Spectroscopy Sample Submission and Data Analysis Information

1) Preparing and submitting samples for ^{1}H-NMR analysis

All ^{1}H-NMR analysis in CHEM 344 is performed upon dilute solutions in $CDCl_3$. Undiluted liquids, biphasic solutions, or solutions containing solids give poor quality NMR data. To prepare and submit a sample for ^{1}H-NMR analysis:

a) For liquids or oils, use a clean Pasteur pipette to transfer **10 drops** of the liquid into a clean sample vial.
b) For solids, add a liberal **spatula-tip full** of compound (40 - 50 mg) into a clean sample vial.
c) With another **clean** Pasteur pipette, add approx. 1.5 mL (~1 pipette load) of $CDCl_3$ to the vial.
d) Mix the two compounds to give a homogeneous solution and then transfer the sample into a clean NMR tube *via* Pasteur pipette. The sample should fill the NMR tube to a volume of ⅓ to ½ full.
e) Once the solution has been transferred, cap the NMR tube ***securely***, and take it to the plastic sample box designated for your laboratory section. Dispose of the glass pipettes in the glass waste bin.
f) Once the NMR tube is placed in the sample box with a firmly attached cap to the correct depth, place the tube in the sample box.
    i) Always use the next available numbered slot in the rack; do not skip spaces.
    ii) Write your initials on the NMR sample submission sheet in the location designated for your section.
    iii) Always include a sample letter or designation when applicable.
    iv) Always write your sample box and location information into your laboratory notebook.

2) Obtaining NMR spectral data for analysis.

All ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR, and ^{31}P-NMR data will be provided as the raw free-induction-decay (fid) data. You will need to convert the raw data to a useable spectrum to be analyzed and interpreted for each lab report. ***You must submit your own spectral data with your lab report - submitting data as your own that you did not obtain is academic misconduct. If you fail to obtain data, you will not be penalized, a stock spectrum is available for analysis for each experiment.***

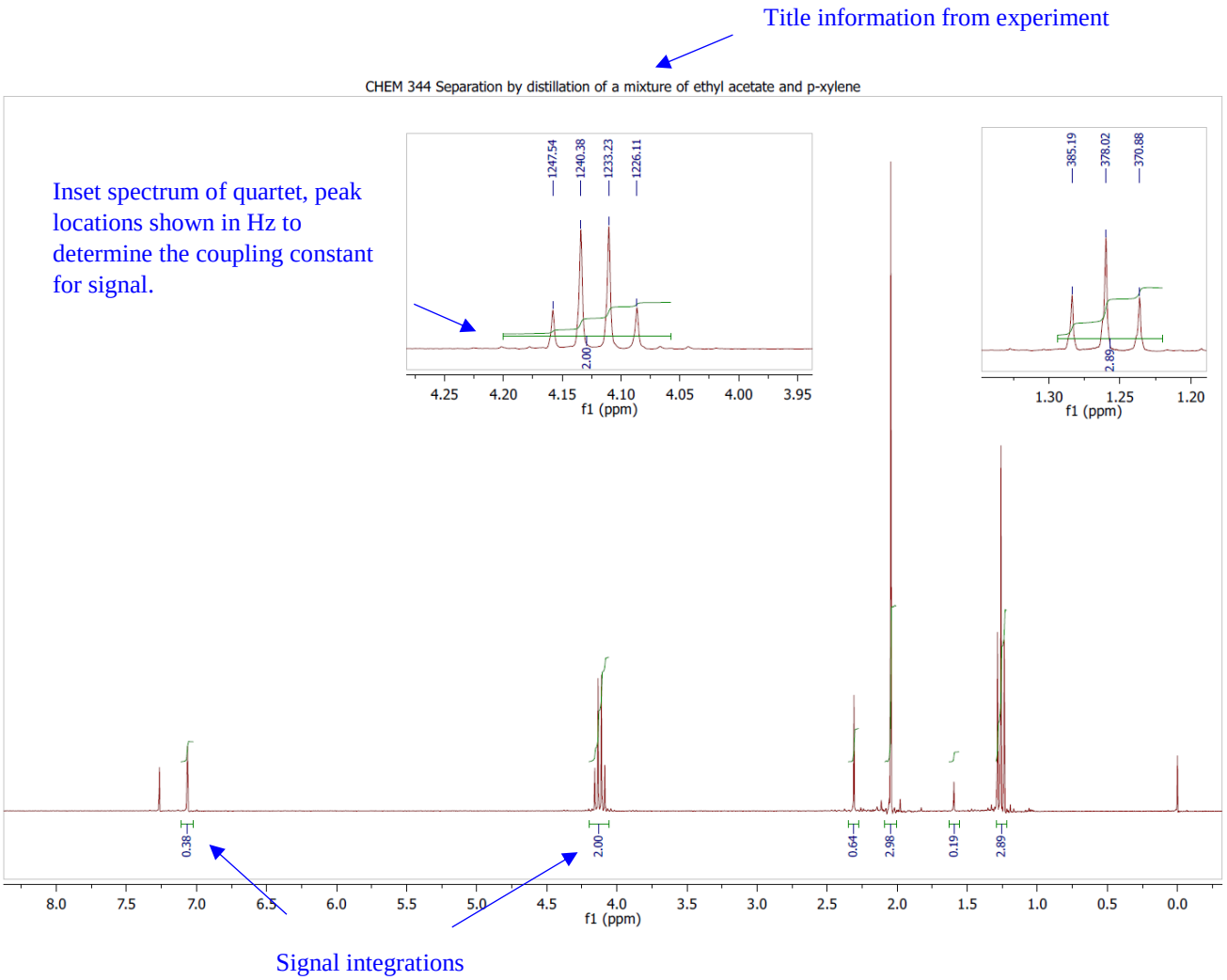
a) Open MestReNova with a properly installed license file (.lic). Instructions are available on the chemistry department NMR facility website.

https://www.chem.wisc.edu/~cic/nmr/main.html

b) Obtain a folder of many files for your NMR data. ***Instructions on how to obtain your data via the chemistry department server are provided below.***
c) Open the fid file in MestReNova. MestReNova will convert the fid from the time-domain (signal intensity vs. time) to the frequency domain (intensity vs. frequency). All NMR spectra in the course are in the frequency-domain, showing intensity vs. chemical shift. Detailed instructions for obtaining MestReNova are on the course website.
d) Work up all spectra by following the directions on the course website for each experiment and in the same manner as the stock spectrum. The directions will change for each experiment, so be sure to consult the example stock spectrum and specific directions each time. A video of how to work up the spectrum will be provided for the early experiments.

i) Make sure the x-axis scale is set to display all important signals are shown in the spectrum.
ii) Make sure that the baseline is relatively flat and correctly phased.
iii) Make sure all signals related to the reagents, products, byproducts, or solvents are integrated (excluding $CDCl_3$ and TMS).
iv) Make sure that all signals that need specific coupling information are peak picked in Hz.

e) Save the MNova spectrum in worked-up format and as a pdf for easy printing. You must include a hard copy of all NMR spectra for each experiment with your laboratory report.



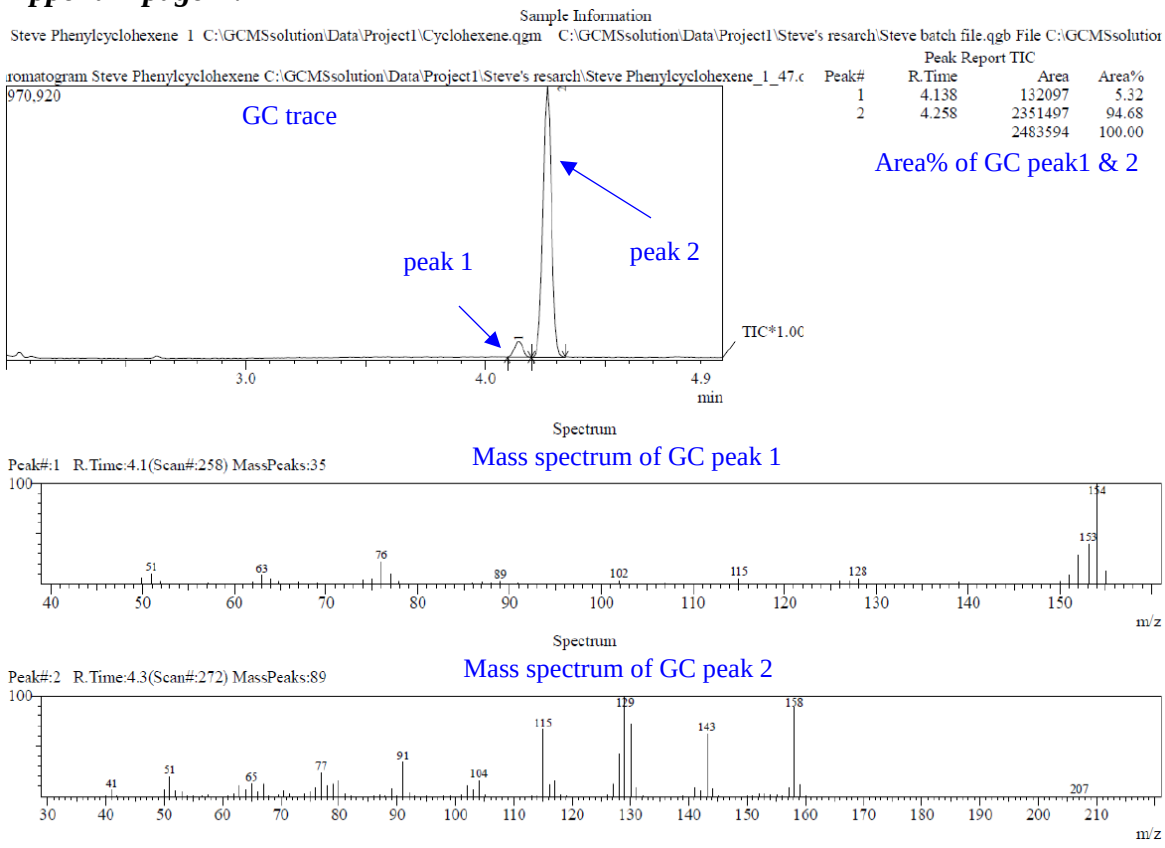
3) Preparing and submitting samples for GC-MS analysis

All GC-MS analysis in CHEM 344 is performed upon dilute solutions **except for the E1 and E2 product samples**. To protect the instrument, it is important that all samples are free of solid particulates. To prepare and submit a sample for GC-MS analysis:

a) For liquids or oils, use a clean Pasteur pipette to transfer **~10 drops** of the liquid into a clean sample vial.
b) For solids, add a liberal **spatula-tip full** of compound (40 - 50 mg) into a clean sample vial.
c) With another **clean** Pasteur pipette, place dichloromethane (CH_2Cl_2 not $CDCl_3$) into the sample vial until it is approx. ½ full.
d) Mix the two compounds to give a homogeneous mixture and then transfer the sample into a clean GC-MS sample vial *via* a **clean** Pasteur pipette.
e) Once the solution has been transferred, attach the screw cap to the GC-MS vial.
f) Place the tube in the sample box.
    i) Always use the next available numbered slot in the row designated for your section; do not skip spaces or put your sample in a different row.
    ii) Write your first name and last initials on the GC-MS sample submission sheet.
    iii) Always include an unknown number or letter when applicable.

4) Obtaining a GC-Mass spectrum for analysis.

Unlike the NMR spectra, the GC-MS data will be provided for you as fully worked up data including a gas chromatogram and its corresponding mass spectra. ***Instructions on how to obtain the pdf your GC-MS data via the chemistry department server are provided below on Appendix page F.***



5) Obtaining an Infrared (IR) spectrum for analysis.
The Bruker Alpha Platinum ATR FT-IR spectrometers are available in the laboratory for student use and spectra can be obtained during the laboratory session.

- **Remove your gloves before touching the mouse or computer!**
- **Do not pull down on the lever and press the pressure device without placing a sample on the crystal!**
- **LEAVE EVERYTHING CLEANER THAN YOU FOUND IT!**

Preparation

a) If not already open, open the program **Opus 7**. **Login:** *Student* **Password :** (*none, leave blank*) Press enter. Click ok. It will take the program a few seconds to setup the instrument.

b) Click the **Measure Background** button. It is critical that the crystal is clean at this point and NO SAMPLE has been placed on the platform. Wait for a short time while the spectrometer completes several scans of the region with no sample and averages the signal. This will allow the spectrometer to accurately measure the IR absorptions due your sample by subtracting the background.

c) Place a small amount of your solid or oil sample directly on the crystal window in the center of the metallic disc. The sample should completely cover the crystal.

d) Pull the lever down until the pressure device locks in place.

Data Collection and Analysis

e) Click the Measure Sample button. Enter a descriptive filename in the general format "STUDENT(S)_NAMES TA_NAME EXPERIMENT MOLECULE." This name will appear on the printout of your spectrum

f) Click the **Start Sample Measurement** Button. Wait for a short time while the spectrometer completes several scans of the region and averages the signal. The spectrometer will use the background spectrum collected earlier to produce the spectrum of your sample.

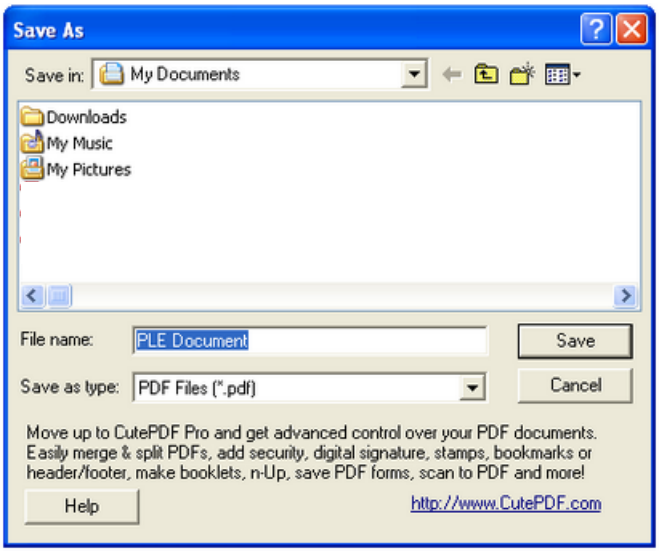
g) Choose **Manipulate > Baseline Correction** from the file menu.

h) Choose **Manipulate > Smooth** from the file menu. Highlight the file name and hit the **Smooth button**. Steps g and h, combined with completing multiple scans, are designed to enhance your spectrum and improve the signal-to-noise ratio of the data.

i) Choose **Evaluate > Peak Picking** from the file menu. Move the target cursor so that all desired absorptions pass below the threshold (horizontal) line. Click the **Store button**. This will place convenient frequency labels next to all picked peaks directly on the spectrum.

Saving Data Via Printing a pdf

j) There is no printer in the lab, but a pdf of the spectrum can be saved by clicking the **Print Report** Button. As before, enter a descriptive filename in the general format "STUDENT(S)_NAMES TA_NAME EXPERIMENT MOLECULE." This will be the name of the pdf file generated for your spectrum. Save the pdf reports in the **designated TA folder on the desktop** only.



k) Use any of the web browsers on the computer to email this file to yourself and your labmates.

Spectrometer Clean-up

l) Clean the pressure device and crystal with an isopropanol soaked wipe and a clean/dry Kimwipe. **CLEAN UP ALL CHEMICAL SPILLS FROM ON AND AROUND THE INSTRUMENT!!!!** Move the pressure device off center. **Throw away all trash!** Unless someone else is directly following you, close all programs.

Troubleshooting

m) We have noticed that after many samples, the communications between the spectrometer and computer may fail. Simply unplug the spectrometer and restart the computer. When both power back up, the communications should be fine.

Obtaining your NMR and GC-MS data

You must be able to electronically access your NMR and GC-MS data. This will be an important part of each experimental analysis. The same connection procedure will enable the MestReNova license file that is necessary for workup of all NMR spectra. ***Being unable to connect will never be an acceptable justification for late work or academic misconduct.***

1) You must be electronically ***on-campus*** to obtain your data. You can be ***on-campus*** in one of two ways, direct connection to a campus network *via* an **ethernet cable** or by connection to the campus virtual private network (**WiscVPN**), which is preferred.

a) An ethernet cable is required if you do not wish to use the VPN. To be on-campus *via* this method you must have a cable plugged in. A campus Wi-Fi connection is **not** equivalent to using an ethernet cable.

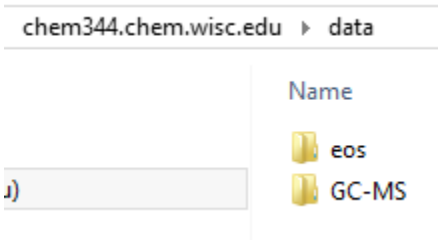
b) You can connect to the campus network and be electronically ***on-campus*** anywhere in the world via WiscVPN or the University of Wisconsin Virtual Private Network.

i) **Download** AnyConnect (https://wiscvpn.doit.wisc.edu/) Enter your campus username and password to begin the downloading process. It may fail. A complete DoIT guide to the install can be found here or importantly a "what-to-do-if-Java-Fails page" with Mac and PC instructions is also available. A google search of "WiscVPN (Mac and Windows)" will get you to these pages.

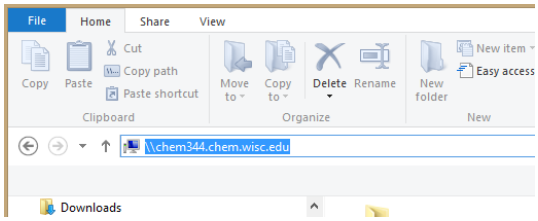
ii) **Install** AnyConnect. After downloading the file, you will need to run the installation. Find where your computer saved the file, click on it, and follow the directions to install the program.

iii) **Run** AnyConnect. You must now activate the program and have it running to allow the network to treat you as being ***on-campus***. This is the only step that you will have to repeat each time you wish to access your data or re-activate you MestReNova license.

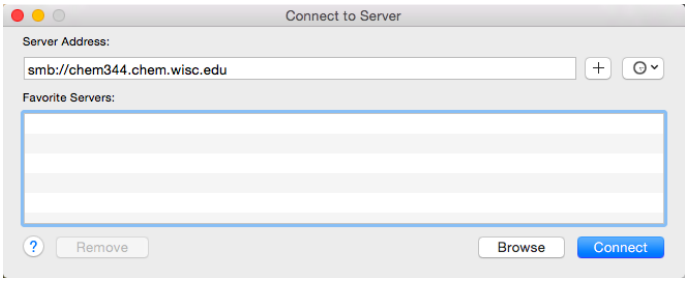
2) You must now navigate to the Chem 344 data server. This server will host your NMR and GC-MS data for the entire semester and you will need to access it after completing the in-class portion of each experiment.



a) Using a PC, navigate in a file browser like windows explorer to \\chem344.chem.wisc.edu Do not use a web-browser and make sure you are using the proper slashes. You may wish to make a shortcut of this location. If you are unable to access this folder, you are likely not properly ***on-campus***. (https://comphelp.chem.wisc.edu/content/connecting-chemistryfs3-chemhome-or-another-server-windows)

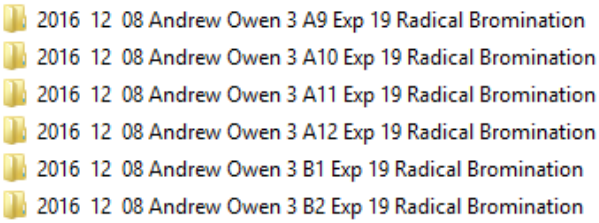


b) Using a Mac, access your "Connect to Server" application. You can do this using the Go option in Finder or by clicking on the background and pressing Apple+K on the keyboard. Once Connect to Server is open, type "smb://chem344.chem.wisc.edu" into the server address. Press connect. (https://comphelp.chem.wisc.edu/content/connecting-chemistryfs3-chemhome-or-another-file-server-mac-osx)



3) Download your data. The data folder will contain a separate folder for each instrument computer to type of instrument. The folder eos contains the NMR data (see above), the folder GC-MS contains the data from the GC-MS instrument.

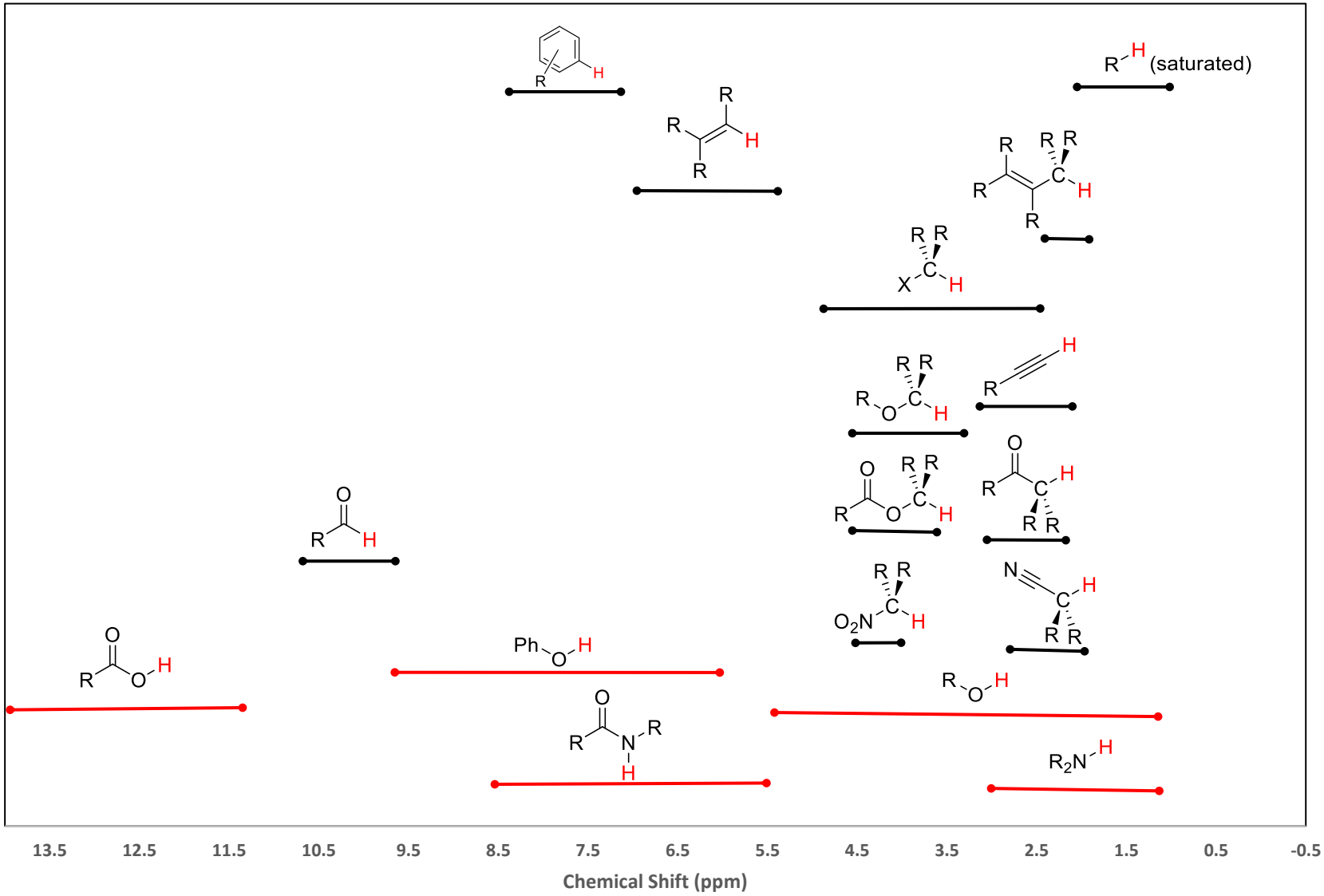
a) Eos (https://en.wikipedia.org/wiki/Eos) is the name of the Bruker Ascend 400 MHz NMR Instrument available for student samples (New in Oct 2016, $350,000). The data will be posted to the Chem 344 data server in real-time. At the end of each experiment's data collection, the data will be moved from the main Eos data folder into an archival folder labeled for each experiment. A scanned copy of each day's submission sheets will be made available. Download the folder of data corresponding to your sample (YYYY MM DD TA_NAME BOX# Slot_Position Exp). The data folder must be imported into MestReNova and worked up properly (see course website for sample processed spectra for each experiment).



b) The instrument used to obtain Chem 344 GC-MS student data is a Shimadzu GCMS-QP2010S. All sample data will be posted to the Chem 344 data server in real-time. Each experiment sample's data will be provided as a pdf with the GC trace and mass spectra as shown on ***Appendix page C***. No further workup is required. The pdf filename format will be TA_NAME_##_##, where the first ## will correspond to the sample number on the submission sheet. A scanned copy of each day's submission sheets will be made available.

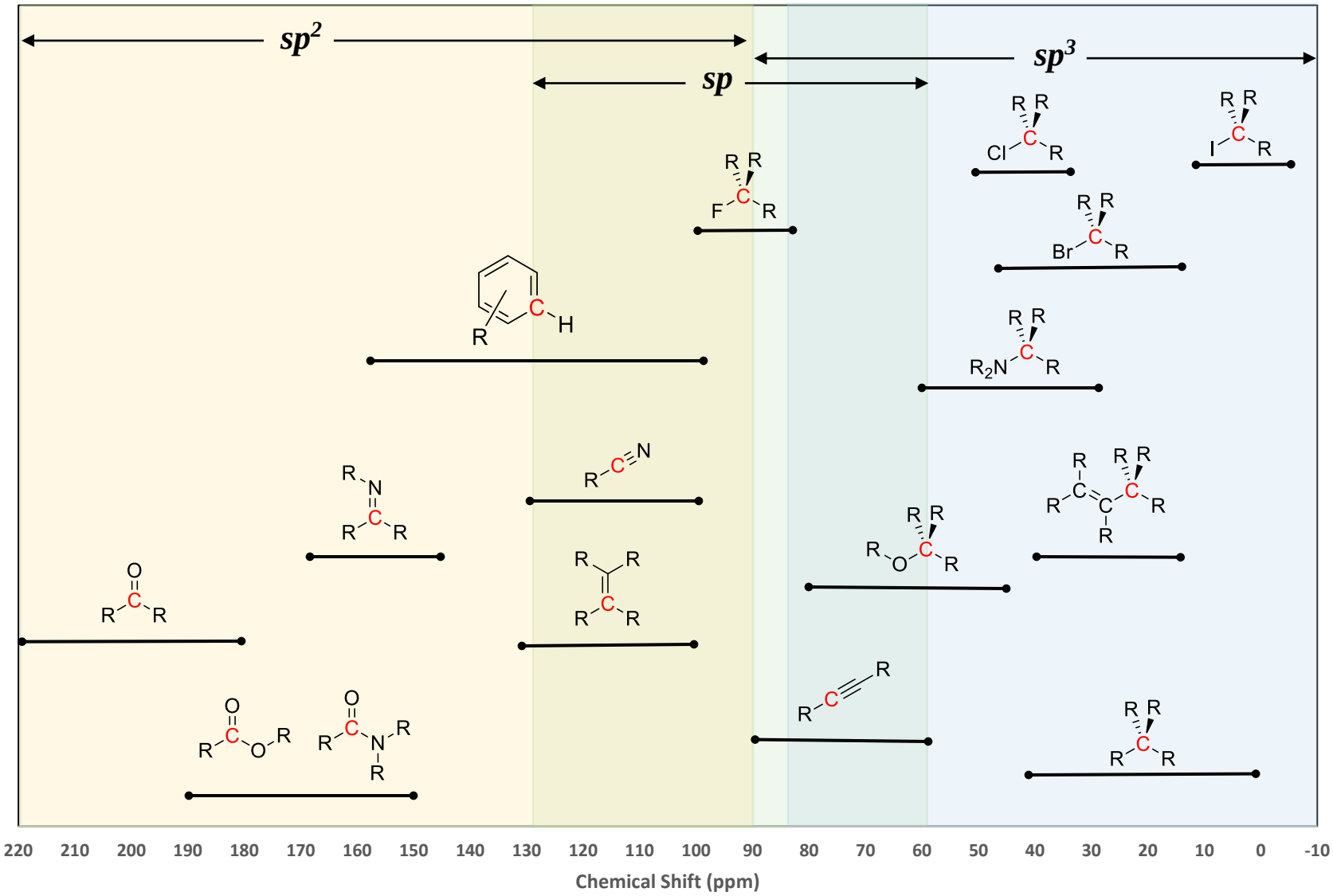
Typical ^{1}H-NMR Chemical Shift Ranges

(in $CDCl_3$ referenced to TMS $\delta = 0$)

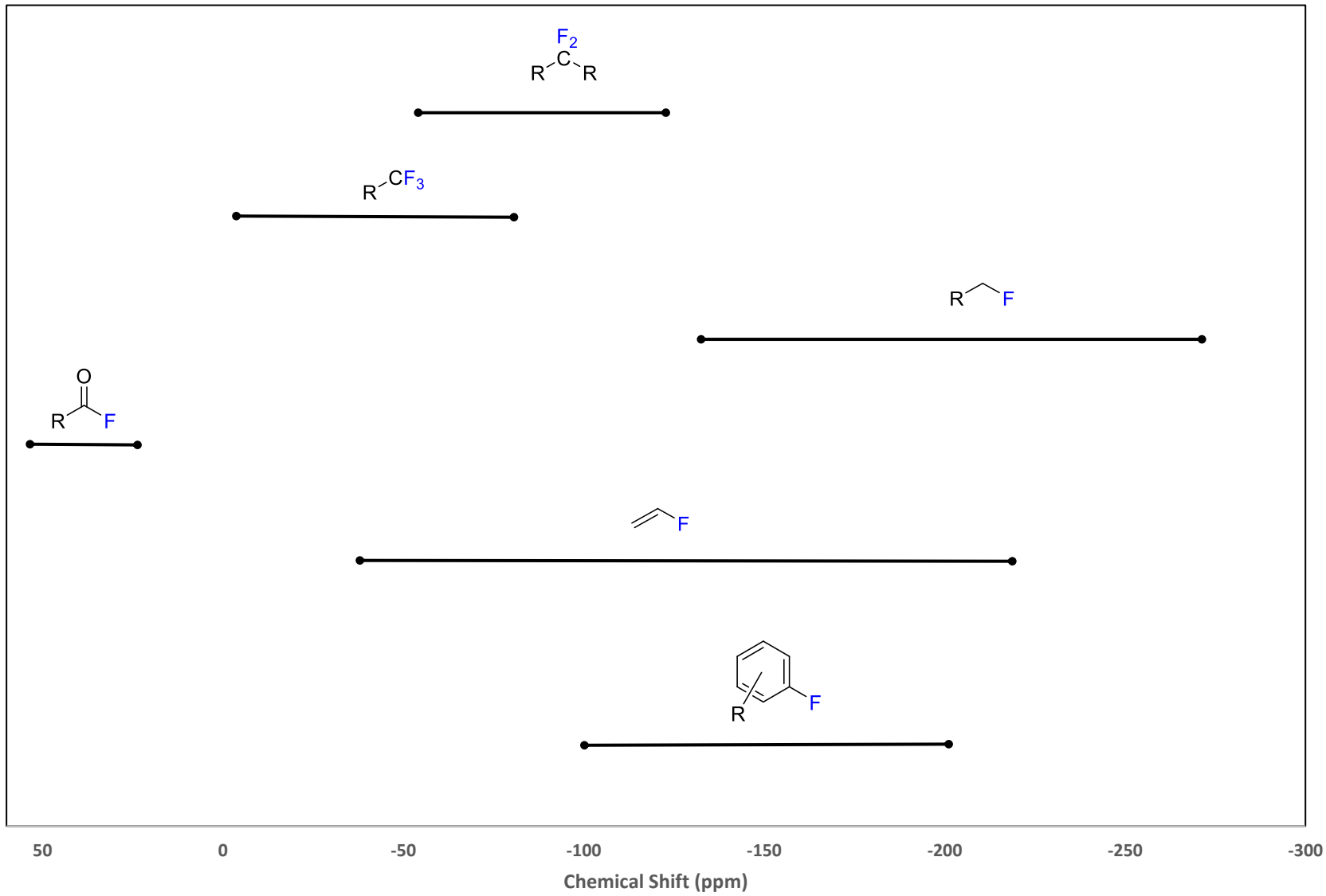


Typical ^{13}C-NMR Chemical Shift Ranges

(in $CDCl_3$ referenced to TMS $\delta = 0$)

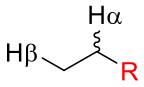


Typical ^{19}F-NMR Chemical Shift Ranges



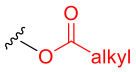
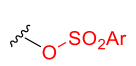
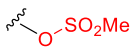
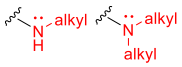
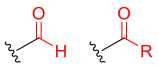
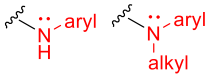
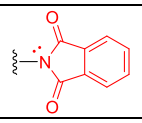
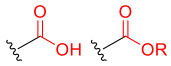
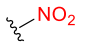
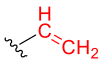
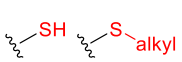
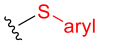
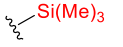
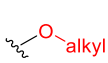
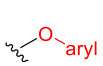
K

Curphy-Morrison Additivity Constants for Proton NMR

α and β Substituent Effects: 

Standard Shift: Methyl (-CH_3) 0.90 δ, Methylene (-CH_2-) 1.20 δ, Methine (-CH-) 1.55 δ

Shift Estimate: δ_H = Standard Shift + $\Sigma_{\alpha\text{-shifts}}$ + $\Sigma_{\beta\text{-shifts}}$

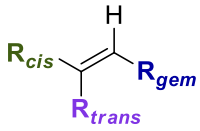
Substituent (R)		α-shift	β-shift	Substituent (R)		α-shift	β-shift
	-CH_3	2.30	0.60		-CH_3	2.90	0.40
	-CH_2-	2.30	0.55		-CH_2-	2.95	0.45
	-CH-	2.55	0.15		-CH-	3.45	----
	-CH_3	1.80	0.80		-CH_3	2.84	0.39(1)
	-CH_2-	2.15	0.80		-CH_2-	2.66(6)	0.28(5)
	-CH-	2.20	0.25		-CH-	3.16(3)	0.32(2)
	-CH_3	1.80	0.80		-CH_3	3.01	0.47(2)
	-CH_2-	2.15	0.80		-CH_2-	2.90(5)	0.43(2)
	-CH-	2.20	0.25		-CH-	2.64(1)	0.61(1)
	-CH_3	1.45	0.35		-CH_3	1.25	0.20
	-CH_2-	1.45	0.55		-CH_2-	1.40	0.15
	-CH-	1.35	----		-CH-	1.35	----
	-CH_3	1.25	0.25		-CH_3	2.08(8)	0.28(10)
	-CH_2-	1.10	0.30		-CH_2-	2.03(12)	0.34(2)
	-CH-	0.95	----		-CH-	2.33(2)	?
	-CH_3	1.70(6)	0.28(4)		-CH_3	2.08(8)	0.28(10)
	-CH_2-	1.64(10)	0.50(3)		-CH_2-	2.03(12)	0.34(2)
	-CH-	1.76(2)	0.76(1)		-CH-	2.33(2)	?
	-CH_3	1.20	0.25		-CH_3	3.50	0.65
	-CH_2-	1.00	0.30		-CH_2-	3.15	0.85
	-CH-	0.95	----		-CH-	3.05	----
	-CH_3	1.10	0.45		-CH_3	2.08(1)	0.45(1)
	-CH_2-	1.10	0.40		-CH_2-	1.45(3)	0.46(1)
	-CH-	0.95	----		-CH-	1.46(2)	-0.22(1)
	-CH_3	0.90	0.05		-CH_3	1.20	0.40
	-CH_2-	0.75	0.10		-CH_2-	1.30	0.30
	-CH-	0.65	----		-CH-	1.30	----
	-CH_3	0.90	0.15		-CH_3	1.47(2)	0.35(2)
	-CH_2-	0.80	0.05		-CH_2-	1.45(8)	0.31(2)
	-CH-	0.35	----		-CH-	1.60(4)	0.01(4)
	-CH_3	2.45	0.40		-CH_3	-0.90(1)	0.06(2)
	-CH_2-	2.30	0.20		-CH_2-	-0.39(2)	?
	-CH-	2.10	----		-CH-	-0.83(8)	?
	-CH_3	2.45	0.30				
	-CH_2-	2.30	0.15				
	-CH-	2.10	----				
	-CH_3	2.95	0.40				
	-CH_2-	2.65(11)	0.45				
	-CH-	3.06(2)	----				

Adapted from: P. L. Fuchs and C. A. Bunnell, "Carbon-13 NMR Based Spectral Problems," John Wiley, New York, 1979. Data with numbers in parentheses were added by H. J. Reich with limited number of examples (number is sample size).

(Adapted from Hans J. Reich, http://www.chem.wisc.edu/areas/reich/nmr/notes-9-hmr-5-curphy-morrison.pdf)

Curphy-Morrison-type Additivity Constants for Calculating Vinyl Chemical Shifts

Substituent Effects on:



Shift Estimate: $\delta_{H\ (vinyl)} = 5.25 + Z_{gem} + Z_{cis} + Z_{trans}$

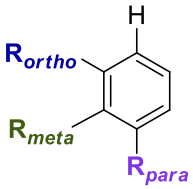
Substituent (R)	Z_{gem}	Z_{cis}	Z_{trans}	Substituent (R)	Z_{gem}	Z_{cis}	Z_{trans}
H	0.00	0.00	0.00	F	1.54	-0.40	-1.02
alkyl	0.45	-0.22	-0.28	Cl	1.08	0.18	0.13
Alkyl (cyclic) [a]	0.69	-0.25	-0.28	Br	1.07	0.45	0.55
CH_2OH	0.64	-0.01	-0.02	I	1.14	0.81	0.88
CH_2SH	0.71	-0.13	-0.22	OR (R = aliphatic)	1.22	-1.07	-1.21
CH_2X (X = F, Cl, Br)	0.71	-0.13	-0.22	OR (R = conjugated)	1.21	-0.60	-1.00
CH_2NR_2	0.58	-0.10	-0.08	O-C(O)R	2.11	-0.35	-0.64
CF_3	0.66	0.61	0.32	NR_2 (R = aliphatic)	0.80	-1.26	-1.21
$C=CR_2$ (isolated)	1.00	-0.09	-0.23	NR_2 (R = conjugated)	1.17	-0.53	-0.99
$C=CR_2$ (conjugated) [b]	1.24	0.02	-0.05	N=N-Ph	2.39	1.11	0.67
C≡C-R	0.47	0.38	0.12	NO_2	1.87	1.30	0.62
C≡N	0.27	0.75	0.55	N-C(O)R	2.08	-0.57	-0.72
COOH (isolated)	0.97	1.41	0.71	N_3	1.21	-0.35	-0.71
COOH (conjugated) [b]	0.80	0.98	0.32	$SiMe_3$	0.77	0.37	0.62
COOR (isolated)	0.80	1.18	0.55				
COOR (conjugated) [b]	0.78	1.01	0.46				
C(O)H (aldehyde)	1.02	0.95	1.17				
$C(O)NR_2$ (amide)	1.37	0.98	0.46				
C(O)Cl (acid chloride)	1.11	1.46	1.01				
C(O)R (ketone)	1.10	1.12	0.87				
C(O)R (conj. ketone) [b]	1.06	0.91	0.74				
CH_2-C(O)R; CH_2-CN	0.69	-0.08	-0.06				
CH_2Ar (benzyl)	1.05	-0.29	-0.32				
Aryl	1.38	0.36	-0.07				
Aryl (*o*-substituted)	1.65	0.19	0.09				

[a] The increment alkyl (cyclic) is to be used when both the substituent and the double bond form part of a ring. (Data for compounds containing 3- and 4-membered rings have not been considered.) [b] The increments 'R conjugated' are to be used instead of 'R isolated' when either the substituent or the double bond is conjugated with further substituents. Numbers in parentheses represent the number of examples used to calculate the parameters.

[1] Pascual, C. *Helv. Chem. Acta* **1966**, *49*, 164.
[2] L'Abbe, G. *Chem. & Ind*. (London) **1971**, 278.

(Adapted from Hans J. Reich, http://www.chem.wisc.edu/areas/reich/nmr/notes-9-hmr-6-vinyl-aryl-shifts.pdf)

Curphy-Morrison-type Additivity Constants for Calculating Benzene Chemical Shifts



Substituent Effects on:

Shift Estimate: $\delta_{H\ (aryl)} = 7.36 + Z_{ortho} + Z_{meta} + Z_{para}$

Substituent (R)	Z_{ortho}	Z_{meta}	Z_{para}	Substituent (R)	Z_{ortho}	Z_{meta}	Z_{para}
H	0.00	0.00	0.00	OPh	-0.36	-0.04	-0.28
CH_3	-0.18	-0.11	-0.21	O-C(O)CH_3	-0.27	-0.02	-0.13
*t*Bu	0.02	-0.08	-0.21	O-C(O)Ph	-0.14	0.07	-0.09
CH_2Cl	0.02	-0.01	-0.04	O-SO_2CH_3	-0.05	0.07	-0.01
CH_2OH	-0.07	-0.07	-0.07	SH	-0.08	-0.16	-0.22
CF_3	0.32	0.14	0.20	SMe	-0.08	-0.10	-0.24
CCl_3	0.64	0.13	0.10	SPh	0.06	-0.09	-0.15
C=CH_2	0.04	-0.04	-0.12	SO_2Cl	0.76	0.35	0.45
C=CHCOOH	0.19	0.04	0.05	NH_2	-0.71	-0.22	-0.62
C≡C-H	0.15	-0.02	-0.01	NMe_2	-0.66	-0.18	-0.67
C≡C-Ph	0.17	-0.02	-0.03	NEt_2	-0.68	-0.15	-0.73
Ph	0.23	0.07	-0.02	$NMe_3^+ I^-$	0.69	0.36	0.31
COOH	0.77	0.11	0.25	NHC(O)CH_3	0.14	-0.07	-0.27
C(O)OCH_3	0.68	0.08	0.19	NH-NH_2	-0.60	-0.08	-0.55
C(O)OPh	0.85	0.14	0.27	N=N-Ph	0.67	0.20	0.20
C(O)NH_2	0.46	0.09	0.17	N=O	0.58	0.31	0.37
C(O)Cl	0.76	0.16	0.33	NO_2	0.87	0.20	0.35
C(O)CH_3	0.60	0.10	0.20	$SiMe_3$	0.22	-0.02	-0.02
C(O)*t*Bu	0.44	0.05	0.05				
C(O)H	0.53	0.18	0.28				
C(NPh)H	0.60	0.20	0.20				
C(O)Ph	0.45	0.12	0.23				
C(O)C(O)Ph	0.62	0.15	0.30				
CN	0.29	0.12	0.25				
F	-0.29	-0.02	-0.23				
Cl	-0.02	-0.07	-0.13				
Br	0.13	-0.13	-0.08				
I	0.39	-0.21	0.00				
OH	-0.53	-0.14	-0.43				
OCH_3	-0.45	-0.07	-0.41				

Data in dilute $CDCl_3$ by Paul Schatz, UW-Madison. Original data from *J. Am. Chem. Soc*. **1956**, *78*, 3043 at 30 MHz with 50% solutions in cyclohexane.

(Adapted from Hans J. Reich, http://www.chem.wisc.edu/areas/reich/nmr/notes-9-hmr-6-vinyl-aryl-shifts.pdf)

^{1}H- and ^{13}C-NMR Chemical Shifts for Common Solvents in $CDCl_3$

Solvent	ρ (g/cm^3)	^{1}H δ (ppm)	^{1}H Signal Multiplicity	^{13}C δ (ppm)
acetone	0.791	2.17	singlet	207.07 (CO) 30.92 (CH_3)
acetonitrile	0.786	2.10	singlet	116.43 (CN) 1.89 (CH_3)
benzene	0.8765	7.36	singlet	128.57 (Ar)
chloroform	1.489 @ 25 ºC	7.27	singlet	77.58 (CD)* 77.44 (CD)* 77.00 (CD)*
dichloromethane	1.3266 @ 20 ºC	5.30	singlet	53.52 (CH_2)
diethyl ether	0.7134	3.48 1.21	quartet triplet	65.91 (CH_2) 15.20 (CH_3)
ethanol	0.789 @ 25 ºC	3.72 1.25	quartet triplet	58.28 (CH_2) 18.41 (CH_3)
n-hexane	0.6548	1.26 0.88	2nd order multiplet triplet	31.64 (CH_2) 22.70 (CH_2) 14.14 (CH_3)
isopropanol	0.786 @ 20 ºC	4.04 1.73	septet doublet	64.50 (CH) 25.14 (CH_3)
methanol	0.792	3.49 variable	singlet broad singlet	50.41 (CH_3)
n-pentane	0.626	1.27 0.88	2nd order multiplet triplet	34.16 (CH_2) 22.38 (CH_2) 14.08 (CH_3)
tetrahydrofuran	0.8892 @ 20 ºC	3.76 1.85	2nd order multiplet 2nd order multiplet	67.97 (CH_2) 25.62 (CH_2)
toluene	0.87 @ 20 ºC	2.36 (CH_3) 7.1 – 7.3 (Ar)	singlet	137.8 (Ar) 129.0 (Ar) 128.2 (Ar) 125.3 (Ar) 21.46 (CH_3)
water	1.00	1.56	singlet	-

Values obtained from the following:

Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. NMR Chemical Shifts of Common Laboratory Solvents as Trace Impurities. *J. Org. Chem.*, **1997**, *62*, 7512–7515.

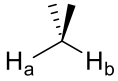
Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist. *Organometallics*, **2010**, *29*, 2176–2179.

Typical ^{1}H-NMR $J_{H\text{-}H}$ Coupling Values*

Coupling

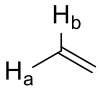
2-bond

gem alkyl



^2J = 2 – 15
(typical -12 Hz)

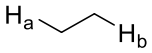
gem vinyl



^2J = 1 – 3

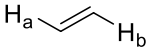
3-bond

vicinal alkyl



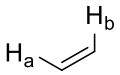
^3J = 2 – 20
(typical 7 Hz)

trans vinyl



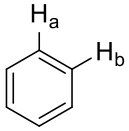
^3J = 12 – 18

cis vinyl



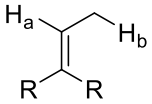
^3J = 6 – 12

ortho aryl



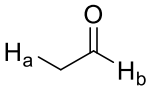
^3J = 8 – 12

vicinal C(sp^2)-C(sp^3)



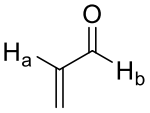
^3J = 3 – 11
(dihedral dependent)

vicinal aldehyde



^3J = 1 – 3

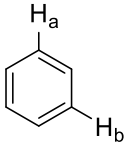
vicinal conjugated aldehyde



^{3}J = 7 – 8

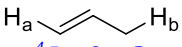
4-bond

meta aryl



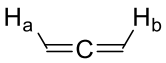
^4J = 2 – 3

allylic



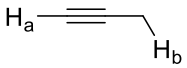
^4J = 0 – 3

allenic



^4J = 6 – 7

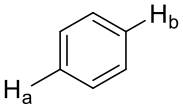
propargylic



^4J = 2 – 4

5-bond

para aryl



^5J = 0 – 1

*values listed as absolute values of coupling in Hz, $|^xJ_{H\text{-}H}|$

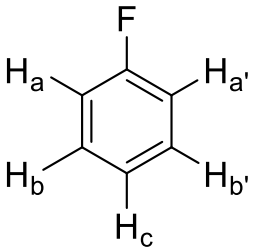
Model $J_{H\text{-}F}$ and $J_{C\text{-}F}$ Couplings

The coupling of ^{19}F in ^{1}H-NMR and ^{13}C-NMR spectra can be interpreted readily using the model coupling constants provided below for fluorobenzene. As with $J_{H\text{-}H}$ values, the size of coupling values ($J_{H\text{-}F}$ and $J_{C\text{-}F}$) for ^{19}F to other nuclei decreases as the number of bonds between the nuclei increases.

$^{3}J_{H\text{-}H}$ = 6 - 12 Hz

$^{4}J_{H\text{-}H}$ = 1 - 3 Hz

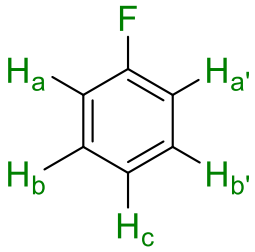
$^{5}J_{H\text{-}H}$ = 0 - 1 Hz



$^{3}J_{Ha\text{-}F}$ = 8.9 Hz

$^{4}J_{Hb\text{-}F}$ = 5.7 Hz

$^{5}J_{Hc\text{-}F}$ = 0.2 Hz

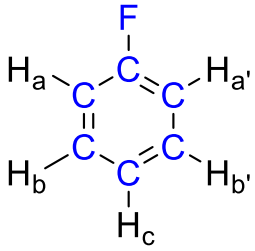


$^{1}J_{Cipso\text{-}F}$ = 245.1 Hz

$^{2}J_{Cortho\text{-}F}$ = 21.0 Hz

$^{3}J_{Cmeta\text{-}F}$ = 7.8 Hz

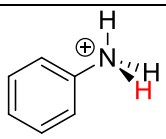
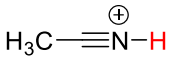
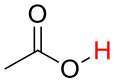
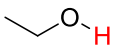
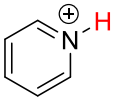
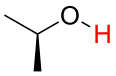
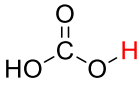
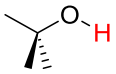
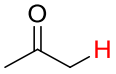
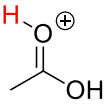
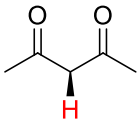
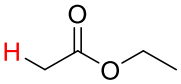
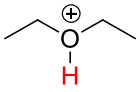
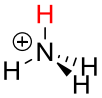
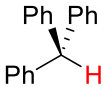
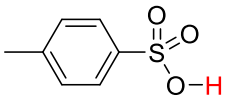
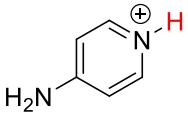
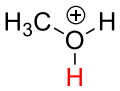
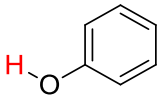
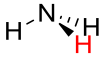
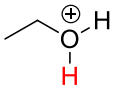
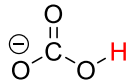
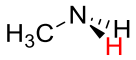
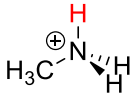
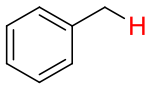
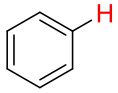
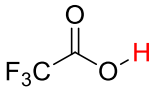
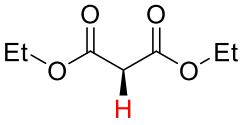
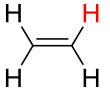
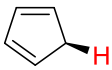
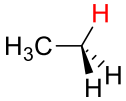
$^{4}J_{Cpara\text{-}F}$ = 3.2 Hz



Infrared Correlation Chart

Group	Type of Vibration		Frequency (cm^{-1})	Intensity
C–H	Alkanes	(stretch)	3000-2850	s
	$-CH_3$	(bend)	1450 and 1375	m
	$-CH_2-$	(bend)	1465	m
	Alkenes	(stretch)	3100-3000	m
		(out-of-plane bend)	1000-650	s
	Aromatics	(stretch)	3150-3050	s
		(out-of-plane bend)	900-690	s
	Alkyne	(stretch)	~3300	s
	Aldehyde		2900-2800	w
			2800-2700	w
C–C	Alkane	not interpretatively useful		
C=C	Alkene		1680-1600	m-w
	Aromatic		1600 and 1475	m-w
C≡C	Alkyne		2250-2100	m-w
C=O	Aldehyde		1740-1720	s
	Ketone		1725-1705	s
	Carboxylic Acid		1725-1700	s
	Ester		1750-1730	s
	Amide		1670-1640	s
	Anhydride		1810 and 1760	s
	Acid Chloride		1800	s
C–O	Alcohols, Ethers, Esters, Carboxylic Acids, Anhydrides		1300-1000	s
O–H	Alcohols, Phenols			
		Free	3650-3600	m
		H-bonded	3500-3200	m
	Carboxylic Acids		3400-2400	m
N–H	Primary and Secondary Amines and Amides			
		(stretch)	3500-3100	m
		(bend)	1640-1550	m-s
C–N	Amines		1350-1000	m-s
C=N	Imines and Oximes		1690-1640	w-s
C≡N	Nitriles		2260-2240	m
X=C=Y	Allenes, Ketenes, Isocyanates, Isothiocyanates		2270-1950	m-s
N=O	Nitro ($R-NO_2$)		1550 and 1350	s
S–H	Mercaptans		2550	w
S=O	Sulfoxides		1050	s
	Sulfones, Sulfonyl Chlorides, Sulfates, Sulfonamides		1375-1300	s
C–X	Fluoride		1400-1000	s
	Chloride		800-600	s
	Bromide, Iodide		<667	s

Original Source Unknown. w = weak, m = medium, s= strong

Acid	pK_a	Acid	pK_a	Acid	pK_a
	-10		4.6		15.7
	-10		4.75		16
	-9		5.2		16.5
	-7.5		6.35		18
	-7		7.0		19.2
	-6.2		9.0		24
	-3.8	H–CN	9.1		25
H–O–SO_3H	-3*		9.2		33
	-2.8		9.2	H–H	35
	-2.5		9.9		38
	-2.4		10.3		38
	-1.74		10.6		41
H–O–NO_2	-1.4		10.7		43
	0.18		10.7		44
H–F	3.2		15		50

*values differ widely depending on source from -9 to -3.

Cyclohexane A-values* (in kcal/mol)

–H	0.0	$–COCH_3$	1.0-1.5
–D	0.006	$–NO_2$	1.1
–CN	0.17	–SH	1.21
–F	0.25-0.42	$–NH_2$	1.23-1.7
–Cl	0.53-0.64	$–CO_2H$	1.4
–Br	0.48-0.67	**$–CH_3$**	**1.74**
–I	0.47-0.61	$–C_2H_5$	1.79
$–OCH_3$	0.55-0.75	$–CH(CH_3)_2$	2.21
–OH	0.60-1.04	$–CF_3$	2.4-2.5
–OPh	0.65	–Ph	2.8
–CHO	0.56-0.8	$– C(CH_3)_3$	4.7-4.9

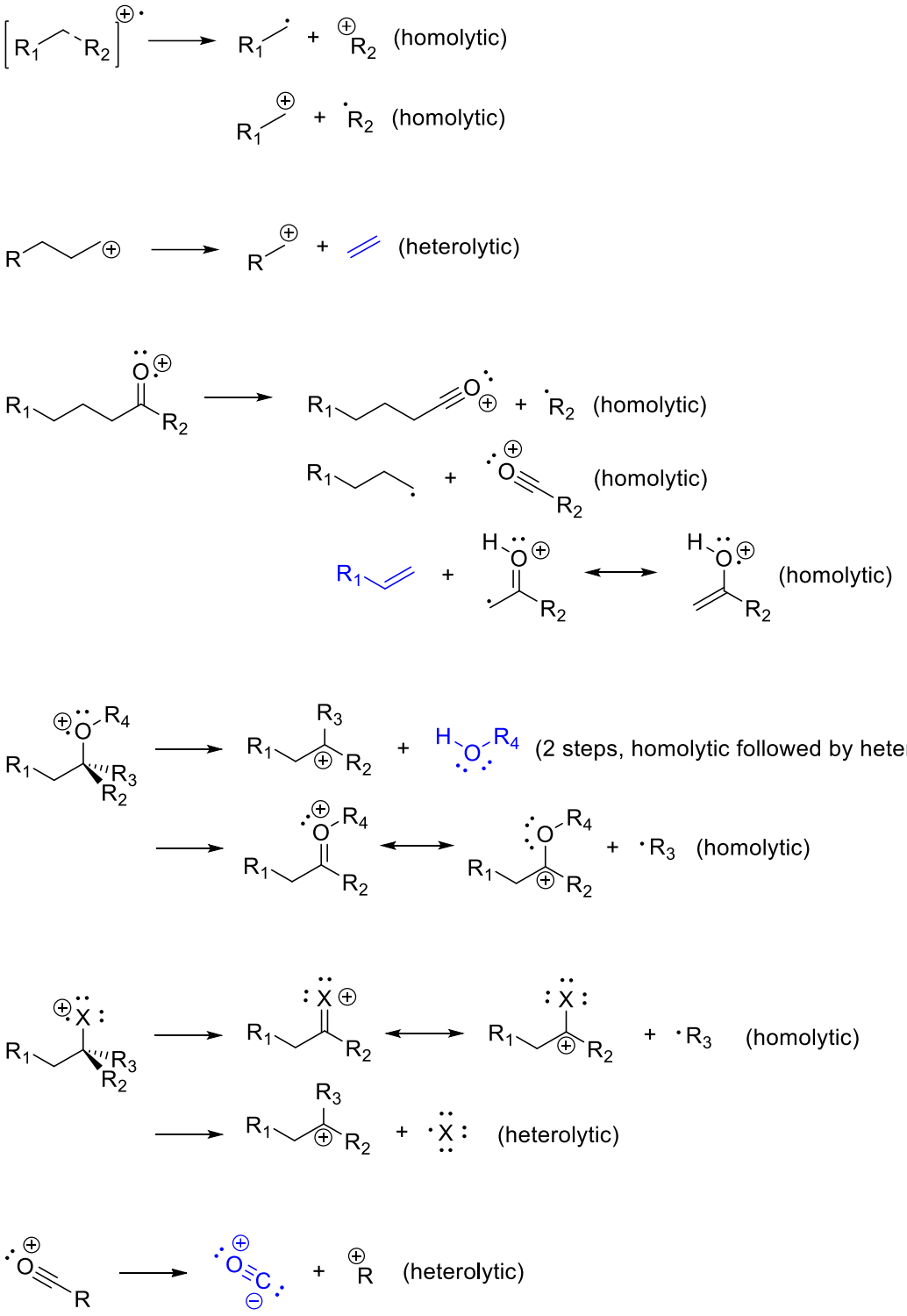
*The energy cost for a substituent to be axial vs. equatorial on a cyclohexane ring.

Adapted from Eliel, E.L.; Wilen, S.H.; Mander, L.N. Stereochemistry of Organic Compounds, Wiley, New York (1994).

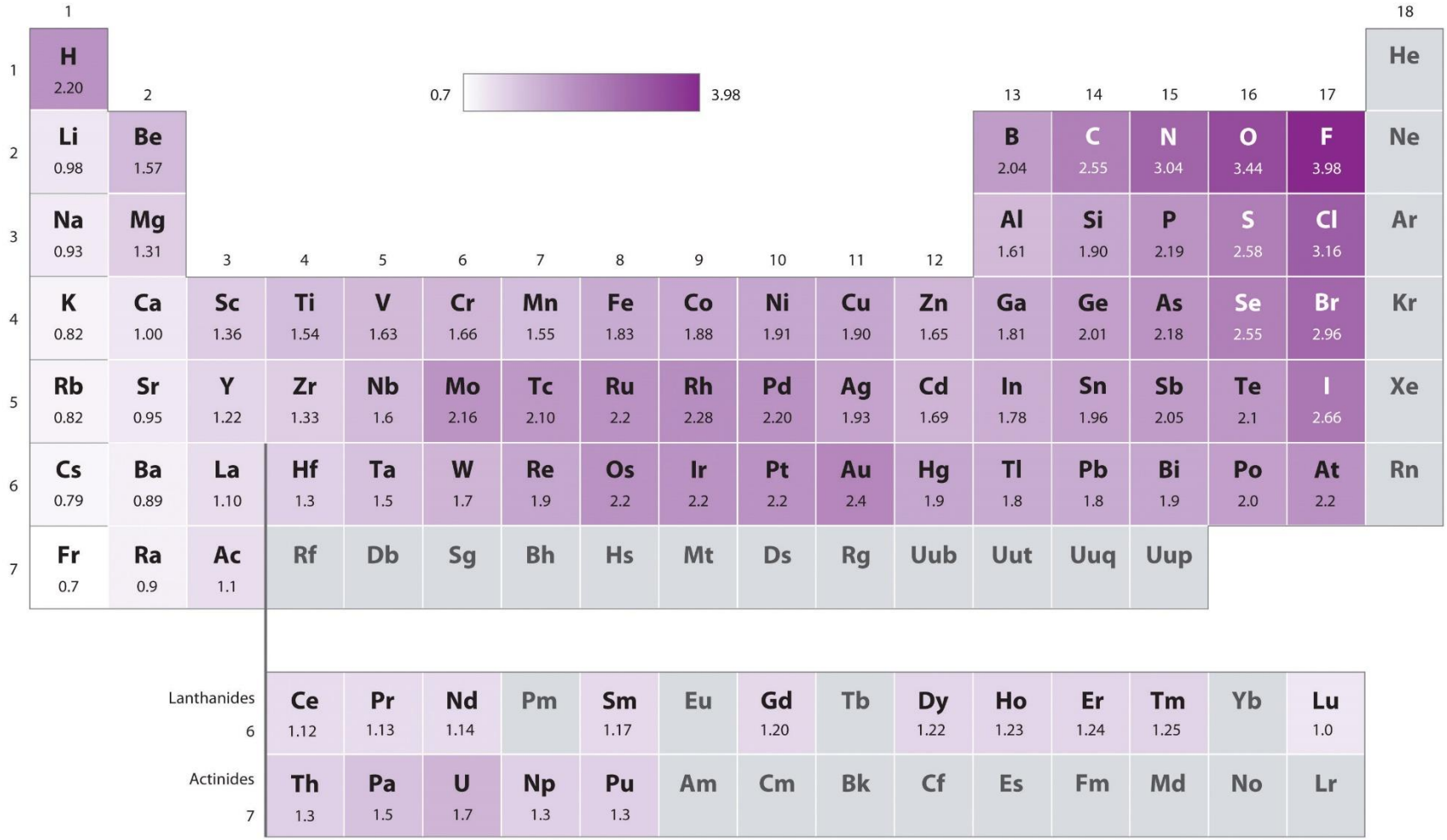
Nuclear Spin, Relative Abundance, and Exact Mass of Several Common Isotopes

Element	Isotope	Nuclear Spin	Exact Mass	Abundance %
Hydrogen	^{1}H	$^{1}/_{2}$	1.007825	99.985
	^{2}H or D	1	2.0140	0.015
Carbon	^{12}C	0	12.0000	98.90
	^{13}C	$^{1}/_{2}$	13.00335	1.10
Nitrogen	^{14}N	1	14.00307	99.63
	^{15}N	$^{1}/_{2}$	15.00011	0.37
Oxygen	^{16}O	0	15.99491	99.759
	^{17}O	$^{5}/_{2}$	16.99913	0.037
	^{18}O	0	17.99916	0.204
Fluorine	^{19}F	$^{1}/_{2}$	18.99840	100.0
Silicon	^{28}Si	0	27.97693	92.21
	^{29}Si	½	28.97649	4.67
	^{30}Si	0	29.97377	3.10
Phosphorus	^{31}P	$^{1}/_{2}$	30.97376	100.0
Sulfur	^{32}S	0	31.97207	95.0
	^{33}S	$^{3}/_{2}$	32.97146	0.75
	^{34}S	0	33.96787	4.22
Chlorine	^{35}Cl	$^{3}/_{2}$	34.96885	75.77
	^{37}Cl	$^{3}/_{2}$	36.96590	24.23
Bromine	^{79}Br	$^{3}/_{2}$	78.91834	50.69
	^{81}Br	$^{3}/_{2}$	80.91629	49.31
Iodine	^{127}I	$^{5}/_{2}$	126.90447	100.0

Common EI-MS Fragmentation Reactions



Periodic Table with Pauling Electronegativities (χ)



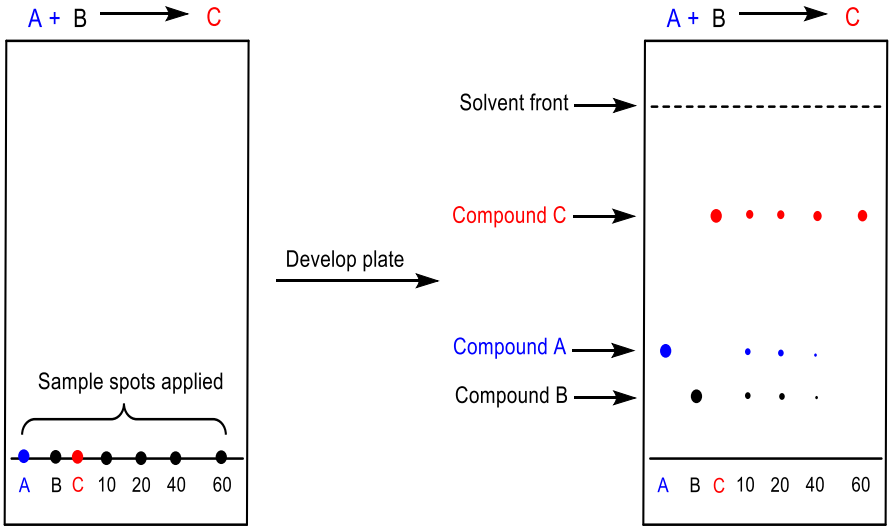
Adapted from Averill, B. A.; Eldredge, P. Chemistry: Principles, Patterns, and Applications, Prentice Hall, (2006)

Thin-Layer Chromatography Background

Thin-layer chromatography (TLC) is a simple analytical technique used for the separation and identification of compounds from mixtures. The TLC technique uses the same principle as extraction to accomplish the separation of compounds: that is, the partitioning of compounds between two phases based on differences in physical properties of the compounds. In the case of TLC, one phase is a mobile liquid solvent phase and the other phase is a stationary solid phase with a high surface area. The **stationary phase** normally consists of a thin layer of finely divided adsorbent, typically silica (SiO_2) or alumina (Al_2O_3) powder, on a supporting material of glass or metal foil. The **mobile phase** is an organic solvent or mixture of solvents.

TLC is routinely used in organic chemistry to monitor the progress of a reaction by observing the disappearance of starting materials and the appearance of products (and byproducts) over time. A solution of the reaction mixture is applied to the edge of the TLC plate as a small spot. The plate is propped vertically in a closed container (developing chamber), with the edge to which the spot was applied resting on the bottom of the chamber in a shallow pool of solvent. The solvent travels up the plate by capillary action, passes over the sample spot and moves the compounds in the mixture along the plate at different rates, resulting in separation of the compounds. This process is termed elution.

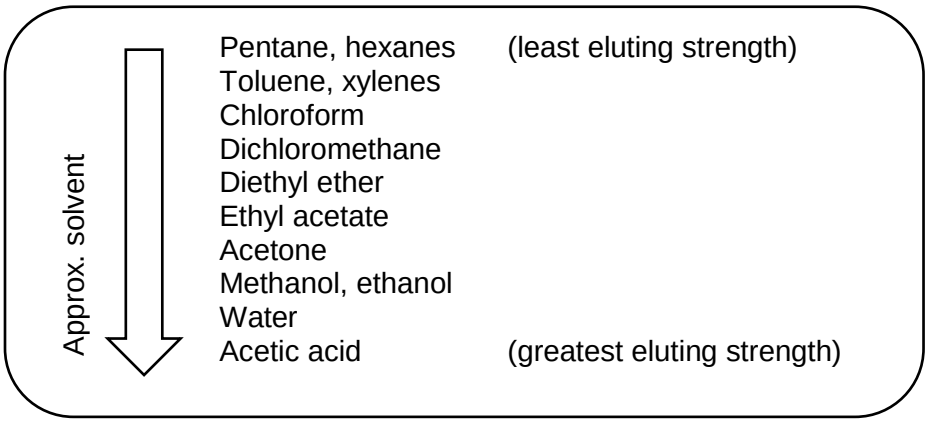
In the example shown below, the reaction mixture A + B → C was sampled at 4 different time periods (10, 20, 40, and 60 min, shown on base of plate). Pure compounds A, B, and C were also spotted for comparison. Development of the plate reveals that compounds A and B react to yield C within 60 min.



An equilibrium is established between the molecules of each compound (A, B, or C) adsorbed onto the surface of the plate and the molecules of the compound which are in solution. Each component of the mixture will differ in solubility and in the strength of its adsorption to the plate, and thus as the mobile phase flows over the surface of the plate each component is carried up the plate to a differing extent. This forms the basis of separation and identification of the components of the A + B → C reaction mixture.

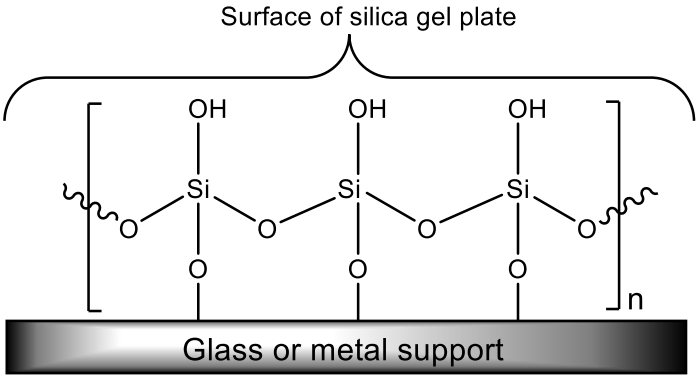
When the solvent front reaches near the top of the plate, the plate is removed from the developing chamber, the solvent front is marked with a pencil, the plate allowed to dry, and the separated components of the reaction mixture (the "spots") are visualized. Visualization is straightforward if the compounds are highly colored. Typically, however, the separated organic compounds are colorless or only weakly colored and so a UV lamp is required to visualize the plates. (The TLC plate is coated with an inert fluorescent dye which glows under UV radiation *except* where an organic compound is on the plate). The overall procedure is referred to as "developing" the TLC plate.

The solvent used as the mobile phase should be able to dissolve all of the compounds to be separated. The solubility of different compounds in the solvent plays an important role in how rapidly they move up the TLC plate. A more important property of the solvent is its ability to be adsorbed onto the plate. To the extent that the solvent has affinity for the adsorbent (typically SiO_2), it can displace the compounds in the reaction mixture thereby "pushing" them up the plate. If the solvent is too strongly adsorbed, it can fully displace all compounds causing them to move up the plate together near the solvent front, resulting in minimal (or no) separation of the mixture. If the solvent is too weakly adsorbed, its solvating power alone may be insufficient to move any compounds along the plate fast enough to effect separation. Ideally, the affinity of the solvent for the adsorbent should be similar to that of the compounds being separated, causing different compounds to move at different rates and resulting in adequate separation of the mixture.



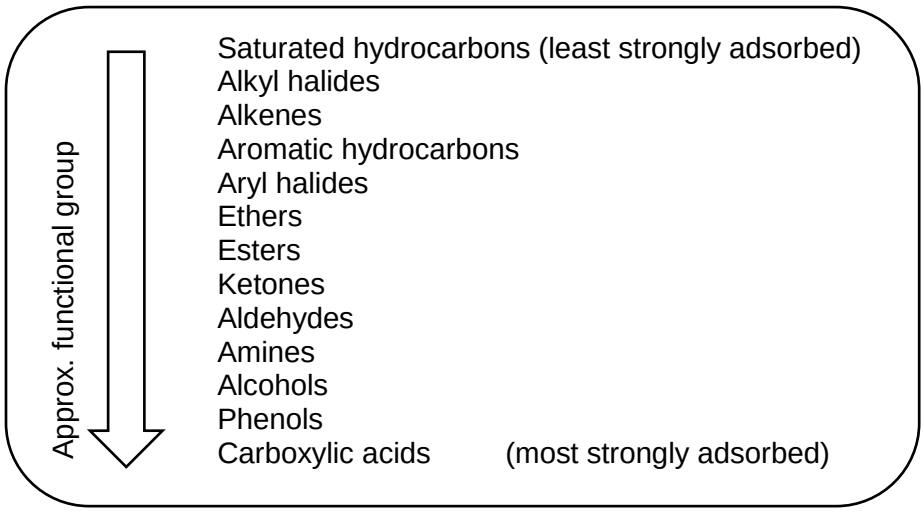
Because the eluting strength of a solvent is primarily related to how strongly it adsorbs onto the adsorbent and because typical adsorbents are highly polar, eluting strength increases with solvent polarity. In practice, mixtures of solvents are commonly used to achieve optimum separations by TLC. When using mixtures of solvents, addition of a minor amount of a polar solvent can result in a large increase in the eluting power of the solvent mixture.

Silica gel (SiO_2) consists of a three-dimensional network of Si-O bonds, with Si-O-H groups on the surface. A silica gel TLC plate is essentially a thin layer of very finely ground pure sand adhered to a metal or glass support.



Molecules featuring a significant dipole interact strongly with the polar Si-OH groups at the surface of the SiO_2 plate and thus will adsorb onto the fine particles of the adsorbent. In contrast, molecules with a weak dipole (or no dipole) interact less strongly with the surface of the polar Si-OH network on the surface of the plate. Molecules with a weak dipole generally move through along the Si-OH network more rapidly than those with a significant dipole and thus appear higher on the plate once it is developed

It is possible to make some approximations about the relative rate of elution of different compounds with a given solvent (or mixture of solvents) on a specific adsorbent, however the specific combination that results in the successful separation of a specific mixture of compounds can be determined only by experimentation. The process begins by consideration of the structures of the compounds to be separated and their relative affinity for the stationary phase. The figure below indicates an approximate order of affinity of organic compounds for SiO_2 sorted by functional group. The strength with which an organic compound binds to the TLC plate depends primarily upon the extent of the dipole-dipole interactions between the molecule and the surface of the plate. Other attractive forces between the adsorbent and the organic compounds (such as hydrogen bonding, dipole-induced-dipole, and van der Waals forces) also play a role in the overall strength of the molecule-surface interaction.

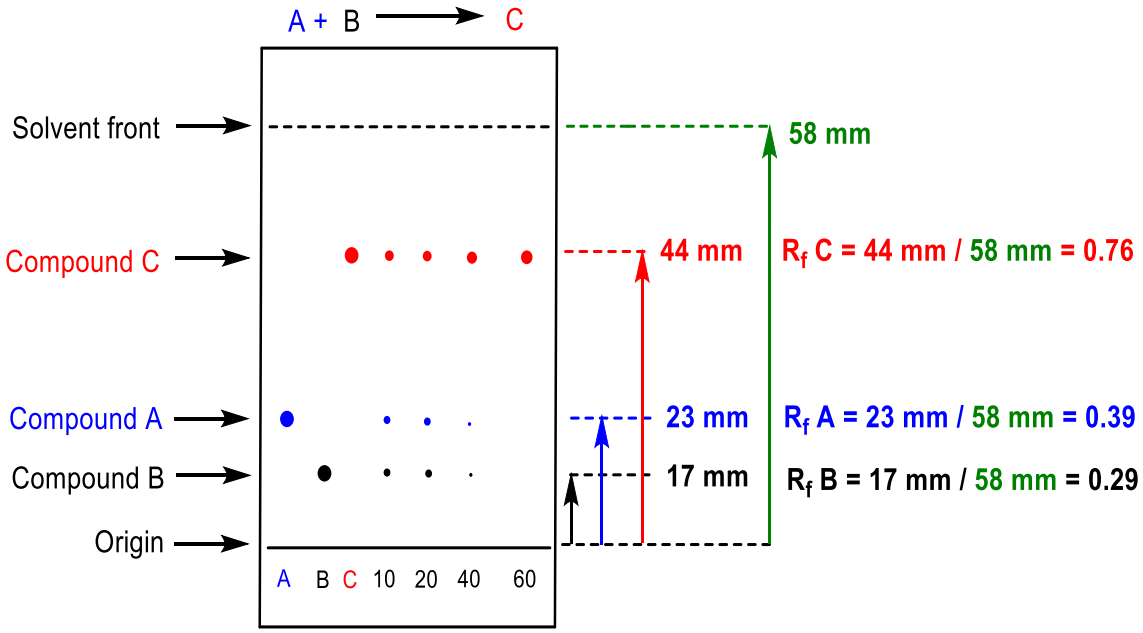


The distance traveled by a compound relative to the distance traveled by the solvent front depends upon the structure of the molecule, and thus TLC can be used to identify substances as well as to separate them. But how is the extent of interaction between the molecule and the plate surface quantified?

The relationship between the distance traveled by the compound(s) and the distance traveled by the solvent front and is expressed as a decimal, termed the **R_f value (retention factor)**. The stronger a compound is bound to the adsorbent, the slower it moves up the TLC plate and thus the lower its R_f value.

In the example below, compound C has traveled furthest up the TLC plate because it is the least strongly adsorbed compound of the mixture and thus has the highest R_f value (0.76). Likewise, B has the lowest R_f value (0.29) and is thus the most strongly adsorbed compound. The figure also shows how to properly calculate R_f values for the components of the reaction mixture A + B → C.

$$R_f = \frac{distance\ traveled\ by\ compound\ (mm)}{distance\ from\ origin\ to\ solvent\ front\ (mm)}$$



Experimental R_f values are strongly dependent upon the nature of the plate surface and the solvent system, and thus experimental R_f values obtained from different TLC runs are not always in agreement. In order to determine whether an unknown compound is identical to a compound of known structure, it is necessary to run samples of the two compounds side-by-side on the same TLC plate, preferably at the same concentration. This concept is illustrated in Figure 1 and 5, where A, B, and C are spotted on the TLC plate as pure compounds in order to compare their R_f values with those obtained from the reaction mixture.