Isotope Effects on NMR Chemical Shifts

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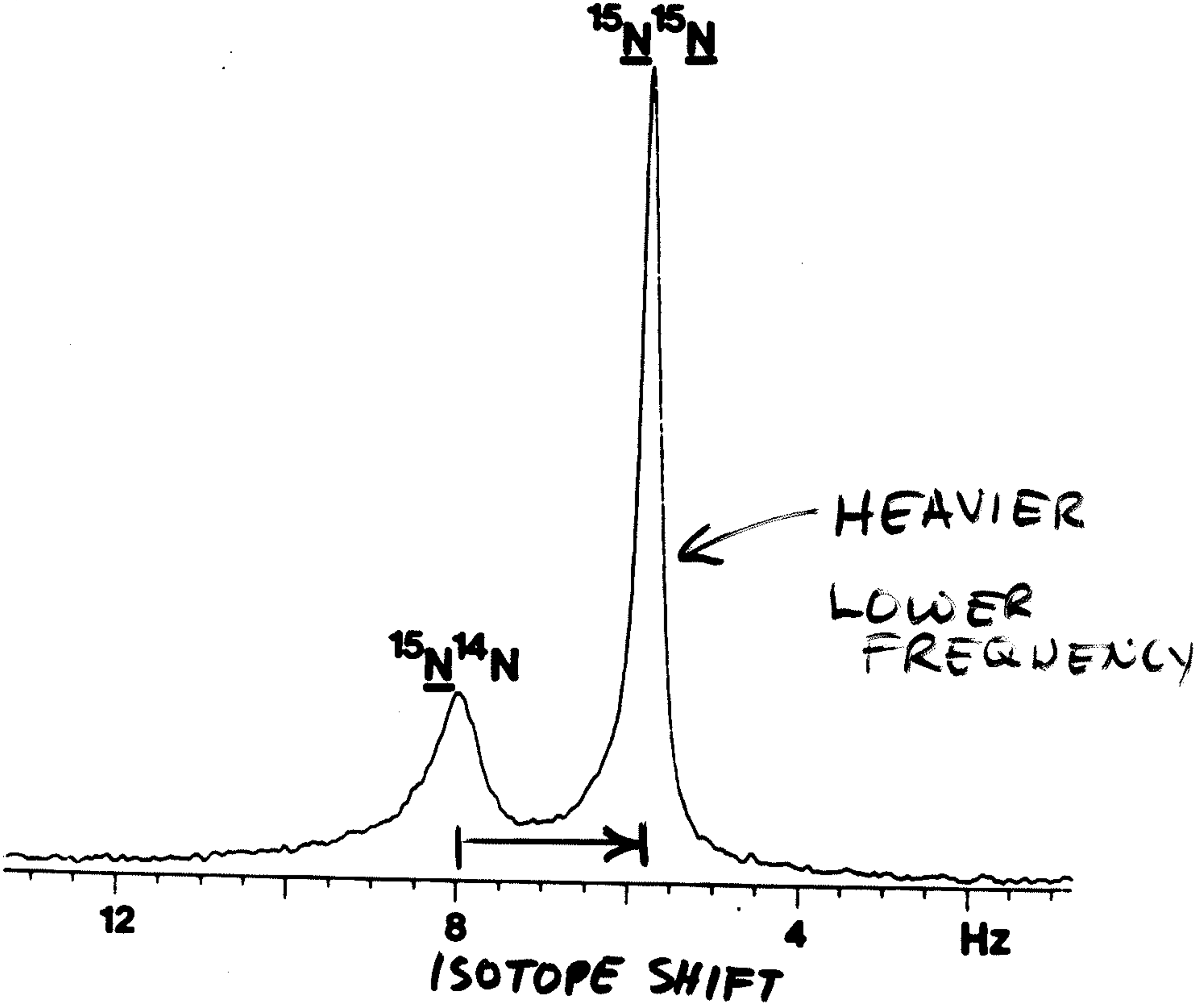
ISOTOPE EFFECTS ON NMR CHEMICAL SHIFTS

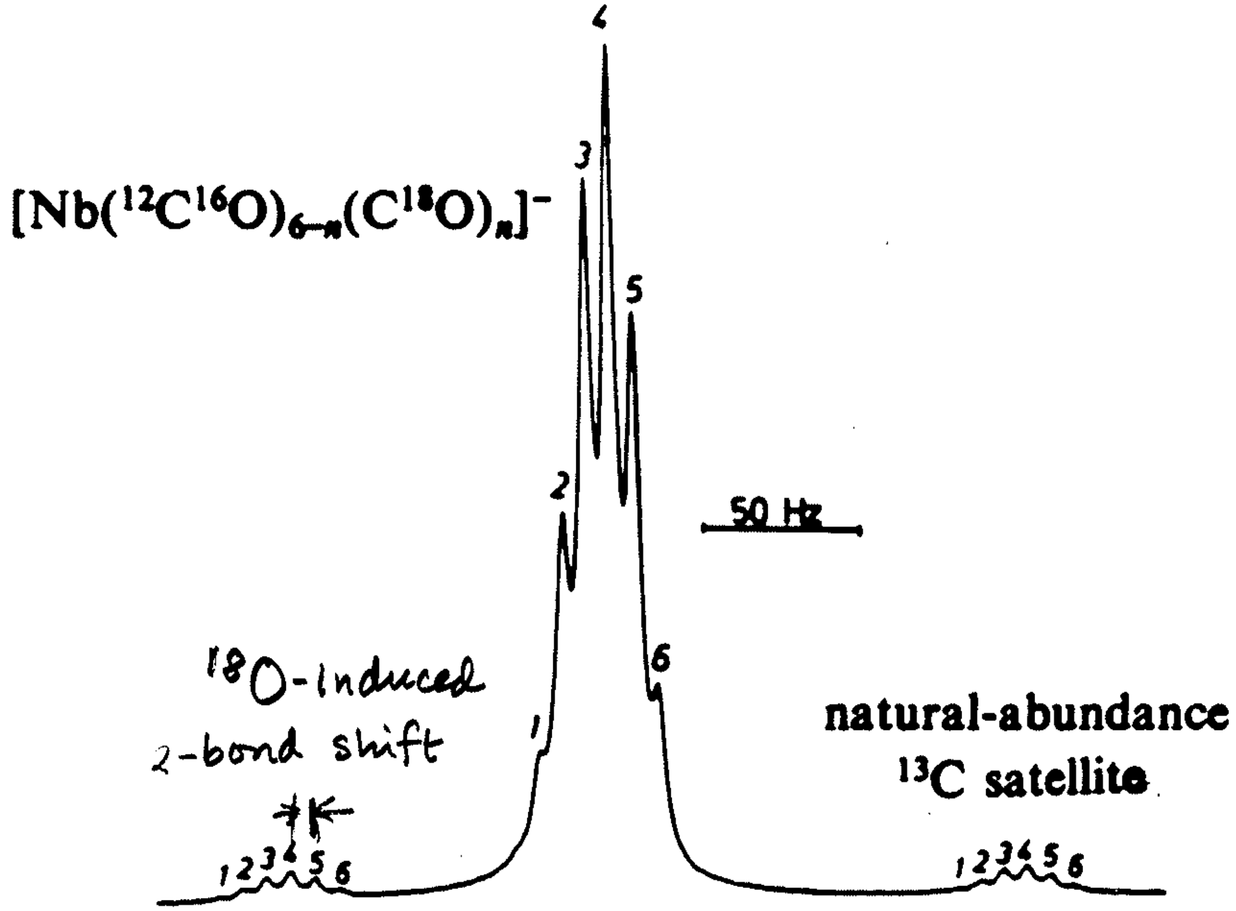
OUTLINE

1. **Some empirical observations**
2. **Summary of empirical observations**
3. **Probability of finding a molecule at a given nuclear configuration**
4. **Dynamic averages :** mass dependence
5. **Nuclear shielding surfaces**
   How does shielding change with increasing bond length and bond angle?
6. **Trends in Electronic Factors**
   a. symmetry
   b. net charge
   c. number of lone pairs
   d. bond order
7. **Temperature dependence**



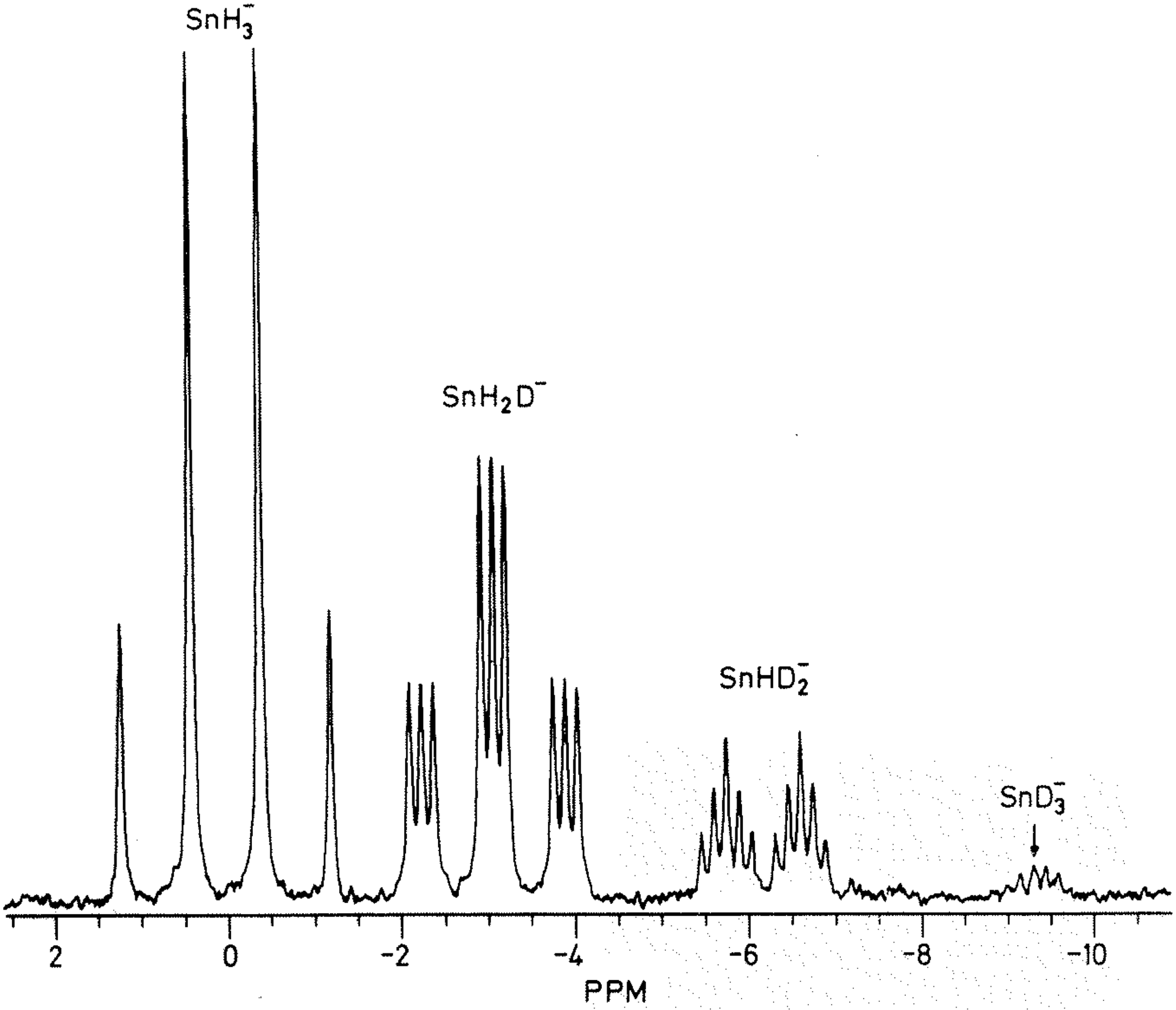
Nitrogen-15 NMR spectrum of $^{14}N^{15}N$ and $^{15}N^{15}N$ at 36.5977 MHz.

R.E. Wasylishen



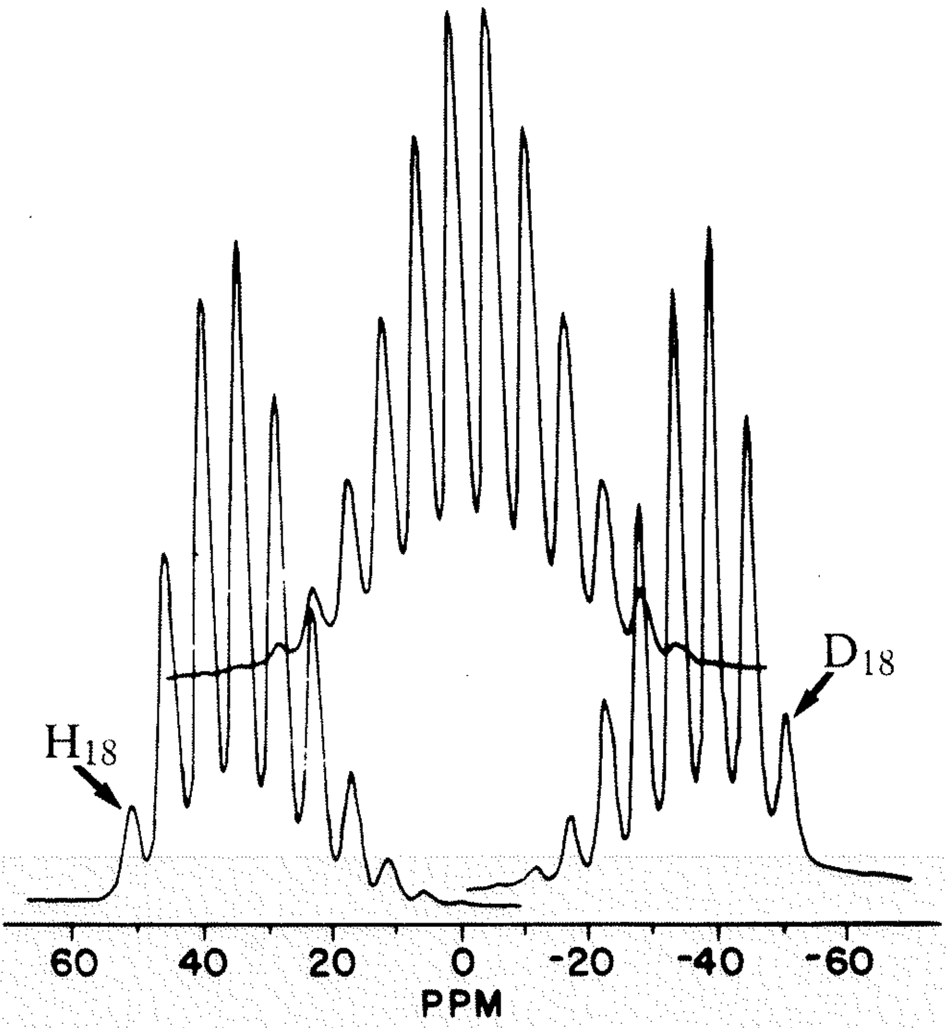
^{93}Nb NMR spectra of [Nb(CO)$_6$]$^-$ ion enriched in C^{18}O taken at 88.29 MHz in acetone solution.

D. Rehder



^{119}Sn D-induced isotope shifts in the deuterated SnH_3^- species are -3.281 ppm / D

Wasylishen and Burford



^{59}Co NMR spectrum of 3 samples of deuterated $^{59}Co[(NH_3)_6]^{2+}$

$$I = \frac{18!}{p!(18-p)!}(1-d)^p(d)^{(18-p)}$$

d = overall deuterium fraction in sample

d = 0.15, 0.50, 0.85 from left to right

Russell and Bryant

Summary of empirical observations about isotope shifts in NMR:

(1) Heavy isotopic substitution shifts the NMR signal of a nearby nucleus toward lower frequency (higher magnetic field).

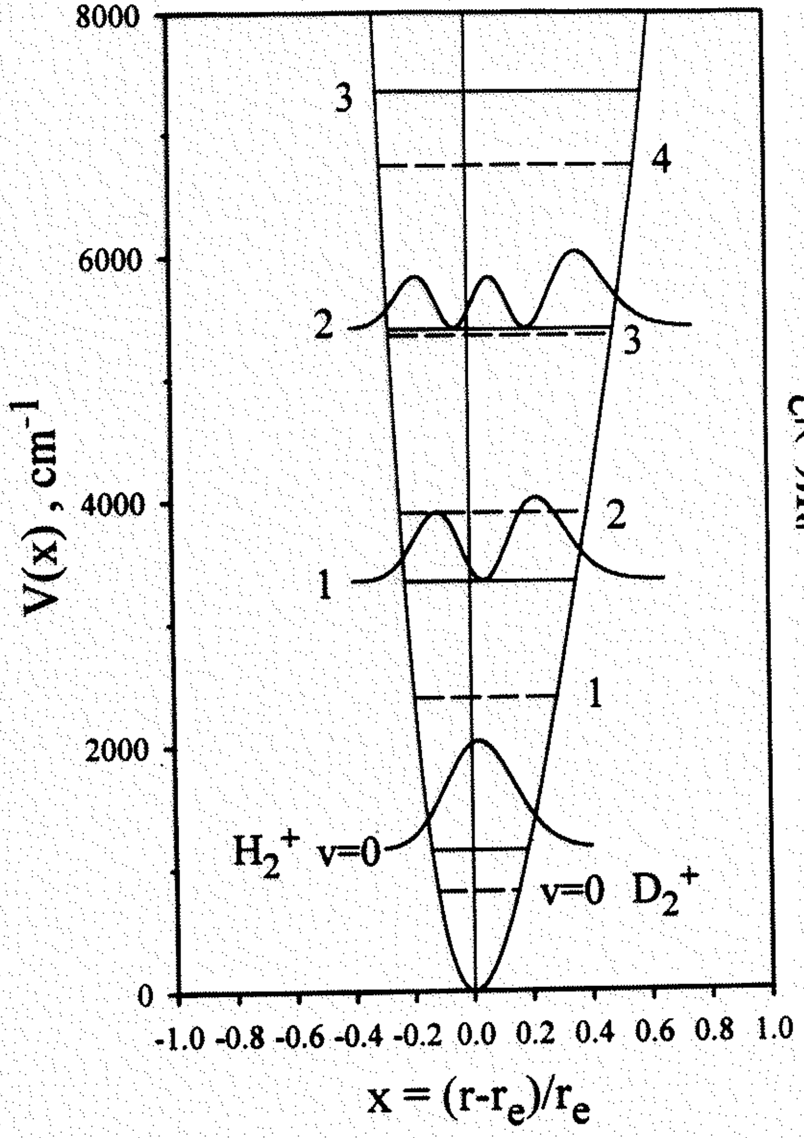
(2) The magnitude of the isotope shift is dependent on how remote the isotopic substitution is from the nucleus under observation.

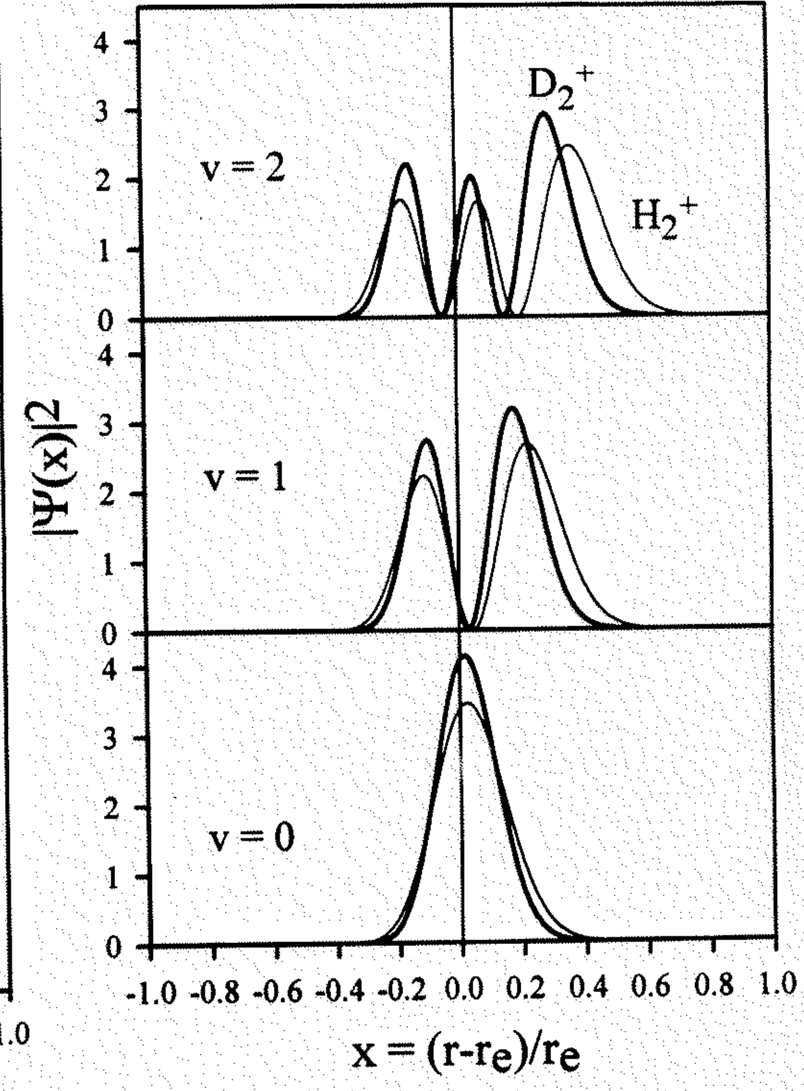
(3) The magnitude of the shift is a function of the resonant nucleus, reflecting the differences in the range of chemical shifts for the nuclei.

(4) The magnitude of the shift is largest where the fractional change in mass upon isotopic substitution is largest. (largest for H →D or T)

(5) The magnitude of the shift is approximately proportional to the number of atoms in the molecule that have been substituted by isotopes.

3. The probability of finding a molecule at a given nuclear configuration is given by $|\Psi_{vib}|^2$.





This is
mass-dependent.

4. Dynamic averages

To get the average value of a molecular electronic property:

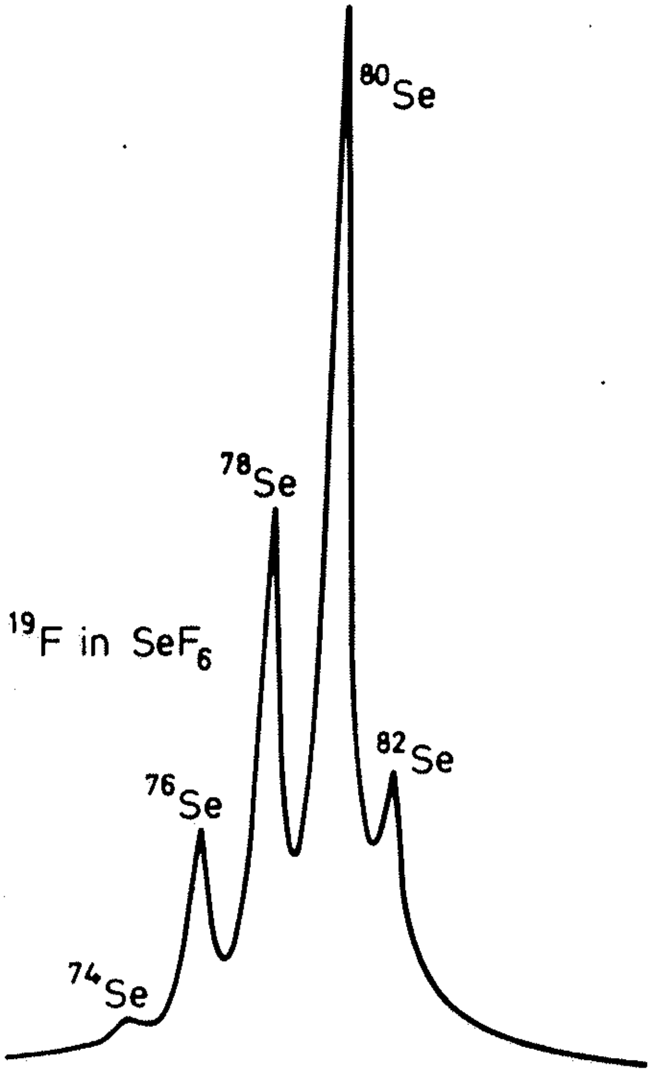
$$\langle P \rangle_v = \int_{-\infty}^{+\infty} \left| \Psi_v(x) \right|^2 P(x) dx$$

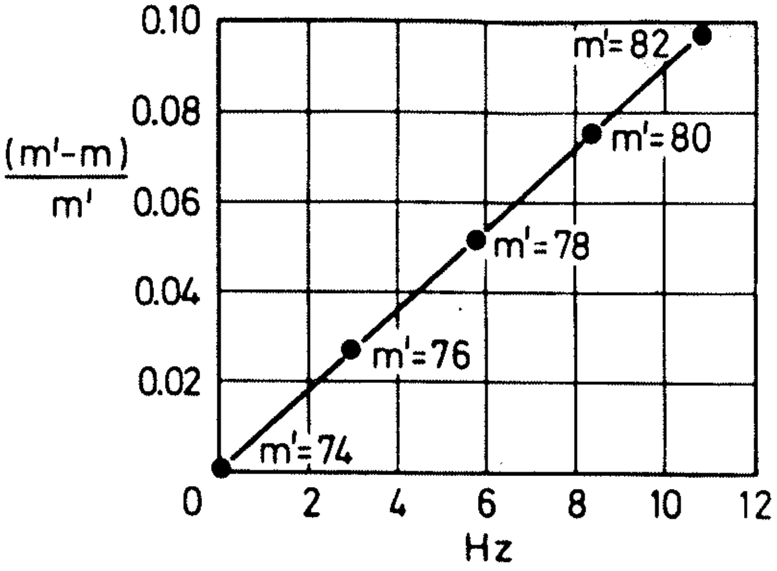
We can also find the rotational average.

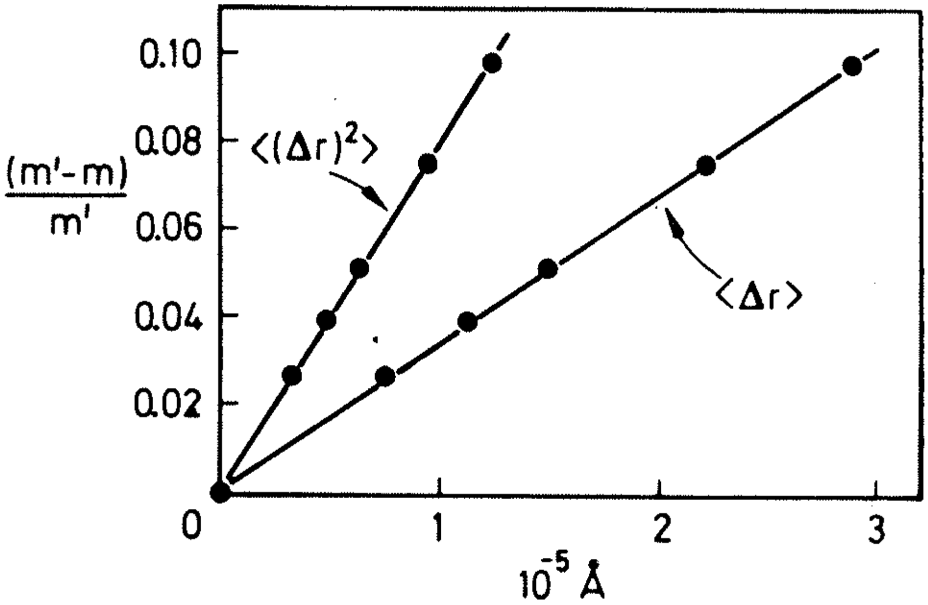
The thermal average is

$$\langle P \rangle^T = \frac{\sum_{v,J,K} (2J+1) g_{Ns} \langle P \rangle_{vJK} \exp(-E_{vJK}/kT)}{\sum_{v,J,K} (2J+1) g_{Ns} \exp(-E_{vJK}/kT)}$$

We can see that the low frequency vibrations are important, but also those vibrational modes that have large $\langle P \rangle_{vJ}$

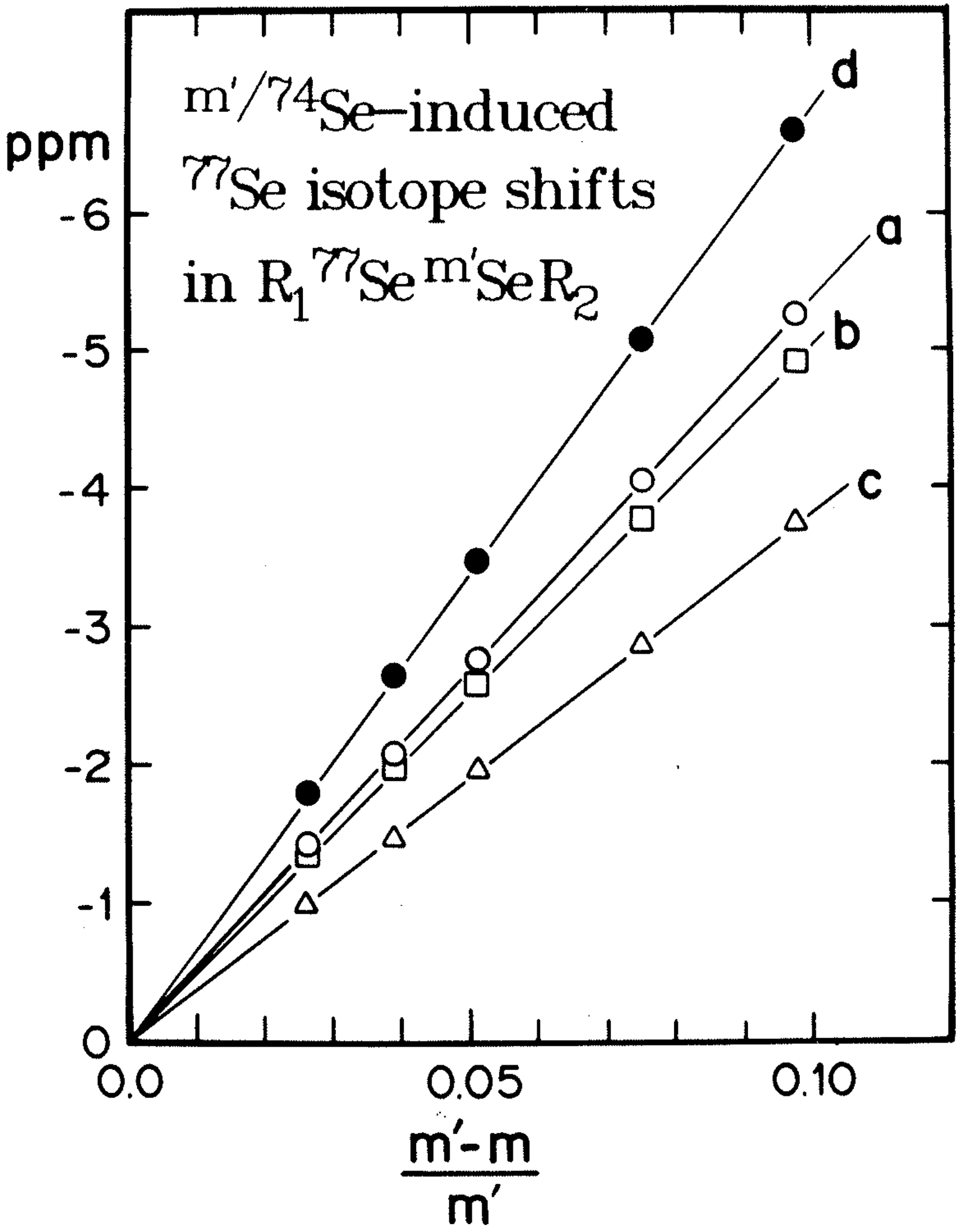

^{19}F in SeF_6
^{80}Se
^{78}Se
^{82}Se
^{76}Se
^{74}Se


$\frac{(m'-m)}{m'}$
0.10
0.08
0.06
0.04
0.02
0
2
4
6
8
10
12
Hz
m'=82
m'=80
m'=78
m'=76
m'=74


$\frac{(m'-m)}{m'}$
0.10
0.08
0.06
0.04
0.02
0
1
2
3
10^{-5} Å
$\langle(\Delta r)^2\rangle$
$\langle\Delta r\rangle$

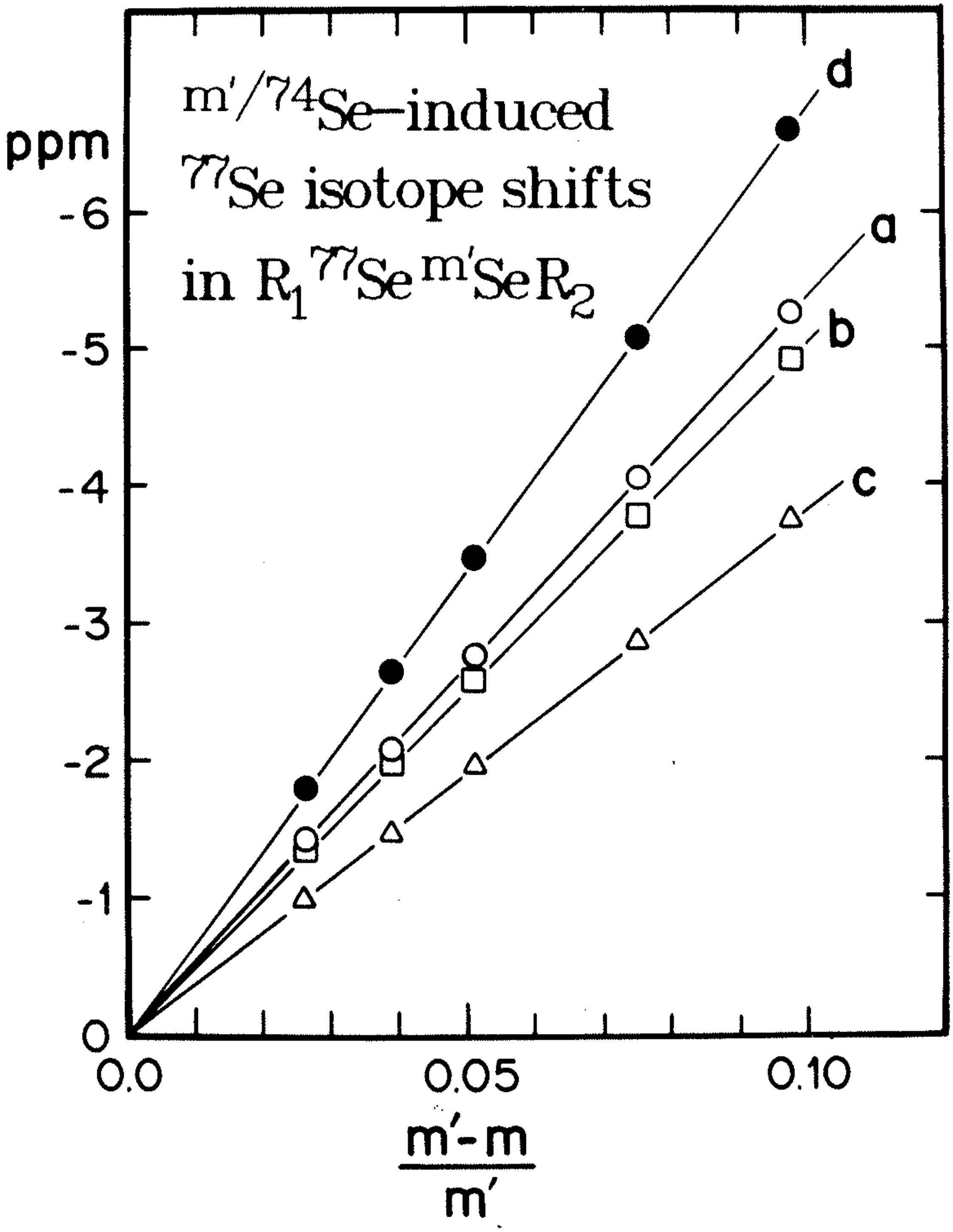
The mass-dependence of the dynamic part is predicted by theory: both $\langle \Delta r \rangle$ and $\langle (\Delta r)^2 \rangle$ depend on (m'-m)/m'. Here m and m' are the masses of the Se isotopes, 74 - 82.

Jameson and Osten, data from Gombler

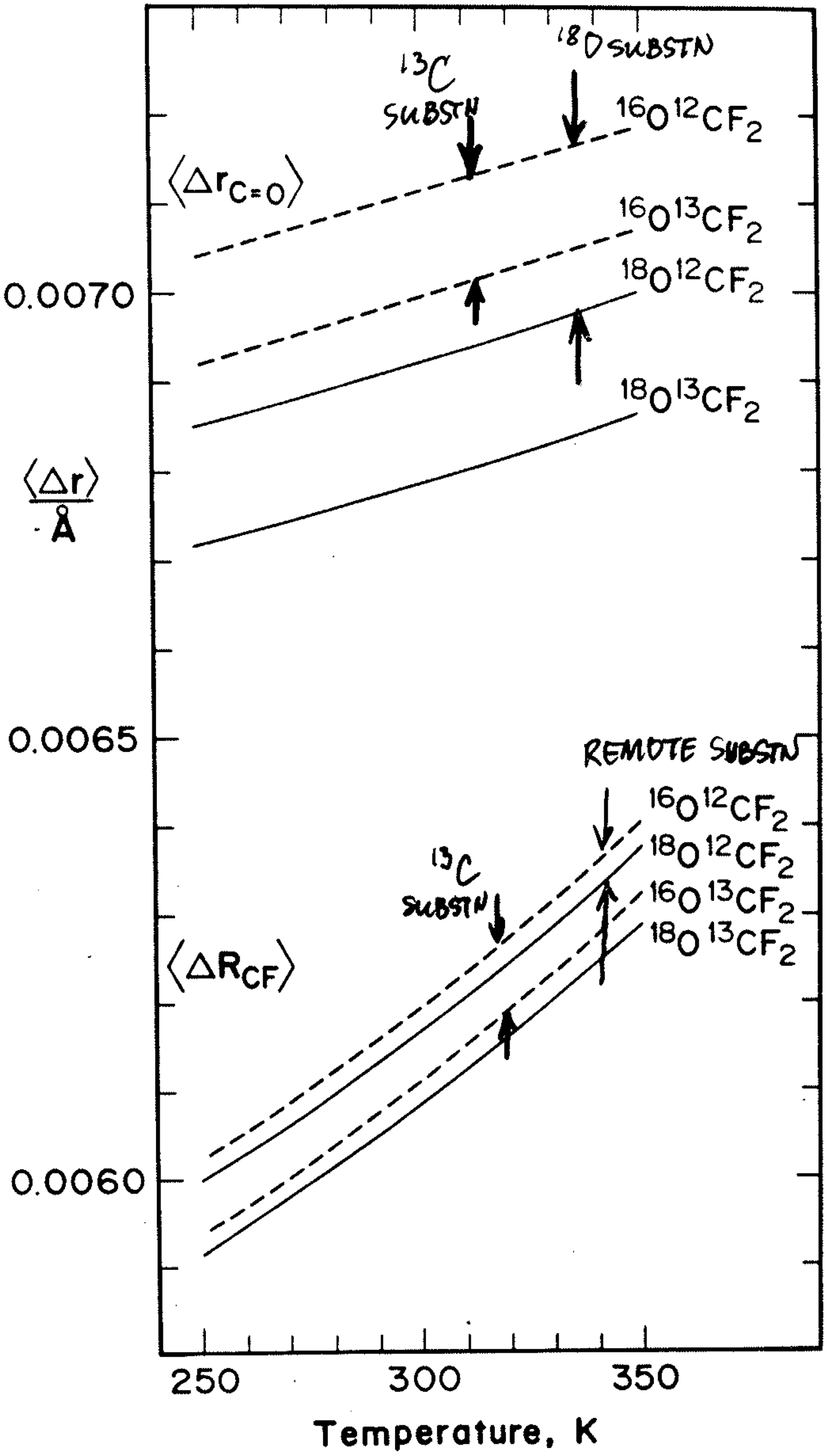


The mass-dependence of the dynamic part is predicted by theory: both $\langle \Delta r \rangle$ and $\langle (\Delta r)^2 \rangle$ depend on (m'-m)/m'. Here m and m' are the masses of the Se isotopes, 74 - 82.

Jameson and Osten, data from Gombler



33



large effects of ^{18}O- or ^{13}C- substitution on O-C bond length

small effect of ^{18}O- substitutio on C-F bond length

5. NUCLEAR SHIELDING SURFACES

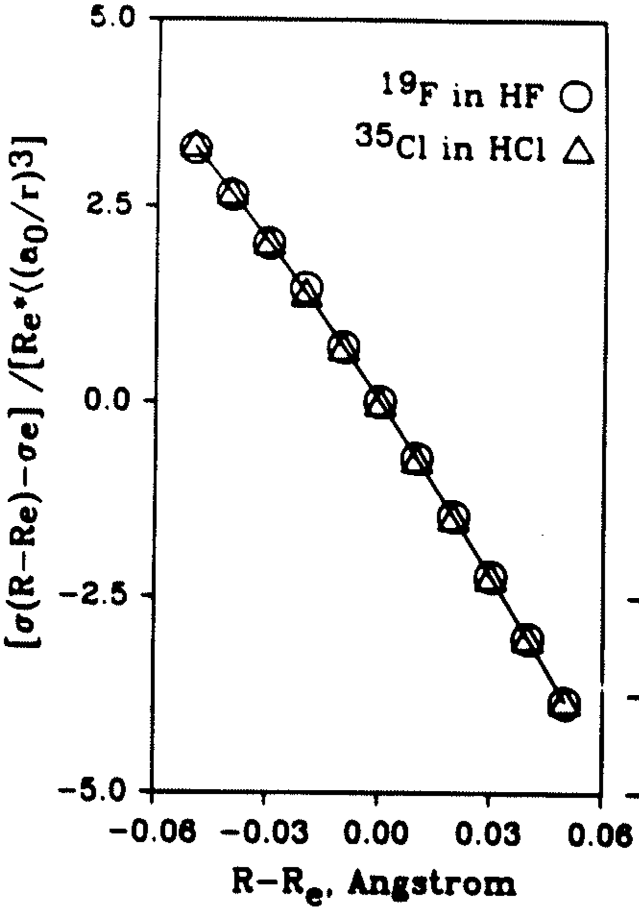
a. How does shielding change with increasing bond length? variation of the derivative $(\partial\sigma/\partial r)$

b. What is $(\partial\sigma/\partial r)_e$ i.e., the value at the equilibrium geometry of the molecule?

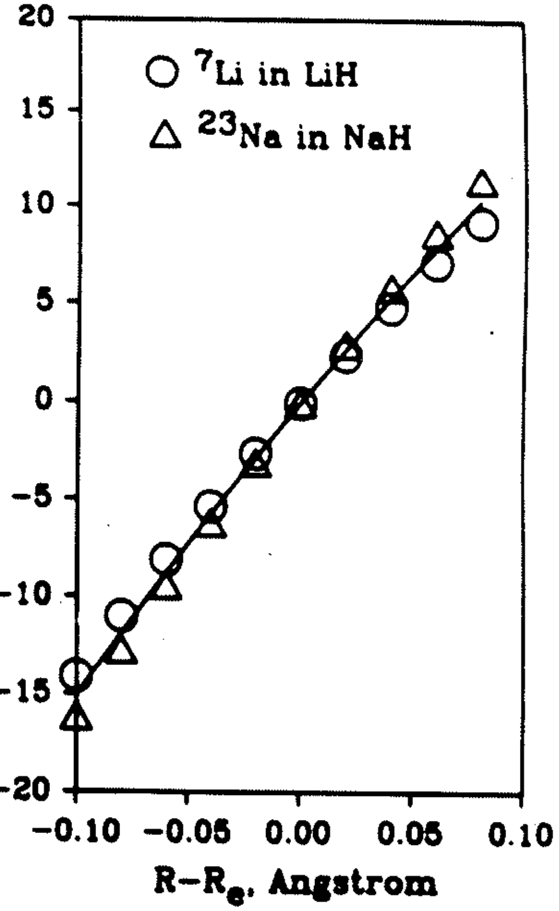
c. How does $(\partial\sigma/\partial r)_e$ change across the Periodic Table?

d. When scaled, does the variation of $(\partial\sigma/\partial r)_e$ across the Periodic Table make sense?

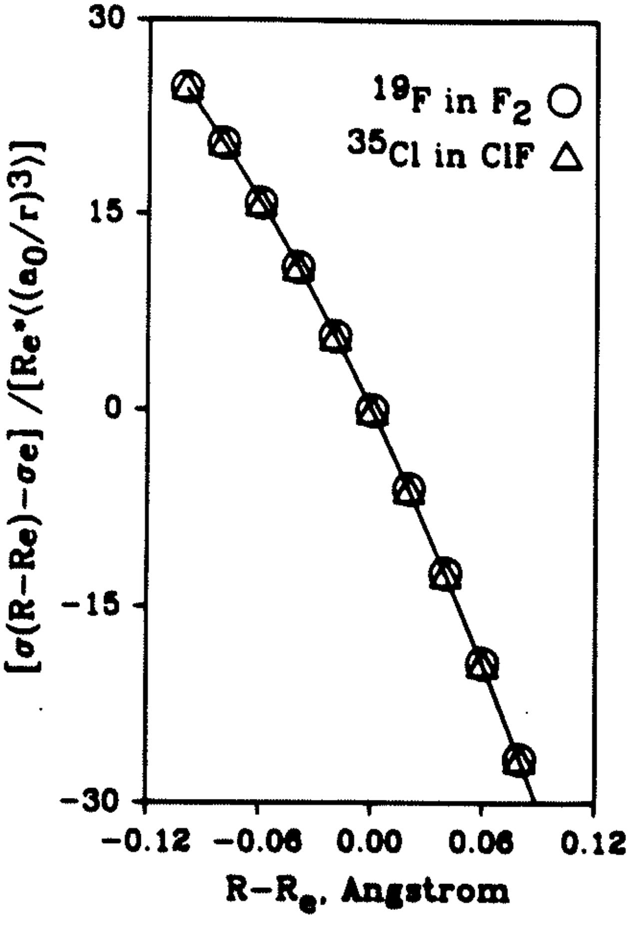
e. Do the different signs of $(\partial\sigma/\partial r)_e$ make sense in terms of the variation of electron density with increasing internuclear distance?



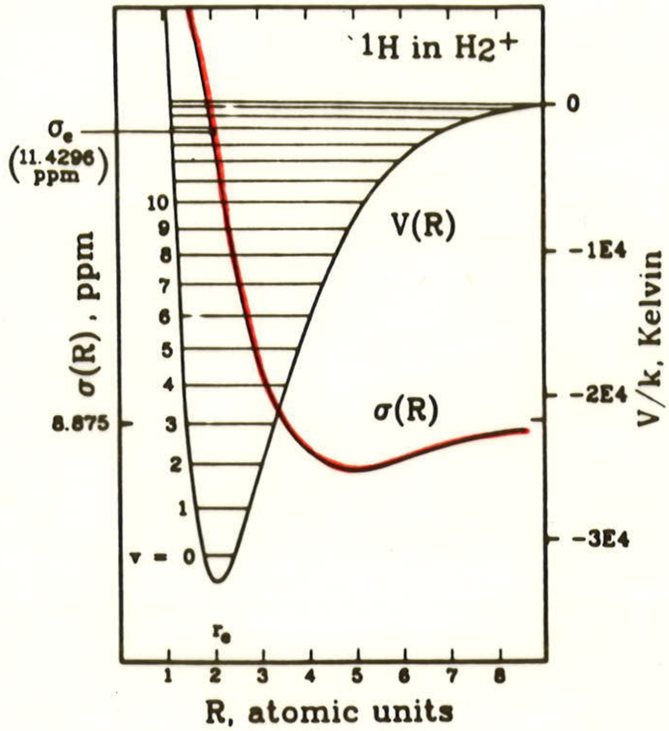
¹⁹F in HF ○
³⁵Cl in HCl △
[σ(R−Re)−σe] /[Re*⟨(a0/r)3⟩]
5.0
2.5
0.0
−2.5
−5.0
−0.06
−0.03
0.00
0.03
0.06
R−Re, Angstrom

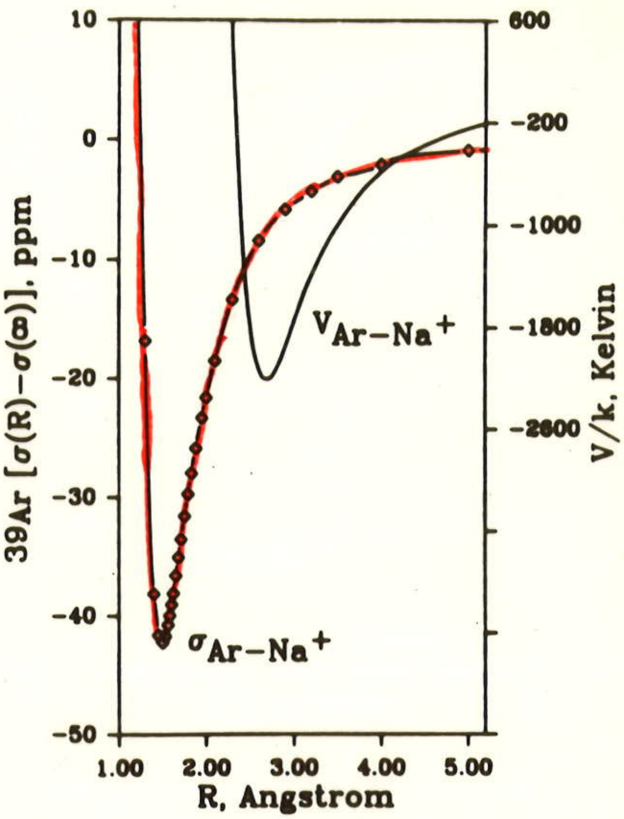


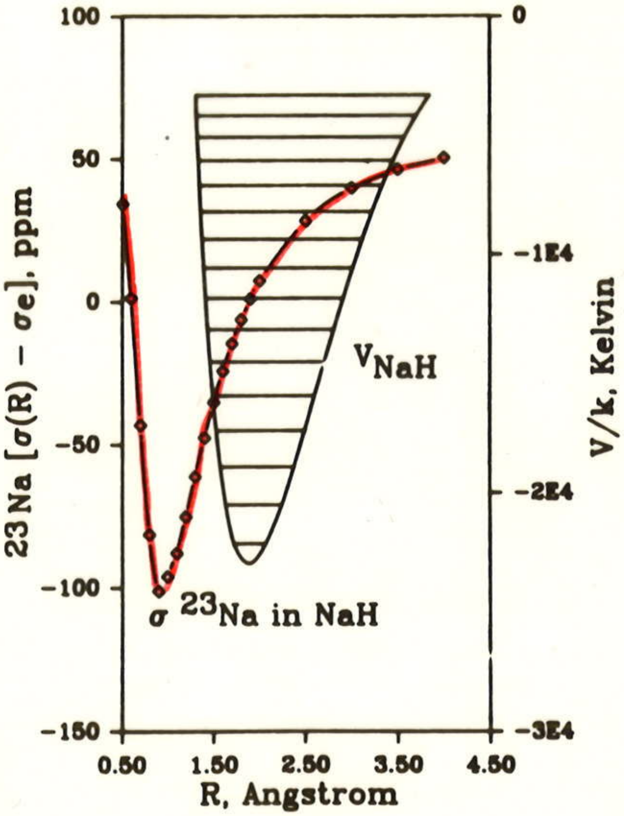
○ ⁷Li in LiH
△ ²³Na in NaH
20
15
10
5
0
−5
−10
−15
−20
−0.10
−0.05
0.00
0.05
0.10
R−Re, Angstrom

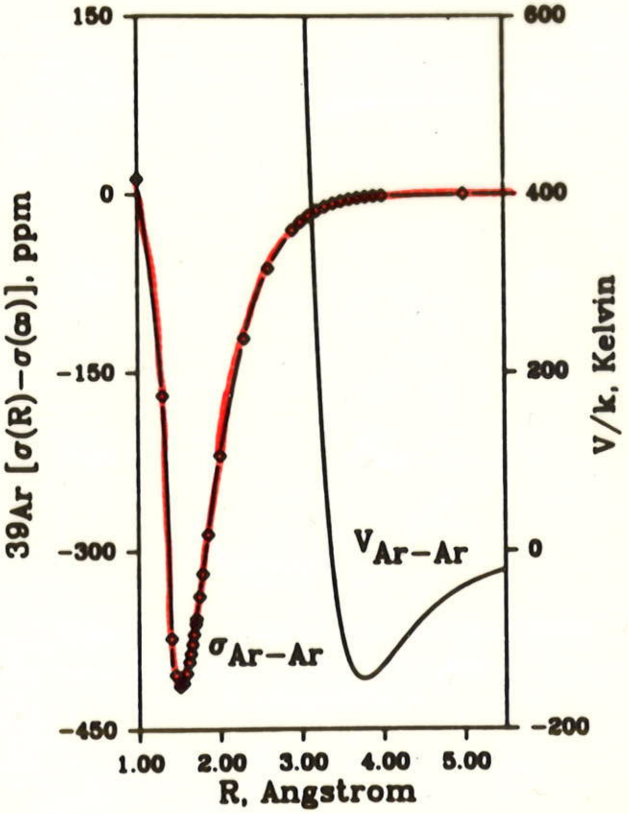


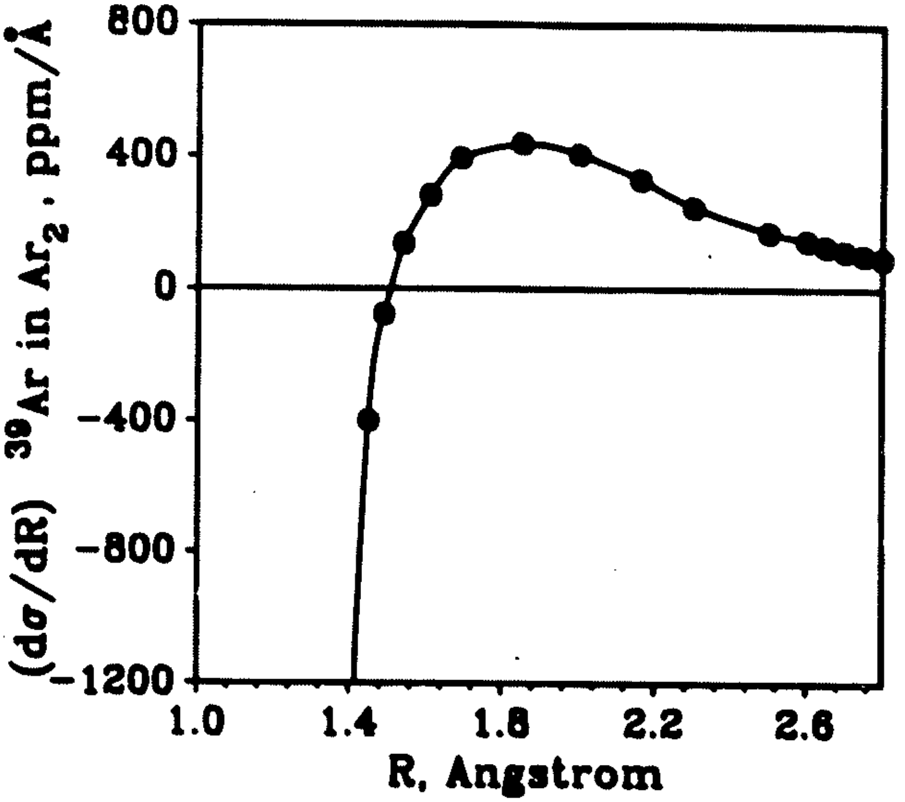
¹⁹F in F2 ○
³⁵Cl in ClF △
[σ(R−Re)−σe] /[Re*⟨(a0/r)3⟩]
30
15
0
−15
−30
−0.12
−0.06
0.00
0.06
0.12
R−Re, Angstrom

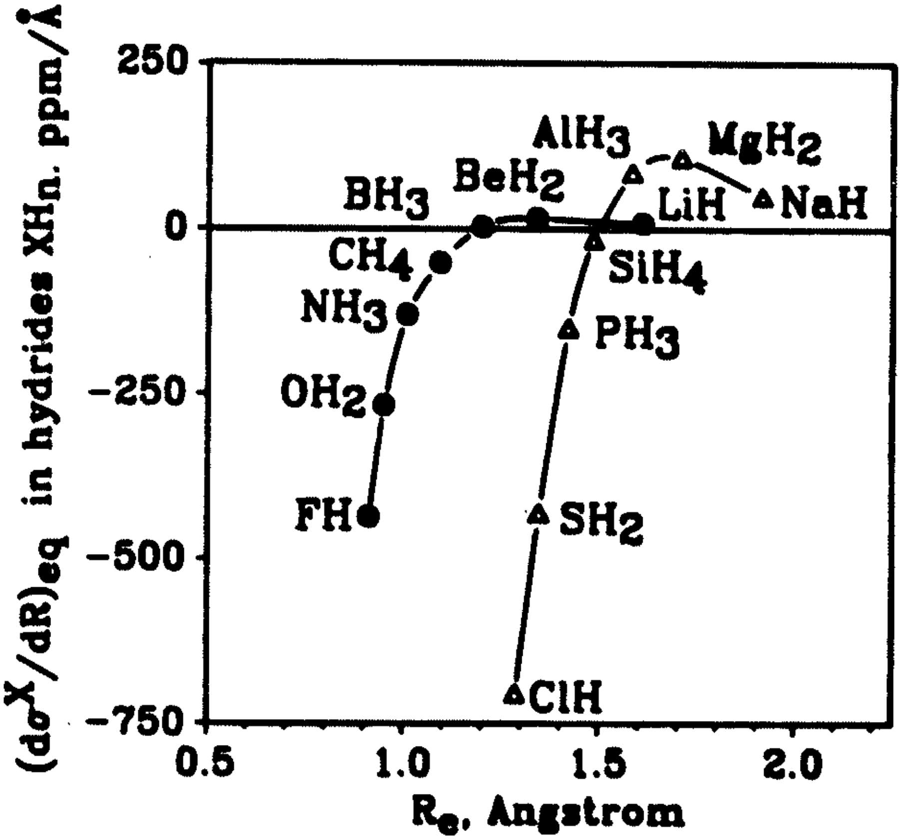

1H in H2+
σe
(11.4296 ppm)
σ(R), ppm
8.875
10
9
8
7
6
5
4
3
2
1
v = 0
re
V(R)
σ(R)
0
-1E4
-2E4
-3E4
V/k, Kelvin
1
2
3
4
5
6
7
8
R, atomic units

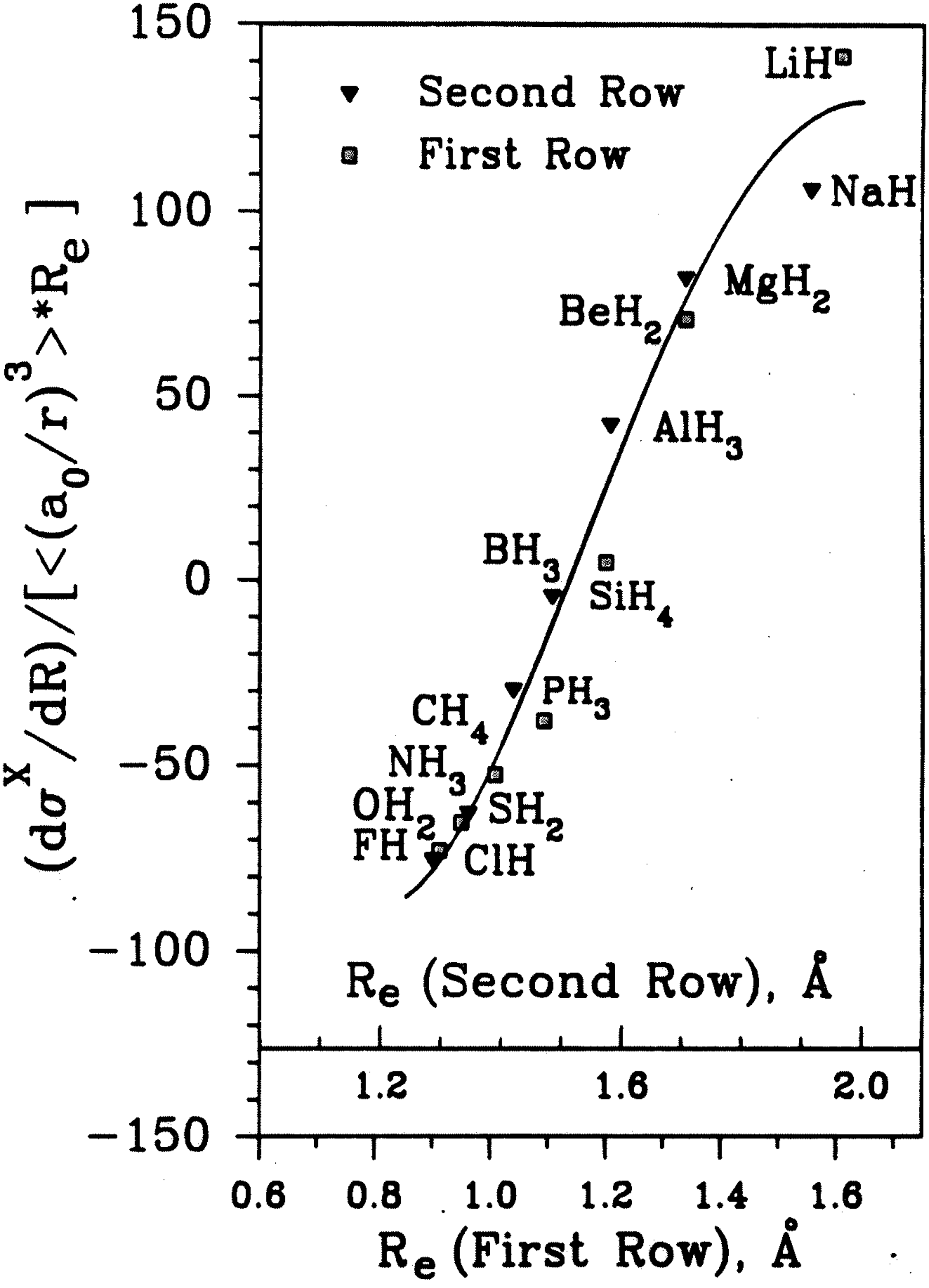

10
0
-10
-20
-30
-40
-50
39Ar [σ(R)-σ(∞)], ppm
VAr-Na+
σAr-Na+
600
-200
-1000
-1800
-2600
V/k, Kelvin
1.00
2.00
3.00
4.00
5.00
R, Angstrom


100
50
0
-50
-100
-150
23Na [σ(R) - σe], ppm
VNaH
σ 23Na in NaH
0
-1E4
-2E4
-3E4
V/k, Kelvin
0.50
1.50
2.50
3.50
4.50
R, Angstrom

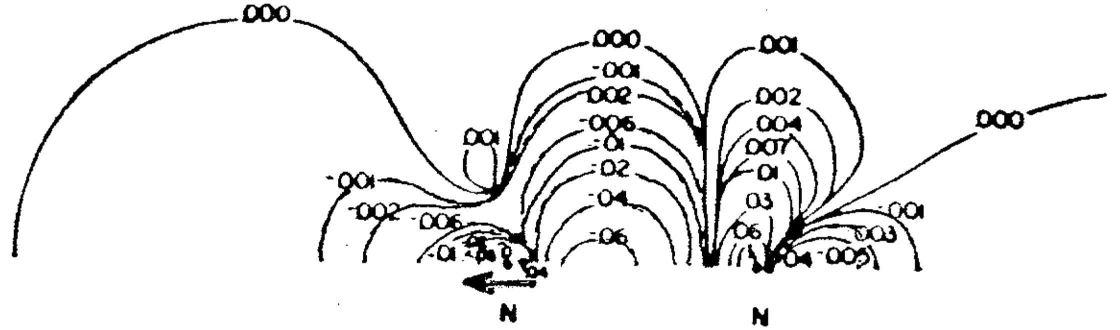

150
0
-150
-300
-450
39Ar [σ(R)-σ(∞)], ppm
VAr-Ar
σAr-Ar
600
400
200
0
-200
V/k, Kelvin
1.00
2.00
3.00
4.00
5.00
R, Angstrom


800
400
0
-400
-800
-1200
1.0
1.4
1.8
2.2
2.6
R, Angstrom
(dσ/dR) ³⁹Ar in Ar₂ . ppm/Å

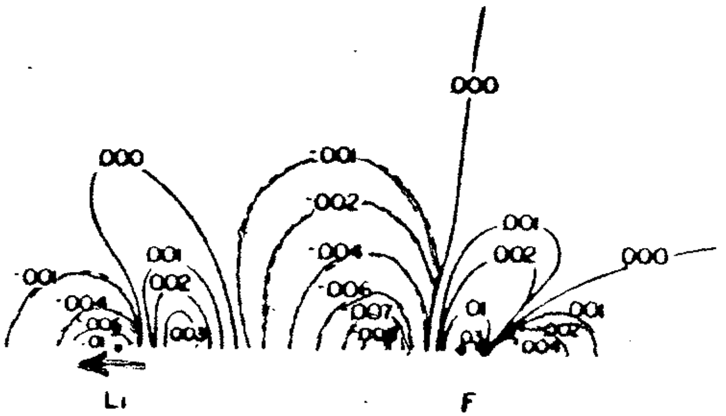

250
0
-250
-500
-750
0.5
1.0
1.5
2.0
Rₑ, Angstrom
(dσˣ/dR)ₑq in hydrides XHₙ. ppm/Å
AlH₃
MgH₂
BeH₂
BH₃
LiH
NaH
CH₄
SiH₄
NH₃
PH₃
OH₂
FH
SH₂
ClH



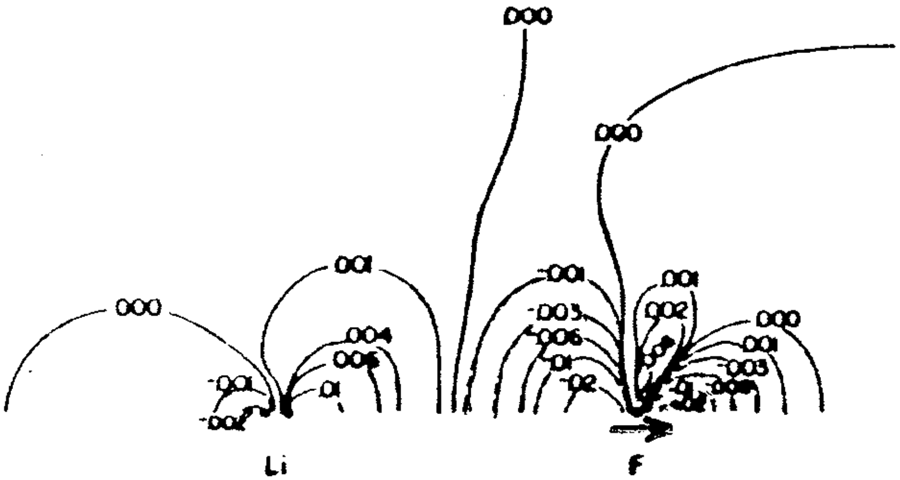
▼ Second Row
▨ First Row
LiH
NaH
MgH$_2$
BeH$_2$
AlH$_3$
BH$_3$
SiH$_4$
PH$_3$
CH$_4$
NH$_3$
OH$_2$
SH$_2$
FH
ClH
$(d\sigma^x/dR)/[\langle(a_0/r)^3\rangle{}^*R_e]$
150
100
50
0
−50
−100
−150
R$_e$ (Second Row), Å
1.2
1.6
2.0
0.6
0.8
1.0
1.2
1.4
1.6
R$_e$ (First Row), Å


.000
.000
-.001
-.002
-.006
-.01
-.02
-.04
-.06
.001
.002
.004
.007
.01
.03
.06
.000
.001
-.001
-.002
-.006
-.01
.04
-.001
.003
.005
N
N

N


.000
.000
-.001
-.002
-.004
-.006
.007
-.001
-.004
.001
.002
.003
.001
.002
.01
.03
.000
.001
.002
.004
Li
F

Li


.000
.000
.000
.001
.004
.006
.01
-.001
-.002
-.001
-.003
-.006
-.01
-.02
.001
.002
.000
-.001
-.003
Li
F

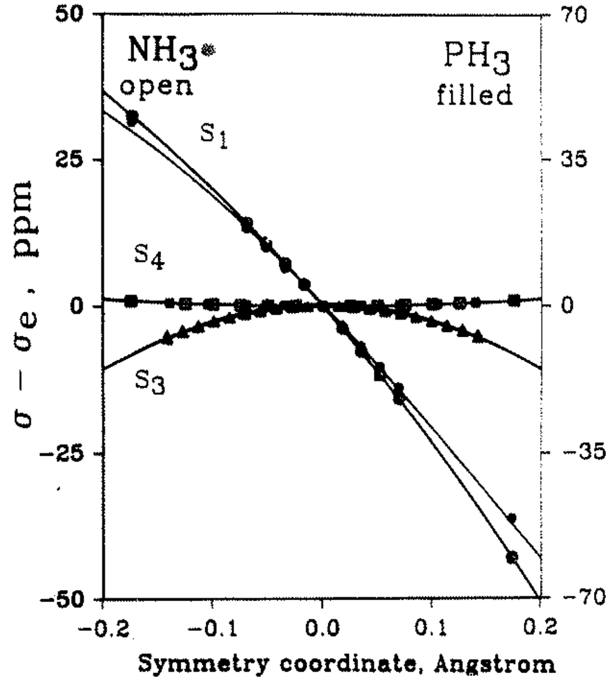
F

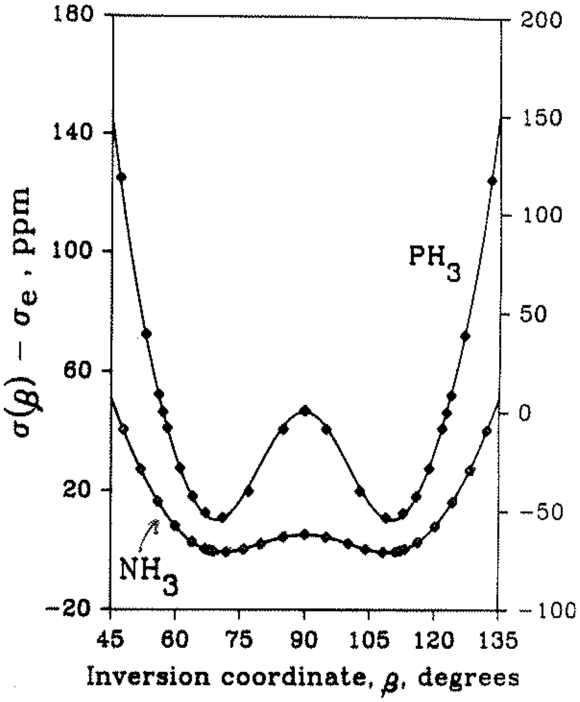
Electron density difference maps showing how electron density changes with bond extension

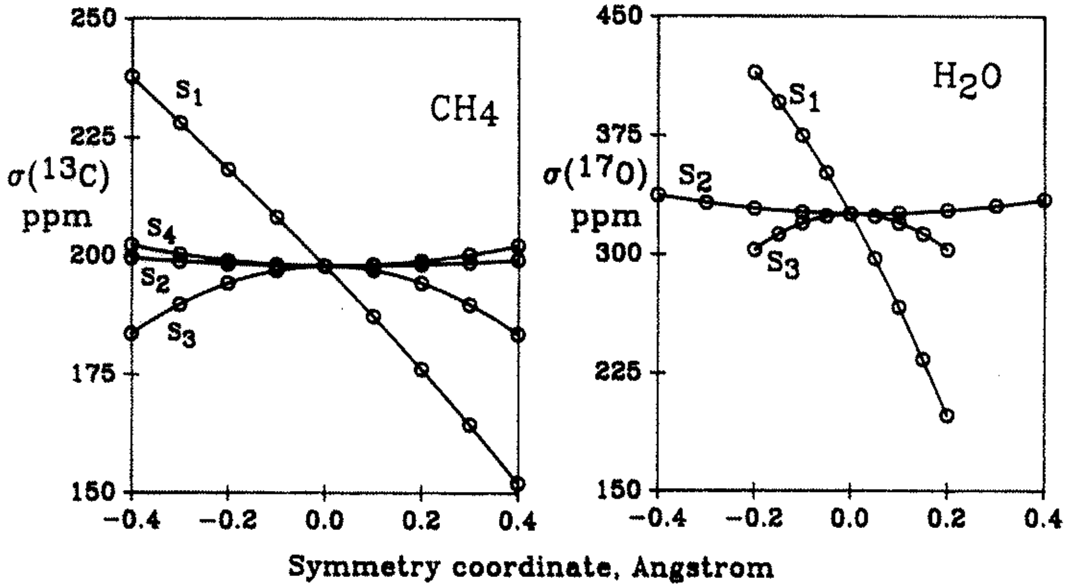
The charge redistribution in diatomic molecules, caused by extension of the bond:

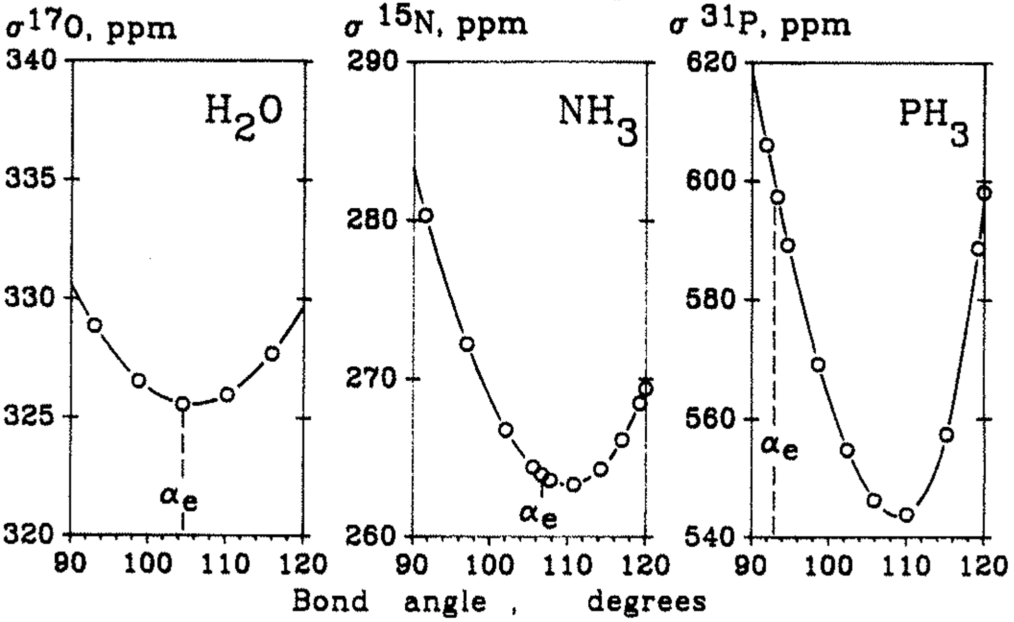
a) Charge is removed from along the internuclear axis and becomes concentrated in the perpendicular region. This leads to a quadrupolar character of the change in charge density, most pronounced for *N* and *F*. This leads to a larger paramagnetic contribution to the shielding, a net deshielding.

b) On the other hand, charge is removed from the overlap region and builds up immediately in front of the *Li* nucleus in *LiF*. This leads to an increase in shielding.


NH3* open
PH3 filled
S1
S4
S3
σ − σe , ppm
50
25
0
−25
−50
70
35
0
−35
−70
−0.2
−0.1
0.0
0.1
0.2
Symmetry coordinate, Angstrom


PH3
NH3
σ(β) − σe , ppm
180
140
100
60
20
−20
200
150
100
50
0
−50
−100
45
60
75
90
105
120
135
Inversion coordinate, β, degrees


CH4
σ(13C) ppm
S1
S4
S2
S3
250
225
200
175
150
−0.4
−0.2
0.0
0.2
0.4
H2O
σ(17O) ppm
S1
S2
S3
450
375
300
225
150
−0.4
−0.2
0.0
0.2
0.4
Symmetry coordinate, Angstrom


σ 17O, ppm
H2O
340
335
330
325
320
αe
90
100
110
120
σ 15N, ppm
NH3
290
280
270
260
αe
90
100
110
120
σ 31P, ppm
PH3
620
600
580
560
540
αe
90
100
110
120
Bond angle , degrees

6. Trends in Electronic Factors

How does the shielding derivative $(\partial\sigma^N/\partial r)$ (and thus also the isotope shift) change with

- a. position of N in the Periodic Table
- b. paramagnetic shielding of nucleus N in the chemical specie
- c. symmetry at site of nucleus N
- d. net charge of the chemical specie
- e. number of lone pairs on atom N
- f. bond order of the bonds to atom N
- g. change in pi density at aromatic site remote from atom N

THE ISOTOPE SHIFT IS GREATER FOR
THE LESS SYMMETRIC ENVIRONMENT

Proc. Natl. Acad. Sci. USA 79 (1982)

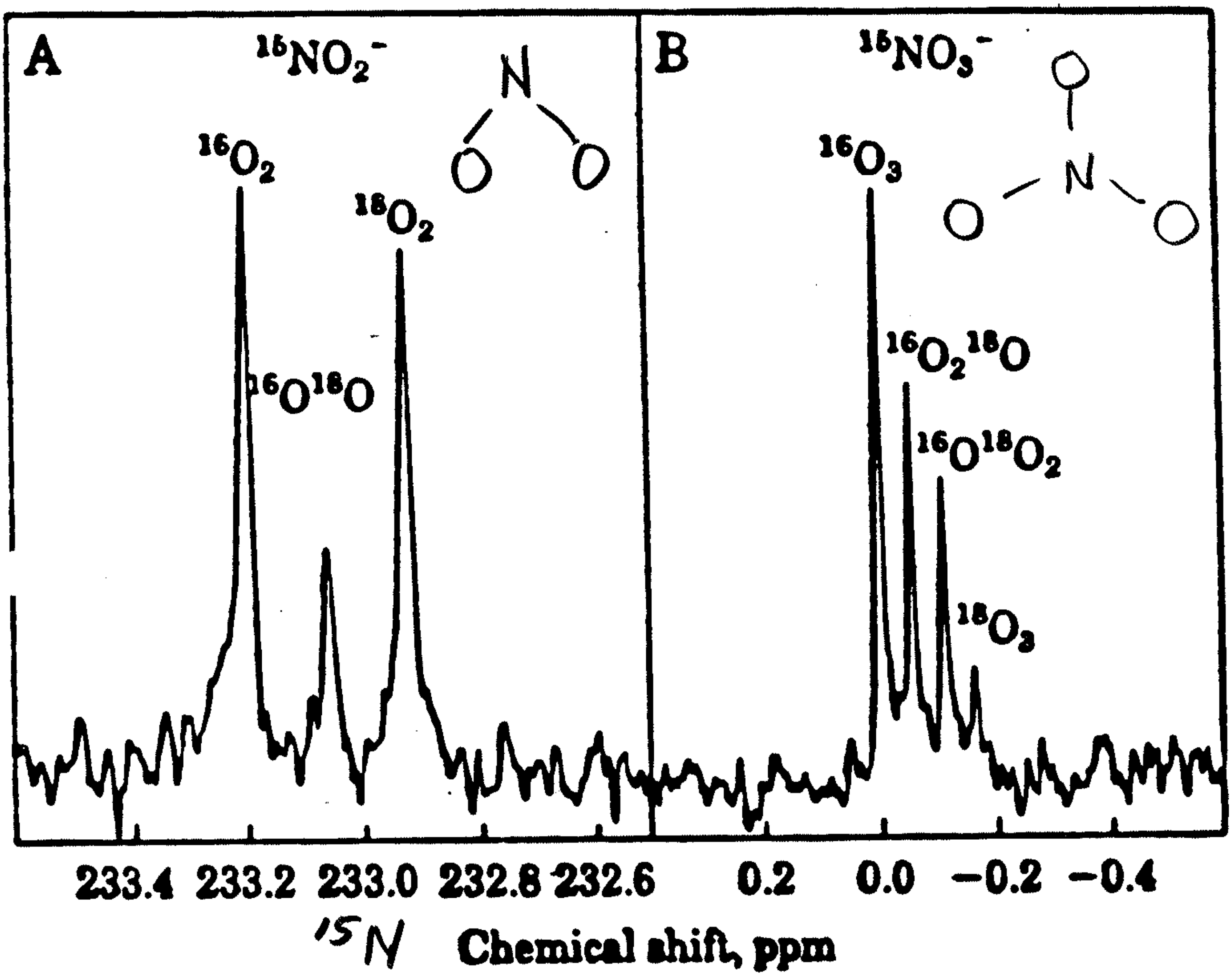


FIG. 1. $^{18}O/^{16}O$ derivatives of nitrite and nitrate resolved by high-resolution ^{15}N NMR. (*A*) Solution of 100 mM [^{15}N]nitrite in 0.25 M phosphate/0.5 mM carbonate/6% $H_2{}^{18}O$, pH 7.5; 180 scans, 12-mm tube (4 ml). (*B*) Solution of [^{15}N]nitrite in 0.25 M phosphate/5 mM rbonate/10% $H_2{}^{18}O$, pH 7.0; 724 scans, 12-mm tube.

Effects of the net charge

	$^{1}\Delta^{119}\mathrm{Sn}(^{2/1}\mathrm{H})$ ppm per D	emp. $(\partial\sigma/\partial r)_e$ ppm $\mathrm{\AA}^{-1}$
^{119}Sn in SnH_4	-0.403	-92
^{119}Sn in SnH_3^+	-0.05 ± 0.03	-10

	theor. $(\partial\sigma/\partial r)_e$ ppm $\mathrm{\AA}^{-1}$
^{11}B in BH_3	-3.5
^{11}B in BH_4^-	-27.
^{27}Al in AlH_3	+84.2
^{27}Al in AlH_4^-	+11.6

	$(\partial\sigma/\partial r)_e$ ppm $\mathrm{\AA}^{-1}$	
	theor.	emp.
^{13}C in HCN	-263	
^{13}C in CN^-	-538.7	-473
^{15}N in HCN	-675.4	
^{15}N in CN^-	-892.2	-872

		number of lone pairs	Average $^1\Delta$ ppm per D
^{15}N	in NH_3	1	- 0.623
	NH_4^+	0	- 0.293
^{17}O	in H_2O	2	- 3.090
	H_3O^+	1	- 0.3
^{31}P	in PH_2^-	2	- 2.760
	PH_3	1	- 0.846
	PH_4^+	0	very small
^{119}Sn	in SnH_3^-	1	- 3.281
	SnH_4	0	- 0.403
	SnH_3^+	0	- 0.05 ± 0.03

Lone pair effects

	Ab initio $(\partial\sigma/\partial r)_e$ ppm Å^{-1}	From expt
N in NH_3	- 130.3 -144 (-70 from LP)	-124
NH_4^+	- 67.9	-60 , -65
P in PH_2^-		-585
PH_3	- 150.8 - 154 (-47 from LP)	-180
PH_4^+	- 52.9	very small
Sn in SnH_3^-		- 750
SnH_4		- 92
SnH_3^+		- 10

EMPIRICAL TREND:

greater bond order, larger isotope shifts

THEORY:

	$(\partial\sigma^{C}/\partial r_{CO})_e$ ppm Å^{-1}	
	empirical	theoretical*
CO	-456	-573.9
O=C=O	-214, -220	-156.4

* GIAO Chesnut

SUMMARY OF TRENDS:

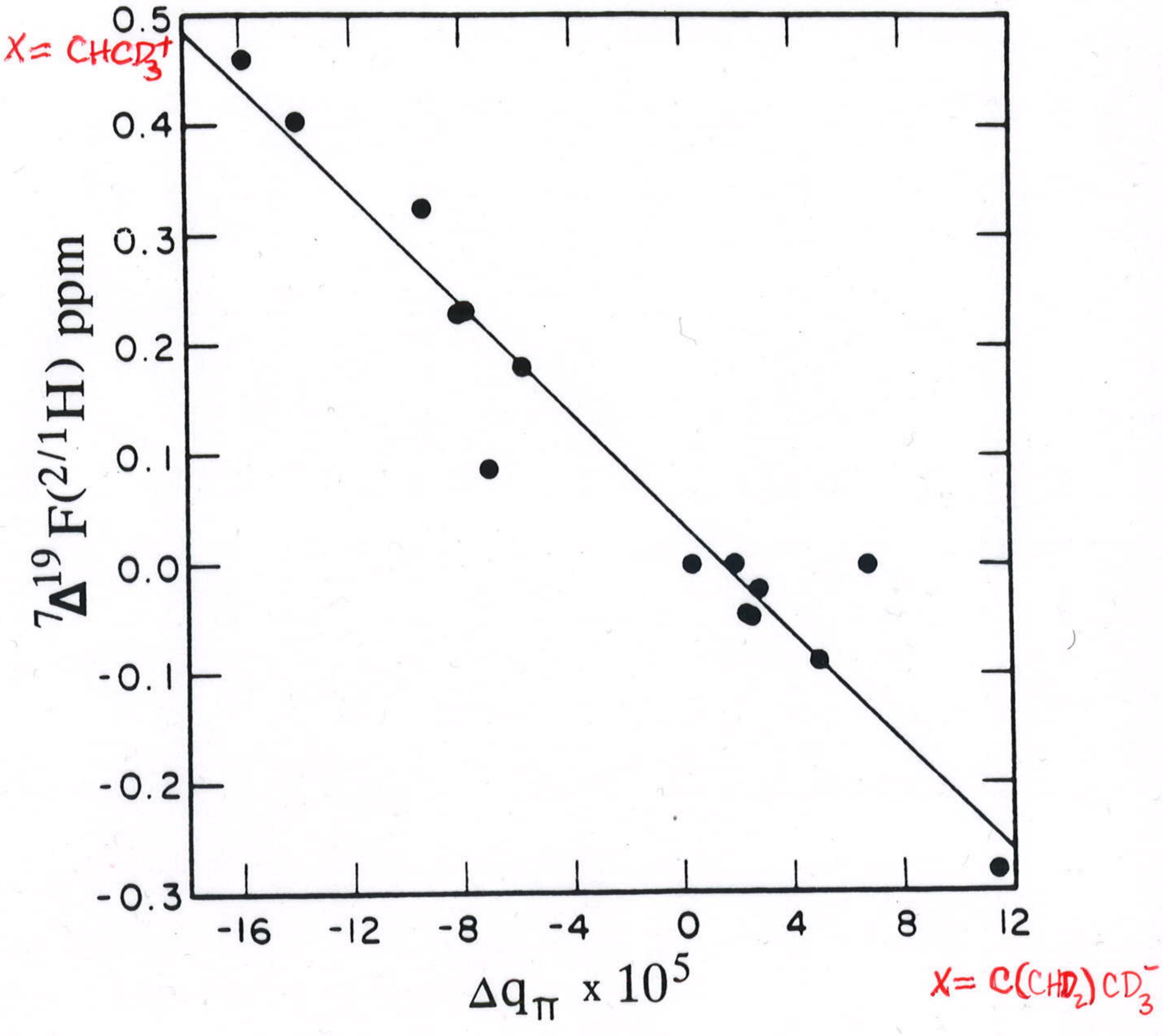
	positive ← $(\partial\sigma/\partial r)_e$ ← large negative		
net charge	positive ion	neutral	negative ion
lone pairs	0	1	2
bond order	1	2	3

- DEPENDENCE of the MAGNITUDE of ISOTOPE SHIFT on the NMR nucleus
- THE SIGN of the ISOTOPE SHIFT

X= $COCD_3$, etc.

^{19}F D-induced isotope shifts in 4-fluorophenyl systems correlate with calculated change in pi density induced by shortening the C-H(D) bond

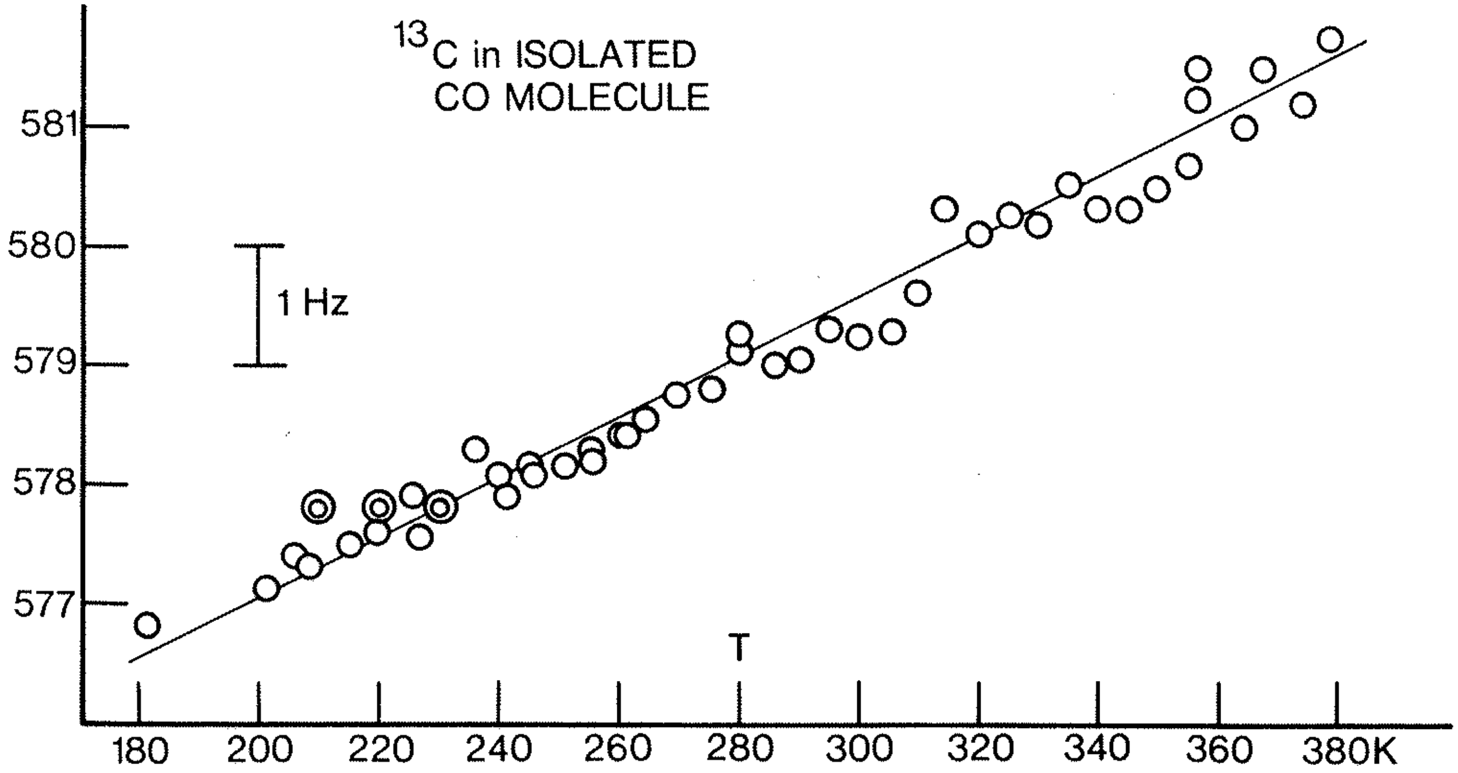
Forsyth and Yang



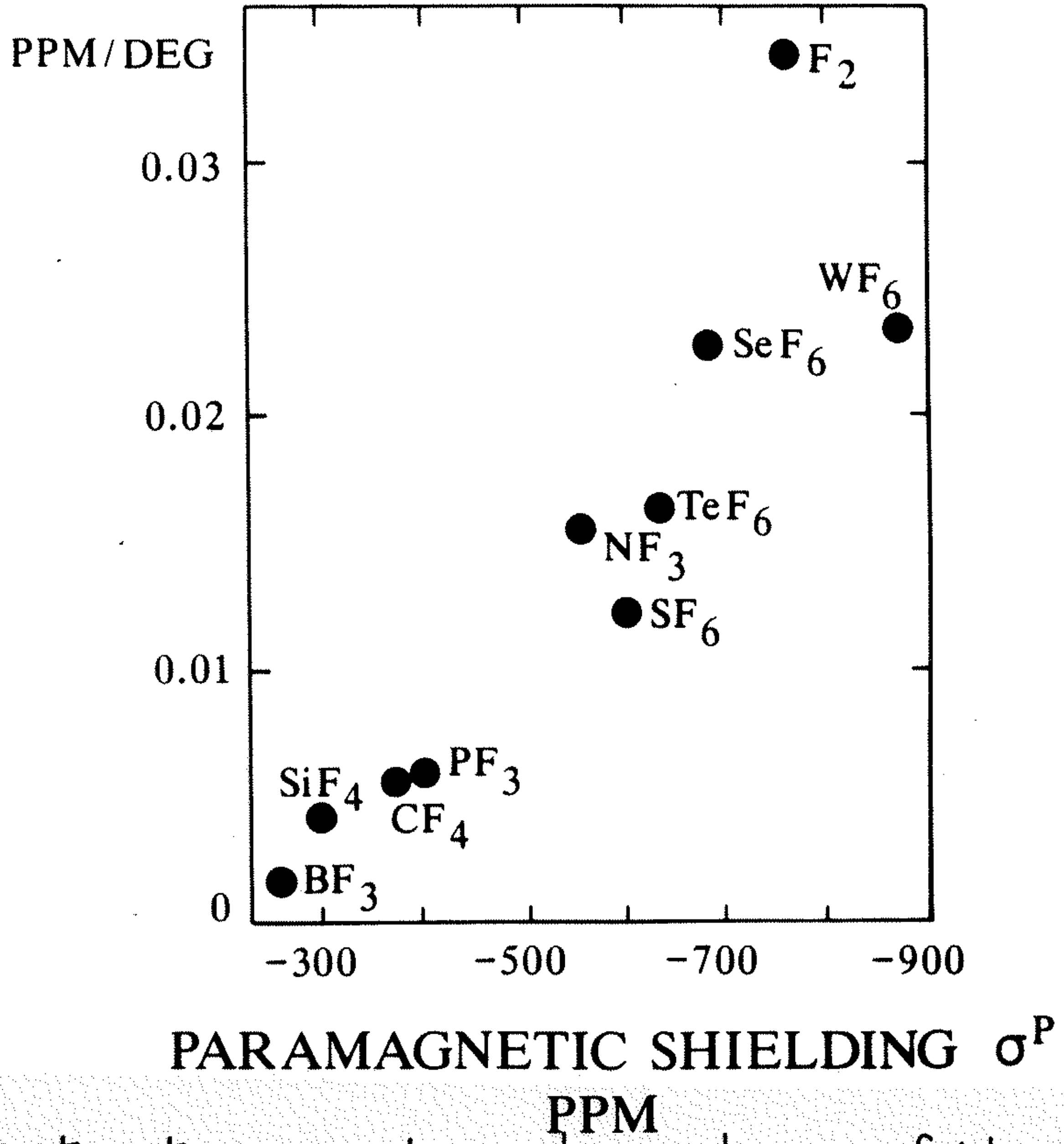
7. Temperature dependence of the chemical shift

a. How the temperature dependence is related to isotope shifts

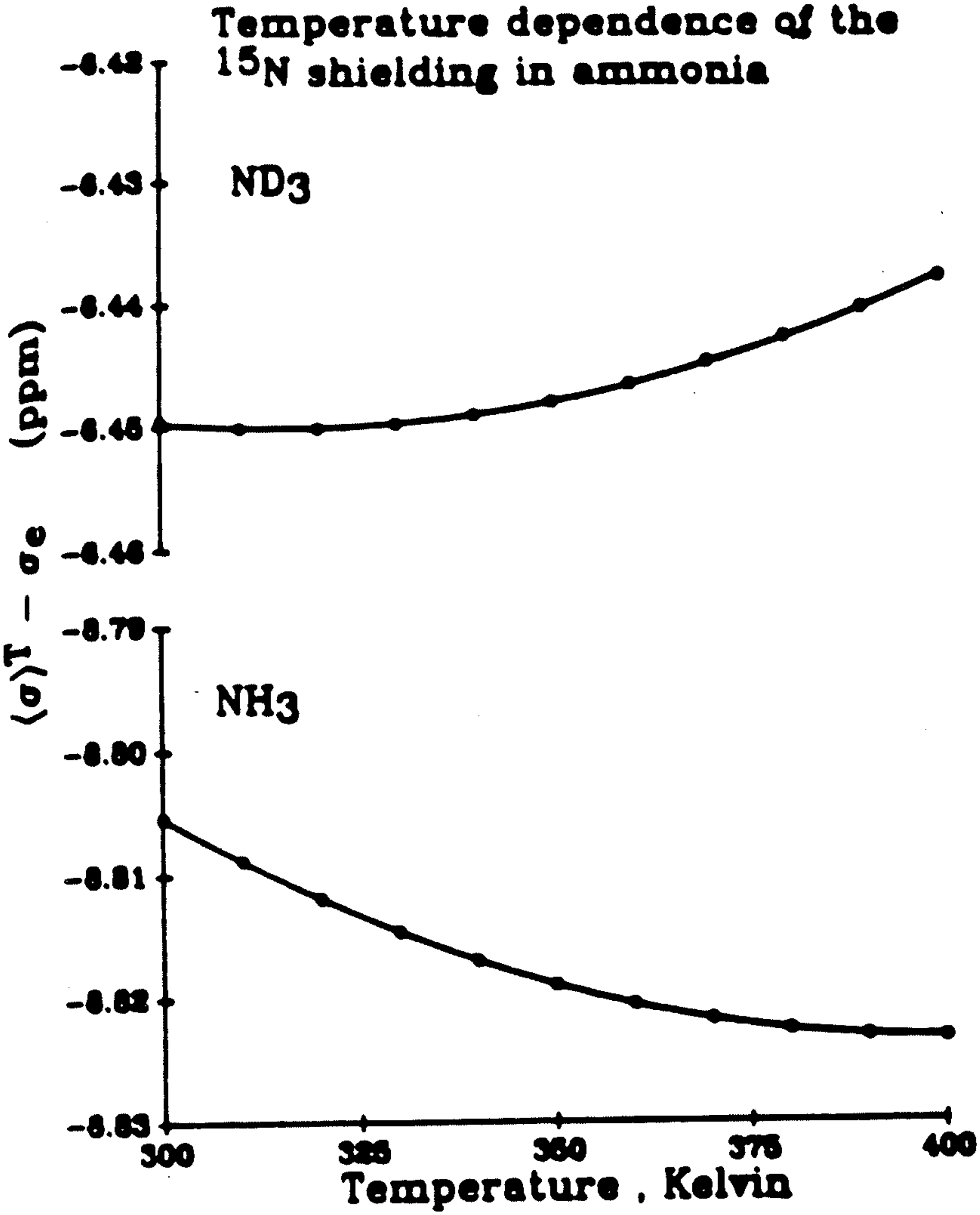
b. How to calculate isotope shifts and their temperature dependence



^{13}C in isolated CO molecule becomes less shielded (moves to higher frequency) with increasing temperature. This is consistent with the sign and magnitude of the ^{18}O-induced isotope shift (lighter isotope, higher frequency).



The greater temperature dependence of the ^{19}F chemical shift goes with the more negative paramagnetic shielding. That is, most of the change in shielding upon bond extension comes from the change in the paramagnetic part.


Temperature dependence of the ^{15}N shielding in ammonia
ND3
NH3
$\langle\sigma\rangle^T - \sigma_e$ (ppm)
-6.42
-6.43
-6.44
-6.45
-6.46
-8.79
-8.80
-8.81
-8.82
-8.83
300
325
350
375
400
Temperature , Kelvin

POTENTIAL ENERGY SURFACE:

$$V = \frac{1}{2!}\sum_i \omega_i q_i^2 + \frac{1}{3!}\sum_{ijk} \phi_{ijk}\, q_i q_j q_k + \cdots$$

PROPERTY SURFACE:

σ in particular, but could be any other molecular electronic property

$$P = P_e + \sum_i P_i q_i + \sum_{ij} \frac{1}{2!} P_{ij} q_i q_j + \sum_{ijk} \frac{1}{3!} P_{ijk} q_i q_j q_k + \cdots$$

To first order

$$\langle P \rangle_n = \langle X_n^{(0)} + \lambda X_n^{(1)} | P | X_n^{(0)} + \lambda X_n^{(1)} \rangle$$

$$= \langle X_n^{(0)} | P | X_n^{(0)} \rangle + 2\lambda \langle X_n^{(0)} | P | X_n^{(1)} \rangle$$

VIBRATIONAL AVERAGE:

$$\langle q_s q_{s'} \rangle = (v_s + \frac{d_s}{2})\delta_{ss'}$$

$$\langle q_{s'} \rangle = -\sum_s (\phi_{sss'}/2\omega_{s'})(v_s + \frac{d_s}{2})$$

non-vanishing only when s′ is totally symmetric

$$+\frac{1}{4\pi c\omega_s}\left(\frac{1}{hc\omega_s}\right)^{1/2} \sum_\alpha \frac{a_{s'}^{\alpha\alpha}}{\left(I_{\alpha\alpha}^{(e)}\right)^2} \langle J_\alpha^2 \rangle \quad \text{rot. contrib.}$$

ONLY THIS TERM HAS FIRST and SECOND DERIVATIVES of the PROPERTY

$$\langle P\rangle = P_0 + \boxed{\sum_s A_s (v_s + \frac{1}{2})} + \sum_{s\le s'} B_{ss'}(v_s + \frac{1}{2})(v_{s'} + \frac{1}{2})$$

where

"MECHANICAL" ANHARMONICITY has only CUBIC force constants

$$\boxed{A_s = \overbrace{P_{ss}}^{\text{ELECTRICAL ANHARMONICITY}}/2 - \sum_{s'} P_{s'}\phi_{sss'}/2\omega_{s'}}$$

$$P_0 = P_e + \sum_s \frac{1}{64}\underline{P_{ssss}} - \sum_s 7\underline{P_{sss}}\phi_{sss}/288\omega_s$$

HIGHER ORDER

$$+ \sum_{s\neq s'} 3\underline{P_{sss'}}\phi_{sss'}\omega_{s'}/32(4\omega_s^2 - \omega_{s'}^2)$$

$$B_{ss} = \underline{P_{ssss}}/16 - \sum_{s'} \underline{P_{sss'}}\phi_{sss'}(8\omega_s^2 - 3\omega_{s'}^2)/8\omega_{s'}(4\omega_s^2 - \omega_{s'}^2)$$

THE OBSERVED THERMAL AVERAGE :

$$\langle P\rangle^T = \frac{\sum_{v,J,K}(2J+1)g_{N_s}\boxed{\langle P\rangle_{vJK}}\exp(-E_{vJK}/kT)}{\sum_{v,J,K}(2J+1)g_{N_s}\exp(-E_{vJK}/kT)}$$

In terms of the [redacted] curvilinear internal coordinates

$$P = P_e + \sum_i \left(\frac{\partial P}{\partial R_i}\right) R_i + \frac{1}{2!}\sum_{ij}\left(\frac{\partial^2 P}{\partial R_i \partial R_j}\right)_e R_i R_j + \frac{1}{3!}\sum_{ijk}\left(\frac{\partial^3 P}{\partial R_i \partial R_j \partial R_k}\right) R_i R_j R_k + \ldots$$

For example, in CH$_4$-type molecules

smaller terms due to non-linear transformation

$$\langle \Delta r_1 \rangle = \boxed{\bar{L}_1^{1}\langle q_1 \rangle} + \frac{1}{2}\bar{L}_1^{2a2a}\langle q_2^2 \rangle + \frac{1}{2}\bar{L}_1^{3x3x}\langle q_3^2 \rangle + \frac{1}{2}\bar{L}_1^{4x4x}\langle q_4^2 \rangle + \ldots$$

$$\langle (\Delta r_1)^2 \rangle = \underline{(\bar{L}_1^{1})^2\langle q_1^2 \rangle + (\bar{L}_1^{3x})^2\langle q_3^2 \rangle + (\bar{L}_1^{4x})^2\langle q_4^2 \rangle} + \ldots$$

SUMMARY

- Where an isotopic label is introduced in a molecule, every neighboring NMR nucleus experiences a slight chemical shift.
- If labeling is less than 100%, the resonant nuclei in both the labeled and the unlabeled molecules are observed, with intensities according to statistical distribution.
- The magnitude of the shift depends on the fractional mass change at the isotope substitution site, on the remoteness of the resonant nucleus from the substitution site, and on the sensitivity of the chemical shift of the resonant nucleus; the latter is reflected by the chemical shift range of that nucleus.

- The isotope shift is just one more powerful tool in which a very selective tag carries with it the same wealth of information as the chemical shift itself.
- Isotope shifts provide a more stringent test of ab initio calculations of chemical shifts in specific molecules, being directly related to the slopes on the mathematical surface that describes the variation of the chemical shift with the molecular geometry.
- In a more general sense, the trends in the thousands of isotope shifts that have been accumulated provide insight into the general nature of these chemical shift surfaces, in terms of the dependence of the details of the surface on the nature of the chemical bond, the net charge of the molecule, bond orders, presence of lone pairs, etc.

- With a method of estimating the dynamic factors in isotope shifts, we educe from tables of data on isotope shifts the general trends in the electronic factors (how the NMR chemical shifts depend on bond length for example), which have been recently verified by ab initio calculations.

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Roskilde Universitet

UNESCO

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Educational, Scientific and
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