Nitrogen-15 Chemical Shifts in Ring-substituted Benzamides and Benzonitriles

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The nitrogen-15 shifts of a series of enriched benzamides and benzonitriles have been measured utilizing the Fourier pulse method. A correlation of the nitrogen shifts with Hammett substituent constants has been observed. π-Density changes are shown to contribute to the observed changes in nitrogen-15 shifts within each series.

THE analytical potential of the less abundant isotope of nitrogen, ^{15}N (natural abundance 0·36%), has long been recognised. Previously, low natural abundance and long relaxation times have limited the number of single resonance studies of this nucleus, and double resonance studies,[1] although accurate, were tedious. Roberts and his co-workers determined the nitrogen-15 shifts of some nitrobenzene derivatives[2] directly and more recently Axenrod *et al.* have measured the positions of the nitrogen-15 absorptions for ring-substituted anilines.[3] Recent advances in instrumental technique[4] and an increase in the number of commercially available enriched materials have facilitated such studies of this nucleus. The scope of nitrogen-15 spectroscopy has been reviewed.[5]

We now report our observations on a selection of ^{15}N-enriched benzamides (I) and benzonitriles (II), data for which are shown in the Table. Spectra were obtained utilizing the Fourier pulse method, which gives a signal-to-noise gain of approximately 25.[4] Wide-band decoupling of the protons was also employed to facilitate the observation of the nitrogen resonances in the benzamides. Thus the nitrogen signal of [^{15}N]-benzamide appears as a singlet instead of a multiplet. Additionally, a signal-to-noise gain of between two and three results from the nuclear Overhauser effect (NOE) associated with the proton decoupling.[4] The multiplet collapse and NOE combine to afford excellent spectra of the amides in less than one quarter of the time necessary to obtain comparable spectra of the nitriles.

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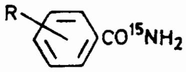
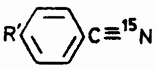


(I)



(II)

No.	R	δ^{15}N/p.p.m.[a,b]	No.	R′	δ^{15}N/p.p.m.[c,d]
1	*p*-NO_2	+3·3	13	*p*-NO_2[e]	+8·8
2	*p*-CN	+2·7	14	*p*-CN[e]	+7·5
3	*m*-NO_2	+1·5	15	*p*-Cl	+2·9
4	*m*-Br	+0·9	16	*p*-Br	+2·7
5	*m*-F	+0·8	17	*p*-H	0
6	*p*-Br	+0·6	18	*p*-Me	−0·3
7	*p*-Cl	+0·5	19	*p*-MeO	−2·7
8	*p*-H	0			
9	*m*-Me	−0·1			
10	*p*-F	−0·1			
11	*p*-Me	−0·8			
12	*p*-MeO	−1·7			

[a] Measured as 1·4*m* solutions in dimethyl sulphoxide. [b] Error estimated to be within ±0·1 p.p.m. [c] Measured as 1·0—2·0*m* solutions in chloroform. [d] Error estimated to be within ±0·2 p.p.m. [e] Saturated solution in chloroform.

A positive δ value denotes a shift to high frequency.

The general approach to the theory of nitrogen shifts has been reviewed.[5,6] The proven assumption of the dominance of the paramagnetic term, σ_p, in the equation for the total screening is made. Further we have made no correction for the smaller diamagnetic term, σ_d, although this approach has recently been advocated.[7]

The high field position of the nitrogen-14 absorptions in amides relative to nitriles has been reported previously.[8] In agreement with this we have observed a ^{15}N chemical shift difference of 153 p.p.m. between benzamide and benzonitrile with the former absorption at higher field. The nitrogen-15 shifts in these compounds relative to the ammonium ion of ^{15}N-enriched ammonium chloride (5M in 2N-HCl) are +77·7 and +231·0 p.p.m., respectively, where a positive sign denotes a shift to high frequency. Compared with the total observed range of nitrogen shifts, $\Delta\delta$, of *ca.* 900 p.p.m., variations within each series of compounds are relatively small (Table); however, the values of 5·0 and 11·5 p.p.m. for the amides and nitriles, respectively, are of the same order of magnitude as the 4·5 p.p.m. range found for ring-substituted nitrobenzenes.[2] For ring-substituted anilines, where a direct mesomeric interaction of the substituent with the aniline nitrogen atom is considered important, a larger nitrogen shift of *ca.* 38 p.p.m. has been observed.[3]

The effect of the ring substituent on the nitrogen shift is observed to be qualitatively the same for both classes of compounds. An electron-withdrawing group produces a low field shift of the nitrogen resonance whereas an electron-donating group produces a shift in the opposite sense. Similar substituent effects have been observed on the i.r. stretching frequencies in benzonitriles [ν(C≡N)] and *NN*-dimethylbenzamides (amide I band), the higher frequencies being associated with electron-withdrawing groups.[9] The C-1 carbon-13 shifts

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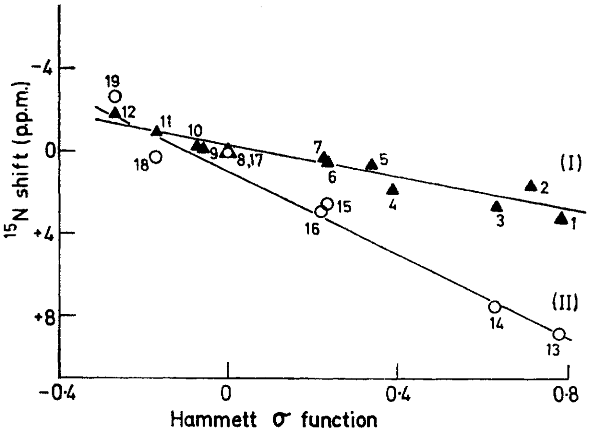
of benzonitriles[10] and benzamides[11] are known to be responsive to substituents. We find the sense of the shifts to be the same for nitrogen as for the C-1 carbon resonances.

The observed ^{15}N shift differences between the *meta*- and *para*-isomers of the benzamide series, allied to the fact that the methoxy-group, which exerts a powerful mesomeric but only a weak inductive effect, produces an appreciable upfield shift of the nitrogen resonance, suggest that changes in π electron density affect the paramagnetic term of the nitrogen shift expression for the nitriles and benzamides. This conclusion appears to differ from that found for substituted nitrobenzenes,[2,12] where the nitrogen shift was found to be insensitive to π electron conjugation. An attempt to relate our data to the Hammett substituent constant, σ, a parameter known to include contributions from π electron densities in aromatic systems, resulted in an approximately linear relationship between σ and the nitrogen-15 shift in both classes of compound. A similar relationship between the Hammett substituent constant and nitrogen-15 shift has recently been observed for ring-substituted aniline derivatives.[3] Attempts to correlate the nitrogen shifts with either σ_p or σ_m afforded less satisfactory results with significant deviations from linearity within each class of compound.



For key to numbering, see Table

Thus we conclude that it is the total electronic effect of the substituent which is important in determining the nitrogen shift.

EXPERIMENTAL

Nitrogen-15 spectra were measured on a Bruker HFX-13 multinuclear spectrometer operating at 9·12 MHz. Solutions were contained inside 5 mm tubes which were inserted concentrically in a 10 mm tube containing neat hexafluorobenzene, the fluorine resonance of which was used to provide a field-frequency lock.

The spectra were obtained by storing the free-induction decays afforded by a series of 40 μs r.f. pulses in a Fabritek 1074 computer of average transients. The resulting interferograms were then each Fourier-transformed utilizing a Digital PDP 81 computer. Line widths were of the order of 2 Hz.

[^{15}N]Ammonium chloride (97 atom % ^{15}N) was obtained from Prochem Ltd. The ring-substituted benzamides were prepared by reactions of the appropriate acid chlorides with [^{15}N]ammonium chloride following the procedure described by Swan and Kelly.[13] Dehydration of the [^{15}N]amides with benzenesulphonyl chloride in pyridine afforded the ring-substituted [^{15}N]benzonitriles. The crude materials had m.p.s and i.r. spectra in good agreement with the literature values and were used without further purification.

The benzamides were measured as 1·4*m* solutions in dimethyl sulphoxide, whereas the nitriles were measured as 1·0—2·0*m* solutions in chloroform. The *p*-cyano- and *p*-nitro-derivatives of benzonitrile were measured as saturated solutions.

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