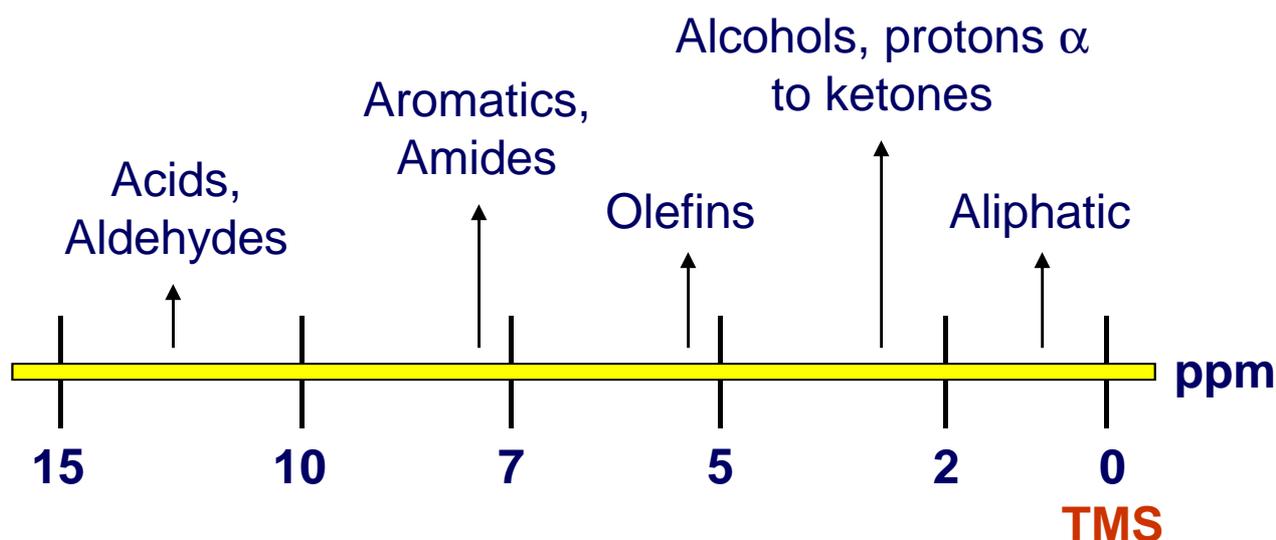# Interpretation of ^{1}H spectra

- So far we have talked about different NMR techniques and pulse sequences, but we haven't focused seriously on how to analyze the data that we obtain from these experiments.

- Now we will do this, starting from the very bottom. The first thing that we will discuss are ^{1}H spectra. As we saw before, the chemical shift range for ^{1}H is pretty small, from 15 to 0 ppm in most cases, although we can get peaks above 20 and below -5 ppm in some cases:

Alcohols, protons α
to ketones

Aromatics,
Amides

Acids,
Aldehydes

Olefins

Aliphatic

ppm

15   10   7   5   2   0

TMS

- As we said before, the chemical shifts of different nuclei in a molecule arise due to differences in the local magnetic field or **shielding** (σ) felt by the nuclei in different spots of the molecule:

$$\mathbf{B_{eff} = B_o - B_{loc}} \quad \text{---} \quad \mathbf{B_{eff} = B_o(1 - \sigma)}$$

Origins of σ (B_{loc})

- The shielding of different nuclei depends on the electron density in its surroundings. We can dissect the contributions to the total shielding:

$$\sigma = \sigma^{dia} + \sigma^{para} + \sigma^{loc}$$

- The term σ^{dia} is the diamagnetic contribution, which arises from the magnetic field opposing **B**$_o$ from the electrons immediately surrounding the nucleus (*s* orbitals).

- σ^{para} is the paramagnetic term, and is generated by electrons in *p* orbitals (as well as bonds…). It is in favor of **B**$_o$.

- The third term, σ^{loc}, is due to neighboring groups, and it can add or subtract from **B**$_o$, depending on the nature of the group and its spatial orientation. σ^{loc} is the term that actually makes nuclei with similar characteristics in a molecule have different shieldings (and therefore chemical shifts).

- If we now consider our main players, ^{1}H and ^{13}C, we can see that since ^{1}H have only a *1s* orbital, σ^{dia} will dominate, while for ^{13}C (and other heavier atoms) σ^{para} will dominate because we have more *p* electron shells that can become occupied (lower energy than *p* orbitals in ^{1}H…)

Origins of σ (continued)

- As we said, what determines the shielding is the electron density, which for an isolated ^1H (which is perfectly spherical), is calculated with the **Lamb formula**:

$$\sigma = \frac{\mu_o\, e^2}{3\, m_e} \int_0^\infty r\, \rho(r)\, dr$$

- We could use the same formula to calculate any chemical shift and forget about the dissection into different terms, but the problem is that in a molecule the equation for $\rho(r)$ is very complicated: We have to consider **s**, **p**, **d**, hybrid orbitals (i.e., **sp^n**), and we also have to consider molecular orbitals.

- This is the realm of quantum mechanical chemical shift calculations, far more than what we want to know.

- However, most of the effects can be qualitatively described by using σ^{dia} and σ^{loc} for protons (remember that σ^{para} has little contributions in ^1H).

- We will start with effects (or contributions) to σ^{dia}. These are known as **inductive and mesomeric effects**, and as we will see, their origin lies in the how the electron density around the ^1H is affected by different species attached to it.

Inductive contributions to σ^{dia}

- As we said, an isolated ^1H atom has a perfectly symmetrical distribution of its **1s** electrons around it. If we use the Lamb formula, we get a value of 17.8 ppm for σ^{dia}:

H (*1s*)
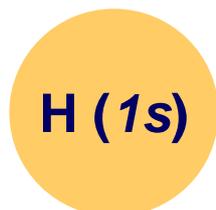
- Now, when we add, say, a -CH_3 to it (and get methane), the electron cloud on the ^1H (on any of the 4) will become deformed, because the **electronegativity** (**E**) of the carbon will pull the **1s** electron of the ^1H towards it:

H (*1s*) **C (*sp³*)**
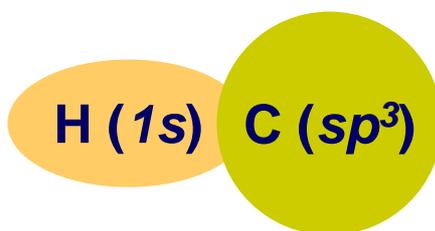
- Since we lower the electron density around the nucleus, it will become **deshielded**, and therefore it will move towards lower fields (higher chemical shift).

- For example, if we consider hydrogen halides, we'll see that the more electronegative the halide is, the drop in shielding constants is inversely proportional to the **E** of the halide:

$$\sigma \text{ (HF)} < \sigma \text{ (HCl)} < \sigma \text{ (HBr)} < \sigma \text{ (HI)}$$

Inductive effects (continued)

- The inductive effect on the shielding of the ^{1}H is not limited to groups bonded directly to it. We have to remember that the electron density around the ^{1}H depends on the molecular orbitals of the whole molecule (i.e., the bonds).

- The effects of electronegativity are 'transmitted' through molecular orbitals (bonds): If we have a very electronegative atom bound to a carbon, protons bonded to that carbon will have their *1s* electrons pulled away more than if we did not have the electronegative group. So, for the methane series we have:

	$H-CH_3$	$H-CH_2I$	$H-CH_2Br$	$H-CH_2Cl$	$H-CH_2F$
E	2.1	2.5	2.8	3.0	4.0
δ	0.23	1.98	2.45	2.84	4.13

- A similar correlation to the one we did with electronegativity can be done in the methane series with the polarity (or polarization) of the C-X bond.

- The group creating the inductive effect does not need to be exclusively an halogen (or a single atom). We can consider the effects of chemical groups as a whole, such as $-NO_2$, $-OH$, $-SH$, $-NH_2$, etc.

Inductive effects (…)

- Furthermore, we don't need a particularly electronegative atom. If we lengthen the carbon chain, the shielding will also increase.

- To demonstrate this, lets look at the chemical shift of different protons in saturated linear hydrocarbons:
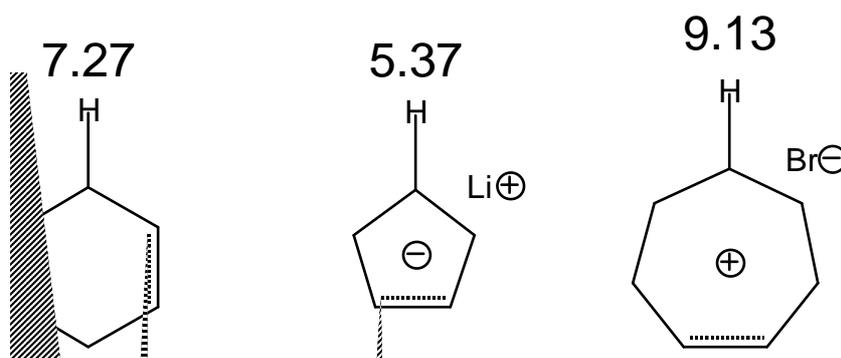
0.23	0.80	0.91
H-CH$_3$	**H-CH$_2$-CH$_3$**	**H-CH$_2$-CH$_2$-CH$_3$**

- Another factor affecting the electron density around the proton and therefore its shielding are partial charges on the carbon atom. This is clearly seen if we compare certain aromatic ions to benzene:

- Note that we have the same number of π electrons in these systems (the **4n + 2** rule is satisfied…). The charge on the carbon of tropolium ion is positive, so it 'sucks' more the [1]H's 1s electrons, and gives us less shielding. The reverse happens for the cyclopentadienyl ion…

Mesomeric effects - EWGs and EDGs

- Now lets look at what happens when we have an olefinic or aromatic proton and we have a substituent that can have different *mesomeric effects* (**+M** or **-M**).

- For example, lets consider ethene and **EWGs** or **EDGs** as substituents. If we consider methylvinylketone, the chemical shifts of the olefinic protons will move downfield considerably, because since the ketone (an **EWG**) is taking electrons away from the double bond, the electron density around the ^{1}H will diminish:
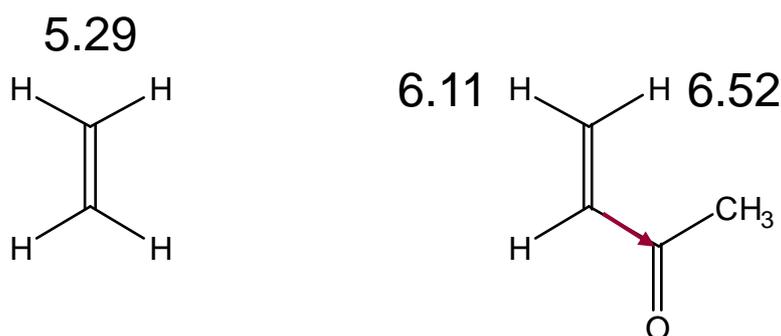
- If on the other hand we consider methylvinylether, the situation is reversed: The methoxy groups (an **EDG**), will donate electrons to the double bond, which will increase the electron density around the ^{1}H and therefore increase the shielding:
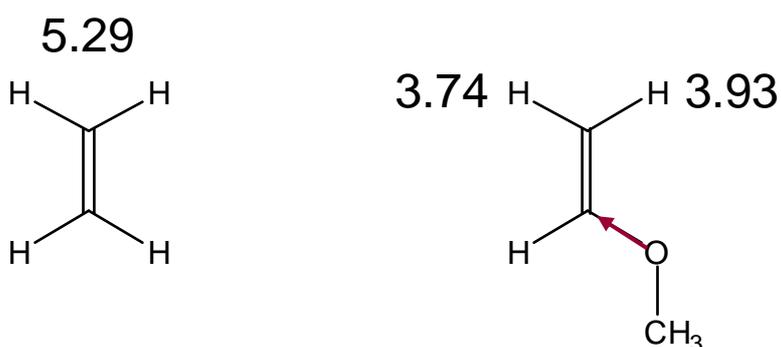
Mesomeric effects (continued)

- A similar reasoning can be used when we analyze the chemical shifts of ^{1}Hs on substituted aromatic systems.

- For example, in aniline we have an **EDG**, which has a **+M** effect. Since we'll have more electron density in the ring, all protons will be more shielded than the respective protons in benzene (7.24 ppm).

- Furthermore, if we draw resonant structures we can see that the **ortho** and **para** positions will have a larger electron density. Therefore, protons attached to the **ortho** or **para** carbons will be more shielded (lower chamical shift):
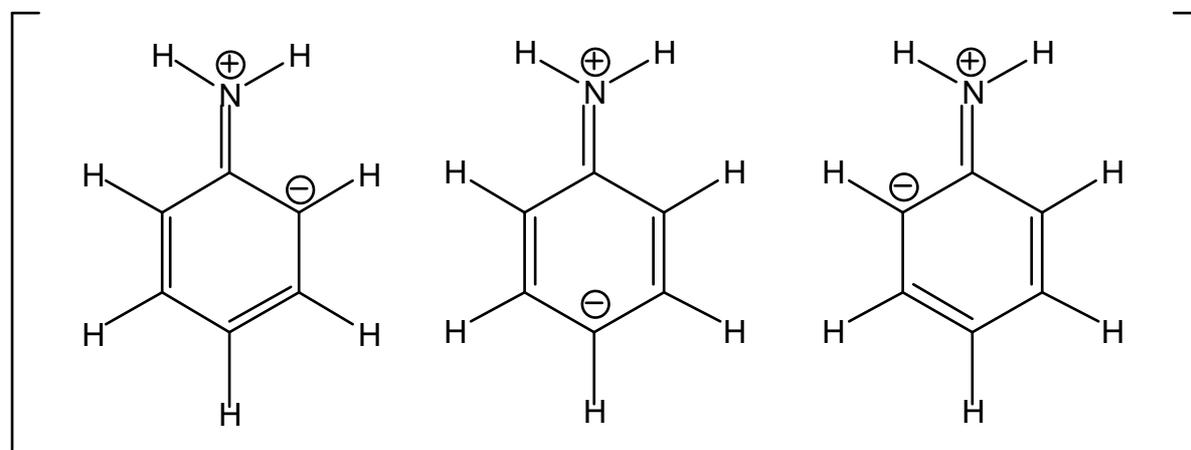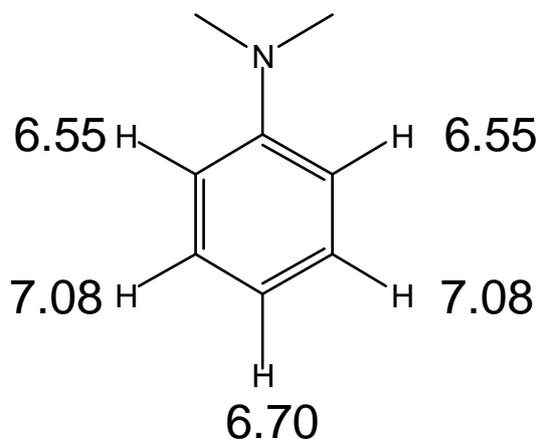
Mesomeric effects (…)

- On the other hand, nitrobenzene, which has an **EWG**, has a **-M** effect. All centers will have a lower electron density, but the ortho and para positions will have a particularly lowered electron density.

- All protons in nitrobenzene will be more deshielded than benzene. In particular, the effect at the **ortho** and **para** positions will be the largest.
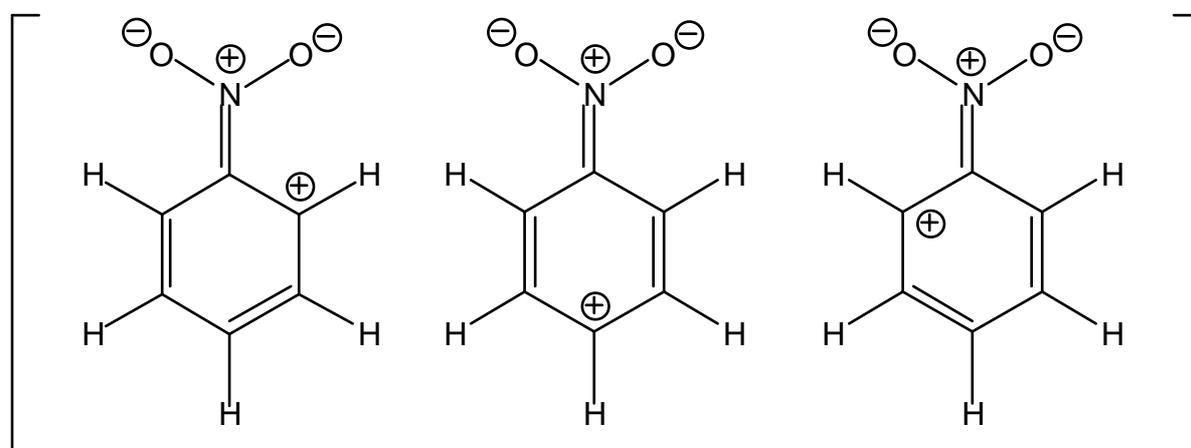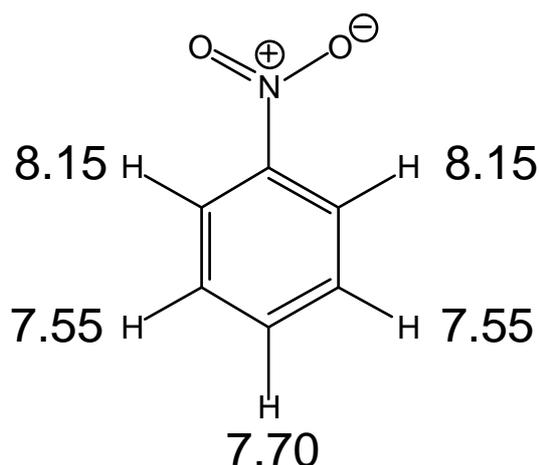
Factors affecting σ^{loc}. Anisotropic effects

- Any chemical bond is inherently anisotropic, i.e., it has a direction in space, and depending from which way we look at it, it will be different.

- When we subject the bonds (electron density) to an external magnetic field ($\mathbf{B_o}$), there will be an induced magnetic moment which will also be anisotropic.

- Therefore, the magnetic environment of ^{1}Hs around these groups will be anisotropic (σ^{loc}). This means, depending were the ^{1}Hs are with respect to the group giving rise to the induced magnetic dipole, the effective magnetic field felt by the proton will vary.

- If we consider a single C-C bond, which has cylindrical symmetry, and think of the induced magnetic dipole to be centered right in the middle of the bond, it will look like this:
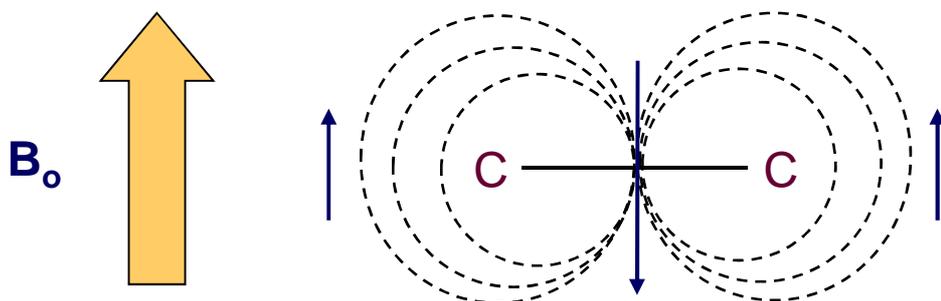
- What we see is that things on the ends of the bond will feel an increased magnetic field, while things sitting above or below will feel a slightly decreased effective field.

Anisotropic effects (continued)

- In order to calculate the magnitude of the induced dipole, we need to know its magnetic suceptibility, χ. We have two of them, one parallel to the bond, $\chi_{||}$, and one perpendicular, $\chi_{\perp}$. The magnitude of the magnetic dipole can then be calculated using the **McConnell** equation:

$$\sigma = \frac{1}{3r^3 \, 4\pi} \, (\, \chi_{||} - \chi_{\perp}) \cdot (\, 1 - 3\cos^2\theta \,)$$

- Here **r** is the distance from the center of the bond to the ^1H under study, and θ is the angle formed by the vector connecting them and the bond direction:

C

C

H θ
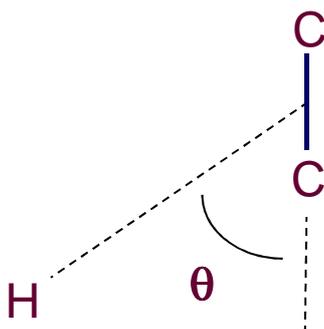
- The formula is an approximation, but it is pretty general, and we can apply it not only to single bonds, but to double and triple bonds, as well as to carbonyl groups, and as a crude approximations, to aromatic systems.

Anisotropic effects (…)

- The most useful thing arising from the equation is that if we plot it, we will get two cones spanning from the center of the bond: Inside the cone, we will be deshielded, on the sides, we'll be shielded. At an angle of 54.7°, the effect is zero:
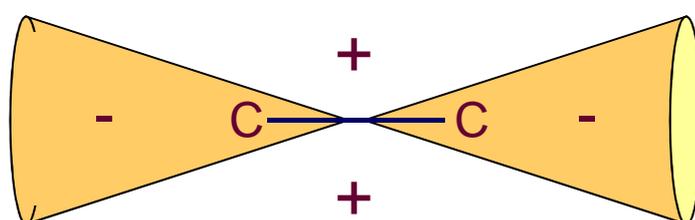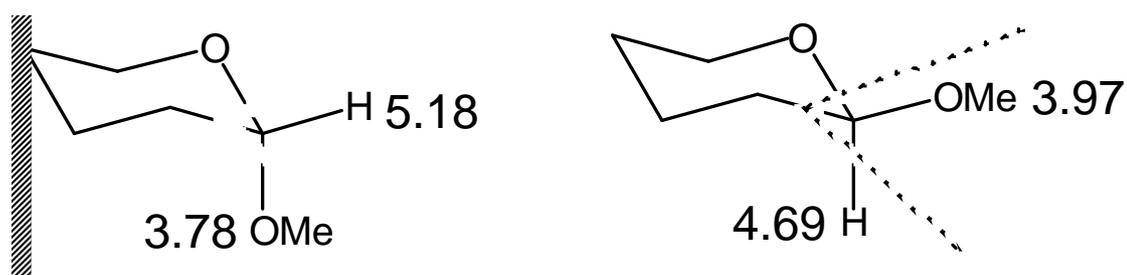

- For double bonds (C=O, C=C), the situation is similar:
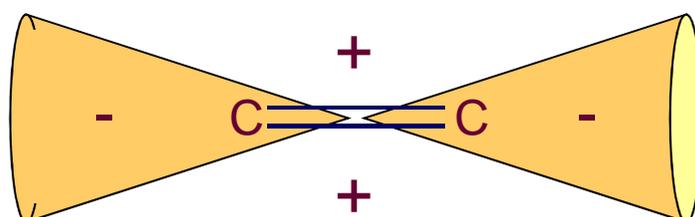
- For triple bonds, the induced magnetic dipole is such that the values of $\chi_{\parallel}$ and $\chi_{\perp}$ are reversed:
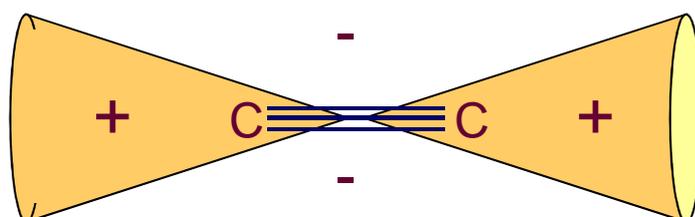
Anisotropic effects (…)

- So, lets look at some examples. In methoxygalactose, we can use this to see which one is α and which one is β.

H 5.18

3.78 OMe

OMe 3.97

4.69 H

- In the α-isomer, the anomeric ^{1}H is in the deshielding area of the cone, while in the β-isomer, it sits in the shielding zone.

- Another typical example are aldehydes. The aldehydic proton is very deshielded for two reasons. First, the proton is attached to a carbon with a double bond to an oxygen - It is very electropositive, which therefore draws a lot of the electron density away from the proton, deshielding it.

- Second, the proton is stuck in the deshielding area of the cone of the carbonyl group, which makes it even more deshielded:
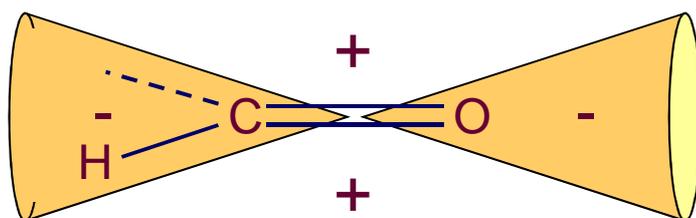
Ring current effects

- One of the most pronounced effects arising from induced magnetic moments on ^1H's are due to aromatic rings.

- The induced magnetic dipole created by an aromatic ring is the easiest to understand. If we consider the ring current of the ring, it will generate a magnetic field perpendicular to the plane of the ring, that will be against the external magnetic field:
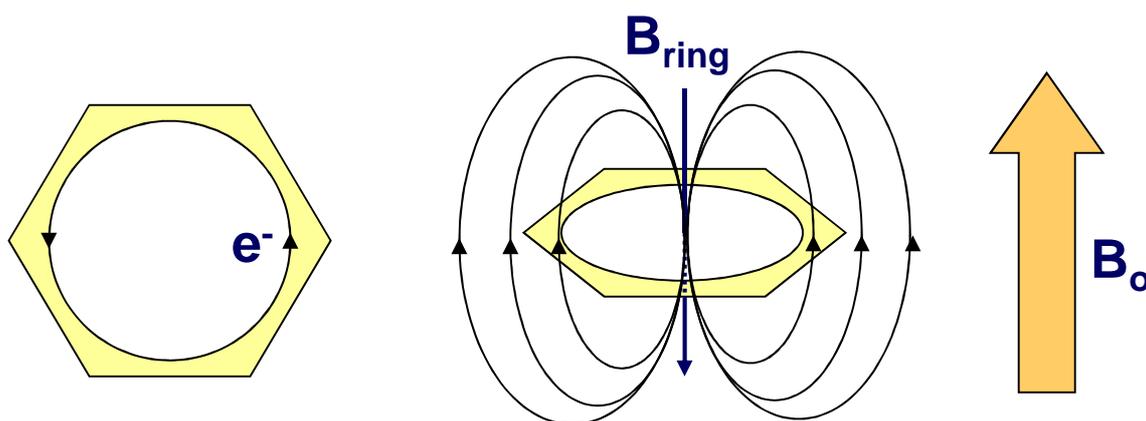
- As we see, the field lines through the ring are against of the external magnetic field (the induced magnetic moment will oppose the effect of B_o), but the 'return' lines, which go on the outside of the ring, are in favor of it.

- Therefore, we can safely assume that protons sitting on the plane of the ring and thereabouts will be deshielded, while those lying on top or below the ring will be shielded (i.e., higher fields and therefore lower chemical shifts.

Ring current effects (continued)

- As we had for simpler systems (single, double, and triple bonds), we can also estimate the degree of shielding as a function of the position of our nuclei around the ring.

- There are several formulas with different degrees of precision, but even the simplest ones give us a pretty decent estimate. The simplest one is the **Polple point-dipole** model:
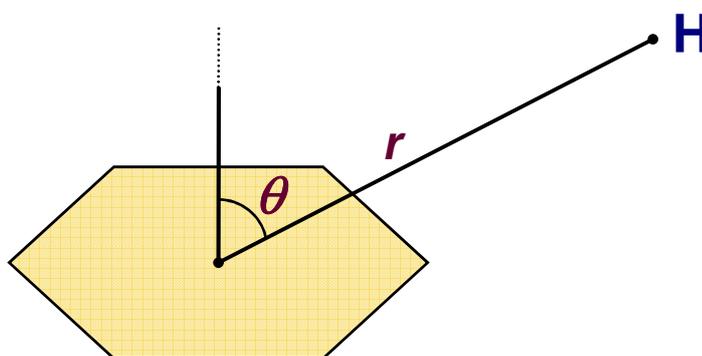

$$\delta_{rc} = C_{pople} \ast i_{rc} \cdot r^3 \cdot (\, 1 - 3 \cdot \cos^2\theta \,)$$

- Here C_{pople} is a proportionality constant, which can be determined by calculations or, most commonly, by parametrizing against experimental data. i_{rc} is the intensity factor of the ring current, and depends on the type of aromatic ring. It is **1.00** for benzene.
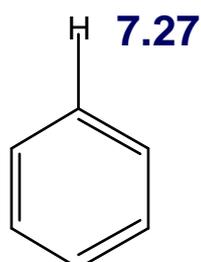
Ring current effects (…)

- As was the case for single, double, and triple bonds, we can plot the shielding as a function of the position in space of the ^{1}H under study. It will also be cone-shaped, with shielding regions (**-**, lower chemical shift), and deshielding regions (**+**, higher chemical shift):

- Protons on the sides of the aromatic ring will feel a higher local field (higher ppm's), while those on top or bottom will feel a lower local field (lower ppm's).
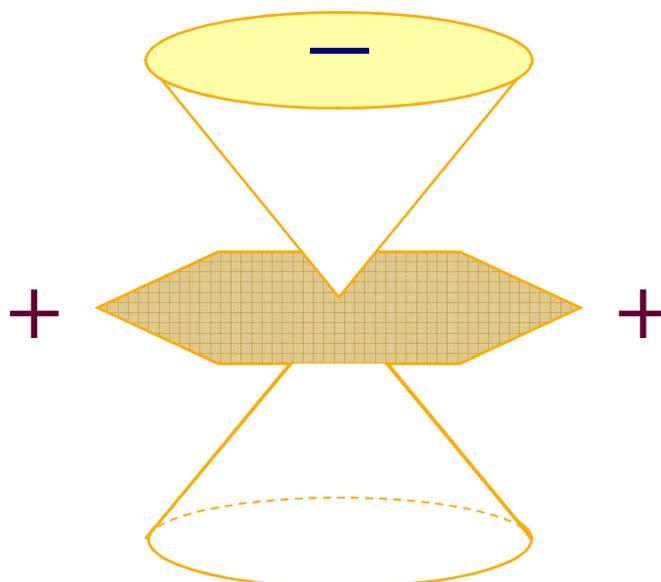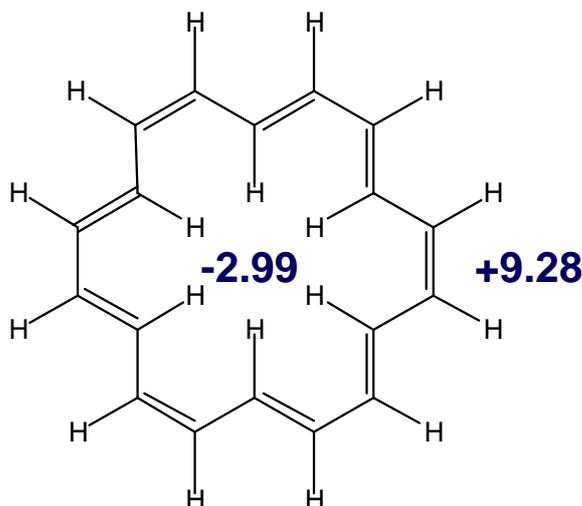

- This is the reason why aromatic protons poking outwards from an aromatic ring have chemical shifts in the 6 to 9 ppm's:


H **7.27**

H **7.79**

H **7.41**
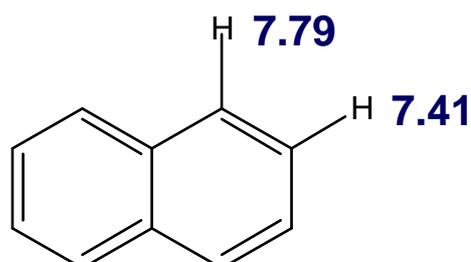
Ring current effects (…)

- There are cases in which the protons of the ring end up inside the shielding cone of the aromatic ring, such as in *[18]annulene*:

-2.99   +9.28

- There is one last example of a ring with a considerable anisotropic effect. **Cyclopropane** is very strained, and has double bond character (carbons have **sp²** character). There is a magnetic dipole perpendicular to the plane of the ring:
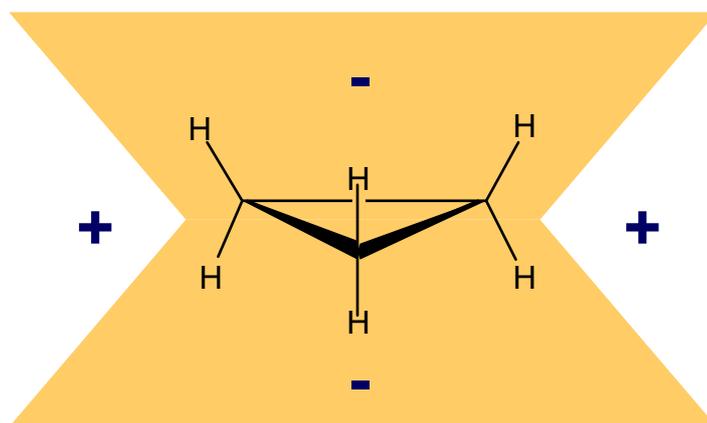

- However, the strain in cyclopropane puts the ¹H's on the shielding region of the cone, and therefore their resonances are shifted upfield approximately 1 ppm from other non-strained cyclic alkanes (shifts of 0.8 to 0.2 ppm's).

Electric field and Van der Waals effects

- Although there are many other factors affecting ^{1}H chemical shifts, we'll finish by describing the effect that polar groups and close contacts have on shifts.

- We can understand pretty intuitively how a charged group will affect the shielding of a proton. Depending on the charge, the electric field will 'pull' or 'push' on the electron density around the proton, deforming it, and therefore affecting the local field.

- Analogously, an uncharged group that sits close to the proton will disturb its electron density due to van der Waals contacts. Both effects are appropriately represented by the *Buckingham equation*:

$$\Delta\sigma = -AE_{C-H} - BE^2$$

C
H
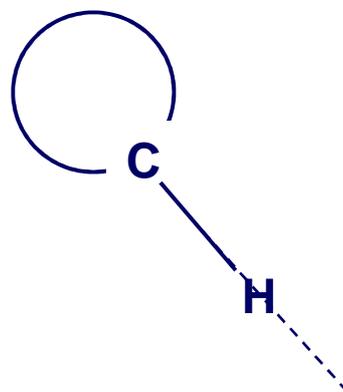
- Here **A** and **B** are constants. E_{C-H} represents the electric field along the C-H bond, and E^2 is the magnitude of the electric field on the proton squared.

- The first part of the equation describes effects of charged groups, as those found in proteins, pretty well. The second one, does the same with van der Waals contacts.

Some examples

- To conclude this discussion of factors affecting chemical shift, lets take a look at some interesting examples in which chemical shift can be used to decide on the structure of different molecules.

- The first one deals with cyclopropane anisotropy. In the following compound, the chemical shift of the indicated protons appears were expected for aromatic protons:
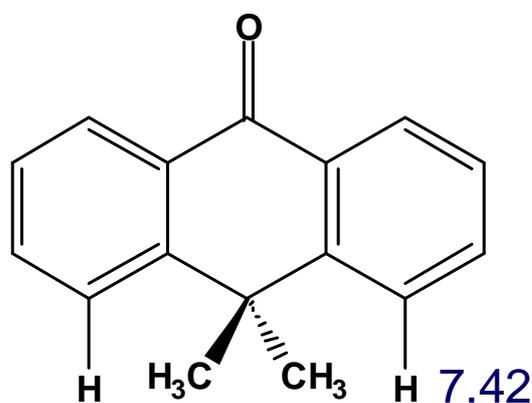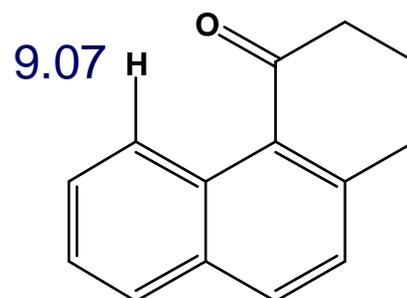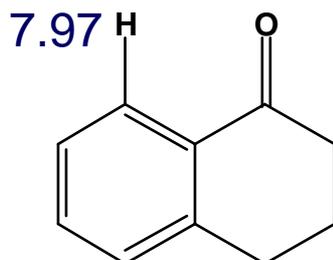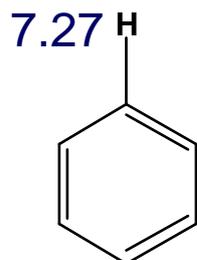

- However, if we just change the two methyls for a spiro cyclopropane ring, the induced magnetic field of the ring, which is perpendicular to the aromatic protons, makes them deshielded, shifting them to higher fields:
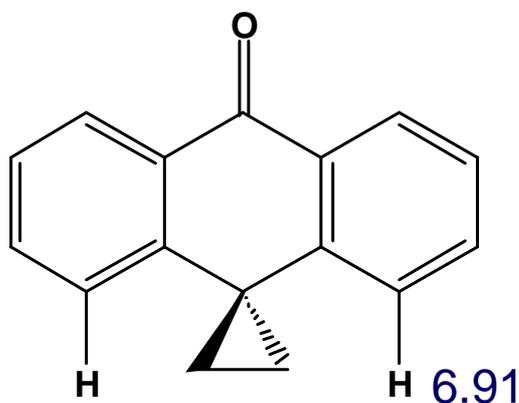
Some examples (continued)

- In the following ketones, we can see the effects of the carbonyl group anisotropy:

7.27 H   7.97 H   O   9.07 H

- Finally, the following example demonstrates that **antiaromatic** systems are paramagnetic (their induced field is in favor of the external magnetic field). In this dihydropyrene, everything shows up were expected for an aromatic with 14 e⁻ (4 x 6 + 2).
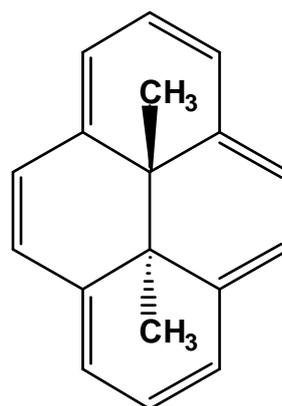
δ (CH$_3$) ~ -4
δ (Ar-H) ~ 8

- When we generate an ion (by reduction with metallic K) we get a system with 16 e⁻ (not 4 x n + 2). This makes it a paramagnetic system, and all the chemical shifts change pretty dramatically.
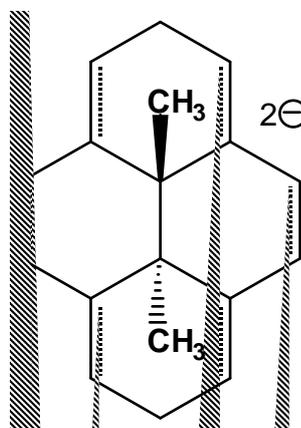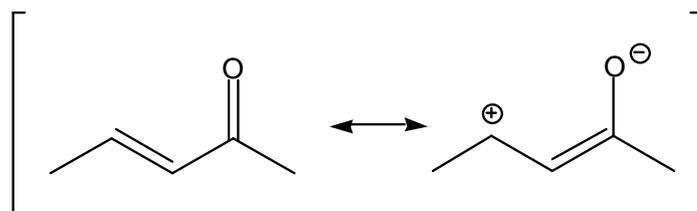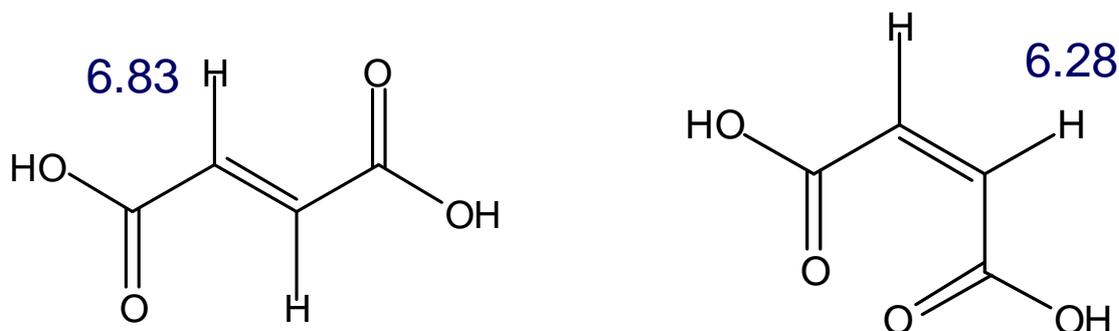
δ (CH$_3$) ~ 21
δ (Ar-H) ~ -4

Some examples (…)

- Another case in which several effects come into play is seen in α,β-unsaturated ketones. Here we resonance (electronic effects) dominating the shift at the β protons:

- We also have CO group anisotropy:

- In **cis-malonates** the deshielding is not as strong because the two **cis** groups bend the molecule out of the plane, reducing its resonance.

- Finally, the following examples show the effects of close contacts on chemical shifts. In these **pagodanes**, the close H···H or H···O contacts produces a dowfield shift (values of σ):
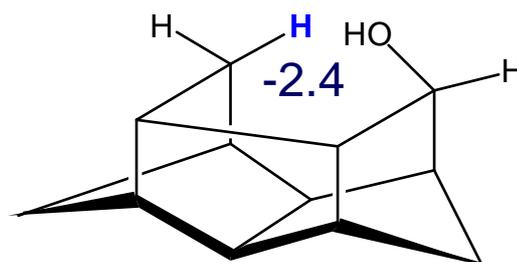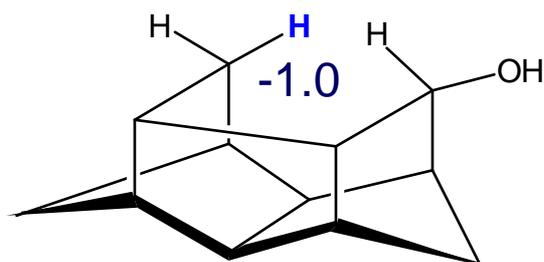
Shoolery chemical shift rules for ^1H

- As we have seen, most of the different effects on ^1H chemical shifts have been tabulated in one way or another.

- Furthermore, we also saw that most of the effects are *additive*, meaning that if we can estimate the different effects on the chemical shift of a certain ^1H from different groups and bonds, we can in principle estimate its chemical shift by adding all the effects together.

- There are several empirical rules, derived mostly by *Shoolery* in the late 50s/early 60s.

- In order to use them, we first have to identify the type of proton we have, such as aliphatic CH_3, CH_2, CH, olefinic CH_2 or CH, aromatic, α or β to a ketone or alcohol, belonging to an a α,β-unsaturated system, etc. They will have a base value.

- Then we look up the contributions from different groups attached to carbons in the surroundings of our system, and add them up to obtain the estimated chemical shift.

$$\delta H = \delta H_{base} + \Sigma \, contributions$$

- We'll analyze several cases to see how they work...

Shoolery rules (continued)

• *Aliphatic compounds*. There are two approaches to the calculation of additive effects on the ^1H chemical shifts.

• The first one is very simple. We just use two 'skeletons' with two base values, $R_1\text{-}CH_2\text{-}R_2$ or $R_1\text{-}CH\text{-}(R_2)\text{-}R_3$, and add the effects from the R_1, R_2, or R_3 groups:

Substituent	δ
Alkyl	0.0
-C=C-	0.8
-C≡C-	0.9
$-C_6H_5$	1.3
-CO-R	1.3
-OH	1.7
-O-R	1.5
-O-CO-R	2.7
$-NH_2$	1.0
-Br	1.9
-Cl	2.0

$$R_1\text{-}CH_2\text{-}R_2$$
$$\delta = 1.25 + R_1 + R_2$$

$$R_1\text{-}CH\text{-}(R_2)\text{-}R_3$$
$$\delta = 1.50 + R_1 + R_2 + R_2$$

• So CH_2Br_2 would be $\delta = 1.25 + 1.9 + 1.9 = 5.05$ ppm, which compares pretty well with the experimental value of 4.94 ppm.

Shoolery rules (…)

- The second method is pretty more general. We start with methane (δ_{base} of 0.23 ppm), and then we add substituent effects directly.

CH_3-	0.47
Cl-	2.53
RO-	2.36
RC(=O)O-	3.13

$$\delta = \delta_{base} + \Sigma\, S(\delta)$$

- Now, if instead of methane we have a longer carbon chain, δ_{base} is 0.933 ppm and we have to consider how many carbons it has, and each carbon will have an increment we will need to add to the base value:

0.248
$— C_2$

0.244
$—C_2—C_3$

0.147
$—C_2{\Large<}^{C_3}_{C_3}$

0.006
$—C_2{\Large<}^{C_3}_{C_3}{}_{C_3}$
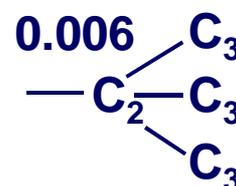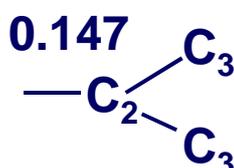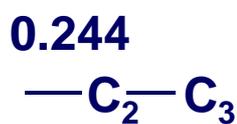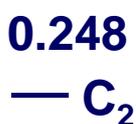
- Furthermore, if the carbons of these chains are substituted, we have to add increments according to their position in the carbon chain.

	C_1	C_2	C_3
HO-	2.47	0.048	0.235
Br-	1.995	0.363	0.023
Cl-	2.170	0.254	0.177
=O	-	1.021	0.004

- It is a lot more more general (and some say more accurate).

Shoolery rules (…)

- **Olefines**. For alkenes we change the tables for the base values, but we also have to consider the stereochemistry of the substituent (*cis*, *trans*, or *gem*):
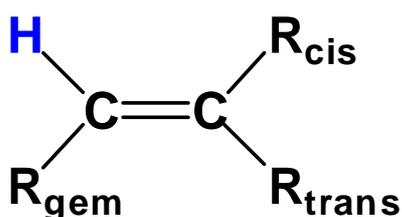
$$\delta = 5.25 + R_{gem} + R_{trans} + R_{cis}$$

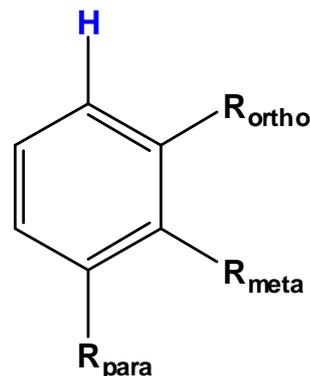| Substituent	δ_{gem}	δ_{cis}	δ_{trans}
H-	0.0	0.0	0.0
Alkyl-	0.45	-0.22	-0.28
-OR	1.21	-0.60	-1.00
-COOH	0.80	0.98	0.32
-Ar	1.38	0.36	-0.07
-C=C-	1.24	0.02	-0.05
-OH	1.22	-1.07	-1.21
-Cl	1.08	-0.40	-1.02

- So for cinnamic acid (*trans* Ph-CH^a=CH^b-COOH), we get that δH^a = 5.25 + 1.38 + 0 + 0.98 = 7.61, and δH^b = 5.25 + 0.80 + 0 + 0.36 = 6.41, pretty close to the reported values of 7.82 and 6.47 ppm.

Shoolery rules (…)

- **Aromatics**. Finally, the Schoolery rules allow us to calculate the approximate chemical shifts in aromatic compounds. Again, we have a different base value of 7.27 (benzene…).
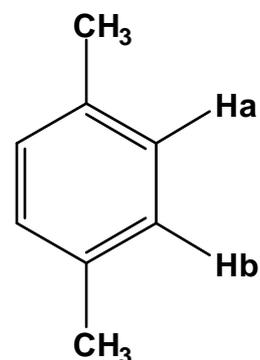
$$\delta = 7.27 + R_{ortho} + R_{meta} + R_{para}$$

Substituent	δ_{ortho}	δ_{meta}	δ_{para}
-H	0.0	0.0	0.0
-CH$_3$	-0.17	-0.09	-0.18
-NO$_2$	0.95	0.17	0.33
-COOH	0.80	0.14	0.20
-OCH$_3$	-0.43	-0.09	-0.37
-Cl	0.02	-0.06	-0.04
-F	-0.30	-0.02	-0.22
-NH$_2$	-0.75	-0.24	-0.63
-C$_6$H$_5$	0.18	0.00	0.08
-SCH$_3$	-0.03	0.00	0.00

Shoolery rules (…)

• For *p*-Xylene:

$\delta H_a = 7.27 - 0.17 - 0.09 = 7.00$ (6.97)
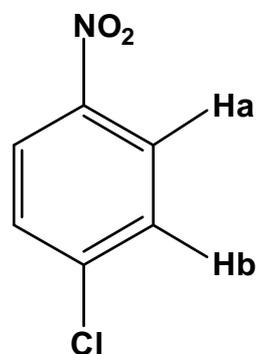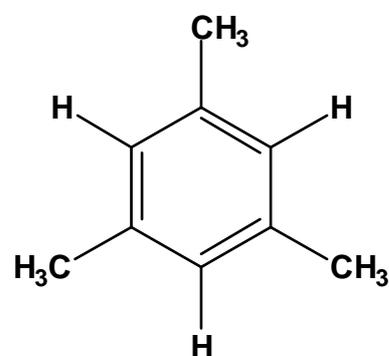$\delta H_b = \delta H_a$

• For 1-Chloro-4-nitrobenzene

$\delta H_a = 7.27 + 0.95 - 0.06 = 8.16$ (8.17)
$\delta H_b = 7.27 + 0.02 + 0.17 = 7.46$ (7.52)

• For mesitylene

$\delta H = 7.27 - 2 * 0.17 - 0.18 = 6.75$ (6.78)

• For 2,4-dinitro-1-methoxybenzene

$\delta H_a = 7.27 - 0.43 + 2 * 0.17 = 7.18$ (7.28)
$\delta H_b = 7.27 + 0.95 + 0.33 - 0.09 = 8.46$ (8.47)
$\delta H_c = 7.27 + 2 * 0.95 - 0.09 = 9.08$ (8.72)