Evidence for Electronic Buttressing in 4-Substituted *NN*-Dimethyl-2-trifluoromethylanilines: Long Range ^{19}F–^{1}H Coupling

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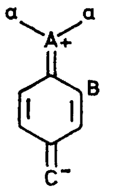
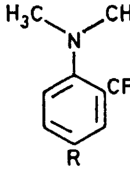
The ^{1}H n.m.r. spectra of a series of 4-substituted derivatives of *NN*-dimethyl-2-trifluoromethylaniline have been examined; a long range ^{19}F–^{1}H coupling $^{6}J(F,H)$ between NCH_3 and CF_3 was confirmed by ^{19}F n.m.r. A linear relation obtains between $^{6}J(F,H)$ in these compounds and the appropriate Hammett *para*-substituent constants in accord with the operation of electronic buttressing; a similar correlation holds between the chemical shift of the *N*-methyl protons and σ_p.

THE stabilisation of aromatic structures with one substituent (Aaa) in a sterically hindered conformation *ortho* to a bulky group (B) *via* conjugation with a *para*-substituent (C) [see (I)] has been termed electronic buttressing.[1] Herrmann and Rae demonstrated[2] the operation of such an effect from measurements of ^{1}H n.m.r. chemical shifts in a variety of nitro-compounds. In 4-substituted 1,2-dinitrobenzenes the magnitude of the electronic buttressing was shown to depend on the conjugative ability of the 4-substituent as indicated by the appropriate Hammett constant.



(I)



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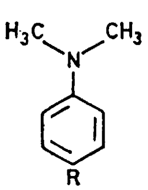

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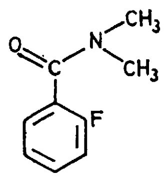


(IV)

We now report an n.m.r. investigation of a series of 4-substituted derivatives of *NN*-dimethyl-2-trifluoromethylaniline (II) in which the spin–spin coupling over six bonds between CF_3 and NCH_3 is also shown to depend on the Hammett σ parameter of the substituent R.

The splitting of the NCH_3 signal into a 1 : 3 : 3 : 1 quartet in the ^{1}H n.m.r. spectrum of the nitro-derivative (II; R = NO_2) was confirmed as originating from spin–spin splitting by a $^{1}H\{^{19}F\}$ double resonance experiment: decoupling from CF_3 collapsed the NCH_3 quartet of the nitro-compound (II; R = NO_2).

Fifteen values of $^{6}J(F,H)$ for this series (II), derived mainly from 100 MHz spectra, are listed in the Table. For those compounds in which splittings were not resolved, $^{6}J(F,H)$ was estimated from the ratio of the widths at half-height of the NCH_3 and tetramethylsilane signals.[3] These values of *J* represent averages of the couplings of CF_3 to both methyl groups since rotation about the ring-nitrogen bond is relatively free at ambient temperature. Now, in a study of internal rotation in certain *para*-substituted dimethylanilines (III), separate ^{1}H n.m.r. signals were observed[4] for the two CH_3 groups at low temperatures with coalescence temperatures between 139 (III; R = $COCH_3$) and 185.5 K (III; R = NO). No perceptible broadening was observed in our work for the NCH_3 signals of the nitro-derivative (II; R = NO_2) in solution in $CFCl_3$–CD_3COCD_3 at temperatures down to 173 K. The chemical shifts of CH_3 in different conformers may be similar or, as is more likely, the sterically compressed $N(CH_3)_2$ group may not have a conformation of significantly lower energy (*cf.* ref. 5).

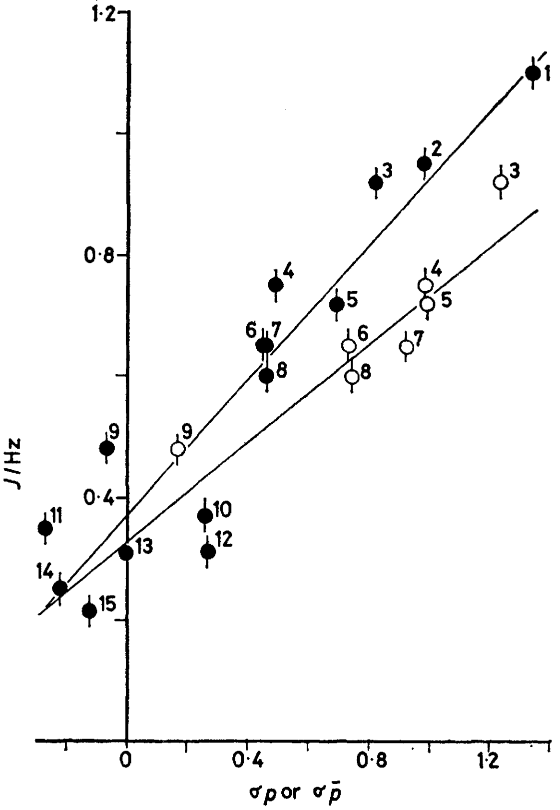
N.m.r. parameters for 4-substituted derivatives of *NN*-dimethyl-2-trifluoromethylaniline (II)

	R	$\lvert ^{6}J(F,H)\rvert$/Hz * ± 0.05	δ_{CH_3} ± 0.01	σ_p	σ_p^-
1	$C(CN)=C(CN)_2$	1.10	3.19	1.33 [a]	
2	$CH=C(CN)_2$	0.95	3.08	0.98 [a]	
3	NO_2	0.92	3.04	0.82 [b]	1.23 [c]
4	CHO	0.75	2.99	0.49 [b]	0.98 [c]
5	CN	0.72	2.95	0.69 [b]	0.99 [c]
6	CO_2H	0.65	2.95	0.45 [d]	0.73 [b]
7	COC_6H_3-(3-CF_3)-(4-NMe_2)	0.65	2.94	0.46 [e]	0.92 [e]
8	CO_2Me	0.60	2.90	0.46 [b]	0.74 [c]
9	$SiMe_3$	0.48 [f]	2.79 [f]	−0.07 [d]	0.17 [b]
10	Br	0.37	2.72	0.26 [b]	
11	NH_2	0.35	2.62	−0.27 [c]	
12	Cl	0.31	2.70	0.27 [b]	
13	H	0.31	2.73	0	
14	NMe_2	0.25	2.62	−0.22 [c]	
15	Me	0.23	2.62	−0.12 [b]	

* Measured directly from splittings for compounds 1—8.

[a] Determined spectroscopically by J. Griffiths and L. R. Mosley, unpublished work. [b] O. Exner, 'Advances in Linear Free Energy Relationships,' eds. N. B. Chapman and J. Shorter, Plenum, London, 1972, p. 1. [c] Ref. 9. [d] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 425. [e] Value for benzoyl taken from ref. 10; *cf.* J. Hine, 'Structural Effects on Equilibria in Organic Chemistry,' Wiley–Interscience, New York, 1975, p. 65. [f] Based on CH_2Cl_2 as reference.

If the observed $^{6}J(F,H)$ in this series (II) is taken to be a through-space coupling,[6] as in the corresponding structure (IV),[7] and therefore dependent on the proximity of the coupled nuclei, a correlation may be expected between ^6J(F,H) and the Hammett σ_p values of R; a similar explanation was adopted by Burdon [8] who showed that ^5J(F,H) between NCH_3 and *o*-F in substituted dimethylanilines increased with increasing electronegativity of the ring substituents. The greater the value of σ_p, the more significant will be the contribution of canonical structures represented by (I) to the resonance hybrid, and hence the greater the time spent by CH_3 close to CF_3. A graph (Figure) shows that ^6J(F,H) increases with σ_p (Table 1) and that the points lie close to a straight line: the correlation (r 0.933) is only slightly improved (r 0.947) by use of the parameter σ_p^- where available for groups capable of mesomeric interaction with $N(CH_3)_2$. ^6J(F,H) could, however, also be correlated with a more complex function of σ_p; there is no reason to expect a linear relationship since the value of a through-space coupling does not depend on the first power of internuclear separation,[6] and a direct proportionality between residence time and ^6J(F,H) cannot be assumed.



Graphs of ^6J(F,H) against σ_p (●) or σ_p^- (○) where appropriate. For key to numbering, see Table

The values of σ_p for the strongly electron donating NH_2 and $N(CH_3)_2$ groups are those recently proposed by Wepster;[9] the values of σ_p recommended hitherto fit the linear correlation with ^6J(F,H) if the sign of ^6J(F,H) for these derivatives [II; R = NH_2 and $N(CH_3)_2$] is taken to be opposite to that for the other compounds given in the Figure. Spin-tickling experiments to determine the sign of ^6J(F,H) were not possible because of the superposition of further, unresolved couplings between ring protons and CF_3. The ^{19}F resonance was therefore a broadened singlet for which the width at half height was proportional to ^6J(F,H) [*e.g.*, 3.0 ± 0.1 Hz for (II; R = NH_2) and 5.0 ± 0.1 Hz for (II; R = NO_2)].

An approximately linear correlation (r 0.969) holds between the chemical shift of NCH_3 (Table 1) and σ_p or σ_p^- for the same compounds which are included in the Figure. The degree of dependence of δ_{CH_3} on σ_p is greater (0.29 ± 0.03 p.p.m. per σ unit) than that reported[10] by Rae and Dyall for the corresponding *para*-substituted dimethylanilines (0.17 p.p.m. per σ unit) in solution in chloroform. Possible explanations of the increased dependence include increased chemical shift contributions in the conformer represented by (I) from the magnetic anisotropy and electric field of CF_3 and/or the attenuation by the bulky CF_3 group of those disturbances due to self-association which tend[10] to reduce the substituent effect.

Preparations.—Several of the compounds (II; R = H, Br, NH_2, and NO_2) have been described previously[11] and others [II; R = Cl, CH_3, CN and $N(CH_3)_2$] will appear elsewhere.[12] The remaining intermediates were mainly derived from 4-bromo-2-trifluoromethyl-*NN*-dimethylaniline *via* the corresponding lithium derivative. 4-Dicyanovinyl-2-trifluoromethyl-*NN*-dimethylaniline was readily obtained from the appropriate aldehyde and malononitrile.[13] The corresponding tricyanovinyl compound was obtained from the dicyanovinyl derivative and potassium cyanide in the presence of lead(IV) acetate;[14] use of an old sample of lead(IV) acetate led to the formation of 4-tricyanoethyl-2-trifluoromethyl-*NN*-dimethylaniline.

EXPERIMENTAL

Ambient temperature ^1H n.m.r. spectra were recorded for solutions in deuteriochloroform on Varian HA 100 and HR 220 spectrometers at the Physicochemical Measurements Unit, Harwell. ^{19}F N.m.r. spectra were obtained on a Bruker HX 90E instrument at 84.67 MHz and 22 °C. Variable temperature ^1H n.m.r. spectra and ^1H spectra with decoupling from ^{19}F were also recorded on the Bruker spectrometer, at 90 MHz.

4-Dimethylamino-3-trifluoromethylbenzoic Acid.—4-Bromo-2-trifluoromethyl-*NN*-dimethylaniline[11] (2.6 g, 0.01 mol) in ether (20 cm³) was added dropwise to butyl-lithium (0.01 mol) in ether–hexane at 0 °C. After 15 min, the mixture was poured onto solid carbon dioxide and the usual work-up gave the *acid* (70%), m.p. 158—160 °C [from light petroleum (b.p. 80—100 °C)] (Found: C, 51.2; H, 4.3; F, 24.4; N, 6.3. $C_{10}H_{10}F_3NO_2$ requires C, 51.5; H, 4.3; F, 24.5; N, 6.0%), τ 1.67 (1 H, d, J_m 2.5 Hz, 2-H), 1.92 (1 H, dd, J_o 9.0, J_m 2.5 Hz, 6-H), 2.91 (1 H, d, J_o 9.0 Hz, 5-H), and 7.05 (6 H, s, NMe_2). The *methyl ester*, b.p. 81 °C at 1 mmHg, m.p. 49 °C, prepared from the acid using boron trifluoride–methanol reagent,[15] was crystallised from light petroleum (b.p. 60—80 °C) after initial distillation (Found: C, 53.4; H, 4.9; F, 23.4; N, 6.0. $C_{11}H_{12}F_3NO_2$ requires

C, 53.4; H, 4.9; F, 23.1; N, 5.7%), τ 1.73 (1 H, d, J_m 2.5 Hz, 2-H), 1.96 (1 H, dd, J_o 9.0, J_m 2.5 Hz, 5-H), 2.88 (1 H, d, J, 9.0 Hz, 6-H), 6.11 (3 H, s, CO_2Me), and 7.10 (6 H, s, NMe_2).

2-*Trifluoromethyl*-4-*trimethylsilyl*-NN-*dimethylaniline*.—4-Dimethylamino-3-trifluoromethylphenyl-lithium, prepared as above, was treated with chlorotrimethylsilane (2.5 g). After 90 min, the mixture was decomposed with water. Removal of solvent from the dried (Na_2SO_4) organic layer and distillation of the residue gave 2-*trifluoromethyl*-4-*trimethylsilyl*-NN-*dimethylaniline* (82%), b.p. 119 °C at 2 mmHg (Found: C, 55.6; H, 6.8; F, 21.4; N, 5.6. $C_{12}H_{18}F_3NSi$ requires C, 55.1; H, 6.9; F, 21.8; N, 5.4%), τ 2.24 (1 H, s, 3-H), 2.33 (1 H, d, J_o 8.5 Hz, 5-H), 2.68 (1 H, d, J_o 8.5 Hz, 6-H), 7.21 (6 H, s, NMe_2), and 9.68 (9 H, s, $SiMe_3$).

4,4′-*Bisdimethylamino*-3,3′-*bistrifluoromethylbenzophenone*.—A solution of 4-dimethylamino-3-trifluoromethylbenzonitrile [12] (4.0 g) in ether (25 cm^3) was added over 20 min to a solution of 4-dimethylamino-3-trifluoromethylphenyl-lithium [from the bromo-compound (5.05 g)]. The mixture, which became dark red, was stirred at room temperature overnight and then decomposed with water. The organic layer was extracted with concentrated hydrochloric acid and the acid extracts were boiled for 6 h. The cooled solution was basified and was then extracted with chloroform. Removal of solvent from the dried organic layer gave a brown solid which was eluted from alumina with chloroform; recrystallisation of the residue from light petroleum (b.p. 30—40 °C) gave pale brown prisms of the *ketone* (65%), m.p. 76—76.5 °C (Found: C, 56.2; H, 4.5; F, 28.5; N, 7.3. $C_{19}H_{18}F_6N_2O$ requires C, 56.4; H, 4.5; F, 28.2; N, 6.9%), τ 1.96 (2 H, d, J_m 2.5 Hz, 2,2′-H), 2.16 (2 H, dd, J_o 9.0, J_m 2.5 Hz, 6,6′-H), 2.86 (2 H, d, J_o 9.0 Hz, 5,5′-H), and 7.06 (12 H, s, 4,4′-NMe_2).

4-*Dimethylamino*-3-*trifluoromethylbenzaldehyde*.—The aryl-lithium derivative, prepared as above from the bromo-compound (30 g), was treated with dimethylformamide (8.2 g). After 1 h, the usual work-up gave the *aldehyde* (89%), b.p. 165 °C at 25 mmHg (Found: C, 55.5; H, 4.7; F, 26.3; N, 6.8. $C_{10}H_{10}F_3NO$ requires C, 55.3; H, 4.7; F, 26.3; N, 6.5%), τ 0.16 (1 H, s, CHO), 1.94 (1 H, d, J_m 2.5 Hz, 2-H), 2.13 (1 H, dd, J_o 9.0, J_m 2.5 Hz, 6-H), 2.89 (1 H, d, J_o 9.0 Hz, 5-H), and 7.01 (6 H, s, NMe_2). The 2,4-*dinitrophenylhydrazone* had m.p. 226 °C (Found: C, 48.4; H, 3.7; F, 14.6; N, 17.6. $C_{16}H_{14}F_3N_5O_4$ requires C, 48.4; H, 3.5; F, 14.4; N, 17.6%).

4-*Dicyanovinyl*-2-*trifluoromethyl*-NN-*dimethylaniline*.—A solution of 4-dimethylamino-3-trifluoromethylbenzaldehyde (4.1 g) in ethanol (40 cm^3) was treated with malononitrile (1.37 g) and piperidine (6 drops). After 36 h at room temperature, the solid was collected and recrystallised from ethanol to give yellow plates of 4-*dicyanovinyl*-2-*trifluoromethyl*-NN-*dimethylaniline* (67%), m.p. 97—97.5 °C (Found: C, 58.9; H, 3.9; F, 21.2; N, 15.9. $C_{13}H_{10}F_3N_3$ requires C, 58.9; H, 3.8; F, 21.5; N, 15.8%), τ 1.92 (1 H, dd, J_o 9.0, J_m 2.5 Hz, 5-H), 2.08 (1 H, d, J_m 2.5 Hz, 3-H), 2.46 [1 H, s, $CH{=}C(CN)_2$], 2.97 (1 H, d, J_o 9.0 Hz, 6-H), and 6.92 (6 H, s, NMe_2).

4-*Tricyanovinyl*-2-*trifluoromethyl*-NN-*dimethylaniline*.—A solution of the dicyanovinyl compound (1.0 g) in dimethylformamide (5.7 cm^3) was treated with a solution of potassium cyanide (0.43 g) in water (1.7 cm^3). The mixture was kept at 25 °C for 5 min and then warmed to 35 °C whereupon a fresh solution of lead(IV) acetate (3.2 g) in acetic acid (6.3 cm^3) was added. After 3 h, the mixture was poured into water, neutralised, and extracted with chloroform. The leading band from a preparative layer chromatogram of the dried extracts on silica was collected. The solid which was recovered was crystallised from chloroform to give the *tricyanovinyl derivative*, m.p. 214 °C, as red needles (Found: C, 57.8; H, 3.0; F, 19.8; N, 19.3. $C_{14}H_9F_3N_4$ requires C, 57.9; H, 3.1; F, 19.6; N, 19.3%), τ 1.70 (1 H, d, J_m 2.0 Hz, 3-H), 1.87 (1 H, dd, J_o 9.0, J_m 2.0 Hz, 5-H), 2.98 (1 H, d, J_o 9.0 Hz, 6-H), and 6.81 (6 H, s, NMe_2). When an old sample of lead(IV) acetate was used, there was obtained 4-*tricyanoethyl*-2-*trifluoromethyl*-NN-*dimethylaniline* (26%), m.p. 106 °C (Found: C, 57.7; H, 3.9; F, 19.5; N, 19.3. $C_{14}H_{11}F_3N_4$ requires C, 57.5; H, 3.8; F, 19.5; N, 19.2%), τ 2.36 (1 H, s, 3-H), 2.40 (1 H, d, J_o 9.0 Hz, 5-H), 2.72 (1 H, d, J_o 9.0 Hz, 6-H), 5.54 [1 H, d, J 5.0 Hz, $CH(CN)CH(CN)_2$], 5.74 [1 H, d, J 5.0 Hz, $CH(CN)CH(CN)_2$], and 7.12 (6 H, s, NMe_2).

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