.2(0.7)	3.1	0.672(0.017)

**Table 2 (cont'd).**  $K_{eq}$ 's of aromatic CN and NO<sub>2</sub> compounds with HMPA in CCl<sub>4</sub> at 22° C

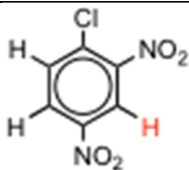
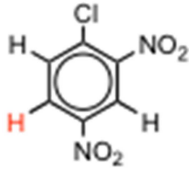
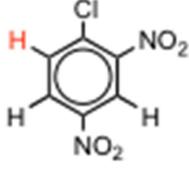
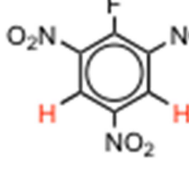
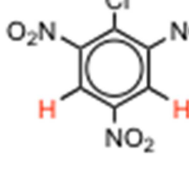
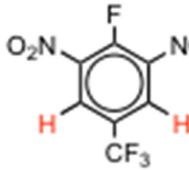
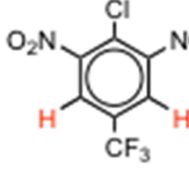
No.	C-H Donor		$K_{eq}, M^{-1}$	$K_{eq}/H, M^{-1}$	$\delta_c - \delta_a, ppm$
16		1,2-Dicyanobenzene	3.4(0.1)	1.7	0.289(0.004)
16			2.05(0.03)	1.0	0.426(0.004)
17		1,3-Dicyanobenzene	3.1(0.07)	3.1	0.194(0.021)
17			3.87(0.29)	1.9	0.307(0.009)
17			2.31(0.02)	2.3	0.495(0.003)
18		1,4-Dicyanobenzene	3.83(0.09)	0.96	0.310(0.004)
19		4-Methylbenzonitrile	1.43(0.11)	0.71	0.081(0.003)
19			0.53(0.01)	0.26	0.303(0.004)

**Table 2 (cont'd).**  $K_{eq}$ 's of aromatic CN and NO<sub>2</sub> compounds with HMPA in CCl<sub>4</sub> at 22° C

No.	C-H Donor	$K_{eq}, M^{-1}$	$K_{eq}/H, M^{-1}$	$\delta_c - \delta_a, ppm$
20	 2,4-Dichloro-5-nitrobenzonitrile	0.66(0.03)	0.66	0.973(0.032)
20	 2,4-Dichloro-5-nitrobenzonitrile	1.16(0.07)	1.16	0.582(0.019)
21	 1,2-Dinitrobenzene	4.5(0.1)	2.25	0.233(0.003)
21	 1,2-Dinitrobenzene	2.80(0.45)	1.4	0.439(0.006)
22	 1,3-Dinitrobenzene	0 <sup>a</sup>	0	n.a. <sup>b</sup>
22	 1,3-Dinitrobenzene	2.7(0.1)	1.3	0.207(0.005)
22	 1,3-Dinitrobenzene	2.72(0.03)	2.7	0.603(0.004)
23	 1,4-Dinitrobenzene	2.75(0.08)	0.7	0.181(0.003)

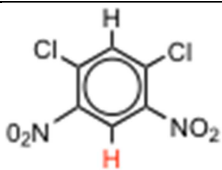
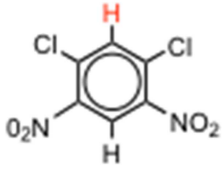
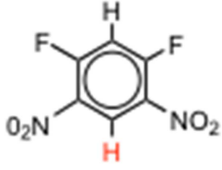
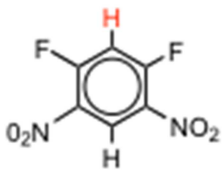
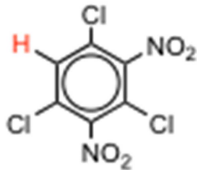
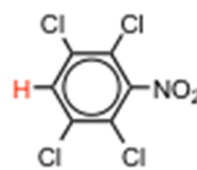
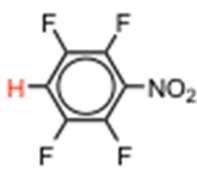
<sup>a</sup>NMR signal (<sup>1</sup>H) moves to higher field, not lower. <sup>b</sup>Could not be measured; *cf.* text.

**Table 3.**  $K_{eq}$ 's of aromatic F, Cl, and  $\text{NO}_2$  compounds with HMPA<sup>a</sup> in  $\text{CCl}_4$  at 22° C

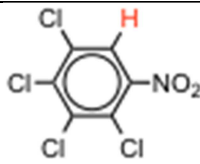
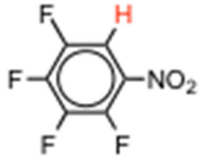
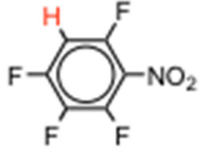
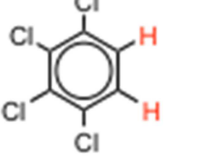
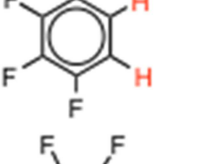
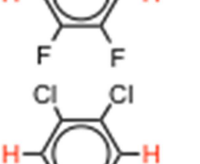
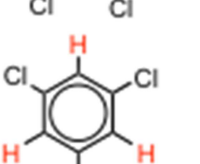
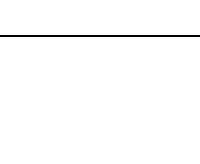
No.	C–H Donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
24	 2,4– Dinitrochlorobenzene	2.9(0.1)	2.9	0.637(0.010)
24		3.52(0.05)	3.5	0.381(0.002)
24		5.6(0.7)	5.6	0.061(0.003)
25	 2,4,6– Trinitrofluorobenzene	10.0(0.09) <sup>a</sup>	5.0	0.050(0.002) <sup>a</sup>
26	 2,4,6– Trinitrochlorobenzene	22.4(0.3)	11.2	0.432(0.001)
26	“	6.8(0.1) <sup>a</sup>	3.4	0.260(0.002) <sup>a</sup>
27	 3,5–Dinitro–4– fluorobenzo– trifluoride	4.9(0.4) <sup>a</sup>	2.4	0.161(0.006) <sup>a</sup>
28	 3,5–Dinitro–4– chlorobenzo– trifluoride	8.3(0.3)	4.1	0.705(0.010)
28	“	3.8(0.2) <sup>a</sup>	1.9	0.424(0.015) <sup>a</sup>



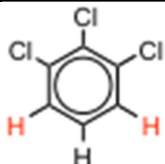
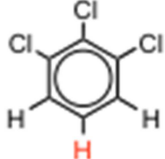
**Table 3 (cont'd).**  $K_{eq}$ 's of aromatic F, Cl, and  $\text{NO}_2$  compounds with  $\text{HMPA}^a$  in  $\text{CCl}_4$  at  $22^\circ\text{C}$ 

No.	C-H Donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
29	 1,5-Dichloro-2,4-dinitrobenzene	5.02(0.08)	5.0	0.601(0.004)
29		1.10(0.06)	1.1	0.735(0.028)
30	 1,5-Difluoro-2,4-dinitrobenzene	6.3(0.8)	6.3	0.050(0.002)
30		5.3(0.2)	5.3	1.080(0.012)
31	 1,3,5-Trichloro-2,4-dinitrobenzene	1.92(0.02)	1.9	1.587(0.009)
32	 2,3,5,6-Tetrachloronitrobenzene	0.60(0.03)	0.60	1.27(0.05)
33	 2,3,5,6-Tetrafluoronitrobenzene	2.82(0.02)	2.82	1.495(0.005)

**Table 3 (cont'd).**  $K_{eq}$ 's of aromatic F, Cl, and  $\text{NO}_2$  compounds with HMPA<sup>a</sup> in  $\text{CCl}_4$  at 22° C

No.	C-H Donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
34	 2,3,4,5-Tetrachloronitrobenzene	1.25(0.05)	1.25	1.04(0.03)
35	 2,3,4,5-Tetrafluoronitrobenzene	1.83(0.02)	1.83	0.603(0.004)
36	 2,3,4,6-Tetrafluoronitrobenzene	2.55(0.04)	2.55	1.42(0.01)
37	 1,2,3,4-Tetrachlorobenzene	0.69(0.01) <sup>b,c</sup>	0.34	0.87(0.01) <sup>b,c</sup>
38	 1,2,3,4-Tetrafluorobenzene	0.68(0.02)	0.34	0.807(0.021)
39	 1,2,4,5-Tetrafluorobenzene	0.77(0.05)	0.38	0.70(0.03)
40	 1,2,4,5-Tetrachlorobenzene	0.30(0.01) <sup>b,c</sup>	0.15	0.76(0.02) <sup>b,c</sup>
41	 1,3,5-Trichlorobenzene	0.20(0.01) <sup>b,c</sup>	0.07	0.55(0.02) <sup>b,c</sup>

**Table 3 (cont'd).**  $K_{eq}$ 's of aromatic F, Cl, and  $\text{NO}_2$  compounds with HMPA<sup>a</sup> in  $\text{CCl}_4$  at 22° C

No.	C–H Donor	$K_{eq}, \text{M}^{-1}$	$K_{eq}/\text{H}, \text{M}^{-1}$	$\delta_c - \delta_a, \text{ppm}$
42	 1,2,3– Trichlorobenzene	0.38(0.01) <sup>b,d</sup>	0.19	0.504(0.010) <sup>b,d</sup>
42		0.48(0.01) <sup>b,d</sup>	0.48	0.755(0.004) <sup>b,d</sup>

<sup>a</sup>Measured with DMF: picryl fluoride reacted rapidly with HMPA and DMSO; *cf.* text.

<sup>b</sup>Measured in cyclohexane;  $K(\text{CCl}_4)$  estimated to be  $1/4 K(\text{cyclohexane})^3$ . <sup>c</sup>Data from Ref. 8;  $K$ s extrapolated from 35° C to 22° C, assuming  $\Delta H^\circ = -3.6 \text{ kcal mol}^{-1}$ . <sup>d</sup>Data from Ref. 8;  $K$ s extrapolated from 27° C to 22° C, assuming  $\Delta H^\circ = -3.6 \text{ kcal mol}^{-1}$ .

The  $K_{eq}$  value for **33** may be added to those of a series of 1-substituted 2,3,5,6-tetra-fluorobenzenes in  $\text{CCl}_4$ <sup>9</sup> published earlier. The resulting plot of  $\log K_{eq}$  vs.  $\sigma$ , their Hammett polar substituent constants, for five points (omitting  $\text{CH}_3$  and  $\text{OCH}_3$ ), gives  $\rho = +1.26 \pm 0.06$ . This value is closely similar to those reported,<sup>9</sup> since  $\log K$  and  $\sigma$  of  $\text{CN}$  and  $\text{NO}_2$  are similar.

### Use of $^{19}\text{F}$ NMR

Table 4 shows data for several F-substituted donors obtained *via*  $^{19}\text{F}$  NMR, and compares them with those from  $^1\text{H}$  NMR. Five of the eight compounds, **3**, **27**, **30**, **38**, and **39** show good agreement between the two sets. The others differ by 20 to 30% of the larger number; for **25**, however, the  $^1\text{H}$  NMR value is nearly twice the  $^{19}\text{F}$  value. This might be due to the very small value of  $\delta_c - \delta_a$  (see below).  $^{19}\text{F}$  nmr, then, affords good “ball park” values of  $K_{eq}$  in some cases.

### 1,3,5-Trinitrobenzene and steric effects

Surprisingly,  $K_{eq}$  for 1,3,5-trinitrobenzene (**4**) could not be measured, because its signal did not move to lower field with added HMPA. Thus,  $\delta_a$  in  $\text{CCl}_4$  was 9.343 ppm, but  $\delta_{\text{obs}}$  with [HMPA] = 0.1, 0.3, and 0.6 M was 9.307, 9.284, and 9.269, respectively. This is a solvent effect, independent of H-bonding. The entry for **4** in Table 1 thus shows  $K_{eq} = 0$ . However, for its monomethyl derivative, TNT (**5**),  $K_{eq}/\text{H} = 3.0$ ; for the tert-butyl analog (**6**)  $K_{eq}/\text{H} = 1.9$ , and for 2,4,6-trinitro-m-xylene (**7**),  $K_{eq}/\text{H} = 3.3$ . Just as strikingly, the aromatic signal of 2,4,6-tris-trifluoromethanesulfonyltoluene (**12**) moved to higher field, so  $K_{eq} = 0$  despite the presence of the methyl group. The same was found for the H's between two nitro groups in **3**, **13**, and **21**, and between two  $\text{CF}_3$  groups in **10**, although not in **2**. Thus  $K_{eq} = 0$  for these protons as well.

**Table 4.** Ks of aromatic halo and nitro compounds with HMPA in CCl<sub>4</sub> measured *via* <sup>19</sup>F nmr

No.	C–H Donor	NMR Method	H No.	K <sub>eq</sub> , M <sup>-1</sup>	K <sub>eq</sub> /H	δ <sub>c</sub> – δ <sub>a</sub> , ppm
<b>3</b>	3,5–Dinitrobenzotrifluoride	<sup>19</sup> F	2,6	3.1(0.2)	1.6	0.261(0.007)
<b>3</b>		<sup>1</sup> H	2,6	2.84(0.06)	1.4	0.058(0.001)
<b>25</b>	2,4,6–Trinitrofluorobenzene <sup>a</sup>	<sup>19</sup> F	3,5	5.4(0.4) <sup>a</sup>	2.7	1.04(0.03)
<b>25</b>		<sup>1</sup> H	3,5	10.0(0.09)	5.0	0.050(0.002)
<b>27</b>	3,5–Dinitro–4–fluorobenzo–trifluoride: CF <sub>3</sub> <sup>a</sup> observed	<sup>19</sup> F	2,6	3.1(0.2) <sup>a</sup>	1.6	1.85(0.05)
<b>27</b>	F <sup>a</sup> observed	<sup>19</sup> F	2,6	4.5(0.5) <sup>a</sup>	2.3	0.17(0.01)
<b>27</b>		<sup>1</sup> H	2,6	4.9(0.4)	2.4	0.161(0.006)
<b>28</b>	3,5–Dinitro–4–chlorobenzo–trifluoride	<sup>19</sup> F	2,6	6.0(0.5)	3.0	0.307(0.012)
<b>28</b>		<sup>1</sup> H	2,6	8.3(0.3)	4.1	0.424(0.015)
<b>30</b>	1,5–Difluoro–2,4–dinitrobenzene	<sup>19</sup> F	3,6	9.9(0.6)	5.0	0.434(0.006)
<b>30</b>		<sup>1</sup> H	3	6.3(0.8)	6.3	0.050(0.002)
<b>30</b>		<sup>1</sup> H	6	5.3(0.2)	5.3	1.080(0.016)
<b>33</b>	2,3,5,6–Tetrafluoronitrobenzene	<sup>19</sup> F	4	2.2(0.05)	2.2	2.39(0.03)
<b>33</b>		<sup>1</sup> H	4	2.82(0.02)	2.8	1.495(0.005)
<b>36</b>	2,3,4,6–Tetrafluoronitrobenzene, 137 ppm	<sup>19</sup> F	5	2.04(0.06)	2.0	4.09(0.05)
<b>36</b>	160 ppm	<sup>19</sup> F	5	2.04(0.06)	2.0	2.47(0.04)
<b>36</b>		<sup>1</sup> H	5	2.55(0.04)	2.5	1.42(0.01)
<b>38</b>	1,2,3,4–Tetrafluorobenzene, 69 ppm	<sup>19</sup> F	5,6	0.72(0.05)	0.36	2.22(0.10)
<b>38</b>	85 ppm	<sup>19</sup> F	5,6	0.64(0.02)	0.32	5.15(0.12)
<b>38</b>		<sup>1</sup> H	5,6	0.68(0.02)	0.34	0.807(0.021)
<b>39</b>	1,2,4,5–Tetrafluorobenzene	<sup>19</sup> F	3,6	0.74(0.05)	0.37	1.32(0.01)
<b>39</b>		<sup>1</sup> H	3,6	0.77(0.05)	0.38	1.45(0.01)

<sup>a</sup>Measured with DMF: picryl fluoride reacted rapidly with HMPA and DMSO; *cf.* text.

By contrast, H's between the following pairs of groups have significant values of K<sub>eq</sub>:

- (a) Two cyano groups in **14**, **15**, and **17**;
- (b) One nitro and one cyano group in **13**, **14**, and **20**;
- (c) One CF<sub>3</sub> and one nitro group in **2**, **3**, **27**, and **28**;
- (d) Two nitro groups in **7** and **24–26**, in addition to **5** and **6**.

The anomalous behavior of 1,3,5–trinitrobenzene (**4**) can be explained by the notion that the nitro groups lie coplanar with the ring. Two consequences may combine to prevent detectable H–bonding with HMPA:

(a) The nitro groups, with negative charge on each O atom, repel the negatively charged O atom of HMPA.

(b) The nitro O atoms can form intramolecular H-bonds with adjacent H's. Evidence for this interaction is found in the large downfield nmr shifts of several protons flanked by two nitro groups which have no *ortho* neighbor. The compounds and  $\delta$  values of such H's appear in Table 5 as the first 4 entries: in all of these,  $\delta > 9.0$  ppm, and reaches 9.34 ppm for compound **4**.

**Table 5.**  $\delta$  Values of protons between 2 nitro groups

No.	Name of Compound	Position of H	$\delta$ , ppm
<b>21</b>	1,3-Dinitrobenzene	2	9.06
<b>13</b>	3,5-Dinitrobenzonitrile	4	9.23
<b>3</b>	3,5-Dinitrotrifluoromethylbenzene	4	9.23
<b>4</b>	1,3,5-Trinitrobenzene	2,4,6	9.34
<b>29</b>	1,5-Dichloro-2,4-dinitrobenzene	3	8.49
<b>30</b>	1,5-Difluoro-2,4-dinitrobenzene	3	8.92
<b>5</b>	2,4,6-Trinitrotoluene (TNT)	3,5	8.78
<b>6</b>	2,4,6-Trinitro- <i>tert</i> -butylbenzene	3,5	8.31
<b>7</b>	2,4,6-Trinitro- <i>m</i> -xylene	5	8.58
<b>26</b>	2,4,6-Trinitrochlorobenzene	3,5	8.79
<b>25</b>	2,4,6-Trinitrofluorobenzene	3,5	9.13

The results of a neutron diffraction study<sup>12</sup> of crystalline **4** support coplanarity: two slightly different structures were present, denoted A and B. Structure B was practically planar, with the nitro groups rotated very slightly out of plane, while A was significantly non-planar, with one nitro group far more out of plane than the other two. The authors also observe distortions in molecular complexes of **4** and attribute them to "packing strain." Thus it is likely that the structure of **4** in solution is nearly completely planar. The intramolecular H $\cdots$ O contacts in B average  $2.42 \pm 0.01$  Å, while four of those in A average  $2.38 \pm 0.02$  Å. These are significantly less than the sum of van der Waals radii, 2.60 Å, of O (1.40 Å) and H (1.20 Å).<sup>13-15</sup> This evidence strongly supports hypothesis (b), but does not rule out a role for hypothesis (a).

In *substituted* trinitrobenzenes, and other nitro compounds, however, *ortho* substituents force the nitro groups to rotate out of coplanarity with the ring. An X-ray diffraction study of TNT (**5**) again revealed the presence of two structures, denoted A and B.<sup>16</sup> The nitro groups were *all* rotated out of the ring plane, 4-nitro groups by 24° and 30°, respectively, and 2- and 6-nitro groups by 43° – 60°. Both intramolecular H-bonding and repulsion of HMPA are expected to diminish or disappear, hence the sizable non-zero values of  $K_{eq}/H$  for (**5**), (**6**), and (**7**). Consistent with the intramolecular H-bonding hypothesis, as also shown in Table 5, the  $\delta$  values of all these protons are less than 9.0, except for (**25**).

It is interesting to compare compounds **22**, **29**, and **30**. The H's between the nitro groups have  $K_{eq} = 0$ , 5.0, and 6.3, respectively. The two chlorines of **29** and the two fluorines of **30** force

the nitro groups out of coplanarity. This effect is probably smaller for the fluorines, but is compensated by the greater electron withdrawing character of the fluorines than of the chlorines. The H's *meta* to the nitro groups all give measurable  $K_{eq}$ 's: that in **30** is the largest, while that in **29** is the smallest. The F's of **30** increase  $K$  relative to **22**, while the chlorines of **29** may sterically hinder approach of HMPA.

A third effect, buttressing,<sup>8,13–15</sup> affects  $K_{eq}/H$  values of crowded compounds, having four or five substituents. In such cases the groups push one another away in the ring plane toward the H, decreasing the space available to the O atom of HMPA. Thus, introducing three methyl groups into **22** to form **8** decreases  $K_{eq}/H$  for the H that is *meta* to both nitro groups from 2.7 to 0.7.  $K_{eq}/H$  for H-6 of **29** is only 1/5 that in **30**. The difference between **37** and **40** (1,2,3,4- and 1,2,4,5-tetrachlorobenzenes, resp.), 0.34 vs. 0.15, may be an example of buttressing in addition to crowding, since **37** has only one Cl adjacent to each H, while in **40** two Cl's flank each H.

Cyano groups, being linear, are unchanged by rotation, and probably little affected by crowding or buttressing. The CF<sub>3</sub> group, being slightly larger than methyl, should be subject to crowding and buttressing, but we have not studied crowded analogs. Table 3 includes several Cl substituted and two F substituted compounds; the order of van der Waals radii is Cl > F > H.<sup>17–19</sup> Crowding and possible buttressing involving Cl has already been mentioned.

### Polar effects

The effect of substituting nitro for H or for a different polar substituent can be substantial. Several examples, detailed in Table 6, show that a nitro group increases  $K_{eq}$  by factors of  $4.5 \pm 1$  when replacing H, and by factors of  $2.5 \pm 0.2$  when replacing trifluoromethyl.

**Table 6.** Effect of substituent changes on  $K_{eq}$

New group	Group replaced	Compounds	$K_{eq}$ values, $M^{-1}$	Ratio of $K_{eq}$ 's
NO <sub>2</sub>	H	<b>14</b> vs. <b>17</b>	12.7 vs. 3.1	4.2
NO <sub>2</sub>	H	<b>32</b> vs. <b>40</b>	0.60 vs. 0.15	4.0
NO <sub>2</sub>	H	<b>33</b> vs. <b>39</b>	2.82 vs. 0.38	7.4
NO <sub>2</sub>	H	<b>34</b> vs. <b>37</b>	1.25 vs. 0.34	3.7
NO <sub>2</sub>	H	<b>35</b> vs. <b>38</b>	1.83 vs. 0.34	5.4
2 NO <sub>2</sub>	2 H	<b>31</b> vs. <b>41</b>	1.92 vs. 0.07	$27 = (5.2)^2$
NO <sub>2</sub>	CF <sub>3</sub>	<b>26</b> vs. <b>28</b>	11.2 vs. 4.1	2.7
NO <sub>2</sub>	CF <sub>3</sub>	<b>25</b> vs. <b>27</b>	5.0 vs. 2.4	2.1
NO <sub>2</sub>	CF <sub>3</sub>	<b>3</b> vs. <b>2</b>	1.42 vs. 0.52	2.7

The order of enhancement of C–H H–Bonding appears to be NO<sub>2</sub> > CN > CF<sub>3</sub> > Cl ~ F, the same as that of their Hammett substituent constants  $\sigma_p$  in the gas phase, 0.78, 0.72, 0.51, 0.29 and 0.19, respectively.<sup>20</sup> The gas phase should be a better model for CCl<sub>4</sub> solution than H<sub>2</sub>O. In the gas phase,  $\sigma_m$  values do not differ greatly from  $\sigma_p$  values (for these 5 substituents the largest difference is 0.06 for both F and NO<sub>2</sub>). One direct comparison of these groups is *via* the 1,3–

disubstituted benzenes **22**, **17**, and **10**, in each of which one H is meta to both substituents; for Cl we will use the 5-H of 1,2,3-trichlorobenzene (**42**): their  $K_{eq}/H$  values are 2.7, 2.3, 0.7, and 0.5, respectively. We may also compare the 1,3,5-trisubstituted analogs **7**, **15**, **1**, and **41**, which have  $K_{eq}/H$  values of 3.3, 3.1, 0.9, and 0.07, respectively. It was necessary to utilize **7** for this comparison because of the nitro group coplanarity problem.

These effects do not depend strongly on whether the substituent is ortho, meta, or para to the H. As already noted, however, nitro may render  $K_{eq} = 0$  for ortho H's. Steric effects complicate the analysis (*vide infra*).

### Limiting shifts

Values of  $\delta_c - \delta_a$ , "limiting shifts", obtained in this study cover a very large range, from as low as 0.050 to 1.587 ppm. The smallest values are listed in Table 7. As with  $K_{eq}$ 's, many of these need to be corrected statistically. Values of  $(\delta_c - \delta_a)/H$ , *i.e.* " $\delta_c - \delta_a$  per H" have been calculated by multiplying  $\delta_c - \delta_a$  by the number of equivalent H's, assuming that when one H is H-bonded,  $\delta_{obs}$  for an equivalent non-H-bonded H is unchanged. For **25** and **27**, values for HMPA have been estimated as described in the footnote to Table 7.

**Table 7.** Low values of  $\delta_c - \delta_a$

Compound	No. equiv. H's	$\delta_c - \delta_a$ , ppm	$(\delta_c - \delta_a)/H$ , <sup>a</sup> ppm
<b>1</b>	3	0.107	0.321
<b>2</b> , H4,6	2	0.110	0.220
<b>3</b> , H2,6	2	0.058	0.116
<b>10</b> , H4,6	2	0.26	0.52
<b>11</b>	4	0.19	0.76
<b>14</b> , H4,6	2	0.184	0.368
<b>17</b> , H2	1	0.194	0.194
<b>19</b> , H2,6	2	0.081	0.162
<b>21</b> , H3,6	2	0.233	0.466
<b>22</b> , H4,6	2	0.207	0.414
<b>23</b>	4	0.181	0.724
<b>24</b> , H6	1	0.061	0.061
<b>25</b>	2	0.083 <sup>b</sup>	0.166 <sup>b</sup>
<b>27</b>	2	0.267 <sup>b</sup>	0.534 <sup>b</sup>
<b>30</b> , H3	1	0.050	0.050

<sup>a</sup> $\delta_c - \delta_a$  multiplied by number of equivalent H's; see text. <sup>b</sup>Measured values with DMF have been corrected, based on the fact that for both **25** & **27**,  $(\delta_c - \delta_a)/H$  with HMPA is 1.66 times that with DMF (*cf.* Table 3).

The presence of two or more Cl atoms greatly increases values of  $(\delta_c - \delta_a)/H$ . Examples are **31** (1.587), with three Cl's, and **32** (1.27) and **34** (1.04), each with four Cl's and just one H. The values found for **37** and **40–42**, with more than one H, are also large, as compared to compounds lacking any Cl's. However, *no* compounds in Table 7 contain Cl.

Among the  $(\delta_c - \delta_a)/H$  values listed in Table 7, those for **3**, **19**, **24**, **25**, and **30** are unusually small: we have rarely found values less than 0.20.<sup>7–9</sup> Values for **1**, **10**, **11**, **14**, **21–23**, and **27** appear more nearly “normal”: all are greater than 0.30. We consider **2** and **17** to be borderline.

## Conclusions

- (a) A large number of benzene derivatives exhibit C–H H–bonding.
- (b) Electron withdrawing substituents on the ring increase equilibrium constants.
- (c) Polar substituent effects may be diminished by electrostatic repulsion of the H–acceptor, intramolecular H–bonding, and/or buttressing.
- (d) Limiting NMR shift changes,  $(\delta_c - \delta_a)/H$ , are largest when one or more Cl's are present, but not F, while in several other cases shifts are unexpectedly small.

## Experimental Section

**General.** Melting points were measured on a MelTemp instrument.  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra were recorded at 300.1 and 282.4 MHz, respectively, on a Varian instrument with an Oxford electromagnet, with  $\text{CCl}_4$  as solvent and acetone- $\text{d}_6$  as external lock. Internal standards were TMS for  $^1\text{H}$  and perfluoromethylcyclohexane for  $^{19}\text{F}$ . All purchased compounds were used as received. One gram of 3,5–dinitrobenzotrifluoride (**3**) was graciously donated by Marshalltown Research Industries, Marshalltown, NC. The 2,4,6–tris–trifluoromethanesulfonyltoluene (**12**) was a gift from the late Professor R. W. Taft. HMPA was stored over molecular sieves. The procedure for preparing solutions has been described;<sup>7–9</sup> 7 samples and a blank were prepared for each run.

**Determination of  $K_{\text{eq}}$  and  $(\delta_c - \delta_a)$  via the Higuchi Equation.** Chemical shifts and concentrations were converted to equilibrium constants,  $K_{\text{eq}}$ , and “limiting” chemical shift changes,  $(\delta_c - \delta_a)$ , via the Higuchi Equation<sup>21</sup> (2), using a program written for the purpose, as described previously.<sup>9</sup> The resulting data were plotted using ProFit, and outliers identified.

$$C_b/(\delta_{\text{obs}} - \delta_a) = (C_a + C_b - C_c)/K_{\text{eq}} + 1/K_{\text{eq}}(\delta_c - \delta_a) \quad (2)$$

where  $C_a$  and  $C_b$  are total added concentrations of “acid,” or H–bond donor, and “base,” *i.e.* HMPA, respectively, and  $C_c$  is the equilibrium concentration of H–bond complex;



$\delta_a$  is the chemical shift of the donor H atom in the absence of HMPA;

$\delta_{\text{obs}}$  is the chemical shift of the H atom at a given HMPA concentration;

$\delta_c$  is the chemical shift of the H atom in the complex.

$\delta_c - \delta_a$  = "limiting chemical shift change" of the H-bonded H atom; when  $^{19}\text{F}$  NMR is used, this quantity applies to the F atom, and thus can be quite different from that for the H atom.

A plot of the left hand side of equation 1 vs.  $C_a + C_b - C_c$  has slope =  $1/K_{\text{eq}}$ , while the intercept =  $1/K_{\text{eq}}(\delta_c - \delta_a)$ . Thus,  $K_{\text{eq}} = 1/\text{slope}$ , and  $(\delta_c - \delta_a) = \text{slope}/\text{intercept}$ .

Since  $C_c$  is initially unknown, the left hand side of equation 1 is first plotted vs.  $(C_a + C_b)$ . Then  $(\delta_c - \delta_a)$  is estimated as slope/intercept.  $C_c$  is estimated from  $C_c = C_a[(\delta_{\text{obs}} - \delta_a)/(\delta_c - \delta_a)]$ , and a new plot is made using this value of  $C_c$ . New values of slope, intercept, and  $C_c$  are obtained, permitting a third plot. This iterative procedure is performed until the results converge to constant values of  $K_{\text{eq}}$  and  $\delta_c - \delta_a$ . Convergence usually requires 10 iterations. The program used provides standard deviations of computed quantities, and an R value, a measure of adherence of points to the least squares line. R values were always at least 0.99, and as high as 0.9999.

**5-Nitro-1,3-dicyanobenzene (14).** The dinitrile was prepared in three steps from 5-nitroisophthalic acid, after unsuccessful attempts to nitrate isophthalonitrile. From the acid (42.3 g, 0.200 mol) and  $\text{SOCl}_2$  (60 mL, 97.8 g, 0.822 mol) in toluene (50 mL), by refluxing for 27 hrs, and then distilling out the reagent and solvent, there was obtained 52 g of an oil, which solidified; lit.<sup>22</sup> mp 66–68° C for 5-nitroisophthaloyl dichloride. All of this material was dissolved in benzene (50 mL) and slowly added with stirring and cooling to concentrated  $\text{NH}_3$  (101 mL, 25.5 g  $\text{NH}_3$ , 1.50 mol). The precipitate was collected, washed with water, and dried, giving the crude, white solid diamide, yield 100%, 41.8 g; lit.<sup>22</sup> mp >300° C. The diamide (10.0 g, 0.048 mol) was mixed with  $\text{P}_2\text{O}_5$  (13 g, 0.092 mol), and the mixture heated for 8 hr at 250° C. Water (28 mL) was added to the dark, hard, solid mass. After 2 days it was broken up, filtered, and let dry. This solid (13.8 g) was extracted twice with glacial acetic acid at reflux, and the mother liquors concentrated. **14**, yellow crystals, 3 crops, yield 23%, 1.79 g, mp 200–210° C (1st crop), lit.<sup>23</sup> 209–210° C.  $^1\text{H}$  NMR (sparingly soluble in  $\text{CCl}_4$ ):  $\delta_{\text{H}}$  8.258 (1H, t,  $^3J_{\text{HH}}$  1.5 Hz, H-2); 8.707 (2H, d,  $^3J_{\text{HH}}$  1.5 Hz, H-4,6).

**2,4-Dinitro-tert-butylbenzene.**<sup>24–27</sup> From tert-butylbenzene (13.4 g, 0.100 mol), 90% nitric acid (28.4 mL, 42 g, 0.60 mol), and 95%  $\text{H}_2\text{SO}_4$  (33.8 mL, 58.8 g, 0.60 mol), in a 125 mL Erlenmeyer flask, and the mixture heated at 160° C for 30 min, was obtained a yellow solid, yield 68%, 18.2 g, mp 45–50° C. Pale yellow crystals, mp 59–62° C (from ligroin), lit. 63.5–64.5 °C<sup>25</sup>; 61–62°C<sup>26</sup>.  $^1\text{H}$  NMR ( $\text{CCl}_4$ ):  $\delta_{\text{H}}$  1.455 (9H, tert-butyl); 7.787 (d,  $^3J_{\text{HH}}$  8.7 Hz, 1H, H-6); 8.135, d,  $^3J_{\text{HH}}$  2.4 Hz, 1H, H-3); 8.238 (d of d,  $^3J_{\text{HH}}$  2.4 & 8.7 Hz, 1H, H-5).

**2,4,6-Trinitro-tert-butylbenzene (6).** The procedure of Liss and Lohmann was used.<sup>27</sup> To 2,4-dinitro-tert-butylbenzene (2.10 g, 0.0094 mol) in a 125 mL Erlenmeyer flask was added 90%  $\text{HNO}_3$  (8.4 mL, 11.2 g, 0.18 mol) and 95%  $\text{H}_2\text{SO}_4$  (42 mL, 73 g, 0.75 mol). On heating to 127° C, then removal from heat, the temperature remained constant for 5 min; heating was continued for 25 min more, then the solution quenched in ice. Pale yellow solid, yield 25%, 0.64 g, mp 110–

115° C. White needles, mp 125–126° C (from 95% EtOH), lit.<sup>28,29</sup> 124° C. <sup>1</sup>H NMR (CCl<sub>4</sub>): δ<sub>H</sub> 1.529 (s, 9H, tert-butyl), 8.309 ppm (s, 2H, aromatic).

**2,4,6-Trinitro-*m*-xylene (7).** To *m*-xylene (10.6 g, 0.100 mol) in a 125 mL Erlenmeyer flask was slowly added 90% HNO<sub>3</sub> (18.9 mL, 28 g, 0.40 mol) with magnetic stirring. The temperature of the deep red mixture was kept below 55° C, then raised to 70° C for a few minutes. Concentrated H<sub>2</sub>SO<sub>4</sub> (22.5 mL, 41.3 g, 0.40 mol) was added gradually with stirring and cooling. The mixture was heated to 90° C, and the heat shut off. The temperature rose to 94° C, when a large amount of solid appeared. After cooling and quenching in ice, there was obtained 25.6 g of white solid having a broad melting range.

A 3.0 g portion of this product dissolved only partially in hot 95% ethanol; the remainder was collected. **7:** White solid, yield 17%, 0.49 g, mp 179–182° C, lit.<sup>30</sup> 179–182° C. <sup>1</sup>H NMR (CCl<sub>4</sub>, very sparingly soluble): δ<sub>H</sub> 2.564 (6H, s, methyl), 8.573 (1H, s, aromatic). The ethanol soluble product is presumably a mixture of 2,4- and 4,6-dinitro-*m*-xylenes.

**2,4-Dinitro-1,3,5-trimethylbenzene (dinitromesitylene) (8).** Product from a student preparation was purified. **8:** White crystals, mp 82–84° C (from 95% EtOH); lit.<sup>31</sup> 86° C. <sup>1</sup>H NMR (CCl<sub>4</sub>): δ<sub>H</sub> 2.231 ppm (s, 3H, 3-methyl), 2.328 ppm (s, 6H, 1,5-dimethyl), 7.058 ppm (s, 1H, aromatic).

**2,4,6-Trinitrochlorobenzene (picryl chloride) (26).** The two-step procedure of Wright, *et al.*<sup>32</sup> was followed. From picric acid (5.24 g, 0.0229 mol) and pyridine (2.0 g, 0.025 mol) was obtained pyridinium picrate, yellow solid, yield 97%, 6.83 g. A solution of this product (6.18 g, 0.0206 mol) and POCl<sub>3</sub> (2.29 g, 0.0143 mol) in benzene (5 mL) was refluxed for 20 min. **26:** Pale yellow crystals, yield 78%, 3.97 g, mp 78–80° C, lit.<sup>32</sup> 83° C. <sup>1</sup>H NMR (CCl<sub>4</sub>): δ<sub>H</sub> 8.788 (2H, s, aromatic), 9.109 (s, very weak, impurity, 2% of height of main signal).

**2,4,6-Trinitrofluorobenzene (picryl fluoride) (27).** Using the method of Shaw and Seaton,<sup>33</sup> 2,4-dinitrofluorobenzene (5.0 g, 0.027 mol), KNO<sub>3</sub> (10.5 g, 0.104 mol), and 20% fuming H<sub>2</sub>SO<sub>4</sub> (29 mL), were heated for 48 hr at 125° C. **27:** White crystals, yield 50%, 3.18 g, mp 125–7° C, lit.<sup>33</sup> 122–3° C. <sup>1</sup>H NMR (CCl<sub>4</sub>): δ<sub>H</sub> 9.12 ppm, (2H, d, <sup>3</sup>J<sub>HH</sub> 5.4 Hz; <sup>19</sup>F (no standard), –114.5 ppm (t, <sup>4</sup>J<sub>HF</sub> 5.4 Hz).

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## References

1. Desiraju, G. R. *Acc. Chem. Res.* **2002**, *35*, 565–573.

- <http://dx.doi.org/10.1021/ar010054t>
2. Vega, I. El D.; Gale, P. A.; Light, M. E.; Loeb, S. J. *Chem. Commun.* **2005**, 4913–4915.  
<http://dx.doi.org/10.1039/b510506d>
  3. Ammer, J.; Nolte, C.; Karaghiosoff\*, K.; Thallmair, S.; Mayer, P.; deVivie–Riedle, R.; Mayr, H. *Chemistry, Eur. J.* **2013**, *19*, 14612–14630.  
<http://dx.doi.org/10.1002/chem.201204561>
  4. Shi, G.; Gadhe, C. G.; Park, S–W.; Kim, K. S.; Kang, J.; Seema, H.; Singh, N. J.; Cho, S. J. *Org. Lett.* **2014**, *16*, 334–337.  
<http://dx.doi.org/10.1021/ol402819m>
  5. Struble, M.D.; Strull, J.; Patel, K.; Siegler, M. A.; Lectka, T. *J. Org. Chem.* **2014**, *79*, 1–6.  
<http://dx.doi.org/10.1021/jo4018205>
  6. Salamone, M.; DiLabio, G. A.; Bietti, M. *J. Org. Chem.* **2012**, *77*, 10479–10487.  
<http://dx.doi.org/10.1021/jo3019889>
  7. Slasinski, F. M.; Tustin, J. M.; Sweeney, F. J.; Armstrong, A. M.; Ahmed, Q. A.; Lorand, J. *P. J. Org. Chem.* **1976**, *41*, 2693–2699.  
<http://dx.doi.org/10.1021/jo00878a007>
  8. Lorand, J. P.; Nelson, J. P.; Gilman, R. D.; Staley, K. L.; Chambers, J. R.; Kirk, H. D.; Moeggenborg, K. J.; Farlow, D. L. *J. Phys. Org. Chem.* **1990**, *3*, 659–669.  
<http://dx.doi.org/10.1002/poc.610031007>
  9. Lorand, J. P. *J. Phys. Org. Chem.* **2011**, *24*, 267–273.  
<http://dx.doi.org/10.1002/poc.1740>
  10. Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Taft, R. W.; Morris, J. J.; Taylor, P. J.; Laurance, C.; Berthelot, M.; Doherty, R. M.; Kamlet, M. J.; Abboud, J–L. M.; Sraidi, K.; Guihéneuf, G. *J. Amer. Chem. Soc.* **1988**, *110*, 8534–8536.  
<http://dx.doi.org/10.1021/ja00233a034>
  11. Bunnett, J. F.; Garbisch, E. W., Jr.; Pruitt, K. M. *J. Amer. Chem. Soc.* **1957**, *79*, 385–391.  
<http://dx.doi.org/10.1021/ja01559a040>
  12. Choi, C. S.; Abel, J. E. *Acta Cryst. B*, **1972**, *28*, 193–201.  
<http://dx.doi.org/10.1107/S0567740872002067>
  13. Taft, R. W. *Steric Effects in Organic Chemistry*, Wiley: NY, 1956; pp 552–554.
  14. Hanford, W. E.; Adams, R. *J. Amer. Chem. Soc.* **1935**, *57*, 1592–1595.  
<http://dx.doi.org/10.1021/ja01312a026>
  15. Rieger, M.; Westheimer, F. H. *J. Amer. Chem. Soc.* **1950**, *72*, 19–28, and 28–32.  
<http://dx.doi.org/10.1021/ja01157a006>
  16. Carper, W. R.; Davis, L. P.; Extine, M. W. *J. Phys. Chem.* **1982**, *86*, 459–462.  
<http://dx.doi.org/10.1021/j100393a009>
  17. “...F and H are so nearly the same size.” Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*, Interscience: NY, 1965; reprinted by the Amer. Chem. Soc., 1981, p 146.

18. From 15 crystal structures, the statistical average van der Waals radius of F is 1.40 Å:  
Zefirov, Yu. V.; Porai-Koshits, M. A. *Zh. Strukt. Khimii* **1980**, *21*, 150–155.
19. Calculated van der Waals radius of H in H<sub>2</sub>, HCl, & HCN is in the range 0.86 to 0.97 Å:  
Ikuta, S.; Ishikawa, M.; Katado, M.; Sano, H. *Acta Cryst.* **1990**, *B46*, 23–27.  
<http://dx.doi.org/10.1107/S010876818901030X>
20. Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.  
<http://dx.doi.org/10.1021/cr00002a004>
21. Nakano, M.; Nakano, N. I.; Higuchi, T. *J. Phys. Chem.* **1967**, *71*, 3954–3959.  
<http://dx.doi.org/10.1021/j100871a034>
22. Bennett, G. M.; Wain, R. L. *J. Chem. Soc.* **1936**, 1108–1114.  
<http://dx.doi.org/10.1039/jr9360001108>
23. Fendler, E. J.; Fendler, J. H.; Arthur, N. L.; Griffin, C. E. *J. Org. Chem.* **1972**, *37*, 812–819.  
<http://dx.doi.org/10.1021/jo00971a002>
24. Malherbe, D. F. T. *Chem. Ber.* **1919**, *52*, 319–324.  
<http://dx.doi.org/10.1002/cber.19190520222>
25. Carpenter, M. S. *J. Org. Chem.* **1951**, *16*, 586–617.  
<http://dx.doi.org/10.1021/jo01144a011>
26. Zook, H. D. *J. Amer. Chem. Soc.* **1955**, *77*, 2501–2503.  
<http://dx.doi.org/10.1021/ja01614a042>
27. Murphy, J. T. *J. C. S. Perkin 2* **1987**(12), 1767–1772.
28. Liss, E.; Lohmann, K. *Chem. Ber.* **1956**, *89*, 2546–2550.  
<http://dx.doi.org/10.1002/cber.19560891110>
29. Adolph, H. G.; Dacons, J. C.; Kamlet, M. J. *Tetrahedron* **1963**, *19*(6), 801–807.  
[http://dx.doi.org/10.1016/S0040-4020\(01\)99330-5](http://dx.doi.org/10.1016/S0040-4020(01)99330-5)
30. Fieser, L. F.; Clapp, R. C.; Daudt, W. H. *J. Amer. Chem. Soc.* **1942**, *64*, 2052–2060.  
<http://dx.doi.org/10.1021/ja01261a014>
31. Bayless, P. L.; Hauser, C. R. *J. Amer. Chem. Soc.* **1954**, *76*, 2306.  
<http://dx.doi.org/10.1021/ja01638a007>
32. Boyer, R.; Spencer, E. F.; Wright, G. F. *Can. J. Res.* **1946**, *24B*, 200–203.  
<http://dx.doi.org/10.1139/cjr46b-025>
33. Shaw, G. C.; Seaton, D. L. *J. Org. Chem.* **1961**, *26*, 5227–5229.  
<http://dx.doi.org/10.1021/jo01070a525>