Origin of Chemical Shifts

BCMB/CHEM 8190
Empirical Properties of Chemical Shift

\[ \nu_i (\text{Hz}) = \gamma B_0 \left( 1 - \sigma_i \right) / 2\pi \]

- The Larmor frequencies of nuclei depend on the electronic structure of the molecule and the electronic environments of the nuclei, and reflect the chemical properties.
- The adjustments to the resonance frequencies to account for electronic structure and electronic shielding of nuclei from the magnetic field are embodied in the shielding constant, \( \sigma \).
- The values of \( \sigma \) are small (10\(^{-6}\)), and reduce the effective field strength by parts per million (ppm) (\( B_{\text{eff}} = B_0(1-\sigma) \)).

Measurements are made relative to a reference peak (TMS). Offsets given in terms of \( \delta \) in parts per million, ppm, + downfield.

\[ \delta_i = (\sigma_{\text{ref}} - \sigma_i) \times 10^6 \]

or

\[ \delta_i = (\left( \nu_i - \nu_{\text{ref}} \right) / \nu_{\text{ref}}) \times 10^6 \]

Ranges: \( ^1\text{H}, ^2\text{H}, 10 \text{ ppm}; ^{13}\text{C}, ^{15}\text{N}, ^{31}\text{P}, 300 \text{ ppm}; ^{19}\text{F}, 1000 \text{ ppm} \)
Importance of Chemical Shifts and Their Origins

- Shieldings are tensor quantities: magnitudes depend on orientation to magnetic field (chemical shift anisotropy)
- In the solid state, different orientations give different shifts
- In solution (rapid molecular tumbling) an average value results
- However, in solution some orientation can be reintroduced in order to exploit available structural information
- Chemical shifts reflect chemical environment, so there is potentially lots of structural information in chemical shifts themselves if we can understand the relationship with structure
Ramsey’s Equation for Chemical Shift


- Classical explanation offered by Ramsey's equation: charged particles moving through a magnetic field ($B_0$) experience a force perpendicular to both $B_0$ and the particle trajectory.

- So, electrons in the molecule (around the nucleus) precess

- The precessing charge generates its own magnetic field ($B'$), which happens to be in the opposite direction to $B_0$

$$\vec{B}' = -(e/c) \frac{(\vec{r} \times \vec{v})}{r^3} = -(e/cm) \frac{(\vec{r} \times \vec{p})}{r^3}$$

- The opposing $B'$ field reduces the effective $B_0$ field for the nucleus, so $B_{\text{eff}} < B_0$, and $B_{\text{eff}} = B_0(1-\sigma)$

- But, how does electronic structure dictate $B'$? $\sigma$? Need QM.
Some Quantum Mechanics Fundamentals

Expectation Values

- To find the value for some observable (i.e. $B'$, $\sigma$), quantum mechanically we calculate the *expectation value*
- Here, the expectation of some property ($\langle O \rangle$) is the result of some operator ($\hat{O}$) operating on an appropriate wavefunction ($\psi$) multiplied (on the left) by the complex conjugate of the wavefunction ($\psi^*$), integrated over all space

$$\langle O \rangle = \langle \psi | \hat{O} | \psi \rangle = \int \psi^* \hat{O} \psi \, d\tau$$

$\hat{O}$ - some operator  $\psi$ - some wavefunction

Wavefunctions

- For calculating $B'$ and $\sigma$, (chemical systems) we'll need *electronic wavefunctions*
  - i.e. atomic electronic orbitals like $\psi = 1s, 2s, 2p_1, 2p_0, 2p_{-1} ...$
  - can write p orbitals as $p_x, p_y, p_z$ (spatial representations) or $2p_1, 2p_0, 2p_{-1}$, (1, 0, -1 are magnetic quantum numbers $m$, p orbitals have total angular momentum of 1)
Some Quantum Mechanics Fundamentals

Wavefunctions

- For calculating spin systems we'll need spin wavefunctions
  \[ \psi = \alpha, \beta \text{ (single spins } 1/2), \alpha\alpha, \alpha\beta, \beta\alpha, \beta\beta \text{ (two spins } 1/2) \]
  - for \( \alpha \) and \( \beta \), \( m=+\frac{1}{2} \) and \( m=-\frac{1}{2} \)
  - for noninteracting spins, can just take products (\( \alpha\alpha, \alpha\beta \), etc.)

- All of these wavefunctions are solutions to Schrödinger's equation
  \[ \hat{H}\psi = E\psi \]
  - \( \hat{H} \) (Hamiltonian operator) operates on \( \psi \) to give back the energy (\( E \)) and \( \psi \)
  - a discrete set of energies and a discrete set of associated \( \psi \)s

- These wavefunctions must be normalized
  \[ \int \psi^* \psi \, dt = \langle \psi | \psi \rangle = 1 \]
  - \( \psi^*\psi \), probability of finding our particle at some point in space
  - so, sum of all probabilities (all space) should = 1
Some Quantum Mechanics Fundamentals

Operators

• The expectation value of the Hamiltonian operator is energy
  \[ \langle \psi | \hat{H} | \psi \rangle = E \]

• For electronic wavefunctions, the energy of interaction of the electrons with their environments are returned

• For spin wavefunctions, the energies of interaction of the nuclei with the magnetic field are returned

  \[ \hat{H}_z = -\hat{\mu} \cdot B_0, \quad E_{z\alpha} = \langle \alpha | -\hat{\mu} \cdot B_0 | \alpha \rangle, \quad E_{z\beta} = \langle \beta | -\hat{\mu} \cdot B_0 | \beta \rangle \]

• Often the Hamiltonian can be understood by substituting operators (that operate on the wavefunctions) into a classical expression

  \[ \hat{\mu}_z = \gamma \hat{I}_z, \quad \mu_z = \gamma I_z = m\gamma\hbar \]

- this gives us the quantum numbers \( m=+\frac{1}{2} \) and \( m=-\frac{1}{2} \), thus

  \[ E_{zm} = \langle \psi_m | -m\gamma\hbar B_0 | \psi_m \rangle = -m\gamma\hbar B_0 \langle \psi_m | \psi_m \rangle = -m\gamma\hbar B_0 \]
Quantum Expression for $B'$

- For calculation of $B'$ and $\sigma$, QM operators are needed
- Below are the classical expression for $B'$ in terms of linear momentum ($p$) and the QM operator for linear momentum

$$B' = -(e/cm)(\vec{r} \times \vec{p}) / r^3 = -e (\vec{r} \times \vec{p}) / [r^3 cm] \quad \hat{p}_0 = i\hbar(\partial/\partial x + \partial/\partial y + \partial/\partial z)$$

- One caveat: a charged particle in a magnetic field feels a force perpendicular to both $B_0$ and its trajectory, causing it to "curl"

- Solution: modify the linear momentum to recognize that the particle does not travel in a straight line, but curves (the "curl")

$$\vec{p} = \vec{p}_0 + e(\vec{B}_0 \times \vec{r}) / (2c) = \vec{p}_0 + (e/c)\vec{A} \text{ where } \vec{A} = (\vec{B}_0 \times \vec{r}) / 2$$

- Here $\vec{A}$ is called the vector potential

- So, now the "corrected" classical expression for $B'$ becomes

$$B' = -e (\vec{r} \times \vec{p}_0) / [r^3 cm] - e^2 (\vec{r} \times \vec{A}) / [r^3 c^2 m]$$
Quantum Expression for $B'$

- Quantum mechanically, calculate the expectation value from the following expression ($\psi_0$ are electronic wavefunctions)

\[
B' = \langle \psi_0 \rangle - e (\vec{r} \times \vec{p}_0) / [r^3 \text{cm}] - e^2 (\vec{r} \times \vec{A}) / [r^3 c^2 \text{m}] \psi_0
\]

paramagnetic \hfil \text{diamagnetic}

- Are two parts to $B'$ (and $\sigma$): paramagnetic and diamagnetic
- Paramagnetic does not refer to paramagnetism or unpaired electrons
- Diamagnetic part accounts for the induced circulation of electrons that shields the nucleus (so $B_{\text{eff}} < B_0$)
- Paramagnetic part comes from change in the electronic wavefunctions
- Paramagnetic component insignificant for hydrogen, but is important for heavier elements (is the cause of large chemical shift ranges)
Diamagnetic Shifts

- For H, only diamagnetic part important
- Only the diamagnetic, or "Lamb", term) explicitly includes $B_0$, so, to first order, need only use this term in $B'$ ($B'_D$)
- Rewrite the diamagnetic part in terms of $\bar{B}_0$ and $\bar{r}$
  \[-e^2 (\bar{r} \times \hat{A}) / [r^3 c^2 m] = -e^2 (\bar{r} \times \bar{B}_0 \times \bar{r}) / [2r^3 c^2 m] \text{ where } \hat{A} = (\bar{B}_0 \times \bar{r}) / 2\]
- So, $B'_D$ is proportional to the applied magnetic field, as expected
  \[B'_D = \langle \psi_0 | -e^2 (\bar{r} \times \bar{B}_0 \times \bar{r}) / [2r^3 c^2 m] | \psi_0 \rangle\]
- Cross product (see "Appendix" of Bloch equations lecture notes)
  \[\bar{r} = [x \ y \ z] \quad (\bar{B}_0 \times \bar{r}) = [(\bar{B}_0 \times \bar{r})_x \ (\bar{B}_0 \times \bar{r})_y \ (\bar{B}_0 \times \bar{r})_z] \quad \text{and unit vectors } \hat{i}, \hat{j}, \hat{k}\]
  \[\bar{r} \times (\bar{B}_0 \times \bar{r}) = [(i (y(\bar{B}_0 \times \bar{r})_z) - z(\bar{B}_0 \times \bar{r})_y) \ j(z(\bar{B}_0 \times \bar{r})_x) - x(\bar{B}_0 \times \bar{r})_z) \ k(x(\bar{B}_0 \times \bar{r})_y) - y(\bar{B}_0 \times \bar{r})_x)]\]
- $B_0$ is along $z$, so only $z$ component is significant. Thus
  \[\bar{r} \times (\bar{B}_0 \times \bar{r}) = [ \hat{k} (x(\bar{B}_0 \times \bar{r})_y) - y(\bar{B}_0 \times \bar{r})_x) ]\]
Diamagnetic Shifts

\[ \vec{r} \times (\vec{B}_0 \times \vec{r}) = \left[ k \left( x (\vec{B}_0 \times \vec{r})_y - y (\vec{B}_0 \times \vec{r})_x \right) \right] \]

- Now need the cross product \( \vec{B}_0 \times \vec{r} \)

\[ \vec{B}_0 = \begin{bmatrix} B_{0,x} & B_{0,y} & B_{0,z} \end{bmatrix} \quad \vec{r} = \begin{bmatrix} x & y & z \end{bmatrix} \] and unit vectors \( \hat{i}, \hat{j}, \hat{k} \)

\[ \vec{B}_0 \times \vec{r} = \begin{bmatrix} i (\vec{B}_{0,y} z - \vec{B}_{0,z} y) & j (\vec{B}_{0,z} x - \vec{B}_{0,x} z) & k (\vec{B}_{0,x} y - \vec{B}_{0,y} x) \end{bmatrix} \]

- So

\[ (\vec{B}_0 \times \vec{r})_y = j (\vec{B}_{0,z} x - \vec{B}_{0,x} z) \quad (\vec{B}_0 \times \vec{r})_x = i (\vec{B}_{0,y} z - \vec{B}_{0,z} y) \]

- Substitute

\[ \vec{r} \times (\vec{B}_0 \times \vec{r}) = \left[ k \left( x (j (\vec{B}_{0,z} x - \vec{B}_{0,x} z)) - y (i (\vec{B}_{0,y} z - \vec{B}_{0,z} y)) \right) \right] \]

\[ = \begin{bmatrix} x (\vec{B}_{0,z} x - \vec{B}_{0,x} z) - y (\vec{B}_{0,y} z - \vec{B}_{0,z} y) \end{bmatrix} = x (\vec{B}_{0,z} x) + y (\vec{B}_{0,y} y) = B_0 (x^2 + y^2) \]

- Finally

\[ B_D' = \langle \psi_0 \mid -e^2 \ (\vec{r} \times \vec{B}_0 \times \vec{r}) / [2r^3 c^2 m] \mid \psi_0 \rangle = \langle \psi_0 \mid -e^2 B_0 (x^2 + y^2) / [2r^3 c^2 m] \mid \psi_0 \rangle \]

\[ = -\left( e^2 / [2c^2 m] \right) B_0 \langle \psi_0 \mid (x^2 + y^2) / r^3 \mid \psi_0 \rangle \]
Diamagnetic Shifts

\[ B'_D = -(e^2 / [2c^2 m])B_0 \langle \psi_0 | (x^2 + y^2) / r^3 | \psi_0 \rangle \]

- So, what does this predict?
- We now have a simple operator, \((x^2 + y^2)/r^3\) that weights the probability density \(\langle \psi_0 | \psi_0 \rangle\)
- \((x^2 + y^2)/r^3 \sim 1/r\) increases as \(r\) (distance of electron from nucleus) decreases (as electron gets closer to nucleus)
- So, this predicts that \(B'_D\) (shielding of the nucleus by the magnetic fields generated by the precessing electrons) increases as electrons get closer to the nucleus (only s orbitals have electron density at nucleus)
- \(p, d, \text{ etc.},\) have zero electron density at the nucleus

Predictions: depends on electron density near to nucleus
opposes magnetic field (shields)

Examples: He 2 1s electrons \(\sigma = 59.93 \times 10^{-6}\)
Ne 10 s electrons \(\sigma = 547 \times 10^{-6}\)
H ~2 1s electrons \(\sigma = \sim 60 \times 10^{-6}\)
HO- O withdraws \sim 10\% \sim 6 \text{ ppm downfield}
Paramagnetic Contribution to Shifts

- This comes from the first term in the quantum expression for $B'$
  \[ B' = \langle \psi_0 \left| -e \left( \vec{r} \times \hat{p}_0 \right) / [r^3 \text{cm}] \right| \psi_0 \rangle \]

- A variation of $B'$ with $B_0$ is expected, but no explicit $B_0$ dependence in the operator as written

- The $B_0$ dependence is introduced when the nuclei are introduced into the magnetic field, because the electronic wavefunctions are perturbed/changed by the magnetic field

- So, a second order perturbation/correction is needed (perturbation theory)
  \[ \psi = \psi_0 + \psi' = \psi_0 + \sum_n \left( \langle \psi_n | \hat{H}' | \psi_0 \rangle / (E_n - E_0) \right) \psi_n \]

- Here, we add a correction factor, introducing changes to the Hamiltonian to account for the interactions of the electrons with the magnetic field, that we neglected to first order

- The correction factor mixes in wavefunctions for excited states

- Depends on the integral of the complex conjugate of the excited state wavefunction multiplied by the result of the corrected Hamiltonian operating on the ground state wavefunction

- Denominator is the energy gap (small differences make big contributions)
Paramagnetic Contribution to Shifts

- $\hat{H}_0$ is the Hamiltonian in the absence of a magnetic field
  \[
  \hat{H}_0 = \frac{1}{2m}\hat{p}_0^2 + V
  \]
  - includes operators representing kinetic energy ($K=p^2/2m$) and the strong electronic (Coulombic) interaction of the electron and nuclear charges ($V$)

- $\hat{H}$ is the Hamiltonian in the presence of a magnetic field
  \[
  \hat{H} = \frac{1}{2m}(\hat{p}_0 + (e/c)\vec{A})^2 + V
  \]
  - recall
    \[
    \vec{p} = \vec{p}_0 + e(\vec{B}_0 \times \vec{r}) / (2c) = \vec{p}_0 + (e/c)\vec{A} \quad \text{where} \quad \vec{A} = (\vec{B}_0 \times \vec{r}) / 2
    \]
  - so the $\hat{p}_0^2$ operator is rewritten as before, including the vector potential $A$, which includes the $B_0$ dependence

- $\hat{H}'$ is the Hamiltonian that we will use, as it includes a linear dependence on $B_0$
  \[
  \hat{H}' = \frac{e}{2mc}\vec{A} \cdot \hat{p}_0
  \]
  - note that
    \[
    (\hat{p}_0 + (e/c)\vec{A})^2 = \hat{p}_0^2 + 2\hat{p}_0(e/c)\vec{A} + ((e/c)\vec{A})^2
    \]
  - so we're making a first order approximation, keeping only the linear $B_0$ dependence (which is what we expect for chemical shift, a linear $B_0$ dependence)
Paramagnetic term continued

- Expand $\vec{A} \cdot \vec{p}_0$ into a more useful form

$$\vec{A} \cdot \vec{p}_0 = \left( (\vec{B}_0 \times \vec{r}) / 2 \right) \cdot \vec{p}_0 \equiv B_0 \cdot (\vec{r} \times \vec{p}_0) / 2 = B_0 \hat{L} \hbar / 2 = B_0 \hat{L}_z \hbar / 2$$

- The cross product $\vec{r} \times \vec{p}$ (distance $\times$ linear momentum) is \textit{angular momentum}

- The $z$ projection operator, $\hat{L}_z$, operating on atomic electronic wavefunctions, returns projections on the $z$ axis

- Here $L$ is the orbital angular momentum quantum number.
  - for s orbitals, $L$ is 0
  - for p orbitals, $L$ is 1, and $m = 1, 0$ and -1 ($2p_1$, $2p_0$, $2p_{-1}$, i.e. $2p_x$, $2p_y$, $2p_z$)

- If only s orbitals (hydrogen), paramagnetic term is insignificant

- Now we can rewrite the Hamiltonian

$$\hat{H}' = (e/(2 mc)) \vec{A} \cdot \vec{p}_0 = (e/(2 mc)) B_0 \hat{L}_z \hbar / 2 = B_0 e \hbar /(4mc) \hat{L}_z$$

- The corrected wavefunction now is

$$\psi = \psi_0 + \psi' = \psi_0 + \sum_n \left( \left\langle \psi_n | \hat{H}' | \psi_0 \right\rangle / (E_n - E_0) \right) \psi_n$$

$$= \psi_0 + B_0 e \hbar / (4mc) \sum_n \left( \left\langle \psi_n | \hat{L}_z | \psi_0 \right\rangle / (\Delta E) \right) \psi_n$$
Paramagnetic term continued

- Here again is the expression for the paramagnetic term
  \[ B_p' = \langle \psi_0 | -e (\hat{r} \times \hat{p}_0) / [r^3 \text{cm}] | \psi_0 \rangle \]

- The corrected expression now is
  \[ B_p' = \langle \psi_0 + \psi' | -e (\hat{r} \times \hat{p}_0) / [r^3 \text{cm}] | \psi_0 + \psi' \rangle = \langle \psi_0 + \psi' | - (e/(\text{cm})) \hat{L}_z / r^3 | \psi_0 + \psi' \rangle \]

- Now substitute in \( \psi' \)
  \[ B_p' = \langle \psi_0 + \psi' | -(e/(\text{cm})) \hat{L}_z / r^3 | \psi_0 + \psi' \rangle \]

- Simplify \( \psi' \) and \( B' \) by getting rid of constants
  \[ B_p' \propto \langle \psi_0 + \psi' | \hat{L}_z / r^3 | \psi_0 + \psi' \rangle \quad \psi' \propto \sum_n \left( \langle \psi_n | \hat{L}_z | \psi_0 \rangle / (\Delta E) \right) \]

- Write \( B' \), keeping only terms linear in \( B_0 \)
  \[ B_p' \propto \sum_n \left[ \left( \langle \psi_0 | \hat{L}_z | \psi_n \rangle \langle \psi_n | \hat{L}_z / r^3 | \psi_0 \rangle \right) / (\Delta E) + \left( \langle \psi_0 | \hat{L}_z / r^3 | \psi_n \rangle \langle \psi_n | \hat{L}_z | \psi_0 \rangle \right) / (\Delta E) \right] \]

- when the \( \Delta E \) between the ground state orbitals and the excited state orbitals (that were mixed in) is small (i.e. low lying excited states), \( B' \) is big (responsible for large chemical shift ranges)

- for p orbitals, if all are equally occupied (spherical distribution), no effect (must be an asymmetric distribution)
Implications for Paramagnetic Term

\[ B_p' \propto \sum_n \left[ \left( \langle \psi_0 | \hat{L}_z | \psi_n \rangle \langle \psi_n | \hat{L}_z / r^3 | \psi_0 \rangle \right) / (\Delta E) + \left( \langle \psi_0 | \hat{L}_z / r^3 | \psi_n \rangle \langle \psi_n | \hat{L}_z | \psi_0 \rangle \right) / (\Delta E) \right] \]

- \( B_p' \propto -\sigma_p \), so \( \sigma_p \) is negative (deshielding, opposite to \( \sigma_D \))

- \( \sigma_p \) is zero unless \( \hat{L}_z | \psi \rangle \) is finite
  - for instance, for "s" orbitals, \( \hat{L}_z | s \rangle = 0 \), so no contribution from paramagnetic term
  - so, chemical shift range for H is small

- \( \hat{L}_z | \psi \rangle \) is finite for p orbitals, so \( \sigma_p \) is finite (when p orbitals are not equally occupied)
  - for \(^{13}\)C, for instance, \( \sigma_p \) is finite (i.e. \( \hat{L}_z | p_i \rangle = 1 \), etc.)
  - for \(^{13}\)C, \( \Delta E \) can be small, so large chemical shift range

- Contributions of all p orbitals are summed, so if all are equally occupied, sum is zero (i.e. \( \sum \hat{L}_z | p \rangle = 0 \)), so, no effect
  - in other words, electron distribution must be asymmetric
  - example: CH\(_4\), all p orbitals occupied (highly shielded, i.e. no deshielding from paramagnetic term)
**$^{13}$C Example: Ethane vs Ethylene**

- For CH$_3$-CH$_3$, $\delta^{13}$C = 6 ppm, for CH$_2$=CH$_2$, $\delta^{13}$C = 123 ppm!
  - for CH$_3$-CH$_3$, nearly symmetrical use of $p$ orbitals, so small $\sigma_p$
  - not so for CH$_2$=CH$_2$, where $p$ orbitals are used for $\pi$ orbitals (very asymmetrical)

- For both, $\sigma_D$ is about the same ($\sim 200 \times 10^{-6}$)
- Consider our paramagnetic shielding contribution equation

$$\sigma_p \propto \sum_n \left[ \frac{\langle \psi_0 | \hat{L}_z | \psi_n \rangle \langle \psi_n | \hat{L}_z | \rho^3 | \psi_0 \rangle}{\Delta E} + \frac{\langle \psi_0 | \hat{L}_z | \rho^3 | \psi_n \rangle \langle \psi_n | \hat{L}_z | \psi_0 \rangle}{\Delta E} \right]$$

-only consider $\psi_n$ functions 2p$_1$, 2p$_0$, 2p$_{-1}$ (s orbitals don't contribute significantly to $\sigma_p$)
-keep in mind $\Delta E$ in denominator: $\Delta E$ likely to be small, so will be important

- In ethylene, is a $\pi$ bond between the C nuclei
  - the $\pi$ bond is comprised of 2 $p$ orbitals, one on each C nucleus (very different than the $sp^2$ bonds to the H nuclei)
  - the $\pi$ bond tends to have low lying excited states (small $\Delta E$)
  - the occupied $\pi$ bond comes from the sum of the two $p$ orbitals on the C atoms, but the first excited state ($\pi^*$) results from the difference

- Consider only the first excited state: $\pi^*=(1/\sqrt{2})(p_{1A}-p_{1B})$
  - fairly low lying, so $\Delta E$ likely to be small, and its contribution to $\sigma_p$ large
Consider Field Parallel to C-C Bond

- Antisymmetric p orbitals of $\pi^*$ bond: perpendicular to plane of other atoms (black - positive, white - negative)
- Here $B_0$ is parallel to C-C bond ("A" and "B" are carbons A and B)

We have an expression for $\pi^*$ that can be rewritten/expanded in terms of $p_1$ and $p_{-1}$ (projections of angular momentum orbitals)

$$\pi^* = \frac{1}{\sqrt{2}} \left( p_{xA} - p_{xB} \right) = \frac{1}{\sqrt{2}} \left( (p_{1A} + p_{-1A}) - (p_{1B} + p_{-1B}) \right)$$

Note the following relationships

$$p_{xA} = (p_{1A} + p_{-1A}), \quad p_{yA} = (p_{1A} - p_{-1A}), \quad p_{xB} = (p_{1B} + p_{-1B}), \quad p_{yB} = (p_{1B} - p_{-1B})$$

Now, operate on $\pi^*$ with $L_z$ operator: it returns projection of angular momentum on $z$ axis (1 for $p_{1A}$, -1 for $p_{-1A}$, etc.)

$$\hat{L}_z \left| \pi^* \right> = \left( i\hbar/\sqrt{2} \right) \left( ((1)p_{1A} + (-1)p_{-1A}) - ((1)p_{1B} + (-1)p_{-1B}) \right)$$

$$= \left( i\hbar/\sqrt{2} \right) \left( (p_{1A} - p_{-1A}) - (p_{1B} - p_{-1B}) \right)$$

$$= \left( i\hbar/\sqrt{2} \right) (p_{yA} - p_{yB}) \text{ antisymmetric combination of } p_y \text{ orbitals}$$

So, when we evaluate $\left< \psi_0 \left| \hat{L}_z \right| \pi^* \right>$, it will be finite if $p_{yA}$ and $p_{yB}$ are populated in ground state $\psi_0$ (so, look at ground state MOs)
Estimating Paramagnetic Contribution

- Ground state molecular orbitals for ethylene (in plane of atoms, p are $p_y$)
- Energies according to number of nodes
- Fill with electrons (2x6 for C, 4 for H = 16)
- 4 in 1s$_C$, 2 in bonding $p_0$ (⊥ to plane), 2 in C-C $\sigma$, 4 in C-H $\sigma$
- Implies can put 4 in MOs

- 2 go in $\psi_1$, but is symmetric ($\langle \psi_0 | \hat{L}_z | \pi^* \rangle$ is zero)
- 2 go in $\psi_2$, antisymmetric, so $\langle \psi_0 | \hat{L}_z | \pi^* \rangle$ is finite, so can attempt to calculate $\sigma_p$..........
- $\sigma_p = -(eh/(2\pi mc))^2 <(1/r^3)>_{2p}$ etc. $\equiv -200 \times 10^{-6}$
- Recall $\sigma_{c-c} = \sigma_D = 200 \times 10^{-6}$ also, so effects cancel approximately (i.e. expect big downfield shift)
**σ Depends on Orientation in Magnetic Field**

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- Shieldings are tensor quantities: magnitudes depend on orientation to magnetic field *(chemical shift anisotropy)*

- What happens (ethylene) if $B_0$ is $\perp$ to plane?

- Now antibonding ($\pi^*$) is made of $p_z$ ($p_0$) orbitals

\[
\pi^* = \frac{1}{\sqrt{2}} (p_{zA} - p_{zB}) = \frac{1}{\sqrt{2}} (p_{0A} - p_{0B})
\]

- Angular momentum projection on $z$ is zero ($\hat{L}_z |p_0\rangle = 0$), $\sigma_p = 0$

- So, shielding in $z$ direction is purely diamagnetic

\[
\sigma_z = \sigma_D + \sigma_p = \sigma_D + 0 = 200 \times 10^{-6}
\]

- Summary: for $B_0$ along C-C bond ($\sigma_x$), $\sigma_p = \sigma_D$, so $\sigma_x = 0$, same for $B_0$ in plane perpendicular to C-C ($\sigma_y = 0$), and $\sigma_z = 200$

- Write as a tensor: isotropic shift = $1/3 \operatorname{Tr} \sigma \approx 70$-100 ppm

\[
\begin{bmatrix}
0 \\
0 \\
200
\end{bmatrix}
- \begin{bmatrix}
-20 \\
120 \\
200
\end{bmatrix}
\]

1H of ethylene are significantly deshielded relative to ethane (5.84 vs 1.96 ppm). The deshielding is due to the paramagnetic B' effect of the $\pi^*$ (remote group effect)

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Waugh, Griffin, Wolff, JCP, 67 2387 (1977) – solids NMR
Alpha and beta carbon chemical shifts are sensitive to structure, and reflect the magnitudes of $\phi$ and $\psi$ angles in proteins.

Below: surface profiles of shielding constants for $^{13}\text{C}\alpha$ and $^{13}\text{C}\beta$ versus $\phi$ and $\psi$.

For $^{13}\text{C}\alpha$, beta sheet more shielded than alpha helix.

For $^{13}\text{C}\beta$, beta sheet less shielded than alpha helix.

α helix, -57, -47; β sheet, -139, 135; Oldfield and Dios, JACS, 116, 5307 (1994)
$^{13}$C shifts and Peptide Geometry

- Conclusions of calculations empirically verified
- Results led to important methods (Talos) to predict $\phi$ and $\psi$ from $\delta^{13}$C

For $^{13}$C$\alpha$, beta sheet more shielded than alpha helix

For $^{13}$C$\beta$, beta sheet less shielded than alpha helix

- Shifts relative to random coil with same amino acid
- Spera and Bax, JACS, 113, 5490 (1991)
- See also: Case, http://www.scripps.edu/mb/case (Shifts)
- See also: Wishart, http://redpoll.pharmacy.ualberta.ca/shiftz
Remote Group Effects

- Paramagnetic shielding effects arise from asymmetric electron distribution
- Nuclei near groups with large paramagnetic contributions to shielding can also be differentially shielded or deshielded, depending on their location

\[ \sigma'_{\text{remote}} = \Delta \chi/r^3 (1-3\cos^2 \theta) \]  

Here \( \Delta \chi \) is a measure of the magnitude of \( B' \) in \( B_0 \)

- Johnson and Bovey, *J. Chem. Phys.*, 29, 1012 (1958)
Fig. 1. "Isoshielding" lines in the neighborhood of a benzene ring. The plot represents one quadrant of a plane passing normally through the center of the ring. The lines represent the shift in the NMR shielding value which will be experienced by protons as a result of the magnetic field of the benzene ring.
Recent Applications of Chemical Shift to Protein Structure Determination

- Shen Y, Bax A, Protein backbone chemical shifts predicted from searching a database for torsion angle and sequence homology JOURNAL OF BIOMOLECULAR NMR 38: 289-302, 2007
Other data can be combined with Chemical Shifts – Protein Targets now up to 25 kDa

• For small proteins, chemical shift data combined with other types of data (Residual Dipolar Couplings, RDC) can be used to "predict" structures to within good agreement with NMR structures determined traditionally (NOE based)

Comparison of traditional NMR structure and predicted structure with chemical shift and RDC data.