

to be more stable than either **6b** or **6b'**. Since the conformation **6b''** has a dimethylamino group in a pseudo-equatorial position, the observed increase in basicity is not unreasonable.

The dissociation constant of the tertiary amine **6c** is quite similar to that of **6b**, suggesting that the two bases may have similar conformations. The basicity of the tetramethyl derivative **8b** is less than that of **8a**. In **8b**, the axial methyl groups at the 2,6-positions may hinder solvation of  $^+NH(CH_3)_2$ , and hence the basicity of the amino group may be reduced.

### Experimental Section

4-Aminooxanes **1a,b,d,e**, **2a,b,d,e**, and **3** were prepared as reported.<sup>9</sup> Preparation of compounds **1c,f-n**, **2c,f-n**, **4a-f**, **5a-f**, **6a-c**, **7a-c**, and **8a**, will be reported elsewhere.<sup>10</sup>

**General Procedure for the Measurement of Dissociation Constants.**<sup>4</sup> The amines were purified by either repeated crystallizations or distillation under reduced pressure. Methyl Cellosolve (2-methoxyethanol) was purified initially by distillation over quick lime and subsequently by fractionation using a Dufton column [bp 124 °C (760 mm)]. Distilled water, free from carbon dioxide, was prepared, and 80% 2-methoxyethanol was used as the solvent.

The amine (about 15 mg) was dissolved in 80% 2-methoxyethanol (25 mL). While the solution was stirred under nitrogen, 0.05 N hydrochloric acid was added dropwise from a buret that could be read to 0.005 mL. The pH values were measured in a pH meter, precalibrated with buffers at pH 4.0 and 9.2 with a glass electrode and a saturated calomel electrode as the reference electrode. All measurements were made at  $27 \pm 0.1$  °C. The equivalence point was determined from a plot of pH against

volume of HCl added. An average value ( $pK_a$ ) of one-fourth, one-half, and three-fourths neutralizations was taken, and at least two independent titrations were carried out on each compound. The pH meter was an Elico Digital pH meter (Model LI-120) with an accuracy of  $\pm 0.01$  pH units.

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**Registry No.** **1a**, 74854-71-0; **1b**, 74854-72-1; **1c**, 85336-31-8; **1d**, 74854-73-2; **1e**, 74854-74-3; **1f**, 85336-32-9; **1g**, 85336-33-0; **1h**, 85336-34-1; **1i**, 85336-35-2; **1j**, 85336-36-3; **1k**, 81158-62-5; **1l**, 81158-63-6; **1m**, 81158-64-7; **1n**, 81158-65-8; **2a**, 74854-79-8; **2b**, 74854-80-1; **2c**, 85336-37-4; **2d**, 74854-81-2; **2e**, 74854-82-3; **2f**, 85336-38-5; **2g**, 85336-39-6; **2h**, 85336-40-9; **2i**, 85336-41-0; **2j**, 85336-42-1; **2k**, 81158-68-1; **2l**, 81158-69-2; **2m**, 81158-70-5; **2n**, 81158-71-6; **3**, 74854-70-9; **4a**, 85336-43-2; **4b**, 85336-44-3; **4c**, 81203-25-0; **4d**, 85404-41-7; **4e**, 81158-66-9; **4f**, 81158-67-0; **5a**, 85404-42-8; **5b**, 85404-43-9; **5c**, 81203-26-1; **5d**, 85404-44-0; **5e**, 81203-27-2; **5f**, 81203-28-3; **6a**, 85336-45-4; **6b**, 81158-72-7; **6c**, 85336-46-5; **7a**, 85336-47-6; **7b**, 81158-73-8; **7c**, 85336-48-7; **8a**, 85336-49-8; **8b**, 85336-50-1.

## Substituent Effects on $^{15}N$ and $^{17}O$ Chemical Shifts in Nitrobenzenes: Correlations with Electron Densities

David J. Craik,<sup>\*1a</sup> George C. Levy,<sup>1b</sup> and Robert T. C. Brownlee<sup>1c</sup>

Departments of Chemistry, Syracuse University, Syracuse, New York 13210, and La Trobe University, Bundoora, Victoria 3083, Australia

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$^{15}N$  and  $^{17}O$  NMR spectra have been measured for a series of para- and meta-substituted nitrobenzenes, and the derived substituent chemical shifts (SCS) have been correlated with  $\sigma_I$  and  $\sigma_R$  substituent constants by using the dual substituent parameter (DSP) equation. The polar nature of the substituent is most important in determining the nitrogen chemical shifts, which follow a "reverse" trend; i.e., electron-withdrawing substituents induce *upfield*  $^{15}N$  shifts. This observation is consistent with a  $\pi$ -polarization mechanism in which the  $N=O$  bonds are polarized by the dipole of the substituent. The proposal that this mechanism is transmitted through space and is not dependent on conjugation between the substituent and side-chain nitro group is confirmed by the observation that substituent effects on  $^{15}N$  SCS values are  $\sim 25\%$  larger in the meta series compared with the para series. Substituent chemical shifts at the oxygen atom are an order of magnitude larger than those at nitrogen and depend strongly on both polar and resonance substituent effects. The  $^{17}O$  shifts follow a normal direction (i.e., donor substituents induce upfield shifts) and are smaller in the meta series than in the para series. Calculated ab initio  $\pi$ -electron densities reproduce the  $^{15}N$  and  $^{17}O$  chemical shift trends.

Over the last decade, NMR chemical shifts have been used extensively as probes of electronic substituent effects.<sup>2-4</sup> Although  $^1H$  chemical shifts show small but

systematic changes with molecular substitution, the larger chemical shift range of  $^{13}C$  and  $^{19}F$  nuclei makes them more useful probes, as has been demonstrated recently in studies of substituent effects at ring<sup>4-6</sup> and side-chain sites<sup>7-9</sup> in

(1) (a) To whom correspondence should be addressed at the School of Pharmaceutical Chemistry, Victorian College of Pharmacy Ltd., Parkville, Victoria 3052, Australia. (b) Camille and Henry Dreyfus Teacher Scholar, 1976-1981. (c) La Trobe University.

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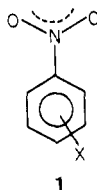
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substituted aromatic derivatives. The utility of NMR chemical shifts as probes of substituent electronic effects relies on there being a linear relationship between measured substituent chemical shifts (SCS) and calculated electron densities. Although there is a good theoretical basis for relating these terms,<sup>10</sup> complicating influences from a number of other factors contribute to chemical shifts, so that precise correlations are not usually obtained, *except* in compounds with closely related structures. The utilization of chemical shifts as electronic probes therefore depends mainly on empirical SCS–electron density correlations in substituted aromatics or similar systems. In this paper we investigate <sup>15</sup>N and <sup>17</sup>O chemical shifts (and corresponding electron densities) in meta- and para-substituted nitrobenzenes (1).



Substituent effects on <sup>13</sup>C and <sup>1</sup>H chemical shifts in the benzene ring of nitrobenzene derivatives are easily measurable and have been previously reported.<sup>6,11</sup> However, studies of substituent effects on nitro-group chemical shifts are more difficult because of the low inherent sensitivity of both <sup>15</sup>N and <sup>17</sup>O nuclei.<sup>12</sup> Despite the growing literature on natural abundance <sup>15</sup>N NMR spectroscopy,<sup>12</sup> there have been relatively few reports pertaining to nitro groups. This results from two factors (in addition to the low natural abundance of <sup>15</sup>N) that make the nitro group particularly insensitive to NMR detection: long spin relaxation times (no nearby protons to assist dipole–dipole relaxation) and small, negative nuclear Overhauser effects, NOE's. Optimization of pulse–flip angles and recycle times in the FT NMR experiment is required to overcome the first difficulty. The second difficulty, i.e., potential signal nulling arising from negative NOE's, can be overcome by gating the proton decoupler on *only* during data acquisition to remove long-range N–H couplings without contributing to a buildup of NOE. For decoupler duty cycles of less than ~5–10%, the NOE is effectively suppressed.

In 1969 Roberts and co-workers<sup>13</sup> reported <sup>15</sup>N chemical shifts for a limited number of substituted nitrobenzenes. That report corrected erroneous <sup>15</sup>N shifts published earlier<sup>14</sup> and also confirmed that the <sup>15</sup>N shifts were in agreement with previously reported <sup>14</sup>N shifts.<sup>15</sup> Our <sup>15</sup>N

SCS measurements essentially corroborate these measurements and extend the range of compounds studied, so that we now have a *uniform* data set for meta- and para-substituted nitrobenzenes where the substituents cover a wide range of electronic properties. In addition, we present ab initio molecular orbital calculations and <sup>17</sup>O-shift data for these systems. Systematic studies of substituent effects on <sup>17</sup>O chemical shifts are just beginning to appear in the literature, with recent reports<sup>16</sup> of <sup>17</sup>O chemical shifts in substituted anisoles, acetophenones, and benzaldehydes showing the potential of this probe as a measure of substituent electronic effects. In his pioneering work some 20 years ago, Christ<sup>17</sup> examined <sup>17</sup>O shifts of some substituted nitrobenzenes; however the high concentrations and small range of substituents used make these data unsuitable for the current analysis. This also applies to the more recent work of Lipkowitz.<sup>18</sup> In this paper we demonstrate the feasibility of obtaining <sup>17</sup>O spectra for natural abundance samples at relatively low concentration. It was necessary to measure the spectra for dilute solutions because intermolecular interactions can markedly affect chemical shifts. If only electronic substituent effects are to be examined, then all extraneous influences must be minimized.

In studies of this type, another important requirement is that the solvent should be relatively inert. Specific solute–solvent interactions with some substituted derivatives and not with others can reduce the validity of correlations between chemical shifts and electronic substituent constants. However, in this study, another important criterion was that of solubility, and for this reason Me<sub>2</sub>SO was chosen as solvent. This proved suitable for the <sup>15</sup>N studies, but for the <sup>17</sup>O measurements it was found advantageous to use a less viscous solvent, and again for solubility reasons CH<sub>3</sub>CN proved the best choice. The <sup>17</sup>O line widths are strongly dependent on the correlation time for molecular motion, with decreased viscosity increasing motion and hence reducing line widths. Line widths for substituted nitrobenzenes in CH<sub>3</sub>CN were found to be on the order of 200 Hz, whereas our initial measurements of <sup>17</sup>O spectra in Me<sub>2</sub>SO gave line widths of up to a factor of 2–3 larger. Since <sup>17</sup>O line widths are inherently broad due to fast quadrupolar relaxation of this nucleus, any factor that brings about a reduction in line widths also brings about a corresponding improvement in the signal-to-noise ratio of the final spectrum.

## Experimental Section

The nitrobenzenes in this study were commercial samples used without further purification. All <sup>15</sup>N and <sup>17</sup>O spectra were obtained at natural abundance for solutions (7–10% w/v) in Me<sub>2</sub>SO (<sup>15</sup>N studies) or CH<sub>3</sub>CN (<sup>17</sup>O studies). Many <sup>15</sup>N chemical shifts in Table I represent the average of two values obtained by using different spectrometers. Most of the para data and all of the meta data were measured on a Bruker WM-360 spectrometer at 36.50 MHz. Twenty millimeter sample tubes were used, and peaks were referenced to a 5-mm concentric capillary containing nitromethane. Internal deuterium lock was achieved by using a mixture of 1 mL of Me<sub>2</sub>SO-*d*<sub>6</sub> and 9 mL of spectroscopic-grade protio Me<sub>2</sub>SO as solvent. Generally, 2000–6000 scans were acquired before Fourier transformation. Typical experimental conditions utilized 30° pulse angles, acquisition times of 0.5 s, and recycle times of 4–10 s. Gated decoupling was employed to provide proton

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decoupling without NOE. Consistency checks on many of the data were carried out on a Bruker HX-270 spectrometer at 27.36 MHz, in the locked mode (1:1 Me<sub>2</sub>SO/Me<sub>2</sub>SO-*d*<sub>6</sub> solvent) using 15-mm diameter sample tubes containing both a substituted and the unsubstituted nitrobenzene. Substituent chemical shifts (SCS) were measured directly from the separation of the two peaks in the spectrum. Some additional <sup>15</sup>N spectra were recorded on a home-built wide-bore superconducting spectrometer (the SEMINOLE) at 15.20 MHz. In this case 25-mm sample tubes were employed and peaks were referenced to the signal from neat nitromethane contained in a 5-mm concentric NMR tube and later converted to SCS values with respect to nitrobenzene. SCS values measured on the two wide-bore spectrometers were generally equivalent to within ±0.1 ppm. Slightly larger deviations were noted for some of the measurements made for samples containing both substituted and unsubstituted derivatives in the 15-mm sample tubes, presumably reflecting increased intermolecular interactions due to the higher effective concentrations in these solutions.

<sup>17</sup>O spectra were measured on a Bruker WM-360 instrument at 48.84 MHz for 20-mm sample tubes containing the substituted nitrobenzenes (7% w/v) in spectroscopic grade CH<sub>3</sub>CN. Field-frequency locking was not necessary, because of the naturally broad line widths of the <sup>17</sup>O signals and excellent stability of the superconducting solenoid magnet. Short acquisition times (~25 ms) between 90° pulses were used to allow rapid accumulation of 10 000–50 000 scans. The spectral signal-to-noise ratio was enhanced by the application of an exponential weighting function to the FID prior to Fourier transformation. This produced a line broadening of 200 Hz in the transformed spectra in addition to the natural line width of 200–250 Hz. Rolling base lines, typically observed in <sup>17</sup>O spectra, were reduced by left-shifting each FID prior to Fourier transformation. This reduced the strong signal in the first few data points of the time-domain signal arising from rf pulse breakthrough into the receiver, or acoustic ringing of the probe, commonly encountered for studies of low-sensitivity nuclei with low magnetogyric ratios. <sup>17</sup>O chemical shifts were measured with respect to the absolute carrier frequency. Repetitive checks of the shift of the parent derivative with respect to the carrier were carried out between runs of the substituted derivatives and revealed no substantial drift of the magnetic field. The <sup>17</sup>O chemical shifts were generally reproducible to within 1 ppm for duplicate runs on the same sample. Substituent chemical shifts are therefore accurate to ±2 ppm. Some additional <sup>17</sup>O spectra were recorded on the SEMINOLE spectrometer, operating at 20.33 MHz, for solutions of the substituted nitrobenzenes in 25-mm tubes. The shifts were consistent with those measured on the WM-360 spectrometer. For all spectra, signal-to-noise ratios were sufficient (>10:1) to accurately measure chemical shifts.

The ab initio molecular orbital calculations were done on a DEC-10 computer using a modified version of the GAUSSIAN70 program.<sup>19</sup> Each molecule required between 0.5 and 3.5 h of central processor computer time. Molecular coordinates were calculated by assuming standard bond lengths and angles<sup>20</sup> for all of the nitrobenzene derivatives. DSP correlations of shifts and electron densities were done by using a least-squares regression program.

### Results and Discussion

<sup>15</sup>N and <sup>17</sup>O NMR chemical shift data for meta- and para-substituted nitrobenzenes are given in Table I. The <sup>15</sup>N SCS values cover a range of less than 6 ppm, while the <sup>17</sup>O shifts are more sensitive to substituent effects and range over nearly 40 ppm. In addition, the direction of substituent effects is different at these two atomic sites, with electron-withdrawing substituents (such as NO<sub>2</sub>, CN, or CF<sub>3</sub>) causing *upfield* <sup>15</sup>N shifts and *downfield* <sup>17</sup>O shifts. In order to account for this observation, it is necessary to dissect the SCS values into polar and resonance compo-

Table I. <sup>15</sup>N and <sup>17</sup>O Substituent Chemical Shifts<sup>a</sup> (ppm) in Meta- and Para-Substituted Nitrobenzenes

X	meta			
	para		<sup>15</sup> N	<sup>17</sup> O
	<sup>15</sup> N SCS <sup>b</sup>	<sup>17</sup> O SCS <sup>c</sup>	SCS <sup>b</sup>	SCS <sup>c</sup>
NH <sub>2</sub>	-0.4	-25.6	0.8	0.8
OCH <sub>3</sub>	-1.0	-9.8		
OH		-6.7	0.1	
F	-2.6	-1.3	-3.0	2.9
Cl	-2.5	0.6		
Br	-2.1		-3.3	4.0
CH <sub>3</sub>	-0.1	-3.3	0.3	-0.4
H	0.0 <sup>d</sup>	0.0 <sup>e</sup>	0.0	0.0
CHO	-1.9	8.1	-2.3	1.9
CF <sub>3</sub>	-3.1	7.7	-3.8	2.7
CN	-3.5	7.5	-4.2	3.5
NO <sub>2</sub>	-4.0	11.5	-5.0	5.0

<sup>a</sup> Positive shifts are downfield. <sup>b</sup> Error ± 0.1 ppm. <sup>c</sup> Error ± 2 ppm. <sup>d</sup> The parent compound has a <sup>15</sup>N shift 9.8 ppm upfield from nitromethane contained in a 5-mm capillary (i.e., δ<sub>nitrobenzene</sub> = ~370 ppm downfield from aqueous ammonia reference). <sup>e</sup> Nitrobenzene has an <sup>17</sup>O chemical shift ~569 ppm downfield from H<sub>2</sub>O.<sup>18</sup>

nents. This can readily be done by using the dual substituent parameter (DSP) (eq 1).<sup>21,22</sup> In this equation, the

$$SCS = \rho_I \sigma_I + \rho_R \bar{\sigma}_R \quad (1)$$

observed SCS value is correlated with a linear combination of the polar and resonance substituent parameters  $\sigma_I$  and  $\bar{\sigma}_R$  (where  $\bar{\sigma}_R$  may be one of  $\sigma_R^-$ ,  $\sigma_R^0$ ,  $\sigma_R^{BA}$ , or  $\sigma_R^+$ ).<sup>21</sup> The derived  $\rho_I$  and  $\rho_R$  values are the relative transmission coefficients of polar and resonance effects.

**A. Para SCS Data.** The appropriate correlations for the <sup>15</sup>N and <sup>17</sup>O SCS values in para-substituted nitrobenzenes are shown below as eq 2 and 3, respectively. For

$$^{15}\text{N SCS} = -6.0\sigma_I - 1.0\sigma_R^0 \quad (2)$$

$$SD = 0.21, f = 0.09$$

$$^{17}\text{O SCS} = 13.5\sigma_I + 15.6\sigma_R^+ \quad (3)$$

$$SD = 1.57, f = 0.15$$

$$^{13}\text{C SCS} = 1.5\sigma_I + 11.3\sigma_R^{BA} \quad (4)$$

$$SD = 0.40, f = 0.10$$

comparison, the correlation<sup>2d</sup> for <sup>13</sup>C SCS values at the *ipso* position (C-1) is shown in eq 4. As discussed previously,<sup>21</sup>  $f$  ( $f = SD/RMS$ ) is the ratio of the standard deviation (SD) of the fit to root-mean-square (RMS) size of the data and provides a means of assessing the goodness of fit.  $f$  values of less than 0.1 indicate excellent fits while those in the range 0.1–0.2 indicate acceptable correlations.

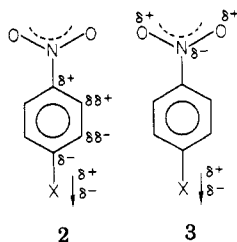
The derived  $\rho_I$  and  $\rho_R$  values for the <sup>13</sup>C SCS data at C-1 have been previously explained in terms of  $\pi$ -polarization and resonance effects, respectively.<sup>6</sup> The large  $\rho_R$  value reflects the strong resonance interaction of the substituent with the para ring site, while the  $\rho_I$  component arises mainly from the substituent's ability to polarize the  $\pi$  electrons of the benzene ring as shown in 2. These  $\rho_I$  and  $\rho_R$  values provide a basis for comparison with the <sup>15</sup>N and <sup>17</sup>O shifts of the nitro side chain. Note that the  $\rho_I$  and  $\rho_R$  values at the <sup>15</sup>N site have the *opposite* sign to those at the adjacent carbon and oxygen. The negative sign reflects the reverse nature of the <sup>15</sup>N shifts. The fact that  $\rho_I$  is the dominant term in eq 2 shows that  $\pi$ -polarization of the

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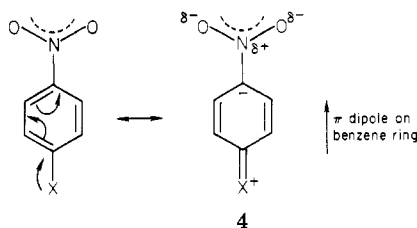
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N=O bonds is the most important contribution to the  $^{15}\text{N}$  shifts. Previously, negative  $\rho_I$  values at unsaturated carbonyl<sup>8,9,23,24</sup> and vinyl<sup>7,25</sup> sites adjacent to a benzene ring have been rationalized<sup>2</sup> by using this mechanism. The present study shows that such effects also occur in N=O partial double bonds.

The nature of this  $\pi$ -polarization is shown in 3. Here, the dipolar substituent X polarizes the N=O bonds to pull electrons from the oxygen atoms toward the nitrogen. Note that the polarity shown on the nitro group in 3 reflects the substituent-induced perturbation and not the absolute bond polarity. It is somewhat surprising that the magnitude of the effect is so large ( $\rho_I = -6.0$ ) since the N=O bonds have only partial-double-bond character. In aromatic carbonyl and styrene derivatives, where the  $\pi$  bond order of the polarizable side-chain bond is larger,  $\rho_I$  values of only  $-2.7 \pm 0.3$  (e.g., see eq 5) are obtained in DSP correlations of  $^{13}\text{C}$  SCS values<sup>2</sup> for the first atom of the side chain. Unfortunately, a quantitative estimate of the relative polarizability of C=O and N=O bonds cannot be obtained from the magnitudes of  $\rho_I$  values derived from  $^{13}\text{C}$  and  $^{15}\text{N}$  SCS studies, since these nuclei may have significantly different shift/charge ratios;<sup>6</sup> i.e., a given change in electron density can result in different changes in  $^{13}\text{C}$  and  $^{15}\text{N}$  SCS values.

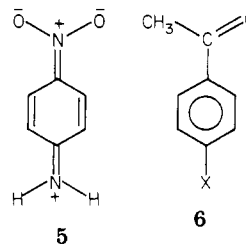
Although the  $\rho_R$  value in eq 2 is small compared with  $\rho_I$ , the fact that it too is negative (i.e., a "reverse" effect) is significant. Reverse resonance effects have not received as much discussion as reverse polar effects, but they do play a role in determining SCS values. In the nitrobenzene series, the negative  $\rho_R$  value for the  $^{15}\text{N}$  chemical shifts most likely arises because of a secondary resonance effect shown in 4.



The substituent induces a dipole in the benzene ring as a consequence of the resonance interaction shown. This dipole (whose magnitude is proportional to  $\sigma_R$  of X) then polarizes the nitro-group side chain. The reverse nature of the effect arises because resonance donor substituents set up a dipole that polarizes electron density away from the nitrogen (toward the oxygen), and resonance-acceptor substituents set up a dipole that polarizes electron density toward the nitrogen.

The large positive  $\rho_R$  value seen in the  $^{17}\text{O}$  chemical shift correlation (eq 3) demonstrates the importance of primary

resonance effects at this site. The fact that the  $\sigma_R^+$  scale is preferred indicates an enhanced interaction for donor substituents, as shown in 5.



A similar effect is seen in the DSP  $^{17}\text{O}$  chemical shift correlation for para-substituted acetophenones (6)<sup>2</sup> (eq 6). For comparison, eq 5 gives the DSP correlation for the C- $\alpha$  site in this series.

$$^{13}\text{C SCS} = -2.6\sigma_I + 0.8\sigma_R^+ \quad (5)$$

$$\text{SD} = 0.18, f = 0.14$$

$$^{17}\text{O SCS} = 18.6\sigma_I + 24.0\sigma_R^+ \quad (6)$$

$$\text{SD} = 2.24, f = 0.14$$

The magnitudes of the transmission coefficients in eq 6 are slightly larger than those for the nitrobenzene series (eq 3), reflecting the larger substituent effect on the  $^{17}\text{O}$  atom of the carbonyl group compared with the nitro group. However, the most interesting features of eq 3 and 6 are the large  $\rho_I$  values. These confirm the importance of  $\pi$ -polarization of N=O and C=O bonds. Another trend is that  $\rho_I$  is larger for the oxygen atom than for its attached atom (compare eq 2 with eq 3 and eq 5 with eq 6).

**B. Electron Densities.** Electron densities for para-substituted nitrobenzenes calculated by using ab initio molecular orbital theory are given in Table II. Substituent effects at the nitrogen and oxygen atoms of the side chain are smaller than at the ring C-1 carbon atom,<sup>6</sup> but systematic trends can be discerned. Resonance donating substituents such as  $\text{NH}_2$  or  $\text{OH}$  increase the  $\pi$  electron density on the oxygen atoms, whereas resonance acceptors such as  $\text{NO}_2$  or  $\text{CN}$  decrease it. This is consistent with the type of resonance interaction shown in 5 and is in agreement with the observed  $^{17}\text{O}$  SCS values.<sup>31</sup> Changes in  $\sigma$  electron density at the oxygen atom are much smaller than changes in  $\pi$  electron density and consequently  $\pi$  and total electron densities are very similar. Different trends are seen at the nitrogen atom. Here, donating substituents cause a decrease in  $\pi$  electron density and acceptors an increase. Qualitatively this shows that the calculations reproduce the reverse effect seen in the  $^{15}\text{N}$  SCS values. Changes in  $\sigma$  electron density at the nitrogen atom are approximately equal and opposite to changes in  $\pi$  electron density, with the result that changes in total electron density are relatively small. These trends reinforce the view<sup>2</sup> that  $\pi$  (rather than  $\sigma$  or total) electron density is the parameter of choice for correlations with SCS values in benzene derivatives.

Figure 1 shows plots of the  $^{15}\text{N}$  and  $^{17}\text{O}$  SCS values vs. calculated  $\pi$  electron densities at the nitrogen and oxygen atomic sites. Although both plots are somewhat scattered ( $r = 0.822$  for the  $^{15}\text{N}$  SCS values and  $r = 0.962$  for the  $^{17}\text{O}$  SCS values), the general linear trends confirm that the SCS values are largely electronic in origin. The slope of the plot for the  $^{17}\text{O}$  data is  $1600 \pm 300$  ppm/electron, which is larger than that typically observed for  $^{13}\text{C}$  shifts in aromatic systems (where the slopes are usually in the range 100–220 ppm/electron).<sup>6</sup> A plot of  $^{17}\text{O}$  SCS values vs. total electron densities yields a similar correlation. On the other hand,

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Table II. Calculated Electron Densities<sup>a</sup> on the Nitro Group in Para-Substituted Nitrobenzenes

X	nitrogen atom			oxygen atom		
	σ	π	total	σ	π	total
NH <sub>2</sub> (pl) <sup>b</sup>	54.8	-67.9	-13.2	-0.1	102.3	102.3
NH <sub>2</sub> (py) <sup>c</sup>	37.2	-48.8	-11.5	-0.7	75.7	75.0
NH <sub>2</sub> (t) <sup>d</sup>	32.7	-43.8	-11.1	-1.0	68.7	67.7
OH	23.3	-31.1	-7.8	-7.3	58.0	50.7
F	-0.3	-6.0	-6.4	-9.2	18.7	9.5
CH <sub>3</sub>	23.8	-16.2	7.6	15.5	-0.5	15.0
H	0.0	0.0	0.0	0.0	0.0	0.0
CF <sub>3</sub>	-39.9	35.8	-4.1	-6.6	-36.9	-43.5
CN	-60.1	54.8	-6.3	-15.7	-57.6	-73.3
NO <sub>2</sub>	-85.3	80.2	-5.1	-21.7	-86.8	-108.5
CHO	-29.6	27.5	-2.1	-1.9	-32.4	-34.3
q(H) <sup>e</sup>	5.6256	1.2313	6.8569	6.8615	1.3996	8.2010

<sup>a</sup> Ab initio (STO-3G) electron densities expressed relative to the hydrogen substituent ( $\times 10^4$ ). A positive value indicates a substituent-induced increase in electron density. <sup>b</sup> Planar amino. <sup>c</sup> Pyramidal amino. <sup>d</sup> Tetrahedral amino. <sup>e</sup> Absolute electron densities in parent derivative.

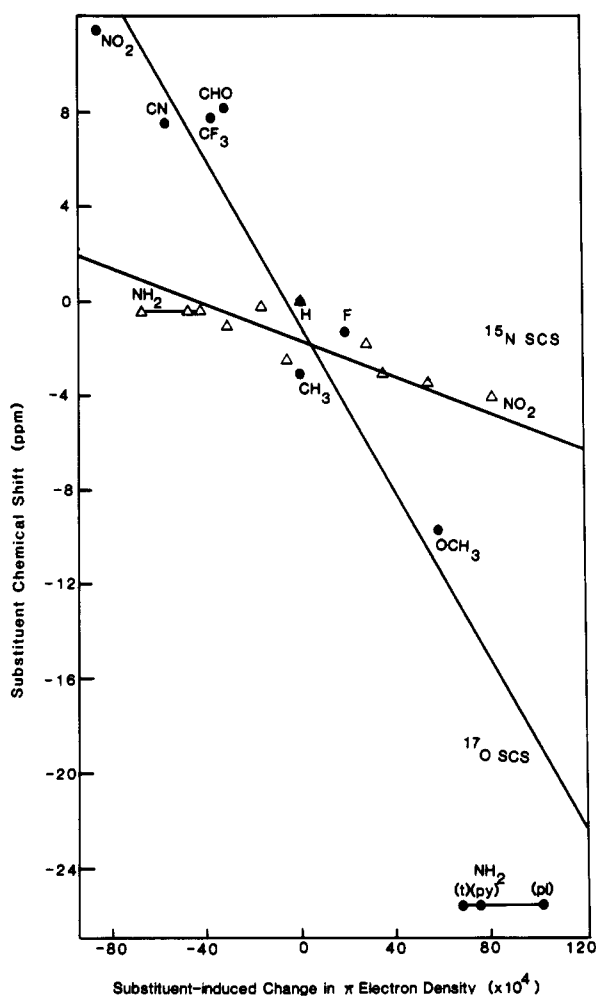


Figure 1. Plot of <sup>15</sup>N (●) and <sup>17</sup>O (Δ) substituent chemical shifts (ppm) vs. substituent-induced changes in electron density ( $\Delta q_\pi \times 10^4$ ) for para-substituted nitrobenzenes. A positive SCS denotes a downfield shift and a positive  $\Delta q_\pi$  indicates an increase in electron density. Electron densities for three conformations of the NH<sub>2</sub> substituent were calculated corresponding to a planar (pl), pyramidal (py),<sup>30</sup> and tetrahedral (t) arrangements of bonds about the nitrogen atom.

$\sigma$  electron densities do not correlate with the <sup>17</sup>O SCS values. The slope of the plot of <sup>15</sup>N SCS values vs.  $\pi$  electron densities is  $300 \pm 100$  ppm/electron. The slope of the corresponding plot using  $\sigma$  electron densities has the wrong sign, although Table II shows that for the nitrogen atom, there is a linear relationship between substituent-induced changes in  $\sigma$  and  $\pi$  electron densities. An increase

Table III. DSP Correlations of Side-Chain Electron Densities ( $\times 10^4$ ) in Para-Substituted Nitrobenzenes<sup>a</sup>

atom	electron density component <sup>b</sup>	resonance scale		SD	f	
		$\rho_I$	$\rho_R$			
N	$\sigma$	-88	-124	$\sigma_R^0$	7.8	0.17
	$\pi$	78	137	$\sigma_R^0$	8.7	0.19
	total	-109	-138	$\sigma_R^{BA}$	10.6	0.18
O	$\pi$	-82	-133	$\sigma_R^{BA}$	10.3	0.16

<sup>a</sup> Calculated electron densities ( $\times 10^4$ ) in Table II were fitted to the DSP equation to yield the above  $\rho_I$  and  $\rho_R$  values. <sup>b</sup> Poor fits ( $f > 0.4$ ) were obtained for the total electron density on the nitrogen atom, and the  $\sigma$  electron density on the oxygen because of the small range of substituent-induced perturbations on these components.

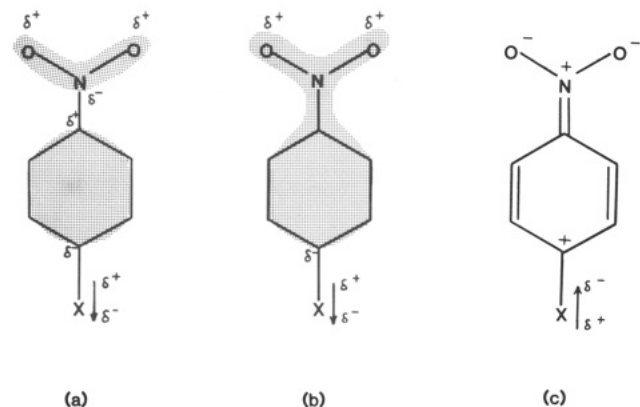
in  $\pi$  electron density is associated with an equivalent decrease in  $\sigma$  electron density (eq 7).

$$\Delta q_\sigma = -0.95 \Delta q_\pi \quad (r = 0.948) \quad (7)$$

This type of relationship has been observed for a number of other systems<sup>6,26</sup> and is related to repulsive interactions between the two electron density components. It is interesting to note that no such trend is observed at the oxygen atom.

A more quantitative insight into the nature of substituent effects can be gained by separating the overall changes in electron densities into polar and resonance components. The appropriate DSP correlations for  $\sigma$ ,  $\pi$ , and total electron densities are given in Table III. Note that because of the sign convention used here (i.e.,  $\Delta q$  is positive for an increased electron density), electron density/DSP correlations with negative signs represent normal effects and those with positive signs represent reverse effects. This is opposite to the signs of normal and reverse effects in SCS DSP correlations. Note also that the derived  $\rho_I$  and  $\rho_R$  values have been scaled up by a factor of  $10^4$ .

The main trend to emerge from the DSP analyses in Table III is that both polar and resonance effects contribute significantly to changes in electron densities at both side-chain sites. The large resonance component of  $\Delta q_\pi$  ( $\rho_R = -133$ ) at the oxygen atoms reflects their conjugation with the substituent, as noted earlier from the SCS data. In addition to this resonance perturbation of  $\pi$  electron density on the oxygen atoms, there is also a significant polar component ( $\rho_I = -82$ ). This confirms the presence of  $\pi$ -polarization of the N=O partial double bonds. In



**Figure 2.**  $\pi$ -Polarization effects: (a) separate localized polarization of the side-chain and ring  $\pi$  systems; (b) extended polarization of the ring and side-chain conjugated  $\pi$  system; (c) possible representation of extended polarization in terms of field induced resonance. The dipolar substituent X stabilizes particular resonance forms, thus bringing about enhanced electron density changes at conjugated sites such as the terminal oxygen atoms. Note that the substituent shown has an electron-donating polar effect (e.g., a methyl group). Electron-withdrawing substituents, which have a dipole opposite to that shown, would destabilize this resonance form.

contrast to the trend seen in the  $^{15}\text{N}$  SCS data, the  $\pi$  electron densities at the nitrogen atom appear to be significantly affected by the substituents resonance effect. This difference between the SCS and  $\Delta q_\pi$  values explains why the plot in Figure 1 is somewhat scattered. The electron densities correctly predict the reverse sign of polar effects at the nitrogen but appear to grossly overestimate the importance of reverse resonance effects.

A comparison of the polar components of  $\Delta q_\pi$  for the nitrogen ( $\rho_1 = 78$ ) and oxygen ( $\rho_1 = -82$ ) shows that substituent-induced  $\pi$ -polarization is not localized in the N=O bonds. If the N=O bonds were polarized independently of the adjacent benzene ring, then the change in  $\pi$  electron density on the nitrogen would be twice that on each oxygen atom. The larger than expected  $\rho_1$  value at the nitrogen atom supports the concept of extended polarization.<sup>23,24</sup> In general, a substituent is able to polarize the N=O bonds in a combination of two ways: (a) in a localized manner (Figure 2a) and (b) in an extended manner (Figure 2b). The latter component represents the ability of a substituent to polarize the whole conjugated  $\pi$  system consisting of the nitro group and benzene ring. The effect may occur in a continuous manner as shown in Figure 2b or, as it has been suggested recently,<sup>27</sup> may reflect contributions from "field induced resonance".<sup>28</sup> In this case, the substituent dipole stabilizes resonance forms such as that shown in Figure 2c. Since the effect depends on the strength of the substituent dipole, and hence is proportional to  $\sigma_I$ , the term field induced resonance is somewhat misleading in this case.

Irrespective of the exact mechanism representing the extended polarization component, (i.e., Figure 2, b or c), its effect is to increase a substituent's polar influence at the terminal atom of a conjugated  $\pi$  system, as is observed in the  $\Delta q_\pi$  data for the nitrobenzenes examined here.

**C. Meta SCS Values.** The meta SCS data in Table I verify the arguments presented for the para data. Each

meta  $^{15}\text{N}$  SCS value is a factor of 20–30% larger than the corresponding para SCS. On the other hand, the meta  $^{17}\text{O}$  SCS values are much smaller than the para SCS values. Both of these observations are also reflected in the DSP correlations shown in eq 8 and 9 for the meta series.

$$^{15}\text{N SCS} = -7.5\sigma_I - 2.5\sigma_R^0 \quad (8)$$

$$\text{SD} = 0.31, f = 0.14$$

$$^{17}\text{O SCS} = 6.5\sigma_I + 0.6\sigma_R^- \quad (9)$$

$$\text{SD} = 0.32, f = 0.12$$

Equation 8 shows that the increased  $^{15}\text{N}$  SCS values in the meta series compared with the para series arise because of an increased polar substituent effect ( $\rho_1 = -7.5$  compared with  $-6.0$  in the para series). This trend is consistent with the concept of polar effects being transmitted *through space* by the  $\pi$ -polarization mechanism. The larger  $\rho_1$  value at the meta position clearly shows that conjugation of the substituent with the side chain is not required for the transmission of polar effects. The observation is also consistent with similar trends seen for meta- and para-carbonyl side-chain derivatives.<sup>23</sup>

A comparison of eq 3 and 9 shows that the dramatic decrease in  $^{17}\text{O}$  SCS values in the meta series compared with the para series arises from a decrease in the  $\rho_R$  term. Again this is expected and, incidentally, confirms the validity of the DSP approach as a means of separating polar and resonance effects and probing changes in these individual components. The polar component,  $\rho_1$ , also decreased by a factor of 2 in going from the para to the meta series. Again, this is consistent with observations in  $^{13}\text{C}$  NMR studies of styrenes,<sup>25,29</sup> where  $\rho_1$  for the C- $\beta$  side-chain atom decreases in the meta series compared with the para series.

## Conclusions

A multinuclear approach to the study of substituent effects allows all sites on the nitrobenzene framework to be examined. This study proves the generality of the  $\pi$ -polarization concept by showing that distant substituents can readily polarize the  $\pi$  electrons of a N=O bond.

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**Registry No.** Nitrobenzene, 98-95-3; 1-methoxy-4-nitrobenzene, 100-17-4; 4-nitrophenol, 100-02-7; 1-fluoro-4-nitrobenzene, 350-46-9; 1-chloro-4-nitrobenzene, 100-00-5; 1-bromo-4-nitrobenzene, 586-78-7; 1-methyl-4-nitrobenzene, 99-99-0; 4-nitrobenzenamine, 100-01-6; 4-nitrobenzaldehyde, 555-16-8; 1-nitro-4-(trifluoromethyl)benzene, 402-54-0; 4-nitrobenzotrile, 619-72-7; 1,4-dinitrobenzene, 100-25-4; 3-nitrobenzenamine, 99-09-2; 1-methoxy-3-nitrobenzene, 555-03-3; 3-nitrophenol, 554-84-7; 1-fluoro-3-nitrobenzene, 402-67-5; 1-chloro-3-nitrobenzene, 121-73-3; 1-bromo-3-nitrobenzene, 585-79-5; 1-methyl-3-nitrobenzene, 99-08-1; 3-nitrobenzaldehyde, 99-61-6; 1-nitro-3-(trifluoromethyl)benzene, 98-46-4; 3-nitrobenzotrile, 619-24-9; 1,3-dinitrobenzene, 99-65-0.

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