BACKDONATION AND INTERRELATIONSHIPS BETWEEN ^{15}N, ^{13}C CHEMICAL SHIFTS AND INFRARED ABSORPTION FREQUENCIES IN HETEROCYCLIC N-OXIDES

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Abstract -- 1) A relationship has been shown to exist between the ^{15}N chemical shifts of a number of N-oxides and their ν_{NO} absorption frequencies.

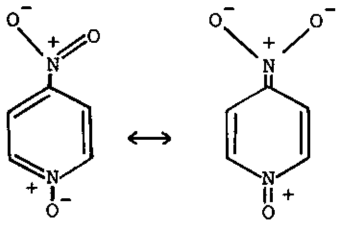
2) A similar relationship exists between the σ_{NO} ionization potentials of N-oxides and their ν_{NO} absorption frequencies.

3) The changes in ^{15}N chemical shifts of these N-oxides are reflected in changes of the ^{13}C chemical shifts of the carbons α to the N-oxide function.

4) By comparing the ^{15}N chemical shift changes of the N-oxides and their oxygen protonated analogs, a measure of the extent of *backdonation*, relatable to the π-deficiency of the N-oxides, has been established.

5) The steric inhibition to backdonation in some appropriately di-substituted N-oxides has been estimated by means of their ν_{NO} frequencies and changes in the ^{13}C chemical shifts of the α-carbons.

The chemical reactivity of pyridine, diazine and 1,2,4-triazine N-oxides can be related to the π-deficiency of these compounds, a factor which influences the extent of double bond character of the N-O bond.[1] The degree of backdonation of the oxide oxygen (1b,2b) is enhanced by the presence of either suitable electron withdrawing substituents (1) or replacement of a ring carbon by a nitrogen atom (2).



a b

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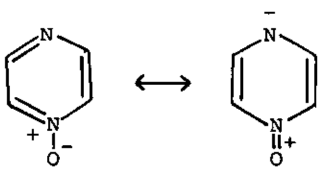

a b

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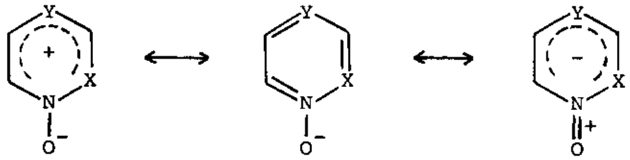
The contribution of resonance structures such as 1b and 2b, to the ground state of these molecules should be reflected by the N-O absorption frequency in the infrared region, the nitrogen and selected ^{13}C chemical shifts and the ionization potentials, among other properties.

It is the purpose of this publication to describe a number of correlations among these various physical properties, to estimate the degree of backdonation and to demonstrate the existence of steric inhibition to backdonation in some substituted N-oxides.

The infrared stretching vibrations in the region 1200 - 1400 cm^{-1} are associated with the N-O bond in N-oxides.[2] In the general structure 3, if either Y and/or X is a nitrogen atom,



a b c

3

the N-O absorption is in the region 1300-1370 cm^{-1}.[3] When neither Y nor X is a heteroatom, the N-O absorption varies from 1220-1290 cm^{-1}.[4] Thus, qualitatively at least, the N-oxide absorption reflects the degree of backdonation.

Nitrogen-15 chemical shifts depend on the local diamagnetic screening (σ^{d}_{loc}), the local paramagnetic screening (σ^{p}_{loc}) and a quantity, σ_{other}, which includes contributions to the nuclear screening from sources such as anisotropy, field effects, solvent effects, etc.[5] It has been shown that among all of these terms σ^{p}_{loc} is the most significantly variable one.

This local paramagnetic term (σ^{p}_{loc}) can be viewed as being comprised of three structurally related contributions:[6]

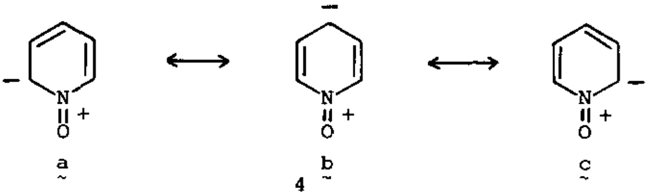
$$\sigma^{P}_{loc} \propto \frac{1}{\Delta E} \cdot \langle\frac{1}{r^3}\rangle \cdot \Sigma Q$$

In this proportionality, ΔE is a measure of the accessibility of low-lying excited states and the $1/r^3$ term relates to the orbital radius of the electrons influencing the ^{15}N chemical shift. The summation ΣQ is derived from the bond orders and charge densities of the bonding electrons. In other words, it is a measure of the degree of multiple bonding to the nitrogen atom.

Thus, it is expected that, as long as closely related systems are compared, the ^{15}N chemical shifts should largely reflect changes in the $1/r^3$ and ΣQ terms, with the latter term predominating. If this is indeed the case, a linear relationship between the N-O infrared absorption frequency of a given heteroaromatic N-oxide and the ^{15}N chemical shift should exist.

The ionization potentials of the sigma N-O bond of the N-oxides should also reflect the degree of backdonation. The more double bond character is present, the greater should be the ionization potential.

The degree of backdonation will affect the electron densities at positions 2-, 4- and 6- of a 6-membered π-deficient heteroaromatic ring system, placing excess negative charges at these sites (4 a → c).



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The difference between the ^{13}C chemical shifts of the α (and γ) carbon of the N-oxides and the corresponding non-oxides will reflect this effect, as well as the shielding caused by the N-oxidations of the nitrogen atom.

Results

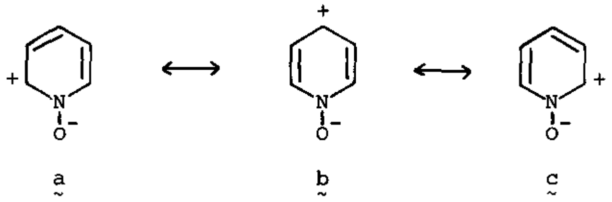
Figure 1 shows the correlation that exists between the N-O absorption frequencies of a number of pyridine, diazine and triazine N-oxides and the ^{15}N chemical shifts of the N-oxide nitrogen. The correlation coefficient (R) for this graph, 0.978 attests to the excellence of this interrelationship.

Thus, as the double bond character of the N-oxide increases so does the amount of deshielding the oxide nitrogen experiences. The relationship between electron donating and electron withdrawing substituents and their effect on the

N-oxide ground-state structure is exemplified by the 4-methoxy (**11**) and 4-nitropyridine (**1**) N-oxides.

Figure 2 demonstrates the interrelationship that exists between the sigma N-O ionization potentials,[7,8] and the N-O absorption frequencies. The coefficient of correlation is 0.974, again, quite good.

The difference in the ^{13}C chemical shifts of the carbons in the azines, etc. (See Table I) and their corresponding N-oxides, is largely due to changes in *electron density (changes in the bonding of the nitrogen, are of course, operative* as well). These changes will, again, reflect contributions such as **4** **a** → **c** and **5** **a** → **c**.



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Contributions from structures **4** will cause shielding with respect to the non-oxides, while structures **5** will cause deshielding. The overall change, when plotted against the ^{15}N chemical shifts affords a measure of the relative electron density changes experienced by the carbons upon N-oxidation. Fig. 3 shows this plot with a coefficient of correlation of 0.983 and a slope of $5.748\ (\Delta\ \delta_{^{13}C}(\text{ppm}))/\delta_{^{15}N}$. So far, we have interrelated the infrared absorption frequencies of a number of N-oxides with their ionization potentials, and ^{15}N as well as ^{13}C chemical shifts. The relevant equations (calculated from Figs. 1 - 3) are:

$\delta_{^{15}N}(\text{ppm}) = 0.543[\nu\text{N-O}] - 391$ (Fig. 1)

$[\text{ioniz. pot. } (\sigma\text{N-O})] = 9.5 \times 10^{-2}\ [\nu\text{N-O}] - 2.57$ (Fig. 2)

$\delta_{^{15}N}(\text{ppm}) = 5.75\ [\Delta(\delta_{^{13}C}\ \text{parent } \alpha\text{-C}) - (\delta_{^{13}C}\text{N-oxide } \alpha\text{-C})] + 232$ (Fig. 3)

The effect of N-oxidation on the ^{15}N chemical shift of π-deficient heteroaromatic systems can be subdivided into the following components:

1) N-oxidation will remove the lone pair of electrons from the nitrogen, thus causing shielding. For example, protonation of pyridine causes shielding by approximately 100 ppm.[6,9]

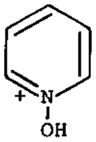
2) The oxygen-nitrogen bond that is formed will cause deshielding of the

nitrogen atom.[6]

3) The degree of deshielding will depend upon the relative charge difference between the N-oxidized nitrogen and the oxygen. For example, the structural feature $\geqslant N^{+}\text{-}O^{-}$ will cause more deshielding of the nitrogen atom than will the $\geqslant N^{+}{=}O$ structure.

In other words, effects 1 and 2 will change the ^{15}N chemical shift in opposing directions, and backdonation, i.e. the presence of $\geqslant N^{+}{=}O$, will cause deshielding.

Thus, in order to establish the degree of backdonation in an N-oxide, one would ideally have to "lock" the N-oxide into a form which cannot have any backdonation occuring. To a reasonable approximation, this should be true when an N-oxide is protonated (6). The difference in the ^{15}N chemical shift of the protonated N-oxide and the N-oxide itself, will be a measure of the change: $\geqslant N^{+}\text{-}O^{-} \rightarrow \geqslant N^{+}\text{-}OH$. This change will be at a maximum in those N-oxides where no backdonation is present. On the other hand, if the N-oxide exists largely in the "backdonated" form (i.e. the charge on the oxygen is small) the change in the ^{15}N chemical shift on protonation of the N-oxide should be minimal.



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Fortunately, Roberts and co-workers[9] reported the ^{15}N chemical shifts of a number of pyridine N-oxides and their O-protonated analogs. A plot of these ^{15}N chemical shifts against each other affords a straight line, with the difference between the N-oxide and its protonated form becoming less as the electron-withdrawing power of a γ-substituent increases.

Since protonation of diazine- and triazine-N-oxides most probably occurs on the non-oxidized nitrogen atoms[10], it is not feasible to obtain the ^{15}N chemical shifts of these N-oxides in their protonated form. However, since it has already been established that a linear relationship exists between ^{15}N chemical shifts and the N-O absorption frequencies, thus establishing a linearity, the ^{15}N chemical shifts of the hypothetical O-protonated diazine and triazine N-oxides are available from the graph of pyridine N-oxides vs N-hydroxypyridinium compounds

(See Fig. 4).

When this is done, the chemical shifts indicated in parenthesis in Table II are obtained. The difference between the chemical shifts of the protonated and non-protonated N-oxides (given in column 3) represents a measure of the "amount" of backdonation present in the various N-oxides.

Thus, the difference between 1,2,4-triazine 1-oxide and its protonated form is only 15 ppm, indicating a very significant amount of backdonation. On the other hand, this difference is 56 ppm in the 4-methoxypyridine N-oxide instance where much less backdonation is indicated.

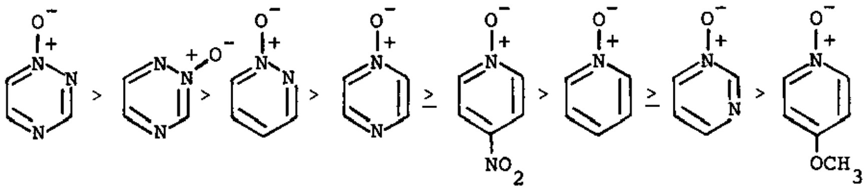
These number also show that the old "adage" that a nitro-group is "equivalent" to a ring nitrogen in π-deficient systems is valid, since the amount of backdonation in 4-nitropyridine N-oxide is the same as that in pyrazine N-oxide.

It has been estimated, from dipole moment measurements of pyridine N-oxide that it exists in approximately equal "amounts" in the forms 12a and 12b. Based on this information, and the estimate


12a


12b

that the chemical shift difference between $>N^{\oplus}$-OR and $>N^{+}$=O should be very small, one can estimate the percent of backbonding of the various N-oxides studied. The following sequence is thus established (while the absolute percentages may be significantly different, the relative differences should be reasonably accurate):



% Back Bonding:	85%	75%	70%	60%	60%	50%	50%	40%

The percentages, based on the various assumptions, are estimated to be correct to within ± 5%.

Table I
Physical Data for a Number of π-Deficient
Heteroaromatic N-Oxides

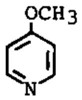
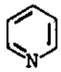
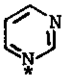
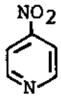
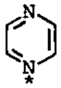
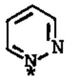
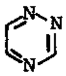
Compound (#)	^{15}N Chemical Shifts[5,6,9,c] ($\delta_{^{15}N}$ = 0, NH$_3$)	νN-O[1-4] (cm^{-1})	Ioniz. Pot.[7] (δN-O, eV)	$\Delta(\delta_{^{13}C}$ α-C's)[12] (ppm)
	279	----		
1-oxide (11)	276	1232		
	302	----	----	
1-oxide (4)	295	1248	9.22	-11.1
	295*	----	----	
1-oxide (7)	289*	1260	9.53	-11.9
	345	----		
1-oxide (1)	309	1283		
	332*	----	----	
1-oxide (2)	312*	1305	9.90	-13
	390*	----	----	
1-oxide (8)	326*	1325	9.95	-17.5
	N$_1$ = 422[11] N$_2$ = 382 N$_4$ = 298	----	----	
2-oxide (9)	N$_1$ = ? N$_2$ = (331)[b] N$_4$ = ?	1330	(10.07)[a]	----

Table I (Continued)

Compound (#)	^{15}N Chemical Shifts[5,6,9,c] ($\delta_{^{15}N}$ = 0,NH_3	νN-O[1-4] (cm^{-1})	Ioniz. Pot.[7] (δN-O,eV)	$\Delta(\delta_{^{13}C}$ α-C's)[12] (ppm)
1-oxide (10)	N_1 = 356 N_2 = 343 N_4 = 252	1370	(10.64)[a]	-20

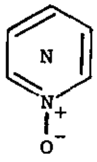
a) from Fig. 2

b) from Fig. 1

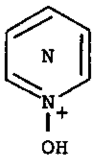
c) ^{15}N chemical shifts are for solutions in CH_3OH, except for the 1,2,4-triazine 1-oxide which is in DMSO.

Table II

^{15}N Chemical Shift Differences (ppm) between



and



B

BH

Compound	B (ppm)	BH (ppm)	B-BH Δ (ppm)
1,2,4-triazine 1-oxide (10)	356	(341)[a]	15
1,2,4-triazine 2-oxide (9)	331	(304)	27
pyridazine 1-oxide (8)	326	(296)	30
pyrazine 1-oxide (2)	312	(275)	37
4-nitropyridine 1-oxide (1)	308^{9b}	269	39
pyridine 1-oxide (4)	295^{9b}	246	49
pyrimidine 1-oxide (7)	289	(238)	51
4-methoxypyridine 1-oxide (11)	276^{9b}	220	56

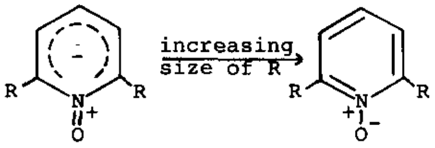
Correlation equation (Fig.4): $\delta_{^{15}N}(\overset{+}{N}-\bar{O}) = 0.655\ [(\delta_{^{15}N}(\overset{+}{N}-OH)] + 133$

(R = 0.997)

a) Numbers in parentheses obtained from Fig. 4

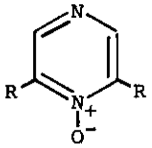
Steric Inhibition of Backdonation:

Since the degree of backdonation of an N-oxide group is reflected not only in the ^{13}C and ^{15}N chemical shifts but also in the infrared absorption frequency of the N-O bond, any one of these techniques should be applicable to the examination of any steric inhibition to backdonation. Thus, if the oxygen of the N-oxide cannot be coplanar with the nitrogen and the two α-carbon atoms, the degree of backdonation will decrease (13 vs 14).



13 14

Pyrazine N-Oxides: Among the pyrazine N-oxides, in going from pyrazine N-oxide (1305 cm^{-1}) to the 2-methyl derivative (15) (1305 cm^{-1}) there is no change in the N-O frequency. However, the introduction of a second ortho-methyl group as in 2,6-dimethylpyrazine N-oxide (16), decreases the absorption frequency to 1294 cm^{-1}. Thus a change of 11 cm^{-1} towards more single bond character takes place. This corresponds to an approximate change of 7% in the degree of double bond character of the pyrazine 1-oxide (Fig. 5).



8 : $R_1 = R_2 = H$: 1305 cm^{-1}

15 : $R_1 = CH_3; R_2 = H$: 1305 cm^{-1}

16 : $R_1 = R_2 = CH_3$: 1294 cm^{-1}

17 : $R_1 = N(CH_3)_2; R_2 = H$: 1275 cm^{-1}

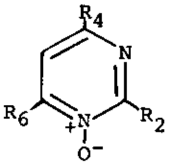
18 : $R_1 = R_2 = N(CH_3)_2$: 1233 cm^{-1}

The introduction of an α-dimethylamino (17) group alters the absorption frequency of pyrazine N-oxide by 25 cm^{-1}. Consequently, the 2,6-dimethylaminopyrazine

N-oxide (18) is expected to have a maximum ν_{NO} of 1255 cm^{-1} (1305 - (2x25)). However, the N-O absorption for the compound is at 1233 cm^{-1}. Thus, the "steric" effect is 12 cm^{-1}, a value corresponding to about 8% change towards more single bond character, than exists in pyrazine N-oxide. The absorption of the N-O bond in 2-chloropyrazine N-oxide is at 1313 cm^{-1}, as compared 1305 cm^{-1} for the parent. Thus, the 2-chloro substituent causes a shift of 8 cm^{-1} towards higher wave-numbers. Based on this, 2.6-dichloropyrazine N-oxide should have a maximum ν_{NO} of 1321 cm^{-1}. The observed value of 1318 cm^{-1} indicates only a minimal possible steric inhibition to backdonation. The major inhibition is observed in 2,3,6-tribromopyrazine 1-oxide (ν_{NO} = 1287 cm^{-1}). The 3-bromopyrazine 1-oxide absorption is at 1331 cm^{-1}, in 2-bromopyrazine 1-oxide ν_{NO} = 1315. Thus one can calculate a value of 1351 cm^{-1} for the 2,3,6-tribromopyrazine 1-oxide. The difference between this value and the observed one is 64 cm^{-1}. Thus, a 30% decrease in the amount of double bond character in comparison to pyrazine N-oxide is present.

The steric inhibition of backdonation in 2,6-dimethylpyrazine 1-oxide (16) is also evident in the ^{13}C chemical shift changes of the α-carbon atoms. The carbon atom in 2-methylpyrazine 1-oxide (15) absorbs at 144.4 ppm, having experienced 9.6 ppm shielding in comparison to its non-oxide.[14] The introduction of another methyl group, to form 2,6-dimethylpyrazine 1-oxide (16), causes more shielding of the α-carbons (less backdonation) in the 2,6-dimethylpyrazine 1-oxide than in the 2-methylpyrazine N-oxide. Consequently, ^{13}C and infrared data lead to the same conclusions.[14]

Pyrimidine N-Oxides: Similar effects of steric inhibition of backdonation are observable in α,α-disubstituted pyrimidine N-oxides:[13]



$R_2 = R_4 = R_6 = H$: 1276 cm^{-1}

$R_2 = CH_3$; $R_4 = R_6 = H$: 1272 cm^{-1}

$R_2 = R_4 = H$; $R_6 = CH_3$: 1278 cm^{-1}

$R_2 = R_6 = CH_3$; R_4 = Et: 1264 cm^{-1}

$R_2 = R_4 = CH_3$; R_6 = Et: 1255 cm^{-1}

The 2,4,6-trimethylpyrimidine 1-oxide should have an N-O absorption of 1274 cm^{-1} (1276 - 4 + 2) maximum. The observed value (1264 cm^{-1}) reflects, again, the degree (about 8%) of steric inhibition of backdonation (10 cm^{-1}). This is even *more pronounced (19 cm^{-1} change, 15%) in the* 2,4-dimethyl-6-ethylpyrimidine 1-oxide.

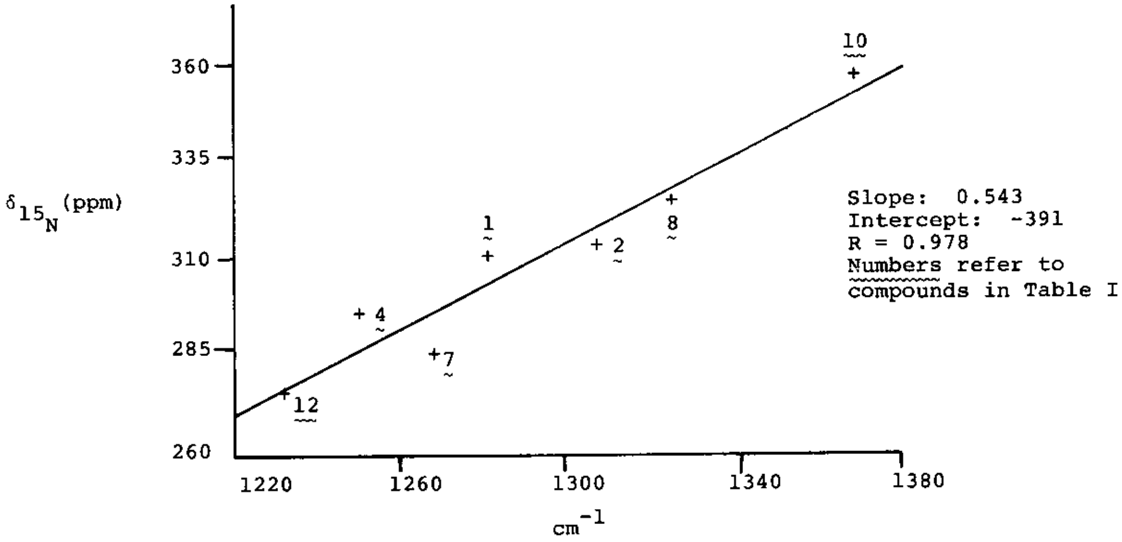
Pyridine N-Oxides: The infrared absorption frequency for the N-O bond in 2-methylpyridine N-oxide (1252 cm^{-1}) is only slightly different from that of pyridine N-oxide *(1250 cm^{-1}). However, ν_{NO} in 2,6-dimethylpyridine N-oxide is at* 1240 cm^{-1},[15] corresponding to a change of 10 cm^{-1}. This difference is the same as those observed in the pyrazine and pyrimidine N-oxide instances, and corresponds to a decrease in the backdonation of about 8% with respect to pyridine N-oxide.

This, relatively small, steric inhibition to backdonation is also reflected in the chemical shift changes of the α carbon in going from 2-methylpyridine to its N-oxide (159.9 - 148.1 ppm) a shielding effect of 11.8 ppm as compared to the N-oxidation effect in 2,6-dimethylpyridine (158.3 - 148.1), 10.2 ppm.[9]

Summary:

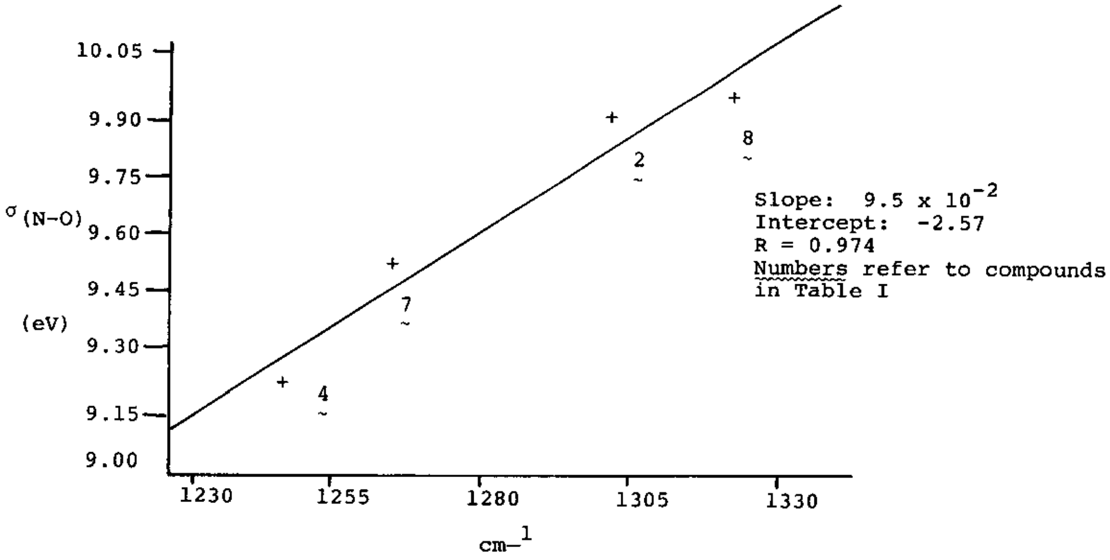
1) A relationship has been shown to exist between the ^{15}N chemical shifts of a number of N-oxides and their ν_{NO} absorption frequencies.
2) A similar relationship exists between the σ_{N-O} ionization potentials of N-oxides and their ν_{N-O} absorption frequencies.
3) The changes in ^{15}N chemical shifts of these N-oxides are reflected in changes of the ^{13}C chemical shifts of the carbons α to the N-oxide function.
4) By comparing the ^{15}N chemical shift changes of the N-oxides and their oxygen protonated analogs, a measure of the extent of backdonation, relatable to the π-deficiency of the N-oxides, has been established.
5) The steric inhibition to backdonation in some appropriately di-substituted N-oxides has been estimated by means of their ν_{N-O} frequencies and changes in the ^{13}C chemical shifts of the α-carbons.

Figure 1: ^{15}N Chemical Shifts *vs* ν_{N-O} of Some N-Oxides



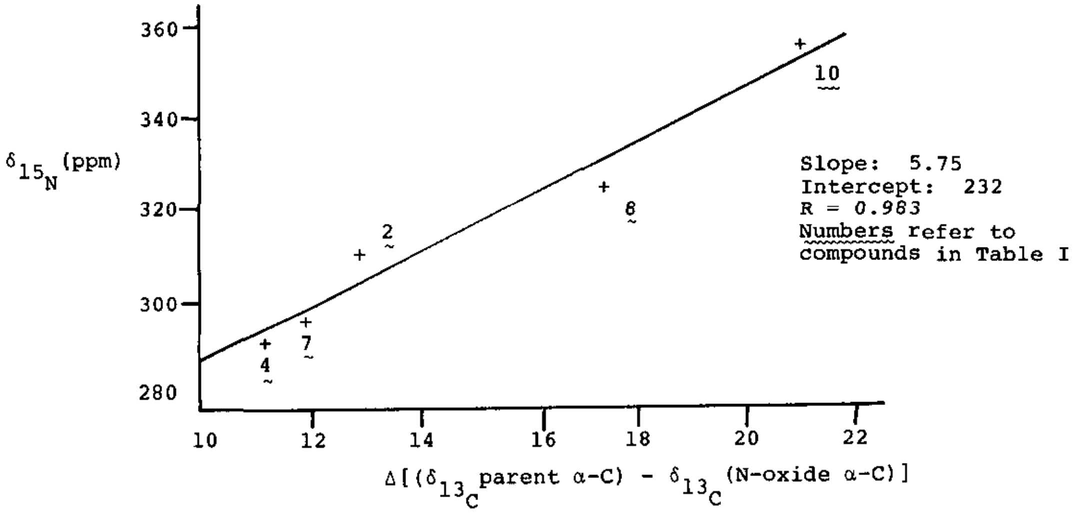
Slope: 0.543
Intercept: -391
R = 0.978
Numbers refer to compounds in Table I

Figure 2: Ionization Potential (σ_{N-O}) vs νN-O of Some N-Oxides



Slope: 9.5×10^{-2}
Intercept: -2.57
R = 0.974
Numbers refer to compounds in Table I

Figure 3: ^{13}C Chemical Shift Differences of α-C's *vs* $\delta_{^{15}N}$ of Some N-Oxides



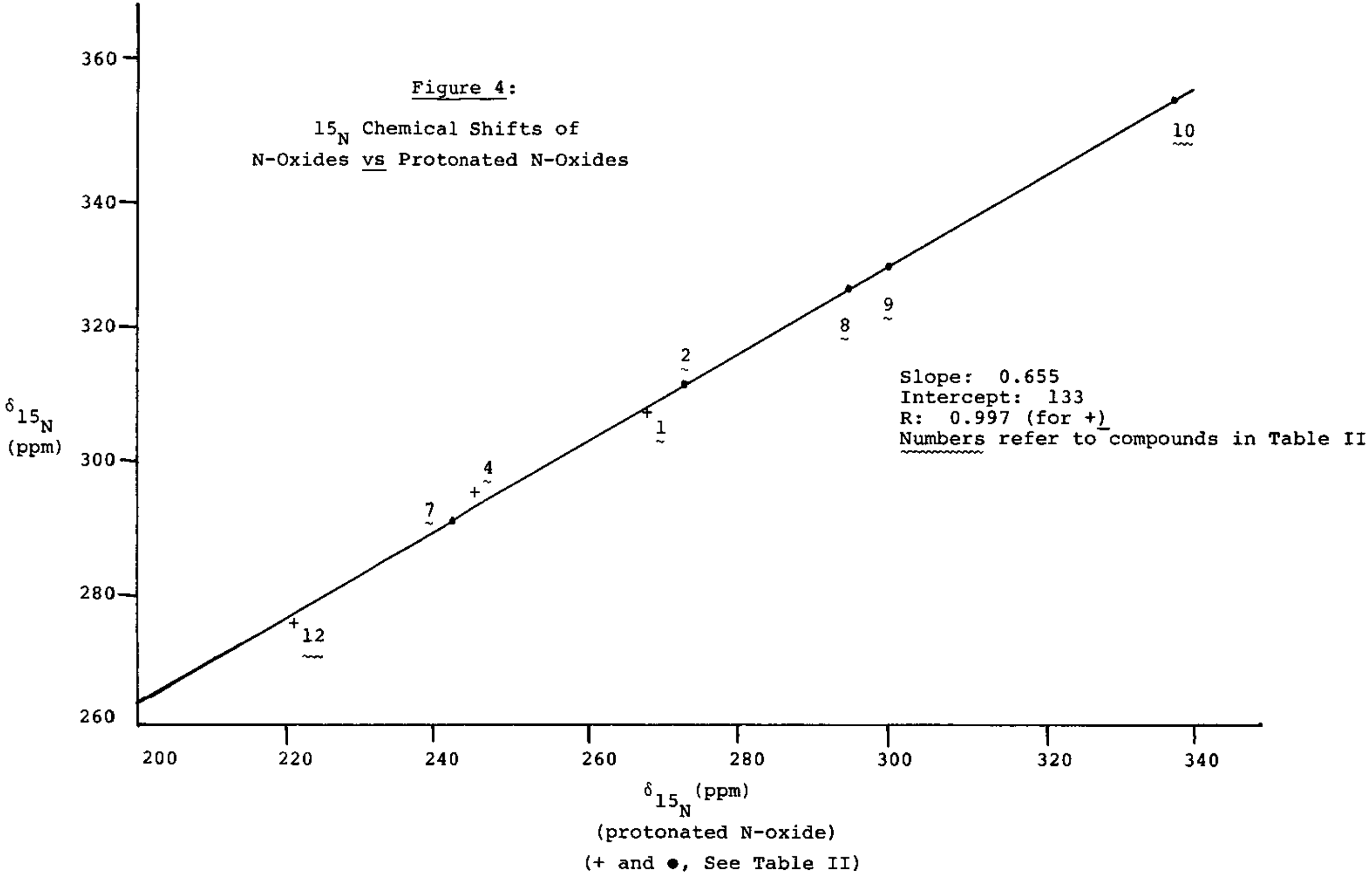


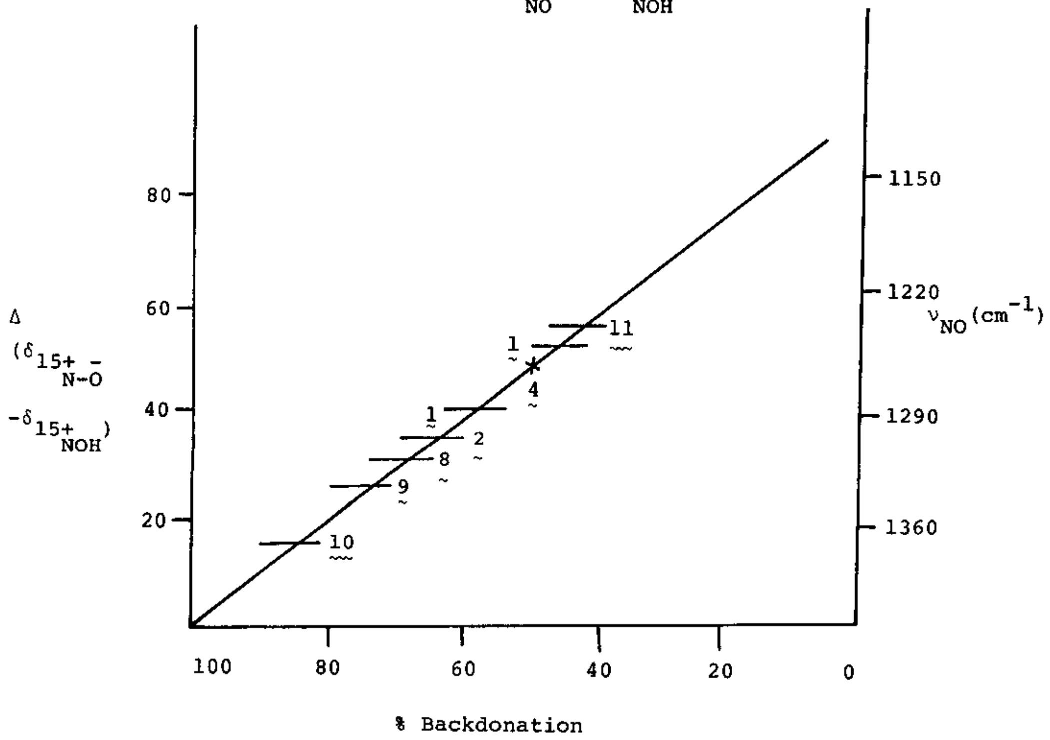
Figure 4:

^{15}N Chemical Shifts of N-Oxides vs Protonated N-Oxides

Slope: 0.655
Intercept: 133
R: 0.997 (for +)
Numbers refer to compounds in Table II

Figure 5

Correlation Estimate between Degree of Backdonation in N-Oxides and ν_{N-O} and $\Delta(\delta_{15\overset{+-}{NO}} - \delta_{15\overset{+}{NOH}})$



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